Intracardiac Ultrasound Guided Systems for Transcatheter Cardiac Interventions

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A thesis submitted in partial fulfillment of the requirements for the Doctor of Philosophy degree in Biomedical Engineering
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Abstract

Transcatheter cardiac interventions are characterized by their percutaneous nature, increased patient safety, and low hospitalization times. Transcatheter procedures involve two major stages: navigation towards the target site and the positioning of tools to deliver the therapy, during which the interventionalists face the challenge of visualizing the anatomy and the relative position of the tools such as a guidewire. Fluoroscopic and transesophageal ultrasound (TEE) imaging are the most used techniques in cardiac procedures; however, they possess the disadvantage of radiation exposure and suboptimal imaging. This work explores the potential of intracardiac ultrasound (ICE) within an image guidance system (IGS) to facilitate the two stages of cardiac interventions.

First, a novel 2.5D side-firing, conical Foresight ICE probe (Conavi Medical Inc., Toronto) is characterized, calibrated, and tracked using an electromagnetic sensor. A point-to-line registration technique is employed to perform the calibration, which is validated using two geometric phantoms. The results indicate an acceptable tracking accuracy within some limitations. A texture mapping-based 3D Slicer module is also developed to visualize the unique conical geometry of the Foresight ICE probe.

Next, an IGS is developed for navigating the vessels without fluoroscopy. A forward-looking, tracked ICE probe is used to reconstruct the vessel on a phantom which mimics the ultrasound imaging of an animal vena cava. Deep learning methods are employed to segment the complex vessel geometry from ICE imaging for the first time. The ICE-reconstructed vessel was compared to the CT-segmented version of the vessel, which showed a clinically acceptable range of accuracy. The average surface distance error was recorded to be less than a millimeter.

Finally, a guidance system was developed to facilitate the positioning of guidewire and tools during a TriClip procedure which is performed to repair the tricuspid valve by reducing the amount of regurgitation as seen in Doppler ultrasound imaging. The designed system potentially facilitates the positioning of the TriClip at the coaptation gap by pre-mapping the corresponding site of regurgitation in 3D tracking space. A user-friendly Slicer module was developed to automatically segment the vena contracta of the regurgitant jet from Doppler ICE and place it in 3D space.
Summary for Lay Audience

Heart surgeries have evolved from high-risk open-heart surgeries to much safer minimally invasive procedures. Transcatheter interventions often involve repairing a structural heart disease by accessing the heart through veins and arteries. Thin, wire-like tools such as a guidewire are inserted in the body via limbs and are then used to traverse the vessels using live x-ray technology called fluoroscopy. Once the tools reach the heart, they are then positioned at the pathological, target site and deployed to deliver therapy. This positioning of tools is often facilitated using an external ultrasound probe. In this work, we explore the potential of using a novel intracardiac ultrasound probe (ICE) to assist transcatheter procedures in an image-guided system (IGS). We augment a Foresight ICE probe (Conavi Medical Inc.) with an electromagnetic tracking sensor so the probe’s position can be always tracked in 3D space. Calibration methods to track the exact location of the ICE image are described as well. The second objective is to demonstrate the feasibility of using a tracked ICE probe in order to generate a vascular roadmap which can then be followed by a tracked guidewire to navigate the vessels. We designed an ultrasound-realistic vessel phantom and reconstructed the vessel in real-time using deep learning methods. The results indicate that ultrasound technology can be used instead of fluoroscopy to visualize and traverse the vessels. The third objective is to develop an IGS to assist the positioning of a therapeutic device during tricuspid valve repair surgery. Current imaging standards produce suboptimal imaging of the tricuspid valve and it can be challenging to identify the site of tricuspid valve regurgitation. We designed an algorithm to automatically detect the location of the regurgitation site from the color Doppler imaging on a tracked ICE probe. This method helps pre-map the location the clinicians have to target with the therapeutic device. This work demonstrates some of the ways an ICE ultrasound technology can improve and assist the existing procedural workflows by providing more information to the clinicians safely and accurately.

Keywords: Intracardiac echocardiography (ICE), Image-guided system (IGS), Transcatheter interventions, Tricuspid valve repair, Vessel reconstruction, Fluoro-free navigation.
Co-Authorship Statement

This thesis integrates several publications that are published or in preparation for submission. Details regarding the author’s contributions to these manuscripts are provided below.

Chapter 2


**Contributions:** This chapter contains work beyond the above-mentioned publication. It also includes an extensive report on the characterization of the Foresight™ ICE probe. My contributions towards the report include experimental setup and design, data acquisition, data analysis and writing of the report. Elvis C.S. Chen assisted with the study design. Terry Peters and Brian Courtney reviewed and edited the report. For the manuscript, my contributions include study design, performing experiments, data collection and manuscript preparation. Natasha Alves and Germain Hwang provided their expertise on the probe design during all stages. Elvis C.S. Chen extended his technical expertise during the calibration process. All authors helped in reviewing and editing the manuscript.

Chapter 3


**Contributions:** My contributions to this study include phantom design, preparation of raw materials, imaging data collection, image analysis, and manuscript preparation. John Moore assisted with phantom making and CAD designs. Roberta Piazza helped with the preparation of materials for the phantoms. Efthymios Maneas extended his expertise in phantom making and editing the manuscript. All authors helped in reviewing and editing the manuscript.

Chapter 4


Contributions: My contributions include the study design, software development, data collection and analysis, and manuscript writing. Leah Groves assisted with the ultrasound reconstruction pipeline and manuscript editing. Leandro Cardarelli-Leite provided his expertise in designing the study and structuring the manuscript. Patrick Carnahan assisted during the software development stage involving deep learning. Djalal Fakim and Humayon Akhuanzada established the ground truth segmentation. David Hocking supervised the process of defining ground truth and made corrections. All authors helped in reviewing and editing the manuscript.

Chapter 5


Contributions: My contributions to this work includes study design, data collection, development of the methods, data analysis, and writing. Djalal Fakim was responsible for the manufacturing of the patient-specific valve models and imaging the beating heart phantom for data acquisition. He also contributed towards the writing of the final manuscript. Daniel Bainbridge provided clinical expertise in designing the research question and establishing the clinical need. All authors helped in reviewing and editing the manuscript.
Acknowledgements

Although as Ph.D. students, we are encouraged to take ownership of our work, I believe it to be a collaborative (ad)venture. This thesis would not be the same if it weren’t for the support of many wonderful individuals – and a cat.

I would like to thank my supervisor, Dr. Terry Peters, for providing me with this opportunity to conduct research and for having faith in my abilities all the way through. From my first interview in a small town in Pakistan to presenting my work internationally in Japan and everything in between (read: 5 years of PhD and a pandemic), Terry has been a constant source of encouragement, guidance, and support. He leads with both brilliance and kindness and has inspired me to be a similar scientist. Thank you for being a mentor to me.

I would also like to thank Dr. Elvis Chen and John Moore for their patience and energy spent in explaining the concepts to me, helping me design studies, as well as giving me the courage to take on challenges. I learned to overcome my fear because John encouraged me to experiment with the new ICE technology and “break a probe”. A great deal of gratitude goes toward the members of my advisory committee – Dr. James Lacefield and Dr. Dan Bainbridge, as well as clinicians – Dr. Hocking and Dr. Leite for their valuable discussions and feedback throughout my degree. Their suggestions have indeed steered this research to be clinically relevant. This work would not have been possible without the research collaboration and support of Conavi Medical Inc. with special thanks to Bogdan Neagu, Feng Patrick Li, and Brian Courtney.

To the members of the VASST lab – thank you for creating a welcoming environment for me and being open to helping solve many, many problems I encountered over the years. A special thanks to Wenyao, Uditha, and Joeana for listening to my rants, and Leah and Patrick for always debugging my code with me. Dan, Djalal, Michellie, Shuwei, and my two Italian geniuses – your presence made the lab a fun place to work in. Thank you to the “Lab Moms” for being there for all of us.

To my friends – Sarah & El, Jo & Jo, and Gavin who gave me a family away from home and took care of me like their own. I owe my sanity to your support and delicious cooking. Gavin, I don’t have the words to describe the amount of faith and encouragement you gave me. Thank you. Last but not least – a ton of gratitude towards my family who supported my dream of being an academic. It was not easy living so far away from you, but your love and prayers kept me going. Thank you Ammi and Abbu for giving me the best possible life – full of love, ease, comfort, science, education, respect, and kindness. My peers, friends, and family – you have always lifted me and talked me into embracing my strengths. I would not have achieved this without your care. I thank God for bringing me to this point in my life and for blessing me with such an amazing support system.
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<tr>
<td>2D</td>
<td>Two dimensional</td>
</tr>
<tr>
<td>2.5D</td>
<td>Two and a half dimensional</td>
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<tr>
<td>3D</td>
<td>Three dimensional</td>
</tr>
<tr>
<td>4D</td>
<td>Four dimensional</td>
</tr>
<tr>
<td>CT</td>
<td>Computed tomography</td>
</tr>
<tr>
<td>ECG</td>
<td>Electrocardiogram</td>
</tr>
<tr>
<td>EM</td>
<td>Electromagnetic</td>
</tr>
<tr>
<td>FOV</td>
<td>Field of view</td>
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<tr>
<td>ICE</td>
<td>Intracardiac echocardiography</td>
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<tr>
<td>IGI</td>
<td>Image guided intervention</td>
</tr>
<tr>
<td>IGS</td>
<td>Image guidance system</td>
</tr>
<tr>
<td>IVC</td>
<td>Inferior vena cava</td>
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<tr>
<td>IVUS</td>
<td>Intravascular ultrasound</td>
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<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
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<tr>
<td>MTS</td>
<td>Magnetic tracking system</td>
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<tr>
<td>MV</td>
<td>Mitral valve</td>
</tr>
<tr>
<td>PVA-c</td>
<td>Polyvinyl alcohol cryogel</td>
</tr>
<tr>
<td>ROI</td>
<td>Region of interest</td>
</tr>
<tr>
<td>SVC</td>
<td>Superior vena cava</td>
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<tr>
<td>TAVR</td>
<td>Transcatheter aortic valve repair</td>
</tr>
<tr>
<td>TEE</td>
<td>Transesophageal echocardiography</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Full Form</td>
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<td>--------------</td>
<td>-----------</td>
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<tr>
<td>TMM</td>
<td>Tissue-mimicking material</td>
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<tr>
<td>TR</td>
<td>Tricuspid valve regurgitation</td>
</tr>
<tr>
<td>TTE</td>
<td>Transthoracic echocardiography</td>
</tr>
<tr>
<td>TV</td>
<td>Tricuspid valve</td>
</tr>
<tr>
<td>US</td>
<td>Ultrasound</td>
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<tr>
<td>VMM</td>
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Chapter 1

Introduction: Ultrasound Guidance in Transcatheter Cardiac Interventions

Transcatheter cardiac interventions face the challenges of invisible tool phenomena, not having a line-of-sight with the anatomy, and relying on 2D fluoroscopic imaging, which is known to cause harmful radiation exposure and spinal issues in the interventional team due to the need to wear heavy lead-lined aprons. In this thesis, we address these challenges by designing image guidance systems (IGS) to facilitate the different stages of a transcatheter cardiac procedure using electromagnetic (EM) tracking technology and intracardiac echocardiography (ICE). We first characterize, calibrate, and track a novel Foresight™ ICE probe so it may be used in an IGS. Then, an ICE-generated vessel reconstruction method is developed to facilitate fluoro-free tool navigation. Finally, the tracked ICE probe is used in a Doppler mode to identify the site of tricuspid valve regurgitation in 3D space and facilitate the device positioning step during valve repair interventions. This chapter provides the necessary background information and overview of the state-of-the-art technology relevant to the work performed in this thesis.

1.1 Cardiology

1.1.1 Cardiac Anatomy

The heart is the heart of the human body as it supplies and regulates blood flow throughout the circulatory system to keep the rest of the body alive. This complex and dynamic organ continuously beats by means of muscular contractions to maintain the blood flow. It is positioned slightly left to the mediastinum in the chest, and in humans, there are four cardiac chambers – two atria and two ventricles, along with two atroventricular valves namely the tricuspid valve (TV) and the mitral valve (MV). The right atrium, the tricuspid valve, and the right ventricle
are collectively referred to as the ‘right-sided heart’. Similarly, the left atrium, the mitral valve, and the left ventricle are called the ‘left-sided heart’. The left and right atria are separated by a thin wall of tissue called the atrial septum, that needs to be punctured when a left-sided transcatheter procedure is performed. From a therapy perspective, there are many differences in the left and right sides of the heart including the anatomy of the atrioventricular valve, the pressures on each side, and the means of access to the desired anatomical structure.

The pressure on the left side of the heart is around three times higher than that on the right side, and by approximately 8mmHg on average and is mainly due to the function each side is performing. The muscles on the left side are stronger as well since they have to pump the oxygenated blood to the entire body including the extremities. On the other hand, the right-sided heart supplies blood to the lungs with fewer vessels and less resistance, thus requiring lower blood pressure and pumped by less powerful heart muscles. For this reason, there is a high risk of perforation during right-sided heart surgery or therapy.

The nature of mitral and tricuspid valve surgeries/therapies differ significantly as these valves differ greatly in their anatomy and positioning. The mitral valve has two leaflets that are connected to the papillary muscles using tendinous chords (chordae tendinae) or “heart strings”. Due to its posterior location, close to the esophagus, the MV can be visualized well using standard cardiac ultrasound or transesophageal echocardiography (TEE) views. As such, mitral valve therapies have been well developed and standard protocols exist in clinical practice. Meanwhile, tricuspid valve therapies and imaging protocols are currently underway. As the name suggests, the tricuspid valve has three leaflets that regulate the blood flow between the atrium and the ventricle. It is positioned such that the TEE probe is parallel to the TV annulus and at a significant distance, thus causing signal dropout in the ultrasound (US) imaging. Moreover, the chordae are more complicated in the case of the TV, with the chordae tendinea attaching the leaflets to the papillary muscles as well as directly to the walls of the right ventricle.

This thesis deals primarily with transcatheter interventions which are often performed to repair structural heart diseases. During these interventions, the heart is accessed using either the inferior vena cava (IVC) or the superior vena cava (SVC) which opens directly into the right atrium. The tricuspid valve can be accessed by entering in the right atrium and bending the catheter at roughly 90 degrees. To access the left atrium or the mitral valve, the catheter first needs to enter the right atrium and then puncture the atrial septum to be advanced into the left atrium. Transseptal puncture is a meticulous procedure with an associated risk of aortic valve puncture or pericardial perforation.
1.2. (R)evolution of Cardiac Therapy

This thesis strongly advocates for percutaneous, transcatheter, cardiovascular interventions as opposed to open-heart surgeries. We, as humankind, have come a long way towards simplifying the surgical procedures for the heart and are still progressing. From the first successful heart surgery by Dr. Ludwig Rehn in 1896 to repair a stab wound, to the revolutionary invention of the cardiopulmonary bypass machine and the development of Cath labs and interventional suites – surgery has continuously improved with technological advances [39, 69]. Today, well-established techniques in cardiac surgery can further benefit from modern technology to enhance patient safety, minimize the concerns of the medical staff, and reduce the time for hospitalization. This section looks at the different categories of cardiac surgery and therapy i.e., the evolution of open-heart surgery, to minimally invasive cardiac surgeries and transcatheter procedures. A comparison of these major surgical categories can be seen in figure 2.

1.2.1 Open-Heart Surgeries

Cardiac surgery was clinically initiated in the early 1940s when only a few procedures, including the closure of a patent ductus to separate the two merged blood vessels, repair of aortic coarctation or narrowing, the Blalock-Taussig shunt to increase the blood flow to the lungs, and the mitral commissurotomy to repair mitral valve stenosis could be performed [189]. Atrial septal defect closure was tried using techniques such as hypothermia and the Gross well [58],

Figure 1.1: Illustration of the cross-sectional view of the heart with common anatomical features [157]
but these approaches could not be adapted for many other procedures, and in particular the repair of structural heart diseases. Dr. Lillehei [58] attempted to repair a ventricular septum defect using a ‘cross-circulation’ technique where the patient’s blood was oxygenated through their mother’s circulatory system. This technique, with the potential of a 200% mortality rate(!), successfully demonstrated the feasibility of a temporary cardiopulmonary bypass in order to perform a cardiac repair.

Open-heart surgeries became more reliable and popular with the advent of the Mayo-Gibbon device – the first truly commercial heart-lung machine made with the design of Dr. Gibbon’s original machine. [57]. Since then, open-heart surgeries became a standard of care for many procedures including aortic valve replacement, valve replacement using a mechanical caged ball-and-set valve, and coronary artery bypass grafting. Open heart surgeries are performed using a technique called median sternotomy where a large, vertical incision is made along the sternum to crack it open while the procedure is performed using conventional surgical tools. The cardiac surgeon has a direct line of sight with the tools and the anatomy while an anesthesiologist maintains the patient under general anesthesia.

Despite successful procedural outcomes, open-heart surgeries have a high rate of postoperative complications, leading to a prolonged stay at the hospital, and overall high treatment cost [42]. These post-operative complications include hemorrhage, respiratory distress syndrome, stroke, infection, and sepsis. Cardiopulmonary by-pass often results in systemic inflammatory response leading to organ failure, atrial fibrillation, hematologic complications, pulmonary adverse reactions including edema and ischemia, and neuro-cognitive deficits, even stroke. Additionally, patients have a longer recovery period to get back to their daily routine. These complications and heavy impact on the patient’s body are the prime reasons that drove cardiac therapy towards minimally invasive procedures.

