# McGill University

**3D Printed Aortic Simulators with Tunable Stiffness to Achieve Physiological Fidelity**

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## Abbreviations

3D: 3 Dimension

AAA: Abdominal Aortic Aneurysm

ACC: American College of Cardiology

AHA: American Heart Association

ATAA: Ascending Thoracic Aortic Aneurysm

AVR: Aortic Valve Replacement

CABG: Coronary Artery Bypass Graft

CAD: Computer Aided Design

CM: Centimeter

CPB: Cardiopulmonary Bypass

CT: Computerized Tomography

CTS: Cardiothoracic Surgery

D: Diameter

FEVAR: Fenestrated Endovascular Aneurysm Repair

HF: High Fidelity

HLHS: Hypoplastic Left Heart Syndrome

IABP: Intra-Aortic Balloon Pump

ICU: Intensive Care Unit

IRAAD: International Registry of Acute Aortic Dissection

LF: Low Fidelity

MCS: Mock Circulatory System

MIMVS: Minimally Invasive Mitral Valve Surgery

MMPS: Matrix Metalloproteinases

MPa: Megapascal

MRI: Magnetic Resonance Imaging

O: Wall Stress

OR: Operation Room

OSCE: Objective Structured Clinical Examination

P: Pressure

PAR: Paravalvular Aortic Regurgitation

PLAAO: Percutaneous Left Apical Appendage Occlusion

PVA: Polyvinyl Alcohol

SMCs: Smooth Muscle Cells

SPE: Speckle Tracking Echocardiography

T: Wall Thickness

TAA: Thoracic Aortic Aneurysm

TAVR: Transcatheter Aortic Valve Replacement

TGPF930: TangoPlus FullCure 930

ToF: Tetralogy of Fallot

TTE SAX: Transthoracic Echocardiography Short Axis

USA: United States of America

USFDA: United States Food and Drug Administration

VATS: Video-Assisted Thoracoscopy Surgery

VSD: Ventricular Septal Defect

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I have no conflicts of interest or disclosure to declare.

## Abstract

In the cardiothoracic surgery field, surgeons require a highly technical skill set that is traditionally acquired through intensive clinical training. For several years now, surgical training has included some form of medical simulation that allows a trainee to repeatedly practice techniques in a controlled environment.

Current surgical simulators for cardiac surgery procedures are offered through idealized phantoms created from commercial tissue substitutes that are often basic tubular models and deficient in specific patient pathologies or from animals or human cadavers. The application of 3D printing technology is evolving in the medical field and can be leveraged to replicate patient-specific geometries with both normal and pathological tissue characteristics.

This thesis is aimed at the design and fabrication of 3D printed aortic models with anatomical and physiological fidelity. To demonstrate physiological fidelity, 3D printed multi-material ascending aortic simulators (2 geometric variants and 2 material variants) were created and evaluated for their capacity to replicate the distensibility of human tissue when perfused at physiological pressures. The aortic simulators were dynamic and echo-compatible with the ability to reproduce the distensibility of real aortas under physiological pressures. Using 3D printed composites offered the capability to tune the stiffness of the simulators which allowed a better representation of the stiffness variation seen in human tissue. This work demonstrates and validates a new generation of aortic simulators that have enhanced physiological fidelity and have the potential to be effective tools for surgical training.

## Résumé

Dans le domaine de la chirurgie cardiothoracique, les chirurgiens ont besoin d'un ensemble de compétences hautement techniques qui sont traditionnellement acquises grâce à une formation clinique intensive. Depuis plusieurs années, la formation chirurgicale comprend une forme de simulation médicale qui permet à un stagiaire de pratiquer à plusieurs reprises des techniques dans un environnement contrôlé.

Les simulateurs chirurgicaux actuels utilisés pour la réalisation de procédures chirurgicales sont généralement des simulateurs idéalisés créés à partir de substituts tissulaires commerciaux qui sont souvent des modèles tubulaires de base et déficients en pathologies spécifiques de patients ou d'animaux ou de cadavres humains. L'application de la technologie d'impression 3D évolue dans le domaine médical et peut être mise à profit pour reproduire des géométries spécifiques au patient avec des caractéristiques tissulaires normales et pathologiques. Cette thèse vise la conception et la fabrication de modèles aortiques imprimés en 3D avec une fidélité anatomique et physiologique. Pour démontrer la fidélité physiologique, des simulateurs aortiques ascendants multi-matériaux imprimés en 3D (2 variantes géométriques et 2 variantes de matériaux) ont été créés et évalués pour leur capacité à reproduire la distensibilité du tissu humain lorsqu'il est perfusé à des pressions physiologiques. Les simulateurs aortiques étaient dynamiques et compatibles avec l'écho avec la capacité de reproduire la distensibilité des vraies aortes sous des pressions physiologiques. L'utilisation de composites imprimés en 3D offrait la possibilité de régler la rigidité des simulateurs, ce qui a permis une meilleure représentation de la variation de rigidité observée dans les tissus humains. Ce travail démontre et valide une nouvelle génération de simulateurs aortiques qui ont amélioré la fidélité physiologique et ont le potentiel d'être des outils efficaces pour la formation chirurgicale.

## Contribution of Authors

**Ali Alakhtar:** designed the experiment, performed the experiment, analyzed the data and wrote the manuscript.

**Alexander Emmott:** performed the experiment, analyzed the data and edited the manuscript

**Cornelius Hart:** performed the experiment and performed 3D printing

**Rosaire Mongrain:** provided the infrastructure and reviewed the manuscript

**Richard Leask:** supervised the study, provided the infrastructure, designed the experiment, reviewed the data analysis and reviewed the manuscript

**Kevin Lachapelle:** supervised the study, provided the infrastructure, designed the experiment, reviewed the data analysis and reviewed the manuscript

# Chapter 1: Introduction

Cardiothoracic surgery demands a high-level of competency and delicate precision that is attained through intensive clinical training. To acquire and hone their skills, surgical trainees require an environment where skills can be practiced safely, repetitively and where they can be effectively assessed. Simulation is an established tool for learning, training and performance assessment [1, 2]. Medical simulation environments provide safe and controlled settings for repeated practice without harming patients and an area to develop and refine skills necessary in providing quality care to patient populations [3]. This is particularly true for surgical trainees when learning skills required for performing complex and intricate surgeries. Studies have shown that when trained in medical simulation environments, surgical trainees have improved knowledge, management skills and bolstered confidence [4].

In the speciality of Cardiac Surgery, much research is being focused on better understanding the pathophysiology of aneurysms which has revealed that the development of dilatation is often accompanied by structural and biomechanical changes in the aortic wall [5]. From the clinician's perspective, there is ongoing work being done on establishing best practices of prophylactic repair of the ascending aorta to avoid the dissection and/or rupture of an aortic aneurysm.

The use of various imaging techniques assists the clinician in determining size, structure and in producing a care plan to better manage the patient. The use of ultrasound is ideal for the use of screening and follow-up of aortic aneurysms but is not without limitations. Computerized Tomography (CT) scan imaging assists in accurately determining aneurysm size and defining the cranio-caudal extent of the aneurysm. Visualization of other anatomical structures is also beneficial with CT imaging. Magnetic Resonance Imaging (MRI) can help show contrast between flowing blood and other adjacent structures. By using multiple imaging techniques, clinicians can better prepare for surgical procedures [6].

The evolution of 3D printing allows for the creation of various patient-specific geometric models to be produced rapidly and with anatomical fidelity and mechanical properties that most accurately mimic human aortic tissue. While this is beneficial in creating simulation models for aortic aneurysm repair it is also essential that simulator materials remain true to human aortic structures and function, including the biomechanical properties of the aorta.

In responding to the learning needs of today's cardiac surgery trainees, it is imperative that research is done to improve upon current simulator models in both function and material composition. Utilizing 3D printing methods that allow for geometrically accurate models to be produced and using multi-material structures could assist with producing simulation models that replicate diseased aortas while achieving both physiological and tissue fidelity of human aortic tissue. Creating such a model could further enhance the learning of surgical trainees and benefit patients requiring such complex surgeries. Therefore, in this thesis, we created models of aortic aneurysm ("simulators") using 3D printing technology that were used to investigate how material and geometric properties of the simulators could be varied to achieve biomechanical and physiological fidelity when compared with human tissue.

## Chapter2: Hypothesis and Objectives

The central hypothesis of this thesis is that a 3D printed multi-material composite physical aortic simulator can provide physiological and biomechanical fidelity with human aortic tissue.

To test this hypothesis, the following objectives were defined:

**Objectives:**

1. Create 3D printed aortic simulators that contain appropriate dimensions and anatomical features of the ascending aorta with a concentric ascending aortic aneurysm.

2. Create a pulsatile flow loop and perfuse the aortic simulators to mimic physiological blood pressures within the human aorta.

3. Image the relative diameter changes of the simulators under physiological pressures using echocardiography to acquire stiffness measurements and compare the results with that of human aorta.

4. Measure the material properties (stiffness and energy loss) of the aortic simulators using biaxial tensile testing and compare the results with that of human aorta.

# Chapter 3: Background

## *Surgical Simulation*

### General Overview

Simulation is an education tool that offers an interactive platform for trainees to perform and learn in an environment that mimics a real-world clinical scenario. While having the opportunity to learn and train in an actual operating room with a real patient would be most beneficial to the learner, it is unrealistic to believe that the trainee would be able to safely and repeatedly hone required complex skills in this environment without causing undo harm to the patient. This is why the need for highly developed simulation environments is key for learning and training.

In healthcare, medical simulation has become an accepted and established tool used in developing medical trainee skills and competencies and boosting levels of confidence in students [4]. Simple-to-complex procedures and techniques are developed and practiced in a safe, realistic environment using methods and equipment that would be seen in real healthcare scenarios. Not only can skills be practiced and honed but medical simulation also allows for appropriate assessment of trainees along with testing of newly developed medical device prototypes to be used in new treatments and therapies.

### Why Simulation?

Ultimately, the goal of any organization is to have employees that are knowledgeable, well-trained and ready to provide service to their clientele. Conferences, e-learning modules and in-house training sessions all contribute to an employee's development and benefits the organizational outcomes. While these methods provide much needed theoretical knowledge, they lack in providing practical training. Knowing things are important but doing things are essential to many professions. In the healthcare profession, a surgeon is not a surgeon unless he or she operates. But knowing how to perform technical manoeuvres takes more than just learning from a textbook or in a classroom. It is important that the theoretical knowledge gets translated into practical work. But it is also important that the practical learning is done in a safe environment that is conducive to learning. Simulation-based training provides a surgical trainee with a learning experience that mimics real life situations and environments. Trainees can actively participate, learn new skills, practice already-acquired skills and receive constructive criticism and feedback all the while being of no risk to patients [7]. Decision-making skills and problem-solving techniques are also key benefits of simulation [7].

Simulation environments not only lend themselves to providing safe and controlled areas for trainees to learn and hone their technical skills, but they can also be used to develop communication and teamwork skills.

Surgery not only requires the surgeon to have flawless surgical techniques, but communication is of utmost importance to the whole multidisciplinary operating team. Behavioural practices and attitudes can be learned and modified during simulation situations and collaboration can be advanced among team members [7]. All these skills will effectively benefit patients especially during long and complex surgical cases.

## *Fidelity in Surgical Simulation*

### Definition of Fidelity

Although the definition of fidelity is undecided and despite the opposing concepts of Low-fidelity (LF) and High-fidelity (HF), it is not uncommon to see both used in medical simulation scenarios. According to Paige & Morin (2013), fidelity is defined by the degree to which a simulator is practical and true to reality [8]. In medical simulation, fidelity can be seen as the likeness and realistic comparability to the anatomy, physiology and behaviour of humans [9].

LF is seen when rudimentary tasks or scenarios are replicated but do not or cannot reproduce human elements like pain and mobility [10]. Cook *et al* (2011), noted that the use of simple models with LF are adequate when simple tasks and/or procedures are to be learned [11]. LF simulation is therefore seen when smaller, more specific tasks are required and is useful for repetitive practice by the trainee until the skill is fully grasped. Suturing techniques can be considered this type of task where LF is seen. A disadvantage of LF simulation models is the difficulty of the trainee to fully comprehend the concept or patient reaction when used in actual medical scenarios [12].

In contrast to LF, HF simulation more closely reproduces real-life scenarios including the mimicking of human reactions, environmental situations and disease processes that trainees can encounter in healthcare but can navigate through without any risk to real patients. Although HF simulation most accurately mimics real scenarios, the use of LF simulation is usually seen as the starting point for training with the progression to HF as the trainees' skills, knowledge and training requirements become more complex, a strategy known as "progressive fidelity" [13, 14].

Despite the lack of studies done to look at complex procedures such as cardiac surgery, it can be presumed that more complex scenarios would require higher fidelity simulation models.

Although it is logical that HF simulation would be more beneficial to more complex learning needs, Meurling *et al* (2014), noted no significant effect on basic technique learning or trainee performance anxiety levels in pediatric emergency care but that HF simulation did benefit in the reduction of performance interruptions and improved the timing between evaluation and treatment introduction [15]. Other studies and reviews show that the use of HF may be unnecessary especially when used by naïve trainees as no significant improvement to performance has been seen [16-19]. Maran & Glavin (2003), also suggested the use of HF necessity should be carefully examined especially when the cost risks outweigh the improvement benefits [20].

Determining the level of fidelity to be used in simulation remains a discussion within the medical community as higher fidelity is not certain to be more beneficial to improved learning. Factors like procedure types needed to be learned and simulation objectives may help determine the simulation fidelity level. It can be concluded that, when deciding between the use of LF and HF simulation, the type of skills to be learned, the learning level of the trainee and the time required to learn the skills should be considered [12]. The expenses versus performance benefit ratio should also be measured as LF simulation is generally less expensive and can be more cost effective in many situations when compared to HF.

### Dimensions of Fidelity

The type of simulator to be used can be dependent on several factors. These factors include emphasized topographies (auditory, functional and tactile), situational use and learner characteristics and needs [21]. Because of these factors it may be naïve to limit simulation characterization to just LF or HF. Hamstra *et al* (2014), identified two different fidelity concepts: functional fidelity and structural fidelity. Functional fidelity (what skills can be taught using the simulator) is crucial in surgical training as simulators replicate active and tissue processes of real patients and permit the repetitive training of basic skills. Structural fidelity (resemblance of simulator to humans) is not necessarily beneficial to trainees' learning as the physical resemblance of the simulator to humans has no direct correlation on educational success [21, 22].

In 2013, Paige and Morin, noted three components in simulation: physical, psychological and conceptual. The physical component includes the type of equipment used (mannequins) and the details of the surrounding environment (sounds, smells etc.). The psychological component denotes the emotional reaction to the activity while the recreation of medical scenario responses (critical thinking) comprises the conceptual component [8].

In comparison, Norman *et al* (2012), referred to psychological fidelity in terms of engineering fidelity [14]. An example of this could be the use of real but simple materials instead of using complicated but poorly executed computer-generated simulators. In this instance, psychological fidelity simulation favours simple materials as they would be more beneficial to trainee learning.

### Importance of Fidelity and Biomechanics in Surgical Simulation

With the shifting paradigm of surgical education and training from the operating rooms to simulation laboratories, the need to evolve the simulation models used by surgical residents is evident. Basic bench-top models assist in the development of skills for particular tasks, but more sophisticated models are required to permit surgical residents to develop and practice multiple techniques to respond to the real complex case scenarios being seen in today's healthcare environment.

