

## **CHAPTER 1**

### **INTRODUCTION**

This chapter briefly introduces cardiovascular disorders, emphasizing aortic valve problems necessary for diagnosing, planning, and treating conditions using medical imaging. In Section 1.1, an overview of aortic valve disease and standard treatment protocols is reviewed. Subsequently, Section 1.2 sets out the research issue statement. Section 1.3 outlines the reasoning behind this research and its objectives. The significance of this study is summarized in Section 1.4. Consequently, Section 1.5 lays out the study's structure in depth.

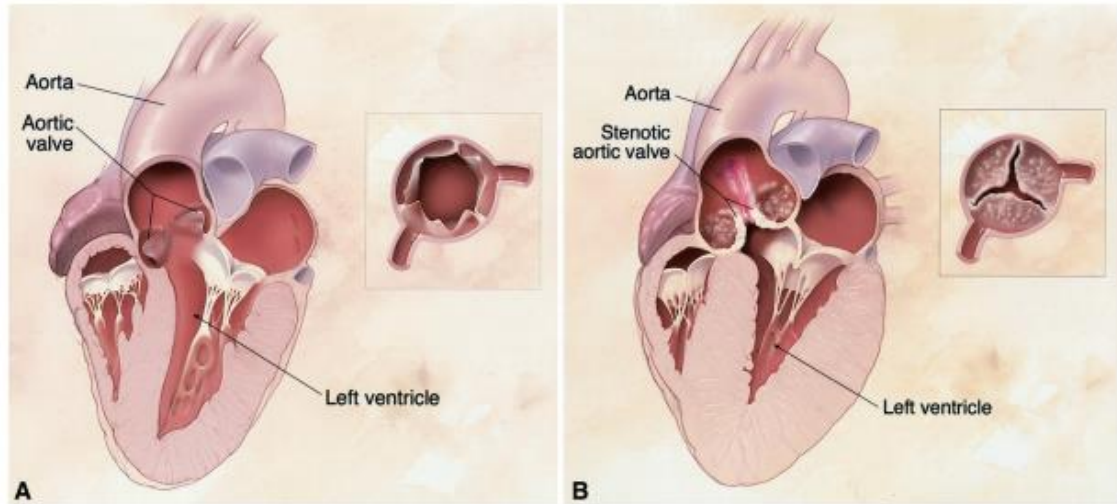
#### **1.1 Research Background**

The heart is the most powerful muscle in the human body, even though it is only the size of a fist. It starts beating from 21 to 28 days after uterine conception, long before birth. Note that the common heartbeats for a person are about 100 000 times every day or approximately two and a half billion times over a 70-year lifetime (Tran & Mahabadi, 2019). The heart pumps blood throughout the body with every heartbeat around 70 times per minute but sometimes can be doubled when exercising or in extreme excitement. Other than that, the pumped-out blood occurs from the left chambers of the heart. It is carried through the diminishing arteries, eventually reaching the capillaries in all tissues, for example, the skin and other body organs. After providing oxygen and nutrients and collecting waste products, the blood is brought back to the right heart chamber through the ever-expanding vascular system. Finally, the waste products are removed during circulation through the liver (Chaudhry & Rehman, 2018).

Cardiac valve illnesses are referred to as "mysterious assassins". They move slowly and indistinctly but are capable of causing rapid and abrupt death. It falls within the Cardiovascular Diseases (CVD) category, encompassing heart and blood vessel disorders (Liu et al., 2014). Globally, CVD is the number one cause of death, and they are projected to occur still. People who died from CVD are estimated at around 17 million, representing 30% of all global deaths in 2005. According to the World Health Organization (WHO), 7.2 million deaths were due to heart attacks, and another 5.7 million were because of cardiac valve diseases and strokes. It is estimated that 23.6 million people will die from CVD by 2030 if current trends continue, mostly from cardiac valve diseases, heart attacks, and strokes (Wang et al., 2020). Note that aortic disease is the most frequent cardiac valve disease recently affecting humanity.