1.2.2 Minimally Invasive Cardiac Surgeries

Over the last few decades, minimally invasive cardiac surgeries have largely replaced open-heart procedures. They are characterized by a small incision made to the chest, usually 8 – 10 cm in length. These surgeries can be performed using many techniques such as mini-thoracotomy, mini sternotomy, clamshell thoracotomy, and robot-assisted methods. The site and shape of the incision varies between the different surgical procedures, depending on the surgical site. Such procedures are performed by cardiac surgeons with specialized tools, often with the assistance of imaging to monitor the patient’s health and for the delivery of therapy while blood circulation is maintained via peripheral cardiopulmonary bypass. However, both on-pump and off-pump techniques have been utilized successfully, and beating heart techniques
can have comparable, if not superior, outcomes with lower complication rates [180]. Similar to open-heart surgery, an anesthesiologist is always present on-site for on-pump techniques. Some studies have shown an increased operational time for minimally invasive procedures but decreased cost due to significantly shorter stays in intensive care.

Minimally invasive procedures have several advantages over the conventional sternotomy methods including earlier extubation (by 1 hour), earlier reintegration into their normal lives (by 7 days) as well as significantly less pain [68]. Nevertheless, these procedures still involve an incision at the chest, and thus leave the patient vulnerable to wound infections, arrhythmia, memory loss, and blood clots as well as significant blood loss. The administration of anesthesia also adds to the net cost and possible complications of the procedure. Furthermore, they carry the same risk of myocardial infarction, stroke, and neurological disorders as the conventional sternotomy [63].

Overall, minimally invasive surgeries have proven to be effective, but procedural safety can be improved. The guiding principle behind the evolution of cardiac therapy is to minimize the ‘side-effects’ of the surgery i.e., any risk or complication not a part of actual therapy such as the incision wound in the case of minimally invasive surgery. The techniques of delivering therapy can thus be employed percutaneously, without opening the chest and inducing the risk of infection along with other complications. This genre of cardiac therapy is known as micro-invasive surgery or transcatheter interventions.

Figure 1.2: Comparison of features between the conventional open-heart surgery (left), minimally invasive cardiac surgeries (middle), and micro-invasive or transcatheter interventions (right)
1.2.3 Micro-invasive Cardiac Surgeries

Micro-invasive surgeries, more commonly known as transcatheter interventions are procedures that are performed entirely percutaneously. Only a small incision is made in the skin to insert specialized, miniaturized tools in order to deliver therapy. During these interventions the patient is placed only under local anesthesia and remains conscious in many cases. One of the earliest procedures, a percutaneous transluminal coronary angioplasty, was performed by Dr. Andreas Gruentzig in 1977 and it began the era of interventional cardiology [46]. Since then, transcatheter procedures have been developed for different fields including pediatric cardiology, electrophysiology, and most prominently in structural heart diseases. Reflecting the focus of this thesis, the various elements of transcatheter interventions are discussed in the next chapter in detail.

1.3 Transcatheter Cardiac Interventions

1.3.1 Introduction

Transcatheter interventions are percutaneous procedures, usually performed using specialized tools and catheters without opening the chest. Catheters are tube-like structures with a therapeutic tool or device at their tips. Each catheter is specialized, and the tip is designed to perform a certain task. Most catheters are steerable which allows the clinician to accurately deliver the therapy [20]. Catheterization refers to introducing catheters into the cardiovascular system and is performed under fluoroscopic guidance in a catheterization laboratory (Cath lab). Cath labs are usually small and lack the facilities for multimodality imaging and surgical operations. On the other hand, an operating room (OR) lacks the angiographic capabilities required for transcatheter interventions. A hybrid OR is an ideal choice for performing interventional procedures, which combines an OR with high-resolution fluoroscopy equipment such as an O-arm. A complete heart team can operate in this suite with a high focus on patient-safety [102,46].

Transcatheter interventions are highly popular for angioplasty, stent placement, and the treatment of structural heart diseases such as the closure of cardiac defects in the adult population including patent foramen ovale closure, atrial septal defect closure, ventricular septal defect closure, and left atrial appendage occlusion [107,46]. These procedures, especially atrial septal defect closure, have a success rate of up to 98% [206]. They have also been adopted by clinicians to perform valve repair such as aortic balloon valvuloplasty, TAVI, transcatheter mitral valve repair, and recently embraced transcatheter tricuspid valve (TV) repair procedures [166]. They have also become the gold standard for electrophysiological treatments, where an ablation catheter is used to treat atrial fibrillation [27]. During this procedure,
a tracked intracardiac echocardiography (ICE) probe is used to reconstruct the atrial chamber from the inside to provide a real-time anatomical model as well as facilitate trans-septal puncture \[175\]. Apart from being used in electrophysiology, ICE is involved in the device closure procedure for the atrial septal defect and patent foramen ovale. But in most of the transcatheter interventions, the current standard for ultrasound imaging employs a transthoracic echo (TTE) preoperatively or a transesophageal echo (TEE) intraoperatively. Real-time intraoperative imaging is essential for accurate navigation, positioning, and deployment of tools at the target site. Therapeutic tools for valvular repair can be categorized as annuloplasty, leaflet repair, and valve replacement devices. Prendergast et al. \[166\] provide a comprehensive overview of the state-of-the-art transcatheter valve repair techniques along with a visual summary that can be seen in figure 1.3.

Figure 1.3: \[166\] – Overview of common transcatheter valve repair therapies

An indispensable tool used during an intervention is a guidewire – a long, thin, metallic wire that can be inserted into the body using a needle, and functions as a guide to introduce larger instruments such as catheters, therapeutic tools, and a central venous line inside the body. A guidewire is an essential tool to interventional cardiology, as its insertion is the first step in any cardiac catheterization, where the goal is to transport a therapeutic device to a surgical site. They are also used to traverse the vessels and reach the target site first, and then the devices or catheters follow, ensuring patient safety as well as allowing the tools to be more flexible in design \[196\]. Guidewires come in many different types, based on their composition, shape
of the tip, torquability, and tactile feedback, and some procedures call for a specific type of guidewire.

1.3.2 Vascular Access

Transcatheter cardiac interventions are usually performed via vascular access, where the heart is accessed through veins or arteries. Catheters are inserted into the vessels using the Seldinger technique, named after Dr. Sven Ivar Seldinger who introduced this method in 1952. The technique is described in his own words as \[200\] “...I had a sudden attack of common sense and knew what to do: needle in, guidewire in through the needle, needle out, catheter in over the wire, and finally removal of the guidewire”. Since then, this technique has been used in interventional cardiology. The Seldinger technique is a safe and effective means of inserting a catheter into a vessel, with the most common complication being a minor haematoma around the vessel. Once the tools, either guidewire or the catheter, are inserted into the vessel, they then navigate the vasculature under fluoroscopic guidance to reach the heart. Transfemoral access is one of the most common routes for vessel navigation to reach the atria, however, in the case of a thrombotic vessel or torturous arterial path, transradial access is preferred. Some of the common vascular access points are indicated in figure 4 with a description given below.

![Common vascular access sites](image)

Figure 1.4: Common vascular access sites used during percutaneous, transcatheter interventions

1. Trans-femoral – is the most common vascular access for transcatheter interventions.
Both the femoral vein and femoral artery are used to gain access to the heart. Trans-femoral access complications include perforation of the iliac vessels, limited flow in femoral artery or vein, and acute limb ischemia [46].

2. Trans-jugular – access is through the jugular vein in the neck. This route is preferred when the femoral access is contra-indicated for the patient.

3. Trans-axillary or subclavian artery access is used in some cases such as aortic valve replacement where a small incision is made at the shoulder.

4. Trans-radial – is a less common means of arterial access, through the arm. This method is avoided as it often leads to blood loss because of high blood pressure in the region.

For structural heart diseases, especially the MV and the TV, the valve is accessed through transfemoral access. A thin, metal guidewire is inserted usually in the femoral vein, and it traverses the iliac vein and then the inferior vena cava (IVC) to reach the right atrium in the heart. When performing the mitral valve repair therapy using MitraClip (Abbott, Chicago), the valve is accessed through the right atrium, by puncturing the atrial septum to reach the left atrium.

1.3.3 Stages

For every micro-invasive or transcatheter cardiovascular procedure, regardless of the specifics of the pathology and the type of therapy, there are two main stages involved – navigation and positioning. The pathological structure within the heart or the vessels is referred to as the ‘target site’ and the process of getting to the target site via vasculature is called navigation, whereas the process of properly orienting the tools at the target site is known as targeting or positioning [136].

Navigation

For a given procedure, once vascular access is established, the next step is for the guidewire to traverse the vessels and reach the target organ or target site. A therapeutic device then follows the path established by the guidewire. Currently, this vascular navigation is achieved under fluoroscopic guidance, often using contrast agents in the form of angiography or a venogram in order to see the vessel walls and branches. Fluoroscopic guidance consists of continuous 2D X-ray projections of the thorax form an appropriate viewing angle. Without contrast agents, the interventionalist is only able to visualize the bony structures and the metal guidewire. Under these circumstances, the vessel navigation stage involves a risk of vessel wall perforation, iliac
vein rounding, and traversing into the wrong vessel branch. According to clinicians, vascular navigation is the less demanding stage in terms of navigation accuracy and is comparatively a lower risk stage of a transcatheter procedure for the patient. However, recent literature shows that the radiation used during both the navigation and positioning stage is harmful to the medical team. The details of radiation-induced complications are discussed later in this chapter.

Positioning

Once a therapeutic device reaches the target site with the help of a guidewire, the next stage is to orient and position the device correctly in order to deliver accurate therapy. Currently, this step is performed using a combination of fluoroscopic and TEE imaging. The accuracy constraints are high for device positioning as it dictates how effective the therapy will be. The interventionalists rely on imaging-derived anatomical landmarks to position the device, which after careful positioning, is finally deployed. In the case of left-sided procedures, a prerequisite step of transseptal puncture is also involved which necessitates tool positioning. A needle-tip catheter must be positioned at a target location on the atrial septum, advanced to puncture the septum wall, and followed by the therapeutic catheter to enter the left atrium.

1.3.4 Interventional Imaging

This subsection reviews the state-of-the-art, non-diagnostic, procedural imaging modalities used to carry out structural heart interventions in a hybrid OR.

X-ray Fluoroscopy

X-ray fluoroscopic imaging is the backbone of most clinical transcatheter procedures, and is the current gold standard for intraprocedural imaging in a Cath lab, due to its large field of view (40cm) and high temporal resolution (a few milliseconds). Contrast agents are often administered to view the vasculature, especially for coronary interventions. For visualization of cardiac soft tissue such as the myocardium, atrial septum, ventricular septum, or the valvular anatomy, a radio-opaque dye must be injected into the heart [103]. Commercial fluoroscopic imaging systems include Alphenix Core (Cannon Medical), Optima / Innova (GE Healthcare), Azurion series (Philips), Trinias C16 unity (Shimadzu Medical Systems), and Artis One (Siemens Healthineers), all of which have a built-in dose monitoring capability and roughly occupy a space of 6x6 m. A typical interventional x-ray system is composed of a ceiling-mounted C-arm gantry, with a 30x40 cm flat-panel detector and a flexible positioning system to permit the desired angled projections.
1.3. Transcatheter Cardiac Interventions

Fluoroscopy is used in both the navigation and positioning stages of an intervention. During the navigation of tools and guidewires, fluoroscopy is part of the standard clinical practice. During device positioning, however, a combination of fluoroscopy and ultrasound is used to guide the tools. In a TAVI procedure, fluoroscopy is used during the aortic valve crossing, positioning the balloon, and deployment of the valve stage, while TEE is used for valve positioning and hemodynamic monitoring [208]. In the case of mitral valve repair interventions, fluoroscopy is used to cross the atrial septum and orient the tools properly at the mitral valve, although ultrasound technology has taken over these tasks because of the complications that arise due to radiation.

Fluoroscopy is an expensive, immobile, and demanding imaging technique, requiring specialized equipment including, but not limited to, lead shielded room, lead apron, eye protection, and a thyroid shield [121]. The preparation of lead shielded rooms alone adds an enormous cost to the hospital. Another major drawback is the presence of harmful X-ray radiation. Guidelines to minimize the damage inflicted by fluoroscopy have been in place for decades and are continuously revised [54]. They include equipment adjustments such as using copper filters and high-frequency generators, use shielding wearables, maintenance of imaging and shielding equipment, continuous monitoring of radiation exposure, and appropriate safety training of medical students. Moreover, there are extensive guidelines for an operator to minimize fluoroscopic time, optimal collimation of x-ray beams, and positional adjustments. These guidelines and precautionary measures help reduce the exposure, but do not eliminate it completely.

In order to minimize radiation exposure and avoid costs of fluoroscopic equipment, near-zero fluoro methods and zero-fluoro surgical workflows have been proposed [80]. Several, predominantly echo-based, image-guided systems have been proposed to eliminate fluoroscopy, especially from electrophysiology lab [187, 151]. In a recent study, Matsubara et al. [135] show the successful clinical implementation of fluoro-less catheter ablation procedure performed without using lead aprons. Fluoro-free IGS for valve repair interventions, transseptal puncture, and general tool navigation and positioning tasks are still in development.

Ultrasound

Ultrasound (US) technology or commonly known as echocardiography is used during all stages of transcatheter interventions including pre-procedural planning and diagnostic imaging, intra-operative image guidance, and post-operative evaluation, and is a vital component of a Hybrid OR to allow for real-time visualization of cardiac soft tissues. During a cardiac intervention, ultrasound guidance is commonly provided using one or more of these echocardiographic methods: trans-thoracic echocardiography (TTE), transesophageal echo (TEE), intracardiac echocardiography (ICE), and Doppler imaging techniques. Among these, TEE has become
Figure 1.5: Image guidance during a tricuspid valve repair intervention using Cardioband where fluoroscopy (left) is used to align the device (pointed by the arrow) perpendicular to the right coronary artery (RCA), followed by the positioning of the device in the right atrium (RA) under intracardiac ultrasound imaging.

a standard for assisting device deployment during structural heart interventions [182]. If the patient is intubated, then TEE is preferred over TTE because of higher image quality, higher resolution, and anatomical views. 3D TEE provides high-quality en-face visualization of the mitral valve and is used during edge-to-edge repair [30]. ICE imaging is routinely used to perform trans-septal punctures during left-sided procedures and is an indispensable component of the electrophysiology lab. Spectral Doppler imaging is used for hemodynamic characterization, while color Doppler imaging is employed for the assessment of valvular regurgitation and paravalvular leaks. Common types of US probes are discussed in detail later in this chapter.

One limitation of any echocardiographic method, is the difficulty in localizing the tools within the US image. Catheters and guidewires can be seen in 2D ultrasound images however it becomes difficult to distinguish the tip from the shaft. 3D ultrasound helps overcome this issue by providing a larger field of view in which the catheter tip can be manipulated. The quality and the accuracy of tip visualization through echocardiography are, however, suboptimal. Other limitations of TEE and TTE include restricted positioning of the probe in the esophagus and limited imaging views, as well as shadowing artifacts from metallic implants, interventional tools, calcium, and air [103]. The restricted positioning of TEE probes makes it ideal for mitral valve procedures, however, for many other interventions such as TAVI and tricuspid valve repair, fluoroscopy is used as the primary imaging modality [46].
Computed Tomography

Even though X-ray and ultrasound are the core intraprocedural imaging modalities, high-quality pre-procedural Computed Tomography (CT) or MRI can greatly facilitate interventions for structural heart diseases. Pre-procedural CT angiography can provide useful contextual information to the interventionalist, allowing for an extensive evaluation of the target region and relative anatomy in the surrounding regions. CT permits high-resolution 3D imaging, with a large field-of-view and enhanced structure identification or tissue characterization. Volumetric CT can also be used to identify the optimal fluoroscopic projection angles for a given target site and a therapeutic device [95]. Schwartz et al. [178] give a detailed comparison of X-ray-based technologies used in a Cath lab including rotational angiography, C-arm CT, and their potential applications in interventional cardiology. In TAVI procedures, pre-operative CT is performed to prepare for the intervention by evaluating the aortic root, measuring the annulus, and assessing the aortic valve [18]. Measurements, such as the orifice area and annulus diameter are also made using the CT. Similarly, for mitral valve interventions, pre-operative CT can help identify the regions of annulus calcification and estimate the suitable intraoperative C-arm angulations [90]. Tricuspid valve interventions have been declared unsuitable using TEE, thus pre-procedural CT has been suggested as an alternative for making measurements of the sub-valvular apparatus [167].

Motion artifacts due to cardiac and respiratory motion are a common concern for CT imaging. Patients are subjected to breath-holding techniques in order to compensate for the motion of the chest. Cardiac motion is counteracted by either retrospective ECG gating or prospective triggering of the imaging at the diastolic cardiac phase [95]. Beta-blockers have also been used to slow down the beating motion of the heart and enhance image quality.

CT or CT angiography faces the disadvantage of being off-line and having limited intraoperative usage. Moreover, it is associated with all the radiation-induced complications in the patients and risk factors in the medical team. The amount of scattered radiations when using an O-arm in the fluoro mode has been calculated to be 5 to 20 times higher than the radiation exposure when using conventional C-arm fluoroscopy [158].