3D printing models are being produced to represent real patient-specific disease processes with data derived from Ultrasound, CT Scan, and MRI imaging. These models can replicate the fidelity of the anatomy and structure based on these images [23]. The more closely the models replicate complex cases, the better surgical trainees can understand and be better prepared to deal with actual case scenarios [24].

The visual replication of 3D printed models is not enough to fully satisfy the learning needs of surgical residents. How the model feels to touch and how it can be manipulated is also of importance. Most models that use hard materials can respond to the anatomical fidelity required in advanced training, but material flexibility and elasticity can better address human pathological tissue characteristics. Manipulation and blending of composite materials to best mimic human tissue are necessary to satisfy learning needs. Trainees that are exposed to models that look and feel like human structures and matter will be able to develop skills required for performing surgical incisions, resections and hone simple and complex suturing techniques [25]. HF, patient-specific 3D printed simulation models have been found to help improve surgical trainees' knowledge, performance and skill development to improve surgical outcomes [26-28].

### *Past and Current Surgical Simulation*

As early as the 18th century, medical simulation has been used to train physicians and surgeons. An early example of this was an obstetrical mannequin, created by the Gregoires, known as "The Phantom,". Consisting of a human pelvis and dead baby, the use of "the Phantom" resulted in the reduction of maternal and infant deaths by enabling obstetrical trainees to learn and practice safe delivery techniques [6]. Other forms of simulation have also been documented. Data from the Middle Ages through to present times, shows the use of various animals in skills training [7]. Aviation Science originated the use of simulation to learn and hone practical skills and is the primary influence in the development of modern medical simulation [6, 7].

The support for medical simulation is growing. The American College of Surgeons as well as The Accreditation Council for Graduate Medical Education both strongly support the use of surgical simulation in surgical training. Furthermore, board certification for General Surgeons now mandates the use of the Fundamentals of Laparoscopic Surgery education module [29]. In cardiac surgery, the use of simulation may reduce the risks often associated with high-demanding and complex cardiac surgeries and may help in the establishment of standard and efficient cardiac surgical training.

### *Current State of Surgical Simulators*

Achieving surgical success requires knowledge and competent technical skills (surgical procedure) and non-technical skills (crisis management, interpersonal and team communication). Historically, surgical training has been attained through an apprenticeship approach with most skills learned in the operating room [30]. With the evolution of modern medicine and technology, surgical training is moving from an operating room (OR) theater setting to a simulation laboratory environment.

General simulation has been used in various industries since the mid 20th century. Medical simulation is more recently becoming a popular mode of medical training, replicating real case scenarios and environments, using low to high fidelity technology [30]. There are various models of simulation available for medical training. Bench-top models use deceased animal tissue or synthetic materials to develop surgical skills or for use in performance assessment. These models are used in a multitude of clinical specialties like General Surgery and Obstetrics and Gynecology with signs showing that bench-top model training promotes skill development [30]. Studies have shown that skill acquisition by medical trainees using bench-top models, irrespective of the level of fidelity used, is easily and successfully transferred to live procedures [31]. Due to the low cost of synthetic materials, bench-top models can be widely used throughout the world where funds are limited therefore are advantageous in medical training in disadvantaged countries. Proficiency achievement, improved efficacy in operating room training, safety and affordability are all advantages of the use of bench-top models in medical simulation training [30]. Despite the low cost and the ability of bench-top models to provide the medical trainee with the opportunity to repetitively fine-tune a specific task, there is a limitation of the true surgical experience when using this type of simulation [32]. Partial task simulation and performance-specific simulation have been used in the development of skills required in performing laparoscopic surgeries with variations in fidelity levels. The use of LF simulation in laparoscopic training allows the development of cutting, clipping and other fine skills [30]. Virtual reality training has demonstrated improved efficiency, time and accuracy in medical trainees with a decrease in errors [33, 34]. Despite eliminating the cost of human resources required when using LF simulation training in laparoscopic procedures, the initial and recurrent costs of virtual reality simulation can be disadvantageous for resource-restricted establishments [30].

Single-Incision Laparoscopic Surgery simulators and Natural Orifice Transluminal Endoscopy Surgery simulators have both been developed for surgery-specific training to develop skills and improve performance when performing such delicate and precise procedures [30]. Simulators replicating robotic surgeries have been developed to address the increasing use of robotic surgeries particularly in the speciality of Urology. Studies are showing that the use of these simulators have a positive influence on robotic surgery performance [35].

Competency among surgical trainees and established surgeons envelops more than just technical skill. Competencies like communication and professionalism are essential to performance and patient outcomes [36]. Standardized patients and standardized family members are being used for Objective Structured Clinical Examination (OSCE) simulation exercises that allow for medical trainees to develop and practice appropriate communication skills and behaviours and allow for constructive feedback. Residents can practice how to approach difficult conversations with patients and families and reflect on best approaches [37]. Team communication and coordination and crisis management are also skills that are used in Non-Surgical Skills simulation environments.

Team communication in the OR is essential to patient safety and these environments permit the development of communication skills that contribute to positive patient outcomes [30]. Such simulation environments are being used in areas like Emergency Departments and Intensive Care Units (ICU) as well as the OR to develop critical thinking and response skills. Despite the need for further studies to determine validity and reliability of such simulations, initial evidence shows improvement in non-surgical performance including communication, leadership and support [30].

### *Cardiothoracic Simulators*

The complexity and high risks in cardiothoracic surgery (CTS) require clinicians with extensive knowledge and fine-tuned skills. With the wide range of CTS techniques, the complexity of open surgery and the advancement in percutaneous and endovascular treatment of cardiovascular disease, the range of skills required of treating surgeons has increased. The use of medical simulation in this specialty may help in addressing these issues, by providing a learning environment where medical trainees and more experienced surgeons can learn and fine tune existing procedures and develop new techniques as technology evolves. Various educational institutions are developing simulation curricula to be included in their organization's medical training [32].

Numerous simulators have been developed in CTS to address training needs in areas of coronary artery bypass (CABG), cardiopulmonary bypass (CPB), aortic surgery, valve surgery, video-assisted thoracoscopic surgery (VATS) resection, bronchoscopy, esophageal procedures and endovascular surgery as well as other cardiac and thoracic procedures [32]. In the following paragraphs, state-of-the-art cardiothoracic simulation will be reviewed.

## Non-3D Printed Simulators

A human performance simulator known as the Ramphal Cardiac Surgery Simulator is primarily used in simulator training for CABG surgery [38]. Its balloon-filled porcine heart is connected to a pneumatic pump (computer-controlled) and permits the ventricles' inflation to mimic that of a beating heart. A life-sized mannequin's anterior chest wall is used as a reservoir for the simulator placement with artificial blood flowing through the system. As a source for HF tissue interaction, this simulator provides opportunity for surgical residents to learn and develop technical and cognitive skills required to perform such types of surgery. It may assist in decreasing costs for smaller centers since residents can receive exposure and training without having to travel to larger centers [38]. The Chamberlain Beating Heart Model provides the learner with a HF simple bench model simulator with its realistic anatomical structure and various speed and rhythmic contractibility [32]. Simple bench models like the Anastomosis Task Station, The Beating Heart Model and the Porcine Heart Model demonstrated improvement in resident skills to perform surgical anastomoses and elevated trainees' confidence levels [39, 40].

The Orpheus Cardiopulmonary Bypass Simulation System and the Turkman simulator are human performance simulators that are used in training OR teams of surgeons, anesthesiologists, nurses and perfusionists in CPB procedures. Hemodynamic and patient parameters can be displayed to familiarize the team with patient reactions as the simulations can be based on real patient cases [11]. Improved knowledge and confidence levels have been demonstrated in this form of simulation and is a preferred method of learning among surgical trainees [41]. The Hicks Perfused Non-Beating Heart Model provides a simple bench model simulator consisting of a porcine heart and thoracic aorta placed in a container and draped to mimic a thoracic cavity. Blood circulation and leakage are mimicked by a pressurized flow of saline. A fairly inexpensive type of model, the

Non-Beating Heart Model provides junior residents with a platform to practice skills like aortic cannulation and to understand CPB principles [42].

Yanagawa *et al* (2019), reviewed cardiac training simulation experiences using a variety of CABG simulators including bench-top and HF models. They found that trainees' efficiency at performing coronary anastomoses improved by 20% when using portable and beating-heart models with similar outcomes when staff surgeons coached trainees using task simulators and porcine heart simulators. When using CPB simulators, trainees' knowledge increased and perceived confidence levels improved when initiating CPB. They concluded that, despite the challenges associated with high costs of some simulators and simulation centers, as well as securing dedicated time for learners to train, cardiac training simulation has an overall positive impact on improving trainees' skills, knowledge and confidence which could then have a positive impact on patient outcomes [43].

Various simulators have been developed to address training needs of various cardiac trainee skills. Two simple bench models, The Chamberlain Group's Mitral Valve Model and another developed by Tavlasoglu and colleagues, provide surgical residents with the opportunity to improve technical skills and performance when doing valve repair and replacement surgeries (The Chamberlain Group) [44, 45]. The Nakao Cardiac Model, used in practicing surgical palpation, is a virtual reality simulator model providing 3D visualization of a beating heart to be used interactively by trainees [46]. Virtual Reality Lobectomy Simulator, developed by Solomon and colleagues, is an interactive simulator for right upper lobectomy training. With both an external and internal view of an OR-positioned patient and the lung field, the surgical resident is able to practice lung dissection, division and tissue ligation and experience the physical constraints of a small operating field. The simulator is capable of generating questions for the user regarding anatomy and physiology and can track surgical performance and errors [32].

A human performance simulator, the Fukuoka University VATS simulator is a simulator with three disposable components connected to a pump. The advantages of this simulator include the ability to videotape the training procedures and then evaluate the user with a checklist method of evaluation [47].

Less expensive simple bench-top simulators have also been produced for VATS training using porcine lungs. The models are developed with holes allowing the trainees to feel and manipulate surgical equipment used during VATS surgery [32]. Advantages with these simulators is the relative low cost, resident exposure to thoracic surgery and accuracy to clinical scenarios [48, 49].

Simple bench model simulators are available for open lobectomy simulation. A simulator model for surgical trainees to practice thoracic surgical skills, namely suturing, knot tying and resecting, Carter and colleagues created a mock chest model with a thoracotomy incision and surrounding a deflated-appearing bovine lung [50]. Tesche and colleagues developed a model of a mock hemithorax with a heart and lung and artificially perfused pulmonary vessels allowing for vessel isolation, resection, ligation and suture and stapling [32].

### Imaging Simulators

Medical simulators focusing on cardiac imaging have been developed to assist in the evaluation of various imaging technologies. Although these simulators can be quite detailed and intricate, their overall use is for non-invasive exercises and not for surgical intervention training. These simulators include human-like chests with replicated heart and aortic aneurysm and can be used in assisting medical trainees in acquiring skills related to transthoracic echocardiography ultrasound imaging [51].

Tavkoli *et al* (2012), described a model used for ultrasound and cardiac magnetic resonance evaluation, consisting of an asymmetric left ventricular motion model capable of reproducing various cardiac pathologies [52]. This phantom is made of polyvinyl alcohol (PVA) and has latex balloons inserted for the heart's dilatations and contractions using air. The same material was used to develop a model of an atherosclerotic coronary artery composed of two layers in which lipid pool was added to evaluate intravascular imaging and mechanical testing [53].

A model with a structurally accurate beating heart, heart chambers and coronary arteries has been developed to evaluate cardiac x-ray and computed tomography (Boltz *et al*, 2010) [54]. A silicone left ventricular model with a water-filled semi-ellipsoidal shape that allows for specific surface pressures to be applied, to assess the effect of motion in cardiac positron emission tomography and single photon emission computed tomography studies [55].

### Medical Device Simulators

There are also models used to test various medical devices. Biglino *et al* (2013), tested the distensibility of TangoPlus FullCure 930 material to assess its use in creating cardiovascular models. Cardiovascular magnetic resonance (CMR) images were used to create 3D models of a patient-specific descending aorta. With varying degrees of wall thickness, several models were printed and tested for compliancy with pressure variations monitored as internal volumes were increased and decreased. Determining distensibility, a design of a hypolastic aorta appropriate in connecting to a mock circulatory loop was created. By comparing distensibility values of the model to the data found in the literature, they determined that the TangoPlus material was suitable in successfully creating a model for such purpose. They also found the cost effectiveness of the material to be of benefit [56].

Testing its suitability for use in endovascular procedure simulation and stent design, Sulaiman *et al* (2008), created a life-sized in vitro aortic arch aneurysm model made of soft and transparent silicone rubber which included the aortic arch and supra-aortic arteries. The patient-specific model was derived using 3D magnetic resonance angiography images. The model was connected to an extracorporeal circulation pump and perfused. They concluded that their realistic 3D model was indeed suited for both procedure simulation and stent design [27].

Kolyva *et al* (2012), designed a polyurethane mock circulatory system (MCS), composed of a left ventricle connected to straightened aorta with fourteen branches for the various peripheral organs, to assess intra-aortic balloon pump (IABP) technology. The model was created with accurate arterial anatomy and peripheral resistance/compliance physiological distribution. They concluded that flow distribution and hemodynamic waveform's mean and phasic characteristics were normal functioning when the MCS assessed IABP technology. With minor modifications to the MCS, they believe the system will be capable of assessing other medical equipment and can be used in further hemodynamic studies [57].

### 3D Printed Aortic Simulators

Cardiac surgical procedures involving aortic structures are complex in nature. Surgeons require extensive knowledge and training to perform such delicate operations. 3D printed aortic models, closely resembling anatomical and physiological features, afford clinicians the opportunity to simulate these intricate surgeries.

Looking at producing and validating realistic training models that could be used in the simulation of complex aortic cases and in the training of novice surgeons, Russo *et al* (2020), produced six 3D printed models made of silicone material and derived from CT images. They required the models to be easy in design and use and to accurately replicate the angles and positioning of human aortic structures and resemble human tissue in both mechanics and tactility. The models each included anatomical structures including aortic valve leaflets, aortic root with coronary ostia, ascending aorta and proximal aortic arch. Six cardiac surgeons with varying degrees of experience were asked to perform an aortic valve replacement on their models. All participants were surveyed and responded to questions regarding the model's usefulness in cardiac surgery simulation training, the accurate replication of aortic structures and mechanics and the ease in which the model could be used. All participants scored the model positively in each section and all agreed that they would use this model in future training simulation exercises. From these results, the authors determined that their 3D printed model represented a useful and easy tool to be used in the development and training of novice and experienced cardiac surgeons [56].

To help improve surgical planning and training for aortic endovascular and transcatheter aortic valve surgeries, Gomes *et al* (2018), looked at creating 3D printed models representing different aortic diseases. Using CT angiography images, they created six patient-specific, built-to-scale models using 3D printing technology. Under fluoroscopy in a hybrid OR that allowed imaging to be done that clearly defined the detailed aortic walls, endovascular simulation was done. They concluded that realistic models replicating various aortic diseases, could be successfully created using 3D printing technology. They determined that preoperative surgical planning and clinician training could be improved by using 3D printed models derived from 2D CT angiography images [57].

Patient-specific 3D aortic arch models and patches were created by Chen *et al* (2018), to be used in surgical simulation and medical training for aortic arch repair in patients with hypoplastic left heart syndrome (HLHS). Aortic arch models derived from preoperative CT images were created using 3D printing technology and postoperative models were designed using images from CT angiography with contrast. The postoperative models were manipulated and "undone" to allow for the creation of customized, digitally designed printable patches. Surgeons were then given the models to manipulate and operate on to assess their usefulness in surgical simulation. They concluded that 3D printed models are a viable choice for surgically simulating aortic arch repairs in patients with HLHS and have the potential to assist clinicians in training and honing skills required for such complex cardiac surgeries [58].