The aortic valve works when the valve is opened to allow blood to flow into the aorta, which then shuts to prevent backflow into the ventricle. Subsequently, the valve opens and closes about 103,000 times a day and over 3.7 billion times in its lifetime (Betti, 2012; Tuna & Brtko, 2018). It opens and closes due to the movement of its three leaflets. To visualize a mental image of the aortic valve in motion, imagine opening and closing three leaflets with each heartbeat, similar to a camera shutter. Although heart valve disorders can harm one's health, aortic valve diseases have more severe repercussions, which consequently attaches higher importance to the functions of this valve (Nishimura, 2002). The usual abnormalities discovered from the aortic valve include the narrowing of the aortic valve opening during systole or aortic stenosis, as well as aortic regurgitation, which happens when the valve leaks back to the left ventricle during diastole (Sequeira et al., 2021). The overall disease burden is estimated at 3% to 4% of adults due to moderate or severe aortic stenosis and regurgitation (Coffey et al., 2021). The prevalence of aortic stenosis and aortic regurgitation increases with

age, estimated in 1% of the population over the age of 55 and 6% of the population over 75 have moderate to severe aortic stenosis or regurgitation.



Source: Nishimura (2002)

**Figure 1.1:** Schematic Heart Illustration During Heart Contraction (Systole)

(A) The Left Ventricle Contracts in A Healthy Person and Fully Opens The Thin Aortic Valve Cusp, Allowing Blood to Flow Freely from The Ventricle into The Aorta  
(B) The Aortic Valve in This Patient with Aortic Stenosis is Abnormally Calcified and Cannot Fully Open. It Produces A Blood Flow Restriction from The Left Ventricle to The Aorta, Causing A Compensatory Increase in The Left Ventricle Thickness

Balloon valvuloplasty and surgical valve repair are two common outcomes of cardiac catheterization, and both are used to assess the health of the heart's arteries. This procedure has a low risk of causing severe complications because it is performed frequently (Manda & Baradhi, 2019). In many instances, balloon valvuloplasty is a catheter-based procedure to treat valve disease by expanding a stenotic or stiff aortic valve with a balloon. This procedure is less invasive than open-heart surgery because it can be performed by inserting a catheter into the blood vessel from the groin instead of open valve replacement methods such as cardiothoracic surgery or another open procedure (Otto et al., 2021).

A decade earlier, a minimally invasive treatment procedure for CVD has grown in demand (Nguyen et al., 2017). If balloon valvuloplasty fails to treat a stenotic valve,

open-heart surgery may be necessary to widen the valve and improve blood flow. These treatments involve the surgeon treating the affected area through a tiny insertion in the patient's chest. However, due to the risk of open-heart surgery, such as possible morbidity, renal injury, and stroke, the surgeon often turns to minimally invasive treatment procedures, such as transcatheter-guided treatment for treating cardiac diseases. During this procedure, an image guidance system is essential in presenting the visual aid of the heart and the diseases to the physician. Ultrasound (US) has been employed recently because of its convenience, low costs, user-friendly, and real-time imaging capacity for this aim (Li et al., 2015a). However, suppose US imaging is now a treatment standard. Certain limitations regarding tissue targets related to surgical instruments can be difficult for blood vessels, particularly with two-dimensional (2D) imaging platforms.

As a result, other three-dimensional (3D) imaging modalities, such as Computed Tomography (CT) and Magnetic Resonance Imaging (MRI), have emerged for treatment. CT and MRI are particularly good at visualizing cross-sectional images of the heart and are helpful in addition to purely anatomical imaging. On the other hand, CT and MRI are essential techniques for cardiac imaging. These imaging tests are regularly performed on patients before therapy. Both CT and MRI provide unique 3D information about the hearts. Currently, a trimodality image-guidance system is unexplored. Although dual-modality fusion and registration is the most popular method to visualize multimodality data, registering and fusing three modalities becomes vital when a patient has three different images to investigate given diseases. A dual-modality image registration (US-CT) has been studied previously (Khalil et al., 2018). However, the surgeon still needed information on both CT and MRI to be presented during the treatment procedures.

Thus, this study proposes investigating the trimodality image registration system for guiding CVD treatment procedures. Trimodality techniques will provide opportunities for innovative ways to display composite structural and valuable knowledge of all modalities. This is done by resolving the issues of temporal synchronization and spatial orientation of moving heart images. These techniques will use intraoperative transthoracic US with preoperative CT and MRI images. The key finding for this study is to investigate trimodality image registrations since it is potentially utilized during intraprocedural navigation for cardiovascular treatment. It involves the preoperative 3D cardiac CT and MRI fused with 2D US intraoperative images.

