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A Patient-Specific Cardiac Phantom for Training and Pre-Procedure Surgical Planning

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A thesis submitted in partial fulfillment of the requirements for the Master of Engineering Science degree in Biomedical Engineering

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Abstract

Minimally invasive cardiac procedures requiring a transseptal puncture are becoming increasingly common. For cases of complex or diseased anatomy, clinicians may benefit from using a patient-specific cardiac phantom for training, surgical planning, and the validation of devices or techniques.

An imaging compatible cardiac phantom was developed to simulate a MitraClip® procedure. The phantom contained a patient-specific cardiac model manufactured using tissue mimicking materials.

To evaluate accuracy, the patient-specific model was imaged using CT, segmented, and the resulting point cloud data set was compared using absolute distance to the original patient data. The phantom was validated using a MitraClip® device to ensure anatomical features and tools are identifiable under image guidance.

Patient-specific cardiac phantoms may allow for surgical complications to be accounted for in pre-operative planning. The information gained by clinicians involved in planning and performing the procedure should lead to shorter procedural times and better outcomes for patients.

Keywords

Patient-Specific, 3D printing, Molding, Surgical Planning, Minimally Invasive, Cardiac

Co-Authorship Statement

This master's thesis includes two articles in part, both of which formulate a chapter. The first article, Chapter 2, is currently published as a conference proceeding from the SPIE Medical Imaging Conference. Chapter 3, is submitted and currently under review by the Journal of Medical Imaging.

Chapter 2: Chapter 2 was adapted from the conference proceeding written for the SPIE Medical Imaging conference in 2017.

Laing, J., Moore, J., Bainbridge, D., Drangova, M., & Peters, T. (2017). Patient-specific atrium models for training and pre-procedure surgical planning (Vol. 10135, p. 101351A–101351A–8). <https://doi.org/10.1117/12.2249693>

The initial motivation prompting this study was presented by T. Peters and M. Drangova. My contributions were to the development of the study procedure under the guidance of T. Peters and J. Moore and to the implementation of the study and data analysis with guidance from D. Bainbridge and M. Drangova. I prepared the initial draft of the manuscript, which was edited by J. Moore and T. Peters and reviewed by all authors. T. Peters was the primary supervisor.

Chapter 3: Chapter 3 was adapted from the submission to the Journal of Medical Imaging that is currently under revision.

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My contribution to this study was to the development of the patient-specific model manufacturing methodology, the design of the cardiac phantom, and the analysis of the validation data under the guidance of J. Moore and T. Peters. I prepared the initial draft of the manuscript which was edited by J. Moore, R. Vassallo and T. Peters and reviewed by all authors. T. Peters was the primary supervisor.

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List of Abbreviations

3D	Three Dimensional
CAD	Computer Aided Design
CT	Computed Tomography
FEM	Finite Element Modelling
LAA	Left Atrial Appendage
MRI	Magnetic Resonance Imaging
PLA	Polylactic Acid
PVA	Polyvinyl Alcohol
PVA-C	Polyvinyl Alcohol Cryogel
STL	Stereolithography

Chapter 1

1 Introduction

1.1 Background

This chapter includes a basic introduction to the physiology of the heart and an overview of the previous works and processes that were used to develop this thesis. With increasing life spans due to more advanced health care, cardiovascular disease has become the number one cause of death around the world, with one in four deaths being attributed to cardiovascular issues and an economic impact totalling over \$320.1 billion USD [1]. Modern lifestyles have led to many people being sedentary, with jobs that require workers to sit for prolonged periods. This has led to an increase in obesity, a reduction in exercise, high blood pressure and poorly controlled diabetes, all which are risk factors for cardiovascular disease.

Medical companies have developed a wide range of tools, devices, and techniques to use as therapies to treat cardiovascular disease and prolong a patient's life. In recent years, to reduce the impact on a patient, these therapies have been transitioning from invasive open-heart surgery to minimally invasive procedures. Such procedures are performed while the heart is still beating using catheters that are inserted into the body and manoeuvred with aid from imaging modalities.

This work was motivated by the ever-increasing complexity of minimally-invasive cardiac procedures. As medical technology continues to progress, the rate at which new tools and systems are coming to market is increasing. With each new procedure, clinicians must learn the necessary skills and motor patterns to provide patients with safe and effective care. It is our hope that the outcome of this thesis will provide clinicians with the ability to practice these new procedures in a safe and realistic environment, allowing them to develop the skills and confidence they require.

1.2 The Human Heart

The human heart is a muscular organ responsible for the distribution of blood throughout the body. The heart acts a pump, distributing oxygenated blood returning from the lungs to the rest of the body and sending deoxygenated blood back to the lungs. To regulate blood flow within the heart there are four chambers and four valves. The four chambers of the heart are the left and right atria and the left and right ventricle (Figure 1). The valves are the mitral, tricuspid, aortic and pulmonary (Figure 2).

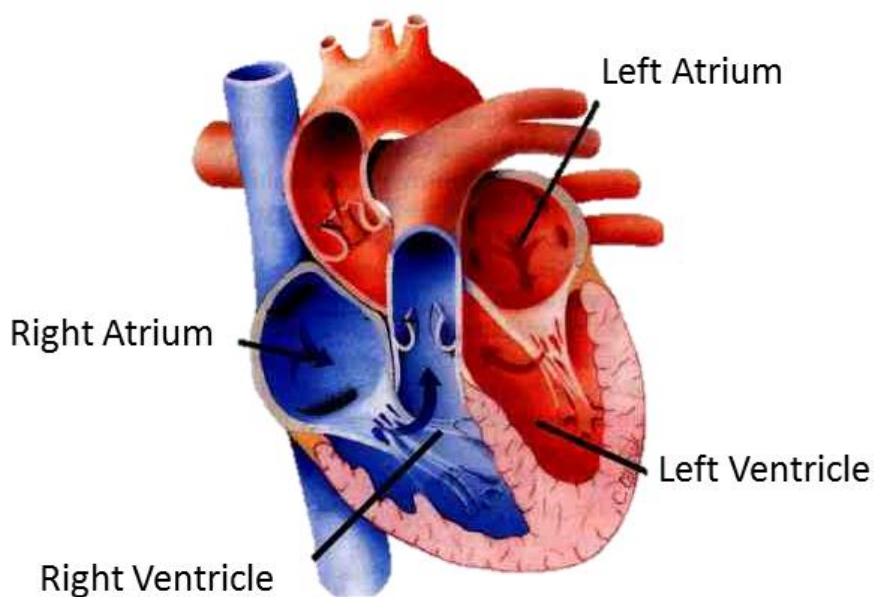


Figure 1.1: Cardiac chambers (Image Courtesy of The Cardio Research Web Project)

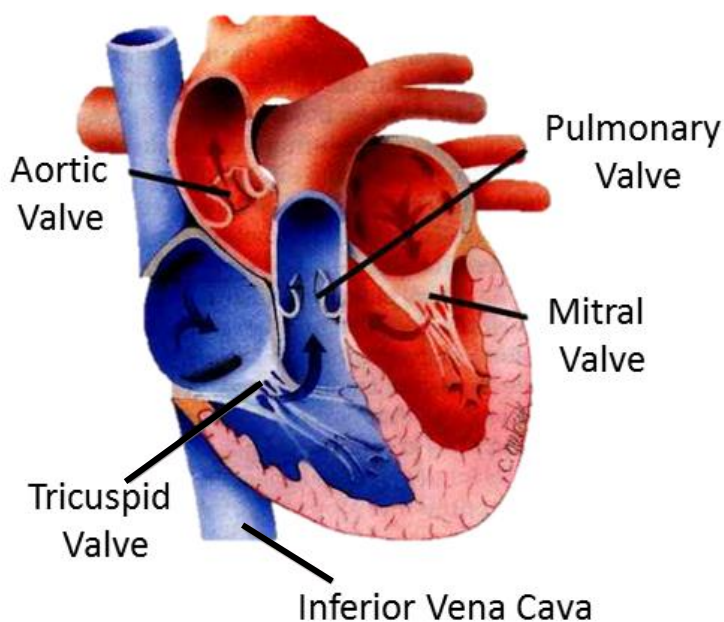


Figure 1.2: Cardiac valves (Image Courtesy of The Cardio Research Web Project)

Blood travels throughout the heart in two systems. The left side of the heart is responsible for the distribution of oxygenated blood to the body. The oxygen rich blood returning from the lungs enters the heart through the pulmonary veins and into the left atrium. As the atrium contracts, the mitral valve is opened and the blood passes into the left ventricle. When the left atrium has relaxed, the mitral valve closes preventing blood from flowing backwards. The left ventricle then contracts, opening the aortic valve, allowing blood to leave the heart and be distributed throughout the body. The right side of the heart receives blood back from the body after the oxygen has been depleted and directs it to the lungs. The deoxygenated blood returns through the inferior and superior vena cava and enters the right atrium. As the right atrium contracts, blood passes through the tricuspid valve and flows into the right atrium. As the right ventricle contracts, the pulmonary valve opens and allows blood to flow back to the lungs.

1.3 Cardiac Surgery

The first successful cardiac operation was performed by Dr. Ludwig Rehn in Frankfurt Germany in 1896 where he successfully repaired a patient's right ventricle. Cardiac

surgeries throughout the early 1900's were performed by accessing the heart through an incision in the chest cavity and operating on a beating heart. It wasn't until 1953 when the cardiopulmonary bypass concept was introduced that a patient could continue to have blood flow throughout the body without the need for the heart to be beating. This allowed for more complex procedures to be performed and led to the development of open heart surgery.

Open heart surgery is the classifications given to procedures where the patient receives a sternotomy in which the chest is opened and the affected cardiac anatomy can be operated on. The patient is connected to a cardiopulmonary bypass machine, allowing the surgeon to arrest the patient's heart, and operate on the affected location without having to compensate for heart's motion. With the use of cardiopulmonary bypass machines, cardiac surgeries were able to become more complex and effective for patients. However, due to the need to crack the patient's rib cage to gain access to the beating heart, there is an increased impact to the patient and a risk of post-surgery complications.

The post-surgical risks to the patient are influenced by the body's negative immunological response and the potential for plaque disruption during the surgery. After undergoing open heart surgery using a cardiopulmonary bypass machine, the body undergoes an innate immune response that manifests as a whole body systemic inflammatory response and can lead to a temporary immunodeficiency [2]. In addition, when performing cardiac surgery, there is a risk of plaques becoming disrupted or rupturing. If this is to happen, the plaque rupture can lead to the formation of a blood clot in the artery and in severe cases, result in a stroke or heart attack.

1.4 Minimally Invasive Cardiac Procedures

To reduce the impact on patients and recovery times that are inherent with open heart surgery, methods have been developed to access the heart using minimally invasive techniques. These procedures rely on catheters inserted through a small incision into specific veins and arteries within the body which allow a catheter to be manoeuvred into the heart. These procedures are beneficial to patients as the recovery time post-surgery is typically drastically reduced when compared to an open-heart procedure [3]. This is also

critical for high-risk or elderly patients as they may not be physically capable of receiving open heart repairs using a bypass machine, but may be eligible to receive a minimally invasive repair.

When performing minimally invasive cardiac surgery, one common access point for the catheter is the femoral vein, through which a catheter can be navigated from the femoral vein, through the inferior vena cava, and into the right atrium. For a clinician to perform common procedures such as atrial ablation, mitral valve repair or replacement or a MitraClip® procedure, a catheter is used to puncture the patient's septal wall and cross into the left side of the heart, accessing the left atrium, left atrial appendage, mitral valve or left ventricle.

The main limitation of these procedures is the need for clinicians to rely on medical imaging such as ultrasound, computed tomography (CT), magnetic resonance imaging (MRI) or fluoroscopy to interpret the patient's anatomy and navigate the catheter while inside the patient. In most cases, an experienced clinician can identify anatomical features while viewed under image guidance. Difficulty may arise however if the patient's anatomy is highly irregular or deformed. This may hinder the clinician's ability to interpret the patient's anatomy and directly impact the clinical outcome for the patient. For very complex cases, patients can be denied care if the clinicians are unable to interpret the preoperative imaging and develop a procedural plan.

1.4.1 Transseptal puncture

The atrial septum is the dividing wall between the left and right atria. An opening in this wall closes during fetal development to prevent blood flow between the two chambers. A transseptal puncture is a common component of minimally invasive cardiac procedures that utilize the femoral vein as the access point. For a catheter to be navigated into the left atrium, clinicians puncture the atrial septum wall to pass the catheter or tool from the right atrium to the left. During minimally invasive procedures, navigating a catheter to puncture the septal wall is performed under fluoroscopy and ultrasound guidance. The tools designed for these minimally invasive procedures can require specific septal wall puncture locations to properly orient them within the left atrium and position them at the

target. Ensuring the septal wall puncture location is correct can greatly increase the duration of the surgery and the radiation dose administered to a patient through fluoroscopy use.