Hossien *et al* (2016), looked at three patients, each presenting with various aortic tears situated in one or more areas of the aorta. Their intent was to create patient-specific virtual digital and physical models (derived from patients' CT images) of the Type A aortic dissections using 3D printing technology and determine if the use of this technology would benefit in determining patient-specific surgical plans for aortic aneurysm repairs. The 3D models facilitated the identification and visualization of the patient's anatomies and precise location and situation of each patient's aortic tear. Not only did they suggest these models were beneficial in surgical intervention planning, but that the use of 3D printed models could improve efficiency and safety in such critical and complex surgeries. They also suggested that the use of these models in simulation environments could help novice and experienced surgeons hone their surgical skills. By further developing and printing models in materials more resembling that of human aortic tissue, they proposed that such models could assist learners in better understanding aortic anatomies and pathologies. Moreover, these models could also be used in facilitating patients' understanding of their disease and intervention options [59].

### 3D Printed Heart Simulators

Three-dimensional simulators can assist clinicians in understanding various challenges seen in ailing hearts. To help improve the learners' understanding of congenital heart defects, White *et al* (2018), suggested 3D printed models be used during didactic training sessions involving pediatric and emergency room residents. To test their theory, they divided the residents into two groups (intervention and control) in a perspective, randomized teaching intervention while the residents learned about 2 congenital heart defects: a) ventricular septal defect (VSD) and b) tetralogy of Fallot (ToF). VSD was considered to be a simple defect while ToF was considered moderately complex. The residents' level of comfort with the anatomy, evaluation and treatment of both defects was determined by using a subjective survey followed by an objective test. Both groups received the same lecture, over the same amount of time which included the use of 2D images of VSD and ToF. The interventional group was also given 3D models of each defect derived from the 2D images used in the lecture. Post-lecture, the groups repeated the survey and test. Post-lecture survey scores showed that all participating residents were subjectively more comfortable with VSD and ToF after receiving the lecture with no difference showing in their baseline scores. The post-lecture test showed the control group scoring higher with VSD while the interventional group scored higher with ToF. The authors concluded that the inclusion of 3D models in congenital heart defect teaching improved both subjective and objective understanding in pediatric and emergency room residents. Although no benefit was seen with a simple defect like VSD, there was in the more intricate defect seen in ToF. This may be explained by lesion complexity and difficulty in spatial relationship visualization. They also feel that further investigation is required to better determine the benefit of the use of 3D printed models in congenital heart defect teaching [60].

At the 2015 Annual Meeting of the American Association for Thoracic Surgery and afterwards at the Congenital Heart Disease Center Symposium in Seoul, Korea and at the Hospital for Sick Children in Toronto, Ontario, Yoo *et al* (2017), used 3D printed heart models for a hands-on training course. Their intent was to introduce 3D cardiac models for surgical simulation and obtain feedback from participants. Using flexible and pliable material, 3D printed models of congenital heart disease, derived from CT and MR angiograms, were created. Eighty-one expert surgeons or trainees (with guidance from experienced surgeons) used the models to perform various simulated surgical procedures with 50 participants responding to the program assessment questionnaire. Although most found the texture and flexibility of the model different than that of human myocardial tissue, all found the quality of the models acceptable or feasible for surgical simulation. All 50 respondents agreed that hands-on training helped in improving their surgical skills and that the 3D models acceptably indicated pathological findings. The authors concluded that 3D printed cardiac models are useful in hands-on training and surgical simulation for congenital heart surgery but further testing of models, using different materials and with improved definition of the cardiac valves, is needed [61].

To assess the effectiveness of 3D printed models in medical education, Lim *et al* (2016), conducted a double-blinded, randomized controlled trial of medical students, all of whom had no prior formal cardiac surgery training. Each participant was given a pre-test to evaluate their cardiac anatomy knowledge and determine a baseline. Pre-test scores were deemed to be not significant with a P-value equaling 0.231. Participants were then randomly divided into 3 groups and participated in self-learning sessions using one of the following: a) cadaver materials; b) 3D prints or c) a combination of both materials. Afterwards, the 52 participants were given a third-party post-test with the 3D print group scoring significantly higher than the other 2 groups (P=0.010; adjusted P=0.012). The authors found this trial suggestive of the benefits of 3D prints in anatomy learning and supportive of their use adjunctive to cadaver-based learning [62].

### 3D Printed Valve Simulators

In the era of minimally invasive cardiac surgery, the use of 3D printed models can help in training and simulation of these operations. Yamada *et al* (2017), developed a 3D printed model specifically for use in mitral valve repair training. The model was created from patient CT images replicating the heart and thoracic cavity, using materials that provided textures and properties seen in porcine hearts. The replication of the model's shape to that of a human heart was confirmed by CT imaging with the model parameters being set to provide bio-texture and tactility of a patient heart. Acknowledging the need for further research and development, they believe that 3D printed models will be revolutionary in other cardiac surgeries and procedures including aortic and tricuspid valve repair. They also believe that such models will benefit in the training of both medical novices and experienced clinicians and could also help in the disease and treatment education of patients and their families [63].

Scanlon *et al* (2018), suggested that transforming congenitally incorrect pediatric heart valves, as viewed on 3D cardiac ultrasound images, into 3D printed models could facilitate the development for surgical valve repair simulation. In doing so, pediatric medical trainees could safely hone their skills that are required for performing successful surgeries in challenging pediatric cardiac patients. They developed several 3D printed models of heart valves from 3D echocardiographic images and compared them to directly printed valves. The molded models were made of soft materials, molded into 3D printed silicone molds and were then evaluated by trained congenital surgeons. The surgeons were asked to perform tricuspid valve annuloplasty on the models and complete a survey comparison, to determine their appropriateness for simulation. The results showed, that for simulation purposes, the molded valve models were more realistic when performing surgical cutting and suturing ($p<0.01$) and annuloplasty suture tightening was more successful ($p<0.01$) when compared to directly printed valves. They concluded that 3D printed molds are beneficial in medical training and obtaining realistic simulation for complex pediatric cardiac valve surgeries [64].

A HF minimally invasive mitral valve surgery (MIMVS) simulator was developed by Nia *et al* (2019), for use in the training of complex heart valve surgeries, including endoscopic and robotic approaches. Experienced mitral valve surgeons were interviewed, and using their requirements, a simulator design was created. The design included a thoracic torso with a disposable mitral valve apparatus, endoscopic and robotic access and a feed-back system. Suturing depths and widths, when using the simulator, were measured and then compared to 3D CT scan images of the same sutures. They found no statistical difference of suture depth ($p=.139$) or width ($p=.865$). They concluded that this simulator could benefit cardiac surgery learners in developing skills required for MIMVS and providing feedback on suture placement and suturing techniques [65].

### *Other Uses of 3D Printing Technology in Cardiothoracic Surgery*

In this section, the general use of 3D printing in cardiac surgery will be reviewed. It will focus on 3D printing technology and its other uses in cardiothoracic surgery.

3D printing is being used in various aspects of cardiac surgery. Experiencing a rapid growth, the use of 3D printing technology is being used for complex surgical planning, research, medical training and patient and family education [66]. Wang *et al* (2020), conducted a systematic review of 43 articles found in PubMed and MEDLINE databases outlining the current uses of 3D printing technology in surgical and catheter-based interventions for adult cardiovascular diseases. They noted that CT and echocardiography images were used most often to produce 3D printed models and that this technology was used most often in patients requiring percutaneous left apical appendage occlusion (PLAAO) at 50.3% followed by those requiring transcatheter aortic valve replacement (TAVR) at 17.6%. One hundred percent of the articles selected and reviewed showed that the use of 3D printing to produce models, benefitted clinicians in decision-making and surgical or interventional planning, intraoperative orientation and medical teaching and training in adult cardiovascular surgeries [67].

The accuracy of 3D printing technology of CT images of aortic aneurysm and aortic dissection anatomies has been studied by Ho *et al* (2017). The models of both aortic aneurysm and aortic dissection, made with rigid and flexible materials, were produced and measurements were done and compared to those of the original CT images, the stereolithographic-formatted computerized model and then contrast-injected CT images of the 3D model. Despite positive results in reproducing the aortic dissection intimal flap, measurements of the aortic diameter were determined outside of standard deviation of 1mm, therefore suggesting further studies needing to be done, in part due to the study's small sample size, before confidence in 3D printing models could be achieved [68].

Three-dimensional printed patient-specific aortic root models, obtained from CT images, were created by Ripley *et al* (2016), to plan complex TAVR surgeries and determine if the models could be used to accurately predict paravalvular aortic regurgitation (PAR). They studied 16 patients and 3D printed models were created using pre-TAVR CT images. Printed valves were then inserted into the aortic root models and then using a light transmission set, they predicted post-implant

PAR. The study showed that the 3D printed models were very accurate in predicting post-implant PAR when compared to results obtained using 2D imaging [69].

Similarly, Qian *et al* (2017), used 3D printing to demonstrate the usefulness of printed simulators to accurately assess and predict paravalvular leaks post-TAVR in 18 patients. By creating patient-specific aortic root models, using tissue-imitating 3D printing technique of CT scans taken of patients pre-TAVR, they were able to insert a valve prosthesis into the model (imitating the TAVR procedure) and then measure the aortic root strain *in vitro*. They found the results from the 3D printed model to be comparable to those found in the patients post-TAVR [70].

With an aging population who have previously undergone CABG and then subsequently requiring aortic valve replacement (AVR), the risk of repeat sternotomies is high and complex. Soudian *et al* (2008), determined that using a patient-specific 3D printed model of the cardiovascular anatomy, derived from CT angiography, could be helpful in both surgical interventional planning and intraoperative orientation for patients requiring valve surgery after previously undergoing CABG. In their created model of an 81-year old woman's cardiovascular anatomy who required AVR for severe aortic stenosis and who had previously undergone CABG, the grafts and the anatomic relationships could be clearly visualized, allowing them to accurately plan the complex surgery. They subsequently used the model in the OR to help them correctly reopen the sternum without causing damage to the previous surgical grafts and other cardiac anatomy. They concluded that creating a 3D printed model is an effective method for planning AVR surgeries in patients who have previously undergone CABG [71].

In 2015, Schmauss *et al* concluded that creating 3D printed models is very useful for the planning of complex cardiac surgeries and interventional cardiology procedures in both pediatric and adult populations. They also concluded that these models are effective simulation instruments to be used by medical trainees to hone skills required for complex cardiac interventions. Between 2006 and 2013, they created 3D printed models of 8 patients (both pediatric and adult populations) identified with complex anatomies and requiring surgery or intervention. The models were made using patients' preoperative CT or MRI images. They concluded that in both the pediatric and adult populations, the creation and use of 3D printed models were beneficial to surgical/interventional planning and orientation. These benefits included the illustration and understanding of congenital heart disease anatomy, aortic pathologies and cardiovascular anatomies, in decision-making and intraoperative orientation as well as in appropriate patient selection for certain interventions and surgeries. They also believed that 3D printed models have a place in medical training and patient education [72].

In response to the United States Food and Drug Administration's (USFDA) limitation on the number of fenestrations (3) available in patient-specific, custom-made, commercially available grafts, Bortman *et al* (2018), created CT-derived, patient-specific 3D printed aneurysm models, to assist in the development of preoperative planning for fenestrated endovascular aneurysm repair (FEVAR). With most surgeons using 4 visceral vessels when performing FEVAR, most custom grafts were created manually by the surgeon but often resulted in anatomic mismatches, aneurysm rupture due to endoleaks and death. Over time, with continued methodology refinement and vascular surgeons' input, the authors were able to demonstrate that, by using 3D printing technology, accurate patient-specific models could be created of abdominal aortic aneurysms thus assisting surgeons in planning for this complex surgery [73].

As seen in the systematic review done by Wang *et al* (2020) [67] and with the support of added research, we have seen that 3D printing has a place in the speciality of cardiothoracic surgery. It has proven useful in surgical planning, intraoperative orientation and medical training and we believe that there are more avenues to explore in 3D printing technology and its multipurpose uses in this field. While 3D printing has proven to be beneficial in cardiothoracic surgery and intervention, further innovative development and testing are required and could change the landscape of cardiothoracic surgery as we now know it [74]. It is for these reasons that we embarked on our project of creating 3D printed aortic models more resembling the structure and tissue component of the human aorta to be used in cardiothoracic surgery simulation environments. We are hoping that our innovative contribution can enhance cardiothoracic surgery training for novice and experienced clinicians and therefore benefitting patient outcomes.

### *Limitation of Current Cardiothoracic Simulation*

Initially, most cardiothoracic simulation models used for surgical training were made of rigid materials with straight tubes used to represent blood vessels. These factors contributed to the limitation in available geometries and the realism desired for a true learning experience. In our search, a limited variety of materials have been mechanically tested to compare with both the normal and aneurysmal tissue seen in human thoracic aortas. With the advancement of 3D printing technology, more flexible and pliable materials require testing to improve the fidelity of 3D printed models with human anatomy and tissue.

Historically, to compensate for the limited availability of simulation models and human cadavers, simulation centers frequently used porcine aortas for training purposes. While more readily available, studies showed that animal aortic tissue was significantly softer than that found in humans ($p < 0.001$) thus lacking representation [75]. A histological study has shown that porcine aortic tissue, when compared to that of humans, has more elastin and less collagen content and may explain the variance between the two tissue types.

Pazos, Mongrain & Tardif (2009), noted that PVA is capable of simulating soft tissues but thermal cycling is required to achieve acceptable crosslinking. Although hyper-elastic isotropic materials like PVA and silicone are seen in simulation models, neither material is a true representation of human aortas. Surgical residents would benefit from simulation models offering various geometries and pathologies that are more representative of human aortic tissue and structure to optimize their training experience. Further development in producing synthetic material models that offer more anatomically correct structures with patient-specific pathologies capable of imitating both healthy and diseased in vivo tissue biomechanics, would improve trainee training and comprehension of the anatomy of the human aorta.

Lastly, the use of 3D printing is a viable option for simulator development as 3D structures of various shapes can be produced using both soft and hard materials. Consequently, the creation of aortic simulation models replicating various tissue characteristics and patient-specific geometries would benefit from the use of 3D printing technology.

### *Aortic Biomechanics*

A 3D printed model should achieve both anatomical and physiological fidelity for optimal use in medical simulation. Unfortunately, much of the materials being used to produce 3D printing models for this purpose, are relatively hard and non-physiological in nature. Ideally, these models would allow learners to see and feel the anatomical structures and the quality of the tissue in both healthy and diseased states. In the following sections, we will study aortic biomechanics to help identify engineering features of the aorta which could be used to construct 3D printed facsimiles with anatomical and tissue fidelity.

The aorta is the largest and main artery in the human body and has 2 major segments: 1) the thoracic stem and 2) the abdominal stem. The aorta originates from the heart's left ventricle and extends upward (aortic root to ascending aorta), arches upward (aortic arch), and then descends into the chest (thoracic aorta), and then continues into the abdomen (abdominal aorta). At this point the aorta then bifurcates to supply the pelvic organs and lower limbs. The primary function of the aorta is to act as an oxygen-rich blood carrier supplying all human body organs.

The ascending aorta is an elastic artery and its wall composed of three layers: the intima (innermost layer), lined by endothelial cells, media and adventitia (outermost layer). The adventitia composes of collagen and elastic fibers, mast cells, and fibroblasts. It also has the vasa vasorum, small arteries that provide the blood to the aortic wall. The elastic medial layer plays a predominant role in mechanical properties of the ascending aorta, contributing in almost 80% of the thickness of normal ascending aorta. It consists of alternating layers of elastic fibers sheets, smooth muscle cells and lamellae (Figure 1). The Collagens (type I, II, IV and V), fibrillar matrix proteins and mucopolysaccharides are interspersed with the elastic sheets. The tensile tissue strength and passive elastic behaviour of the aorta is largely defined by elastic lamellae and collagen fibrils [76-79].

