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Mock Tricuspid Valve for Right Heart Simulator

The thesis is submitted to University College Dublin
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Abstract

Keywords:
Tricuspid Valve Simulation, Biomedical Engineering, Heart Valve Mechanics, Cardiac Simulator, Prosthetic Valve Development, Material Testing, Design Prototyping, Physiological Accuracy,

This thesis presents the comprehensive development of a mock tricuspid valve designed to enhance the fidelity and functionality of heart valve simulators used in biomedical engineering education and research. The primary objective of this study was to engineer a tricuspid valve model that authentically replicates the anatomical and biomechanical characteristics of the natural valve while integrating seamlessly into a right heart simulator. This tool is intended for widespread use in educational settings and experimental research, aiming to improve the understanding and handling of cardiac valve dynamics among medical professionals and researchers.

The development process involved a systematic approach combining innovative design methodologies, material testing, and iterative modifications based on empirical data. Challenges such as replicating the intricate motion dynamics of the valve, ensuring material compatibility, and maintaining physiological accuracy under simulated conditions were addressed. Solutions included the utilization of cutting-edge materials that mimic the viscoelastic properties of native valve tissues and the application of advanced modelling techniques to predict and optimize the valve's performance in real-time physiological scenarios.

▸ Furthermore, the thesis elaborates on the implications of these developments for future enhancements of cardiac simulators. By achieving a higher degree of realism and functional accuracy, the new model sets a benchmark for developing surgical training aids and pre-surgical planning tools. These advancements are poised to significantly impact cardiac healthcare by improving the precision of surgical interventions. This work contributes to the academic field and has practical implications for improving patient outcomes in cardiac care.

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Oscar DALY

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List of Acronyms

Notation	Description	Page List
CVD	Cardiovascular Disease	2
TV	Tricuspid Valve	3
CT	Computed Tomography	20
FSI	Fluid Structure Interaction	14
BHV	Bioprosthetic Heart Valve	16
PU	Polyurethane	19
PET	Polyethylene Terephthalate	19
TTVR	Transcatheter Tricuspid Valve Replacement	18
TAVR	Transcatheter Aortic Valve Replacement	18
CAD	Computer Aided Design	6
PLA	Polylactic Acid	36
MRI	Magnetic Resonance Imaging	20
PIV	Particle Image Velocimetry	17
SLA	Stereolithography	35
FDM	Fusion Deposition Moulding	54

Part I

PROLOGUE

1

Introduction

1.1 Background

1.1.1 *Understanding the Need for Heart Valve Simulators*

- **Cardiovascular Diseases Prevalence**
  CVD's, including heart valve diseases, are the leading cause of global mortality and a significant contributor to disability. The Global Burden of Disease Study 2019 revealed that prevalent cases of total CVD nearly doubled from 271 million in 1990 to 523 million in 2019, with the number of CVD deaths increasing from 12.1 million to 18.6 million over the same period. The study highlights the continuing rise in CVD burden, especially in low- and middle-income countries, and a concerning trend of increasing age-standardized rates of CVD in some high-income countries where rates were previously declining.[Roth et al. 2020]

- **Valvular Heart Diseases Prevalence**
  Valvular heart diseases, a subset of CVDs, are characterized by abnormalities in the heart's valves, affecting blood flow within the heart chambers. These diseases encompass many conditions, including valvular stenosis, regurgitation, and prolapse, with the most common types affecting the aortic and mitral valves. Another study by [Nkomo et al. 2006] emphasizes the substantial prevalence of valvular heart diseases in the general population, affecting approximately 2.5% of the US population, with the prevalence increasing with age. This underscores valvular heart disease as an important public health problem.

- **Challenges in Heart Valve Treatment**
  Treating heart valve diseases involves complex surgical and non-surgical interventions, facing several limitations, highlighting the need for inno-

vative solutions. The challenges include the invasive nature of current treatments, the requirement for high precision in surgery to avoid complications, and the limited availability of treatment options for certain patient groups. [Musumeci et al. 2018]

1.1.2 *The Role of the Tricuspid Valve in Cardiac Function*

- Anatomical and Physiological Overview

The TV, an essential component of the heart's right side, plays a vital role in cardiac physiology. It is located between the right atrium and the right ventricle, acting as a one-way gate that ensures unidirectional blood flow. Structurally, the TV is complex, comprising an annulus, usually three leaflets (anterior, posterior, and septal), the supporting chordae tendineae, and the papillary muscles. This valve is crucial for electrically isolating the two cardiac chambers and maintaining efficient blood flow, with the variability in the number, length, and shape of the chordae tendineae and papillary muscles having significant clinical implications for valve function. [Sanders and Pluchinotta 2014]

- Pathologies Affecting the TV:

TV diseases, such as tricuspid regurgitation or stenosis, significantly impact heart function. Tricuspid regurgitation, where the valve fails to close properly, allows blood to flow back into the right atrium during systole, while stenosis restricts blood flow from the atrium to the ventricle. These conditions can lead to heart failure if left untreated. In these diseases, the annulus dilates, and leaflet tethering is disrupted due to right ventricular remodelling, which is the main mechanism responsible for most cases of tricuspid regurgitation. [Buzzatti et al. 2018]

These conditions underscore the need for accurate simulation models to improve diagnostic and treatment strategies. The complexity of the TV's anatomy and the prevalence of its pathologies highlight the necessity for innovative solutions to provide precise and personalized treatments, making the development of realistic simulation models critical for advancing cardiac care.

1.1.3 *Technological Advances in Heart Valve Simulation*

- Evolution of Heart Valve Simulators

The journey of heart valve simulators from early mechanical models to today's advanced computer simulations marks a significant evolution in cardiovascular medicine. Initially, simulators were simplistic, focusing on the basic mechanical functions of heart valves. [Takashina et al. 1990] developed one of the early cardiac auscultation simulators that digitally recorded, modified, and played back heart sounds characteristic of various heart diseases, marking a pivotal moment in the simulation technology for educational purposes.

Advancements continued with the introduction of tissue-based simulators for surgical training. [Ramphal et al. 2005] described a high-fidelity, tissue-based cardiac surgical simulator that significantly enhanced training realism, enabling surgical residents to practice various cardiac procedures risk-free.

- **Current State of TV Simulators:**

The focus has shifted towards creating highly realistic and patient-specific models. The Living Heart Project represents a groundbreaking step towards integrative simulators for human heart function. This simulator for a four-chamber human heart model created from imaging data illustrates the electrical and mechanical response of the heart, including its valves, throughout the cardiac cycle, offering a sophisticated tool for exploring heart function under various conditions. [Baillargeon et al. 2014]

Despite these advancements, current TV simulators still face gaps in realism, accessibility, or functionality. These limitations include the challenge of accurately replicating the intricate biomechanics of the TV and its interaction with the right heart dynamics under physiological and pathological conditions.

1.1.4 *The Importance of Realistic Simulation Models*

- **Benefits for Medical Training and Surgical Planning**

Realistic heart valve simulators have emerged as critical tools for medical education and surgical planning. These simulators allow practitioners to gain hands-on experience without any risk to patients, bridging the gap between theoretical learning and practical application. They are essential in pre-surgical planning, enabling surgeons to explore intervention strategies and anticipate challenges in a controlled environment. This aspect is crucial for complex procedures like heart valve surgery, where understanding the intricate details of the valve's anatomy and predicting the outcomes of surgical interventions can significantly affect patient outcomes.

▸ CONTRIBUTION TO PROSTHETIC VALVE DEVELOPMENT
Accurate simulation models contribute immensely to the design and testing of prosthetic valves. They enable the identification of design considerations that affect performance and longevity, such as the impact of geometric variations on valve mechanics. By simulating the dynamic behavior of valve leaflets and the surrounding blood flow, engineers and surgeons can refine prosthetic designs to enhance their functionality and durability, ultimately leading to improved patient outcomes.

1.2 Aims, Scope and Limitations

▸ PRIMARY OBJECTIVE

- To develop a mock TV that accurately replicates the anatomical structure and physiological function of the human TV for use in a heart simulator.

▸ SECONDARY OBJECTIVES

- To evaluate the realism and functionality of the developed valve model compared to existing simulators.
- To assess the potential of the modular sub-valvular aparatus such as the chordae tendineae.
- To explore the model's utility in testing and improving prosthetic valve designs.

Achieving these objectives will not only fill the current technological void but also potentially revolutionize how heart valve diseases, especially those affecting the TV, are understood, taught, and treated.

1.2.1 *Scope*

The primary focus of this research is the design, development, and testing of a mock TV intended for integration within a specifically designed right heart simulator. This project aims to utilize advanced biomedical engineering principles and methodologies to create a valve that closely mimics the physiological behaviours and properties of a natural human TV. The research will leverage materials known for their biocompatibility and mechanical resilience, ensuring the mock valve's functionality.

Additionally, the project will employ state-of-the-art CAD technologies to optimize the valve's performance under various physiological conditions and to refine the design in terms of anatomical accuracy. The scope will also include the iterative design process, fabrication techniques potentially involving 3D printing with various materials, and a series of validation tests within the simulator environment to evaluate hemodynamic performance, durability, and response to simulated physiological variations.

1.2.2 *Limitations*

There are inherent limitations associated with studies replicating biological function, this impacts the results and their applicability. Firstly, the complexity of replicating the exact physiological environment and dynamic conditions of the heart poses a significant challenge. The material selected for the mock TV, while similar, may not perfectly mimic the viscoelastic properties of natural heart valve tissue, potentially leading to differences in hemodynamic/hydrodynamic performance when compared to a biological valve. Additionally, the scale and scope of the study are focused exclusively on the TV, excluding other cardiac structures and valves, which may limit the understanding of the valve's interaction within the complete cardiac system. The research is also conducted within a simulator environment, which, despite its advanced design, cannot replicate every aspect of human physiology or the potential effects of systemic factors such as neurohormonal feedback. [Chatterjee 2005]

These limitations underscore the importance of interpreting the findings within the context of the study's controlled conditions, with an understanding that further research and testing are necessary to bridge the gap between simulation and real-world application.

1.3 Research Questions and Hypotheses

Based on the outlined objectives, the following research questions and hypotheses are formulated to guide the study and provide a clear framework for investigation:

1. Research Question: How accurately can the developed mock TV replicate the anatomical and physiological characteristics of the human TV?

    - Hypothesis: The developed mock TV will significantly replicate the anatomical structure and physiological function of the human TV, as evidenced by comparative analyses with clinical data(video).

2. Research Question: In what sense does the new valve model improve upon existing heart valve simulators?
   - Hypothesis: The new valve model will demonstrate superior realism and experimental adaptability compared to existing heart valve simulators, providing a more effective and versatile tool for medical training and surgical planning.
3. Research Question: What is the potential impact of the developed valve model on surgical training, planning, and the design of prosthetic valves?
   - Hypothesis: Integrating the developed valve model into surgical training and planning processes will lead to enhanced learning outcomes, more accurate surgical interventions, and informed prosthetic valve design, contributing to improved patient care and treatment outcomes.

1.4 Problem Statement

Current in-vitro simulators for heart valve diseases, particularly those affecting the TV, fall short in accurately replicating the valve's intricate anatomy and physiology. This gap limits their utility in characterizing prosthetic valves, a critical step in the development and evaluation process. Despite advancements in ex-vivo and in-silico simulation technologies, there's a distinct need for a TV simulator that closely models the real-world behavior of valves under various physiological conditions. This research addresses this by developing a TV simulator that enhances anatomical and physiological realism while maintaining the accessibility of prosthetic interventions and measurement systems like particle image velocimetry and pressure transducers.

▸ In summary, the research embodies a significant stride towards enhancing medical training, advancing prosthetic valve development, and filling a vital research gap in cardiovascular simulation technology, with the potential to impact broadly across the fields of biomedical engineering, and patient care.

2

Literature Review

2.1 Heart Valve Anatomy and Physiology

2.1.1 *Introduction to the Heart Valve System*

The heart valve system plays a pivotal role in the circulatory system, ensuring the unidirectional flow of blood through the heart and maintaining cardiovascular health. The cardiovascular system, as a closed circulatory network, is divided into two primary circuits: one that pumps blood from the heart to the lungs for oxygenation, the right, and another that distributes this oxygenated blood to the body's organs, the left. The heart comprises four chambers: two atria for receiving blood and two ventricles for pumping blood to the body. To maintain the blood's unidirectional flow, the heart has a valve in each chamber each of which are unique to the geometry of the chamber and have their own unique pathologies, they're strategically located between the atria and ventricles and between the ventricles and the arteries that emerge from the heart. [Frater 1962]

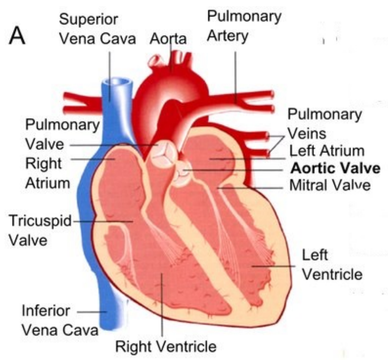

Figure 2.1: Heart Valve System [Rock et al. 2014]

The functionality and integrity of heart valves are essential for cardiovascular health. Heart valves open and close with each heartbeat, totalling over 3 billion times in a lifetime. This continuous operation occurs under significant pressure and within flowing blood, a viscous fluid rich in minerals, proteins, lipids, and cells. When valves become defective, they critically affect heart performance, leading to valve diseases requiring surgical intervention without curative drug treatments. Currently, diseased valves are replaced with artificial devices designed to emulate the valves' mechanical functions and restore heart functionality. However, these artificial valves can fail due to design flaws, material imperfections, or biocompatibility issues, often requiring risky reoperations. [Simionescu 2006]

Biomedical engineering strives to enhance treatments for valvular diseases, potentially impacting millions worldwide. This interdisciplinary field combines efforts from medicine, biology, engineering, and mechanics to improve device biocompatibility and explore tissue-engineering approaches that could enable the complete regeneration of valve tissues. [Simionescu 2006]

2.1.2 *Anatomy of the tricuspid valve*

The TV, an integral component of the heart's valve system, is located between the right atrium and right ventricle. It plays a crucial role in ensuring unidirectional blood flow from the atrium to the ventricle, thus maintaining the efficiency of the cardiac cycle. The TV's anatomy is complex and consists of several key structures: the annulus, leaflets, chordae tendineae, and papillary muscles.

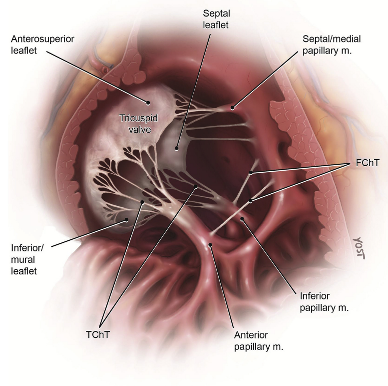

FIGURE 2.2: Sub-System of Tricuspid Valve [*Yost - Drawing Detailed View of Tricuspid Valve - English Labels | AnatomyTOOL* n.d.]

- Annulus: The annulus is a fibrous ring that anchors the valve leaflets and maintains their spatial configuration. It is the foundation to which the leaflets are attached, providing structural support for the entire valve apparatus.
- Leaflets: Typically, the TV has three leaflets named according to their position: the anterior, posterior, and septal leaflets. These leaflets act as one-way doors that open to allow blood flow from the atrium to the ventricle and close to prevent backflow.
- Chordae Tendineae: These are thin, string-like structures that connect the valve leaflets to the papillary muscles. The chordae tendineae ensure the leaflets close securely and prevent them from inverting when the ventricle contracts.
- Papillary Muscles: These muscles extend from the inner walls of the right ventricle and attach to the valve leaflets via the chordae tendineae. During ventricular contraction, the papillary muscles contract, pulling the chordae tendineae taut and ensuring the valve leaflets close properly.

The TV's structure is characterized by its adaptability and variability. The number, length, and shape of the chordae tendineae and the papillary muscles can vary significantly among individuals, which can be clinically significant. Dysfunctional papillary muscles or dysplastic chordae can lead to valve dysfunction, emphasizing the importance of understanding this complex anatomy for clinical assessment and intervention [Sanders and Pluchinotta 2014]

Furthermore, the TV is part of a dynamic apparatus that includes closely linked structures such as the annulus, leaflets, chordae, papillary muscles, and the right ventricle itself. Understanding the precise anatomy and function of these components is crucial for the success of percutaneous and surgical interventions aimed at addressing TV pathologies [Buzzatti et al. 2018]

2.1.3 *Physiological Functioning*

The human heart contains four main valves: the mitral, tricuspid, aortic, and pulmonary valves. These valves play a critical role in ensuring unidirectional blood flow through the heart's four chambers, contributing to the cardiovascular system's efficiency. Pressure changes in the heart chambers during the cardiac cycle tightly regulate the opening and closing of these valves.