Magnetic Resonance Imaging (MRI)

MRI in cardiac interventions is an evolving field. This ionization-free imaging technique overcomes the challenges from the aforementioned imaging modalities by providing enhanced soft-tissue characterization, 3D anatomical structures, and an added ability to perform cardiac functional assessment [168]. Dukkipati et al. [70] suggest that MRI-guided ablation therapy can be used as an alternative to the current electro-anatomical mapping technique. Currently, interven-
Figure 1.6: [82] (left) Pre-procedural assessment of the tricuspid valve anatomy using CT volume by measuring the TV annulus diameters. (right) Assessment of right ventricular volume and remodeling using cardiovascular MRI.

tional magnetic resonance is used for pre-procedural diagnostic assessment during right-sided heart catheterization [170], and is the gold standard for measuring the RV size and the assessment of systolic function without using any contrast medium in TV disease [82] (figure 6). Although limited in its application, interventional MRI has also been used for structural heart interventions like aortic coarctation angioplasty, femoral artery angioplasty, and pulmonary valvuloplasty. The progress in this domain is limited by the compatibility of medical instruments with MRI and the monetary investment involved. Another limitation of this technology is the low temporal resolution and the need for ECG gating over multiple cardiac cycles.

1.3.5 Advantages

Since the objective of this thesis is to develop advanced imaging systems for transcatheter cardiovascular interventions, it must be understood why we are advocating this percutaneous method of therapy. Literature shows that transcatheter interventions have the same, if not better, long-term efficiency as the previously established gold standard of open-heart surgery [116, 22]. In a study, Sondergaard et al. [184] conclude that a percutaneous approach for aortic and coronary interventions exhibits similar outcomes as the gold-standard surgical and open heart techniques in terms of safety and efficacy. While surgery has shown great technical success in delivering therapy, it is limited by the risks, impact on the patient, and the costs involved. Hospitals and clinicians are adopting more transcatheter procedures as they have several added benefits – primarily the increased patient safety and fewer complications associated with the
percutaneous, transcatheter approach. In-hospital major adverse events, including death, are almost 3 times more likely to occur after surgery than a percutaneous intervention [22]. In comparison to its surgical former gold standard, TAVR is linked with a significantly lower risk of all-cause death as well as cardiovascular death at one year [111]. Transcatheter repair is also associated with lower rates of post-operative complications such as atrial fibrillation, excessive bleeding, stroke, and acute kidney injury [111, 116, 113]. However, some studies have shown an increased rate of paravalvular leakage [111, 22] in transcatheter interventions compared to surgical valve repair indicating the room, and need for improvement in current transcatheter procedures. IGS employed using the beating heart, transapical approach (where cardiac access is established through the apex of the heart) has shown to improve procedural outcomes [140].

As a result of fewer perioperative complications, the patients recover faster and experience a shorter stay at the hospital. As such, transcatheter procedures are associated with a shorter length of stay in the hospital in comparison to surgery [29]. In the case of transcatheter TV repair, there is a reduced rate of mortality and hospitalization due to heart failure [37]. Latif et al. [116] report similar outcomes for TAVI where the hospital stay was 3.6 days shorter on average compared to the surgery. They also report that the procedure time was 170 min less than the surgical alternative.

Transcatheter interventions are also associated with a lower cost or a better cost-to-benefit ratio. According to a 2018 systematic review, the cost of transcatheter mitral valve repair and aortic valve interventions, in comparison to the cost of medical management, indicates that transcatheter interventions are an economically attractive treatment option as well, that result in a greater number of gained-life years and quality-adjusted life expectancy [86]. An economic and clinical comparison of TAVR versus surgery shows that transcatheter interventions have a lower long-term cost to them [33].

Another benefit is the avoidance of general anesthesia. The use of local anesthesia with conscious sedation has been a favorable option for transcatheter procedures. However, TEE imaging is not possible in this case. Instead, fluoroscopic guidance, angiography, TTE, or ICE may be used to assist the procedure. Local anesthesia has several advantages, including stable hemodynamics, minimal need for medications, lack of endotracheal ventilation, reduced vascular access sites, shorter time of the procedure, and shorter stay at the hospital afterwards [71].

1.3.6 Complications

Transcatheter interventions do face a few risks of perioperative complications including vaso-vagal reaction, myocardial infarction, pulmonary edema in patients with aortic/mitral valve stenosis, cardiac tamponade, and in some cases stroke due to the presence of plaque, thrombi,
or emboli. Most complications are procedure-specific and depend on the device and the therapeutic technique chosen for the intervention. Here I discuss some of the common complications that are induced because of the imaging techniques currently employed in interventional procedures.

**Fluoroscopy-related complications**

1. Radiation hazards – Cath lab procedures are primarily guided by x-ray imaging in the form of fluoroscopy, angiography, or venography which exposes the patient and medical staff to harmful radiations. A radiation-induced high-grade skin injury is often observed in Cath-lab patients, following a percutaneous coronary intervention \[110, 32\]. Continuous exposure to x-rays is neither healthy for the patient, nor the surgical staff. The problem of radiation exposure also extends to medical students in training as they attend multiple procedures per day and are exposed to radiation each time. Radiation exposure limits the number of procedures attended by the surgeons, staff, and medical students annually, even after using various radiation-minimizing techniques \[112\]. The occupational hazards of X-ray fluoroscopy also tend to be underestimated. Due to their proximity to the patient, the interventionalists are exposed to radiation whose effect accumulates with each procedure performed. Interventional cardiologists can reach an annual exposure of more than 5mSv \[162\] and a lifetime exposure of up to 200mSv which corresponds to the dose associated with receiving 10,000 chest x-rays \[26\]. Prolonged radiation exposure to the less protected regions of the body has been suspected to cause cancer among interventionalists. Roguin et al. \[171\] investigate the prevalence of brain and neck tumors among interventional cardiologists. Occupational exposure is said to increase the risk of cancer among medical professionals by 3.6% \[121\], and several non-cancer diseases have also been reported in the literature. In the case of pregnant female medical professionals, radiation exposure can be harmful to the fetus leading to congenital defects and malformations. Cardiologists have reported developing eye cataracts in their mid-career \[97\], as well as reproductive organ damage \[117\] and thyroid gland disease \[202\], and Andreassi et al. \[25\] conclude that exposure to ionizing radiation is associated with early vascular aging and atherosclerosis in the medical staff.

2. Interventionalist’s disc disease – In order to protect themselves from the radiations in the Cath lab, the interventionalists employ many dose reduction techniques \[190\] including wearing lead shielding equipment. Heavy lead aprons can weigh up to 7 kg and must be worn throughout the procedure, and have been notorious for causing orthopedic issues, as identified by Ross et al. \[172\] who coined the term ‘interventionalist’s disc disease’.
Despite the mass awareness of the issue, inadequate measures are in place to eliminate the root cause of the problem. Interventionalists are now performing more procedures than ever and have been reporting cases of neck pain, backache, knee and ankle problems, spinal issues, and disc disease [109].

3. Renal failure – To visualize the vessels and cardiac soft tissues, X-ray contrast agents are used to enhance fluoroscopic imaging. These agents are potentially nephrotoxic, and can cause renal impairments and allergic reactions. Acute renal failure was observed in roughly 3% of the patients undergoing transcatheter valve repair [127]. This complication often calls for hemodialysis and is linked to a low survival rate [137].

**TEE-induced complications**

Transesophageal echocardiography (TEE) is routinely used for diagnostic and intraoperative monitoring of cardiac anatomy during transcatheter procedures. Although widely adopted, TEE is not innocuous and has several associated minor and major complications. Furthermore, longer procedure time corresponds to an increased prevalence of TEE-induced major complications [85]. A comprehensive list of TEE-induced complications can be seen in figure 7 [61]. Some of the common TEE-induced complications include:

- Dental trauma
- Failed intubation
- Bleeding tonsils
- Jaw dislocation
- Vocal cord paralysis
- Laryngeal nerve paralysis
- Pharyngeal ablation
- Sore throat
- Dysphagia
- Perforation
- Vascular compression leading to arrhythmia
- Infective endocarditis
- Embolization
- Esophageal laceration
- Perforation and tears
- Bleeding
- Occult perforation
- Airway trauma
- Aspiration
- Respiratory distress
- Tracheal intubation
- Pilot cuff damage
- Laryngospasm
- Airway compression
- Pulmonary edema

Figure 1.7: List of complications induced due to the use of a TEE probe in an intervention

1. Gastrointestinal injuries – The insertion of TEE-probe can cause injuries to the upper gastrointestinal tract including dental trauma, bleeding tonsils, and submucosal hematoma [59].
Elderly patients are also at a high risk of developing esophageal lesions. Tears and perforations in the esophagus can occur at abdominal, intrathoracic, and even trans-gastric levels due to the potential inexperience of the TEE user. TEE-induced intraoperative bleeding due to mucosal trauma as well as late-bleeding due to ulceration has also been reported.

2. Cardiovascular effects – Intubation of the esophagus is a semi-invasive maneuver that induces vasovagal reactions as well as sympathetic reactions like hyper or hypotension, trachy-arrhythmia, and in severe cases angina, atrial fibrillation, and myocardial ischemia [19]. Vascular compression is also observed in the pediatric population, which can lead to cardiovascular complications.

**Procedural Complications**

There are a number of complications associated with any transcatheter procedure, with most of them being specific to the pathology, technique, and device used in the procedure. In this section, we discuss some of the complications that can occur in the majority of transcatheter procedures.

1. Vascular complications may occur in a transcatheter procedure during the deployment of a device. In transcatheter aortic valve repair (TAVR) procedures, 16% of the cases have reported major vascular complications [92] including vascular rupture, perforation, and fistulas. Such problems may occur due to sheath size mismatch, incorrect puncture, intraluminal buildup, or failure of a suture-based closure system. Depending on the severity of the complication, the treatment may include compression, thrombin injections, covered stent implantation, or another surgery.

2. Device embolization is a rare but alarming complication where a device such as a clip, stent, or even a central line may become detached and move freely in the cardiovascular system. In such cases, another intervention is needed to retrieve the free device using either a snare, another stent, pigtail catheter, or using biopsy forceps [73]. Device detachment occurs when a device is incorrectly deployed due to insufficient information or misinformation from 2D fluoroscopic imaging.

3. Pericardial tamponade, or the overfilling of the pericardium sac with fluids especially blood, is a major complication that often requires interventions to convert to surgery. Tamponade may occur as a result of ventricular wall puncture or annulus rupture [127], that can potentially be caused due to a lack of anatomical information available to the interventionalist or other interventional challenges discussed below.
1.3. Transcatheter Cardiac Interventions

1.3.7 Interventional Challenges

Above, I have discussed a few of the many medical complications that arise during surgery. Medical complications are often a result of poor imaging or other challenges, and below I discuss some of the challenges that are inherent to any percutaneous, transcatheter procedure and which can potentially be overcome by advanced technological solutions such as an image-guidance system.

While the evolution of cardiac surgery resulted in less pain, risk, and recovery time on the part of the patient, the introduction of a minimally invasive or a transcatheter procedure called for further knowledge, learning, and dexterity on part of the clinicians. Edmondson et al. [72] investigated this shift in the operating room and the changes to be learned by the medical team for performing minimally invasive techniques. One surgeon gave them a humorous interview about minimally invasive cardiac procedures saying – ” [This procedure] represents a transfer of pain–from the patient to the surgeon.”, thus highlighting the learning curve a clinician has to go through. With the advent of percutaneous interventions, the dynamics within the operating room (or the Cath lab) changed and presented new challenges such as the visualization of the anatomy and tools, as well as their locations relative to each other.

A shift from cardiac surgeries to transcatheter interventions also meant that the nature of tools has changed from being hand-held to catheter-based. Once the tools are inserted into the body, it becomes a challenge to know their location relative to the overall anatomy. In the field of image-guided interventions, this is referred to as the “invisible tool phenomenon”. Currently, fluoroscopy is used to visualize the tool during the navigation phase while a combination of

Figure 1.8: (left) A case of device embolization as seen in a projected fluoroscopic image where the arrow points to a misplaced device inside the body, and (right) a case of tamponade resulting in pericardial effusion [127].
fluoroscopy and TEE imaging is used to locate the tool during the positioning phase.

Another challenge faced by the interventionalists and their team, is the lack of information about the real-time anatomy of the patient. This challenge is observed during both the planning and the procedural step. Unlike open-heart procedures, a transcatheter intervention is fully percutaneous and therefore the clinicians lack a direct line of sight with the anatomy. Imaging modalities, either on their own or via fusion, are used to visualize the anatomy for diagnostic and therapeutic purposes. Commonly, angiography, venography, and TEE ultrasound are used to visualize the anatomy. In some procedures, a pre-operative CT or MRI is used along with real-time ultrasound to facilitate the viewing of the target anatomy.

Cardiac procedures often include multimodality imaging – along with a combination of preoperative and intraoperative imaging. Cardiologists rely on their previous knowledge, judgment, their sense of spatial orientation to perform a mental fusion of these different images to extract useful information. This process of mental registration requires experience and expertise on the part of the clinician and has a bearing on the accuracy of the procedure [136]. Relying on multiple imaging modalities, the mental coordination, and the lack of tactile feedback places a heavy cognitive load on the interventionalist. Mental exhaustion or cognitive overload can impair the performance of a clinician during complex or unexpected events [62].

1.4 Image Guidance Systems (IGS)

Image guidance systems (IGS) are methods/workflows that are used to carry out image-guided interventions (IGI) – a term introduced just a few decades ago. Within the literature, there are many definitions of IGI with a popular description from Cleary and Peters [56] as “Image-guided interventions are medical procedures that use computer-based systems to provide virtual image overlays to help the physician precisely visualize and target the surgical site”. In 2020, Gimenez et al. [87] reported that a consensus was held among key opinion leaders in the field where they defined image-guided surgery and intervention as “The synergy between interdisciplinary collaboration and convergence of multiple technologies (eg, guidance systems, immersive technologies), providing extensive visual information layers (eg, spectrum, resolution, transparency) and making them intuitive, upgrading existing surgical skills and forging new ones. Due to its comprehensive mindset (planning, guidance, control), a breakthrough transformation emerges to enforce state-of-the-art procedures and develop others, thereby achieving precision”. Loosely speaking, an IGS is a system designed to be used during minimally or micro-invasive surgery/interventions utilizing advanced technology that enhances an interventionalist’s view of the tools and the anatomy to deliver precise therapy.

IGS caters to some of the aforementioned procedural complications and cardiac interven-
tional challenges by providing an “eye” into the heart, allowing the clinicians to observe the spatial relationship between the therapeutic tool and the target anatomy, thus reducing the cognitive load on the medical team, adding a layer to patient safety, and enhancing procedural outcomes. Luz et al. [129] performed a comprehensive review to identify the impact of various goals of an IGS such as increased patient safety and reduced surgery time, and the overall results indicate that IGS perform similar or better than conventional methods. An overview of the various objectives of an IGS and their impact after a review [129] is given in table 1.1.
Table 1.1: Objectives of an Image guidance system (IGS) and their impact

<table>
<thead>
<tr>
<th>IGS OBJECTIVE</th>
<th>RESULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Improve patient safety and surgical outcomes</strong></td>
<td>Strong evidence of the positive impact of IGS on patient safety and improved surgical outcomes.</td>
</tr>
<tr>
<td><strong>Reduce surgery duration</strong></td>
<td>Among different studies, the surgical duration with an IGS was found to be less, more, and the same as the conventional methods, thus producing mixed results. However, the longer surgical time was associated with studies with increased preparation and set-up time.</td>
</tr>
<tr>
<td><strong>Enhance situation awareness</strong></td>
<td>The results were inconclusive, and the sample size was small. However, some studies [47, 188] conclude that IGS improves the intraoperative orientation of surgeons. This review also suggests that IGS “improves the intraoperative orientation of surgeons and helps them to identify anatomical structures that lead to improved patient safety and surgical outcome”</td>
</tr>
<tr>
<td><strong>Decrease workload and stress</strong></td>
<td>Results indicate a mixed amount of stress on clinicians using IGS, with increased subjective workload indicated by clinicians when a new surgical workflow is introduced, as well as increased frustration score due to technical false alarms. Two studies [134, 128] found reduced physiological effort and stress when using an IGS. Overall, IGS decrease stress levels during a procedure.</td>
</tr>
<tr>
<td><strong>Easier acquisition and maintenance of surgical skills</strong></td>
<td>Some authors [35] suggest that IGS improve the surgical skill acquisition process, while others [142] argue that IGS makes the surgeon dependent on the system resulting in skill loss. No studies however support the negative effects of an IGS.</td>
</tr>
</tbody>
</table>
1.4.1 Barriers

Literature in the last few decades is filled with innovative solutions for challenges in surgery and interventions, however, these solutions have rarely manifested themselves in clinical practice. The lack of clinical translation of IGS is a challenge on its own and a number of studies have been performed to understand and report the possible causes for this restricted uptake of the IGS. In a joint meeting to discuss issues arising for IGS [65], experts in the field identified four major challenges in the clinical adaptation of image guidance systems – reusability of IGS components, validation and performance evaluation of a system, design of clinically-relevant IGS, and stronger industrial partnerships for optimal use of the available devices and design of the new ones. Discussing similar issues, Carroll et al. [45] share that advances in coronary angiography are limited by the clinically-focused studies, adaptability of the clinicians, medical staff training, and associated costs with the new technology.

Linte et al. [123] provides a detailed analysis of barriers towards the clinical implementation of the advanced IGS with two major categories – technical and clinical, where they conclude that for IGS “the lack of adequate validation and evaluation is a major obstacle to the clinical introduction of augmented reality”. This reason is also recently identified by Dilley et al. [64] as a key hindrance towards the clinical uptake of guidance systems, as their review identified that most IGS-related studies focused on traditional clinical outcomes rather than clinician or user-focused metrics. Thus, they developed a framework for researchers as their guide toward complete and comprehensive evaluation and validation of an IGS which is depicted in figure 1.9.

Figure 1.9: Proposed framework by Dilley et al. [64] for the evaluation of an image guidance system
Chapter 1. Introduction

Other technical barriers described by Linte et al. [123] include preparation of required hardware especially the incorporation of tracking sensors to existing devices, spatial calibration of imaging techniques such as ultrasound, correction for temporal differences and latency, and timely, accurate and intuitive methods of data visualization.