1.4.2 Atrial Ablation

Atrial ablation is a minimally invasive procedure used to treat atrial fibrillation, which is an abnormal heart rhythm with periods of rapid or irregular beating. In a normal beating heart, the electrical signals generated by the sinoatrial node are propagated to the myocardium and cause the heart to contract. For a heart with atrial fibrillation, the signals generated by the sinoatrial nodes are interrupted by electrical discharges occurring at the openings of the pulmonary veins within the atria. This interference causes the heart to beat irregularly and out of rhythm. The treatment for atrial fibrillation is commonly radiofrequency ablation or cryoablation, in which a catheter generates scar tissue around the area producing the electrical discharges (Figure 3). The scar tissue does not conduct electricity and contains the electrical discharges within the ablated area. The ablation stops the propagation of the interfering electrical signals and treats the atrial ablation.

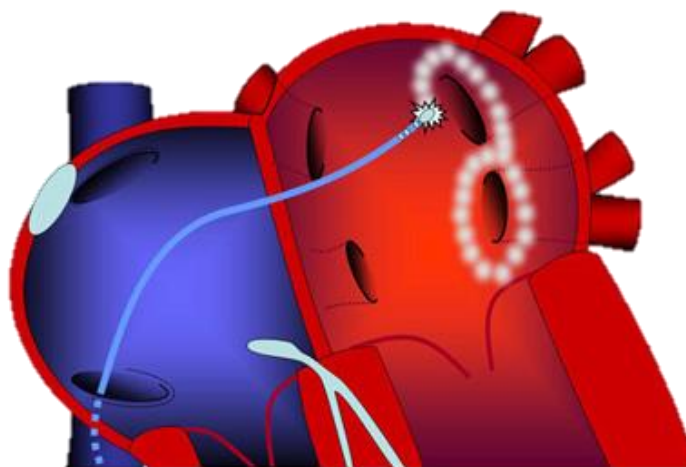


Figure 1.2: Illustration of the atrial ablation of the pulmonary vein openings (image courtesy of the London Arrhythmia Centre)

1.4.3 MitraClip ®

A MitraClip ® procedure is a common minimally invasive intervention to repair a mitral valve when it is not closing effectively and allowing blood to regurgitate from the left ventricle back into the left atrium. Regurgitation reduces the amount of blood being distributed to the body, resulting in an increased work load for the heart, which can lead to cardiac remodelling or other complications. To perform a MitraClip ® procedure a catheter is guided from the femoral vein into the right atrium, where the septal wall is punctured and the deployment catheter (Figure: 4) can be aligned with the mitral valve.



Figure 1.3: MitraClip ® tool used for the treatment of mitral valve regurgitation (Image Courtesy of Abbott)

Using ultrasound imaging the catheter is guided to the location of the regurgitation and a clip(s) is deployed, holding the two leaflets of the mitral valve together while allowing blood to pass through the valve (Figure 5).

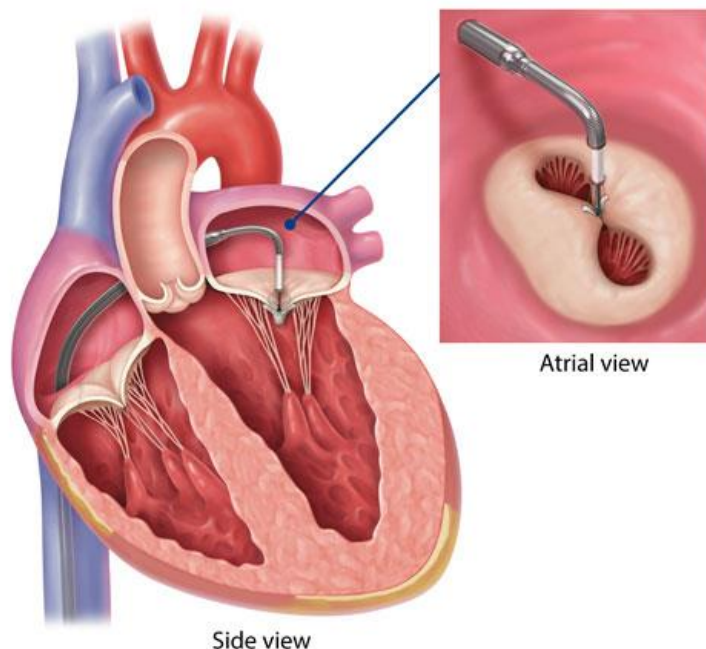


Figure 1.4: MitraClip ® tool aligned with the mitral valve and deployed (image courtesy of Abbott)

If the clip is placed correctly the patient's mitral regurgitation can be reduced or eliminated, greatly impacting their quality of life.

1.4.4 Atrial Appendage Closure

The left atrial appendage (LAA) is a tubular hooked structure (Figure 6) connected to the muscle wall of the left atrium. There are several common types of LAA with some examples seen in Figure 6, however, each patient may have unique variations. In healthy patients as the heart contracts, blood is pushed from the left atrium and LAA into the left ventricle. When a patient has atrial fibrillation the left atrium no longer contracts properly, which can cause blood to pool within the LAA and form blood clots. According to the Cleveland Clinic, people who experience atrial fibrillation are 5 to 7 times more likely to have a stroke because of a blood clot than people without atrial fibrillation [4]. Currently blood thinners are prescribed to prevent blood from clotting with the LAA, however, there can be unfavourable side effects and consequences of the use of blood thinners. Another approach to preventing blood clots is the use of LAA occlusions devices such as the Boston Scientific Watchman device. This device is inserted into the

LAA and designed to create a seal between the left atrium and the LAA. If properly sized and deployed (Figure 7, 8) the device prevents any blood flow into the LAA and over time tissue grows over the device creating a complete and long lasting barrier.

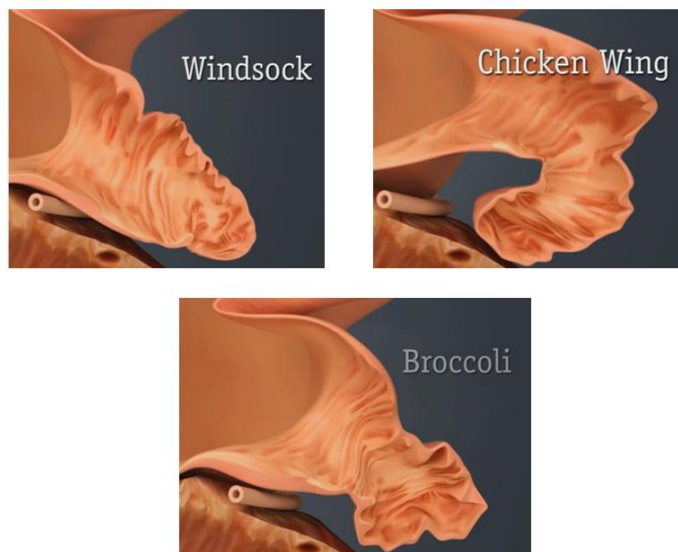


Figure 1.5: Common atrial appendage shapes (Image Courtesy of Boston Scientific)

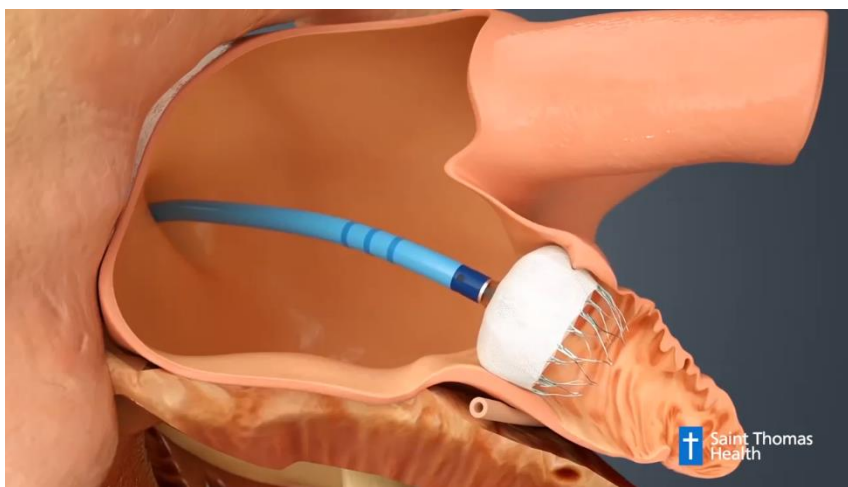


Figure 1.6: Watchman Appendage Closure Device deployed inside the an atrial appendage (Image Courtesy of Boston Scientific)

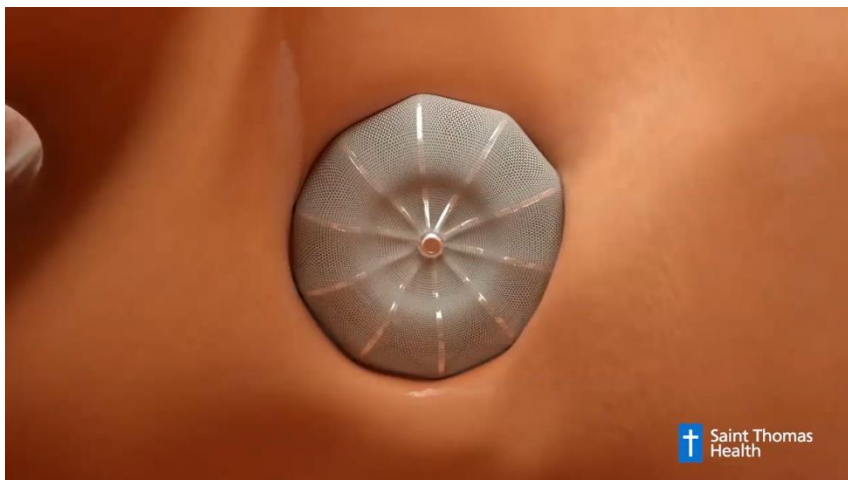


Figure 1.7: Watchman Appendage Closure Device deployed and fully sealing the atrial appendage opening (Image Courtesy of Boston Scientific)

1.5 Image Guidance

Image guidance refers to the different imaging modalities used in diagnostic and therapeutic imaging. For minimally invasive procedures, clinicians rely on a combination of preoperative and intraoperative imaging to provide visual feedback on the patient's anatomy and the location of tools. Preoperative imaging allows clinicians to gain a comprehensive view of the patient's anatomy and pathology and develop a plan for the procedure. During the procedure, the clinician uses intraoperative imaging to navigate and position the catheter or tool to the desired location. The preoperative imaging can be used to supplement intraoperative imaging, ensuring the clinicians have a comprehensive understanding of the patient's anatomy and pathology.

Currently, several imaging modalities can be used to visualize anatomy within a surgical environment. This can include MRI, CT, fluoroscopy, ultrasound and positron emission tomography. These modalities each have their own advantages and can be used in combination with each other to best visualize the anatomy and tools.

1.5.1 Preoperative Image Guidance

Preoperative image guidance allows clinicians to diagnose and develop a plan for the procedure. Clinicians perform preoperative diagnostic scans aimed at locating areas of

interest in the patient's anatomy and pathology. If the clinicians determine that the pathology requires intervention, these preoperative scans can be used to plan the operation, including the optimal route for catheter navigation, sizing of tools or devices to be inserted into the patient, or the target location for the intervention to take place, such as the area to be ablated. In cases where the patient's anatomy or pathology is complex, preoperative imaging may be difficult to interpret, making procedural planning more difficult and leading to a higher risk to patients, or patients not receiving treatment that they need.

1.5.2 Intraoperative Image Guidance

As minimally invasive procedures develop and increase in complexity, the need for intraoperative imaging is becoming more important. These procedures rely on visual feedback from imaging modalities to interpret a patient's anatomy and locate the tool(s) within the patient. For minimally invasive cardiac procedures, catheters need to be navigated from common access points such as the femoral vein or the femoral artery, into the heart and positioned near the area of interest. To navigate catheters towards the heart from the access point, clinicians can use a combination of magnetic tracking if available, intraoperative imaging and the preoperative images.