- MECHANISM OF VALVE FUNCTIONING:
  - During diastole, the mitral and TVs open in response to pressure differences, allowing blood to flow from the atria to the ventricles.
  - As the ventricles contract in systole, the mitral and TVs close to prevent backflow of blood into the atria. Concurrently, the aortic and pulmonary valves open, allowing blood to be ejected from the ventricles to the aorta and pulmonary artery, respectively.
  - When ventricular pressure falls below that in the aorta and pulmonary artery at the end of systole, the aortic and pulmonary valves close to prevent the backflow of blood into the ventricles.

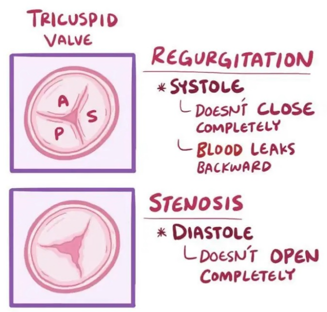

FIGURE 2.3: Illustration of Regurgitation vs Stenosis [*Tricuspid Valve Disease* n.d.]

- IMPLICATIONS OF VALVE MALFUNCTION:
  - Valvular Stenosis: Stenosis of a valve leads to a narrowing of the valve opening, restricting blood flow. This results in an increased workload for the heart chambers upstream of the affected valve, potentially causing hypertrophy and, ultimately, heart failure.
  - Valvular Regurgitation: Valve regurgitation occurs when a valve does not close properly, allowing blood to flow backwards. This leads to volume overload in the affected chambers, requiring the

heart to work harder to pump the additional volume, which can also lead to heart failure over time.

Both conditions, if severe, can significantly impair cardiac function and may require surgical intervention, such as valve repair or replacement, to restore normal blood flow dynamics and prevent further cardiac damage. For instance, afterload mismatch in valvular heart disease, particularly in aortic stenosis, occurs when the left ventricle cannot generate sufficient pressure to overcome the increased afterload caused by the stenosed valve, leading to decreased cardiac output. Surgical therapy, like aortic valve replacement, can relieve this mismatch and improve cardiac function, underscoring the importance of timely intervention in patients with valvular heart disease [Ross 1985].

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2.1.4 *Variability and Pathologies*

The TV is an essential component of the heart's right side and plays a critical role in the unidirectional blood flow from the right atrium to the right ventricle. Its anatomy and functioning can be affected by various factors, highlighting the importance of understanding its variability and pathologies;

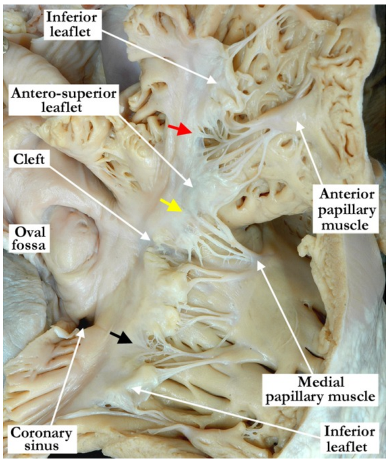


FIGURE 2.4: Disssected tricuspid valve with common anomaly of having 4 leaflets [Tretter et al. 2016]

- ANATOMICAL VARIABILITY:
  The TV typically features three leaflets (anterior, septal, and posterior), supported by chordae tendineae and papillary muscles. However, there can be considerable anatomical variability, including the number and size of leaflets, the structure of the subvalvular apparatus(papillary muscles, chordae tendineae and free wall), and the annular size. Such variations can impact valve function and are crucial for distinguishing between normal anatomical diversity and pathological alterations. In some instances, additional leaflets or unusual leaflet sizes are observed, affecting the valve's competence and flow dynamics. Understanding these variations is essential for accurate diagnosis and treatment planning, especially in surgical repairs and replacements . [Tretter et al. 2016]

- PATHOLOGIES AFFECTING VALVE FUNCTION:
  TV pathologies can be classified into primary, involving intrinsic valve anatomy alterations, and secondary, resulting from functional modifications due to other cardiac or systemic conditions.

  - Primary TV disease encompasses congenital abnormalities, infective endocarditis, rheumatic disease, and degenerative changes.

- Secondary TV disease is often related to left heart diseases or pulmonary hypertension, leading to tricuspid annular dilation and right ventricular remodelling. These changes can result in tricuspid regurgitation or, less commonly, tricuspid stenosis, significantly impacting cardiac function and patient prognosis.

Advanced imaging techniques are crucial for the detailed evaluation of TV anatomy and pathology, aiding in the accurate assessment and management of these conditions. [Shah and Raney 2008] One key aspect of tricuspid regurgitation that this study is looking to capture is the remodelling effects that tricuspid regurgitation has on the right ventricle and the valvular apparatus, some key variables that changes are the annular dilation, annular height, and circularity, which have been shown to increase in [Nam et al. 2023] and chordal/papillary muscle lengths in [Obase et al. 2016]. All of these parameters are hoped to be captured over the study.

- Need for Effective Simulation Models:
Given the complex anatomy of the TV and the wide range of pathologies that can affect it, there is a growing need for effective simulation models. These models, computational and experimental, can help in understanding the functional impacts of anatomical variability and pathological changes on the TV, facilitating the development of more precise diagnostic tools and treatment strategies. Such models are particularly valuable in planning surgical interventions and predicting their outcomes.

2.2 Advances in Heart Valve Disease Treatment

The landscape of treatments for TV disease has been evolving, incorporating both surgical interventions and transcatheter approaches to offer alternatives for patients with varied risk profiles. Surgery remains the standard treatment for TV disease, with techniques such as annuloplasty, leaflet repair, or valve replacement being common. However, surgical intervention is often reserved for patients without significant comorbidities due to the invasive nature of the procedures and the associated recovery times.

- Transcatheter Developments:
Transcatheter techniques have emerged as a forefront innovation for treating TV disease, especially for high-risk patients for whom traditional surgery is not viable. Transcatheter TV repair and replacement therapies

have shown promise in reducing tricuspid regurgitation and improving patient outcomes with less invasiveness than traditional surgery.

- In transcatheter tricuspid valve repair, various devices and techniques are being developed and tested, including coaptation devices, annuloplasty systems, and heterotopic caval valve implantation. These approaches aim to reduce tricuspid regurgitation by improving leaflet coaptation or reducing annular dilatation, offering symptomatic relief and functional improvement to patients with severe tricuspid regurgitation. [Hell et al. 2021]

- Transcatheter tricuspid valve replacement involves the percutaneous placement of a new valve within the native tricuspid annulus or a previously implanted surgical valve. This method has been advantageous for patients with severe TV disease who are ineligible for surgical repair or replacement, demonstrating comparable safety and short-term outcomes. [Gales et al. 2018]

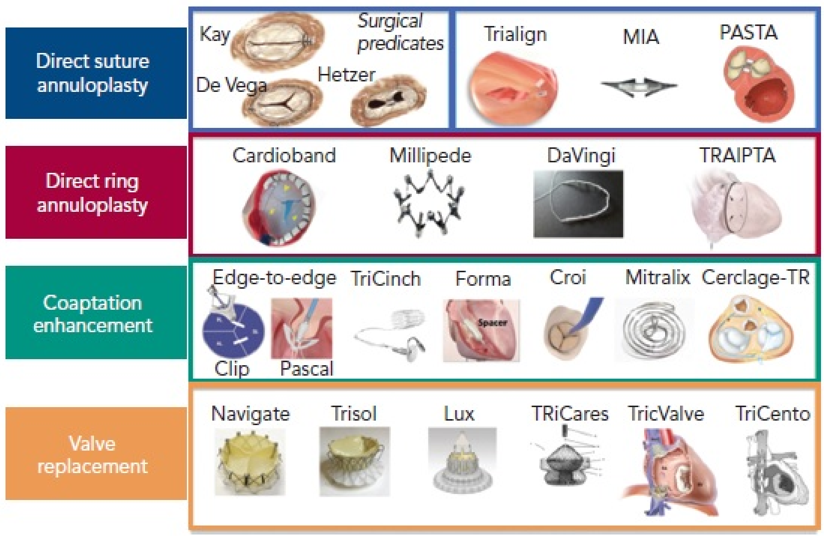


Figure 2.5: Current landscape of tricuspid valve replacement/repair products being used surgically [Curio et al. 2019]

Impact of Valve Modelling and Simulation:

Advancements in valve modelling and simulation have significantly impacted the development of new therapeutic techniques for TV disease. High-fidelity models created from patient-specific anatomical data have been instrumental in the design and testing of transcatheter devices, allowing for the precise customization of treatments. Computational simulations have also been crucial in understanding the biomechanical properties of the TV under various physiological conditions, aiding in optimising device designs for improved durability and performance. These innovations in modelling and simulation can potentially enhance treatment outcomes for TV disease, paving the way for the development of more effective and less invasive therapeutic options.

2.3 Current Models and Simulators

2.3.1 *Early Developments and Evolution of Physical Simulators*

The development of simulators in the field of cardiac care has a rich history, tracing back to the mid-20th century when the first conceptual models of blood flow dynamics and heart mechanics were introduced. These early models were primarily analogue systems that used electrical circuits to mimic the hydraulic and hemodynamic properties of the heart. A pivotal innovation during this period was the development of the Windkessel model [Westerhof et al. 2009], which was crucial in understanding arterial load and its effects on cardiac function; it described the haemodynamics of the arterial system in terms of resistance and compliance. It explained aortic pressure decay in diastole but fell short in systole. The development of physical simulators has come hand in hand with clinical, computational and biological research advancements. Increases in computational power have allowed for the development of more advanced finite element models of the heart, which can simulate complex interactions between blood flow and heart valve mechanics. Software advancements have also played a critical role, with tools capable of simulating FSI in the heart. Tangental clinical and biological studies have given more reason to develop physical simulators as new hypotheses can now be drawn from their learnings and then tested in a physical model.

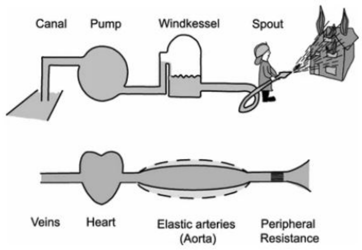


Figure 2.6: Concept of the WindKessel Model [Westerhof et al. 2009]

The advent of 3D printing and CAD technologies has revolutionized the fabrication of physical heart valve simulators. These technologies allow for high precision and customization of simulator components, enabling the production of complex valve geometries that accurately represent diverse anatomical variations seen in the population. This capability is vital for developing simulators that can be used for specialized surgical training and pre-surgical planning.

2.3.2 *Current State of the Art Simulators*

Heart valve models and simulators have significantly advanced, providing diverse tools for educational purposes, surgical planning, and research. These models range from low-fidelity simulators for basic educational use to high-fidelity, patient-specific models for complex surgical planning and research on prosthetics or interventions.

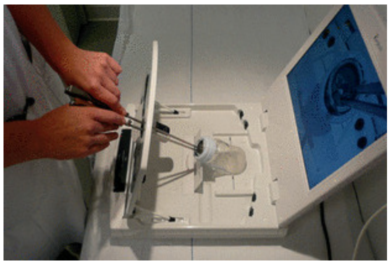


FIGURE 2.7: Set up for minimally invasive training [Verberkmoes and Verberkmoes-Broeders 2013]

- SURGICAL PLANNING AND EDUCATIONAL MODELS:
 Low-fidelity models, often made from commonly available materials, are used primarily for educational purposes. They provide an accessible and cost-effective means for trainees to develop surgical skills and understand valve anatomy and function. For instance, novel simulators made from components like baby bottles, combined with dental dam, offer simulation training in mitral and TV surgical techniques almost anywhere, at minimal cost. These models have been evaluated positively for their ability to replicate anatomy and surgical handling, proving very useful as training tools for cardiac surgery [Verberkmoes and Verberkmoes-Broeders 2013]

One attempt at such an educational simulator took an entirely tissue-based approach. [Ramphal et al. 2005] This offered a realistic environment for training cardiac surgical residents, replicating various cardiac surgical procedures. They are instrumental in low-volume cardiothoracic surgery units, providing trainees with pre-clinical experience and helping them respond to clinical situations associated with heart-lung bypass machine operation and changes in patient clinical parameters.
 Advanced, high-fidelity models are developed for surgical planning and research, employing technologies like 3D printing and silicone casting to create patient-specific valve models. These models enable simulation under dynamic physiologic conditions, allowing for the testing of surgical repairs and interventions with considerable accuracy. For example, dynamic ventricular simulators, capable of testing the quality of simulated heart valve procedures, utilize 3D printed valve suspension chambers and model pulsatile pumps to provide close-to-physiologic hemodynamic conditions for education and training in cardiac surgery [Zilinskas et al. 2022]

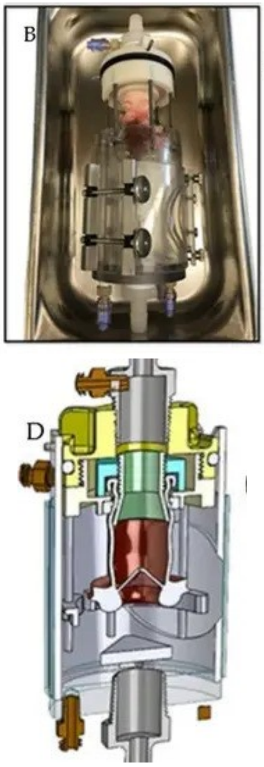


FIGURE 2.8: 3D valve suspension chamber with sutured valve [Zilinskas et al. 2022]

Simulation models for valve surgery, like those for mitral valve repair, offer detailed physiological simulation, including real-time feedback mechanisms. These models incorporate integrated sensors to generate, record, and display quantitative data on trainee performance, significantly enhancing the learning experience [Tozzi et al. 2022]

Utilizing 3D printed valve suspension chambers and model pulsatile pumps, these simulators offer close to physiologic hemodynamic conditions. They have been validated for testing aortic valve leaflet repairs and replacements, demonstrating the potential for extensive educational use in cardiac surgery. [Zilinskas et al. 2022]

Computational models are developed based on patient-specific data to predict clinical outcomes, aiding in planning medical procedures such as percutaneous pulmonary valve implantation and surgical repair of congenital heart diseases. These simulations have agreed well with clinical decisions, demonstrating their utility in personalized cardiovascular treatments. [Capelli et al. 2017]

- Research-focused Models:
  Simulators that can replicate the heart's mechanical and hemodynamic environment under various conditions are utilized for research, especially in developing prosthetics and testing interventions. These include both native heart valve simulations and artificial heart valve simulations, categorized based on the prototype model. Such models are pivotal in studying valve biomechanics, facilitating predictive surgical planning, and aiding in the design and evaluation of repair devices and prostheses [Zhong et al. 2014]

  Simulators designed to house an entire explanted heart subjected to pulsatile fluid-dynamic conditions enable the hemodynamic analysis of simulated surgical procedures. These setups benefit device testing, offering a platform for in-depth investigation of valvular surgeries and interventions. [Leopaldi et al. 2012]

- Fidelity to Human Anatomy and Physiology in Simulators:

  - Some BHV's, such as the Texas TriValve 1.0, have made significant strides in computationally capturing the kinematics and kinetics of the native TV. This model, reverse-engineered from a beating human heart, showcases how finite-element models can closely mimic the natural function of the TV, including disease-induced and repair-induced changes. This level of detail offers a promising platform for simulating surgical and transcatheter interventions, aiming to improve patient outcomes. [Mathur et al. 2022]

- Advanced simulators and models, especially those using 3D printing and computational simulations, have demonstrated a high degree of anatomical and physiological accuracy. These models can replicate complex heart valve geometries and dynamics, providing realistic conditions for training, surgical planning, and device testing. [Rabbah et al. 2013]

- Anatomical and Mechanical Studies: Comparative studies have been crucial in understanding the mechanical, morphological, and microstructural differences between the mitral and tricuspid leaflets and chordae tendineae. These studies reveal that while there are no major differences in leaflet mechanics between the two valves, chordal mechanics can vary significantly, influenced by anatomical location and valve type. This information is vital for surgical and computational applications, especially considering the TV's unique stresses and strains. [Pokutta-Paskaleva et al. 2019]

▸ PAPER RELEASED MARCH 2024 - POST THESIS WORK CONDUCTED

- A research group in Heidelberg [Karl et al. 2024] developed a rig for mitral valve investigations like the aims of this project as they worked to investigate the effects of the MitraClip device. The rig was designed with less anatomical accuracy and did not allow PIV measurement; however, this allowed the group to implement fixturing for motorized chordae tendineae adjustment and a camera system very close up and head-on to the valve to capture the coaptation process. This study ran a few different experiments: one with a mitral valve prosthesis, one with a mechanical valve, two with ex-vivo valves that were sewn onto an oversized elliptical frame and one experiment most close to the nature of this thesis where an in-vitro valve was

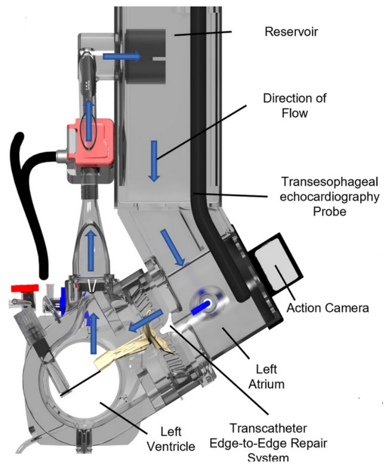


FIGURE 2.9: Side cross-section of simulator with dynamic state camera attachment [Karl et al. 2024]

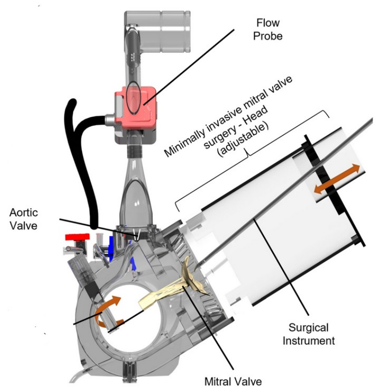


FIGURE 2.10: Side cross-section with static state surgery attachment [Karl et al. 2024]

▸ IMPACT ON UNDERSTANDING VALVE MECHANICS AND PATIENT OUTCOMES: Simulators play a crucial role in understanding the intricate mechanics of heart valves under various physiological and pathological conditions. They provide a risk-free environment for exploring new surgical techniques and device interventions, which is critical for advancing cardiac care. By allowing for the simulation of complex cardiac procedures and the testing of prosthetic valves and annuloplasty rings, these tools help improve surgical precision and patient outcomes. The feedback and data generated from simulators enable continuous learning and adaptation of best practices in heart valve surgery and intervention.