Some of these limitations are more challenging than the others, with two critical issues being proper evaluation and validation of IGS, and acceptability of the new technology. It is challenging to define the metrics to evaluate the clinical accuracy of an IGI since the evaluation should be procedure-specific and it is difficult to control multiple variables during an in-vivo experiment. Moreover, as Linte et al. [123] describes “The translation of clinical accuracy expectations into engineering accuracy constraints is also difficult to formulate, especially when accuracy errors in the image guidance platforms begin to affect clinical performance”. Another clinical debate is around the cost-vs-benefit ratio of the IGS, however, it must be understood that the benefits cannot be evaluated at an early stage and must be analyzed once the technology is widely adapted.

Despite the technical challenges, the cost associated with an IGS, and the validation metrics employed, much of the opposition relates to the acceptability of the new technology. When designing an IGS, it is suggested to make the new systems look like those they are replacing so that the technology is openly welcomed by the user or the clinician. Advanced imaging and visualization techniques like 3D rendering and augmented reality systems can often be intimidating and can cause information overload, resulting in hesitation on part of the user to accept the technology [176]. Along with user-dependent challenges, IGS also face the issue of introducing workflow changes and new equipment in the operating room, leading to a high learning curve and time investment which is often not well-received by the clinicals and industrial partners.

1.4.2 Components

The field of IGS has developed and evolved in its complexity, however, there are a few basic components that are critical, such as imaging, tracking devices, registration, and visualization as identified by [159]. Figure 1.10 shows the major subprocesses involved in an IGI [159, 17].

Spatial Tracking

Transcatheter interventions are inherently faced by the challenge of the invisible tool phenomenon, where the tool tip cannot be seen relative to the anatomy, therefore, tool tip localization or tracking becomes crucial to perform a procedure. Currently in a Cath lab, the tools are visualized using fluoroscopic imaging which is 2D in nature and provides limited infor-
1.4. Image Guidance Systems (IGS)

Figure 1.10: Major components of an image guidance system (IGS)

Information about the anatomy. Image guided interventions (IGI) and surgeries employ real-time tracking systems, most commonly either optical or magnetic / electromagnetic (EM) tracking systems to continuously localize the tool with respect to the anatomy. Prior to their development, several other technologies were invented and tested with the first tracking system being a stereotactic frame introduced in the late 1920s to establish the relationship between the patient anatomy, pre-operative imaging, and surgical tools mounted on the frame during a neurological surgery [159]. With the innovations in CT and MRI technology, tracking was soon replaced by frameless stereotaxy, followed by the use of mechanical digitizers in neurosurgery. By 1990s optical tracking was introduced, which allowed for the tracking of multiple devices simultaneously. Optical tracking system are highly reliable and accurate, and function by estimating the triangulation between the markers and the camera. In spite of their high tracking accuracy (better than 1 mm), optical trackers have limited use in transcatheter interventions as they require a direct line of sight between the optical markers and the tracking camera [185]. For transcatheter interventions, this limitation is overcome by using electromagnetic tracking technology.

Electromagnetic (EM) or magnetic tracking systems (MTS) are composed of two basic components – a field generator emitting magnetic fields of known geometry and tracking sensors containing small solenoid. Franz et al. [84] provide a detailed analysis of applications and validation of magnetic tracking technology in the medical field. The most widely used MTS are the Aurora (North Digital Inc.) and a 3D guidance system from Ascension Technology Corporation. In this thesis work, I have employed a tabletop MTS (Aurora by NDI) since cardiac interventions often involve transfemoral catheterization which uses the entire thoracic
region. In the case of the Aurora tabletop field generator, the varying magnetic field volume is 3D ellipsoidal in shape and can measure up to a height of 600mm (fig 1.11). The characteristic measurements of the Aurora tabletop field generator are reported in table 1.2. This device also features a built-in barrier to minimize any field distortions due to the presence of conductive and ferromagnetic materials underneath the generator.

Note that the Aurora tracking systems by NDI are truly "magnetic" tracking systems as the measurements do not depend on the "electric" component of the electromagnetic wave. Such systems are historically called "electromagnetic" tracking systems and therefore, the term EM tracking system and MTS are used interchangeably in this thesis.

![Figure 1.11: (left) Aurora tabletop field generator by NDI (Waterloo, ON), and (right) its magnetic field measurement volume](image)

Figure 1.11: (left) Aurora tabletop field generator by NDI (Waterloo, ON), and (right) its magnetic field measurement volume

<table>
<thead>
<tr>
<th>NDI Aurora Tabletop Field Generator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dimensions</td>
</tr>
<tr>
<td>Weight</td>
</tr>
<tr>
<td>Thickness</td>
</tr>
<tr>
<td>Mounting</td>
</tr>
<tr>
<td>Measurement Volume</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

Table 1.2: Characteristics of Aurora v2– an electromagnetic tabletop field generator
Even though magnetic tracking sensors do not compete with optical tracking systems in terms of accuracy, their potential for tracking flexible catheters and interventional tools using embedded miniaturized sensors has given them an advantage to allow them to be used during transcatheter image-guided interventions. Tracking sensors can be of two types depending on the measurements they can make or the degrees of freedom (DOF) of measurement required – either 5 DOF sensors measuring the translation in three dimensions and rotation in two dimensions (pitch and yaw), or 6 DOF sensors additionally quantifying the spin or roll rotation. Figure 1.12 shows the difference between the size and transformations of 5DOF and 6DOF sensors.

![Aurora 5DOF Sensor Dimensions: ø0.45 x 8.2 mm](image1) ![Aurora Micro 6DOF Sensor Dimensions: ø0.92 x 9.4 mm](image2)

**Figure 1.12:** 5 DOF and 6 DOF electromagnetic tracking sensors by NDI [3]

### Registration

Registration is the process of bringing multiple data sets into a common coordinate system by means of a transformation. Image registration is the backbone of an IGS as it establishes the relationship between the patient and the virtual environments such as the imaging or tool tracking domains. In general, the space where the patient (or a phantom) exists is called the “world” coordinate system to which the other environments are registered. In the case where external tracking such as MTS is used, the patient lies within the tracking space and the tracker coordinates act as the world coordinates. Many different reviews exist in literature for different subcategories of image registration including medical image registration [153], ultrasound registration [49] and cardiac image registration [131]. The two main categories for image registration are identified as geometry-based methods and intensity-based methods. These methods can be used to perform either rigid or non-rigid image registration. In this thesis, geometry-based, rigid registration is used to bring pre-operative imaging such as CT into the common
“world” or tracking coordinate system where the phantom experiments take place. The ultrasound imaging is linked to the world/tracking coordinates via tracking sensors and calibration methods which are discussed in detail in Chapter 2.

Geometry-based registration methods either include paired-point or surface-based techniques. For both the methods, the data may come from the anatomical structures or the fiducial markers. Point-based registration methods have been widely adopted as they have a closed form solution and a unique output transformation exists. In paired-points method, two sets of at least three non-collinear points are required, and the points are matched to minimize the distance between them to obtain a transformation matrix that aligns the two coordinate systems. This pair-wise landmark registration can be solved using the least square fitting [152] that minimizes the distance error between fixed point data \((Y_i)\) and transformed point data \((X_i)\) using equation (1.1)

\[
\text{Dist.error} = \sum_{i=1}^{N_p} ||R \ast X_i + t - Y_i||,
\]

where \(R\) is the rotation matrix, \(t\) is the translation and \(N_p\) represents the number of points in each dataset. This technique is used throughout the thesis to register phantom or tracking space to imaging space.

1.5 Interventional Ultrasound

Since the arrival of ultrasound technology in the 1990s [132], it has been used in numerous clinical departments including neurosurgery, cardiac therapy, and abdominal procedures. Ultrasound is an indispensable imaging modality to perform minimally invasive and transcatheter cardiac interventions [161]. Ultrasound’s ability to visualize soft-tissue, blood, and flow motion in real-time without the risk of ionizing radiation makes it a favourable choice of imaging peri-procedural monitoring and even diagnosis. US technology is inexpensive, mobile, and compatible with other medical equipment. Although inferior in image quality compared to CT or MR imaging, US can provide excellent soft tissue visualization. Depending on the task at hand, the interventionalist may prefer a 3D US volume to acquire a larger spatial volume, or they may opt for 2D images with finer details.

1.5.1 Types of Echocardiography

US probes differ by the number of piezoelectric elements, the shape of transducer, size, and level of invasiveness. Below are some of the common US probes used in cardiology – each
1. **Interventional Ultrasound**

1. **Transthoracic Echocardiography (TTE)** – TTE is able to provide both structural and functional information, commonly using the parasternal, subcostal, apical, and suprasternal views. The transducer usually incorporates a phased array design, is 2 – 3 cm long, and consists of 64 – 128 elements with a central frequency between 2 – 7.5 MHz. These hand-held probes are easy-to-use, entirely non-invasive, and while they allow freedom of motion, due to the presence of ribcage and lungs, the acoustic window for cardiac imaging is quite limited. Image quality is also limited in the case of obese patients as more layers of tissues must be penetrated before the heart can be imaged. Similarly structures at the back of the heart such as the left atrial appendage are challenging to be viewed by the TTE.

2. **Transesophageal Echocardiography (TEE)** – These probes are widely used in interventional procedures as they are able to sit in the esophagus and closely view the cardiac anatomy. The transducer for 3D TEE usually contains a matrix array of roughly 2500 elements arranged at a tip of size 12x12 mm, and with a frequency range of around 2 – 7 MHz. TEE probes are excellent at visualizing the mitral valve, aorta, pulmonary artery, left atrial appendage and the coronary arteries. TEE is routinely used in minimally invasive and transcatheter interventions to provide visualization, functional evaluation, and monitoring of the procedure [197]. Unlike TTE, these probes are slightly invasive as they are introduced into the esophagus, which necessitates the use anesthesia during the procedure. Patient sedation and handling of the TEE probe may increase the time duration of the therapy. Common locations for the probe placement include mid-esophageal, trans-gastric, and in some cases deep trans-gastric. Because of the restricted locations where the TEE can be positioned, the anatomical views it can acquire are also limited. For example, the tricuspid valve is anterior in its location and is thus difficult to be seen via TEE.

3. **Intravascular Ultrasound (IVUS)** – employs catheter-like ultrasound probes that are inserted into the heart via vessels originating near the groin. Unlike TTE and TEE, IVUS provides an inside-out imaging of the vessels along with information about the vessel wall composition. IVUS can provide high-resolution, cross-sectional 2D images with a 360 degree view. The transducer can be of many different types, but a common configuration is a single-element transducer, mounted on a rotating shaft, and are able to provide high quality imaging due to the high frequency transducers of 10 – 50 MHz, but at the cost of a smaller depth of field (usually 2 – 3 cm) [195]. IVUS is used for diagnostic purposes and making vessel wall measurements, especially for coronary artery disease.
During interventions, it is utilized for optimizing the stent deployment process, monitoring the percutaneous coronary intervention, and assessment of the abdominal aneurysm. The applications of IVUS in cardiac interventions have been somewhat limited due to its inability to visualize the anatomy surrounding the vessel.

4. **Intracardiac Ultrasound (ICE)**—This imaging modality is another form of catheter-based ultrasound technology. In terms of specifications, it lies between the IVUS and TEE technology, having a frequency range of 5 – 10 MHz and an imaging depth of approximately 15 cm [101]. ICE in an indispensable component of electrophysiology procedures, as well as it facilitates the transeptal wall puncture, interventional closure therapy, and evaluation of intracardiac thrombus. There are two major classes of ICE probes:

(a) Radial or rotational ICE – uses a single-element transducer that rotates 360 degrees, acquiring a cross-sectional, circular image perpendicular to the long-axis of the catheter [74]. They are more useful for near field imaging up to a depth of 8 cm.

(b) Phased-array ICE – uses a 64-element transducer mounted at the tip of the catheter and acquires a traditional wedge-shaped ultrasound image. These systems offer a higher field of view than their mechanically rotating alternative, imaging up to 15 cm of depth, as well as easier maneuverability, and a Doppler imaging capability. Due to these features, phased array probes have been preferred over rotational probes for interventional imaging.
Since the focus of this thesis is a novel Foresight™ ICE probe, the next two sections discuss the commercial ICE systems available at the time of beginning of this thesis, and why we decided to pursue the Foresight™ system.

### 1.5.2 Intracardiac Echocardiography

Although the clinical use of ICE is currently limited, it is expected to rise with the growing number of cardiovascular diseases contracted and the awareness about the benefits of transcatheter interventions. By 2028, the catheter-based ultrasound probe market is expected to grow by 5.2% and size up to 1,163 Million USD [16]. At the beginning of this thesis, there were only a handful of ICE probes available in the market with the most popular ones being Ultra ICE [6], ViewFlex Xtra [15], AccuNav [11], and Foresight™ ICE probes [5]. A comparison of their features and characteristics is given in Table 1.3.

### 1.5.3 Foresight™ ICE

As the comparison of commercial ICE probes in Table 1.3 shows, the Foresight™ ICE probe by Conavi Medical Inc. clearly stands out due to its ability to view forward at multiple angles, thus allowing for a hands-free manipulation of the viewing angles – a feature greatly desired by the interventionalists. Among the commercially available options, it is also the only ICE probe with 3D imaging capability as well as Doppler imaging feature in a rotational/radial type ICE. The Foresight™ ICE probe further allowed for a high-resolution radial imaging at a depth of 8cm at a user-specified angle. The angle can be adjusted to acquire side-looking views similar to an IVUS or Ultra ICE probe, or it can be changed to acquire forward-looking views allowing the clinicians to see ahead of the probe tip location. Foresight™ ICE was able to achieve many of these features due to controlled tilt motion of the single-element transducer – a characteristic novel to any catheter-based ultrasound probe. Considering the novel and superior attributes of this device, this thesis was designed to explore its potential use and possibilities to assist cardiac interventions. The imaging characteristics of this novel technology are discussed in detail in chapter 2, with ICE-guidance systems presented in chapters 4 and 5.

### 1.6 Thesis Outline

The global objective of this work is to design and evaluate image guidance systems for transcatheter cardiac interventions in effort to improve patient and staff safety by minimizing the use of fluoroscopy and employing radial ICE imaging as an alternative. While this thesis
Table 1.3: Comparison of common intracardiac echocardiography (ICE) probes commercially available in 2017.

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Ultra ICE</th>
<th>ViewFlex Xtra</th>
<th>AccuNav</th>
<th>Foresight™</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manufacturer</td>
<td>Boston Scientific</td>
<td>St. Jude Medical</td>
<td>Biosense Webster</td>
<td>Conavi Medical</td>
</tr>
<tr>
<td>Transducer</td>
<td>Radial, single-element</td>
<td>Phased array, 64-element</td>
<td>Phased array, 64-element</td>
<td>Radial, single-element</td>
</tr>
<tr>
<td>Image type</td>
<td>Panoramic 360°, side-viewing</td>
<td>Side-firing</td>
<td>Side-firing</td>
<td>Conical 360°, side and forward-viewing</td>
</tr>
<tr>
<td>Imaging depth</td>
<td>12 cm (diameter)</td>
<td>18-21 cm</td>
<td>16 cm</td>
<td>16 cm (diameter)</td>
</tr>
<tr>
<td>Frequency</td>
<td>9 MHz</td>
<td>4.5-8.5 MHz</td>
<td>5.5-10 MHz</td>
<td>6-12MHz</td>
</tr>
<tr>
<td>Shaft diameter</td>
<td>8.5 F</td>
<td>9 F</td>
<td>8 or 10 F</td>
<td>10 F</td>
</tr>
<tr>
<td>Shaft rotation speed</td>
<td>1800 RPM</td>
<td>NA</td>
<td>NA</td>
<td>700 RPM</td>
</tr>
<tr>
<td>Maneuverability</td>
<td>Non-steerable</td>
<td>Four-way steering, 120° deflection</td>
<td>Four-way steering, 160° deflection</td>
<td>Steerable</td>
</tr>
<tr>
<td>Doppler and Color flow</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>3D volumetric imaging</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>
explores the potential of Conavi’s Foresight™ ICE probe, the materials and methods are applicable to any radial ultrasound imaging modality.

As discussed earlier, there are two stages of a transcatheter cardiac intervention - navigation and positioning. In this thesis, two IGSs are presented: to facilitate the tool navigation through the vasculature (Chapter 4) and to facilitate tool positioning during tricuspid valve repair therapy (Chapter 5). The preceding chapters explain the methods for developing the supporting technology required to conduct the IGS-related experiments i.e. tracking and calibration of a radial ICE probe (Chapter 2) and the construction of an ultrasound-realistic vessel phantom (Chapter 3). A short summary of each chapter is as follows.

1.6.1 Chapter 2: Characterization and Calibration of a 2.5D Radial Ultrasound

This chapter serves as a starting point for using the Foresight™ ICE probe in an IGS. The work explores the different features and aspects of the ICE system including how the US images are acquired, stored, displayed, and manipulated. It also includes various visualization techniques that can be used to represent the 2.5D ICE images. Finally the chapter describes the spatial and temporal calibration methods, as well as the challenges and limitations of this novel US technology. The chapter concludes that tracking a forward-looking ICE probe is a demanding task as any bending motion in the catheter can introduce calibration errors.