Commonly in minimally invasive procedures, clinicians will rely on fluoroscopy and ultrasound for intraoperative imaging. Due to the radiation from the fluoroscopy, there is a desire to limit its use during surgery and only use as needed, preventing clinicians from seeing the tool in real time and only while imaging is being used. More complex surgeries can require extra fluoroscopy to guide the catheter, increasing the radiation dose to patients and their risk of potential long-term complications. To navigate the catheter or tool under image guidance can require a high level of dexterity and skill as the clinician must interpret the anatomy as it appears under image guidance and mentally map the route for the catheter between uses of fluoroscopy.

1.6 Clinical Challenges

When relying on imaging modalities to diagnose and perform a procedure there are several factors that can influence the clinician's ability to perform the procedure

effectively. The dependence on imaging modalities means the quality, age, and calibration of the scanner can directly impact the images the clinicians see. In the surgical planning phase, clinicians must make decisions regarding the tools and devices that are best suited for the pathology, in addition to planning for the target location, device size, and implementation based solely on the preoperative images. In many cases, preoperative imaging provides sufficient information to allow clinicians to make informed decisions and confidently perform the procedure. In cases where a patient has complex anatomy or the disease has caused cardiac remodelling, clinicians must take extra care in planning, or in some cases may have to refuse treatment to patients if the risk of failure is too high.

For procedures with target locations in the left atrium using the femoral vein as the access point, such as atrial ablation or mitral valve repair, the procedure must include a septal puncture. The ideal location of the puncture may be different for each procedure depending on the design of the surgical tool. In the case of the MitraClip®, the design of the system requires the puncture to occur near the highest point of the septal wall. This is important, as once inside the left atrium the catheter must bend adequately to align with the mitral valve. If the initial puncture does not occur in the proper location, the clinicians may have to perform the puncture a second time, increasing the use of fluoroscopy, the procedure time, and the risk to the patient.

Due to variations in patient anatomy, the duration and use of fluoroscopy during a MitraClip® procedure can vary drastically. In a study from 2011, the average duration of the procedure was 172.1 minutes \pm 82.9 [5], a variation that can be attributed to limitations in visualizing the septal wall under image guidance, variations in cardiac anatomy from patient to patient or from remodelling due to disease. For complex cases, according to clinicians, the septal wall puncture can account for up to 50% of the duration of a MitraClip® procedure. As the time spent on the septal puncture increases, so does the use of fluoroscopy, increasing the dose of radiation experienced by the patient, creating a need for improved procedural planning tools for difficult cases.

Finally, there can be difficulties sizing and properly positioning devices such as valve replacements or atrial appendage closure devices that are to be implanted within a patient.

In the case of the Boston Scientific Watchman atrial appendage closure device, the atrial appendage is imaged preoperatively using ultrasound. The resulting image is used to measure the size of the appendage and determine the optimal placement location. The quality of the ultrasound image can greatly impact the results of the preoperative planning. If the device is not properly sized, when implanted into a patient it may leak and not fully block off the appendage, leading to future complications for the patient and not resolving the patient's current issue.

1.7 Clinical Training

The goal of clinical training is to prepare clinicians with the knowledge and skills to interact with and treat patients effectively. The training of new clinicians is commonly approached using the, “see one, do one, teach one” method, using the assumption that a clinician can be trained to perform a procedure through watching another clinician. The clinician should then be able to effectively perform the procedure and subsequently teach a new clinician. Invented by William Halsted in 1890 at John Hopkins Hospital, to formalize the training of new clinicians, this method has remained largely unchanged and is still the main form of training today. Despite the method’s longevity, critics have argued that this method is no longer sufficient when used independently from simulations [6], [7]. The authors argue that in using just the “see one, do one, teach one” method, there is a higher level of risk for patients who will be treated by inexperienced clinicians who may lack the skills and confidence of a more experienced practitioner. A study in 2003 found that 42% of young doctors felt inexperienced in performing a practical surgery without supervision [8]. This finding leads to a need for more comprehensive training for new clinicians or new procedures.

With the development of new tools and surgical techniques, there is a need for clinicians to continue to learn and train throughout their careers. As new procedures are adopted by hospitals, it requires clinicians to work with new tools, learn new motor patterns and skills. It is imperative that clinicians are properly trained with the new equipment in a realistic training environment. Currently, in addition to the “see one, do one, teach one” method, training for new clinicians or new techniques may include the use of fresh cadavers or animals. Cadavers offer realistic anatomy, but there is no motion from

respiration or blood flow. Depending on the surgical application, a live animal may be more relevant. Animal training, typically using pigs, allows for training on an animal that is still breathing and has blood flowing throughout the body. The anatomy of these animals may present limitations as they do vary from humans, however, this does create a realistic training environment. Unfortunately, due to the cost of animals or fresh cadavers, along with ethical concerns, clinicians may still have limited training opportunities. Thus, new procedures may be performed by clinicians who have very limited time and training with the device and may have never performed the specific procedure on a live human.

For new clinicians, or those performing new or infrequent procedures, there can be an increased risk to the patient. Studies have shown a direct relationship between the volume of procedures performed and the overall outcome for patients, with patients receiving a procedure performed by a clinician who frequently performs the operation having a higher chance of a positive outcome [9]–[11]. To allow for clinicians, new or experienced, to practice in a safe, realistic and cost effective way, there needs to be a method of supplementing the current training methodology to increase the time and frequency that clinicians are able to spend practising.

1.8 Surgical Simulation

Surgical simulations are the imitation of a real surgical scenario. Simulations can be performed on cadavers, animals, models or on surgical simulators. Simulators can offer the ability to train a clinician's skills, problem-solving or clinical judgment. The earliest medical simulations occurred with cadavers, anatomical models and by using standardized patients or actors. Cadavers and models allowed clinicians to practice procedures and skills in a safe environment without putting a patient at risk, however, in modern times these can be expensive and need to be ethically approved. When learning bedside manner and skills for patient interactions, medical students use standardized patients to recreate real life interactions and create clinical scenarios. These standardized patients allow students to work with real people and develop the skills needed to communicate and interact effectively with patients [12].

As medical technology, has developed, more complex procedures including minimally invasive cardiac techniques have required more complex simulations. These new procedures required clinicians to develop new skill sets, both in navigating tools and interpreting the patient's anatomy through image guidance. To bring the efficacy of simulations using standardized patients into minimally invasive surgery and expand on the "see one, do one, teach one" method, surgical simulators can be used. Simulators can provide a realistic training environment using generalized or patient-specific anatomy that can be designed to be compatible with various imaging modalities. Simulators like the LAP MENTOR™, from 3D Systems, can offer a repeatable and safe environment in which the clinicians can make errors and learn from mistakes while training using real tools for laparoscopic surgery.

Development of surgical mannequins and task-specific trainers, such as CentraLineMan from Simulab, have allowed for surgical tasks to be trained in a hands-on environment without the need for an operating room. These trainers aim to create a realistic environment in which the clinician develops the controls, knowledge, and decision-making abilities to perform the procedure effectively. Task-specific trainers have been developed to teach clinicians a portion of a surgical procedure, an example of which is hand-eye coordination for a laparoscopic environment using the Laparoscopic Training Box (Laptrainer) by US Surgical or more general trainers that are designed to recreate a surgical scenario. Simulators have been developed for ophthalmology [13], orthopaedics [14], endovascular intervention [15], cardiac interventions [16], [17] and other procedures [18], [19]. The literature has found that incorporating surgical simulations into the educational process may improve clinical training and reduce negative outcomes for patients [20], [21]. Each trainer aims to recreate a surgical scenario such that the skills developed on the trainer can be transferred to the procedure on a patient.

1.9 Surgical Guidance Validation

In addition to creating a realistic training environment for clinicians, surgical simulators also act as a tool for the validation of new image-guided virtual and augmented reality techniques. To ensure these systems will accurately assist clinicians and reduce cognitive load during surgery, they are validated and tested using accurate anatomical models. This

can be done with cadavers, animal studies, and more recently using surgical phantoms [22]–[24]. Surgical phantoms are designed to use patient-specific or generalized models that allow for the interaction and/or simulation of a procedure. Surgical simulators are ideal for the validation of augmented or virtual reality techniques as they allow the user to precisely position the anatomical model(s), creating a gold standard. In addition, a phantom is much more accessible and offers a solution that greatly reduces the cost and difficulty of performing validation studies throughout development.

1.10 Models for Surgical Planning

For cases of complex anatomy and pathology, there has been an increasing acceptance from clinicians towards the use of patient-specific models as a tool to better view and interpret anatomy [25], [26] when preparing the pre-procedural plan. These models typically come in two forms, as computational or physical models. The computational models are digital renderings that can be used for interpretation and finite element modelling (FEM) [27], [28]. Physical models are typically created using three dimensional (3D) printing technology [29]–[31], which allows them to be held, measured and interacted with. In both forms, the patient's scan is segmented and used to generate a tessellated computer model that gives clinicians a three-dimensional perspective of the anatomy and pathology.

1.10.1 Computational Models

Computational 3D models can be used with FEM to reproduce a surgical technique and attempt to predict surgical outcomes prior to the surgery [32]. As this technology continues to develop, the ability to examine different options for repair may allow clinicians to choose the ideal repair technique for individuals based on simulated results [32]. This could lead to more positive outcomes for patients by ensuring each patient is receiving the best treatment available. In addition to FEM models, the computer models can be used by clinicians to closely examine the potential pathways for catheter navigation and to evaluate the target location for the procedure. This can be useful in choosing the correct size of a device in a procedure such left atrial appendage closure, or examining the fossa ovalis and measuring the proper catheter puncture location.

1.10.2 3D Printed Models

In addition to computational models, 3D printers have made it possible to quickly and reliably create a physical representation of a patient's anatomy [26], [33]. Many previous studies have examined the use of rigid 3D printed models as a preoperative planning tool [34]–[36]. These models are becoming increasingly popular as clinicians realize the value that three-dimensional models can add in the preoperative phase for measuring, evaluating and interacting with the anatomy. The current state of the art allows for models to be printed using multiple materials, giving clinicians the ability to print anatomical features in a variety of colours, or using materials of different properties, combining both flexible and rigid features [37], [38], [39]. Varying colours allows anatomical features to be more easily identified, and by using materials with different properties the models will have more realistic visual and haptic characteristics. Producing high-quality models utilizing multiple or flexible materials can add significant cost to the surgical workflow, as these models require the need for high-end 3D printers, which implies either a large investment into purchasing or outsourcing to companies that charge a premium to print.

Despite the cost, there are benefits to flexible, over rigid, models, as they are more representative of a patient's anatomy, and they provide some ability to interact with the models that rigid models do not. This may include fitting surgical tools or devices into the models or allow for a procedure to be simulated or practised on the model. With the material properties being controlled by the manufacturer, the flexible models can be constrained and may not be suitable for all anatomical representations. In addition, as most of these procedures are minimally invasive, requiring the use of image guidance. For patient-specific 3D models to be incorporated into the simulation of a surgical procedure, these models would need to be representative of human tissue while viewed under common imaging modalities. Currently, the state of the art flexible 3D printed materials does not sufficiently represent human tissue under image guidance, resulting in a need for new materials or alternative methods of producing anatomical models.

1.10.3 Flexible Models

Therefore, to develop a patient-specific model that is both flexible and compatible for use with common surgical imaging modalities such as ultrasound, MRI or CT, these models need to be produced from specific materials that currently cannot currently be 3D printed. For ultrasound applications, the material polyvinyl alcohol cryogel (PVA-C) is often used as it can be produced to mimic the mechanical properties, the speed of sound and attenuation of human tissue [40]. The material itself can be limited as it is 90% water, requiring the model to be stored in a sealed container to prevent it from drying out and shrinking.

In addition to PVA-C, many flexible silicones offer the ability to reproduce a patient's anatomy with a high degree of accuracy. Silicone can be highly flexible, durable and offers a wide variety of material properties that can be modified depending on the application. Using moulding as the manufacturing method, silicone has been used to create flexible patient-specific models that are capable of being used as tools to analyze a patient's anatomy, simulate a surgical procedure or measure and size a device to be inserted into the patient [41], [42]. Silicone has imaging properties that are dependent on the brand and product line that is used. For use with ultrasound, silicone has higher attenuation than cardiac tissue, but if the wall of the model is thin, then silicone may still be suitable for the application.

The use of flexible, rather than rigid 3D printed models increases the number of potential applications for the user. Flexible models, like rigid models, can act as useful pre-procedure tools to guide clinicians, make measurements and aid in planning the procedure. Unlike rigid models, flexible models with imaging properties representative of human tissue may be used in applications of surgical simulation. Surgical simulators offer great potential for the medical field. Specifically, a surgical simulator that uses patient-specific anatomy could offer a safe and comprehensive training experience for new or inexperienced clinicians. They can also be used to validate new surgical tools or image guidance techniques while in the development stage, helping to reduce the need for animal trials. Finally, they may allow for the simulation of a surgical procedure

preoperatively, using different tools and techniques to evaluate each method's efficacy for the patient.