2.4 Materials and Methods in Valve Modeling

2.4.1 *Materials Used in Valve Modeling*

The development of heart valve models utilizes a range of materials, from biological tissues to synthetic polymers. These materials are selected based on their ability to simulate the natural behaviour of heart valves, which is critical for ensuring the models' effectiveness in clinical training, pre-surgical planning, and device testing.

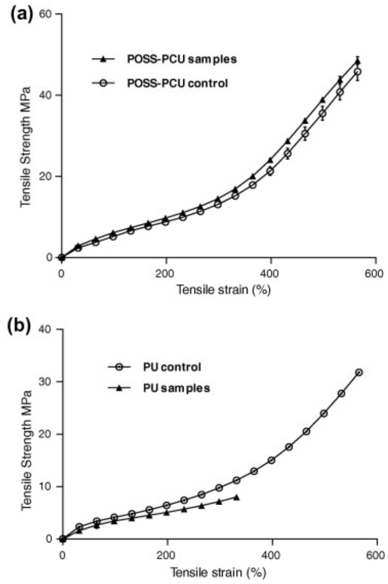


Figure 2.11: Comparison of polyurethane and poly(carbonate-urea)urethane for heart valve performance [Ghanbari et al. 2010]

- Biological Tissues:
  Biological tissues have been a cornerstone in heart valve modelling, particularly for BHV constructs. These tissues, typically derived from porcine or bovine sources, undergo treatments to enhance durability and reduce immunogenicity. The inherent biological properties of these tissues, such as their biomechanical behaviour and hemocompatibility, make them suitable for simulating natural heart valve function. Limitations such as potential calcification, immune reactions have been shown however porcine and bovinepericaridium remains commonplace in current TTVR and TAVR respectively. [Filová et al. 2009]

- Emerging Materials and Technologies:
  Recent advancements have led to the exploration of nanocomposite polymers [1] and hydrogels for heart valve modeling. Nanocomposite polymers, such as poly(carbonate-urea)urethane integrated with polyhedral oligomeric silsesquioxanes, exhibit enhanced mechanical properties and biostability. These materials show reduced calcification potential under in vitro conditions, making them attractive for the development of synthetic leaflet heart valves [Ghanbari et al. 2010]

  Hydrogels, derived from natural or synthetic sources, are being investigated for their potential in valve tissue engineering due to their biocompatibility and ability to support cell adhesion and proliferation. Challenges exist in balancing the bioactivity and mechanical durability of hydrogels to meet the demands of heart valve function.[Zhang et al. 2015]

[1] essentially adding nano-sized building blocks into the polymer matrix which enhances durability while maintaining flexibility and processability

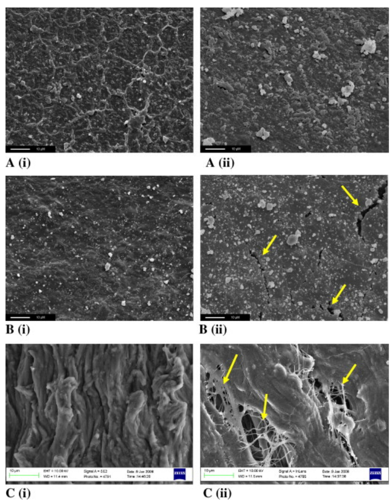


Figure 2.12: Comparison surfaces in fatigued (a) polyurethane (b) poly(carbonate-urea)urethane (c) valve leaflets showing tissue failure and fibre dehiscence marked by the yellow arrows in each [Ghanbari et al. 2010]

2.4.1.1 *Synthetic Polymers:*

Synthetic polymers offer an alternative to biological tissues with advantages in consistency, durability, and the potential for customization. Silicone rubber, PU and PET are among the polymers explored for heart valve modelling. PU, in particular, has shown promise due to its excellent tear resistance and similarity to the mechanical properties of natural valve tissue. The flexibility and durability of PU make it an appealing choice for synthetic heart valve leaflets, though challenges remain in mimicking the viscoelastic properties of natural valves. [Baxter et al. 2006] [2]

[2] In the context of this project, choosing a synthetic material is desirable due to the need for longevity, so finding a PU similar to those in TTVR devices that can mimic the TV's function is ideal.

- **Silicone Mitral Valve Studies**
  [Engelhardt et al. 2019] successfully developed a silicone mitral valve model for low-fidelity surgical training in annuloplasty procedures. The proven efficacy of the casting process in this is a good resource for this project.

Figure 2.13: Video of annuloplasty being performed on silicone mitral valve **(click to view video)**

Previous work on mitral valves [Ginty et al. 2018] also showed silicone to be a useful material for this purpose with utilization of silicone mould die to cast with, however, neither studies implemented their model in a dynamic environment.

- **Polyurethane Mitral Valve Study**
  [Luo et al. 2012] performed work modelling mitral valves, in their work they modelled the valve with a medical polyurethane (PURSPAN) and found efficacable results in thicknesses down to 0.125mm and chordal diameters of 0.7mm. This model was tested dynamically and simulated

computationally, so these material choices will be useful for reference in the later stages of prototype development.

Work from [Liao and Vesely 2003] (Vesely being a CroíValve Alumni) conducted work on porcine mitral tendineae mainly in tensile testing, finding a relationship to chordal thickness and extensibility/tensile modulus and also a range of average chordal thicknesses for the varying types of tendineae. This work provides a great baseline for basing judgments on what material to use for the polyurethane model.

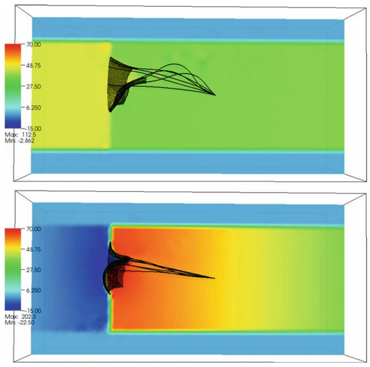


FIGURE 2.14: Fluid pressure field from FSI simulation of mitral valve model in [Luo et al. 2012]

2.4.2 *From Anatomical Data to Model*

- PRECEDENT OF LEFT HEART VALVE MODELS:

In the process of translating anatomical data from CT scans and MRI into functional heart valve models, researchers have developed sophisticated methods to accurately capture the complex geometry and dynamics of the heart's valvular apparatus. This transition from imaging data to practical, patient-specific models is pivotal in advancing cardiac care, offering insights for surgical planning, device testing, and personalized treatment strategies.

[Ionasec et al. 2010] introduced one of the first automatic computational systems for patient-specific modelling and quantification of the left heart valves, operating on cardiac CT and transesophageal echocardiogram data. Their method leverages discriminative learning and estimates parameters from volumetric slices, enabling a holistic representation of the aortic and mitral valves that account for anatomical variations.

In a similar vein, [Grbic et al. 2012] proposed a patient-specific model of cardiac valves from 4D cardiac CT data. Their model addresses the anatomical, functional, and hemodynamic aspects of the heart, utilizing a constrained Multi-linear Shape Model conditioned by anatomical measurements. This approach offers a more detailed representation of the heart's valvular structures and dynamics, facilitating the study of valvular pathologies and interventions.

One research group has done multiple studies on making anatomical models for procedure planning and device testing. The group 3d printed semi-flexible material to implant the MitraClip device[Vukicevic, Puperi, et al. 2017] and later did the same for the tricuspid valve [Vukicevic, Faza, et al. 2020] however models lacked physiological accuracy.

- CHALLENGES WITH RIGHT HEART:

The challenges of the right heart stem primarily from the complex anatomical and functional nature of the TV, which can be more difficult to capture accurately due to several factors:

- The TV's structure includes multiple leaflets (usually three) and a complex subvalvular apparatus, which are not symmetrically arranged. This complexity makes it harder to capture and model accurately using standard imaging techniques compared to the more symmetrically structured mitral valve.
- Both CT and MRI rely on good contrast resolution to differentiate between structures. The right heart's lower pressure and flow conditions can result in poorer contrast enhancement of the TV, further complicating accurate imaging and subsequent modelling. [Ahn et al. 2021]
- The tricuspid valve is subject to significant motion during the cardiac cycle, and capturing its dynamic behaviour accurately with CT and MRI is challenging due to potential motion artifacts. [Suh et al. 2017]

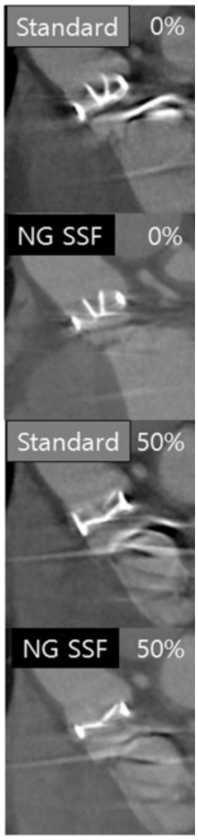


FIGURE 2.15: Example of CT image sets with and without motion correction of a 47-year-old-female with a prosthetic aortic valve, at a heart rate of 70bpm [Suh et al. 2017]

While these challenges have slowed progress, research on the right heart is catching up and with techniques like CT motion-correction algorithms and wide-detector CT with low radiation doses [Ahn et al. 2021; Suh et al. 2017] so the benefits of patient-specific modelling can be extended to the right heart as well.

2.4.3 *Evaluation and Testing Methods*

The evaluation and testing of heart valve models are crucial to ensure their functionality, mechanical properties, durability, and physiological accuracy. Several methodologies have been developed to assess these aspects, employing both in vitro and computational simulation techniques.

▸ MECHANICAL PROPERTIES AND DURABILITY TESTING:

- Bench Testing to ISO Standards: [Stasiak et al. 2020] reported on the design, development, and testing of a polymeric heart valve, including bench testing according to ISO 5840:2015 standards. Their study highlights the importance of rigorous testing in evaluating valve hydrodynamics, durability (tested to over 1.2 billion cycles), and preliminary biocompatibility in short-term animal

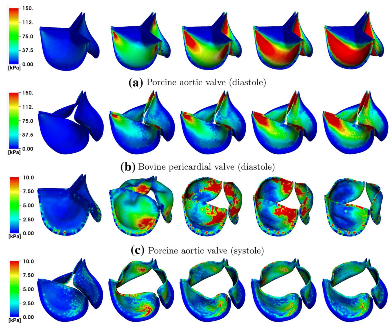
Resources:

- Revised ISO Overview

models. This comprehensive approach ensures that new valve designs meet international safety and performance standards before clinical application.

- In-vitro & ex-vivo Testing: In studies like those discussed previously many methods used to evaluate durability, one particular study [Walker 2010] developed a novel test chamber for an automated mock circulatory loop to evaluate the mechanical performance of heart valves. This method allows for simulating physiological flow conditions to assess valve functionality and durability. Such setups are vital for understanding how artificial heart valves would perform under real-life conditions.

- [Thomas et al. 2019] implemented a multiscale modelling approach to predict extracellular matrix microstructural changes in response to tissue-level mechanical stimuli in the TV's anterior leaflet. This study highlighted the importance of understanding microstructural alterations under mechanical loading for developing new tissue-engineered replacements.



(a) Porcine aortic valve (diastole)
(b) Bovine pericardial valve (diastole)
(c) Porcine aortic valve (systole)
(d) Bovine pericardial valve (systole)

FIGURE 2.16: Von Mises stress (kPa) on the porcine aortic (a, c) and bovine pericardial (b, d) valves during diastole (a, b) and systole (c, d) [Lee et al. 2020]

▸ PHYSIOLOGICAL ACCURACY AND FSI MODELS:

- [Lee et al. 2020] developed dynamic computer models of BHVs in an experimental pulse duplicator based on the immersed boundary method for FSI. These models simulate porcine tissue and bovine pericardial BHVs under conditions used to assess performance in commercial and custom pulse duplicators. The agreement between computational simulations and experimental data for bulk flow rates, pressures, and valve opening areas underscores the potential of FSI modelling in valve design and evaluation.

- [D'Amore et al. 2018] introduced double component deposition, an electrodeposition technique for fabricating valve scaffolds with controlled macro-scale morphology, mechanics, and microstructure. This method allows for the creation of fully assembled stentless multi-leaflet valves, demonstrating the capability of emerging fabrication techniques in producing scaffolds that closely mimic natural valve behaviour.

- [Laurence et al. 2019] conducted an investigation into the regional variations in the biaxial mechanical properties and stress relaxation behaviours of porcine atrioventricular heart valve leaflets. Their findings underscored the significance of accounting for regional differences in valve biomechanics to refine computational models for predicting diseased or surgically altered valve function. This approach allows for a more accurate simulation of heart valve dynamics and mechanical behaviour under varying physiological conditions.

These studies are very important to reference when conducting work on physical simulators, and they can provide key insights that will inform valve design and testing. Visualizing where stress buildup occurs in heart valve structures is particularly useful for understanding where fatigue might occur in physical valve prototypes.

2.5 Regulatory and Ethical Considerations

2.5.1 *Regulatory Standards for Valve Models and Simulators*

A comprehensive regulatory environment governs the development and use of heart valve models and simulators, particularly those intended for biomedical engineering or pre-surgical planning. This framework ensures that these tools meet stringent standards for accuracy, safety, and efficacy before being implemented in clinical settings.

- Experimental Validation and ISO Standards:
  The experimental validation of cardiac simulators, as described by [Bazan and Ortiz 2016-Mar-Apr], is a critical step in developing prosthetic heart valves. Their work underscores the importance of adhering to physiological conditions and meeting the requirements of ISO 5840 standards, which set global benchmarks for cardiovascular implants and cardiac valve prostheses. This ensures that simulators provide a suitable environment for testing valve performance in the mitral, aortic and tricuspid positions under varying heart rates.

- Living Heart Project and Integrative Simulators:
  The Living Heart Project represents a significant advancement in simulating human heart function through a four-chamber heart model. This integrative simulator showcases the potential of computational models of the whole heart, including its valves. Such initiatives illustrate how regulatory standards can evolve to include advanced computational methods and integrative simulators for heart valve research and development [Baillargeon et al. 2014] and how other research work can contribute to

new regulatory standards and set a precedent for how future heart valve simulators should be conducted.

2.5.2 *Ethical Implications*

The development and deployment of physical heart valve simulators involve significant ethical considerations, especially concerning patient safety, informed consent, and access to innovative technologies.