1.6.2 Chapter 3: Towards Vessel Navigation: Ultrasound-realistic, Dual-layered Vessel Phantom

In this chapter we design a PVA-c vascular phantom that produce realistic images upon ICE ultrasound imaging. Unlike conventional phantoms, we aimed to develop two layers for the vessel including a layer that represents the vessel wall and a layer representing the surrounding tissues. Different concentrations of talcum powder, as an additive, were tried and tested to obtain the desired reflections from both the layers. The geometric evaluation of the phantom was also performed by comparing against the CT scan of the phantom. This phantom was used in the development of an ICE-guided navigation system described in the next chapter.
1.6.3 Chapter 4: Towards Vessel Navigation: Deep Learning-based ICE-Guidance System to Generate a Vascular Roadmap

Vessel navigation is routinely performed as part of transcatheter cardiac interventions under fluoroscopic guidance which can be harmful for the patient. Interventionalists are at a risk of developing back and spine issues due to wearing heavy lead shielding equipment to protect themselves from harmful radiations. In this chapter, we propose an US-based IGS to generate a vascular roadmap using tracked ICE imaging which can then be used by a tracked guidewire to navigate towards the heart without using fluoroscopy. A complete 3D Slicer module is designed and presented which uses a deep learning technique to perform vessel segmentation from the ICE images. The 3D US-based vessel surface reconstruction is validated against the 3D vessel extracted from the phantom’s CT scan, where the results show promising accuracy to perform the task of vessel navigation.

1.6.4 Chapter 5: Towards Tool Positioning: Localization of Regurgitation Site in Tricuspid Valves using ICE

In this chapter we describe the use of ICE imaging to facilitate clip positioning during repair procedure for the "forgotten" tricuspid valve (TV) regurgitation disease. Valve repair interventions are often performed under fluoroscopic and TEE guidance, however TV has been declared "TEE-unfriendly". We present the first advanced IGS for TV interventions which uses tracked ICE imaging in Doppler mode to pre-map functional information such as the regurgitation site - an important target location for tool positioning. Experiments were performed and validated in a dynamic, beating heart setting with patient pathology-specific TV models. We hypothesize that providing more contextual information in 3D space can potentially enhance the spacial orientation of the clinicians, thus reducing their cognitive load and improving procedural outcomes.

1.6.5 Chapter 6: Conclusion and Future Directions

This chapter summarizes the contributions of this thesis in the field of biomedical engineering. I also discuss some of future directions this work can take as well as the latest technological advancements in the fields of interventional ultrasound and cardiology.
Chapter 2

Characterization and Calibration of Foresight™ ICE

Foresight™ ICE is an ultrasound probe with novel features such as radial, forward-looking imaging with 3D and Doppler capabilities. This chapter aims at understanding the working and display of ICE imaging on the Hummingbird console, as well as discussing the methods to prepare the ICE probe so it may be used in a tracked, guidance environment. The ICE probe is characterized and spatially and temporally calibrated to be tracked using an electromagnetic tracking sensors.

This chapter includes materials from the following manuscript:


Foresight™ is a recently introduced intracardiac echocardiographic (ICE) probe, designed and manufactured by Conavi Medical Inc. (Toronto, Canada). The Foresight™ ICE probe was invented with a vision of guiding minimally invasive surgeries and cardiovascular interventions. The sophisticated design of the probe includes a single-element ultrasound transducer, which can spin in all 360 degrees as well as tilt physically, thus generating a 2D conical surface ultrasound image lying in 3D space. Due to this unique configuration, we refer to this conical image as 2.5 dimensional. Foresight™ ICE is a catheter-based ultrasound probe which has the unique ability to generate both 2D and 3D imaging, as well as Doppler imaging. This radial design of the probe allows for imaging at multiple views – forward viewing and looking at the sides and constantly switch between multiple views, all without having to move the body of the probe. These features make the Foresight™ ICE probe a rare one-of-its-kind
ultrasound catheter with great utility and potential for advanced image guided systems for cardiac interventions. Some potential applications include transseptal puncture guidance, vascular navigation, structural valve repair, localization of valve regurgitation site, and freehand visualization of dynamic anatomical structures. To utilize the Foresight™ ICE probe in the design of an image guided system, the features and behaviors of imaging system need to be understood in depth. In addition, the system must be integrated into a tracking environment and ultrasound probe may need to be calibrated. The VASST lab at Robarts Research Institute is one of the very early adopters of this technology. In 2017, soon after this novel probe was introduced commercially, the lab acquired this ultrasound system. As one of the early research users of the Foresight™ ICE probe, many of the parameters essential for enabling the use of this device in an image-guided intervention system, were unknown at that time. Since then, I have performed extensive analysis of the imaging system and explored some of the potential applications as well. This chapter presents the (I) characterization of the Foresight™ ICE image, (II) multiple ways to visualize the unique 2.5D conical imaging, (III) the process to calibrate the ultrasound probe and use it in a tracking environment, and (IV) the study and characterization of its spatial calibration.

2.1 ICE Image Characterization

A forward-looking ICE probe presents numerous opportunities for advanced image guided system designs, holding the potential to simplify and improve the cardiovascular and abdominal transcatheter interventions. To utilize the Foresight™ ICE probe in an image guided system based on spatial tracking, it is necessary to understand how the ultrasound image is presented on the screen and the image variability with respect to changing parameters such as depth, imaging angle, frequency, of the ultrasound, as well as inter-variability of image between probes.

In this section we describe experiments to evaluate the appearance of the image on the screen and characterize the display of the 2.5D forward looking ICE probe. In all these experiments, data were acquired as real-time screenshots of the console screen using an Epiphan (Epiphan Video, Canada) frame-grabber. The following questions were considered to perform image characterization for the Foresight™ ICE system.

1. **Image Geometry**: How the echogenic data is acquired by the ICE probe? What are the different operating modes the system has to offer?

2. **Image Orientation**: What is the orientation of conical image when displayed as a circle on the console screen?
3. **Image Data Acquisition**: How to acquire imaging data in real time from the console screen?

4. **Image Display Size**: What is the size of the circular image displayed on the console screen? And how it changes with variability in imaging angle and imaging depth? How do these changes compare between probes?

5. **First Scan Line Consistency**: Are the ultrasound images consistent with each other? In other words, does the 12 o’clock position of the radial image always represent the same physical position with respect to the probe?

6. **Imaging Angle Consistency**: What are the factors affecting the value of imaging angle?

7. **Image Artifacts**: What image artifacts are observed, unique to the Foresight™ ICE probe?

### 2.1.1 Image Geometry

The ultrasound imaging acquired through Conavi’s Foresight™ ICE probe is a 2-dimensional surface image, in the shape of a cone, lying in 3-dimensional space. We sometimes refer to this original conical surface image as 2.5-dimensional. The hexagonal transducer element transmits and receives a single echo beam. The range or depth of this ultrasonic beam can be controlled and lies between 30mm and 80mm. This parameter is referred to as the scanning direction, the field-of-view (FOV), or the radial depth (r). The unique geometry is attained by the 360-degrees spinning motion of a single-element transducer. One complete spinning motion also referred to as the angular rotation, generates an ultrasound image. In spherical coordinates, this motion is represented by the theta (θ). This parameter is referred to as the angle of rotation or rotational angle (θ). The transducer element further can tilt in its position, causing the shape of the cone to change. The users have the option to control this tilt angle in multiple ways – manually set a value, continuous change from minimum to maximum tilt angle, and continuous imaging between the pre-set values for tilting. In spherical coordinates, the tilt is represented by the angle phi (ϕ). This parameter is referred to as the imaging angle (ϕ) or the tilt angle. A schematic of ultrasound acquisition and geometry for the Foresight™ ICE imaging can be seen in figure 2.1.

The Foresight™ ICE probe provides a unique opportunity to not only look at all the four sides around the tip of the probe but also look ahead in space using a smaller imaging angle. The ICE probe is said to operate in side-viewing mode when the imaging angle is between 89 and 70 degrees, and in forward-looking or forward-viewing mode when the imaging angle is
Figure 2.1: Ultrasound image acquisition by the Foresight™ ICE probe as a conical geometry less than 70 degrees. Figure 2.2 shows an example of the shape of the conical ICE image in the side-viewing and the forward-viewing mode.

Figure 2.2: (a) Side-viewing and (b) forward-viewing modes of Conavi’s Foresight™ ICE probe with larger imaging angle and smaller imaging angle respectively.

2.1.2 Image Orientation

Although the ultrasound images acquired by the Foresight™ ICE probe are 2.5D in nature, they occupy space in all three dimensions. However, since the Hummingbird console includes a traditional flat monitor screen that displays two-dimensional information, a question arises of how and in what view is the conical image displayed on the screen.

The 2.5D conical surface image, generated by the Foresight™ ICE probe, is displayed on the 2D monitor screen as a circular image by default. This circular image is the apical view of the conical image, as seen from outside the cone shape. The image can be rotated via
touch screen to view the conical surface from different angles. At each of these views, the image is displayed as a parallel projection of the 2.5D conical surface image on the monitor screen. Figure 2.3(a-d) shows different views of the same ultrasound image where figure 2.3(d) represents the default or ‘home’ view for that image. When the imaging angle is decreased, the cone becomes more forward-looking and the circular image becomes somewhat smaller in diameter (see figure 2.3(e,f)).

Figure 2.3:  (a)(b) Different views of conical ICE image in side-viewing mode as seen on Hummingbird console. (c) ICE image view, as seen from inside the cone. (d) Default or ‘Home’ view of the ICE, as seen from the apex of the cone. (e) A forward-looking ICE image at a smaller imaging angle and (f) its default apical view.

2.1.3 Image Data Acquisition

As described earlier, Conavi’s Foresight™ ICE probe acquires the ultrasonic information in shape of a 2D conical surface, displayed on a traditional flat monitor screen as a circle. Though this circular image contains all the necessary anatomical information a clinician might need, it is inherently misleading in terms of spatial arrangement of the viewed anatomy. The system includes an option to rotate the conical image and view the conical ultrasound image from all angles. The “home” button resets the view to the default cone orientation i.e., apical view of the conical image seen from the outside of the cone shape. Figure 2.4 shows the console layout and highlights the common buttons and parameters to use.
Figure 2.4: Screenshot of Conavi’s Hummingbird console, displaying a conical ICE image from the apical view.

As seen in figure 2.3, different views of the conical image can be seen by rotating the shape on the screen. The angle of the cone itself is controlled by using the (+) and (-) buttons on screen, next to the displayed value of imaging angle. The primary software we have used is 3D Slicer [79] – an open source platform for medical image processing and visualization. In all our experiments, the ultrasound data are acquired as a screenshot of the console screen in 2D form using a frame-grabber (DVI2USB 3.0, Epiphan Video, USA). The data are transferred to the 3D Slicer environment through a PLUS server application [114]. The imaging angle is extracted from the screen in degrees using an optical character recognition (OCR) algorithm integrated within the PLUS server. The image is cropped to obtain only the circular region-of-interest (ROI). The 2.5D conical information is then reconstructed from the 2D circle images. The circular image (in x, y space) is reconstructed to a conical surface image, lying in 3D space, using the equation below. The schematic of this mathematical conversion is described in figure 2.5.

\[
\begin{bmatrix}
  x_{3D} \\
  y_{3D} \\
  z_{3D}
\end{bmatrix}
= 
\begin{bmatrix}
  1 & 0 & -o_x \\
  0 & 1 & -o_y \\
  0 & 0 & \| (x_{2D}, y_{2D}) \| tan(90 - \phi) \|
\end{bmatrix}
\begin{bmatrix}
  x_{2D} \\
  y_{2D} \\
  1
\end{bmatrix}
\] (2.1)

where ox, oy represents the centre of the planar image or the apex of the conical image, and x,y, and z represent the spatial coordinates of imaging pixels. The conical image is reconstructed with the origin of the image set to the apex of the 3D cone image or the centre of the
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2D circle image.

Figure 2.5: Reconstruction of the 2.5D conical surface image from a 2D circular image, given a value for imaging angle φ.

2.1.4 Image Display Size

Figure 2.4 shows a screenshot of the Hummingbird console. The screen display includes many controlling parameters including ‘Field of View’ (FOV) and imaging angle, as well as the ultrasound image in a circular shape. This ultrasound-only portion of the image is referred to as the ‘Region of Interest’ or ROI in this study. It was observed that the radius of the ROI is not fixed and changes by variation of imaging angle parameter available in the system. Characterization of this relationship may be required for the design of certain IGS procedures where measurements need to be made outside of the console, in an external software. We aimed to determine and describe this relationship between the size of the ROI and the imaging angle as well as the FOV of the ICE image. Experiments were performed to identify behaviors within a probe as well as to characterize the inter-probe variations in these characteristics.

Methods: To characterize the radial size of the circular image, as displayed by the Foresight™ ICE probe, three probes (A, B, and C) were tested. The ultrasound probe was held motionless in open-air using a clamp. Imaging contrast was set to ensure maximum brightness in the circular image and obtain a sharp boundary against the dark background (see figure 2.4). The size of the full image captured was 1920x1080 pixels. The imaging depth, also referred to as the field-of-view (FOV), was set to 80mm for the initial configuration. The imaging angle was
swept manually between the minimum and maximum achievable values, thus acquiring the console image at 18 different angles. For probe A, these imaging data were acquired for each of the following FOV values: 75, 70, 65, 60, 55, 50, 45, 40, 30, 20, and 10mm. For probes, B and C, a less exhaustive dataset was acquired, at a FOV of 65mm and at 18 different imaging angle values.

From each ultrasound image, the radius of the circular image was computed using an automated approach to ensure consistency. The radius was defined in terms of the number of pixels. The relationship between ROI radius and imaging angle was determined by fitting a curve to the data. A similar approach was used for all data collected for probes A, B, and C. A relationship was also established for normalized radial data points to provide a generic relationship in case a different image resolution is used. By normalization, we mean that the relationship is provided with respect to the maximum achievable imaging angle for a given probe.

**Results:**

For probe A, the radius of the circular ROI was measured for 12 different imaging depths or FOVs. The results, as seen in Figure 2.6, indicate that the relationship between displayed ICE image radius and imaging angle remains the same regardless of the imaging depth or FOV settings. They also indicate a strong direct relationship between the imaging angle and the size of the ROI.

![Circle Radius vs. Imaging Angle at different Field Of Views](image)

Figure 2.6: Radius of the circular echo image displayed on the console vs. the imaging angle at which the ICE image is acquired. Each color represents a different imaging depth or FOV for which the imaging angles are swept from minimum to maximum.

For probes B and C, the imaging angles are swept at an imaging depth of 65mm. The radius
observed at this FOV is shown in figure 2.7.

Figure 2.7: Radius of the circular echo image displayed on the console vs. the imaging angle at which the ICE image is acquired for probe B (left) and probe C (right) at 65mm FOV. Data points are subsampled for display purpose only.

A second-degree polynomial was fitted to the individual datasets for each probe. Visual validation reveals that all three probes follow a similar trend (figure 2.8) with minor variability. The data from the three probes were combined to form a generic equation. Fitting a curve to this combined dataset produces a generic quadratic equation which can be used to calculate the radius of the ICE display given a certain value for imaging angle, at any FOV. The equation is given as:

\[
\text{Radius (in pixels)} = -0.06 \varphi^2 + 10.88 \varphi - 56.92 \quad (2.2)
\]

where \( \varphi \) represents imaging angle in degrees. It should be noted that the maximum imaging angle present in this dataset is 78 for which the radius becomes 430 pixels.

For a more specific calculation tailored to a probe with a different maximum achievable angle, an alternative/normalized equation can be used, which is acquired by dividing the equation (2.2) by maximum radius value (Rmax). One manual measurement for the maximum radius value will be required in this case. Figure 2.9 shows the curve fitting to the normalized radius vs imaging angle combined-probe dataset. A more fitted equation to calculate the absolute radius of ICE is given as

\[
\text{Radius (in pixels)} = (-0.14 \varphi^2 + 25.31 \varphi - 132.38) \times 10^3 \times (R_{\text{max}}),
\]

where \( \varphi \) represents imaging angle in degrees and \( R_{\text{max}} \) represents the absolute radius value.
Figure 2.8: Curve fitting to the absolute radius vs imaging angle dataset acquired at 65 mm FOV for probes A, B and C in pixels for the maximum imaging angle achievable by the chosen probe.

Note: The curve is expected to become flatter for angles higher than 78. Some probes can achieve imaging angles up to 87 degrees, and if such a probe is used, it is recommended a few data points be taken to establish a closer fitting curve and a more accurate equation.

Conclusion:

The curves for the three probes were similar but not the same. These differences might have been introduced by the potential discrepancy between the true angle and the displayed imaging angle of the ultrasound image. In the above experiments, the size of the displayed ICE image is described in terms of the radius of the ROI i.e., the circular echo image displayed on the screen. From the results, we can conclude that:

- The size of the displayed ultrasound image is a function of the imaging angle.
- The radius of circular ROI varies positively and quadratically with the imaging angle.
- The radius of the ROI is independent of the FOV or imaging depth value chosen during imaging.
- The quadratic relationship between the radius of the ROI and imaging angle is fairly consistent between different probes as well.

\[ A = (-0.06)x^2 + (10.56)x + (-49.69) \]

\[ B = (-0.07)x^2 + (11.91)x + (-95.02) \]

\[ C = (-0.05)x^2 + (10.40)x + (-45.45) \]
2.1. ICE Image Characterization

Figure 2.9: Curve fitting to the normalized radius vs imaging angle dataset acquired at 65 mm FOV for probes A, B and C. Data points are subsampled for display purpose only.

2.1.5 First Scan-Line Consistency

Ultrasound probe tracking and calibration algorithms require that the ultrasound images are consistent with each other. For planar ultrasound imaging, this requirement includes that the first and last scan lines originate from the same transducer elements for each image acquired during the procedure. In the case of a single-element radial ultrasound, the first echo beam must be always generated from the same radial position. For the Foresight™ ICE probe, this translates to the angle of rotation ($\theta$) of the first scan line being identical for each ultrasound image in its position in 3D space.