1.11 Summary

Currently, the use of 3D models, both computational and physical, can help provide extra information in the planning stage of a procedure. Using these models clinicians can get a better understanding of the anatomy they are operating on, helping to avoid extra cognitive load while interpreting image guidance during a procedure. The state of the art 3D printers are able to produce models that are flexible, multi-material, and multicoloured, which can aid in interpreting anatomical features, measuring key locations or interacting with the patient's anatomy. These models are still limited from a materials standpoint, where they are not representative enough of cardiac tissue in regards to imaging or mechanical properties. Employing materials that provide more realistic properties for mimicking cardiac tissue may allow clinicians to better interact and use moulded 3D models that mimic anatomical features.

Due to an increased rate of development of surgical tools, devices and techniques there is an increasing need for clinicians to have access to systems that allow them to learn, practice and simulate interventions. This need is emphasized in clinical evidence where the frequency a clinician performs a procedure can directly impact the outcome of a patient [9]. To address this concern, companies have developed physical, augmented and virtual reality simulators that are designed to recreate surgical scenarios for training clinicians, allowing them to receive feedback regarding their performance while learning the motor patterns and skills for a specific procedure.

Due to the nature of minimally invasive cardiac surgery, with each procedure comes a different set of tools, motor skills, and clinical objectives. The clinicians must be trained using the new systems to ensure they are fully prepared to perform the procedure on a patient. To meet training needs of clinicians, a simulator needs to be developed, that can incorporate different catheters, tools, and devices, to allow for current and future procedures to be practised. To ensure the surgical phantom sufficiently simulates a procedure, the phantom should include patient-specific models with material properties

that are representative of cardiac tissue both physically and under image guidance. This allows clinicians to learn the motor patterns while experiencing the same cognitive load of interpreting image guidance as when performing a real procedure. The patient-specific model incorporated within the phantom should include all anatomical features relevant to the procedure and the model should be interchangeable to allow for different scenarios to be trained or to allow for a specific patient's anatomy to be simulated.

1.12 Objective 1

At the outset of this work, there was not a concrete methodology for manufacturing flexible patient-specific cardiac models. As there is evidence that 3D printed models can provide clinicians with beneficial information for procedural planning, the first objective of this thesis was to develop a methodology to produce thin walled patient-specific atrial models using tissue mimicking materials and validate the manufacturing method for accuracy. The methodology and results of the validation study are reported in Chapter 2.

1.13 Objective 2

Building on the results from chapter 2, it was decided the second objective would be to further expand these models to include all clinically relevant anatomy needed to simulate a minimally invasive procedure. These models would be utilized within a surgical phantom that would be imaging compatible. These tools would then be evaluated for accuracy and functionality by simulating a MitraClip® procedure. The results of the model development and surgical simulation are described in Chapter 3.

Chapter 2

2 Patient-Specific Atrium Models for Training and Pre-Procedure Surgical Planning

2.1 Introduction

For cases of abnormal or diseased patient anatomy, the ability to view and interact with patient-specific models in addition to being able to simulate interventional conditions may provide valuable information for the pre-procedure plan. A review paper published in 2016 [29] examined the results of 14 studies that used 3D printed models to help with surgical planning for a variety of procedures involving congenital heart defects. The consensus of this review was that the models were beneficial in planning the procedure.

Building on the work done for creating models of other cardiac anatomy, the development of patient-specific atrial models could lead to improved clinician training, better surgical planning, and more informed decisions, ultimately decreasing surgery times and resulting in better outcomes for patients. In broad terms, the intent of this investigation is to increase the amount of information that surgical teams have access to for pre-procedure surgical planning. More specifically, we aim to create a workflow for creating patient-specific left and right atria that have realistic tissue and imaging properties. These models can benefit clinicians in planning particularly complex interactions with a patient's anatomy prior to performing any incisions. This methodology will be used to evaluate the efficacy and feasibility of creating pre-operative models of a patient's left and right atria. The models will be validated to determine their accuracy and their ability to reproduce anatomical features that are key to minimally invasive cardiac procedures.

2.2 Methods

2.2.1 Overview

The atrial models were developed to include important anatomical features that are used throughout surgery as access points, spatial identifiers, or potential areas of repair. This list includes access into the atria through the inferior and superior vena cava, the atrial

transseptal wall, the left atrial appendage, the left atrial opening for the mitral valve and the right atrial opening for the tricuspid valve. These features ensure that the preoperative models will contain the information needed to analyse areas of concern for a wide variety of minimally-invasive cardiac surgeries.

2.2.2 Imaging

After REB approval, a cardiac patient's CT data were anonymized and used for the preparation of the atrial models. The patient was scanned using the GE Discovery CT750 HD with 64 slices and a voxel size of 0.5 x 0.5 x 0.625 mm.

2.2.3 Tissue Segmentation

The internal blood pools within the heart were segmented using the software "itk-snap" [43] (<http://www.itksnap.org>) and the resulting volumes modified to only include the blood pool within the left and right atria. The segmentations ended at the mitral and tricuspid annuli. The blood pool models were segmented using automatic threshold segmentation and then manually corrected to ensure all layers contained the required anatomy. Geometric models which enclosed all the segmented voxels were then generated to allow for the data to be modified with computer aided design (CAD) software. The geometric models were exported in the stereolithography (STL) format (Figure 9: Step 1).

2.2.4 Computer-aided Design STL Manipulations

The STL models were then imported into the software, MeshLab [44], where the number of triangulated faces were reduced using decimation, and the overall model smoothed using the Taubin Filter [45] to remove artefacts generated during the segmentation or scanning processes.

With the models corrected, they were then modified using the computer aided design software, SpaceClaim (<http://www.spaceclaim.com>) to add features (Figure 9: Step 2). These features included: uniformly offsetting the blood pool models by 3 mm to generate outer walls of the atria, and adding an indentation to act as the fossa ovalis (the most common location for atrial septal wall punctures). All relevant anatomical features that

were added to the models were identified by a clinician to ensure accuracy. Finally, features were added to allow for the models to be 3D printed and moulded, including cut-outs for the mitral and tricuspid valve annuli and alignment pegs.

2.2.5 3D Printing Technologies

The modified STL models were then printed using fused deposition modelling on the Ultimaker 2+ 3D printer (<https://ultimaker.com>). Models were printed using Cura version 15.04.6. The settings used for the prints were: layer height of 0.1 mm; shell thickness 0.8 mm; 0.6mm fill for the bottom/top thickness; fill density 20%; and extruder nozzle diameter, 0.4 mm. Support material was used everywhere as required. The models were printed using polylactic acid (PLA) filament with a diameter of 2.85 mm. The settings chosen for these prints were used to reduce error in the final part and replicate the patient's anatomy as closely as possible. Printing time for all four components (inner and outer left and right atria), was approximately 40 hours.

2.2.6 Post Processing

After the models were printed, they were post-processed to remove artefacts added by the 3D printer. The first step was to remove all the support material used during the printing process, after which the models were sanded using low grit sand paper to remove any small artefacts such as stepping in between layers and any material left connected after breaking away the support structure. Next, the models were coated with Smooth-On XTC-3D® (<https://www.smooth-on.com>) to assist in sealing the components and remove any remaining stepping artefacts between layers which are generated by the 3D printer (Figure 9: Step 3). After allowing the XTC-3D® to cure the models were then sanded again to remove any final artefacts and to ensure an even coating of the sealant.

2.2.7 Molding

To date, there is no flexible material with material properties to adequately mimic atrial tissue that can be directly 3D printed. Hence, to make patient-specific models from materials that simulate the properties of cardiac tissue, the models must be moulded. To build a mould, the rigid models representing the 3-mm offset from the blood pool

segmentation were used as a mould positive. The moulds were created by pouring Smooth-On Mold Star® 16 Fast silicone around the 3D printed models. This process was performed to create a 2 or 3-part mould depending on the model complexity. Upon curing of the silicone, the 3D printed models were removed from the mould (Figure 9: Step 4). The 3D printed models of the internal blood pool were then inserted into the moulds and tissue mimicking material, either silicone or polyvinyl alcohol (PVA) cryogel, was used to make the hollow patient-specific model. The silicone material used was Smooth-On Ecoflex® 00-30 as it has high flexibility and durability. To optimize echogenicity, the two-part silicone is mixed and then degassed in a degassing chamber to remove any air that has been mixed into the silicone while stirring. When it appears that all the trapped air bubbles have been removed the material is poured into the mould and left to cure. To produce a PVA-C model, the PVA mixture is created by dissolving 10% by weight PVA crystals in hot (95°C) water. When the mixture has cooled, it can be poured into the mould and the material allowed to sit, so that trapped air bubbles rise to the surface and escape. On completion of this process, the mould is placed into a freezer at -20°C and left to freeze for 12 hours, after which the mould can gradually warm to room temperature in a cooler. This cycle is repeated for three freeze-thaw cycles, to create a flexible material which exhibits a speed of sound and attenuation coefficient similar to that of cardiac tissue, while maintaining a realistic flexibility [40]. Once the material, either silicone or PVA-C, is fully cured, the 3D printed parts of the internal blood pools can be removed, leaving a hollow model of patient-specific atria (Figure 9: Step 5).

2.3 Validation

Validation of the final patient-specific model was performed using a cone-beam CT scanner. The model was scanned using a Medtronic O-Arm ® scanner with a voxel size of 0.415 x 0.415 x 0.833 mm. The left and right atria model were held in a typical anatomical pose using a custom 3D printed stand (Figure 9: Step 6). The stand offers support to the model at the inferior and superior vena cava, all four pulmonary vein openings, and employs hooks located at the mitral and tricuspid openings to reduce sagging. The stand was developed using CAD software, and 3D printed using the same printer and parameters as the patient-specific models. The completed high-resolution 3D

CT scan was then segmented and used to create a geometric model (Figure 9: 7). This model was then exported as an STL file where it was used to compare the final model to the original patient data. Using the software program CloudCompare [46] (www.danielgm.net/cc), the final model was registered to the original patient STL model using the original iterative closest point algorithm [47]. The registered models were then used to measure absolute distance between point cloud data sets (Figure 9: Step 8) to determine the accuracy of the physical models.

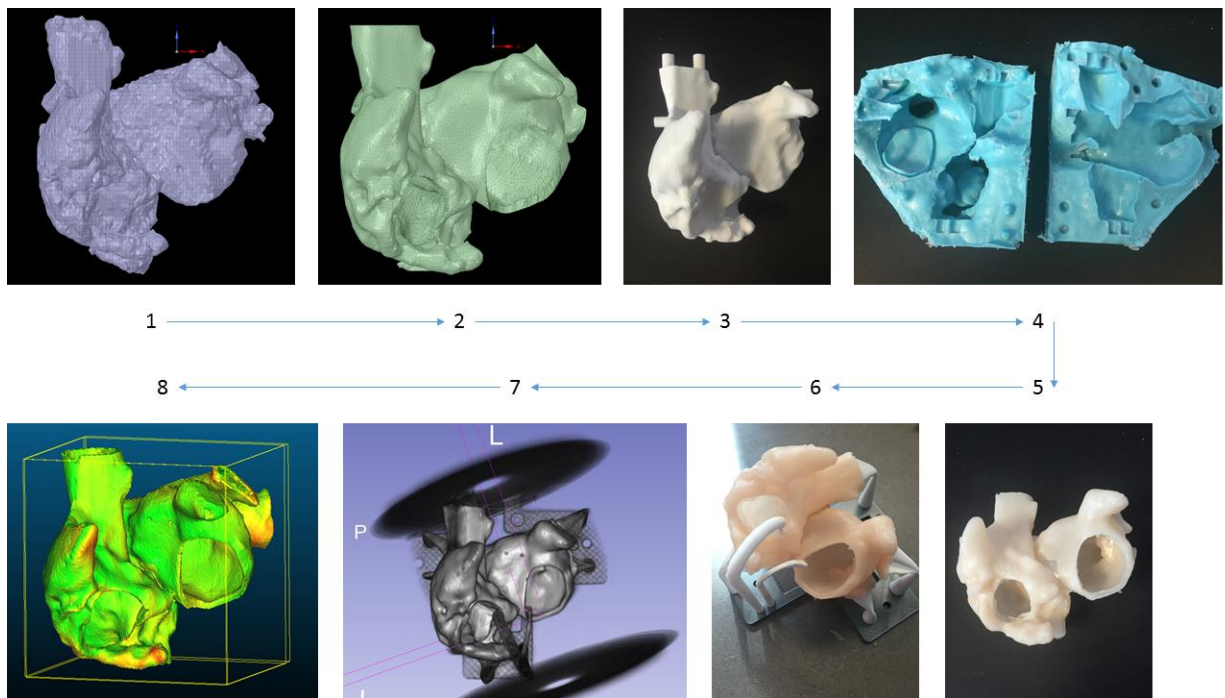


Figure 2.1: Workflow showing the progression from segmentation of patient CT data to silicone model. Step 1 is an STL model generated after segmentation of the patient's blood pool. Step 2 is the blood pool model smoothed and modified using computer aided design to prepare it for 3D printing. Step 3 is a 3D printed blood pool model with alignment pegs that are used for molding. Step 4 is the flexible silicone mold used for generating the flexible models. Step 5 is a hollow silicone atria model. Step 6 is the silicone model inside a 3D printed fixture that hold the model in an anatomical orientation during CT scanning. Step 7 is the result of the CT scan of the silicone atria model. Step 8 is the result of the comparison of the scanned silicone model to the original patient model.