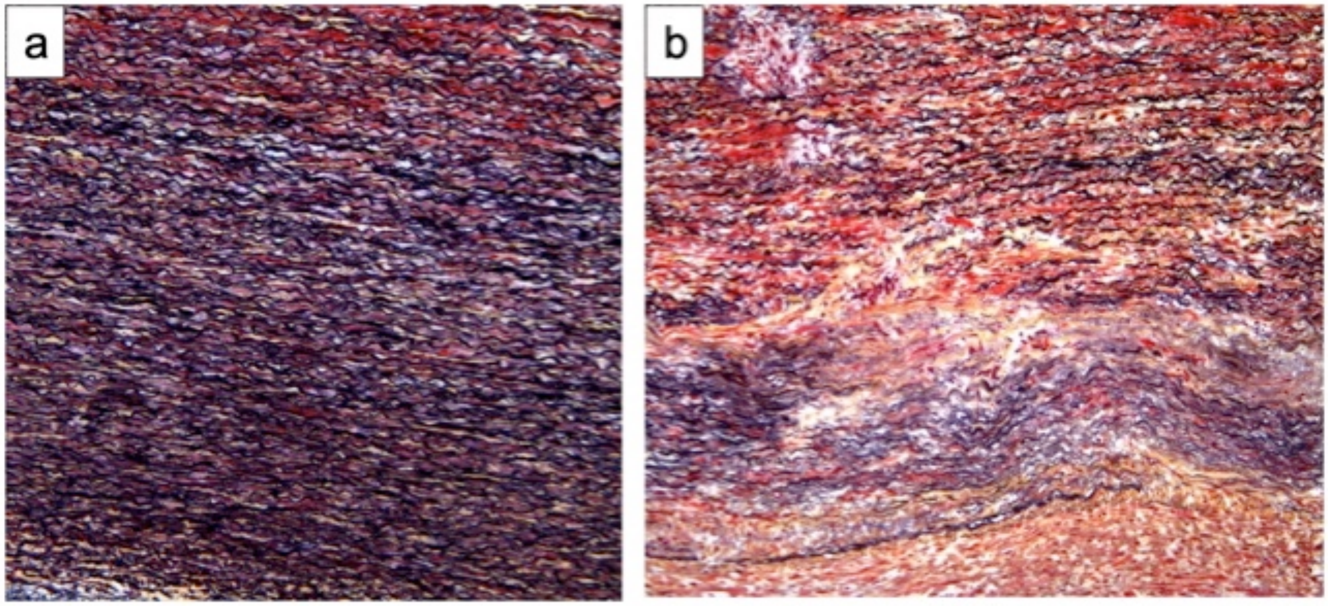


*Figure 1. Histopathology of the ascending aorta using Movat pentachrome staining, a) relatively healthy non-dilated ascending aorta and b) a 5.8-cm dilated ascending thoracic aortic aneurysm with medial degeneration and elastin fragmentation. Black indicates elastin; red/purple, smooth muscle cells; blue, mucopolysaccharides; and yellow, collagens*

The heart's pumping ability, regulated by peripheral resistances, generates arterial blood pressure. The mechanical variables that affect the arterial wall hemodynamic load include kinetic energy (blood velocity), pulsatility (heart frequency) and blood pressure. The largest artery in the human body, the aorta has a diameter measurement of ~3cm in the ascending aorta (origin), ~2.5cm in the descending segment (thoracic aorta) with the abdominal aortic component measuring at 1.8-2cm in diameter.

Blood flows into the aorta as the aortic valve opens (cardiac systole) and is then circulated to the peripheral organs. As a secondary function, the aorta acts as a buffer through its visco-elastic properties (compliance). The aorta's capability to expand at each systole allows blood stroke volume with this elastic energy being used during diastole (recoiling of aortic tube) then flows to the periphery. This behaviour is known as the Windkessel Effect.

Stress, defined as force per area, is caused by mechanical loads on cardiovascular tissue. The predominant source of tissue stress in the aorta arises because of blood pressure, causing circumferential tension in the wall as described by Laplace's Law for a pressures cylinder:

$\sigma = PxD/(2xt)$, where $\sigma$ is the wall (or "hoop") stress, D is the diameter, and T is the wall thickness. Since the aorta is elastic, the cardiac blood pressure waveform therefore generates periodic stresses in the aorta that lead to a constantly changing diameter as the aorta distends and recoils. This distension under mechanical stress is best defined by the *stiffness* of the aorta. In particular, the stiffness is the tissue's ability to resist strain (or, in other words, change in diameter) as the wall stress increases.

Aortic aneurysms and aortic stenosis may be caused by either the basic tendency for the aortic wall to expand in response to normal biomechanics as seen in Marfan syndrome or bicuspid valve, or in response to arterial segment pathological biomechanics [80].

### *Pathophysiology of Aortic Aneurysms*

Non-atherosclerotic aortic disease is often associated with disease located proximal to the ligamentum arteriosum contrary to atherosclerosis which is linked to disease found distally to the ligamentum arteriosum [81]. These differences could be explained by embryonic origins of the smooth muscle cells (SMCs) of both ascending aorta and descending aorta, which have the effect in formation of the aneurysm through their release of many proteolytic factors. The neural crest cells are the embryonic origin of ascending aorta and great vessels SMCs, whereas the paraxial mesoderm gives raise for the descending aorta [82, 83]. The lateral plate mesoderm gives raise for the aortic valve [82]. It is highly suggestive that abnormal aortic tissue extending into the distal arch or the proximal descending aorta is closely associated with aortic valve abnormalities like bicuspid aortic valve [84].

Degenerating alterations in vascular wall biology leading to the loss of structural integrity and aortic wall strength are present in most thoracic aortic aneurysms (TAA) [85-87]. Although the underlying triggers found in degenerative TAAs are not well known, similar processes are found to be responsible for degenerative abdominal aortic aneurysms (AAA).

The mechanical factors and protein degradation together are thought to be reason for medial degradation, which will have the appearance of elastic fiber degeneration and SMC necrosis associated with mucoid material filling the cystic spaces [88]. Media cystic degeneration of the aorta is associated with aging process but accelerated by hypertension and other factors.

Various matrix metalloproteinases such as elastase, collagenase, various metalloproteinases (MMPs) and plasmin play a key role in the breakdown of extracellular matrix proteins (elastin and collagen) as emphasized by many theories when discussing this process [89-92]. The proteolytic factors are released from smooth muscle cells and endothelial cells as well as the inflammatory cells that are infiltrating the media and adventitia [92].

Similar pathogenic pathways are shared by familial TAAs, TAAs associated with genetic syndromes and degenerative aneurysms although some unique differences are noted in relation to known genetic defects [93, 94]. For example, Mutation in the Fibrillin-1 gene is associated with Marfan syndrome which is mostly located at aortic root and may involve the ascending aorta as well. A high risk of aortic complications in relatively young patients and accelerated expansion are associated with these aneurysms compared to degenerative aneurysms [95-97].

Most patients presenting with thoracic aortic dissection present with thoracic aortic diameters between 4.0cm and 5.5cm which is considered low risk for rupture as the risk of dissection/rupture increases with aortic diameter. In a review of the International Registry of Acute Aortic Dissection (IRAAD), 591 patients presenting with Type A dissection had a mean aortic diameter of 5.3cm. Sixty percent of these patients had aortic diameters of <5.5cm and 40% measured at <5.0cm [98].

The growth of TAA is naturally slow in progression. Historically, an increase in diameter from 0.1cm to 1.0cm per year is seen but is dependent upon factors including TAA etiology, diameter and where it is situated within the aorta. Potentially adding a crucial dimension in the surgical management of patients, a novel assessment technique was presented in a previously published article by our group.

### *Ex Vivo Tensile Mechanics*

The "gold standard" for characterising the biomechanics of human tissues is *ex vivo* tensile testing. This methodology uses testing segments that have a defined geometry and stretches them while precisely measuring the forces generated in the specimens as they deform. With respect to the aorta, the most common form of *ex vivo* mechanical characterisation is through biaxial tensile testing. In this setup, a segment of the aorta is connected to a tester and cyclically stretched in its principle axes (circumferential and longitudinal) while measuring the forces generated in both axes. In doing so, one can generate a characteristic stress-strain curve (Figure 2) which, for the aorta, is both hyperplastic (stresses increase non-linearly with strain) and viscoelastic. Viscoelasticity leads to differences in stress depending on whether the tissue is being stretched or relaxed. Two common parameters are calculated from the stress-strain relation. The first, *stiffness*, is defined as the slope of a tangent line to the curve and is formally called the "apparent modulus of elasticity." To compare stiffness values between different specimens, the stiffness is measured at a consistent level of strain (e.g., 40% strain). The second, termed *energy loss*, is a measure of the tissue's viscoelasticity and describes the amount of elastic energy the is unrecovered after stretching. It is calculated as the area between the loading and unloading curve divided by the area under the loading curve.

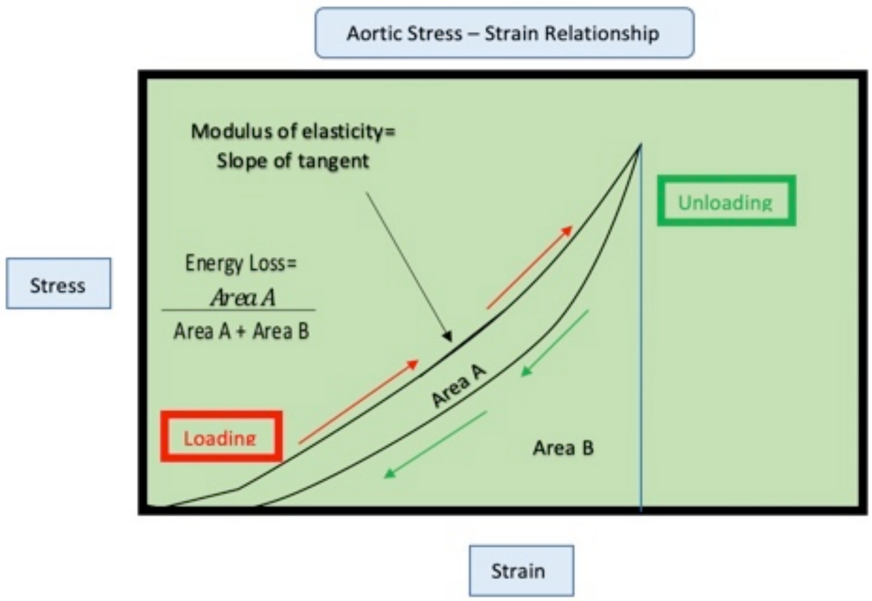


*Figure 2. The stress-strain relationship of the ascending aorta and definitions of 2 biomechanical parameters: The apparent modulus of elasticity (stiffness) and the energy loss. Adapted from Chung et al., 2014 [80].*

Studies have shown that both stiffness and energy loss vary in the aortic wall of patients with degenerative aneurysm [99-101] Generally, normal ascending aorta has relatively low stiffness and energy loss (0.15 MPa and 25 %) and these values increase significantly with aneurysm (0.3 MPa and 40 %).

*In Vivo Mechanics Using Echocardiography*

Echocardiography provides a tool for assessing thoracic aorta and part of the abdominal aorta. Transthoracic echocardiography enables a view of the ascending aorta and aortic arch and also offers evaluation of atherosclerotic plaque, aortic aneurysms and sinus of Valsalva aneurysms. Transthoracic echocardiography is recommended for evaluation of ascending aortic aneurysm as per the 2011 American College of Cardiology/ American Heart Association (ACC/AHA) practice guidelines [102]. In this thesis, an echocardiography modality was used to measure the stiffness (β Stiffness Index) of the aortic simulators under physiological pressures in a perfusion loop. The β Stiffness Index (β) is a dimensionless number and is defined as the following [103]:

$$\beta = \ln(P_{Sys}/P_{Dia})/[(D_{Sys} - D_{Dia})/D_{Dia}]$$

where $P_{Sys}$ and $P_{Dia}$ are the systolic and diastolic pressure (or the maximum and minimum of a sine pressure waveform) and the $D_{Sys}$ and $D_{Dia}$ are the systolic and diastolic diameters, respectively. The diameter measurements where obtained using the caliper function short-axis (transverse) echo images of the aortic simulators.

Echocardiographic measurements of aortic dimensions (leading edge to leading edge) are consistent with images obtained by computed tomography CT (inner-wall to inner-wall). The best conformity TTE SAX results is acquired using the end-diastolic L-L method for ascending aorta and mid-diastolic for the sinuses measurements [104]. Although the data comparing the measurement of echocardiography and CT are limited, one of the studies showed that aortic diameters of echocardiography correlates well with that of CT measurement [105]. Transthoracic echocardiography is an accurate and feasible technique to assess and follow-up thoracic aortic diameter in patients with ascending aortic aneurysm. In assessing aortic wall stiffness using long axis views to measure aortic diameter change, young patients with Marfan Syndrome were found to have more aortic wall stiffness when compared to the control groups [106]. Another method is using short axis views with speckle tracking, a process that tracks the regional deformation of the wall, which is a well-known method to assess left ventricular strain [107].

Current clinical studies view the TAA as a dysfunction of the vessel wall mechanics that can be derived by size. Indeed, this metric is limited and cannot tale the variation, complexity and dynamic nature of aortic disease. Pathology identification and aneurysm risk assessment goes beyond aortic size alone. The key to defining and validating new standards requires tensile testing of both healthy and diseased ascending aortic tissue.

In conclusion, there is a strong correlation between histopathological markers and *in vivo* measured biomechanics of aortic disease with ultrasound-derived biomechanical parameters including stiffness index and Cardiac Cycle Moduli [108]. For future consideration in patient selection for surgical intervention, ultrasound-derived biomechanics parameters should be studied to determine aortic wall integrity, in conjunction with existing aneurysm-size guidelines. By developing echo-compatible 3D printed models, the trainee will be able to perform *in vivo,* and *ex vivo* experiments. This development could also allow for the validation of new strain imaging technology.

### *3D Printer Technology*

The use of a 3D printer enables objects of various materials to be created to replicate real-life structures. Multiple materials, ranging from rigid to flexible, can be used to print models with tunable properties and smooth surfaces regardless of the geometric complexity of the object. The advantage of such technology allows for the printing of two or more composite materials at the same time assisting in achieving physiological fidelity of real objects (Objet500 Connex3, Stratasys, Eden Prairie, USA).

# Chapter 4: Expanded Methodology

This section is expanding upon the methodology presented in the manuscript. Here we provide additional details regarding the creation and 3D printing of our aortic simulators.

## *3D Printed Aortic Simulator Materials and Geometries*

In this study, computer-aided aortic model designs were developed using a combination of two software programs (SolidWorks [Dassault Systèmes, Waltham, USA]; Rhinoceros 3D [Robert McNeel & Associates, Seattle, USA]) and 3D printed with a Connex3 Objet500 printer (Statasys, Eden Prairie, USA). To understand the role that material composition and geometry has on physiological fidelity, two different geometries were created. These geometries were developed using two different material compositions (Figure 3). Similar to our previous work [109] a Connex3 Objet500 printer was used to 3D print our echogenic-proven material models [110].