- Patient Safety:
  The primary concern in the development of new heart valve simulators is to ensure patient safety. As these simulators are used in educational and pre-surgical planning, it is crucial that they accurately mimic human physiology to prevent potential errors during actual surgeries. Ensuring the safety and efficacy of these simulators involves rigorous testing and validation processes to avoid any adverse consequences during training sessions or surgical planning. [Rajab et al. 2013]

- Informed Consent:
  Although physical simulators are not implanted in patients, obtaining informed consent is crucial when they are used in scenarios that involve patient interaction, such as educational demonstrations or pre-surgical planning. Patients and participants should be fully informed about the procedures being simulated, the use of their data (if applicable), and the nature of the demonstrations to uphold ethical standards of autonomy and consent. [Fletcher 1983]

- Access to Innovation:
  Access to high-quality educational tools and advanced simulators should be equitable to ensure that all medical professionals, regardless of their institution's economic status, can train with the best available tools. This is essential for maintaining high standards of healthcare globally and ensuring that advancements in medical training are accessible to all healthcare providers. [Aultman et al. 2018]

2.6 Research Strengths and Gaps

2.6.1 *Research Strengths*

- Advancements in Imaging and Computational Simulations:
  In recent years, significant advancements in imaging techniques and

computational simulations have been witnessed, enhancing the understanding and modelling of heart valve mechanics. High-resolution imaging modalities such as 4D CT and MRI have enabled detailed anatomical and functional assessments of heart valves in real-time. These advancements have facilitated the development of more accurate computational models that can predict how valves behave under various physiological and pathological conditions.

- Integration of Patient-Specific Data into Valve Design:
  Incorporating patient-specific anatomical data into the design and testing of heart valves is a major strength in current research, and it can significantly enhance the efficacy and safety of treatments as outcomes can be predicted. This approach has led to the development of customized prosthetic valves instead of one-size-fits-all valves where there is an increased risk of failure. [Kidane et al. 2009]

2.6.2 *Research Gaps*

- Anatomical Variability:
  The significant anatomical variability of the TV presents challenges in creating universally applicable models. For example, the presence of additional leaflets or variations in chordae tendineae and papillary muscles can significantly impact valve function and complicate the design of surgical interventions or prosthetic valves. Understanding and incorporating this variability into models remains a challenge. [Tretter et al. 2016]

  Being able to, with the same piece of equipment, account for changes like these in real-time would be greatly beneficial to studies on the TV devices and interventions.

- Material Properties and Biomechanics:
  Accurately simulating the material properties and biomechanical behaviour of the TV leaflets and subvalvular apparatus is complex. Finite element modelling studies have attempted to address this by adjusting material parameters and considering different collagen fibre distributions. However, these models still face limitations in accurately representing shear behaviour and the complex interactions within the TV apparatus under various physiological and pathological conditions. [Stevanella et al. 2010]

Developing materials that can mimic the viscoelastic properties of natural valve tissues and withstand the mechanical stresses of long-term operational testing is a critical gap in the field. This would afford researchers the time to gather more data on the same specimens in testing, increasing the reliability and statistical significance of the results.

- DYNAMIC BENCH-TOP SIMULATION CAPABILITIES:
Enhancing the dynamic response of simulators to replicate real-time cardiac motions and valve mechanics accurately. This includes the ability to simulate different heart rates, pressures, and pathological conditions to understand their impacts on valve function and durability. Materials that accurately mimic the biomechanical properties of natural heart tissues are also challenging due to the complex nature of biological tissues. These materials must withstand the mechanical stresses of long-term operation to be effective for training and testing.

Current simulators have often opted to integrate dissected porcine hearts into their setups rather than develop synthetic materials that can only withstand a very limited amount of testing before failure. This is a significant gap in the field as it limits the ability to perform long-term projects investigating aspects of valve design and function.

Authors & Year	**Key Findings**	**Study Objective**	**Methodology**	**Relevance to Your Study**	**Key Learnings**
Filová et al. 2009	Calcification of PU in vivo	Overview of tissue-engineered heart valves	Meta-Analysis	Material Choice	Limited sample size
Baxter et al. 2006	Flexibility and durability of PU	Overview of synthetic materials in heart valves	Tearing energy and crack growth rate tests	Material Choice	Performs even better at elevated temperatures
Aggarwal et al. 2013	Converting CT to 3D	To map patient-specific aortic valves	Spline-fitting with mathematic models using echocardiographic images	Modelling / Morphology	Maps microstructure of leaflets
Leopaldi et al. 2012	Comparative data for experimental and simulatory flow-loop	To develop a flow loop with a porcine heart	Endoscopic imaging and hemodynamic measured with ultrasound flowmeter and piezoelectric transducers	Simulator Development	Compares pressures and flow rates
Zilinskas et al. 2022	Simulator succesfully used for performing valve replacement training	To develop a surgical training simulator using porcine aortic roots	Porcine aortic valve dissected and tether to chamber	Simulator Development	Demonstrates efficacy of bench-top simulators

TABLE 2.1: Comparison of key points in the literature review

Part II

METHODOLOGY

3

Design and Prototyping

▸ SYNOPSIS In this chapter the mock valve modelling and prototyping is discussed from conception to completion. Different approaches are disccused in regards to the steps the core design went through;

- Flat Valve: The simplest approach involves creating a flat valve model with leaflets cut to proportion. This design is straightforward to fabricate and provides a basic representation of the TV form.
- Ballooned Valve: A more anatomically accurate design involves creating a balloon-shaped valve similar to regurgitant valves. This approach aimed to mimic the physiological behavior of the TV more closely in the diseased state.
- Ballooned Valve with Chordae Tendineae: Building upon the previous design, this approach incorporates chordae tendineae to simulate the TV's complex structure more accurately with practical considerations to how the valve would be modelled, fully represenatively or a simple tri-leaflet valve.
- Anatomical Valve without Chordae Tendineae: This approach involved converting CT scans of an anatomical valve models, providing a highly realistic representation of the TV capturing the likeness very proportionally.

As well as the design of the other components such as the chordae tendineae and fixturing design.

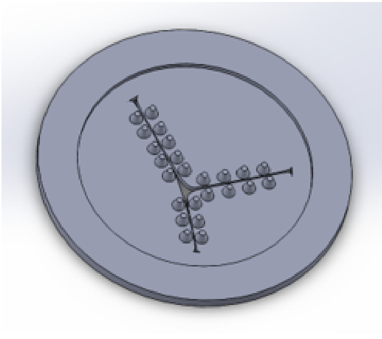


FIGURE 3.1: Flat Valve Model

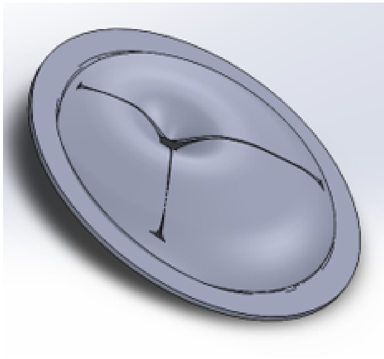


FIGURE 3.2: Billowed Valve Model

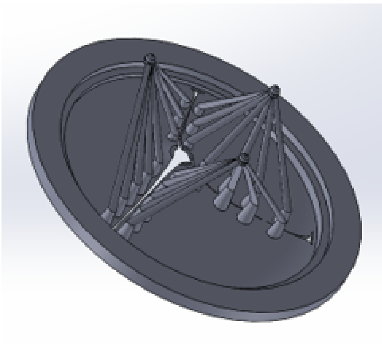


FIGURE 3.3: Billowed Valve with Chordae Tendineae Model

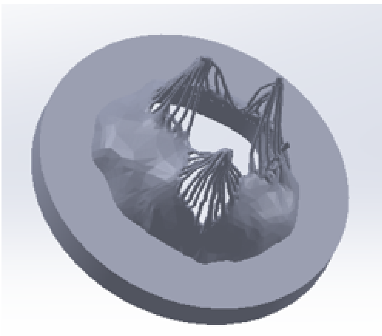


FIGURE 3.4: Anatomical Model

3.1 CONCEPTUALISATION AND INITIAL DESIGN

The essence of a design process is inherently iterative and exploratory. It takes the form of a cycle of conception, experimentation, evaluation, and refinement. This iterative cycle is fundamental to translating abstract ideas into tangible solutions that meet set goals.

At the heart of the design process lies trial and error—a methodical yet flexible approach that takes the discovery of unexpected challenges and leverages them as opportunities for learning and input. Initial ideas are transformed into preliminary models, serving as the first step in a series of continuous interactions between designing, testing, and iterating.

The dynamic nature of this process sets a strong base to pivot strategies, incorporate new technologies/materials, and adapt to findings in real-time. The design changes throughout this project were not merely reactions to setbacks but were driven by a pursuit of optimization, whether in response to material limitations, fabrication challenges, or new modelling insights.

The initial vision of the in-vitro TV was formed on reflection of the literature review. It is crucial to consider both the anatomical fidelity required for effective simulation and the technical feasibility of creating a functional model when developing initial concepts which can then be adapted as the project moves forward and firmer boundaries are discovered.

The approach taken was to start prototyping with the simplest design and gradually increase complexity as the project progressed. This allowed for a more systematic exploration of the design, ensuring that each iteration built upon the insights gained from the previous one with respect to all stages of manufacturing. A minimal time investment in preliminary modelling allowed the prototyping process to be refined in tandem. This was essential to finishing with a refined final model, balancing anatomical fidelity with fabrication feasibility and functional performance.

3.2 Design Criteria

The design criteria were established to guide the development of the mock TV. These criteria were informed by the project's objectives, the gaps in the literature, and the technical constraints of the fabrication process. The design criteria were as follows:

- **Criterion 1: Anatomical Fidelity**
  The mock TV should precisely resemble the anatomical structure of the TV, capturing the key features of the valve's leaflets, annulus and chordae tendineae and, where possible, to account for the variations.

  - Justification: To maintain a realistic simulator, an effort must be made to ensure representative geometry to provide a realistic evaluation tool for medical devices.

- **Criterion 2: Functional Performance**
  The mock TV should exhibit the functional characteristics of the TV, including the ability to open and close in response to fluid flow, and the capacity to simulate regurgitation simulating the physiological and pathological conditions of a natural TV.

  - Justification: Without these functional characteristics, the mock valve would be limited in applicability for integration and characterisation of a prosthetic valve device.

- **Criterion 3: Material Compatibility**
  The materials used in the fabrication of the mock TV should be flexible, durable, and suitable for the intended application, ensuring that the valve can withstand fluid flow and mechanical stresses.

  - Justification: The valve, once integrated into the right heart simulator, will be subjected to continuous fluid flow and mechanical forces over a long period, necessitating the use of materials that can withstand these conditions over a long period.

- **Criterion 4: Fabrication Feasibility**
  The design of the mock TV should be amenable to the fabrication process, considering the limitations of the 3D printing and moulding techniques used in the project.

  - Justification: Some aspects of TV performance depends on biological factors that are difficult to replicate, such as collagen fibre alignment. This design should be able to be fabricated in a way that can be easily replicated and improved upon in the future.

- **Criterion 5: Scalability and Modifiability**
  The design of the mock TV should be scalable, allowing for the creation of multiple valve moulds easily by hot-swapping the scanned and refined CT models with varying anatomical features and functional characteristics

  - Justification: As the overarching project of the right heart simulator progresses past this thesis, the valve should be easily replicated and improved upon again so that future goals can be met.

3.3 Modelling and Design Iterations

3.3.1 *Simplified Valve Designs*

- Flat Valve: As illustrated in Figure 3.1, the flat valve was the first to be developed, with the idea being to use it as a basis for developing the complexity. The shape of the leaflets was designed by overlaying images of regurgitant valves from a study which modelled the TV at different stages of regurgitation [Nam et al. 2023] in systole normal to the annulus of the valve over a disc in SolidWorks and then drawing a spline aligned with the leaflet shapes. In later iterations of this basic structure, considerations started to be made for the chordae tendineae, including whether to include them and how. There were two schools of thought on this method:

    - Having the tendineae attached within the mould and casting the part all of the same material.
    - Casting the valve part without tendineae and then attaching tendineae after being made from another material.

  It wasn't until outcomes in the prototyping phase, section:§ 3.4.3 that this was fully decided on based on experimental results.

- Billowed Valve:
  The next layer of complexity for the valve to visually replicate an anatomical valve was adding the billowed effect. The literature review section:§ 2.1.4 showed how in regurgitant valves the annulus dilates, tendineae weaken and the valve develops a partial prolapse, this was reflected in later iterations by creating a revolve feature in SolidWorks in a 'U' shape which was centred within the leaflets (as opposed to the annulus) to overlay the cusp cut on top of. Later iterations of this model included the chordae tendineae and added extrusions on the leaflet cusps to allow the leaflets to coapt properly; however, as prototyping

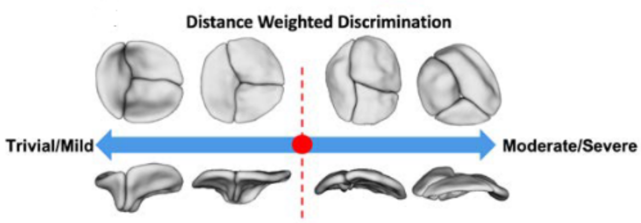


Figure 3.5: Visual representation of regurgitant valve morphological progression [Nam et al. 2023]

progressed and the possibility for using a model converted from a CT scan grew brighter, the work on the representative models was put on hold.

3.3.2 *Represenative Valve Designs*

- Anatomical Valve Model:

While development on the mock valve was progressing, the idea for a more anatomically accurate valve began to look favourable, for it aligned more closely with the project's aims. The idea was to use a CT scan of a TV and then convert this into a 3D model. There were a few options for this; a software package like Mimics can be used to do it quickly; however, this package is very expensive, or open-source programs like Ostrix. Due to the difficulties in capturing the geometry of tricuspid valves in CT and the less user-friendly interface of Osirix, it was decided that a pre-existing model from an online STL repository would be used as a base instead and then refined to fit the project's needs.

With this approach, the traceability of the model is lost, but with confirmation from the designer that it was developed from imaging from a human, it was deemed fit for purpose.

Harnessing the converted model presented many unexpected challenges; this was discovered when initially trying to import the STL model into SolidWorks, and many zero-thickness geometries were present. The main technical issues with this model were:

- Self-intersecting faces,
- Non-manifold edges
- Holes throughout the surface
- Inaccuracies in the model
- Widely varying leaflet thickness

The development of this model had originally been intended to provide educational illustrations of the anatomy, not to be produced physically, so work began to refine it for physical production.

3.3.3 *Model Refinement*

Several software packages were tried and tested to tackle these issues and get the converted model to a usable state to see which could effectively resolve the problems. The leading software used was Meshlab, Meshmixer, Blender, AutoCAD NetFabb, and SolidWorks.

Meshlab is an open-source software for processing and editing unstructured 3D triangular meshes. Mesh-lab is a very low-level[3] program; it was used to try and remove the non-manifold edges; however, the methods to do so require knowledge of advanced mathematical equations and how to manipulate them. With initial attempts and references to online tutorials resulting in the model being distorted and unusable, the decision was made to find more user-friendly software.

[3]Low-level programming involves direct manipulation of hardware resources, offering granular control but requiring detailed hardware knowledge.

AutoCAD NetFabb seemed a fitting replacement as mentioned in many online forums discussing MeshLab's limitations. Initially designed for additive manufacturing pre-processing, it also contained a diverse suite of valuable tools to repair the model. Personalised repair kits could be designed to fix specific issues for the TV and, most importantly, had been developed for higher-level applications.