2.4 Results

The two-point cloud models were compared using Euclidean offset distance. For this trial, which only includes 1 patient data set, when comparing the point cloud of the physical model to the original data set, the results have a maximum distance of 4.5 mm, an average of 0.5 mm and a standard deviation of 0.6 mm with a full histogram of the results seen in Figure 10. A colour map of the absolute distances between the scanned model and the original patient data can be seen in Figures 11 and 12.

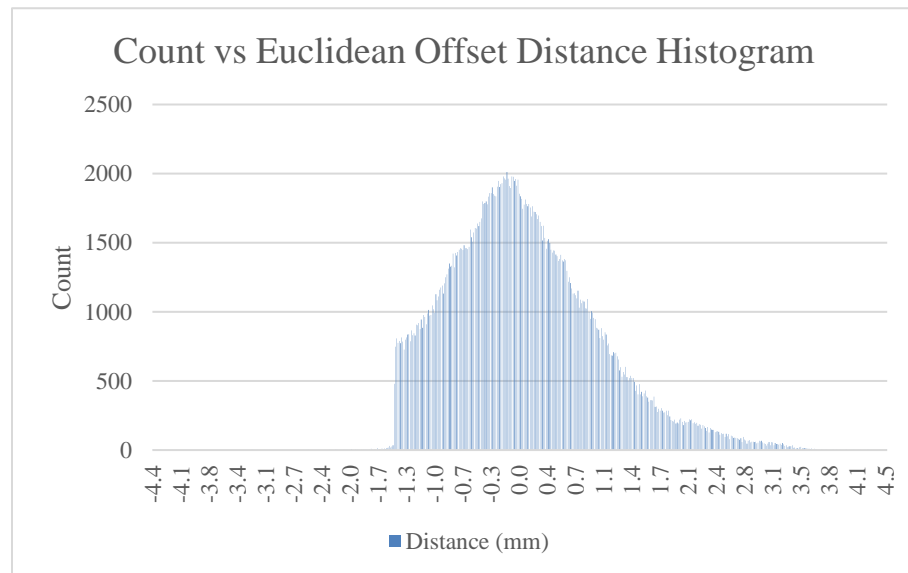


Figure 2.2: Histogram showing the results of the Euclidean offset distance when comparing the physical model to the original patient data set

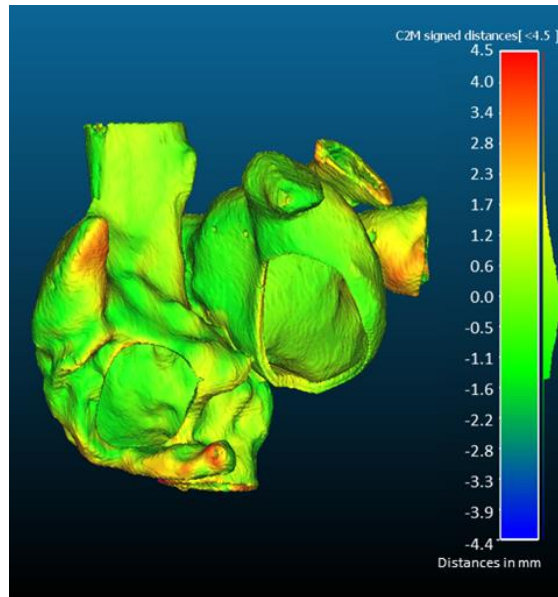


Figure 2.3: Distance map comparing the segmentation of the CT scan from the silicone atria model to the segmentation of the original patient data

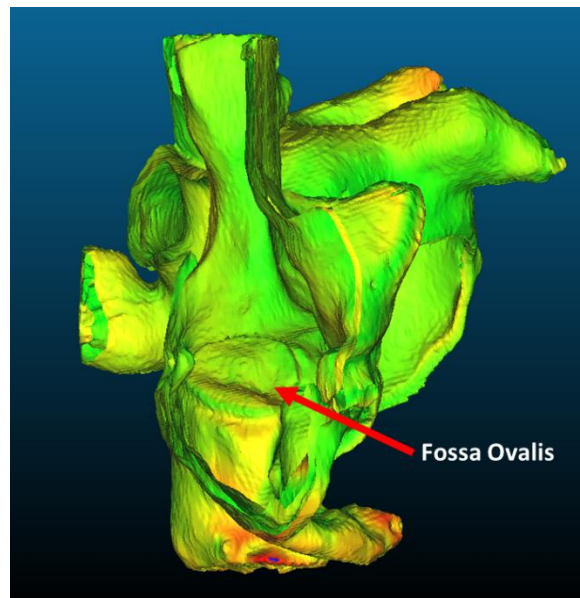


Figure 2.4: Cross section view of the right atrium, showing the fossa ovalis and the results of the Euclidean distance mapping

The results of this study demonstrate the ability of this methodology to accurately replicate a patient's cardiac anatomy with a high degree of accuracy. Using this methodology, models of a patient's left and right atria could be generated as a tool for

pre-procedure surgical planning and would act as an accurate replica of what the clinician could expect to see during the surgery.

2.5 Discussion

We have demonstrated a methodology to accurately build patient-specific models of cardiac atria, and which has the ability to recreate important anatomical features as seen in a patient's CT scan in a physical, flexible model. These models can be made from tissue mimicking materials, such as PVA-C and silicone. For surgeries requiring the use of ultrasound during the repair, the model can be made of PVA-C. PVA-C is a material with variable mechanical properties depending on the number of freeze/thaw cycles, and a speed of sound that is very similar to human tissue [48], resulting in the ability to image the physical models and plan how to best utilise ultrasound throughout the surgery.

In addition to PVA-C, models can be made from silicone. Silicone offers a variety of material properties, colours, and the ability to create highly detailed parts. Models made from silicone are useful as tools for physical inspection and for testing surgical repairs. Silicone is stable at room temperature, is long lasting and can be physically manipulated without easily tearing. Surgical teams can use silicone models for the identification of anatomical features, measurements and gaining visual information regarding diseased areas. These models make it possible for clinicians to gain insight into areas of concern due to diseased or complicated anatomy, for example by selecting the optimal size for LAA closure, or assessing septal puncture locations for MitraClip® delivery. This should allow for a more informed surgical plan, which could lead to shorter surgical times and better patient outcomes.

Many previous studies have examined the use of rigid 3D printed models as a preoperative planning tool [34]–[36], [49]. These studies have demonstrated the value that three-dimensional models can add in the preoperative phase. There have also been studies examining the potential of directly 3D printing flexible models for surgical repair simulation and as training tools [37]. These directly 3D printed models are reliant on the material properties of what can be purchased for their 3D printers. Currently, the materials available on the market do not have imaging properties that can adequately

represent cardiac tissue while under ultrasound, and the printers themselves are quite expensive. As material science evolves, it is possible that a new material will be developed to meet this need. Currently, however, due to this limitation, we have chosen to utilize moulding to create flexible models. This gives us the option of using significantly more materials in creating flexible models. The ability to use PVA-C gives us a tissue mimicking material with ultrasound properties that are very close to cardiac tissue. It is our hope that this ability will allow for us to create patient-specific models that are representative both visually (with ultrasound and MRI) and physically representative of cardiac tissue.

We report a maximum error of 4.5 mm, however, these areas are primarily found in regions where the model was sagging, as a result of the model not being properly supported during the CT scan. A solution to this would be to change the validation procedure to instead scan the models while they are in a neutrally buoyant solution, to ensure the model is in the correct position without requiring specific supports. The current workflow is labour intensive and requires upwards of 2 weeks after receiving the data from a patient's scan to prepare and build a heart model for one of three distinct applications, surgical planning, as a training tool, or for validation. For surgical planning, the current 2-week period creates a time-consuming and expensive addition to surgical planning. For this methodology to be included, it would require optimizations that reduce the manual labour and potential costs to hospitals. In regards to using these models as training tools or as models for validation, the 2-week time period is acceptable. Multiple different models can be created simultaneously, and once a mould has been completed, models can be built with as little as an hour of labour.

Chapter 3

3 A Patient-Specific Cardiac Phantom for Training and Pre-Procedure Surgical Planning

3.1 Introduction

To meet the needs of clinicians and researchers, we have developed a cardiac phantom employing patient-specific cardiac models to recreate minimally invasive cardiac procedures. The phantom is designed to use a model of a patient's cardiac anatomy held within an acrylic chamber that allows clinicians to simulate cardiac procedures that utilize the femoral vein, the femoral artery or the apex of the left ventricle as access points. The simulator is intended to be ultrasound compatible with access for a transesophageal echocardiogram probe to be inserted into the simulated oesophagus, in addition to being fully compatible with MRI, CT, and fluoroscopy.

This phantom will provide the opportunity to simulate a variety of minimally invasive cardiac procedures. These simulations can be used for testing difficult cases, training new clinicians on basic or complex pathologies, and acting as a validation tool for new medical devices or augmented reality guidance techniques.

3.2 Methods

The phantom was developed in three stages. First, patient-specific models were manufactured using silicone moulding and tissue mimicking materials. Next, the valves were produced and attached to the cardiac model. Finally, the phantom was designed and constructed to best simulate minimally invasive cardiac procedures.

The patient-specific cardiac model was designed to include important anatomical features that are used throughout surgery as access points, spatial identifiers, or potential areas of repair. This list includes access into the atria through the inferior and superior vena cava, the atrial transseptal wall, the left atrial appendage, a partial left and right ventricle and anatomically correct mitral and tricuspid valve annuli. After moulding the cardiac wall, a patient-specific mitral valve and a generalized tricuspid valve were manufactured and attached to the cardiac model. These features ensure that the patient-specific models

contain the information needed to analyze areas of concern for a wide variety of minimally invasive cardiac procedures.

We have previously developed a methodology for creating flexible patient-specific models using materials compatible with various imaging modalities[42]. Here we expand on this methodology to include more complex anatomical features that are required for the simulation of minimally invasive cardiac procedures, in addition to adding the necessary features to allow for the model to function within the cylindrical chamber of the phantom.

3.2.1 Imaging

As outlined in the previous chapter, the patient-specific model was produced following REB approval, using an anonymized patient's CT data. The patient was scanned using the GE Discovery CT750 HD with 64 slices and a voxel size of 0.5 x 0.5 x 0.625 mm.

3.2.2 Tissue Segmentation

To maintain the critical features within the heart, the internal blood pools of the CT data were segmented using the software 3D Slicer [50]. The segmentations were performed using an automatic threshold in combination with manual techniques to correct any errors on each slice. Geometric models which enclosed all the segmented voxels were then generated to allow for the data to be modified with CAD software (Figure 13: step 1). The geometric models were exported as an STL file.

3.2.3 Computer-aided Design STL Manipulations

Using the method outlined in 2.2.4 the models were corrected and simplified in MeshLab [44]. The model was then imported into SpaceClaim and modified by cutting crossing the left and right ventricle to allow for the model to be integrated into the heart phantom. Next, the model was uniformly offset by 3 mm to generate an artificial myocardium for the cardiac model. Finally, a flange was added to the patient-specific model, allowing it to be connected to the phantom container in the correct orientation.

3.2.4 3D Printing Technologies

The STL models were then printed using the printer and settings outlined in section 2.2.5. Printing time for the components: outer cardiac model (Figure 13: step 2), inner cardiac model (Figure 13: step 3), flange and mould container, was approximately 80 hours.