## 1.2 Problem Statement

CVD, such as coronary artery disease, valvular disease, and stroke, are a leading cause of mortality worldwide. When evaluating treatment options, surgeons frequently consider the risks associated with open-heart surgery, such as the possibility of morbidity, renal injury, and stroke (Jankowski et al., 2021). Therefore, they often choose minimally invasive procedures to treat cardiac diseases, such as transcatheter-guided treatments.

In these procedures, the surgeon makes only a small incision in the patient's chest to reach the affected area. An image-guiding system is essential in these interventions by providing visual cues to the physician. The surgeon may see the heart and any abnormalities or disorders in real-time using an image guidance system. This visual help improves their ability to navigate and carry out essential interventions.

There are many benefits to using an image guidance system during these types of minimally invasive treatments. It enables the surgeon to precisely target and localize the damaged area, which aids in both decision-making and the execution of the treatment. Furthermore, the system gives vital real-time feedback, allowing the physician to examine the efficacy of the treatment and make any necessary adjustments as needed.

The development of the US has revolutionized minimally invasive valve procedures by providing valuable temporal and spatial information about cardiac structures and device components. It is widely used as an imaging modality since it is inexpensive and does not expose patients to radiation. Despite its widespread application, the US has several drawbacks, the most significant of which is a lack of precision in locating and orienting the target tissue (Dave et al., 2018). The limited visualization window constrains the imaging range, which is further compounded by the presence of speckle noise. Due to their small size, the heart and blood vessels are extremely vulnerable to damage from even the slightest misalignments. As a result, there is a need for a better image-guided system that can give surgeons accurate visual feedback throughout treatment procedures.

CT and MRI are two methods that provide complete remedies to these drawbacks. They go beyond US's limitations by giving functional and anatomical images. As complementary approaches to solely anatomical imaging, CT and MRI shine when visualizing cross-sectional images of the heart. Furthermore, CT and MRI are frequently used in patients before treatment as critical tools in cardiac imaging (Hussain et al., 2022). These two modalities can capture different but complementary spatial dimensions of the heart. A trimodality US-CT-MRI technique can integrate this level

of detail with the US during operations. By combining imaging modalities, physicians would have access to more precise and accurate visual data, allowing for more precise and accurate therapy with fewer complications.

Integrating an image guidance system in transcatheter-guided interventions substantially enhances these minimally invasive procedures' safety, accuracy, and overall efficacy (Liu et al., 2019). The system provides visual aid and facilitates precise navigation, allowing surgeons to administer effective treatments for cardiac diseases while reducing the potential risks associated with more invasive surgical techniques.

In addition, recent trimodality imaging improvements have expanded the capability of intra-procedural navigation in minimally invasive procedures. Accurate navigation during the surgery is frequently dependent on this method since it provides vital spatial and temporal information regarding relevant cardiac structures and device components.

In conclusion, using an image guidance system during transcatheter-guided procedures increases the treatment's efficacy, precision, and safety. The integration of CT and MRI with the US has led to the development of trimodality imaging, offering crucial spatial and temporal information for intra-procedural navigation. This imaging modality combination improves visualization and guidance capabilities, allowing surgeons to execute minimally invasive treatments with improved precision and efficacy.

### **1.3 Research Objectives**

This research aims to investigate the trimodality image registration system for guiding CVD treatment procedures. By addressing challenges related to the temporal synchronization and spatial orientation of moving heart images in trimodality techniques, new possibilities arise for comprehensive visualization of structural and functional details from all modalities. This research combined intraoperative transthoracic US with preoperative CT and MRI images. This integration enables innovative approaches to present structural and functional information derived from all three modalities. The main research objectives included in this research to achieve the purpose are:

1. To investigate a temporal registration system for CT-MRI-US.
2. To investigate a spatial registration system for CT-MRI-US.
3. To determine the image registration validation procedures based on the clinical indices for the trimodality image registration.