- Repair Scripts

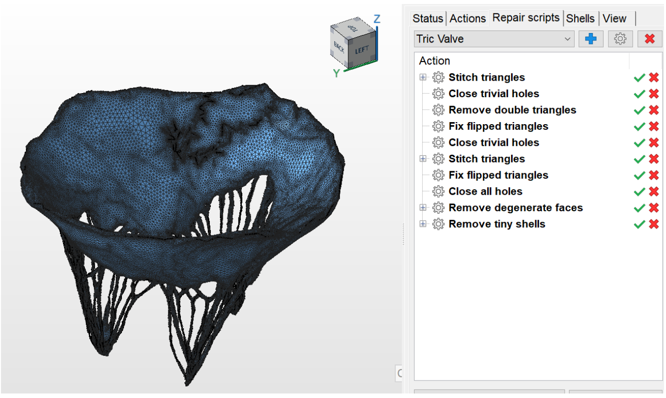


FIGURE 3.6: Netfabb Repair Scripts

- Shell

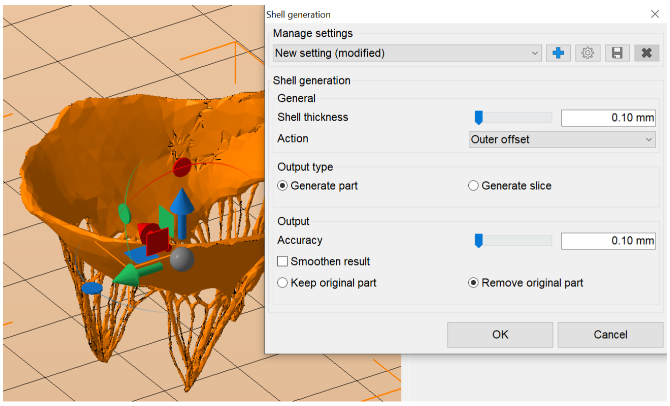


FIGURE 3.7: Netfabb Shell Tool

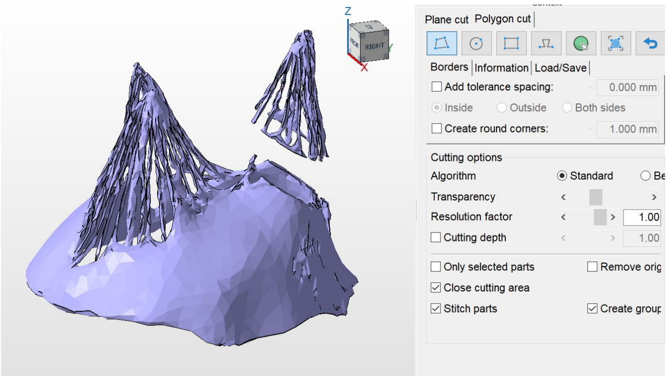


FIGURE 3.8: Netfabb Cutting Tool

After the repairing and hollow shell process was complete, the model could trial some prototyping methods; the model was given a retainer ring to allow for easy mounting and printed with a FormLabs SLA printer. From initial attempts at fabrication using the silicone moulding method, it was evident that casting the tendineae would not be feasible, so a tool within NetFabb was found to remove them from the geometry.

From here, the model was imported into Blender to further refine it, as NetFabb was not capable of detailed mesh sculpting to refine the model by hand. In Blender, the main objective was to smooth out the bumps in the leaflets left from the cuts and ensure they were of a uniform thickness without straying too far from the original geometry.

Meshmixer was used in tandem with Blender as it contained a handy thickness analysis tool which could be used to see the varying thicknesses of the leaflets in the imported model. Blender was then used to manually edit the model using its sculpting tools to thicken or thin the surface where appropriate. This would have been much easier if a dynamic thickness overlay had been developed in Blender and attempts to do so were made. Still, as the coding for personalised tools in the open-source program wasn't well documented, it was abandoned for the former method.

Once the final valve model was finalised, the decision was made to flatten the saddle shape of the geometry to simplify the moulding and mounting processes; some surgical studies like [Mahmood et al. 2010] showed that for mitral valves, it does have a structural disadvantage; however, this did not reduce the ability to coapt correctly.

3.4 PROTOTYPING

3.4.1 *Mould Die Iterations*

FIGURE 3.9: Silicone Mould Design

- PRELIMINARY PROTOTYPING METHODS The prototyping method went through a few key stages. Throughout the simplified valve modelling stage, the running methods were creating PLA prints of the flat and billowed valve models and then using a silicone mould to capture its likeness. Through feasibility testing, it was found this method was not suitable as;

  - Silicone moulds were not firm enough in casting to maintain sub 1mm thicknesses and deformed under their own weight.
  - The mould release agent was less effective on PU-Silicone interfaces than expected.
  - The moulds, even with appropriate vent holes and degassing, would still have large air bubbles and not fill out to the edges of the part.

  As it seemed no amount of optimization of this method would improve results, further work was done to find a more suitable method.

- PRESS MOULDING This new method involved designing blocks in SolidWorks as a separate body to the valve part and using the 'Combine' tool to subtract the valve part. This hollowed block could then be split in the middle to create a two-part mould.
  The PU resin could then be poured into the cavity part, and the lid part pressed on top with a C-clamp to create a tight seal.

  This method was trialled on the simplest flat valve model to seek learnings for my complicated designs; some such learnings were;

  - To measure the volume of the 2-part casting fluid with precision scales instead of doing it by eye, having the mixture slightly off resulted in gross discolouring and an extremely sticky surface.
  - To develop a new chordal attachment method as the trialled insertion buds were ineffective.

FIGURE 3.10: Press Mould Design and cast part for Flat Valve

As the modelling stages evolved in complexity, so did the prototyping; in trialling preliminary anatomical valves for press moulds, it was discovered that due to STL interaction issues with solid CAD geometries, the valve could not be moulded directly, and so a mould die was designed and prototyped of the valve part mould die, making it a two-step process to work around this modelling issue.

A deep-cast epoxy was used to pour into these die to form the moulds for the valve; the key learnings from this process were;

- Thin, easily breakable walls for the mould die were imperative as the epoxy parts were difficult to remove; this had a downside of making the die single-use. This was hoped to be avoided with notches to pry the epoxy part out, but ultimately, it wasn't effective.

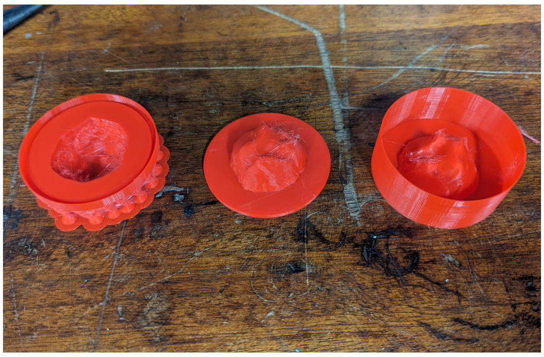
- A split mould was trialled as it was thought to make demoulding the casted part easier; however, this resulted in significant lines being apparent and didn't help significantly in demoulding, so it was abandoned.

- Embossing and debossing key slots in the die ensured the moulds could be aligned correctly.

- Sanding down the PLA prints to a smooth finish, so, in combination with a mould release, grease greatly eased the demolding of the die.

- Initial drafts of the mould die joined the cusps of leaflets directly; however, it was found that extruding the cusps axially stopped excess material from curing past the cusp of the leaflet and also acted as a central large key slot for pressing the moulds into each other.

(a) First draft mould die



(b) Later iteration of mould die

(c) Split mould trialing

(d) Draft and casted part of epoxy moulds

FIGURE 3.11: Iterations of epoxy mould die method

3.4.2 *Casting Material Considerations*

The two main options for material under consideration were PU and silicone; with needing a low shore hardness and casting viscosity for the initial mould designs, a shore 30a PU from Xencast was chosen as it had much lower viscosity than popular silicones of the same hardness. It also similar properties to the PURPLAN PU used in [Luo et al. 2012] which yielded good results, efforts to get samples of PURPLAN were made but lead times and costs were prohibitive so the XencastPX30 was the closest alternative within budget.

Once successful PU parts had been cast, the eco-flex 00-20 silicone was trialled to see if it performed similarly. Results were unsuccessful with the silicone parts, coming out not fully cured after extended curing times were tried, this might have been due to the low temperature in the lab however was not investigated further as PU parts were successful.

Technical specifications:

- PX30
- PURPLAN

3.4.3 *Chordae Tendineae*

Initial conceptualization of the chordae tendineae involved having the valve as one homogenous material with the tendineae attached within

FIGURE 3.12: Failed silicone casting trial part

the mould. However, as the project progressed and the complexity of the valve increased, it was decided that the tendineae should be a separate part that could be attached after the valve was cast. This was decided on as the elastic modulus of the tendineae was vastly different as they function to be pulled taut to stop the leaflets from prolapsing.

▸ DESIGN OF CHOICE: A 0.1mm nylon fishing wire was chosen to represent the tendineae as it was thin enough to be completely collapsible and not interfere with the opening in the diastolic phase. The attachment to the valve was the more challenging aspect, a few methods were considered and tested:

(a) Embedded method trialing (b) Cyanoacrylate method trialing

FIGURE 3.13: Testing the methods for attaching the chordae tendineae to leaflets

- Suture patterns along the cusp of the leaflets.
  - A short continuous suture was used to attach a few tendineae to the leaflets on a sample piece of PU how on a gentle tensile test the suture ripped out as the PU wasn't strong enough to hold.
- Using a small hole in the leaflet to thread the tendineae through and then knotting it on the other side.

- This method also failed as the elasticity of the PU made it so the knot would have to be PU would rip anyway.

• Embedding the wire in the PU leaflets.

- While hopeful the embedding technique proved not feasible as the wire just slipped out, there was an attempt made with thick and thin layers of additional PU but to no avail.

• Gluing the tendineae to the leaflets with a cyanoacrylate adhesive.

- While this method showed initial promise as the adhesive was strong enough to hold the tendineae after seconds of curing when 24 hours passed, the adhesive would harden much stiffer and deform the leaflets, making them very rigid.

• Gluing with B7000 adhesive.

- The B7000 adhesive was chosen as it was a flexible adhesive, initial tests weren't fruitful but if left to set fully over 24 hours the bond became very strong and the leaflets retained their flexibility while also only needing a minuscule amount for a good hold so the very thin thickness of the leaflets wasnt negated.

3.4.4 *Fixturing*

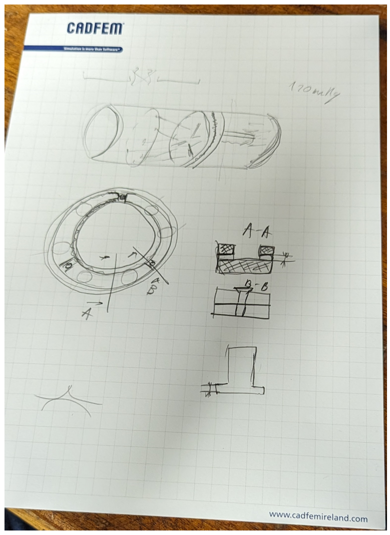


FIGURE 3.14: Initial Sketch of Fixturing

The design criterion was considered carefully before modelling the test fixturing. The main desired outcomes from the testing that the fixturing should facilitate were:

• The chordae tendineae should have anchors which are fully adjustable axially and angularly to allow for a range of testing positions.

• The valve should be mounted in a way that the leaflets are not obstructed so the valve can be viewed from multiple angles for thorough evaluation.

▸ DESIGN OF CHOICE: A combination of 3D printed parts, off-the-shelf components and hand-cut threaded rods were used to emulate the initial sketch of the rig

The threaded rods allowed for the anchoring points of the tendineae to be adjusted axially. Attached to the rods was the ring system with notches that could be adjusted angularly which the mock tendineae were passed through and fastened to with a rubber wedge.

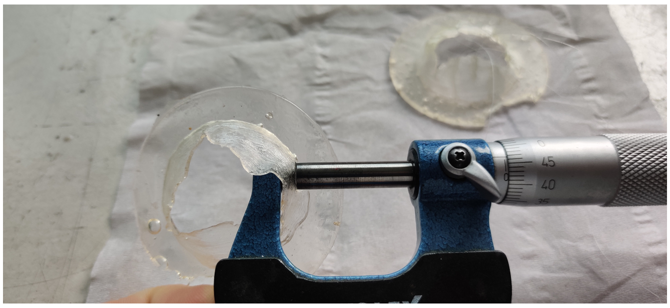
4

Experimental Setup and Testing

4.1 Design Validation

To investigate the experimental thickness of the valve model and compare to the theoretical thickness from the CAD model a series of micrometer measurements were taken on the leaflets. This was done for both models with chordae tendineae attached and without to also get a measured estimate of how much thickness the nylon wire and adhesive adds to the leaflets.

(a) Testing the thickness with the chordae tendineae attached



(b) Testing the thickness without the chordae tendineae attached

Figure 4.1: Thickness investigation for the experimental model of the valve

4.2 Assembly of Fixturing

The assembly process began with seating the valve in its ring holder and passing the chordae tendineae through the evenly spaced notches of the ring fixture.

The chordae tendineae were tensioned evenly by hanging the two-part fixture in a retort stand and manually pulling the wires through the notch fixture until visibly evenly tensioned, at which point Buna-N rubber wedges were inserted to hold the tension in place.

The assembly fixturing, being all one piece, was inserted through the distal end of the polycarbonate tubing. Once the end cap was press-fit into the tubing, a hook tool was used to manoeuvre the seated valve into place 10cm from the edge of the chordae ring.

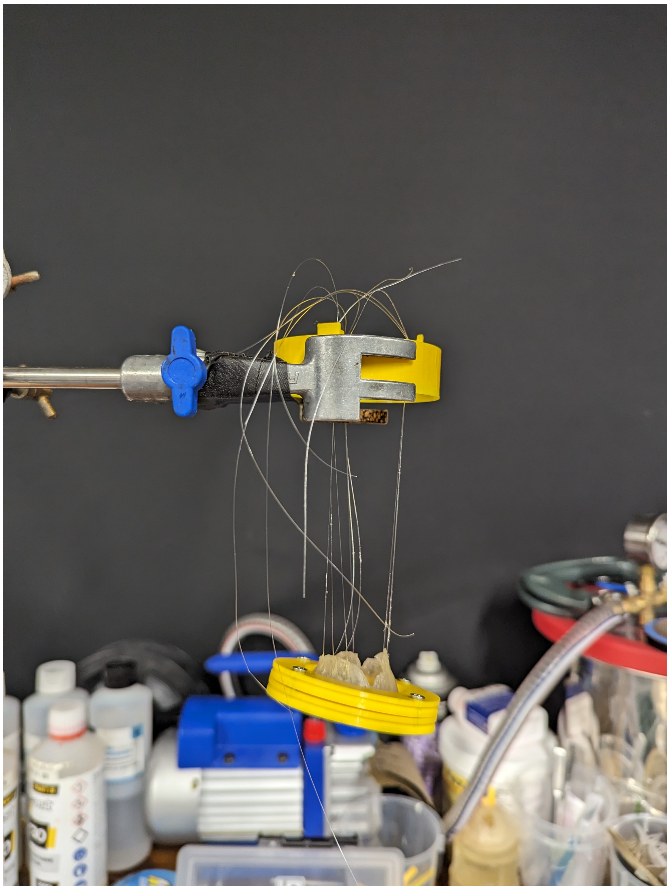


FIGURE 4.2: Tensioning of chordae tendineae

4.3 Rig Assembly

Once the core testing apparatus was assembled, the various adapters for routing the pulsatile flow loop to the valve and valve to the reservoir were wrapped in Teflon tape to secure the connections from leaks.

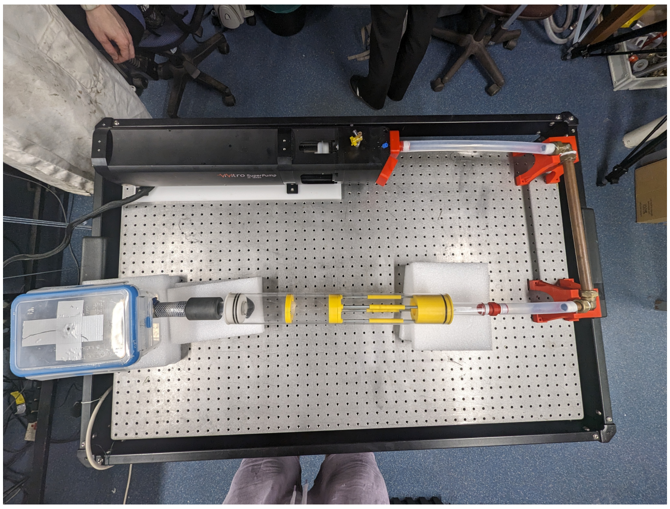


FIGURE 4.3: Bird's eye view of the test rig

When all connections were securely tightened, the components were levelled by eye with styrofoam pads.

4.4 Testing Procedure

4.4.1 *Pilot Checks*

Prior to the main testing, a series of system leakage checks were performed to ensure minimal leaking throughout the main tests. Leakage in coaptation testing results in a great loss in the differential pressure across the valve, resulting in a reduced coaptation for the same pump displacement.

The reservoir was filled, and the leur lock valve on the pulsatile pump was opened so the system could fill with fluid. The system was then purged of air bubbles by using a guide wire and syringe to pull the air out. As leakage spots were observed, they were sealed with blue tack.

4.4.2 *Coaptation Testing*

Once leaks were adequately sealed and air bubbles removed, the pulsatile flow loop was started. The pulsatile pump had a set displacement and frequency. This was sequenced to remove new bubbles, which the system leaks introduced as the testing progressed, obscuring the valve's visual appearance and performance. The valve was observed and recorded for coaptation at multiple angles. To see if the valve presented failure from cyclic stress at the chordae tendineae attachments, the system was left to run for a few minutes longer.