3.2.5 Post Processing

Once printing was completed all of the 3D printed components were post processed using the same methodology as section 2.2.6.

3.2.6 Molding

Currently, the state of the art for materials that can be 3D printed do not have adequate mechanical or imaging properties to mimic cardiac tissue. Therefore, to develop a patient-specific cardiac model using materials that simulate cardiac tissue, the models must be moulded. Due to the complex nature of cardiac anatomy, we have chosen to use a flexible silicone mould (Figure 13: Step 4), that allows for the complex organic shape to be manufactured. To build the flexible mould, a custom housing was 3D printed. The rigid model representing the 3-mm offset from the blood pool segmentation was aligned within the mould housing and used as a mould positive. The mould was created by pouring Smooth-On Mold Star® 16 Fast silicone around the 3D printed model into the 3D printed mould housing. The housing was designed to have alignment features that ensured the blood pool model and 3 mm offset model could be aligned such that the production of all subsequent models would produce consistent results. By designing a custom container for moulding we produced a flexible, single part mould that can generate the patient-specific cardiac model.

When the silicone mould had cured, the 3D printed models were removed, resulting in the negative of the outer cardiac wall (Figure 13: step 5). The 3D printed models representing the internal blood pool were then inserted into the mould utilizing the alignment features to ensure the models were in the correct orientation (Figure 13: step 6). Tissue mimicking materials, either silicone or PVA-C, were used to make the hollow patient-specific model. Production of the silicone model was performed using the method

outlined in 2.2.7, where the Ecoflex® 00-30 material, is mixed, degassed and poured into the mould.

To produce a PVA-C model, the PVA mixture is created by dissolving 10% by weight PVA crystals in hot (95°C) water. When the mixture has cooled, it can be poured into the mould and the material allowed to sit, so that trapped air bubbles rise to the surface and escape. The mould is then placed into a Test Equity 1000 Temperature Chamber in which it goes through three freeze-thaw cycles. Each cycle ramps from room temperature to -20°C and holds for 24 hours, after which the chamber gradually warms to room temperature, and holds for 12 hours. As this cycle is repeated the liquid PVA-C mixture gradually changes into a flexible material which exhibits a speed of sound and attenuation coefficient like that of cardiac tissue while maintaining a realistic flexibility [40].

The final step in the production of both a silicone and PVA-C model is to remove it from the mould (Figure 13: step 7). The 3D printed models of the internal blood pool are removed from the model, leaving a hollow patient-specific cardiac model (Figure 13: Step 8).

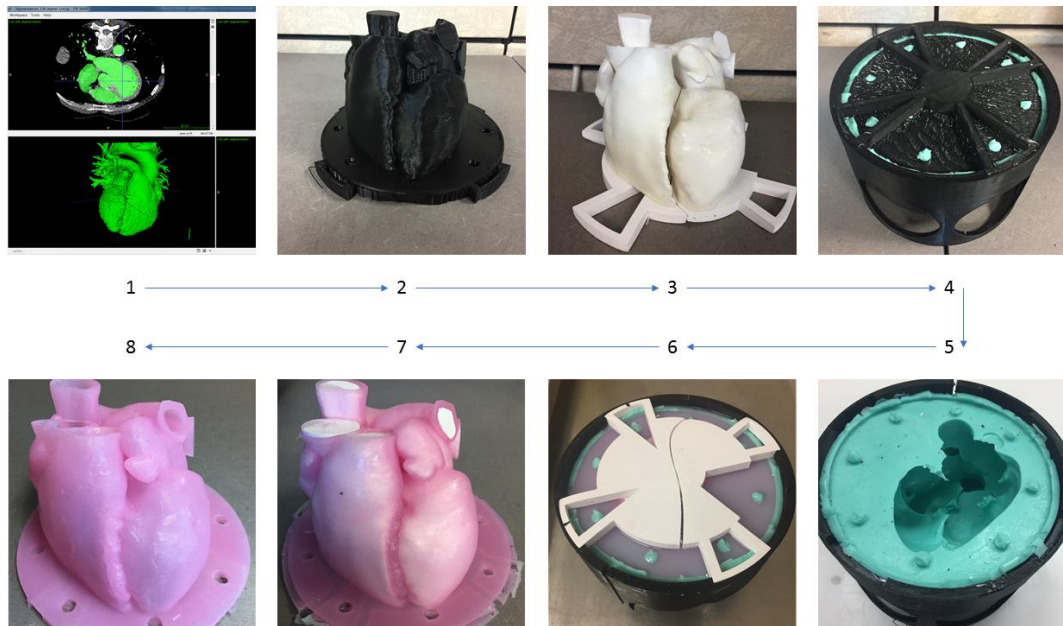


Figure 3.1: Workflow showing the manufacturing of a patient-specific cardiac model. Step 1 is the entire segmentation of the blood within the patient's heart at the time of the scan. Step 2 is the 3D printed thickened atria model. Step 3 is the 3D printed blood pool model. Step 4 is the 3D printed mold container with the thickened blood pool model aligned within. Silicone has been poured into the mold container around the 3D printed model and has cured. Step 5 is the cured and completed silicone mold. Step 6 is the blood pool model aligned inside the mold container with silicone poured into the mold. Step 7 is the silicone heart model completed with the 3D printed blood pool still inside. Step 8 is the complete silicone model.

3.2.7 Valve Manufacturing

Due to imaging constraints associated with a CT scan, it can become difficult properly visualize and segment the valves within the heart at the time of the scan. The valves act as important landmarks and guides when imaging the heart, so it is important that the models still contain valves to aid clinicians in interpreting the patient's anatomy and for guiding the catheter within the model. To overcome this, we have developed a methodology for creating both patient-specific [51] and generalized valve models. As we did not have a TEE scan from this patient, a different patient's TEE scan was used to generate a mitral valve model, with the only modification being scaling of the computational model to fit the other patient. In addition, we have also developed a generalized tricuspid valve using the same manufacturing methods that can be added to the patient-specific cardiac model.

These valves are constructed using a 3D printed mould made of PLA (Figure 14: step 1). Silicone is painted onto the mould and allowed to cure. The silicone chosen for these models is Smooth-On Ecoflex® 00-30, as it is highly durable and flexible, resulting in realistic valve movement within a phantom. Chordae are simulated within the valve by including strings at key locations in the model that maintain the valve's shape. When the silicone has cured, the valve model can be removed from the mould by peeling the silicone off the 3D printed part (Figure 14: step 2). Both the mitral and tricuspid valves were added to the patient-specific model using Smooth-On Sil-Poxy, a single cure bonding silicone (Figure 14: step 3 and 4).



Figure 3.2: Workflow showing the manufacturing of a patient-specific valve model. Step 1 is the 3D printed valve model that is used as a mold. Step 2 is the cured silicone mitral valve model. Step 3 is the mitral valve attached to the full silicone cardiac model. Step 4 shows the silicone mitral and tricuspid valve models inside the silicone heart model.

3.3 Phantom Design

The phantom container was designed to accommodate the patient-specific cardiac model and allow for the simulation of minimally-invasive cardiac procedures. A part of this process, clinicians were consulted to develop the design specifications that would ensure the phantom would perform as required. This included tool access at common access points large enough for a variety of catheters and compatibility with TEE ultrasound, CT, and fluoroscopy to visualize tools and anatomical features within the model. To accomplish this, both the phantom chamber and the model had to be made using materials that would not cause distortion for imaging modalities. In addition, the phantom is designed as a water-filled container to permit the use of ultrasound as an imaging modality and to help simulate blood within a patient's heart during a procedure.

3.3.1 Phantom materials and shape

For the phantom to be compatible with the imaging modalities used throughout a minimally invasive cardiac procedure, it was designed to contain no metal and use components that do not distort imaging of the patient-specific model within the chamber. The outer cylindrical chamber and walls of the phantom were constructed using acrylic as it does not distort the patient-specific model within the chamber. The stand used was 3D printed using the Ultimaker 3 using PLA material, and all the fasteners used were nylon

or plastic. The overall length of the phantom is 15.24 cm, the cylindrical container has an outer diameter of 25.4 cm and an inner diameter of 22.86 cm as seen below in Figure 15.

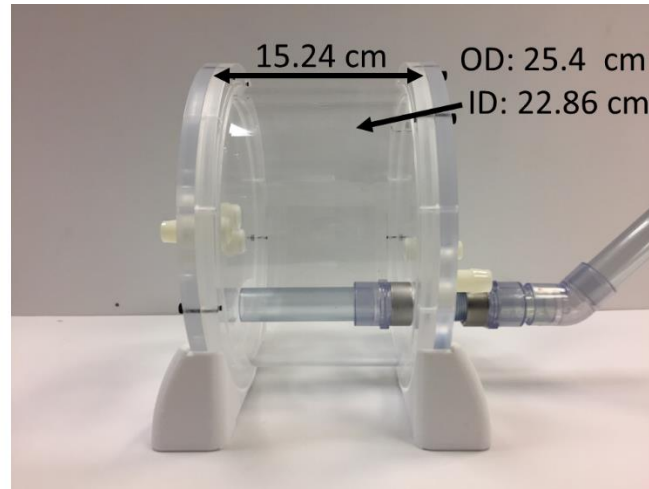


Figure 3.3: Side view of the cardiac phantom container with outer and inner dimensions

3.3.2 Access Points

The phantom container was designed to have 5 access points into the cardiac model at strategic locations. The access points are located at the inferior and superior vena cava, right and left ventricle and in line with the aortic arch. These locations can be used to simulate catheter insertion locations for cardiac procedures or as locations for flow to be added to the phantom. Each access point is capable of accommodating tools up to 1.47 cm in diameter and will fit all catheters up to and including 40 French (Figure 16). The phantom container also has access for a TEE probe to be inserted into a simulated oesophagus. Within the phantom there are two options for the oesophagus, a rigid acrylic tube, or a flexible PVA-C model, which constrain the movement of the probe within the phantom and to provide realistic material properties to the oesophagus.

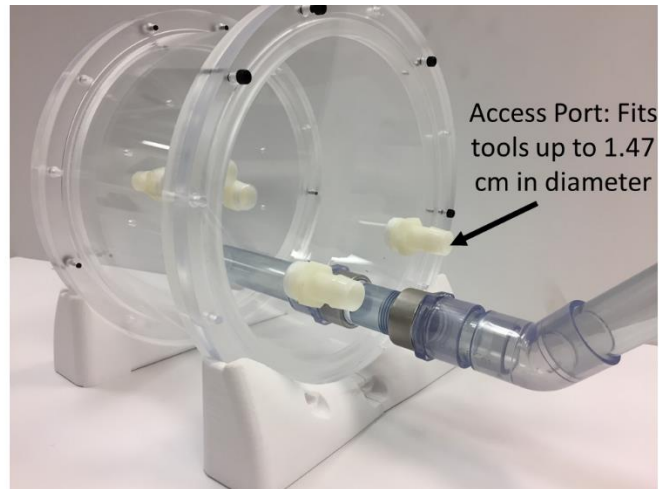


Figure 3.4: Cardiac phantom container access points and dimensions

3.3.3 Model Accommodation

The patient specific model is held within the phantom using a series of 8 nylon screws. Each screw connects the flange of the model to the wall of the phantom securing it in place. A 3D printed interfacing component applies uniform pressure onto the model flange helping to maintain the position of the cardiac model throughout a simulated procedure (Figure 17). The model itself is contained entirely within the phantom container. In use, the phantom is filled with water, which helps to prevent the model from sagging due to gravity and maintains the anatomical position.