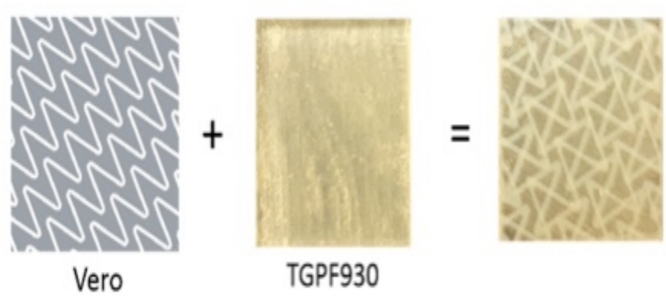


*Figure 3. Composition and materials used to control the softness, strength and directional dependency of soft TGPF930 structures, as well as a tunable, soft but strong three-material composite.*

### Rigid Material

According to manufacture VeroPureWhite is a rigid opaque photopolymer and is good for use in engineering prototypes, product assemblies and room temperature vulcanization molding patterns. With modulus of elasticity (stiffness) 2000-3000 MPa, rigid materials provide deep visualization and can be combined with other polymers to alter characteristics like hardness, flexibility, translucency and resistance (VeroPureWhite, Stratasys, Eden Prairie, USA).

### Flexible Material

TangoPlus is a rubber-like material that simulates applications that require flexible characteristics and can range in hardness values from rubber bands to tire treads to shoe heels. Although Stratasys does not report the stiffness of TangoPlus, it is reported as having a Shore A hardness of 28, which is a rubber-like polymer (TangoPlus, Stratasys, Eden Prairie, USA). We do report the stiffness of pure TangoPlus in our study.

### Geometry of 3D Printed Models

Straight tube models and an idealized ATAA geometry were created with and without inlaid fibers (Figure 5, 6). Homogeneous, isotropic and elastic TGPF930 (TangoPlus FullCure 930, Stratasys, Eden Prairie, USA) was used to create single-material models. Literature has shown the previous use of this 3D printed resin however, limitations were noted due to its inability to tune mechanical properties. By imitating the mechanics and geometry of collagen fibrils, a two-material composite (Figure 3) was designed to largely replicate natural aortic structure. The two-material composite was characterised by VeroWhitePlus (Stratasys, Eden Prairie, USA) zigzag fibers implanted into the flexible TGPF930 material to simulate the elastin lamellae. The ability to control softness **(feel**

**or haptic)**, strength (**deformation resistance)** and the material's mechanical dependency has been shown using this structure [109].

### *CAD and 3D Printing*

Computer-aided design (CAD) was used to produce the straight tube and idealized aortic aneurysm models that were tested as aortic simulators. The 3D design was done in SolidWorks and the following dimensions were implemented in each of the two simulator geometries:

| **Tube** | **Aneurysm** |
| --- | --- |
| Length: 110 mm | Length: 190 mm |
| Diameter: 25 mm | Diameter (Aneurysm): 40 mm |

To embed a fibre network into a cylindrical or idealized aortic aneurysm model, two separate models must be produced: one for the model itself, soft material (Tango Plus), and a second for the rigid fibres (VeroWhite). Both of these models are first built separately in Solidworks CAD software. The fibres are created as an array of sinusoidally extruded strands.

Two layers of these fibres were built orthogonal to each other as this was one of the configurations for testing the flow loop. The more complex phase of building these models is the embedding of the fibrous array. This is some through a series of operations in Rhinoceros 3D manipulation software (Seattle, United State). The process is shown as a series of diagrams in (Figure 4).

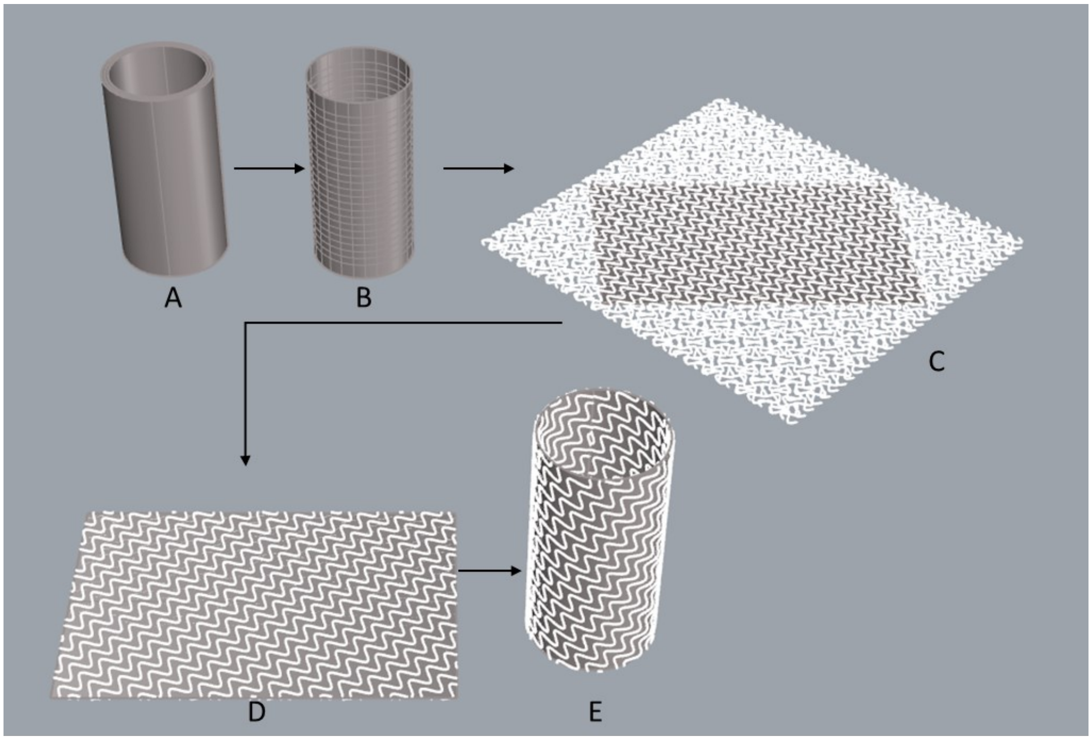


*Figure 4. Process for embedding fibers. A: importing solid object; B: extracting surface between the two external surfaces; C: unroll this surface and superimpose fiber array on top; D: trim fibers to the surface geometry; E: Use "Flow along surface" com command to wrap fibres around surface*

A command called “flow along surface” can be used to deform a given object around a target. To do so, a surface through the midline of the cylinder is extracted (Figure 4 B), and the fibre array is placed on top of it (Figure 4 C). The extra fibres are trimmed (Figure 4 D), and the “flow along surface” command is used to wrap the sinusoidal fibres around the target surface (Figure 4 E). Since this surface lies in the middle of the solid cylinder, the fibre layers are slightly off centre. One is slightly to the outside of the midline and the other is slightly inside of the midline.

The 2 simulator geometries designed and studied in this thesis are presented as 3D design images with their respective fibre inlays: 1) Tube (Figure 5) and 2) Aortic Aneurysm (Figure 6).

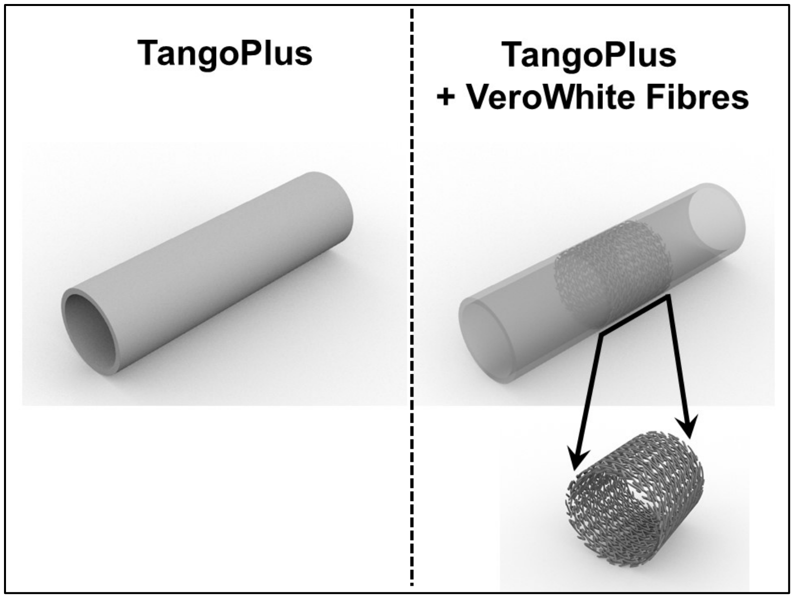


*Figure 5. Tube simulator 3D geometry with pure TangoPlus (Left) and with TangoPlus with embedded VeroWhite fibres (Right).*

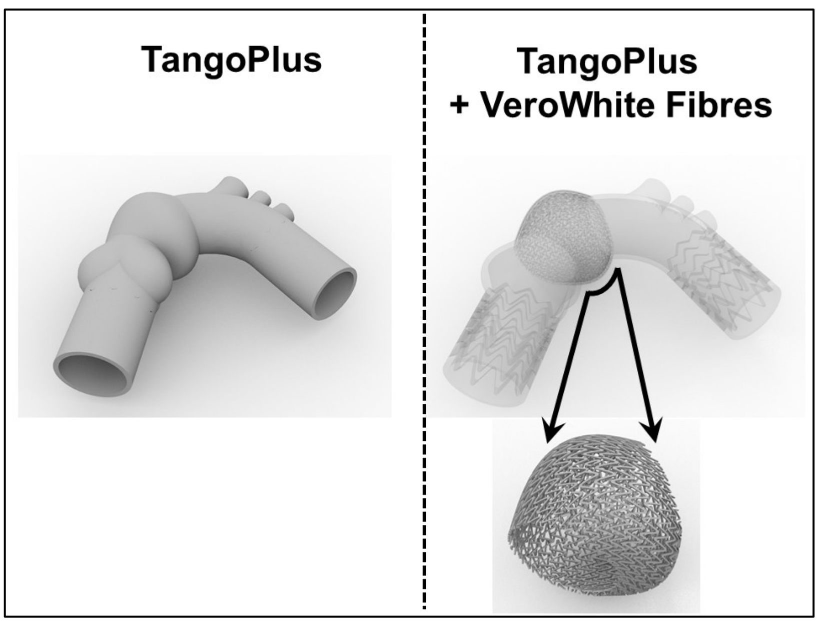


*Figure 6. Aortic aneurysm simulator 3D geometry with pure TangoPlus (Left) and with TangoPlus with embedded VeroWhite fibres (Right).*

## Chapter 5: Manuscript

The following manuscript is in preparation for submission to Journal of Surgical Simulation.

The manuscript discusses the creation of dynamic and echo-compatible ascending aortic simulators with physiological fidelity for surgical simulation.  In this study, we created 3D printed multi-material ascending aortic simulators (2 geometric variants and 2 material variants) and evaluated their capacity to replicate the distensibility of human tissue when perfused at physiological pressures. As described in the expanded methodology section in Chapter 4. These models are a step towards achieving better simulator fidelity and have the potential to be effective tools for surgical training.

The study abstract has been accepted to be presented at the American College of Surgeons Surgical Simulation Conference 2021.

**Ali Alakhtar:** designed the experiment, performed the experiment, analyzed the data and wrote the manuscript.

**Alexander Emmott:** performed the experiment, analyzed the data and edited the manuscript

**Cornelius Hart:** performed the experiment and performed 3D printing

**Rosaire Mongrain:** provided the infrastructure and reviewed the manuscript

**Richard Leask:** supervised the study, provided the infrastructure, designed the experiment, reviewed the data analysis and reviewed the manuscript

**Kevin Lachapelle:** supervised the study, provided the infrastructure, designed the experiment, reviewed the data analysis and reviewed the manuscript

**3D printed ascending aortic simulators with physiological fidelity for surgical simulation**

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**Abstract**

**Introduction:** We created 3D printed multi-material ascending aortic simulators (2 geometric variants and 2 material variants) and evaluated their capacity to replicate the distensibility of human tissue when perfused at physiological pressures.

**Methods:** 3D printed ascending aortic models were developed by computer-aided design and then 3D printed with a multi-material Connex3 Objet500 printer. Two simulator geometries were compared: 1) a straight tube and 2) an idealized aortic aneurysm, containing a sinus of Valsalva, a spherical aneurysm and an aortic arch. Two different material variants were implemented in our simulators: 1) pure elastic material (TangoPlus) and 2) TangoPlus with embedded fibers (Verowhite). Our simulators were connected to a pulsatile flow loop with a sinusoidal pressure wave of 120/80 mmHg ($P_S/P_D$) to replicate the physiological environment of the aorta. Using diameter measurements ($D_S$, $D_D$) from GE Vivid ultrasound and Echopack software, β Stiffness Index ($\beta=\ln(P_S/P_D)/([D_S-D_D]/D_D)$ was calculated to compare stiffness between our simulators and human ascending aortas.

**Results:** β Stiffness Index increased with the addition of VeroWhite fibers while no differences were observed between simulator geometries. The aortic simulators composed of pure TangoPlus had statistically similar β Stiffness Index values to human ascending aorta. The simulators with embedded VeroWhite fibres were stiffer than human tissue; however, they exhibited data point overlap with human tissue in the top quartile suggesting that they can replicate human aortic tissue with severe medial degeneration.

**Conclusion:** We developed dynamic ultrasound-compatible aortic simulators with the ability to reproduce the distensibility of real aortas under physiological pressures. Using 3D printed composites, we were able to tune the stiffness of our simulators which allows us to better represents

the stiffness variation seen in human tissue. These models are a step towards achieving better simulator fidelity and have the potential to be effective tools for surgical training.

## Introduction

Surgeons require a highly technical skill set that is traditionally acquired through intensive clinical training. For several years now, surgical training has included some form of medical simulation that allows a trainee to repeatedly practice techniques in a controlled environment. When compared to traditional approaches, simulation avoids the inherent risk of harming patients [3, 111] while resulting in improved knowledge retention, confidence and management skills of surgical trainees [4, 112].

Establishing the cost-benefit of using high fidelity (HF) or low fidelity (LF) simulators in medicine is determined based on learning objectives. Motor skills literature shows that novice learners benefit from using simpler models especially when practicing skills like repetitive suturing [113, 114].

LF simulation is therefore seen when smaller, more specific tasks are required and is useful for repetitive practice by the trainee until the skill is fully grasped. A disadvantage of LF simulation models is the difficulty of the trainee to fully comprehend the concept or patient reaction when used in actual medical scenarios [12].

In contrast to LF, HF simulation more closely reproduces real-life scenarios including the mimicking of human reactions, environmental situations and disease processes that trainees can encounter in healthcare but can navigate through without any risk to real patients. Although HF simulation most accurately mimics real scenarios, the use of LF simulation is usually seen as the starting point for training with the progression to HF as the trainees' skills, knowledge and training requirements become more complex, a strategy known as "progressive fidelity" [13, 14].

Preparing a trainee for multifaceted challenges like cardiac surgery requires more complex simulations that benefit from a high level of simulator fidelity [115]. To improve knowledge retention, high fidelity cardiac surgical simulations should involve anatomically and physiologically realistic components of the cardiovascular system.

Unfortunately, current vascular simulators remain simplified with basic tubular shapes made of synthetic materials [116-119] or require the use of animal or cadaver tissue that lack pathological fidelity. New 3D printing technologies can be used to produce complex and/or patient-specific geometries quickly [120] but are limited in the material properties of the printed material.