In this section, we evaluate the consistency among the radially acquired ultrasound images in terms of the angle of rotation (theta) for the Foresight™ ICE. The Foresight™ ICE probe has a sophisticated design with a single transducer element, supported by a vertical fulcrum, surrounded by a metal shield. The element undergoes two primary motions – spinning and tilting, as described in section IG (figure 2.7). At a certain imaging angle, the 360-degree spinning motion forms the conical image. During ultrasound imaging, when the imaging is ‘paused’, the spinning motion comes to a halt. Because of the momentum, the element may initially stop at a different radial position than from where it started. The Foresight™ ICE probe has built-in functionality that further spins the transducer until it is positioned at the starting (first scan line) position. In this study, we observe how the first scan line may change both during an imaging session due to the pause feature, and between different studies.
**Methods:**

To check the consistency of scan lines for a given ICE probe, we designed a simple and effective experimental configuration. An ICE probe was fixed in one position while submerged in a water bath. A needle was placed at a fixed position in the imaging field of view of the ICE to provide a fixed reference object, and the scanner parameters were set to an imaging depth of 80mm and an imaging angle of 70 degrees. Multiple sample images were acquired for different conditions and trials. Each image was cropped to acquire an ROI of size 850x850 pixels. From the first image, the automatically computed centroid of the needle reflection was used as a reference for a scan line. For each subsequent ultrasound image, the centroid was again computed using the same method. Given that the probe and the needle are fixed throughout the experiment, if there is no change in the angular position of the first scan line, then all the centroid points should coincide. The differences and offsets in the reference scan line were measured in terms of linear and angular displacement. The displacement measurements are described in terms of the number of pixels as well as in SI units i.e. millimeters. The pixel spacing was used to convert the number of pixel errors to real-world measurements, as calculated based on the following equation, where the radius was set to 80mm as set in the experiments.

\[
\text{Radius}(\text{mm}) = \text{Pixelspacing}(\text{mm/pixel}) \times \text{Number of pixels(pixel)} \quad (2.4)
\]

\[
80\text{mm} = \text{Pixelspacing} \times 850/2\text{pixels} \quad (2.5)
\]

\[
\text{Pixelspacing} = 0.188\text{mm/pixel} \quad (2.6)
\]

The scan line consistency was checked for the following conditions: use of the pause feature; beginning a new study; re-plugging the ICE probe in the PIM (Patient Interface Module) connector; and restarting the entire Conavi Hummingbird console. The following steps (Figure 2.10) were followed, and imaging samples were collected for this experiment.

- **Trial 1)** Open a new study, sample, pause, sample, pause, sample, exit study.
- **Trial 2)** Open a second study, sample, pause, sample, pause, sample exit study.
- **Trial 3)** Open a third study, sample, pause, sample, pause, sample exit study.
- **Trial 4)** Re-plug the probe into PIM, open a fourth study, sample, pause, sample, pause, sample, exit study.
- **Trial 5)** Plug out the ICE probe, restart the console, plug in the probe, open a fifth study, sample, pause, sample, pause sample, exit study.
2.1. ICE Image Characterization

Figure 2.10: Action steps for trials 1-5. The camera icon represents where the image was acquired.

Results:

After obtaining centroids of the needle reflection from each of the ultrasound images, all the centroid points were displayed on a single image. Figure 2.11 (left) shows all the centroids placed on the first image from the first trial. It can be seen that none of the points overlap. A closer observation of the point distribution can be seen in figure 2.11 (right), which shows that the points from trial 4 and trial 5 are significantly farther away from those collected from the other trials.

Figure 2.11: (left) Reference image from Trial 1 overlayed by the centroids from all the trials. (right) Looking closely at the spatial distribution of centroids obtained.

Relative linear and angular displacement was measured with respect to the centroid point from the first image of the first trial, as shown in figure 2.12. It should be noted that only the
angular displacement is the measure of interest here since the variable parameter during radial scanning is the angle of rotation (theta).

When looking at the displacement with respect to the first image of the first trial, the maximum relative linear displacement was observed to be 14 pixels or 2.5mm. The maximum relative angular displacement was observed for trial 5 with a difference of almost 7 degrees.

Within each trial, we measured the displacement of each sample point relative to the first sample of that trial. On average, the linear displacement within trials is almost 1 pixel (1.2 pixels) or 0.2mm. The angular displacement incurred through the use of the “Pause” function is 0.6 degrees on average which is negligible. Some of the errors in this experiment can also be attributed to the systematic fiducial localization error introduced by the large size of a needle reflection.

**Conclusion:**

Looking at the spatial distribution of points, changes between trials, and relative changes within each trial, we can conclude that:

- The first scan line remains similar as long as the probe is plugged in.
- Pausing the imaging during a study does not lead to any significant changes in the angular position of the first scan line.
- Starting a new study, without plugging out the probe, also does not cause any significant change in the angular position of the first scan line.
• The first scan line for a probe will change its angular position once the probe is re-plugged or the system is rebooted.

Based on the results and conclusions derived from it, we can infer the following guidelines when operating the Foresight™ ICE probe.

• In a clinical setup, where the probe is plugged only once and is not re-used, the first scan line remains consistent. This means that no additional measures for probe calibration and tracking are required in a real clinical scenario with one-time use of the ICE probe.

• In an research and development setup, where one probe is potentially reused for multiple experiments, the first scan line may not be the same each time. This implies that the probe should either be recalibrated or the calibration to be manually adjusted each time it is plugged in for a study.

2.1.6 Imaging Angle Accuracy

The imaging angle or tilt angle ‘phi’, displayed on the screen is a major factor in image reconstruction and 3D image processing, since inaccuracies in this measurement will result in faulty 3D image reconstruction. The angle is determined by the sensors embedded within the ICE catheter. While the user can control the imaging angle manually, nevertheless some unintentional changes were observed in this parameter. The trueness, precision, and behavior of the imaging angle may depend on some internal or external factors to the ICE probe.

**Internal factor – Angle accuracy:** The accuracy of the imaging angle is said to be in the range of ±5 degrees, as reported by the manufacturer. Studies were conducted in our lab to characterize the inaccuracy in imaging angle, however the results were inconclusive due to the hypersensitivity of the imaging resolution. Our setup required target localization in the image and even a difference of one pixel in localization would change the predicted imaging angle by one degree.

It should be noted that while a 10-degree offset can cause inaccuracies in a 3D guidance system, this error is unlikely to cause any adverse effects during the intended use of the ICE probe in intraoperative ultrasound imaging situations.

**External factor – Probe rotation:** The imaging angle of the conical ICE image also changes with respect to the physical orientation of the probe. For example, if the probe is horizontally positioned and the imaging angle is 75 degrees, then the angle can decrease by as much as 6 degrees (to 69 deg) when the probe is held vertically. This change in angle is also captured by the angle sensor and reported on the console display. Therefore, this change
in angle will neither cause a discrepancy in intraoperative imaging nor in an image guidance system.

### 2.1.7 Image Artifacts

Foresight™ICE probe is a radial ultrasound imaging technology and can experience all the same imaging artifacts as a planar ultrasound, such as acoustic shadowing, enhancement, reverberations, etc. Apart from the common imaging artifacts, we have observed three atypical effects namely: donut, ring, and sprinkler artifact.

**Donut artifact:** The Foresight™ICE probes have an inherent hollow circular region, either completely bright or dark, in the centre of the image at the apex of the cone. This absolute ‘black-out’ or ‘white-out’ zone in the middle is inherent to each catheter. Imaging is not possible in this region. The width of this region is predefined to be at least 5mm. In the DICOM files, these pixel locations store some of the header information. Figure 2.13 shows an example of a white-out donut artifact.

![Figure 2.13](image_url)

**Figure 2.13:** ICE imaging in water bath showing (a) central white-out donut artifact and ring artifact, (b) ring artifact overlaying a reflection from a silicone sheet. Ring artifact is minimized by using the ‘magic-wand’ button a (c) medium and (d) highest setting.
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**Ring artifact:** The central hollow region is surrounded by a series of bright, concentric rings that can occupy up to a few millimeters of radial space in the ICE image. This ring artifact is a result of near-field noise present in the catheter. It is unique to each ICE probe and may change between multiple uses of a single probe. The appearance of the rings is overlayed on top of the echo image and ultrasound reflections can be seen within the region of the ring artifact. It is worth noting that the rings are constant during a study and do not present any motion or changes in brightness. Thus, the operator’s eyes, when focused on ultrasound imaging, can easily accommodate the presence of these rings. However, these artifacts do present a challenge in the design of image processing techniques. Nevertheless, the appearance of the rings can be minimized by manually adjusting the windows and level functionality or using the automated “magic-wand” function included in Conavi’s Hummingbird console (see figure 2.13(b-d)).

**Sprinkler artifact:** The Foresight™ ICE probe was used in a tracking environment as well. In a table-top tracking system (Aurora, NDI), there is an ellipsoidal volume of low-intensity varying electromagnetic field. In the presence of varying electromagnetic field, interference was observed in the ICE imaging causing a sprinkler effect (figure 2.14). This artifact includes a series of bright speckles in a curved line along with the radial depth of the ICE image. The speckles rotate with the spinning of the transducer. The intensity of the bright speckles decreases as the probe is moved farther away from the tracking system. The artifact can be seen in the images whether the ICE probe is equipped with an EM tracking sensor. Similar to the ring artifact, these bright speckles can cause an issue in the design of an image-guided system that relies on magnetic tracking of the probe, and which involves processing the ultrasound image captured directly from the screen.

![Figure 2.14: (a) Sprinkler artifact seen as a foreground. (b) Sprinkler artifact variation (enhanced) seen in the background and (c) brightness adjusted to minimize the background sprinkler effect.](image-url)
2.2 ICE Image Visualization

2.2.1 Volume Reconstruction and Rendering

The ICE image is visualized on the console monitor screen as a 2D circular image. To visualize the true, conical ultrasound image lying in 3D space the circular image must first be converted into 3D volume form, followed by processing with a volume rendering technique. All processing and off-line visualization is performed within the 3D Slicer [79]. We implemented a Slicer module called ‘ICE Reconstruction’ which performs the 3D reconstruction of the 2D ultrasound image, as well as the rendering of foreground of the volumetric image. The module implements the mathematical reconstruction described in the section IDA. The slicer-compatible python function for the reconstruction of ICE image is added in appendix A. The module utilizes the existing ‘Volume Rendering’ module to render the 3D conical ICE image. Since this visualization technique is composed of voxel information, the volume rendering shows the foreground echo information while blanking out the background / dark regions from the ICE volume. Figure 2.15 shows a sample ICE image and its volumetric reconstruction and rendering via the designed Slicer module. On a typical desktop computer (without GPU), the volume reconstruction takes almost 100ms.

Figure 2.15: (a) ICE image as seen on the console, (b) after volume reconstruction and rendering in 3D space, and (c) after texture mapping to a cone model via Slicer module.

2.2.2 Surface Texture Mapping

Another way to visualize the 3D conical image is to texture map an image on to the surface of a cone, which is implemented in 3D Slicer using VTK (Visualization Toolkit), an open-source platform for observing and handling scientific data. In the texture mapping technique,
an image (as a texture) is mapped on to a surface model. In this case, the ultrasound image, cropped to focus on the ROI, serves as the texture image. Thus the image is set as an input to the function vtkTexture. Then to create a surface model, a cone shaped model (vtkConeSource) acts as a planar surface. Finally, the vtkTextureMapToPlane method is used to map the textured image on to the cone, where the cone source is set as the input connection or the “plane”. For accurate mapping, the textured image coordinates need to align with the geometry of the cone according to figure 2.16. The centre of the cone, which lies midway on the major axis of the cone connecting the apex to the base of the cone, should align with the centre of the image. The texture mapped cone is now ready to be rendered in any 3D visualization software. To view this cone in 3D Slicer, the cone source is rendered as a model and can be manipulated or compounded with spatial transforms. An example image and its texture mapped visualization can be seen in figure 2.15(c). On a typical computer, texture mapping can take up to 17ms, which is adequate for real time visualization and data streaming. A Slicer-compatible python function for texture mapping an ICE image, given an imaging angle, is included in appendix A. A complete module is also available online.

2.2.3 DICOM reconstruction and custom interpolation

The Foresight™ ICE probe has a single element transducer and acquires the ultrasound data radially. As such, when the ultrasound is stored as a DICOM file, there is an obvious change in geometry and the appearance of image in an image-viewing software. Figure 2.17 shows how
each radial echo beam is stored as one complete row in the DICOM file. As the element spins the angle of rotation increases, and the subsequent echo beams are stored as the next rows.

Figure 2.17: Schematics of storing radial and spinning ultrasound beams (right) acquired via Foresight™ ICE probe as DICOM file (left)

The first few pixels in any row, representing the donut-artifact area near the apex of the conical image, are overwritten with supplementary header information, while the rest contain the true echogenic information. Some of the important header information to reconstruct a conical image and their respective DICOM access code are given below:

1. A value for imaging angle (phi) – [0x15, 0x1000]
2. A value of angle of rotation for each row or echo beam – [0x15, 0x1004]
3. Spacing information along the radius. – [0x28, 0x0030]

The value for imaging angle (phi) is already available in degrees. The values for rotational angle (theta) however are encoded and must be converted to degrees using equation:

$$\theta_{\text{degrees}} = \frac{\theta_{\text{encoded}}}{1024 \times 360}$$  \hspace{1cm} (2.7)

In order to reconstruct the 2.5D conical image, we find the Cartesian coordinate location of each pixels using the information above i.e., radial echo sample, radial spacing, theta and phi. The complete code for reconstruction is added in appendix A. It should be kept in mind that each ultrasound frame, consisting of one spinning motion, contains roughly 350 radial beams. When the DICOM file for one frame is reconstructed, the radial beams are sparse, lying far
apart in 3D space as can be seen in figure 18(a). In the appended code we add an additional function to interpolate the image. The interpolation is performed on the DICOM file before the reconstruction. The user chooses the degree of interpolation and rows are added between existing row image-data accordingly. The improvement in visualization upon interpolation can be seen in figure 2.18(b, c).

![Figure 2.18: (a) Conical ultrasound image reconstructed from the DICOM file and with interpolation factor of (b) 5 and (c) 15.](image)

### 2.3 ICE Probe Calibration

Image guidance is critical to percutaneous cardiac interventions because of the absence of the direct line of sight. Ultrasound imaging systems are suitable for cardiac imaging due to their safety, relatively low cost, high soft tissue contrast and compatibility with surgical tools. Transthoracic and transesophageal ultrasound imaging are capable of providing high contrast 2D and 3D imaging of soft tissues in real-time, but they are constrained in their views as they are used from outside the heart. In contrast, intracardiac echocardiography (ICE) is often used to guide these minimally invasive cardiac procedures by advancing the probe inside the heart and providing real-time imaging of the heart anatomy [100]. Conventional ICE images are 2D, planar and limited in their resolution and field of view. The Foresight™ ICE system [60] acquires ultrasound data in spherical coordinates where the transducer rotates along the azimuthal angle $\theta$ at a specific polar angle or imaging angle $\phi$ to generate a hollow cone shaped image (Fig. 2.19). Foresight™ ICE is also capable of generating 3D volume images by acquiring multiple 2.5D cone shaped images at varying imaging angles, which offers new opportunities for improving existing ICE guidance as well as potentially new clinical applications.

Ultrasound-based image guidance systems typically employ tracked tools and a tracked
Imaging probe. The use of EM tracking with ultrasound imaging facilitates the registration between patient anatomy, ultrasound images and other imaging modalities such as preoperative CT and MRI, and even electrophysiology maps to guide atrial ablation procedures. Tracking also simplifies the navigation of catheters towards a surgical target, generating 3D models using volume stitching, and visualization of compound 3D volumes from 2D images. Tracking is achieved using position and orientation (pose) sensors attached to the imaging probe. The tracking system generates a transformation between the sensor attached to an ultrasound device and the reference/world coordinate system, but the pose of the ultrasound image with respect to this reference coordinate system is unknown. Therefore, ultrasound calibration is required to determine the transformation between the coordinate system of the image volume and the sensor attached to the probe. The overall accuracy of an image-guidance system is dependent on the accuracy of this calibration as well as the accuracy of tracking system, the dimensions of the pose sensors, and the quality of imaging. However, only calibration can be controlled and improved to minimize errors in the overall system. Many calibration techniques have been described in the literature for ultrasound probes [138]. Calibration methods for 2D planar ICE probes have been described and evaluated to provide image guidance during interventional procedures such as left atrial ablation therapy [125]. However, all such calibration methods are designed for 2D planar ultrasound images. The Foresight™ ICE system, being unique in its image acquisition technique and 2.5D conical images, has not yet included methods for tracking and calibration in the commercially available version of the technology.

In this chapter, we present and evaluate an intracardiac ultrasound spatial and temporal calibration method designed for 2.5D conical ICE, where line-phantom based methods are used to perform calibrations of the ultrasound probe. We validate these calibrations by quantifying precision at different imaging angles, and the overall system by localizing a point source and computing the centroid of a sphere object.
2.3.1 Methods

In all our experiments, tracking is achieved using an electromagnetic tracking system (Aurora, NDI, Canada)\cite{8}. The Conavi Hummingbird console along with a Foresight\textsuperscript{TM} ICE probe is used to generate ultrasound images. Since we do not have access to the voxelized 3D data of the 2.5D conical images, we acquire the images using a frame-grabber (DVI2USB 3.0, Epiphan Video, USA). An additional step is required to convert the fiducial points from the coordinates of a planar 2D image to that of 3D space in which the ultrasound is acquired. Eqn. 4.1 is used to represent the relationship between the two image coordinate systems.

\[
\begin{bmatrix}
    x_{3D} \\
y_{3D} \\
z_{3D}
\end{bmatrix} = \begin{bmatrix}
    1 & 0 & -o_x \\
    0 & 1 & -o_y \\
    0 & 0 & \| (x_{2D}, y_{2D}) \| \cdot \tan(90 - \phi)
\end{bmatrix} \begin{bmatrix}
    x_{2D} \\
y_{2D} \\
1
\end{bmatrix} \tag{2.8}
\]

where \((o_x, o_y)\) represents the centre of the planar image or the apex of the conical image.