### **1.4 Scope of Research**

This research aims to investigate a trimodality image registration system designed to guide treatment procedures for CVD. The study will be carried out in three major stages: 1) temporal registration development, 2) spatial registration development, and 3) validation of the trimodality image registration scheme. The three imaging modalities employed in this investigation are CT, MRI, and US. It is important to note that the images captured by each modality are acquired at different time points. Therefore, in the initial stage, the CT, MRI, and US images will be aligned and synchronized in terms of temporal correspondence.

The second stage aims to align the modalities in a uniform spatial coordinate system or location. It will be accomplished by combining rigid and nonrigid geometrical transformations into the spatial registration method using a mutual information technique. This stage ensures that images from various modalities are precisely registered and spatially aligned, allowing for complete analysis and evaluation.

In the final stage, the trimodality image registration procedure is validated qualitatively and quantitatively. Note that the visual output quality will be evaluated along with the accuracy of the registration method. This validation aims to ensure the accuracy and consistency of the trimodality image registration method.

This study will focus on patients diagnosed with CVD at Hospital Serdang who underwent CT, MRI, and US procedures between 2015 and 2020. It also offers the potential to obtain valuable insights regarding the utilization of trimodality image registration within the framework of CVD diagnosis and treatment planning. These insights may ultimately contribute to the advancement of clinical practice and the improvement of patient care.

### **1.5 Significance of Research**

Due to the alarming rise in the number of individuals diagnosed with CVD, physicians must enhance their treatment decisions to obtain more accurate diagnostic information. This investigation has led to an improved approach to cardiac treatment procedures by implementing trimodality image registration and enhancing the image-guided system. As a result, patients suffering from heart disease now have access to safer and more effective treatment options instead of undergoing the high-risk open-heart surgery procedure. The enhanced techniques proposed in this research aim to minimize the post-monitoring expenses for heart patients compared to those associated

with open-heart surgery. Hence, the use of trimodality US-CT-MRI highlights the importance of imaging in guiding cardiovascular treatment procedures by leveraging the strengths of these methods while mitigating their limitations. The decreased cost of cardiovascular treatment enables more heart patients to receive care, reducing mortality rates related to heart diseases. Furthermore, trimodality image registration constitutes a significant advancement and technique in medical diagnostics, fostering essential discoveries.

## **1.6 Outline of the Research**

This thesis consists of five chapters, each devoted to a different study area. Chapter 1 provides an overview of the research framework, the problem statement, the research objectives, and the significance of the study. Furthermore, the chapters outline the research framework, which is crucial for designing an effective research structure.

Chapter 2 briefly gives an overview of the literature review performed in this study, with a specific emphasis on trimodality image registration techniques for diagnosing CVD using CT, MRI, and US. The chapter is organized into three parts, each dedicated to investigating theoretical elements and explaining various methodologies and modalities used in diagnosing CVD. Other than that, the significance of trimodality in clinical contexts is emphasized, particularly its role in aiding registration functions, highlighting its usefulness in practical medical applications. In addition, this chapter presents the fundamentals of image processing in the medical field and its relevance to trimodality techniques. A thorough overview of prior research on multimodality and trimodality for image processing is also provided, as is an examination of various surgical applications guided by medical imaging.

Chapter 3 of this thesis comprehensively explains the methodology employed in this study. It includes a detailed description of the procedures utilized for CT, MRI, and US imaging. Furthermore, the chapter discusses the technique employed for image registration, which involves aligning and combining multiple imaging modalities to create a cohesive and accurate representation. The chapter also goes into the validation procedure, evaluating the registration technique's correctness and ensuring that the registered images match the ground truth and fulfil the desired precision and quality standards.

Chapter 4 presents an array of qualitative and quantitative outcomes generated by the automated pipeline of trimodality registration, introduced in Chapter 3. The registration method underwent rigorous validation using a dataset comprising 20 patient data sets. This chapter also discusses and analyses the results obtained from the proposed techniques, highlighting their clinical significance within the context of cardiovascular imaging. Apart from that, a detailed comparison is made between the findings of this study and those of earlier studies on the subject. It is vital to highlight that this chapter acknowledges and discusses numerous limitations observed during the study. Because of these limitations, helpful suggestions to enhance the current method are presented, providing insights for further research and development in trimodality image registration.

Chapter 5 summarizes the study, emphasizing the main findings that can be drawn from this research. It also presents the current contributions of the study and suggests potential directions for future research.