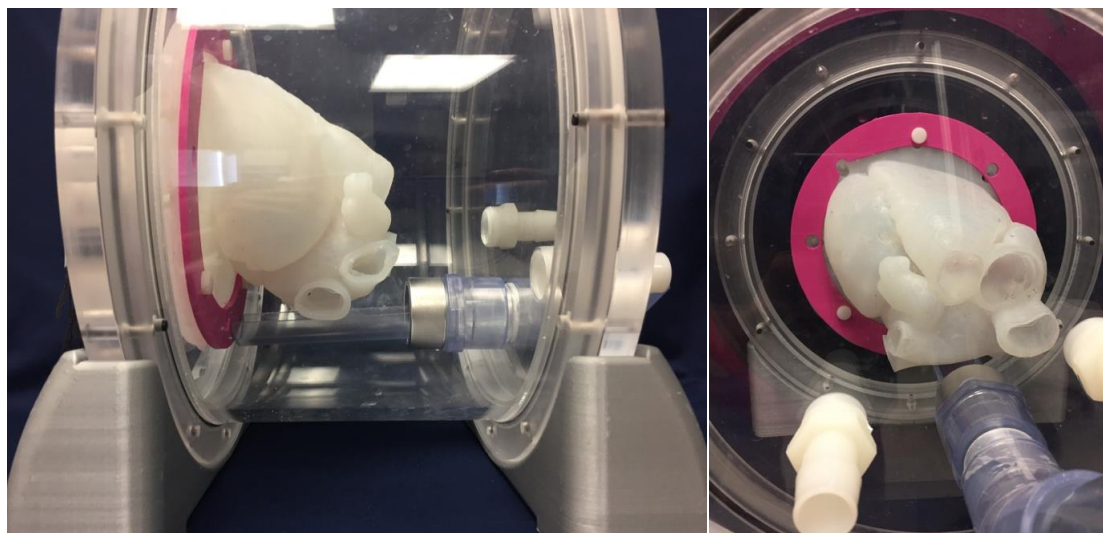


Figure 3.5: The full cardiac phantom with the silicone patient-specific model contained inside

3.4 Validation of the Model

Validation of the final patient-specific model was performed using a cone-beam CT scanner. The model was scanned using a Medtronic O-Arm[®] scanner with a voxel size of 0.415 x 0.415 x 0.833 mm. The model was scanned within the phantom container, positioned as it would be for a simulation. The material properties of silicone were sufficiently stiff to keep the model from sagging noticeably and to hold it in a stable position. The completed high-resolution 3D CT scan was then segmented and used to create a geometric model. This model was then exported as an STL file where it was used to compare the final model to the original patient data. Using the software program CloudCompare [46] the final model was registered to the original patient STL model using the original iterative closest point algorithm [47], as seen in Figure 18 where the blue model is the reference and the red model is the scanned silicone model. The registered models were then used to measure absolute distance between point cloud data sets (Figure 19) to determine the accuracy of the physical models.

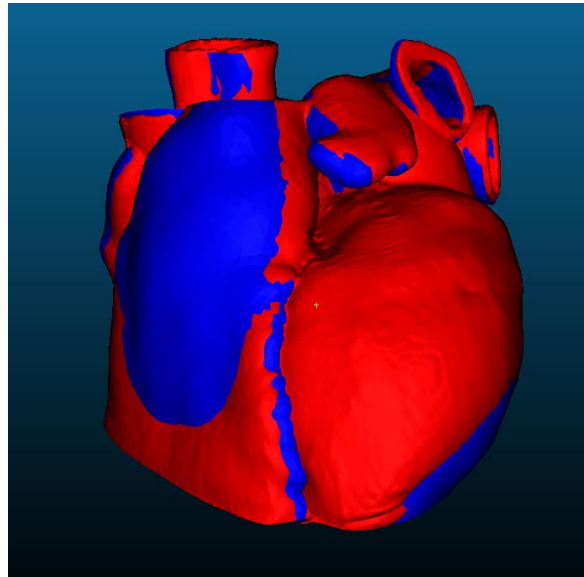


Figure 3.6: The segmentation of the original patient data registered or the segmentation of the CT scanned silicone cardiac model. Blue is the original data set and red is the silicone cardiac model.

3.4.1 Validation of the Phantom

The phantom was validated to determine its ability to realistically display anatomical features and surgical instruments within the phantom. For the phantom to accurately represent a heart during a cardiac procedure, the imaging parameters, including tool visualization need to be correct. This was performed by replicating a MitraClip[®] procedure and positioning the tool at important landmarks for the procedure. The procedure was simulated using a Medtronic O-Arm[®] scanner for both CT and fluoroscopy, and the model was also viewed under TEE ultrasound guidance using the Phillips iE33 Ultrasound machine. Images were acquired by an experienced anaesthetist who simulated the standard views used during a MitraClip[®] procedure. The tool was manipulated by an Abbott Canada MitraClip[®] representative who is experienced in the use and positioning of the tool. The device was positioned and imaged at the septal wall and within the left atrium of the model. The images acquired from the simulator were evaluated qualitatively and compared to patient images used in the Abbott Canada MitraClip[®] training guide.

3.5 Results

To verify the accuracy of the cardiac model, the two-point cloud models were compared using Euclidean offset distance. For this trial, which only includes 1 patient data set, when comparing the point cloud of the physical model to the original data set, the results have a maximum distance of 7.7 mm, an average of 0.98 mm and a standard deviation of 0.91 mm with a full histogram of the results seen in Figure 19.

A colour map of the absolute distances between the scanned model and the original patient data can be seen in Figure 20.

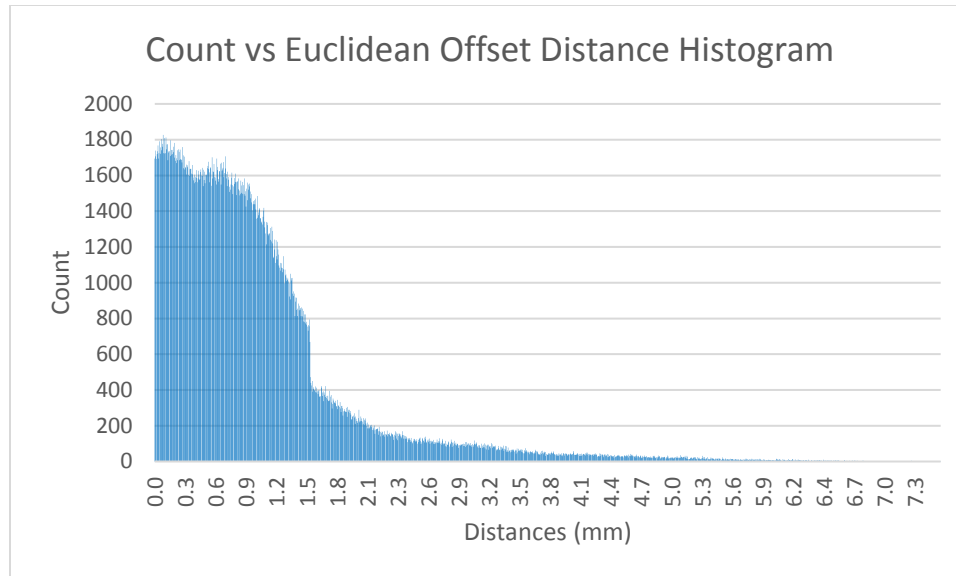


Figure 3.7: Histogram showing the results of the Euclidean offset distance between the silicone model and the original patient data set

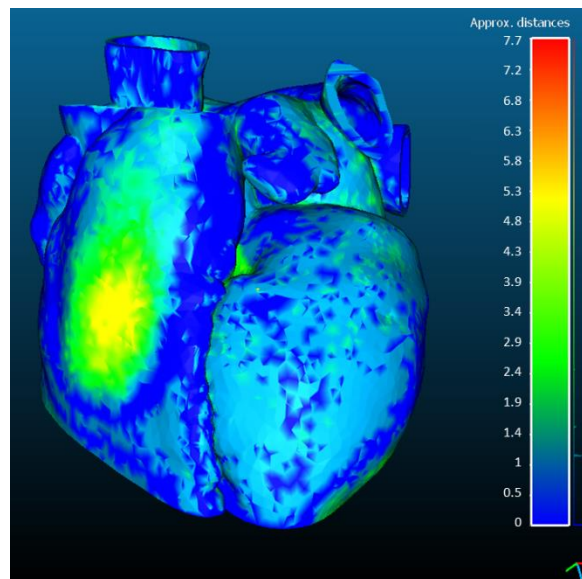


Figure 3.8: Results of the Euclidean distance comparison between the silicone and reference model

When comparing the ultrasound and fluoroscopy images of the cardiac model within the simulator to the training images from Abbott Canada, there are some key points to note. The tool is clearly visible within the cardiac model at the key points evaluated, across the

septal wall, and within the left atrium. This ensures that the tool will be visible during a simulated procedure and will provide realistic visual feedback for the clinician.

As the tool is manoeuvred through the femoral vein to the inferior vena cava and into the right atrium the clinician begins to track the tool using ultrasound guidance. Upon entry into the right atrium, the tool is aligned with the fossa ovalis to puncture the atrial septal wall. In a MitraClip® procedure, the tool must puncture the septal wall at a targeted position to allow for sufficient space within the left atrium to bend the catheter and align the tool head with the mitral valve.

The images were acquired without the use of a septal wall puncture catheter, the MitraClip® introducer, or sheath. This resulted in some disparity in the images at the septal wall. Although the introducer and sheath are not present, the MitraClip® tool head and catheter are visible under image guidance across the septal wall (Figure 21). This is useful for cases of septal wall puncture as a clinician would be able to both identify the fossa ovalis and a catheter under image guidance to perform a simulated septal puncture. The tool was visible under ultrasound guidance within the phantom on both sides of the septal wall. This results in sufficiently realistic imaging and catheter guidance within the phantom for replication a septal puncture from an imaging perspective.

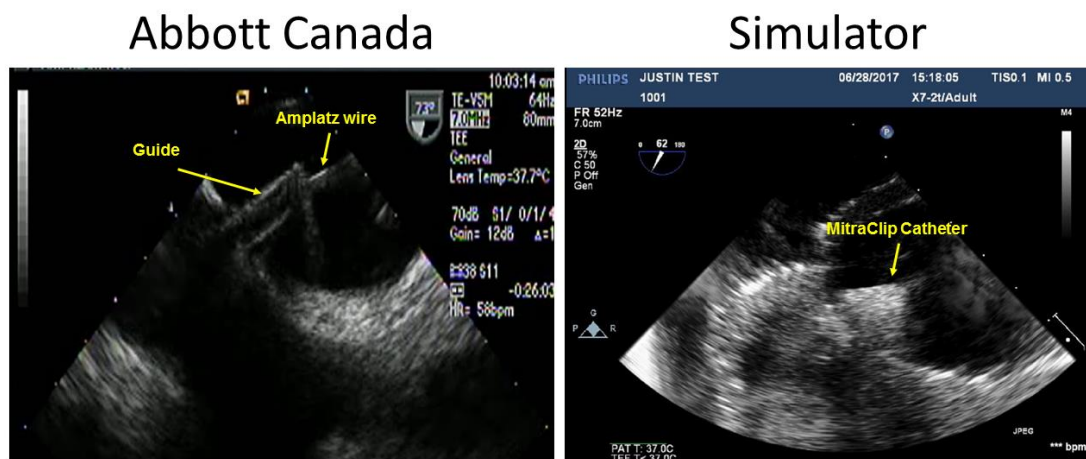


Figure 3.9: Comparison of the MitraClip® tool under ultrasound image guidance crossing septal wall (right), to and image from the Abbott training manual (left) of a tool cross the septal wall of a patient

Once across the septal wall, the clinician manoeuvres the tool to position it in line with the valve. To do this they must be able to see the tool within the left atrium and identify the location of the tool's graspers. This enables the clinicians to align the tool with the flailing leaflet. When evaluating the phantom, the tool was placed within the left atrium and the graspers of the tool were opened. Both arms of the MitraClip® are visible and identifiable under ultrasound (Figure 22) and fluoroscopy imaging (Figure 23).