Both the magnetic tracking system and the frame-grabber are connected to the PC using PLUS\cite{114} library and the time-stamped data are imported to 3D Slicer\cite{79}.

2.3.2 Calibration

Owing to the unique 2.5D conical configuration of the images acquired by the Foresight\textsuperscript{TM} ICE system, standard cross-wire phantoms or Z-fiducial phantoms \cite{138} cannot be used as they are designed for conventional 2D planar images. For the same reason, popular temporal calibration techniques and modules like fCal\cite{114} cannot be used directly with 2.5D conical images. Therefore we use needle-based methods described by Chen et al.\cite{53} and Gobbi et al.\cite{88} for spatial and temporal calibration respectively.

Spatial Calibration

We formulate ultrasound probe calibration as a registration problem between a point and homologous line \cite{51}, using a tracked needle (a line) and its hyperechoic reflection in ultrasound image (a point) as the basis for calibration. While the Foresight\textsuperscript{TM} ICE generates a conical ultrasound image in real time, it is displayed on a conventional 2D monitor as a disc-shaped image in a 2D polar coordinate system (Fig. 5.2a). Given the imaging depth \(r\) and the imaging angle \(\phi\), the 2D pixel location in the original disc image can be converted to a 3D coordinate system as per Eqn 4.1. In this manner, the point-line based calibration \cite{51} is directly applicable to the Foresight\textsuperscript{TM} ICE probe calibration, where efficient solutions exist \cite{53}.

A Foresight\textsuperscript{TM} ICE probe was augmented with a 6 DoF magnetic tracking sensor rigidly attached to the outer sheath, close to the probe tip. A water bath was scanned at room temperature
using tracked a Foresight\textsuperscript{TM} ICE probe. A pre-calibrated needle (Aurora Needle, 18 G/150 mm, NDI, Canada\cite{4}) was used to model a line. The pose of the needle is defined by a point of origin and a direction vector. The needle was oriented at multiple positions and angles to produce point fiducials on the cone shaped 2.5D images, along the radius and at varying azimuthal angles $\theta$. For this initial assessment, the imaging angle $\phi$ was kept constant at 80°. Clamps were used to minimize jitter and overcome inaccuracies caused by temporal misalignment. 15 point fiducials were recorded using screen-capture of the Conavi console, along with the tracking information for both the probe and the needle. Fiducial points from the 2D images were converted using Eqn. 4.1 to their correct representation in 3D space.

The coordinate systems are represented in Fig. 5.2b, with that defined by the magnetic tracking system being considered as the world coordinate system. Let $w$, $n$, $pr$ and $img$ represent coordinate systems as defined by the tracker, needle sensor, ICE probe sensor and ultrasound image volume, respectively. As the needle is pre-calibrated, the transform $P_1$ from needle tip to the sensor on the needle is known. The pose of the line fiducials can be defined in coordinate system of the ultrasound probe using:

$$P_2 = ^{pr}T_{img} = (^wT_{pr})^{-1} (^wT_{n})P_1 \tag{2.9}$$

where $^wT_{pr}$ and $^wT_{n}$ are the locations of the probe sensor and needle respectively, as reported by the magnetic tracking system. Fiducial point coordinates in 3D space and pose information of the line fiducials ($P_2$) are used to solve for the affine calibration transformation comprising of anisotropic scaling, followed by rotation and translation.
Temporal Calibration

We use a temporal calibration method described by Gobbi et al. [88] and extend it to work for the 2.5D images. This approach compares the positions of a tracked, line-shaped object in real space to those of the reflection of that object as seen in a B-mode ultrasound images. We use a wooden shaft (4 mm diameter) to represent a line and its reflection is seen as a point in the ultrasound image. Wood is employed to reduce the amplitude of the reflection at the shaft-water interface. The line is kept almost perpendicular to the 2.5D imaging plane to obtain a bright and well-defined reflection in the ultrasound image. A 6 DoF magnetic tracking sensor is rigidly attached to the shaft representing the line to track its motion. Accuracy of this method is highly dependent on the linear motion of the line with respect to the ultrasound image. To ensure smooth and unidirectional motion of the line-object, we fashioned a simple, plastic building-block assembly which moved along the tracks at the bottom of the water bath. The Foresight™ ICE probe remained static at one position. The block assembly carrying the wooden line-object is moved forward and backward along the tracks to generate a sinusoidal motion pattern. Reflections in the image appear in and out of the imaging angle accordingly. Five measurements were taken with the imaging angle fixed at 85°. For every measurement, at least 2 motion cycles were recorded.

Segmentation of the line reflection from the images was performed automatically using 3D Slicer. The centroid of each segmented reflection from the images was extended to 3D space using Eqn. 4.1. The distance of this point from the origin ‘O’ of the conical image is recorded to represent the positional information of the object in the image (‘img_dist’). To obtain the positional information of the line-object in real space (‘obj_pos’), the tracking sensor data were analyzed to find the linear direction of motion using Principal Component Analysis [205] and record the projection of sensor position along the principal axis. The two signals representing position of the object in space (‘obj_pos’) and its reflection in the image (‘img_dist’) were normalized by subtracting the mean followed by division by the standard deviation of the measurements. Finally, the temporal offset was calculated by finding the time delay which provides the highest cross-correlation between the two signals.

2.3.3 Validation

We validated our calibration both qualitatively and quantitatively. Qualitative assessment was performed by generating a model of the needle used for spatial calibration and displaying its intersection with the 2.5D ultrasound image in a virtual reality environment. The calibration system was validated by evaluating the precision of spatial calibration parameters and time offset as computed by the temporal calibration. To validate the overall
Chapter 2. Characterization of Foresight™ ICE

system accuracy, two experiments were performed: point source localization and calculation of the centroid of a spherical object. We designed a phantom which can be used to model both the point source and a sphere object and compare the point and centroid location with pre-experiment reference positions defined by the CT scan of the phantom.

Calibration Precision

Conventionally, calibration precision is evaluated at multiple depths and transducer excitation frequencies. Variability of parameters, as calibration is performed at different depths and frequencies, is extensively discussed in literature \[138\]. Since Foresight™ ICE has the functionality of adjustable imaging angle \( \phi \) of the cone shaped image, we intended to observe the trends in variability, if any. We repeat our spatial and temporal calibration experiment at multiple imaging angles to evaluate the precision of spatial calibration matrix parameters: translation along Cartesian axes, Euler rotation angles and scaling along Cartesian axes as well as the time delay observed via temporal calibration.

For spatial calibration, in all the experiments the probe was physically restrained using a clamp and the imaging angle \( \phi \) was changed through the buttons on the console. Automatic segmentation was performed using 3D Slicer to locate the needle point fiducial in the 2D images. The remainder of the procedure was as described in section \[2.3.2\]. Similarly for temporal calibration, the experiment was repeated multiple times at three different imaging angles; keeping the probe still and only changing the imaging angle through the console.

Point Source Localization

A 140 mm by 140 mm phantom was designed with 4 pillars in each corner, one in the middle and 7 divots. The divots help define the reference coordinate frame via point-point registration of divot locations from tracker coordinate system to CT coordinate system. The corner pillars secure the wires going across and intersecting at one point, which is considered as the target point source (Fig. 2.21). The wires were roughened near the intersection to improve their echogenicity. The cross-wire phantom was submerged in a water bath and scanned using the calibrated Foresight™ ICE probe to image the point source. A 5 mm thick layer of silicone was poured into the bottom of the phantom to help reduce reflections. Care was taken to position the probe such that the point fiducial lies in the middle of the cone shaped image along the radius, in order to minimize the beam profile effect and associated errors. Points are converted to 3D space using Eqn. [4.1] followed by calibration transformation and conversion to reference coordinate system defined by the CT scanner. The ground truth is established by the point location in the 3D CT scan. Point reconstruction accuracy is described in terms of standard
error and 95% confidence interval along $x$, $y$ and $z$ axis.

Figure 2.21: Validation phantom: (a) cross wire to model a point source, (b) as seen in 2.5D ultrasound and (c) sphere ball, (d) as seen in 2.5D ultrasound.

**Spherical Phantom Centroid**

The same phantom was adjusted to remove wires and add a 30 mm radius, water-filled table-tennis ball to model a sphere. The phantom was imaged at multiple poses to identify points along the outline of the sphere at different cross-sections (Fig. 2.21). Then, similar to the point source localization method, the points were transformed to the reference coordinate system. Spherical fitting was applied to these points to find the centre and radius of the sphere. These centroids of the sphere were compared to the one estimated in the reference coordinate system.
2.3.4 Results

2.3.5 Calibration

Spatial Calibration

Spatial calibration of a fixed-angle Foresight™ ICE probe, with a magnetic sensor attached to the outer sheath, was performed using a needle phantom and point to line registration algorithm. Results depict an overall calibration accuracy (fiducial registration error, or FRE) of 1.74 mm.

Temporal Calibration

The tracked long wooden rod was moved in and out of the conical 2.5D surface plane of the Foresight™ ICE probe fixed at an angle of 85°. Correlation was used to find a temporal offset between the two sinusoidal signals: position of line in 3D space (‘\textit{obj\textsubscript{pos}}’) and distance of point reflection from the centre of the image (‘\textit{img\textsubscript{dist}}’). A time delay of 72 ms was observed in this experiment. Figure 2.22 shows the normalized signals before and after temporal calibration.

![Normalized signals](image)

Figure 2.22: Normalized signals, derived from the tracker position of the line-object and its reflection in the ultrasound image, before and after temporal calibration is applied.

2.3.6 Validation

For initial validation, a qualitative assessment was performed. The 2.5D images were reconstructed from the 2D images obtained from the screen capture of the Conavi console. Transformations were applied to a virtual needle model and the reconstructed volume. Figure 2.23
shows the needle passing through the needle reflection or point fiducial seen in the image, providing preliminary validation of the calibration method.

![Figure 2.23: Qualitative validation of calibration method in virtual space. Needle passing through the reconstructed 2.5D ICE image: (a) side view, and (b) top view.](image)

**Calibration Precision**

Spatial calibration of Foresight™ ICE probe with a unique 2.5D image was repeated at 5 different angles to observe the translation, rotation and scaling factors of the calibration. Table 2.1 shows the precision of different parameters of spatial calibration.

<table>
<thead>
<tr>
<th>$\phi$ ($^\circ$)</th>
<th>$t_x$ (mm)</th>
<th>$t_y$ (mm)</th>
<th>$t_z$ (mm)</th>
<th>$r_x$ (°)</th>
<th>$r_y$ (°)</th>
<th>$r_z$ (°)</th>
<th>$s_x$ (mm/pixel)</th>
<th>$s_y$ (mm/pixel)</th>
<th>$s_z$ (mm/pixel)</th>
</tr>
</thead>
<tbody>
<tr>
<td>85°</td>
<td>-2.68</td>
<td>-1.02</td>
<td>6.22</td>
<td>-0.20</td>
<td>-0.01</td>
<td>2.56</td>
<td>0.16</td>
<td>0.16</td>
<td>0.59</td>
</tr>
<tr>
<td>80°</td>
<td>-2.85</td>
<td>0.18</td>
<td>8.87</td>
<td>-0.34</td>
<td>0.28</td>
<td>2.56</td>
<td>0.16</td>
<td>0.17</td>
<td>0.16</td>
</tr>
<tr>
<td>75°</td>
<td>-2.26</td>
<td>-1.00</td>
<td>0.54</td>
<td>-0.30</td>
<td>-0.12</td>
<td>2.36</td>
<td>0.16</td>
<td>0.15</td>
<td>0.30</td>
</tr>
<tr>
<td>70°</td>
<td>-0.74</td>
<td>-0.51</td>
<td>9.92</td>
<td>-0.28</td>
<td>-0.19</td>
<td>2.43</td>
<td>0.15</td>
<td>0.14</td>
<td>0.25</td>
</tr>
<tr>
<td>65°</td>
<td>-4.77</td>
<td>0.19</td>
<td>8.33</td>
<td>-0.03</td>
<td>-0.29</td>
<td>2.35</td>
<td>0.17</td>
<td>0.17</td>
<td>0.11</td>
</tr>
<tr>
<td>Mean</td>
<td>-2.66</td>
<td>-0.43</td>
<td>6.78</td>
<td>-0.23</td>
<td>-0.07</td>
<td>2.45</td>
<td>0.16</td>
<td>0.16</td>
<td>0.28</td>
</tr>
<tr>
<td>RMS</td>
<td>1.29</td>
<td>0.54</td>
<td>3.34</td>
<td>0.11</td>
<td>0.20</td>
<td>0.09</td>
<td>0.01</td>
<td>0.01</td>
<td>0.17</td>
</tr>
<tr>
<td>$\pm 95%$</td>
<td>$\pm 1.13$</td>
<td>$\pm 0.47$</td>
<td>$\pm 2.93$</td>
<td>$\pm 0.09$</td>
<td>$\pm 0.17$</td>
<td>$\pm 0.08$</td>
<td>$\pm 0.01$</td>
<td>$\pm 0.01$</td>
<td>$\pm 0.15$</td>
</tr>
</tbody>
</table>

Table 2.1: Precision of spatial calibrations performed at different imaging angles. The overall mean, root mean square (rms) error and 95% confidence interval is given for estimated spatial calibration parameters: translations ($t_x, t_y, t_z$), Euler rotations ($r_x, r_y, r_z$) and scaling factors ($s_x, s_y, s_z$).

We observe high variations along $z$-axis with root-mean-square error in translation ($t_z$) going as high as 3.3 mm. This behavior was expected for two reasons. First, the imaging angle $\phi$
changes along the z-axis and there may be up to 5° of uncertainty between the imaging angle displayed on the screen and the true physical angle of the conical image in 3D space. Second, the calibration is performed using 3D reconstruction of the 2D screen-capture of the ultrasound image based on the imaging angle $\phi$. This reconstruction is prone to some error because of possible data loss from projecting a 2.5D image to a 2D console screen and then reconstruction back to 3D space.

A non-tracked Foresight™ ICE probe was held still in place while a wooden rod was moved to reflect sinusoidally in a 2.5D image plane and generate sensor position ‘$obj_{pos}$’ and reflection position ‘$img_{dist}$’ signals. The experiment was repeated at 3 different angles with at least 5 measurements at each angle. Every measurement includes a minimum of two sinusoidal motion cycles. Results are summarized in Table 2.2.

<table>
<thead>
<tr>
<th>$\phi$</th>
<th>Mean temporal offset (ms)</th>
<th>Standard deviation (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$85^\circ$</td>
<td>98.6</td>
<td>±12.8</td>
</tr>
<tr>
<td>$75^\circ$</td>
<td>86.7</td>
<td>±16.9</td>
</tr>
<tr>
<td>$65^\circ$</td>
<td>93.7</td>
<td>±21.6</td>
</tr>
</tbody>
</table>

Table 2.2: Precision of temporal calibrations performed multiple times at different imaging angles

An overall mean temporal offset of 93 ms was observed. While a 93 ms offset may account for an appreciable portion of a patient’s cardiac cycle (particularly at higher heart rates), this time delay does not make a perceptible difference in a clinical setting for most applications such as ablation therapies and visualization. However for some applications involving rigorously moving structures, such as segmentation of mitral valve leaflets, this time offset may cause errors. Therefore, for general purposes it is not crucial to correct for temporal offset but some interventions might require it to achieve higher accuracy.

**Point Source Localization**

The cross-wire phantom was secured firmly in a water bath and imaged using a freehand technique. The intersection of the wires, considered as a point source, was imaged from all 4 crossing angles to have a better estimate and reduce bias. B-scan images of the point source are acquired at 15 different positions. Points were manually segmented and converted to the reference coordinate system defined by the CT image volume. All the points were compared to the ground truth defined by the CT of the phantom. Standard error and 95% confidence limit for point reconstruction accuracy is given in Table 2.3.
Spherical Phantom Centroid

The spherical phantom was scanned freehand from different sides. 20 images were acquired and almost ten points along the outline of the sphere were identified in each image. These points were randomly rearranged into 30 groups to enable unbiased distribution of points along the surface of sphere in each measurement. After reconstruction to 3D space, sphere-fitting and coordinate system conversion, the centroids were computed from each group of points and compared to the centroid defined by the CT coordinate system. Using the points on the surface of the sphere, we can also compute accuracy for radial distance and volume measurement, however they were deemed unreliable due to low ultrasound image quality. Table 2.3 summarizes the results for locating a sphere centroid in a 2.5D ultrasound image.

<table>
<thead>
<tr>
<th>Validation method</th>
<th>Mean error (mm)</th>
<th>95% Confidence interval (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>x</td>
<td>y</td>
</tr>
<tr>
<td>Point source localization</td>
<td>5.07</td>
<td>5.0</td>
</tr>
<tr>
<td>Sphere centroid localization</td>
<td>1.75</td>
<td>0.91</td>
</tr>
</tbody>
</table>

Table 2.3: Accuracy of calibrated and tracked Foresight™ ICE probe described in terms of mean standard error and 95% confidence limits for point source localization and sphere location estimation.