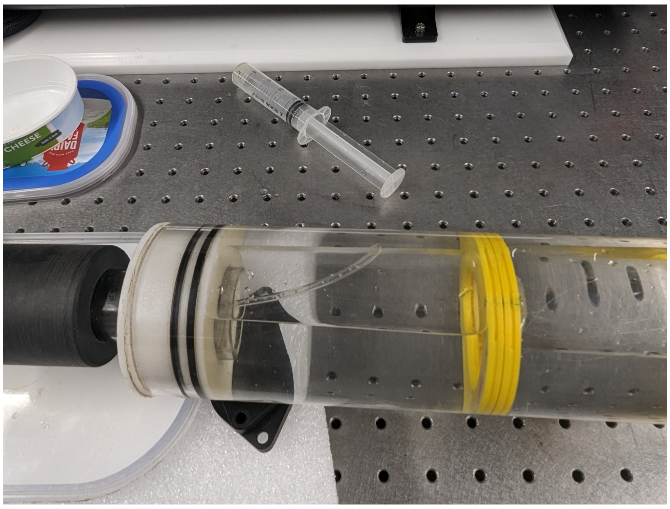


FIGURE 4.4: Removing air bubbles from the system

Part III

RESULTS, ANALYSIS, AND DISCUSSION

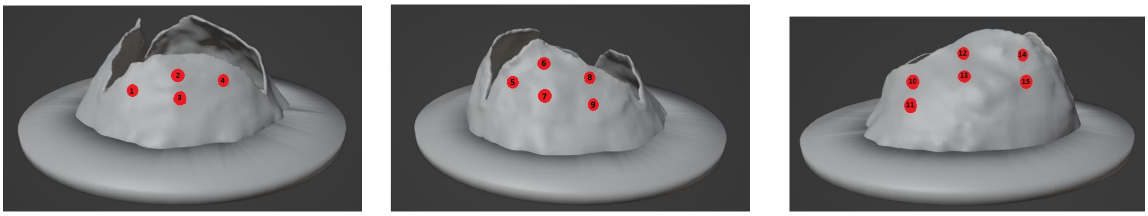
5

Results

The results of the testing of the proof of concept rig are presented in this chapter. The results are presented in a qualitative manner as the rig was not designed to provide quantitative results. The goal of the testing was to determine if the proof-of-concept rig could simulate the coaptation of the tricuspid valve and the flow of blood through the valve. If the valve leaflets and chordae tendineae could sustain the systolic pressure developed from coaptation, the valve's functionality would be verified for use in the right-heart simulator and later integrated into CroiValve DUO.

5.1 Design evaluation and thickness investigation

The cast valve models showed very good homogeny in thickness, with leaflets thickness having a standard deviation of 0.02mm and an average of 0.40mm



(a) Posterior Leaflet (b) Anterior Leaflet (c) Septal Leaflet

FIGURE 5.1: Locations of points chosen for thickness measurements on the valve models

Measurement ID		Without Tendineae	With Tendineae	CAD Model
Posterior	1	0.38	0.45	0.40
	2	0.38	0.41	0.41
	3	0.39	0.41	0.41
	4	0.39	0.50	0.40
Anterior	5	0.40	0.50	0.45
	6	0.40	0.72	0.44
	7	0.42	0.45	0.45
	8	0.43	0.56	0.47
	9	0.43	0.44	0.47
Septal	10	0.45	0.52	0.46
	11	0.40	0.43	0.42
	12	0.42	0.56	0.43
	13	0.39	0.52	0.43
	14	0.43	0.50	0.44
	15	0.40	0.45	0.42
Standard Deviation		0.021104695	0.078392654	0.023211538
Average		0.407333333	0.494666667	0.433333333

TABLE 5.1: Results of thickness measurements of cast and CAD valve models (mm)

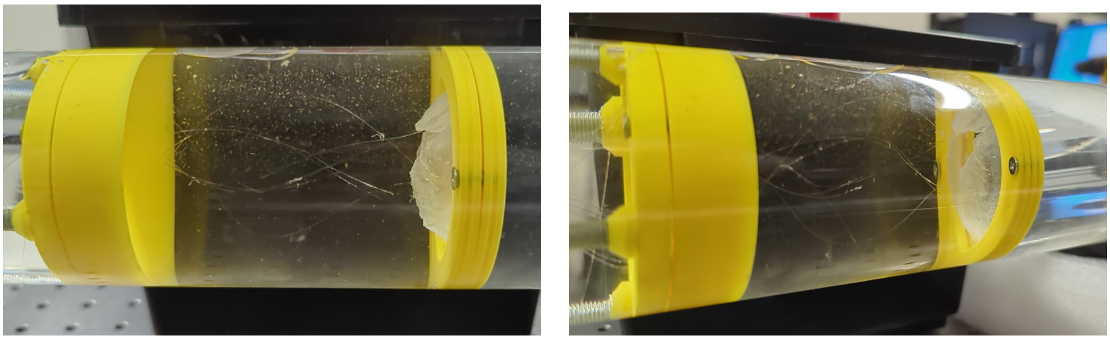
5.2 Pilot Tests

The Teflon tape worked very well where applied; however, the 3D-printed end cap of the core testing chamber leaked a lot even after an attempt to seal with tack. This was due to a misfitting of the O-ring used on the part.

5.3 Coaptation Test

The valve part coapted well, septal and posterior leaflets in particular, the cusp of the anterior leaflet however didnt coapt with either of the adjacent two creating a larger regurgitant orifice than expected. This is likely due to;

- The material properties of the PU used not being elastic enough.



(a) Head-On View (b) Oblique View

FIGURE 5.2: Frame from video of valve coapting during testing **(click to view video)**

- The thickness of the leaflets being too thick making them less flexible.
- The overlapping length of nylon wire on the leaflets making them stiffer.
- The natural saddle shape of the valve annulus being flattened off to fit in the seating fixture.
- Leaflet length loss from the processing of the valve model.

The chordae tendineae held up well under the pressure and prevented the valve from prolapsing. They were tensioned to a point where the valve was allowed to partially prolapse, similar to how native TV's do in regurgitant cases, and an expected degree of prolapse occurred as a result.

During assembly one of the chordae on the posterior leaflet broke leaving just two, however, this didn't affect results.

6

Discussion

▸ Synopsis In this discussion, the good and bad of the methodology and the results obtained from the testing of a tricuspid valve rig are discussed. The focus is on the challenges encountered and the insights gained from the design and manufacturing processes, particularly in the areas of mold die design and valve prototyping. The successful coaptation and functional testing of the valve, the challenges in achieving anatomical accuracy due to material properties and design limitations, and the durability and functionality of the chordae tendineae.

6.1 Challenges and the Various Explored Approaches

6.1.1 *Modelling Challenges*

▸ Mould Die Design

The decision in the early stages of the project of working off of a pre-constructed anatomically accurate valve geometry spawned many issues; it didn't allow for feature interaction in SolidWorks, which prompted some very suboptimal prototyping choices that ended in a huge amount of time investment for an avenue that was eventually made obsolete upon later findings. The series of 2-stage epoxy moulds developed as discussed in Figure 3.11 had a 72 hour curing time, which made the turnaround for learnings very slow to implement and iterate.

This process became obsolete when the SolidWorks package being used was arbitrarily updated in later stages. It was discovered that the 'Segment Mesh' tool previously attempted to be used to convert the STL to a mesh body and then mesh body to solid part had been overhauled to allow more complex geometries to be segmented. On this discovery, the part was successfully converted to a solid body, which allowed for features like body subtraction to remove it from an encompassing cylindrical body as originally planned before encountering the bug, which was then split into what were the foundations of the final design press mould pieces.

From this point, further iterations of the press mould were exponentially quicker, taking only 4-5 hours, reducing the print-to-casting time by 95%, and taking only 20 hours for finalised designs where print settings were maximised for quality and strength of the part.

FIGURE 6.1: Final cast of anatomical valve

▸ VALVE DESIGN

Another area that caused an excess of time consumption was the post-processing of the anatomical valve geometry, in becoming acquainted with STL modelling[4] on the various programs trialled throughout the study, the model was transferred across systems to utilise the different tools each had, for example, Blender had great sculpting tools but lacked simple geometry analysis which was required for monitoring the surface as the thickness was homogenised.

[4]Software packages like Blender use mainly sculpting tools that are used to modify the surface as opposed traditional CAD programs like SolidWorks where parts are built up from a tree of features

While Blender has the capability to manipulate shaders to render this kind of information, due to it being an open-source program, developing a custom shader for this was very complex and deemed not worth the time for other trialled programs like MeshMixer could suffice albeit added unnecessary steps. If further work was conducted with many patient-specific models being developed, it would be likely the most efficient option to develop a custom tool however.

6.1.2 *Manufacturing Challenges*

▸ Chordae Tendineae Prototyping

The tendineae attachment to the leaflets was another highly contested and thought-out design factor. Balancing the rigidity that is added to the leaflets by some methods in attaching the nylon wire and the adhesion to the leaflet is very difficult; for the scope of this study it was found that B7000 adhesive worked well as the tendineae could be effectively attached with minimal disruption to the mechanics of the valve however this did add thickness to the leaflets which not only adds rigidity that hinders coaptation in experimental use but also brings many issues for potential computational simulations that could be conducted in tandem to a study of this nature.

Studies like [Karl et al. 2024] only published in the end stages of the study use a method of embedding their chordae tendineae within the leaflets, containing a medical gauze matrix, so that the tendineae do not detach under tensile forces like was seend in section:§ 3.4.3 with the embed tests. An approach like this could prove very effective in application to this study as it would simplify the manufacturing process in that the tendineae can be attached to the gauze matrix prior to PU casting ensuring accurate and repeatable placement across multiple fabrications without any added thickness to the part.

▸ Valve Prototyping

The prototyping conducted through the study for finalised parts, fixturing, and the experimental rig revealed a few key insights into the rapid prototyping landscape. For each print, the printer's configuration was tailored to the purpose of the parts being produced. Parts being made in early iterations were set to a faster infill and layer height setting, whereas finalised ideas were set to slower, higher resolution settings.

These dense high-definition settings needed for an accurate and rigid mould die had issues that took many iterations and failed prints to perfect. They often resulted in a large amount of stringing, a printing defect that was often not solvable via post-processing. To circumnavigate this the researchers in the UCD print lab were consulted. Tailored settings in Prusa Slicer were programmed for the geometry where the resulting gcode would stop the nozzle from crossing the perimeter of the valve moulds, retraction settings would stop the printer from leaving blobs of residue on the interior of the mould and z-axis seams were aligned to not interfere with the geometry.

In the earlier stages of the study, a resin SLA printer was used to manufacture an anatomic model for the silicone mould method discussed in Figure 3.9, however, it was not feasible to develop further iterations from resin due to the printer being in a separate lab and having a much higher cost with proprietary resins. Two major benefits to SLA printing are;

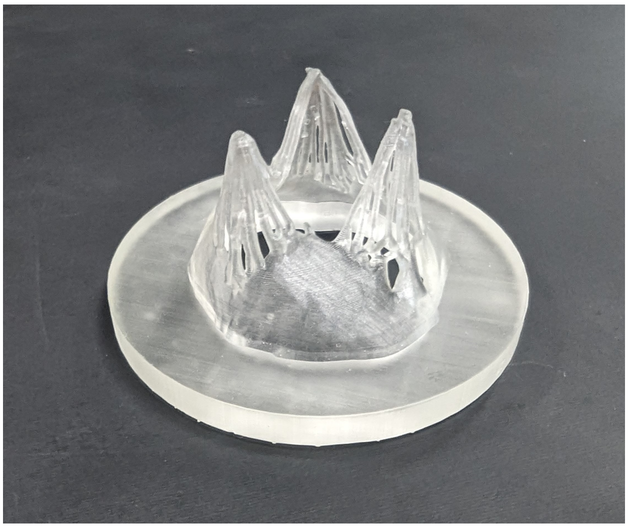


FIGURE 6.2: Early revision SLA print of anatomical valve

Resources:

- Prusa TDS
- FormLabs TDS

- The vastly increased tolerance of resin printing making parts much more accurate
  Prusa FDM:0.3mm
  FormLabs SLA:0.01mm

- The reduced layer height that resin printing is capable of
  Prusa FDM:0.05mm
  FormLabs SLA:0.025mm

This has two main benefits regarding this study;

- Minimizing layer height results in mould parts reducing surface affects

- Reducing adhesion of cast part to mould, this is minimized on PLA parts with mould release and sanding however with casted parts on this degree of thickness there can still be an increased risk of breakage in the demoulding process.

Another option worth considering is machining from either steel or a performance plastic like delrin [Li et al. 2022]; this would be more expensive however, it could be worth the cost for moulds that need to be used for many castings as well as increasing the precision over multiple casts since 3D printed parts warp under the pressure of the clamping.

The importance of transparency for the part was a consideration for further work on the valve as the integration into the right heart simulator would involve PIV measurement where maintaining transparency would allow for a measured flow field uninterrupted by the leaflets, this was an issue in studies like [Rabbah et al. 2013] and the efficacy on dynamic transparent parts in PIV rigs has been shown in studies like [Büsen et al. 2017].

6.2 Contextualizing Results

The results of this study have shown how the development of imitative synthetic heart valves can be a valuable tool in cardiac simulators. The coaptation tests on the valve show great promise for a technology of this nature, surpassing limitations of previous work in simulational studies such as [Rabbah et al. 2013] dissected porcine valves, [Ginty et al. 2018] rigid valves and [Raghav et al. 2018] non-anatomically representative valves, Each have major limitations in their ability for a wider range of experiments.
Some such limitations of these valves are;

- The longevity of porcine for repeated experiments. While it can be stored in the likes of formalin the tissue degrades over time which leads to an irrepeatability in testing and eventual need for replacement.
- Semi-rigid valves can't be used in flow studies as they can't deform to coapt.
- Non-anatomical valves can coapt but don't represent true geometry, which won't yield accurate results.

6.2.1 *Design Validation Testing*

The thickness testing of the casted and CAD models gives a good idea of shrinkage percentages of the PU material used and also discrepancies added from the process of tethering the nylon wire for chordae tendineae, these parameters are important as for computational studies being conducted in tandem require precise geometries. The results show a 5% shrinkage in the material which could make a significant difference.

There are however some limitations that limit the strength of these results. Micrometres have a measurement force of 0.5-2N, which acts on the leaflets as the gauge is tightened. While low, this force is enough to deform the leaflets slightly, leading to small but noticeable discrepancies in the results. Using a laser micrometre would be a good solution to this as it would allow for non-contact measurement of the thickness of the leaflets in much more precise locations; combining this with an adjustable platform to seat the valve in would yield much more accurate and perfectly repeatable results to assess shrinkage.

The locations of measurements were purposefully chosen to overlap with the attached tendineae as much as possible to assess their added thickness, this disruption to the geometry is not ideal as the surface acts much less predictably and be replicated in CAD models since it is done by hand.

6.2.2 *Coaptation Testing*

- Chordae Tendineae Performacnce:
  The coaptation test illustrated how the chordae tendineae can be used in a synthetic part to prevent prolapse and aid coaptation. The aligns well with how it had been done before such as in [Rabbah et al. 2013] and [Karl et al. 2024] where native and synthetic tendineae were used respectively. Such works also show how this part of the model can be manipulated with motors to simulate the contraction of papillary muscles, which while not applicable to the current design of the right heart simulator, could be developed for future iterations or simpler rig designs like that of the tube-based coaptation test Figure 5.2

- Leaflet Performance:
  The area with the most room for improvement is likely the leaflets. The final iteration from this study came very far relative to the initial iterations in terms of rigidity, transparency and geometric precision, it also performed better than similar attempts from other studies like [Ginty et al. 2018] although in regards to the initial design criteria from section:§ 3.2 it is lacking in functional performance and scalability

  Not all the leaflets coapted together, which was the objective, however, it was supposed to occur from annular dilation and chordal loosening, not from the geometry not allowing it, this is most likely due to the model of the valve being based on a valve in the diastolic phase, so the full length of the leaflets were malformed in CT conversion as they were not under load from the pressure systolic pressure which would stretch to there full length. This can be seen in Figure 5.2:B, where the leaflets move back but are not long enough to meet each other. The work of [Karl et al. 2024] capture this well in their mitral valve design, they did well with leaflet length however theyre design was not anatomically representative, building off this to capture both physiological replicity and functional performance would be a first of it's kind for in-vitro tricuspid valve testing.

Part IV

EPILOGUE

7

Conclusions and Future Work

7.1 Conclusions

In this thesis, a mock tricuspid valve was developed to improve the accuracy and functionality of right heart simulators. Through careful design and development, a model was created that accurately replicates the anatomical and biomechanical properties of the natural tricuspid valve and integrates effectively with existing simulation systems.