Optimal cardiovascular simulators require that physiological properties of blood vessels, such as how the tissue is deformed by the dynamics of blood flow, how it sutures and how it cuts, need to be considered [120, 121]. This is especially pertinent when training residents to put a patient on, or wean from, cardiopulmonary bypass where the surgeon requires visual feedback from the distension and recoil of the aorta to safely cannulate and cross clamp the aorta. In this regard, an adequate surgical simulator would be perfused with pulsatile flow and exhibit realistic pressure-diameter fidelity for a variety of pathological states. For example, ascending aortic aneurysms increase tissue stiffness when compared to normal ascending aortas [122, 123] caused by elastin degradation and an increased collagen synthesis [124]. This increased stiffness alters the deformation of aneurysmal aortas and the touch and feel of the tissue to the surgeon.

The creation of a new generation of dynamic aortic simulators suitable for mock flow circulation would therefore need to provide realistic deformation of the ascending aorta to enhance cardiac surgical training. Our objectives in this study, therefore, were 1) to leverage 3D printing technology to create distensible pseudo-tissues that can be used to mimic the biomechanical properties of human aortic tissue and 2) to 3D print these pseudo-tissues into idealized aortic geometries to observe the effect of simulator anatomy on the measured biomechanical indices. Specifically, we evaluated the capacity of the aortic simulators to replicate the pressure-mediated deformations of real aortic tissue as measured by echocardiography (ultrasound) which is the common intraoperative imaging modality used in cardiac surgery for evaluating the heart and great vessels and is commonly used to measure the in vivo biomechanical properties of human aorta [108]. By using a typical imaging modality in the procurement of our measurements, we aim to demonstrate not only simulator fidelity but also the ability to use point-of-care imaging technologies with our simulators.

## Materials and methods

### *Geometries and Materials of the 3D-Printed Aortic Simulators*

3D printed ascending aortic models were developed by computer-aided design with a combination of two software suites: Solidworks (Dassault Systèmes, Waltham, USA) and Rhinoceros 3D (Robert McNeel & Associates, Seattle, USA), and then 3D printed with a multi-material Connex3 Objet500 printer (Stratasys, Eden Prairie, USA). Model geometry and material composition were each varied in two configurations resulting in four simulator variations, **Figure 7**. The model geometries were 1) a straight tube with an inner diameter of 25 mm and length of 110 mm and 2) an idealized aortic aneurysm, containing a sinus of Valsalva, a spherical aneurysm of 40 mm diameter and an aortic arch. Each model had a wall thickness of 2 mm. These geometries were designed based on typical aortic dimensions and wall thickness to represent both an idealized non-dilated aorta (tube) and an anatomical idealized aortic aneurysm with curvature through the aortic arch.

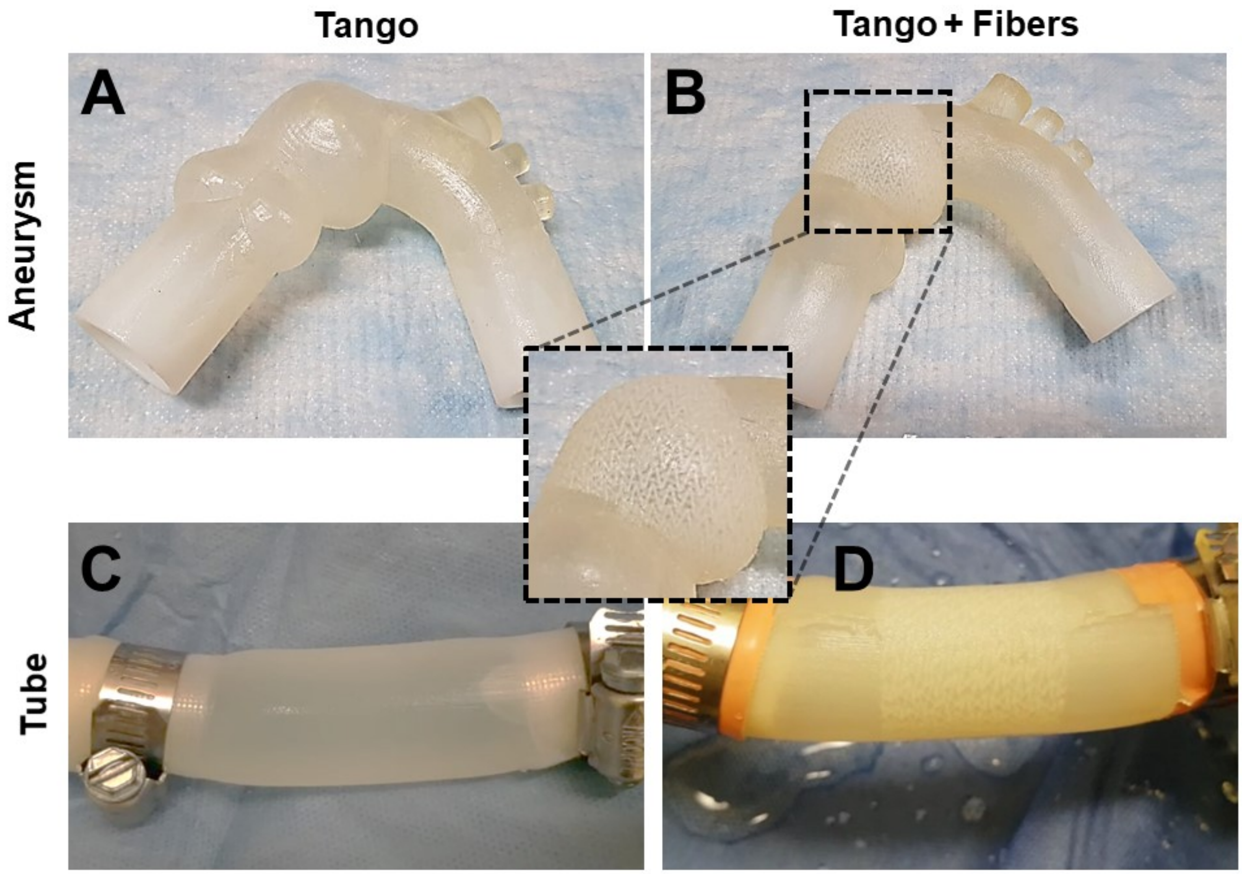



*Figure 7. 3D printed aortic simulators were designed with 2 geometries: an idealized aortic aneurysm (A & B) and a cylindrical tube (C &D) each with a wall thickness of 2 mm. For each model type, two material variants were investigated: pure elastic TangoPlus (A & C) or TangoPlus with embedded ridged VeroWhite fibres (B & D).*

To replicate the compliant (elastin) and stiff (collagen) composite nature of the human aorta, two material variants were produced for each geometric configuration, **Figure 7**. The first variant was homogenous elastic TangoPlus Fullcure 930 (Stratasys, Eden Prairie, USA) while the second variant used the same TangoPlus Fullcure 930 structure with embedded rigid zigzag fibres composed of VeroWhite (Stratasys, Eden Prairie, USA). VeroWhite is a rigid opaque photopolymer with a reported modulus of elasticity (stiffness) of 2000-3000 MPa, while TangoPlus is a photopolymer that has a reported shore A hardness of 28 which qualifies it as a soft rubber-like material [125]. These materials were selected because they were known to be echogenic and have previously demonstrated haptic, strength and isotropic similarity to human tissue [121].

*Mechanical Analysis by Echocardiography*

A water-fed pulsatile flow loop was used to mimic the physiological environment of the aorta to make echocardiographic measurements of stiffness, **Figure 8**. In this setup, a piston pump (Cardioflow MR 1000, Shelley Medical, Toronto, Canada) and resistance valve were used to generate a 0.5 Hz sinusoidal pressure wave within the model that oscillated between 120 mmHg and 60 mmHg. Pressure was recorded from a transducer (86A, TE Connectivity Measurement Specialties) that was connected to a port at the model's inlet. All subsequent echo measurements were made with the simulators submerged in a water-filled box that permitted the transmittance of ultrasound. Furthermore, all 3D printed simulators were tested within a week of printing.

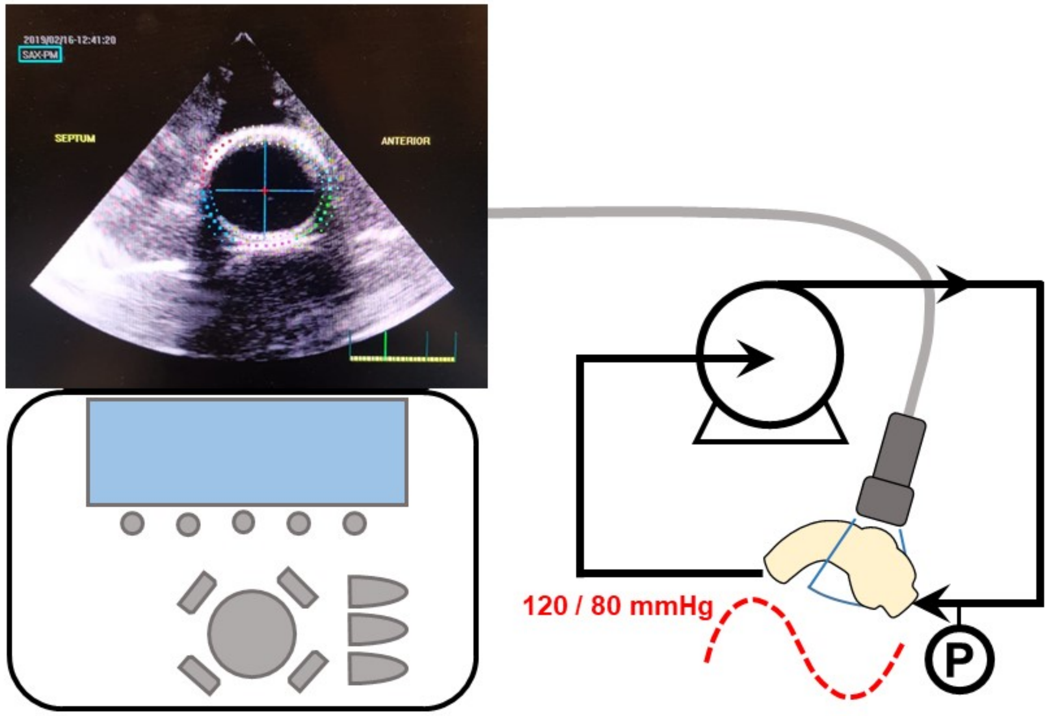



*Figure 8. Perfusion system setup for the echocardiographic measurements of the aortic simulator. A GE Vivid E95 echo machine captures a cross section of the simulator suspended in a shallow bath of water. A closed-loop piston pump generates a sinusoidal pressure wave that oscillates between 120 and 80 mmHg with the pressure measured by a transducer in the model inlet.*

A GE Vivid E95 echocardiographic machine (GE Healthcare, Chicago, IL, USA) was used to obtain a cross-sectional view of the simulator for 3 cycles of the pressure waveform to ensure a single non-truncated cycle. Each measurement used a 2.3/4.6 MHz cardiac probe (M5Sc) placed on the surface of the tubular model or on the belly of the aneurysm, respectively.

Analyses were performed on the cross-sectional view of the simulators following the methods described in Emmott *et al*., 2018 [108, 126]**.** The caliper function in GE EchoPac (GE Healthcare, Chicago, IL, USA) was used to measure the maximum and minimum cross-sectional diameters ($D_{Max}$ and $D_{Min}$, respectively).

The β Stiffness Index was used as a surrogate measure of vessel stiffness and is defined as the following [103]:

$\beta$ Stiffness = ln ($P_{Max}$/$P_{Min}$)/([$D_{Max}$ - $D_{Min}$]/ $D_{Min}$); (Equation 1)

where $P_{Max}$ and $P_{Min}$ are the maximum and minimum pressures that were recorded by the transducer for a single period.

*Mechanical Analysis by Biaxial Tensile Testing*

Equi-biaxial tensile testing is a common method used to evaluate the *ex vivo* material properties of aortic tissue [124]. For each of the 3D printed aortic simulators, a 1.5x1.5 $cm^2$ testing square was isolated from the simulator at the equivalent location of the echocardiographic measurement. The testing squares were attached to an ElectroForce TestBench (TA Instruments, New Castle, DE, USA) with 4-0 hooked silk sutures in a bath of distilled water at room temperature. Each sample underwent cyclic loading-unloading to 40% strain at 0.4 mm/s for ten preconditioning cycles followed by three data cycles at a displacement rate at 0.1 mm/s. Two mechanical indices were calculated from these data:

1) stiffness as defined as the incremental modulus evaluated at 40% strain and 2) the energy loss. Stiffness is a point measure of the rigidity of a material and describes the material's resistance to deformation. Energy loss is a viscoelastic measurement of a material's ability to function as an elastic capacitor to store and return elastic energy. Each of these parameters is commonly reported for human aortic tissue [122, 127-129].

*Human Ascending Aortic Aneurysm Measurements*

Informed consent was obtained from twenty-one patients with aortic aneurysms receiving elective Aortic Replacement surgery at the Royal Victoria Hospital (Montreal, QC, Canada). Expansion and recoil of the ascending aorta was measured by transesophageal echo at the time of surgery and followed the methodology presented in Emmott *et al*., 2018 [128]. Blood pressure was obtained from an invasive radial artery trace. A specimen of the resected aorta was obtained and stored in normal saline at 4°C for subsequent tensile testing. From these human data, equivalent β Stiffness Index and tensile measurements were made following similar protocol. However, tensile measurements on human tissue were made in a bath of normal saline at 37°C to maintain an environment similar to the intraoperative measurements.

*Statistical Analysis*

Data are presented as interquartile box-whisker plots with individual measurements presented as unique dots with N=5 replicates for all geometry and material configurations of the aortic simulators. Multiple comparison analyses were done using 1-Way or 2-Way ANOVA with Tukey post-hoc tests. P-Values $<0.05$ were considered significant.

**Results**

This study assessed the physiological fidelity of 3D printed aortic simulators with different anatomy and material type. Two variants of ascending aortic anatomy were produced: 1) a simplified straight tube aorta ("Tube") and 2) a complex aortic aneurysm ("Aneurysm"), complete with an aortic sinus, a concentric aneurysm and curvature through the aortic arch. For each anatomical model, two variants of materials were selected to produce either a relatively compliant

(TangoPlus, “Tango”) or stiff wall (TangoPlus with embedded VeroWhite fibres, “Tango + Fibres”).

*Mechanical Comparison of Aortic Simulators by Echocardiography*

An echocardiography (ultrasound) imaging modality was used to measure the relative apparent stiffness (β Stiffness Index) when the aortic simulators were perfused under physiological pressures of 120/80 mmHg, **Figure 9**. Models with embedded VeroWhite fibres had higher β Stiffness Index values compared to the equivalent models composed of pure TangoPlus ($P<0.001$, Two-Way ANOVA), **Figure 9**. No statistical difference was measured in β Stiffness Index between the straight tube and aneurysmal geometries ($P=0.062$, Two Way ANOVA). Post-hoc multiple comparison tests showed that for each geometry, there was a significance difference between the models with Tango and Tango + Fibres (Tube: $P=0.020$, Aneurysm: $P=0.001$) and between the Aneurysm, Tango and the Tube, Tango + Fibres ($P<0.001$).