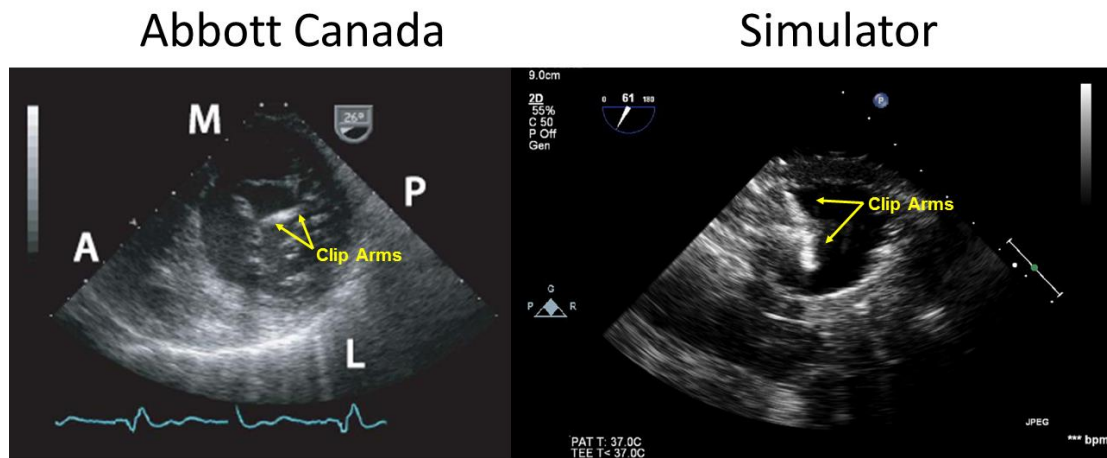


Figure 3.10: Comparison of the MitraClip® tool under ultrasound guidance within the left atrium of the silicone phantom (right), to an ultrasound image from a MitraClip® procedure with the tool within the patient's left atrium (left)

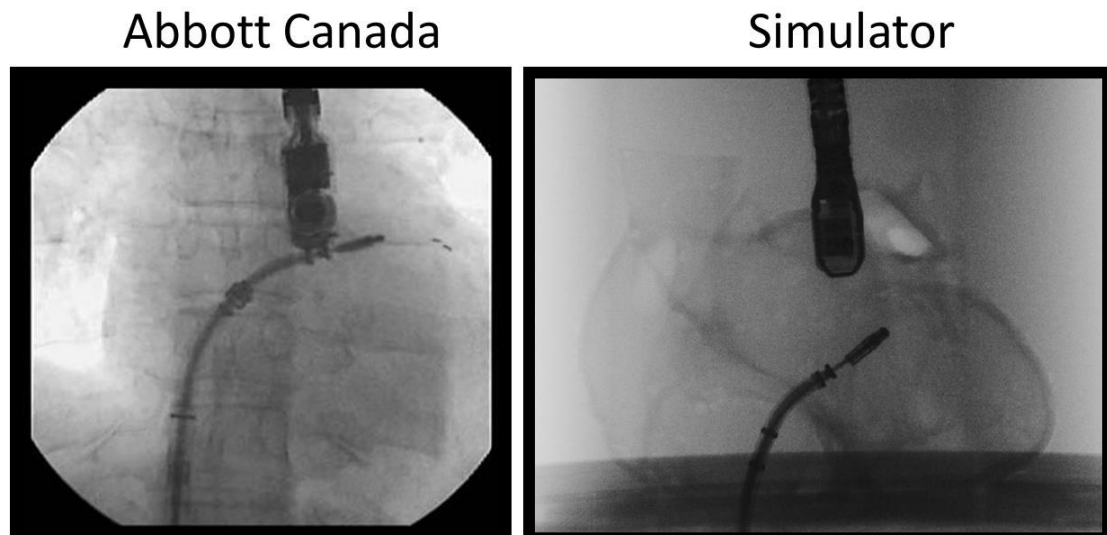


Figure 3.11: Comparison of the MitraClip ® tool under fluoroscopy guidance in the left atrium of the silicone cardiac phantom (right) and an image from the Abbott training manual (left) of the intervention being performed on a patient

The simulated procedure ended prior to deploying a clip onto the valve to maintain the integrity and usability of the tool, as it can only be deployed once. The results of this study demonstrate the ability of this methodology to accurately replicate a patient's cardiac anatomy with a high degree of accuracy and simulate under image guidance a minimally invasive cardiac procedure. Using this methodology, a patient-specific cardiac model can be generated as a tool for pre-procedure surgical planning and would act as an accurate static replica of what the clinician could expect to see during the surgery.

3.6 Discussion

We have demonstrated a methodology to accurately build patient-specific models of cardiac anatomy that can be used within a surgical phantom for simulation of minimally invasive cardiac procedures. The cardiac model recreates important anatomical features as seen in the patient's CT scan in a physical, flexible form. These models can be made from tissue mimicking materials such as PVA-C and silicone, allowing the user to control the material properties of the model. In the simulated procedure employing a MitraClip ® tool, we have shown the ability to display anatomical features that are compatible with ultrasound and fluoroscopy imaging. This allows the phantom to be used as a simulator with patient-specific models, a training tool for imaging or clinicians, and as a means for validating new image-guided techniques.

Patient-specific models made from tissue mimicking materials could make it possible for clinicians to gain insight into areas of concern due to diseased or complicated anatomy, for example by selecting the optimal size for a left atrial appendage closure device, or assessing septal puncture locations for MitraClip ® delivery prior to a surgery. Clinicians have the ability to fully examine, plan, and test fit devices within the models prior to performing a procedure. Furthermore, employing these models in combination with a surgical phantom allows clinicians to simulate and practice the procedure. Used as a

surgical planning tool these models may allow for a more informed surgical plan, which could lead to shorter surgical times and better patient outcomes.

The model was scanned and validated within the chamber to evaluate the efficacy of the phantom to accurately support and maintain the model's functionality during use. To fully demonstrate the accuracy of the manufactured model, it could be scanned with the 3D printed blood pool inside the flexible silicone. This would ensure the model was being supported as effectively as possible, but would not demonstrate the accuracy of the model within the phantom. We report a maximum error of 7.7 mm; however, this offset distance is primarily found in areas where the model was sagging, because of the model not being entirely supported during the CT scan.

The use of surgical phantoms in replicating minimally invasive cardiac procedures is a developing field that aims to provide the opportunity to recreate the experience of a minimally invasive procedure outside of the operating room. This ability will allow for clinicians learning or maintaining their skill level to work on a phantom and hone their skills without any risk to patients or the need for animals. In addition, this allows for a measure of quality control between hospitals where the number of procedures performed may be drastically different. There is evidence that the frequency at which a clinician performs a procedure can directly impact the outcome for a patient[9]. Allowing clinicians to train using a realistic surgical phantom may help to bridge the skill gap between institutions, and help to provide better and more consistent care for patients.

As surgical phantoms are increasingly used as simulators and training tools, the number of patient-specific models will increase. This will result in a catalogue of models with varying anatomy and pathologies. Training clinicians can develop their skills, learning on common models and working up to abnormal or atypical cases that may be very rare to experience in the operating room. Ultimately surgical phantoms could provide the clinicians with a training environment that allows them to experience complex surgical scenarios with no risk to patients.

The phantom was made to accommodate a wide range of heart sizes, allowing it to be compatible with a range of pathologies and models. Thus, to prepare a model for

simulation, training or validation, the limiting factor is the manufacturing time of the silicone or PVA-C model. Using the current workflow, the time required to manufacture the patient-specific cardiac model requires upwards of 2-weeks from the time we receive the patient's scan. For surgical planning, the current workflow of 2-weeks is within the typical time frame between a patient's scan and the surgery. Although labour intensive, developing these models for patients with complex pathologies may provide clinicians with the information they need to perform the procedure. For clinical training and validation, the time to produce the models is sensitive. Using the current workflow, multiple different models can be created simultaneously, and once a mould has been completed, models can be built with as little as an hour of labour.

This work describes our workflow for manufacturing patient-specific cardiac models and the validation of a patient-specific cardiac phantom to be used by clinicians for training, pre-procedure surgical planning and the validation of tools and image guidance techniques. These cardiac phantoms aim to allow for clinicians to work with cardiac models outside of the operating room, for procedure simulation and in a training environment. The use of patient-specific cardiac models within heart phantom will help to promote new research that aims to enhance minimally invasive cardiac surgeries, making them more efficient and effective.

Chapter 4

4 Conclusions and Future Work

4.1 Conclusions

The purpose of this thesis was first to develop a methodology for manufacturing patient-specific cardiac models using tissue mimicking materials, and second to use these models within a cardiac phantom to allow clinicians to train, simulate procedures and validate new tools and systems. The thesis was therefore divided into two chapters based on the objectives stated in Chapter 1. The conclusion of both chapters are discussed hereafter.

In Chapter 2, we outlined a methodology for creating patient-specific left and right atria models from pre-operative CT scans. This methodology has the ability to create flexible models that have material properties similar to cardiac tissue and can accurately represent the patient's anatomy. It is our hope that these models will help to provide clinicians with more information in the pre-procedure surgical planning phase. In cases of difficult anatomy, these models may be able to provide the necessary information to allow for adequate planning and preparation to avoid potential risks and harms to the patient.

In chapter 3 we presented a methodology for building patient-specific cardiac models from pre-operative CT scans and the incorporation of them into a cardiac phantom. Using this methodology, we have demonstrated the ability to simulate a minimally invasive cardiac procedure by performing a MitraClip® intervention using a patient-specific cardiac model. The phantom is capable of the visualization of surgical instruments within the cardiac model, in addition to providing a simulation environment sufficient for the training of minimally invasive procedures and surgical planning. It is our hope that this cardiac simulation system will provide, new clinicians the opportunity to train using surgical tools in a realistic surgical environment, with both basic and complex models. In addition, the simulator can be used by researchers to test and validate new image guided techniques and augmented reality systems. Finally, we hope to see the simulator used in pre-procedure planning for cases where a patient would not be eligible to receive treatment due to their complex anatomy or pathology.

4.2 Future Work

Medical simulators have the potential to allow for clinical training for new and experienced clinicians in ways that have not been possible for minimally invasive surgery. The availability of simulators may allow new clinicians to develop confidence and skills with surgical tools without the need for animal or cadaver studies, which would drastically impact ethical concerns and the cost of training. Clinicians can learn from mistakes and develop strategies and skills through repetition that are not possible with current training opportunities.

For minimally invasive cardiac procedures, we have demonstrated the ability to design and produce a cardiac simulator capable of simulating minimally invasive cardiac techniques. To further increase the realism and power of the simulation, there are several areas of future work that could improve the simulation or the time required to produce a patient-specific model.

The current manufacturing methodology for producing the patient-specific model using the tissue mimicking materials is labour and time intensive. There is great promise with 3D printing to quickly produce patient-specific models, with the state of the art being able to do so using flexible materials. To bring 3D printing to the development of these models, it will require new material science to develop a flexible and imaging compatible material that can be 3D printed or to develop a 3D printing system capable of 3D printing with the currently used materials, silicone, PVA-C, agar or ballistics gel. The ability to produce a new patient's model directly on a 3D printer would allow for the generation and adaptation of a patient's model to the current simulator within 48 hours of receiving the patient's scan.

Other future work includes the adaptation of the static cardiac model into a dynamic state. The current phantom is designed to allow for flow to be added to the system at key locations within the model to create realistic mitral and tricuspid valve motion. This is highly important as the valves within the system currently act as spatial identifiers for clinicians, and their motion allows them to be more easily located under ultrasound guidance, aiding clinicians in interpreting anatomical features within the heart. With the

current phantom design, the access ports allow for connection to a reciprocating pump that provides suction and outflow, such that when integrated with the phantom, should allow for valve motion within the patient's model.

Additionally, the simulator could be further enhanced with the use of tool tracking and augmented reality to provide clinicians with feedback regarding the tools locations within the phantom and/or the optimal tool path to follow. Augmented reality could be used as a training tool to help interpret the tools location, target, and the patient's anatomical features under image guidance. As the user's skills advance, these augmented aids could slowly be reduced, greatly lowering the barrier to entry for new clinicians and allowing the clinician to develop and work on specific skill sets. By integrating tool tracking, the clinician's tool path, puncture location or device placement could be evaluated against the ideal location, providing useful feedback to the user, allowing them to improve and learn from each training session.

Each area of future work is aimed at improving the user's experience when working with the simulator. Currently we have demonstrated that the phantom can be used as a training tool, however, there are many avenues to improve the phantom and develop systems that can improve the training experience. I hope that this thesis has laid the ground work for further developments in surgical simulation and patient-specific modelling, such that future research can build on this work and continue to develop tools and systems that will aid in clinical training, pre-procedure planning and system validation.

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- MEng in Biomedical, Faculty of Engineering,** 2017
Western University, London, Ontario
 Thesis: A Patient-Specific Cardiac Phantom for Training and Pre-Procedure Surgical Planning
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- BEng in Mechanical, Faculty of Engineering, With Professional Internship** 2010-2015
Western University, London, Ontario

HONORS AND AWARDS

- The Canadian Academy of Engineering Bruce Aubin SAE Aerospace Design Award** 2017
- Imaging Network Ontario Conference Poster Award:** 2017
3rd Place
- Dean's List** 2012-13, 2014-15
Western University, London, Ontario

RELATED WORK EXPERIENCE

- Graduate Research Assistant** 2015-2017
Robarts Research Institute, Western University, London Ontario
- Graduate Teaching Assistant: Mechanical Components Design** 2016-2017
Faculty of Mechanical and Mechatronics Engineering, Undergraduate
- Graduate Teaching Assistant: Properties of Materials** 2016
Faculty of Engineering, Undergraduate
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Faculty of Chemical and Biochemical Engineering, Undergraduate
- Hudson Boat Works: Mechanical Engineer** 2015
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- Trudell Medical International: Mechanical Engineering Intern** 2013-2014
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PUBLICATIONS

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SPIE Medical Imaging Conference - Oral Presentation	2017
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