Challenges related to material compatibility and complex valve dynamics were addressed through advanced material testing and iterative design modifications. A prototype was produced, setting a new standard for realistic and functional heart valve simulators and potentially improving patient outcomes in cardiac care.

This work establishes a foundation for future research, suggesting further innovations in material technology and dynamic simulation capabilities. The anticipated integration of sophisticated computational models and exploration of new materials is expected to advance the capabilities of heart valve simulators significantly, bridging the gap between theoretical research and clinical application, and advancing biomedical engineering in cardiac care.

▸ In conclusion, this study shows how the design process can be fraught with many more obstacles of many more varieties than expected. It resulted more in learnings of the iterative process of design and prototyping compared to test method development than expected.

7.2 Future Research Directions

Briefly touched on in the discussion were a few areas that further development in this project is very promising, continuing to decrease valve thickness will likely yield even more representative results and weaving chordal attachments into the leaflets will improve repeatability of fabrication while also aligning models more closely to that of CAD designs for computational models.

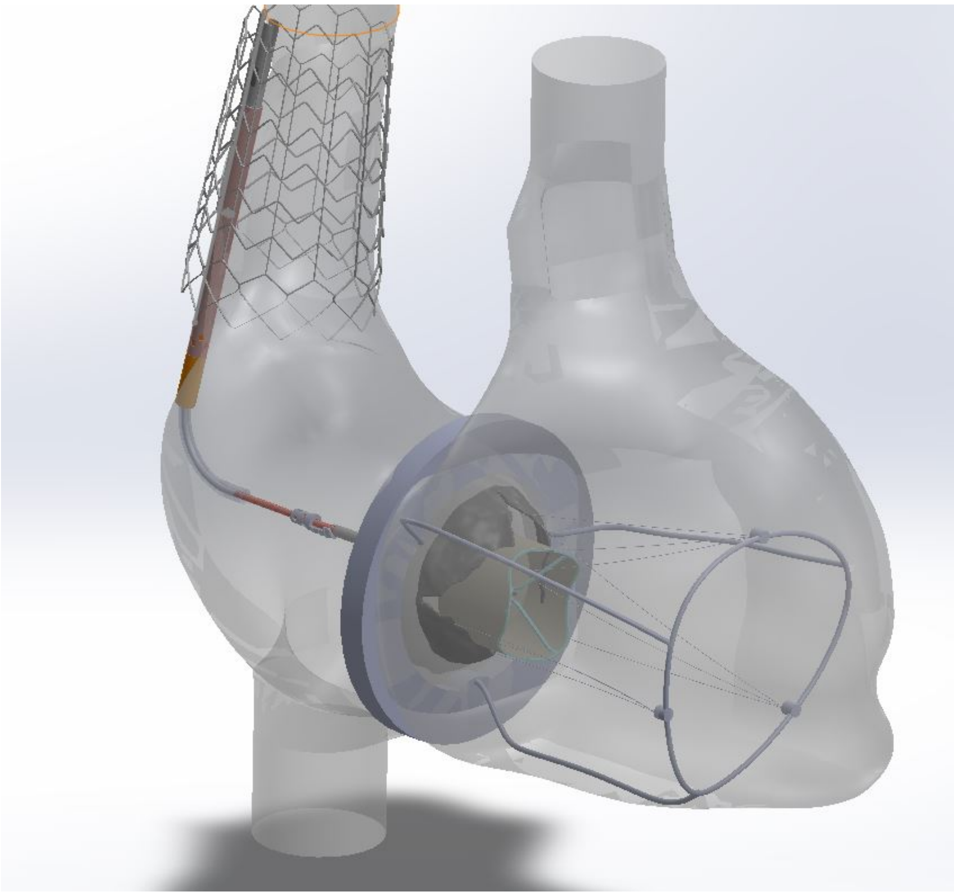


FIGURE 7.1: An assembly of the CroiValve DUO device in the right heart simulator

The next steps in this research will primarily be to fully integrate this valve into the right heart simulator. From there the rig be enhanced to involve TTVR devices to characterize their efficacy on regurgitant valves. The main prospective device to integrate is the CroiValve DUO device which partially occludes the annulus of the valve reducing regurgitant flow. While not reaching full fabrication due to time constrants, an assembly of what this would look like was created to illustrate how this would look. The models of the right heart simulator was used in designing the fixturing to them flush against the heart chamber for minimal flow disturbance.

Integration of the DUO device system could be carried out quite simply by implanting it aligning with the clinical procedure by anchoring the stent in the superior vena cava of the right heart simulator.

Appendix

Solidworks drawings

Bibliography

1. Roth, Gregory A. et al. (Dec. 22, 2020). "Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019: Update From the GBD 2019 Study". In: *Journal of the American College of Cardiology* 76.25, pp. 2982–3021. ISSN: 0735-1097. DOI: 10.1016/j.jacc.2020.11.010 (cit. on p. 2).

2. Nkomo, Vuyisile T, Gardin, Julius M, Skelton, Thomas N, Gottdiener, John S, Scott, Christopher G, and Enriquez-Sarano, Maurice (Sept. 16, 2006). "Burden of Valvular Heart Diseases: A Population-Based Study". In: *The Lancet* 368.9540, pp. 1005–1011. ISSN: 0140-6736. DOI: 10.1016/S0140-6736(06)69208-8 (cit. on p. 2).

3. Musumeci, Lucia, Jacques, Nicolas, Hego, Alexandre, Nchimi, Alain, Lancellotti, Patrizio, and Oury, Cécile (May 14, 2018). "Prosthetic Aortic Valves: Challenges and Solutions". In: *Frontiers in Cardiovascular Medicine* 5. ISSN: 2297-055X. DOI: 10.3389/fcvm.2018.00046 (cit. on p. 3).

4. Sanders, Stephen P. and Pluchinotta, Francesca R. (2014). "Tricuspid Valve: Embryology and Anatomy". In: *The Tricuspid Valve in Congenital Heart Disease*. Ed. by Alessandro Giamberti and Massimo Chessa. Milano: Springer Milan, pp. 1–11. ISBN: 978-88-470-5400-4. DOI: 10.1007/978-88-470-5400-4_1 (cit. on pp. 3, 10).

5. Buzzatti, Nicola, De Bonis, Michele, and Moat, Neil (Jan. 1, 2018). "Anatomy of the Tricuspid Valve, Pathophysiology of Functional Tricuspid Regurgitation, and Implications for Percutaneous Therapies". In: *Interventional Cardiology Clinics*. Transcatheter Tricuspid Valve Intervention/Interventional Therapy for Pulmonary Embolism 7.1, pp. 1–11. ISSN: 2211-7458. DOI: 10.1016/j.iccl.2017.08.005 (cit. on pp. 3, 10).

6. Takashina, T., Masuzawa, T., and Fukui, Y. (1990). "A New Cardiac Auscultation Simulator". In: *Clinical Cardiology* 13.12, pp. 869–872. ISSN: 1932-8737. DOI: 10.1002/clc.4960131210 (cit. on p. 4).

7. Ramphal, Paul S., Coore, Daniel N., Craven, Michael P., Forbes, Neil F., Newman, Somara M., Coye, Adrian A., Little, Sherard G., and Silvera, Brian C. (May 1, 2005). "A High Fidelity Tissue-Based Cardiac Surgical Simulator". In: *European Journal of Cardio-Thoracic Surgery* 27.5, pp. 910–916. ISSN: 1010-7940. DOI: 10.1016/j.ejcts.2004.12.049 (cit. on pp. 4, 15).

8. Baillargeon, Brian, Rebelo, Nuno, Fox, David D., Taylor, Robert L., and Kuhl, Ellen (Nov. 1, 2014). "The Living Heart Project: A Robust and Integrative Simulator for Human Heart Function". In: *European Journal of Mechanics - A/Solids*. Frontiers in Finite-Deformation Electromechanics 48, pp. 38–47. ISSN: 0997-7538. DOI: 10.1016/j.euromechsol.2014.04.001 (cit. on pp. 4, 23).

9. Chatterjee, Kanu (May 2, 2005). “Neurohormonal Activation in Congestive Heart Failure and the Role of Vasopressin”. In: *The American Journal of Cardiology*. Hyponatremia in Congestive Heart Failure 95 (9, Supplement 1), pp. 8–13. ISSN: 0002-9149. DOI: 10.1016/j.amjcard.2005.03.003 (cit. on p. 6).

10. Frater, R. W. M. (Dec. 1, 1962). “ARTIFICIAL HEART VALVES”. In: *The Lancet*. Originally Published as Volume 2, Issue 7266 280.7266, p. 1171. ISSN: 0140-6736. DOI: 10.1016/S0140-6736(62)90938-8 (cit. on p. 8).

11. Rock, Christopher, Han, Lin, and Doehring, Todd (Jan. 21, 2014). “Complex Collagen Fiber and Membrane Morphologies of the Whole Porcine Aortic Valve”. In: *PloS one* 9, e86087. DOI: 10.1371/journal.pone.0086087 (cit. on p. 8).

12. Simionescu, Dan T. (2006). “Artificial Heart Valves”. In: *Wiley Encyclopedia of Biomedical Engineering*. John Wiley & Sons, Ltd. ISBN: 978-0-471-74036-0. DOI: 10.1002/9780471740360.ebs1455 (cit. on pp. 8, 9).

13. *Yost - Drawing Detailed View of Tricuspid Valve - English Labels | AnatomyTOOL* (n.d.) (cit. on p. 9).

14. *Tricuspid Valve Disease* (n.d.). *Tricuspid Valve Disease: Video, Anatomy & Definition | Osmosis* (cit. on p. 10).

15. Ross, John (Apr. 1, 1985). “Afterload Mismatch in Aortic and Mitral Valve Disease: Implications for Surgical Therapy”. In: *Journal of the American College of Cardiology* 5.4, pp. 811–826. ISSN: 0735-1097. DOI: 10.1016/S0735-1097(85)80418-6 (cit. on p. 11).

16. Tretter, Justin T., Sarwark, Anne E., Anderson, Robert H., and Spicer, Diane E. (2016). “Assessment of the Anatomical Variation to Be Found in the Normal Tricuspid Valve”. In: *Clinical Anatomy* 29.3, pp. 399–407. DOI: 10.1002/ca.22591. eprint: https://onlinelibrary.wiley.com/doi/pdf/10.1002/ca.22591 (cit. on pp. 11, 25).

17. Shah, Pravin M. and Raney, Aidan A. (Feb. 1, 2008). “Tricuspid Valve Disease”. In: *Current Problems in Cardiology*. Tricuspid Valve Disease 33.2, pp. 47–84. ISSN: 0146-2806. DOI: 10.1016/j.cpcardiol.2007.10.004 (cit. on p. 12).

18. Nam, Hannah, Flynn, Maura, Lasso, Andras, Herz, Christian, Sabin, Patricia, Wang, Yan, Cianciulli, Alana, Vigil, Chad, Huang, Jing, Vicory, Jared, Paniagua, Beatriz, Allemang, David, Goldberg, David, Nuri, Mohammed, Cohen, Meryl, Fichtinger, Gabor, and Jolley, Matthew (Mar. 3, 2023). “Modeling of the Tricuspid Valve and Right Ventricle in Hypoplastic Left Heart Syndrome With a Fontan Circulation”. In: *Circulation. Cardiovascular imaging* 16, e014671. DOI: 10.1161/CIRCIMAGING.122.014671 (cit. on pp. 12, 32).

19. Obase, Kikuko, Weinert, Lynn, Hollatz, Andrew, Farooqui, Farhan, Roberts, Joseph D., Minhaj, Mohammed M., Tung, Avery, Chaney, Mark, Ota, Takeyoshi, Jeevanandam, Valluvan, Yoshida, Kiyoshi, Mor-Avi, Victor, and Lang, Roberto M. (May 1, 2016). "Elongation of Chordae Tendineae as an Adaptive Process to Reduce Mitral Regurgitation in Functional Mitral Regurgitation". In: *European Heart Journal - Cardiovascular Imaging* 17.5, pp. 500–509. ISSN: 2047-2404. DOI: 10.1093/ehjci/jev314 (cit. on p. 12).

20. Hell, Michaela M, Emrich, Tilman, Kreidel, Felix, Kreitner, Karl-Friedrich, Schoepf, U Joseph, Münzel, Thomas, and von Bardeleben, Ralph Stephan (June 1, 2021). "Computed Tomography Imaging Needs for Novel Transcatheter Tricuspid Valve Repair and Replacement Therapies". In: *European Heart Journal - Cardiovascular Imaging* 22.6, pp. 601–610. ISSN: 2047-2404. DOI: 10.1093/ehjci/jeaa308 (cit. on p. 13).

21. Gales, Jordan, Krasuski, Richard A., and Fleming, Gregory A. (Sept. 1, 2018). "Transcatheter Valve Replacement for Right-sided Valve Disease in Congenital Heart Patients". In: *Progress in Cardiovascular Diseases*. Update on Adult Congenital Heart Disease 61.3, pp. 347–359. ISSN: 0033-0620. DOI: 10.1016/j.pcad.2018.09.003 (cit. on p. 13).

22. Curio, Jonathan, Demir, Ozan M., Pagnesi, Matteo, Mangieri, Antonio, Giannini, Francesco, Weisz, Giora, and Latib, Azeem (Mar. 21, 2019). "Update on the Current Landscape of Transcatheter Options for Tricuspid Regurgitation Treatment". In: (cit. on p. 13).

23. Westerhof, Nico, Lankhaar, Jan-Willem, and Westerhof, Berend E. (Feb. 1, 2009). "The Arterial Windkessel". In: *Medical & Biological Engineering & Computing* 47.2, pp. 131–141. ISSN: 1741-0444. DOI: 10.1007/s11517-008-0359-2 (cit. on p. 14).

24. Verberkmoes, Niels J. and Verberkmoes-Broeders, Elizabeth M.P.C. (Feb. 1, 2013). "A Novel Low-Fidelity Simulator for Both Mitral Valve and Tricuspid Valve Surgery: The Surgical Skills Trainer for Classic Open and Minimally Invasive Techniques†". In: *Interactive CardioVascular and Thoracic Surgery* 16.2, pp. 97–101. ISSN: 1569-9293. DOI: 10.1093/icvts/ivs451 (cit. on p. 15).

25. Zilinskas, Kasparas, Kwon, Jennie H., Bishara, Katherine, Hayden, Kaila, Quintao, Ritchelli, and Rajab, Taufiek Konrad (June 2022). "Physiological Ventricular Simulator for Valve Surgery Training". In: *Bioengineering* 9.6 (6), p. 264. ISSN: 2306-5354. DOI: 10.3390/bioengineering9060264 (cit. on pp. 15, 16).

26. Tozzi, Piergiorgio, Solida, Alessandra, Siniscalchi, Giuseppe, and Ferrari, Enrico (June 2022). "A Heart Surgery Simulator With an Integrated Supervision System for Self-Learning the Key Steps and Pitfalls of the Mitral Valve Repair: Initial Investigation". In: *Simulation in Healthcare* 17.3, p. 192. ISSN: 1559-2332. DOI: 10.1097/SIH.0000000000000590 (cit. on p. 15).

27. Capelli, Claudio, Sauvage, Emilie, Giusti, Giuliano, Bosi, Giorgia M., Ntsinjana, Hopewell, Carminati, Mario, Derrick, Graham, Marek, Jan, Khambadkone, Sachin, Taylor, Andrew M., and Schievano, Silvia (Dec. 15, 2017). “Patient-Specific Simulations for Planning Treatment in Congenital Heart Disease”. In: *Interface Focus* 8.1, p. 20170021. DOI: 10.1098/rsfs.2017.0021 (cit. on p. 16).

28. Zhong, Qi, Zeng, Wen Hua, Huang, Xiao Yang, and Wang, Bo Liang (2014). “Numerical Simulation of the Dynamics of Heart Valves: A Literature Review”. In: *Applied Mechanics and Materials* 444–445, pp. 1211–1217. ISSN: 1662-7482. DOI: 10.4028/www.scientific.net/AMM.444-445.1211 (cit. on p. 16).

29. Leopaldi, A. M., Vismara, R., Lemma, M., Valerio, L., Cervo, M., Mangini, A., Contino, M., Redaelli, A., Antona, C., and Fiore, G. B. (Apr. 30, 2012). “*In Vitro* Hemodynamics and Valve Imaging in Passive Beating Hearts”. In: *Journal of Biomechanics* 45.7, pp. 1133–1139. ISSN: 0021-9290. DOI: 10.1016/j.jbiomech.2012.02.007 (cit. on p. 16).