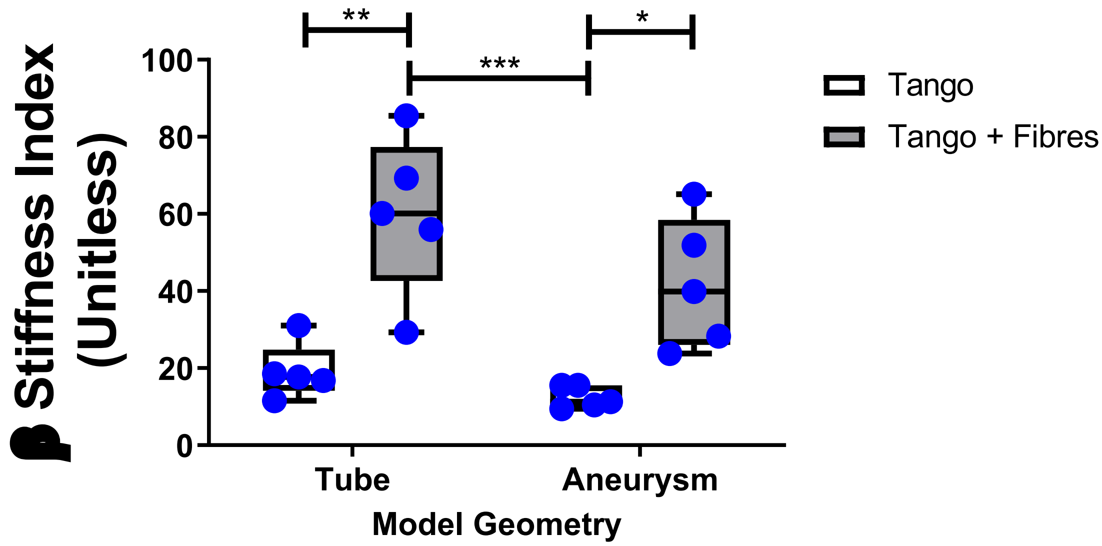
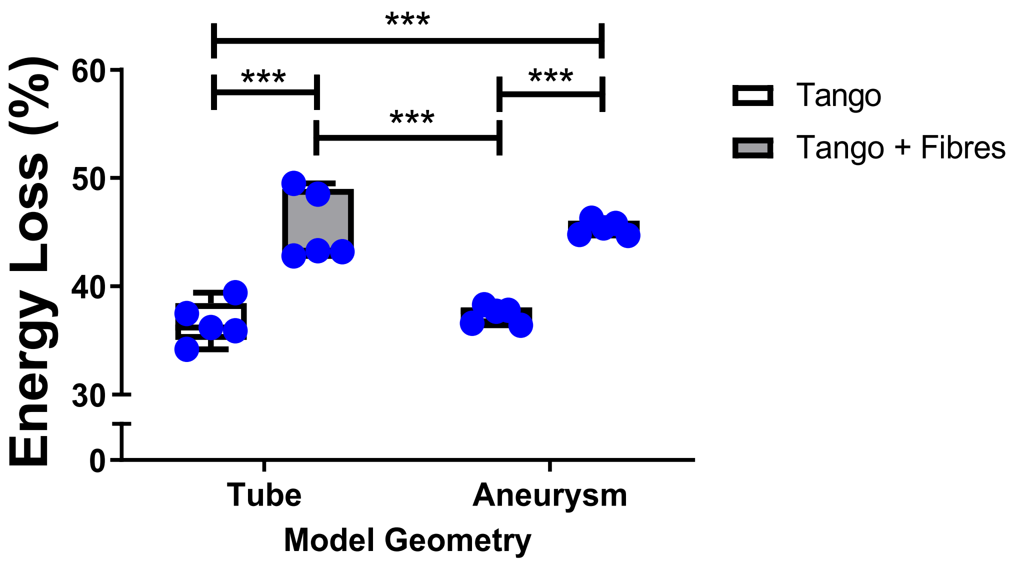



*Figure 9. Mechanical comparison of pressurized 3D printed aortic simulators by echocardiography-measured β Stiffness Index. Statistical analysis by 2-way ANOVA: significant overall effect of material composite, P<0.001, and not-significant overall effect of simulator geometry, P=0.06. Intergroup differences were measured using a Tukey post-hoc multiple comparisons test with significance indicated as * (P<0.05), ** (P<0.01) and *** (P<0.001).*

*Mechanical Comparison of Aortic Simulators by Tensile Testing*

Biaxial tensile testing of specimens from each simulator was used to assess the planar mechanical properties—incremental modulus (i.e., stiffness) and energy loss—for the different material composites and geometries, **Figure 10**. Models with embedded VeroWhite fibres had significantly higher stiffness and energy loss as compared to models of pure TangoPlus for either the tubular or aneurysmal geometries (Stiffness: P<0.001, Energy Loss: P<0.001, Two-Way ANOVA). The geometry of the aortic simulator did not statistically affect the stiffness or energy loss (Stiffness: P=0.221, Energy Loss: P=0.713, Two-Way ANOVA). Post-hoc multiple comparisons showed that there was a significant difference between all Tango and Tango + Fibres (P<0.001) variants for both stiffness and energy loss, regardless of the geometry of the model.



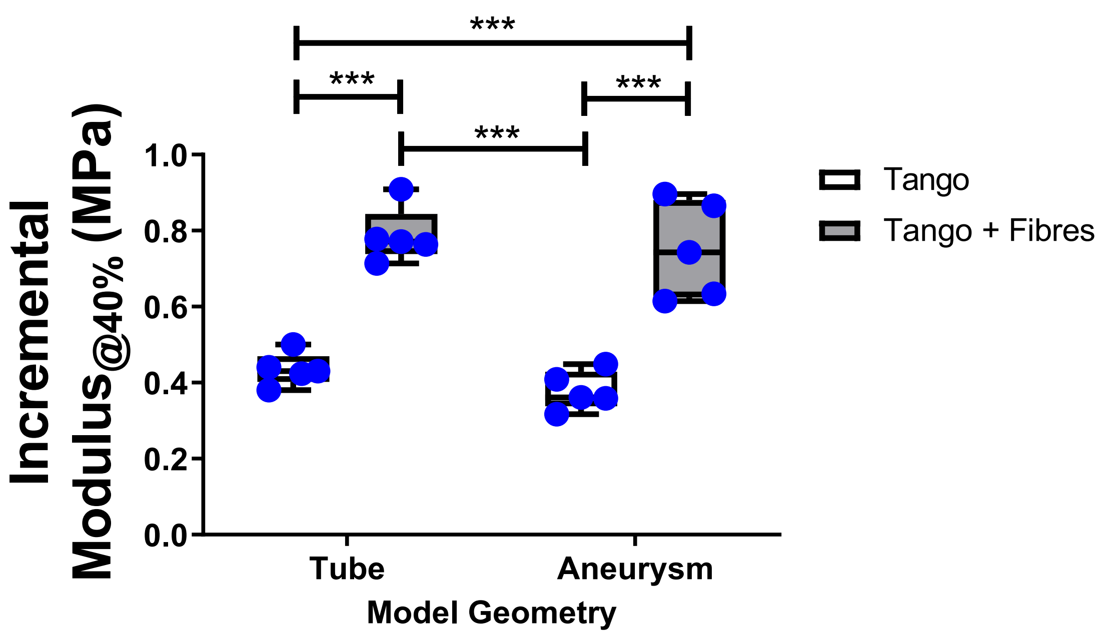




*Figure 10. Mechanical comparison of pressurized 3D printed aortic simulators planar biaxial testing: A) incremental modulus at 40% strain (i.e., stiffness) and B) energy loss. Statistical analysis by 2-way ANOVA: effect of material composite, A) P<0.0001, B) P<0.0001; effect of simulator geometry, A) P=0.2, B) P= 0.7. Intergroup differences were measured using a Tukey post-hoc multiple comparisons test with significance indicated as *** (P<0.001).*

*Mechanical Comparison of Aortic Simulators with Human Tissue*

As the geometry did not alter the mechanical measurements, we proceeded with the aortic aneurysm geometry to compare our aortic simulators with human tissue. Human ascending aortic aneurysm tissue was obtained from twenty-one patients undergoing aortic replacement surgery at the Royal Victoria Hospital in Montreal, Quebec.

Comparison of β Stiffness Index between human tissue and the material composite variants of the aortic simulator by 1-Way ANOVA ($P<0.001$) demonstrated that the aortic simulator with pure TangoPlus was statistically similar to human tissue ($P=0.345$), **Figure 11**. The simulators with embedded fibres, however, were stiffer than human tissue with statistically higher β Stiffness Index values ($P<0.001$). However, the fibre-embedded variant of the aortic simulator exhibits datapoint overlap with human tissue in the latter's top quartile range suggesting that it can replicate human tissue that is exceedingly stiff, **Figure 11**.

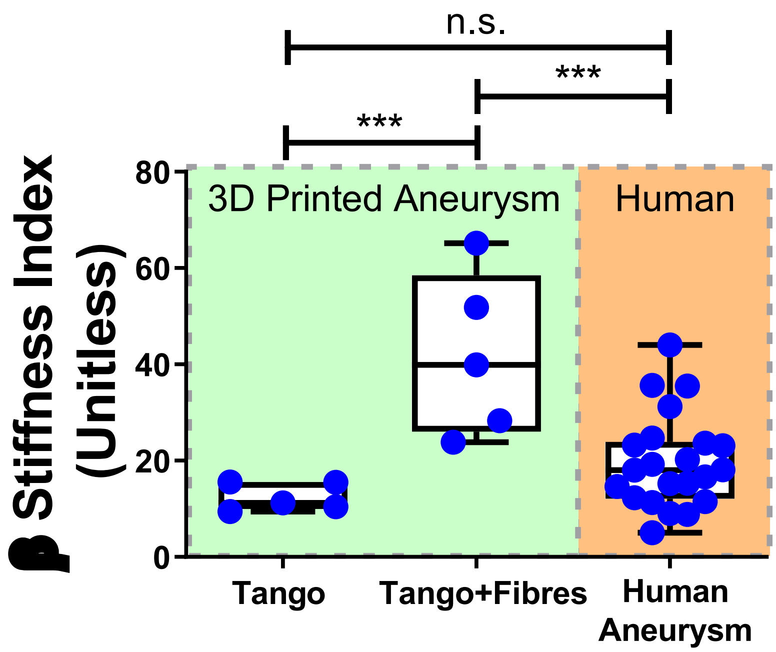



*Figure 11. Mechanical comparison of 3D printed aneurysmal aortic simulators and human ascending aortic aneurysmal tissue by echocardiography-measured β Stiffness Index. Statistical analysis by 1-way ANOVA: effect of grouping, P=0.0002. Intergroup differences were measured using a Tukey post-hoc multiple comparisons test with significance indicated as *** (P<0.001).*

Biaxial tensile measurements of incremental modulus (i.e., stiffness) and energy loss demonstrated significant statistical differences between both material variants and human tissue by 1-Way ANOVA (Stiffness: P<0.001, Energy Loss: P<0.001), **Figure 12**. Post-hoc multiple comparisons showed that both the pure TangoPlus and the TangoPlus with VeroWhite fibres aortic simulators were stiffer than human ascending aortic aneurysmal tissue (P<0.001 and P<0.001, respectively). Similarly, energy loss in each variant was higher than in human tissue (Tango: P=0.016, Tango + Fibres: P<0.001); however, energy loss values from the pure TangoPlus simulator demonstrated datapoint overlap with human tissue in the latter's top quartile range, **Figure 12**.

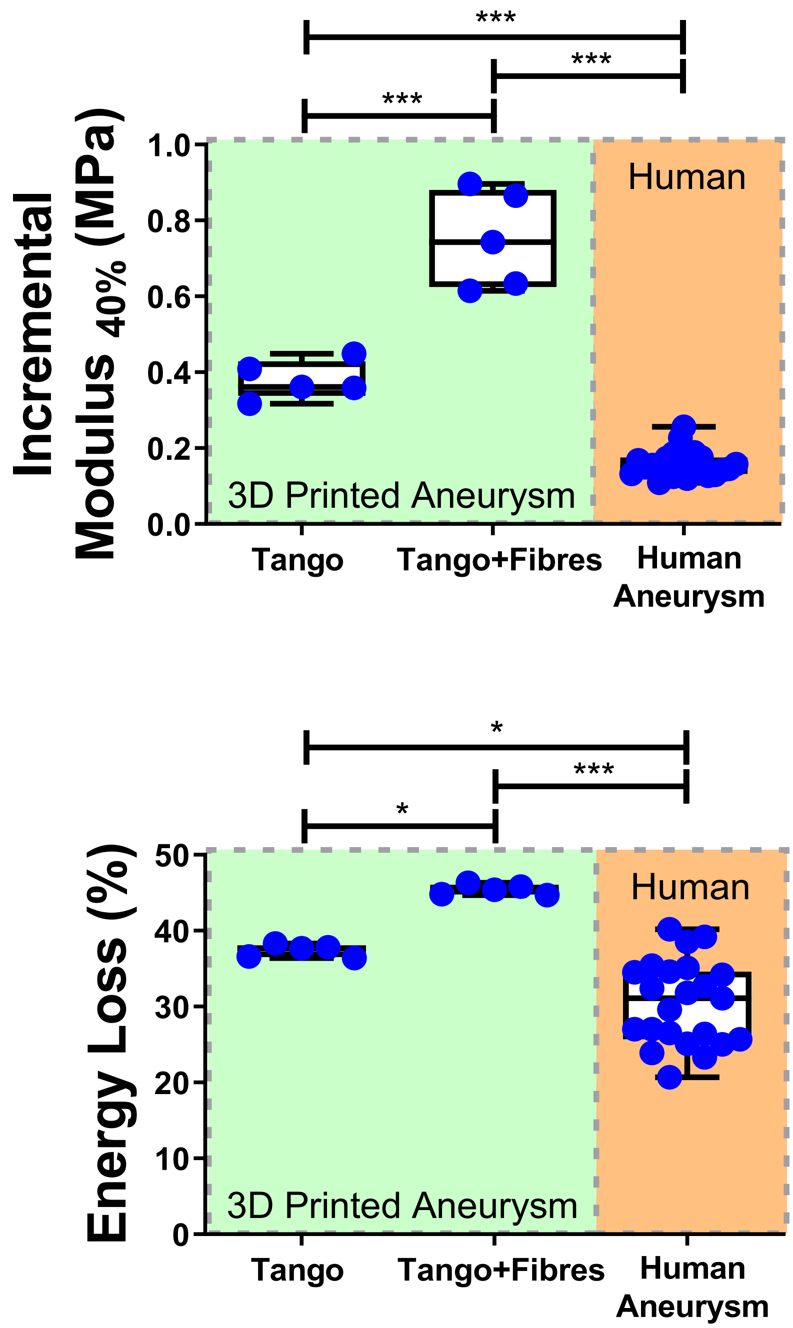



*Figure 12. Mechanical comparison of 3D printed aneurysmal aortic simulators and human ascending aortic aneurysmal tissue by planar biaxial testing: A) incremental modulus at 40% strain (i.e., stiffness) and B) energy loss. Statistical analysis by 1-way ANOVA: p= (***). Multiple comparisons with Tukey post-hoc test.*

Finally, stiffness measurements from planar biaxial testing were re-assessed to account for an expected 25% pre-strain in the human tissue [108, 126]. In this analysis, the incremental modulus of the aortic simulators was measured at 15% strain while that of human tissue was measured at 40% (a difference of 25%), **Figure 13**. A 1-Way ANOVA with a Tukey post-hoc analysis demonstrated that both the pure TangoPlus and the TangoPlus with VeroWhite fibres had statistically similar stiffness to human tissue.