30. Mathur, Mrudang, Meador, William D., Malinowski, Marcin, Jazwiec, Tomasz, Timek, Tomasz A., and Rausch, Manuel K. (Oct. 1, 2022). “Texas TriValve 1.0 : A Reverse-Engineered, Open Model of the Human Tricuspid Valve”. In: *Engineering with Computers* 38.5, pp. 3835–3848. ISSN: 1435-5663. DOI: 10.1007/s00366-022-01659-w (cit. on p. 16).

31. Rabbah, Jean-Pierre, Saikrishnan, Neelakantan, and Yoganathan, Ajit P. (Feb. 1, 2013). “A Novel Left Heart Simulator for the Multi-modality Characterization of Native Mitral Valve Geometry and Fluid Mechanics”. In: *Annals of Biomedical Engineering* 41.2, pp. 305–315. ISSN: 1573-9686. DOI: 10.1007/s10439-012-0651-z (cit. on pp. 17, 55, 56).

32. Pokutta-Paskaleva, Anastassia, Sulejmani, Fatiesa, DelRocini, Marissa, and Sun, Wei (Feb. 1, 2019). “Comparative Mechanical, Morphological, and Microstructural Characterization of Porcine Mitral and Tricuspid Leaflets and Chordae Tendineae”. In: *Acta Biomaterialia* 85, pp. 241–252. ISSN: 1742-7061. DOI: 10.1016/j.actbio.2018.12.029 (cit. on p. 17).

33. Karl, Roger, Romano, Gabriele, Marx, Josephin, Eden, Matthias, Schlegel, Philipp, Stroh, Lubov, Fischer, Samantha, Hehl, Maximilian, Kühle, Reinald, Mohl, Lukas, Karck, Matthias, Frey, Norbert, De Simone, Raffaele, and Engelhardt, Sandy (Mar. 1, 2024). “An Ex-Vivo and in-Vitro Dynamic Simulator for Surgical and Transcatheter Mitral Valve Interventions”. In: *International Journal of Computer Assisted Radiology and Surgery* 19.3 (3), pp. 411–421. ISSN: 1861-6429. DOI: 10.1007/s11548-023-03036-4 (cit. on pp. 17, 53, 56, 57).

34. Ghanbari, Hossein, Kidane, Asmeret G., Burriesci, Gaetano, Ramesh, Bala, Darbyshire, Arnold, and Seifalian, Alexander M. (Nov. 1, 2010). “The Anti-Calcification Potential of a Silsesquioxane Nanocomposite Polymer under in Vitro Conditions: Potential Material for Synthetic Leaflet Heart Valve”. In: *Acta Biomaterialia* 6.11, pp. 4249–4260. ISSN: 1742-7061. DOI: 10.1016/j.actbio.2010.06.015 (cit. on p. 18).

35. Filová, E., Straka, F., Miřejovský, T., Mašín, J., and Bačáková, L. (2009). "Tissue-Engineered Heart Valves". In: *Physiological Research* 58 Suppl 2, S141–S158. ISSN: 0862-8408. DOI: 10.33549/physiolres.931919. pmid: 20131932 (cit. on p. 18).

36. Zhang, Xing, Xu, Bin, Puperi, Daniel S., Wu, Yan, West, Jennifer L., and Grande-Allen, K. Jane (2015). "Application of Hydrogels in Heart Valve Tissue Engineering". In: *Journal of long-term effects of medical implants* 25.0, pp. 105–134. ISSN: 1050-6934. pmid: 25955010 (cit. on p. 18).

37. Baxter, S., Busfield, J. J. C., and Peijs, T. (Jan. 1, 2006). "Chapter 12 - Selection of Elastomers for a Synthetic Heart Valve". In: *Elastomers and Components*. Ed. by V. A. Coveney. Woodhead Publishing, pp. 171–177. ISBN: 978-1-84569-100-4. DOI: 10.1533/9781845691134.2.171 (cit. on p. 19).

38. Engelhardt, Sandy, Sauerzapf, Simon, Preim, Bernhard, Karck, Matthias, Wolf, Ivo, and De Simone, Raffaele (July 1, 2019). "Flexible and Comprehensive Patient-Specific Mitral Valve Silicone Models with Chordae Tendineae Made from 3D-printable Molds". In: *International Journal of Computer Assisted Radiology and Surgery* 14.7, pp. 1177–1186. ISSN: 1861-6429. DOI: 10.1007/s11548-019-01971-9 (cit. on p. 19).

39. Ginty, Olivia, Moore, John, Peters, Terry, and Bainbridge, Daniel (June 1, 2018). "Modeling Patient-Specific Deformable Mitral Valves". In: *Journal of Cardiothoracic and Vascular Anesthesia* 32.3, pp. 1368–1373. ISSN: 1053-0770. DOI: 10.1053/j.jvca.2017.09.005 (cit. on pp. 19, 55, 56).

40. Luo, X. Y., Griffith, B. E., Ma, X. S., Yin, M., Wang, T. J., Liang, C. L., Watton, P. N., and Bernacca, G. M. (July 1, 2012). "Effect of Bending Rigidity in a Dynamic Model of a Polyurethane Prosthetic Mitral Valve". In: *Biomechanics and Modeling in Mechanobiology* 11.6, pp. 815–827. ISSN: 1617-7940. DOI: 10.1007/s10237-011-0354-7 (cit. on pp. 19, 20, 38).

41. Liao, Jun and Vesely, Ivan (Aug. 1, 2003). "A Structural Basis for the Size-Related Mechanical Properties of Mitral Valve Chordae Tendineae". In: *Journal of Biomechanics* 36.8, pp. 1125–1133. ISSN: 0021-9290. DOI: 10.1016/S0021-9290(03)00109-X (cit. on p. 20).

42. Ionasec, Razvan Ioan, Voigt, Ingmar, Georgescu, Bogdan, Wang, Yang, Houle, Helene, Vega-Higuera, Fernando, Navab, Nassir, and Comaniciu, Dorin (Sept. 2010). "Patient-Specific Modeling and Quantification of the Aortic and Mitral Valves From 4-D Cardiac CT and TEE". In: *IEEE Transactions on Medical Imaging* 29.9, pp. 1636–1651. ISSN: 1558-254X. DOI: 10.1109/TMI.2010.2048756 (cit. on p. 20).

43. Grbic, Sasa, Ionasec, Razvan, Vitanovski, Dime, Voigt, Ingmar, Wang, Yang, Georgescu, Bogdan, Navab, Nassir, and Comaniciu, Dorin (July 1, 2012). "Complete Valvular Heart Apparatus Model from 4D Cardiac CT". In: *Medical Image Analysis* 16.5, pp. 1003–1014. ISSN: 1361-8415. DOI: 10.1016/j.media.2012.02.003 (cit. on p. 20).

44. Vukicevic, Marija, Puperi, Daniel S., Jane Grande-Allen, K., and Little, Stephen H. (Feb. 1, 2017). "3D Printed Modeling of the Mitral Valve for Catheter-Based Structural Interventions". In: *Annals of Biomedical Engineering* 45.2, pp. 508–519. ISSN: 1573-9686. DOI: 10.1007/s10439-016-1676-5 (cit. on p. 20).

45. Vukicevic, Marija, Faza, Nadeen N., Avenatti, Eleonora, Durai, Ponraj Chinna, El-Tallawi, Kinan Carlos, Filippini, Stefano, Chang, Su Min, and Little, Stephen H. (July 2020). "Patient-Specific 3-Dimensional Printed Modeling of the Tricuspid Valve for MitraClip Procedure Planning". In: *Circulation: Cardiovascular Imaging* 13.7, e010376. DOI: 10.1161/CIRCIMAGING.119.010376 (cit. on p. 20).

46. Ahn, Yura, Koo, Hyun Jung, Kang, Joon-Won, and Yang, Dong Hyun (Dec. 1, 2021). "Tricuspid Valve Imaging and Right Ventricular Function Analysis Using Cardiac CT and MRI". In: *Korean Journal of Radiology* 22.12, pp. 1946–1963. ISSN: 1229-6929. DOI: 10.3348/kjr.2020.1507 (cit. on p. 21).

47. Suh, Young Joo, Kim, Young Jin, Kim, Jin Young, Chang, Suyon, Im, Dong Jin, Hong, Yoo Jin, and Choi, Byoung Wook (Nov. 1, 2017). "A Whole-Heart Motion-Correction Algorithm: Effects on CT Image Quality and Diagnostic Accuracy of Mechanical Valve Prosthesis Abnormalities". In: *Journal of Cardiovascular Computed Tomography* 11.6, pp. 474–481. ISSN: 1934-5925. DOI: 10.1016/j.jcct.2017.09.011 (cit. on p. 21).

48. Stasiak, Joanna R., Serrani, Marta, Biral, Eugenia, Taylor, James V., Zaman, Azfar G., Jones, Samantha, Ness, Thomas, Gaetano, Francesco De, Costantino, Maria Laura, Bruno, Vito D., Suleiman, Saadeh, Ascione, Raimondo, and Moggridge, Geoff D. (Aug. 11, 2020). "Design, Development, Testing at ISO Standards and in Vivo Feasibility Study of a Novel Polymeric Heart Valve Prosthesis". In: *Biomaterials Science* 8.16, pp. 4467–4480. ISSN: 2047-4849. DOI: 10.1039/D0BM00412J (cit. on p. 21).

49. Walker, Antonio (Aug. 13, 2010). "In Vitro Evaluation of Mechanical Heart Valve Performance Using a Novel Test Chamber in an Automated Mock Circulatory Loop". In: *Theses and Dissertations*. DOI: 10.25772/D5GZ-EE71 (cit. on p. 22).

50. Thomas, Vineet S., Lai, Victor, and Amini, Rouzbeh (Aug. 1, 2019). "A Computational Multi-Scale Approach to Investigate Mechanically-Induced Changes in Tricuspid Valve Anterior Leaflet Microstructure". In: *Acta Biomaterialia* 94, pp. 524–535. ISSN: 1742-7061. DOI: 10.1016/j.actbio.2019.05.074 (cit. on p. 22).

51. Lee, Jae H., Rygg, Alex D., Kolahdouz, Ebrahim M., Rossi, Simone, Retta, Stephen M., Duraiswamy, Nandini, Scotten, Lawrence N., Craven, Brent A., and Griffith, Boyce E. (May 2020). "Fluid-Structure Interaction Models of Bioprosthetic Heart Valve Dynamics in an Experimental Pulse Duplicator". In: *Annals of Biomedical Engineering* 48.5, pp. 1475–1490. ISSN: 1573-9686. DOI: 10.1007/s10439-020-02466-4. pmid: 32034607 (cit. on p. 22).

52. D'Amore, Antonio, Luketich, Samuel K., Raffa, Giuseppe M., Olia, Salim, Menallo, Giorgio, Mazzola, Antonino, D'Accardi, Flavio, Grunberg, Tamir, Gu, Xinzhu, Pilato, Michele, Kameneva, Marina V., Badhwar, Vinay, and Wagner, William R. (Jan. 1, 2018). "Heart Valve Scaffold Fabrication: Bioinspired Control of Macro-Scale Morphology, Mechanics and Micro-Structure". In: *Biomaterials* 150, pp. 25–37. ISSN: 0142-9612. DOI: 10.1016/j.biomaterials.2017.10.011 (cit. on p. 22).

53. Laurence, Devin, Ross, Colton, Jett, Samuel, Johns, Cortland, Echols, Allyson, Baumwart, Ryan, Towner, Rheal, Liao, Jun, Bajona, Pietro, Wu, Yi, and Lee, Chung-Hao (Jan. 23, 2019). "An Investigation of Regional Variations in the Biaxial Mechanical Properties and Stress Relaxation Behaviors of Porcine Atrioventricular Heart Valve Leaflets". In: *Journal of Biomechanics* 83, pp. 16–27. ISSN: 0021-9290. DOI: 10.1016/j.jbiomech.2018.11.015 (cit. on p. 22).

54. Bazan, Ovandir and Ortiz, Jayme Pinto (2016-Mar-Apr). "Experimental Validation of a Cardiac Simulator for *in Vitro* Evaluation of Prosthetic Heart Valves". In: *Brazilian Journal of Cardiovascular Surgery* 31, pp. 151–157. ISSN: 0102-7638, 1678-9741. DOI: 10.5935/1678-9741.20160041 (cit. on p. 23).

55. Rajab, Taufiek, Rivard, Andrew L., Wasiluk, Karen R., Gallegos, Robert P., and Bianco, Richard W. (Jan. 1, 2013). "Chapter III.2.7 - Ethical Issues in Biomaterials and Medical Devices". In: *Biomaterials Science (Third Edition)*. Ed. by Buddy D. Ratner, Allan S. Hoffman, Frederick J. Schoen, and Jack E. Lemons. Academic Press, pp. 1425–1431. ISBN: 978-0-12-374626-9. DOI: 10.1016/B978-0-08-087780-8.00135-2 (cit. on p. 24).

56. Fletcher, J C (Dec. 1983). "Cardiac Transplants and the Artificial Heart: Ethical Considerations." In: *Circulation* 68.6, pp. 1339–1343. DOI: 10.1161/01.CIR.68.6.1339 (cit. on p. 24).

57. Aultman, Julie M., Peshel, Emanuela, Harfouche, Cyril, S.Firstenberg, Michael, Aultman, Julie M., Peshel, Emanuela, Harfouche, Cyril, and S.Firstenberg, Michael (Nov. 5, 2018). "The Ethics in Repeat Heart Valve Replacement Surgery". In: *Advanced Concepts in Endocarditis*. IntechOpen. ISBN: 978-1-78923-627-9. DOI: 10.5772/intechopen.76844 (cit. on p. 24).

58. Kidane, Asmeret G., Burriesci, Gaetano, Cornejo, Patricia, Dooley, Audrey, Sarkar, Sandip, Bonhoeffer, Philipp, Edirisinghe, Mohan, and Seifalian, Alexander M. (2009). "Current Developments and Future Prospects for Heart Valve Replacement Therapy". In: *Journal of Biomedical Materials Research Part B: Applied Biomaterials* 88B.1, pp. 290–303. ISSN: 1552-4981. DOI: 10.1002/jbm.b.31151 (cit. on p. 25).

59. Stevanella, Marco, Votta, Emiliano, Lemma, Massimo, Antona, Carlo, and Redaelli, Alberto (Dec. 1, 2010). "Finite Element Modelling of the Tricuspid Valve: A Preliminary Study". In: *Medical Engineering & Physics* 32.10, pp. 1213–1223. ISSN: 1350-4533. DOI: 10.1016/j.medengphy.2010.08.013 (cit. on p. 25).

60. Mahmood, Feroze, Gorman, Joseph H., Subramaniam, Balachundhar, Gorman, Robert C., Panzica, Peter J., Hagberg, Robert C., Lerner, Adam B., Hess, Philip E., Maslow, Andrew, and Khabbaz, Kamal R. (Oct. 1, 2010). "Changes in Mitral Valve Annular Geometry After Repair: Saddle-Shaped Versus Flat Annuloplasty Rings". In: *The Annals of Thoracic Surgery* 90.4, pp. 1212–1220. ISSN: 0003-4975. DOI: 10.1016/j.athoracsur.2010.03.119 (cit. on p. 35).

61. Li, Ye, Chen, Joseph C., and Ali, Wamda Mohamed (Sept. 1, 2022). "Process Optimization and In-Mold Sensing Enabled Dimensional Prediction for High Precision Injection Molding". In: *International Journal on Interactive Design and Manufacturing (IJIDeM)* 16.3, pp. 997–1013. ISSN: 1955-2505. DOI: 10.1007/s12008-021-00800-1 (cit. on p. 54).

62. Büsen, Martin, Arenz, Christian, Neidlin, Michael, Liao, Sam, Schmitz-Rode, Thomas, Steinseifer, Ulrich, and Sonntag, Simon J. (Sept. 1, 2017). "Development of an In Vitro PIV Setup for Preliminary Investigation of the Effects of Aortic Compliance on Flow Patterns and Hemodynamics". In: *Cardiovascular Engineering and Technology* 8.3, pp. 368–377. ISSN: 1869-4098. DOI: 10.1007/s13239-017-0309-y (cit. on p. 55).

63. Raghav, Vrishank, Sastry, Sudeep, and Saikrishnan, Neelakantan (Sept. 1, 2018). "Experimental Assessment of Flow Fields Associated with Heart Valve Prostheses Using Particle Image Velocimetry (PIV): Recommendations for Best Practices". In: *Cardiovascular Engineering and Technology* 9.3, pp. 273–287. ISSN: 1869-4098. DOI: 10.1007/s13239-018-0348-z (cit. on p. 55).