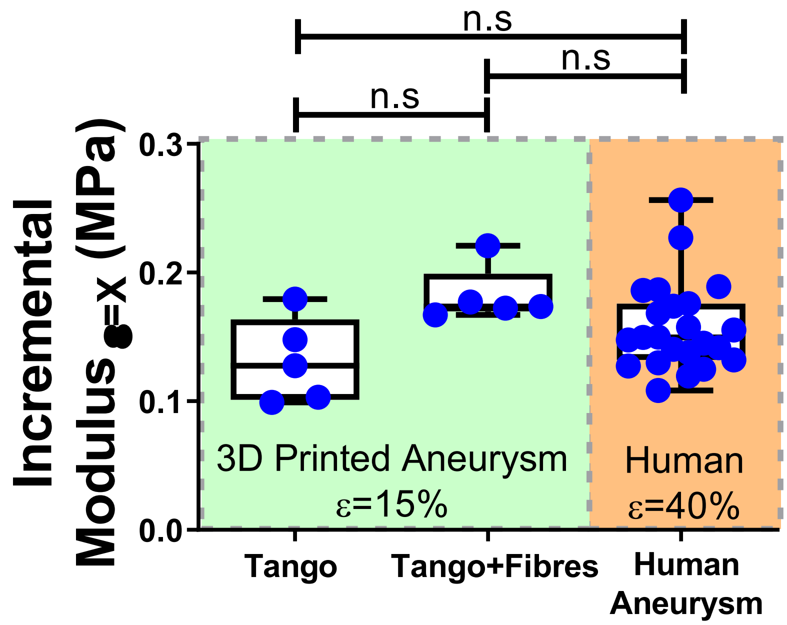



*Figure 13. Stiffness of 3D printed aneurysmal aortic simulators and human ascending aortic aneurysmal tissue by incremental modulus measured at 15% and 40% strain, respectively. Statistical analysis by 1-way ANOVA: p= (n.s.). Multiple comparisons with Tukey post-hoc test.*

## Discussion

Cardiac surgery requires high-level cognitive and technical skills that are developed through intensive clinical training. Recently, medical simulation has been introduced as another form of training to hone these skills [112]. However, the benefit to using cardiovascular simulators is limited due to the current lack of fully immersive open cardiac simulators which mimic the complex physiological processes and the disease state of human tissue seen in cardiac surgery. Our study looked at leveraging novel 3D printing technologies to create more realistic models of the ascending aorta that can be perfused with pulsatile flow and exhibit biomechanical fidelity with human tissue.

The pressure-diameter relation of our simulators was measured using typical point-of-care echocardiography through the β Stiffness Index (equation 1) which is a typical stiffness index for human aorta [130, 131]. Simulators made of pure TangoPlus had statistically similar β Stiffness Index values to those measured on human ascending aortic aneurysms. Although statistically stiffer, simulators with embedded VeroWhite fibres demonstrated datapoint overlap with the stiffest 25% of human data from this cohort (**Figure 11**). This shows that tuning the mechanical properties with the addition or removal of fibres can achieve a broad range of disease states. This is not limited to replicating the increase in stiffness associated with age or medial degeneration, as is common in ascending aortic aneurysm [124], but by changing the local fibre density should also be able to mimic the stiffening associated with calcification (porcelain aorta) [132] and the suture line of anastomoses [133] seen in reoperation.

The production of two geometric variants allowed us to test whether anatomical configuration appreciably changed the β Stiffness Index measurements. Ascending aortic aneurysms can exhibit a variety of morphologies–aneurysms can be saccular or fusiform and can present anywhere from the aortic root to the aortic arch [85]. We demonstrated that either a tubular or a complex spherical aneurysm exhibited the same β Stiffness Index measurements given the same pressure swing (**Figure 9**), signifying that 3D printing aneurysms of different anatomical forms shouldn't appreciably change the pressure-diameter relation in simulation under physiological pressures.

Achieving tissue-like pressure-diameter fidelity of a perfused aorta is centrally important when simulating cardiopulmonary bypass (CPB). Placing patients on CPB is universal in cardiac surgery and requires significant visual, haptic and pressure-distension feedback from the aorta to the surgeon to correctly perform this stage of surgery [134]. The stiffness of the aorta provides resistance when cannulating, cross clamping and inserting the cardioplegia line. Mastery of these techniques avoids unnecessary tearing and bleeding that can extend the operation time and increase the risk of patient mortality/morbidity.

Tensile testing of specimens from the simulator wall was used to measure the mechanical properties of the simulators independent of the perfusion flow loop. Both tensile stiffness and energy loss were tunable in both simulator geometries by adding or removing embedded VeroWhite fibres from a TangoPlus base (**Figure 10**). This result builds upon proof of principle work we've done with planar 3D printed specimens [121] to confirm that tunable multi-material composites can be implemented into complex 3D geometries.

A comparison of the tensile mechanics of the aortic aneurysm simulator with human tissue found that 3D printed models had higher stiffness and energy loss to that of human tissue (**Figure 12)**. Small differences in energy loss from that of human tissue should not be perceptible to a trainee since energy loss describes the viscoelastic recoil of the vessel. Tensile stiffness, however, is a measure of the rigidity of a material and can be perceived through touch and may need additional refinement in the future for the simulator to be used for sewing, cutting and handling.

A variety of materials have been used to replicate vascular models such as latex, polyurethane, silicone and PVA [135-138]. Although compliant 3D printed materials are a novel development and therefore commercially-limited, they have already demonstrated their utility in medical simulation [139]. The overwhelming advantage to 3D printing versus traditional mould production, animal or human cadaver  is the ability to rapidly print a desired structure, such as patient-specific anatomy from CT or MRI [120]. In addition, by using a multi-material composite, the mechanics can be selectively tuned to achieve global or regional differences in model behaviour and, if desired, can even generate material anisotropy (e.g., circumferential vs. longitudinal oriented fibres). Collagen and elastin fibre orientation in the aortic wall leads to mechanical anisotropy [140] (both stiffness and energy loss) and can change considerably with disease [129, 141]. Conversely, preparing simulators from moulded or cured materials generally produce tissue analogues that have globally homogenous and isotropic material properties [25, 142, 143].

**Conclusion**

Cardiac surgery is moving towards advanced specialties that include complex aortic surgeries. Prophylactic ascending aortic repair to prevent dissection and rupture of an aneurysm is commonplace in most large cardiac centers. With this, the development of simulation materials closely mimicking aortopathies will assist residents in more safely and accurately refining techniques to address these issues.

In our study, we developed dynamic echo-compatible aortic simulators with the ability to reproduce pressure-diameter dynamics mimicking the properties of real aortas to better achieve physiological fidelity. Furthermore, by introducing pulsatile flow through our 3D printed models we are moving towards a more realistic and controlled environment where medical residents can practice complex procedures. Future studies will examine the educational impact of these aortic simulators when used by surgical trainees and develop standardized surgical training modules to enhance medical simulation.

## Chapter 6: Discussion

Preoperative and intraoperative preparation is essential for all surgical procedures. Inadequate groundwork and training of all medical personnel can lead to mild or severe surgical complications and may even possibly result in death. As part of enhanced training, medical simulation is being recommended for use in many medical teaching institutions by students, residents and attending physicians to learn and practice new and established skills in safe learning environments.

In the speciality of Cardiac Surgery, various medical models are used in simulation labs to replicate surgical procedures such as CABG, aortic resection, AVR and CPB due to limitations and challenges live operating procedures present [144]. Recent studies show that positive patient outcomes as well as improved surgical trainee technical skills and confidence levels directly correlate to training within a simulation environment [145].

Historically, training and simulation using animal hearts as well as active observation in operating rooms were the best and most viable options for medical learning. Despite the low risk, these options did not come without limitations (different pathologies and anatomy, passive participation). As research advanced, medical models evolved more closely replicating human anatomy. Limitations still existed as materials used in developing the models remained very stiff lending to lower fidelity. With the evolution of 3D printing and availability of more elastic and flexible materials, medical models are being developed with higher fidelity more closely replicating human anatomy and pathologies. Three-dimensional molded models showed promising results when compared to direct printing models for training simulation. The use of 3D printing technology, with various molding materials, is proving to be beneficial in developing and honing surgical skills when used by novice and expert surgeons [64]. Systematic reviews of 3D printing in cardiac surgery show that this technology and the development of 3D cardiac models can be beneficial in medical training as well as in surgical intervention planning, intraoperative optimization and patient education [67].

The development and use of aortic models in cardiac surgery is multipurpose. 3D printed models are effective tools for patient teaching. They allow healthcare providers a visual cue when explaining to patients and their families their disease process and planned surgical intervention. Some research has shown that patients show a greater appreciation and understanding of their disease when a 3D model is used in preoperative patient education and may contribute to practitioners more easily obtaining informed consent for surgical interventions [146].

The use of aortic models in medical simulation helps improve the dexterity and psychomotor skills of surgical trainees. They allow for repetition to learn and hone surgical techniques and with the evolution on model materials, more accurately replicate true OR environments.

Aortic aneurysms and dissections are complex and potentially lethal medical conditions that require skill and precision when requiring surgical resections and repair if medical management is unsuccessful. The surgery is complex in nature and carries significant risk to the patient [146, 147]. The use of various medical imaging techniques (echocardiography, CT, MRI) help physicians to determine appropriate individualized patient surgical treatments. These imaging tests also help in creating patient-specific 3D printed models and assist clinicians in identifying and visualizing anatomy and pathologies to create more accurate and individualized patient treatments [59]. With the availability of medical models in simulation environments, clinicians can also rehearse surgical techniques for these complex cases.

With the shifting paradigm of surgical education and training from the operating rooms to simulation laboratories, the need to evolve the simulation models used by surgical residents is evident. Basic bench-top models assist in the development of skills for particular tasks, but more sophisticated models are required to permit surgical residents to develop and practice multiple techniques to respond to the real complex case scenarios being seen in today's healthcare environment.

3D printing models are being produced to represent real patient-specific disease processes with data derived from Ultrasound, CT Scan, and MRI imaging. These models can replicate the fidelity of the anatomy and structure based on these images [23]. The more closely the models replicate complex cases, the better surgical trainees can understand and be better prepared to deal with actual case scenarios [24].

High fidelity simulation models, replicating human anatomy and disease processes, are beneficial in the training of future surgeons and can be used to learn and perfect various types of cardiothoracic surgeries. Models representing the anatomy of various components of the heart and its surrounding structures permits clinicians to practice established, as well as new and innovative approaches to surgeries, like CABG, aortic and mitral replacement surgeries and aortic aneurysm repair. Their use will continue to produce strong surgical technicians and contribute to future innovative approaches to complex cardiothoracic surgeries [144]. Our study looked at leveraging novel 3D printing technologies to create more realistic models of the ascending aorta that can be perfused and exhibit biomechanical fidelity with human tissue.

Ultimately, we were able to produce aortic aneurysm simulators, capable of demonstrating similar pressure-diameter expansion dynamics when compared to human tissue (**Figure 11**). The β Stiffness Index (equation 1), a physiological metric of stiffness for human aorta [130, 131], was used to measure the pressure-diameter relation. The β Stiffness Index measurements of human ascending aortic aneurysms were statistically similar to simulators created from pure TangoPlus.

Although statistically stiffer, simulators with embedded VeroWhite fibres demonstrated data point overlap with the stiffest 25% of human data from this cohort (**Figure 11**). This demonstrates that a vast range of disease states can be replicated by adding or removing fibres to tune the simulators' mechanical properties. This is not limited to replicating the increase in stiffness associated with age or medial degeneration, as is common in ascending aortic aneurysm [124], but by changing the local fibre density should also be able to mimic the stiffening associated with calcification (porcelain aorta) [132] and the suture line of anastomoses [133] seen in reoperation.

Testing of anatomical configuration changes on the β Stiffness Index measurements were tested by producing two geometric variants. Ascending aortic aneurysms can exhibit a variety of morphologies, aneurysms can be saccular or fusiform and can present anywhere from the aortic root to the aortic arch [85]. Given the same pressure swing, we proved that β Stiffness Index measurements were the same with both tubular and complex spherical aneurysms **(Figure 9)** suggesting that different anatomically formed 3D printing aneurysms should not significantly alter simulation pressure-diameter under physiological pressures.

When simulating CPB, attaining perfused aortic tissue-like pressure-diameter fidelity is centrally significant. Patients undergoing various cardiac surgeries are placed on CPB requiring substantial visual, haptic and pressure-distension feedback from the aorta to the surgeon in order to properly perform this surgical stage [134]. Aortic stiffness provides resistance when performing cannulation, cross clamping and cardioplegia line insertion. Needless tearing and bleeding resulting in operating time extension and increase in patient mortality/morbidity risk can be avoided by perfecting these essential techniques.

Simulator mechanical properties, independent of the perfusion flow loop, were measured using tensile testing of simulator wall specimens. Both tensile stiffness and energy loss were tunable in both simulator geometries by adding or removing embedded VeroWhite fibres from a TangoPlus base (**Figure 10**). This result, confirming that tunable multi-material composites can be implemented into complex 3D geometries, builds upon proof of principle work we've done with planar 3D printed specimens [121].

A comparison of the tensile mechanics of the aortic aneurysm simulator with human tissue found that 3D printed models had higher stiffness and energy loss to that of human tissue (**Figure 12**). Vessel viscoelastic recoil can be described by energy loss, with small differences between energy loss and human tissue being unnoticeable to a trainee. However, material rigidity measurement (tensile stiffness), may be perceived through touch and may require further simulator enhancement for future use in sewing, cutting and handling techniques. Further development in 3D printing technology and testing of model materials to more closely replicate human tissue may additionally assist clinicians to better understand aortic anatomies and pathologies [59, 64]

Latex, polyurethane, silicone and PVA are various materials that have been used when replicating vascular models [135-138]. Newly developed and commercially limited compliant 3D printed materials have already demonstrated their use in medical simulation [139]. 3D printing is overwhelmingly advantageous for desired structure rapid printing (patient-specific anatomy from CT or MRI) [120]. Non-3D printed materials require curing within a negative mold to produce a geometric structure. This process adds extra time-intensive steps to create negative molds with internal cavity inserts that are needed to recreate patient-specific anatomies. Additionally, when using a multi-material composite, mechanics can be selectively tuned for achieving global or regional differences in model behaviour and can create material anisotropy (circumferential vs. longitudinal oriented fibres), if so required. Aortic wall collagen and elastin fibre orientation results in mechanical anisotropy [140] (both stiffness and energy loss) and changes substantially with disease [129, 141]. Conversely, globally homogenous and isotropic material propertied tissue analogues are generally produced when preparing simulators from moulded or cured materials [25, 142, 143]. Furthermore, by introducing pulsatile flow through our 3D printed models we are moving towards a more realistic and controlled environment where surgical residents can practice complex procedures.

# Chapter 7: Conclusion and Future Work

## *Conclusion*

In this study, we developed dynamic echo-compatible aortic simulators capable of reproducing motion reflective of human aortas when perfused under normal pulse pressure (physiological fidelity). This study also determined that manipulating the 3D printed material composite impacted the overall model mechanics while changing the model geometry had no effect on the model mechanics. Furthermore, biaxial tensile testing validated the conclusions made using echocardiography. These aortic surgical simulators would therefore enhance surgical simulation training making them ideal for learning and honing skills for complex aortic aneurysm repair surgeries.

## *Future Direction*

Designing patient specific aortic simulation models will benefit patient outcomes and assist surgical residents in determining treatment options and in training for complex aortic aneurysm repair procedures. For future consideration, more composite combinations will need to be examined to determine the *ex vivo* and/or *in vivo* mechanical properties of such blends. This will then help to adapt the structures to more accurately reflect patient specific aortas. A larger collection of patient data will need to be amassed to reflect patient population properties. Data analysis will allow us to create more realistic simulators with local mechanical variations to mimic exact tissue responses. Furthermore, circuit testing with a more realistic blood-mimicking fluid will enhance medical training and model validation by medical experts.

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