2.3.7 Discussion

In this work, a calibration method for the unique 2.5D cone-geometry images acquired using a single-element, mechanically scanning intracardiac ultrasound probe was presented and evaluated. Qualitative analysis in a virtual environment shows that the needle intersects with the point fiducial in the 2.5D conical images after calibration. The FRE of the calibration was 1.741 mm in the initial study. However FRE alone does not accurately depict the overall efficacy of a tracking and calibration system. We quantify both the calibration methods and our overall tracking system. We perform point source localization to compute the target registration error (TRE) of the system. Results indicate mean standard error up to 5.07 mm. The 2.5D ultrasound images generated by a single-element mechanically scanning probe is a relatively new concept, and calibration accuracy may be improved once the image generation, acquisition and processing are better understood. Attaching a sensor on the outer sheath of the ultrasound probe also introduces errors in this tracking system. Ideally, the sensor would be integrated rigidly inside the probe, close to the transducer and does not cause any magnetic interference.
One major source of error is the large beam profile associated with the single-element transducer. The ultrasound beam is narrow in the centre of the image, or near the apex of the cone, and becomes wider at greater depths. With a wider beam, a point source does not appear as a single bright spot in the image but instead as a blurry and spread out ellipsoid and it becomes difficult to define a specific point in the image. Blurring may also be observed as a result of mechanical scanning rotations in the ultrasound probe. These factors can cause large target localization error which introduces errors in our system accuracy assessment. Beam profile is an inherent property of ultrasound and cannot be improved by the design of an image guidance system. Another source of error, which can potentially be improved as well, is the interchange of coordinate systems. The ultrasound image is generated in 3D space in spherical coordinates, projected on to a 2D screen and then reconstructed back to a 3D Cartesian coordinate system by our system. System accuracy can be improved if these conversions are avoided or performed more efficiently. In spite of these effects potentially causing errors in the system, with the mean error for point source localization appearing to be large, this calibration method may still yield acceptable accuracies, with literature suggesting that for most intracardiac interventions accuracy in the order of 5 mm is required[122].

We also performed an experiment to image the surface of a sphere and compute its centroid. The results indicate much smaller errors in localization of the centroid of the sphere. We suspect that this behavior is observed because some of the sources of error, such as beam profile and image reconstruction, are biased in a certain direction. Collecting points, distributed over the surface, reduces the overall bias and the centroid computed based on multiple, distributed points is more accurate.

It must be noted that the frame-grabber transmitting ultrasound images, and the magnetic tracking system inherently transmit data at different frame-rates. However, we use PLUS library to acquire data from both channels and the time stamps are applied by the PC. The PLUS library module estimates and synchronizes the data for the user, thus recording data from both the channels at same time instances, while it is not possible for the user to control this data acquisition protocol with PLUS library, the data we collect appears to be intrinsically synchronized, i.e., both the tracker and image data are acquired at the time instant, but in reality this is not completely accurate. That being said, the approximations made by the PLUS library are sufficiently close in time that they do not cause any errors of significance in our workflow and can be assumed correct.

Furthermore, these timestamps are not evenly spaced. In temporal calibration, the correlation is computed between ‘\textit{img}_{dist}’ and copies of ‘\textit{obj}_{pos}’ signal B shifted by a certain number of samples. The temporal offset is given by the number of samples to be delayed in order to achieve maximum correlation between ‘\textit{img}_{dist}’ and ‘\textit{obj}_{pos}’ signals. Since the sampling inter-
val of the magnetic tracking system is not constant throughout the signal, the temporal offset estimation from the number of samples is not factual. These differences however are in the order of a few milliseconds at maximum and can be neglected as they do not make a difference in practice.

System accuracy is directly affected by the uncertainty in the imaging angle \( \phi \). The probe calibration and tracking method is greatly affected as it is based on the imaging angle displayed on the screen. Small errors in the displayed approximate imaging angle can cause noticeable deviations in the system. While the error may be small near the apex of the cone, it increases as moving towards the distal end of the image. Our future work includes quantifying the imaging angle using a phantom, studying the effect of beam profile on accuracy, and demonstrate an application of tracked single-element ultrasound in intracardiac interventions.

### 2.3.8 Conclusion

Intracardiac ultrasound probes and their tracking is a vital part of interventional cardiology and cardiac surgery. The accuracy of such a tracking system is dependent on the quality of ultrasound calibration. We describe and validate methods that work for the spatial and temporal calibration of unique 2.5D cone shaped images acquired using Conavi’s Foresight™ ICE system. We use needle or line based methods for both spatial and temporal calibration. Our workflow enables tracking of the ICE probe with the ability to locate a point with the accuracy of 5 mm. The TRE for our system appears to be higher than most calibration methods for planar ultrasound images, primarily because of the large beam profile associated with the single-element ultrasound transducer used in this study. Moreover the unique 2.5D configuration of the image introduce errors when generating a B-scan image at an angle \( \phi \) and when projecting on 2D screen. Even with these limitations, the accuracy of the Conavi Foresight™ ICE tracking system is still more than acceptable for the image guidance system to be used in a clinical settings to perform intracardiac interventions.

### 2.4 Characterization of ICE Calibration

We performed spatial calibrations with the probe affixed in one position and varied the imaging angle. A calibration matrix was obtained with ultrasound images acquired at an angle (phi) of 50 degrees. Similarly, one calibration was performed for each of these imaging angles – 55, 60, 65, and 70 degrees. Immediately following each calibration, error metrics were computed as well. The calibration procedure described previously, gives an error metric called fiducial localization error (FLE). To obtain a more realistic error metric i.e., target registration error
(TRE), we used a point-based validation technique. The tip of a tracked and pre-calibrated 5DoF needle (NDI) served as the target point. The probe was fixed at one position and imaging angle, while the needle was carefully moved to its tip in the ultrasound image. The position of the needle tip in EM tracking space is compared to the position of its reflection as seen in the image, after application of the probe calibration and tracking information. The linear displacement between the two points provides an error or TRE value corresponding to that image. Multiple needle tip placements and associated ultrasound images furnish us with a series of validation points and TREs. We refer to this as a point-cloud validation technique.

Figure 2.24: Outline of experimental steps taken to collect data for the characterization of calibration and tracking behavior of the Foresight™ ICE probe

A minimum of 8 different images, with reflections from the needle tip, were acquired with target points spread throughout the image plane. The entire process was repeated three times to assess the repeatability of the results. The probe was held constant within each trial, although the probe was re-plugged and moved after the first trial.

These experiments were performed to address several questions related to calibration specific to the forward-looking, radial, Foresight™ ICE probe. The questions are designed from both industrial and clinical perspectives. These experiments test the repeatability of calibration, ideal imaging angle for calibration, radial distance and error relationship, and the angle-calibration error relationship as well. It should be noted that the study is post-hoc, such that the questions were designed after the data had been acquired and that the data is not biased to favor any conclusion. Each section below describes the relevant questions, methods employed, results and the conclusion derived to answer those questions.

### 2.4.1 Repeatability of Spatial Calibration

In this section, we validated the spatial calibration technique by evaluating the repeatability of the calibration process for a single probe. The aim is to check the reliability of the calibration method with respect to a probe and answer the following question:
Is the process of spatial calibration valid and reliable for the Foresight™ ICE probe? Is the calibration/tracking accuracy consistent for multiple calibrations performed on the same probe?

**Method:**

We tested the intra-probe variability of calibration accuracy by comparing the error metric TRE between the three trials. TRE was calculated by using the validation dataset acquired at 50 deg ICE imaging along with calibration performed at 50 deg (the same angle) and so on. The TREs from trials 1, 2, and 3 were compared to check whether they are significantly different from each other.

**Result:**

The analysis of variance (ANOVA) testing for the errors among the three trials resulted in a p-value of 0.367 which means that we cannot reject the null hypothesis that the trials are similar. The box plot results are shown in the figure 2.25.

![Figure 2.25: Error distribution among the three trials](image)

**Conclusion:**

The three boxes lie on the same horizontal line indicating that the three trials are not significantly different from each other. Based on this evaluation, we conclude the following:

The spatial calibration is reliable in terms of its repeatability for the same probe.

### 2.4.2 Intra-procedural positioning

In the radial Foresight™ ICE probe, smaller sized reflections are observed towards the centre of the image or the apex of the cone, and wider needle reflections are seen towards the periphery. With respect to tracking, we want to determine whether the same behavior is observed with target registration error (TRE) as well. Clinically, it is important to know whether measurements made in a tracked environment are more accurate when made in one portion of the
image than the other. The clinical question becomes:

To make accurate measurements intraoperatively, should the targeted structure/anatomy be placed near the apex of the cone? Is the effective error dependent on the radial distance from the centre of the ICE image?

Method:
To determine whether the TRE is a function of radial distance, we used the TRE information from the previous section. Since the three trials were similar, we combined the data from the three trials into one. For each TRE, there is an associated ultrasound image with a needle reflection. The radial distance is calculated between the apex of the cone (centre of the image) and the centroid of the needle reflection. The TRE was plotted against the radial distance, and the significance of their relationship is evaluated using spearman’s correlation coefficient. Spearman’s rho was chosen over the Pearson’s correlation coefficient since it is better at handling datasets with outliers and skewed variables. Spearman’s alternative hypothesis is that the two variables are correlated.

Result:
The TRE vs radial distance graph can be seen in figure 2.26. The graph itself shows no visible pattern or relationship between distance and error. Spearman’s rho value is calculated to be 0.223 with a significance of $p < 0.01$, indicating that we can moderately accept the null hypothesis and reject the alternative hypothesis that the variables – TRE and radial distance are correlated.

Figure 2.26: Target registration error (vertical axis) plotted against the radial distance at which it was observed.

Conclusion:
By observing figure 2.26 and the correlation coefficient, we can conclude that there is no
significant relationship between TRE and radial distance. Intraoperatively, measurements can be made freely as the errors introduced due to tracking are almost the same throughout the imaging plane. Thus we can answer the question as:

The effective error is independent of the radial distance from the centre of the image. In a tracking environment, measurements made near the apex of the cone will not be significantly more accurate than those made at the periphery.

2.4.3 Calibration Uniformity wrt Imaging angle

Spatial calibration is a well-established procedure in literature, described and tested for planar ultrasound imaging. In the case of Conavi’s Foresight™ ICE, there is another parameter involved, namely the angle of the cone or the imaging angle. When changing the imaging angle on the Foresight™ ICE probe, the angle of the cone itself changes but the apex of the cone remains at the same position. Since spatial calibration is performed with the origin of the image set to the apex of the cone, the calibration should be valid for imaging at all different angles.

In this section, we evaluate whether the calibration performed at a specific angle is only valid for tracking images at that specific angle, or whether it can track ICE images acquired at other angles with the same accuracy.

If a probe is calibrated at a certain angle, is it suitable/accurate for ultrasound imaging only at that same angle? Does a calibration matrix produce equally accurate tracking regardless of the imaging angle of the ICE?

These questions are of high clinical importance as they determine whether a clinician can freely switch between forward-looking and side-looking imaging with a tracked ICE probe and achieve the same level of accuracy.

**Method:**

We use all the data collected for trials 2 and 3 in this study. Data from trial 1 could not be used due to a technical issue. For each calibration matrix acquired with imaging at a specific angle, the TRE is computed for all the available validation datasets with imaging performed at 50, 55, 60, 65, and 70 degrees. For each pair, we obtained a point cloud and then a set of TREs. The average TRE and standard deviation in error for each pair are represented in the form of a heatmap.

**Result:**

Average TREs for each pair and the standard deviation in error for Trial 2 and Trial 3 can be seen in Figures 2.27 and 2.28 respectively.

**Conclusion:**

It can be seen in each of the four heatmaps that the diagonals are consistently green com-
Figure 2.27: (left) Average TRE and (right) standard deviation in TRE heatmaps when the probe is calibrated at a certain angle and validated with imaging at certain angles for Trial 2.

<table>
<thead>
<tr>
<th>Angle of Probe Calibration</th>
<th>Average TRE</th>
<th>Standard Deviation in TRE</th>
</tr>
</thead>
<tbody>
<tr>
<td>50°</td>
<td>0.8</td>
<td>0.6</td>
</tr>
<tr>
<td>55°</td>
<td>14.6</td>
<td>7.6</td>
</tr>
<tr>
<td>60°</td>
<td>9.5</td>
<td>5.2</td>
</tr>
<tr>
<td>65°</td>
<td>9.7</td>
<td>6.1</td>
</tr>
<tr>
<td>70°</td>
<td>3.2</td>
<td>1.7</td>
</tr>
</tbody>
</table>

Figure 2.28: (left) Average TRE and (right) standard deviation in TRE heatmaps when the probe is calibrated at a certain angle and validated with imaging at certain angles for Trial 3.

<table>
<thead>
<tr>
<th>Angle of Probe Calibration</th>
<th>Average TRE</th>
<th>Standard Deviation in TRE</th>
</tr>
</thead>
<tbody>
<tr>
<td>50°</td>
<td>1.7</td>
<td>0.9</td>
</tr>
<tr>
<td>55°</td>
<td>10.5</td>
<td>6.0</td>
</tr>
<tr>
<td>60°</td>
<td>4.1</td>
<td>2.1</td>
</tr>
<tr>
<td>65°</td>
<td>10.2</td>
<td>6.0</td>
</tr>
<tr>
<td>70°</td>
<td>1.8</td>
<td>0.7</td>
</tr>
</tbody>
</table>
pared to the rest of the values, indicating that the TRE is minimum when the tilt angle of imaging is the same as that used during the calibration of the ICE probe. Therefore the answer to the question becomes:

The error is minimum when imaging is performed at the same angle at which the calibration was acquired. Thus, a calibration matrix is valid but might be less accurate when the imaging angle of ICE is different.

2.4.4 Tracking accuracy wrt Imaging Angle

From the previous section, we have established that tracked imaging is most accurate when acquired at the same imaging angle at which it was calibrated. In this section, we discuss the accuracy of tracked imaging in association with the imaging angle of the conical ultrasound. The Foresight™ ICE probe is considered more reliable and less noisy when imaged in a side-viewing mode rather than at a forward-looking angle. We investigate whether this trend is translated for tracked imaging as well. The question becomes:

Is there a relationship between target registration error and the angle at which it is calibrated? Is side-viewing imaging more accurate than forward-looking imaging?

Answering these questions will give a clinical context as to which angles to use to obtain the most accurate spatial information from the ultrasound.

Method:

Since the data from the three trials are not significantly different (section 2.4.1), we combined the TRE-angle dataset resulting in 135 samples in total. We used one-way ANOVA testing to determine whether there are any significant differences between the angle groups. The null hypothesis is “all the angle groups are the same”. A Tukey test was further conducted to determine where those differences may lie.

Result:

Figure 2.29 shows the mean error for each of the angle groups along with a 95% confidence interval. Qualitatively, there is no visual pattern to observe. Testing with the entire dataset, the ANOVA results showed that there are statistically significant differences \( p < 0.05 \) between the angle groups. The results of Tukey tests were unable to define which two angle pairs have significant differences between them since each angle pair had a \( p_{tukey} > 0.05 \).

Conducting the ANOVA for the dataset without outliers, the results showed that there is no significant difference between any of the angle groups.

Conclusion:

Due to the contradicting nature of the results it is difficult to draw any strong conclusions. However, the absence of any significant angle-pair from the Tukey test would indicate that the
results of ANOVA using a full dataset may be biased due to the presence of outliers. Based on this assumption, we can conclude that

The tracking accuracy of an ICE probe is independent of the imaging angle used during a study.

2.5 Challenges and Conclusion

One of the biggest challenges faced when working with the tracked ICE probe, is the motion of the transducer element relative to the body of the ICE catheter. It was observed that the calibration and tracking were accurate when the probe is held stationary, however, any linear or rotational movement of the catheter introduced exceptionally high errors in the system. Once the probe is moved following calibration, the tracking becomes inaccurate due to a rotational angular offset. This offset is caused by the relative motion between the innermost part of the catheter with the transducer and the external sheath of the ICE probe where the sensor is attached. Figure 2.30 demonstrates this challenge visually. The left image represents the state of imaging and tracking immediately after probe calibration when the ICE catheter is not moved. The virtual needle can be seen intersecting the needle reflection in the ultrasound image. The right image shows the ultrasound imaging after the probe is moved. The error can be seen as the needle reflection follows the virtual needle at a rotational offset. This rotational offset was observed to go up to 60 degrees.
Figure 2.30: (a) Slicer view of a tracked needle (virtual green line) intersecting its reflection in the ICE image right after calibration is performed, holding the ICE probe static. (b) Error introduced into the tracking environment when the probe is moved.

Due to the relative motion between the inner and outer layers of the ICE catheter, there are inaccuracies introduced into the tracking environment. This challenge adversely affects the design of any external tracking-based image-guided system. To address this limitation, an ideal solution would be to integrate the sensor on the innermost layer of the probe right next to the ultrasound transducer instead of the outer sheath. However, this solution requires a major redesign of the hardware which is outside the research scope of our lab.

To mitigate the challenge throughout the research and experiments performed, the probe was used with limited motion. The rest of the work presented in this thesis was designed to accommodate this limitation. Therefore, most experiments involve minimal to no linear probe movement. A small offset that might have been introduced in the time between ICE probe calibration and an experiment’s data collection was corrected manually using the Transforms module in 3D Slicer.

The manufacturers of the Foresight™ ICE probe - Conavi Medical Inc. and an associated research group at SunnyBrook Hospital (Toronto, Canada) were also working towards the integration of a tracking sensor in the ICE probe, employing extensive methods to solve for the relative motion between the sensor and the transducer. However, they came to the same conclusion as ours that the task of sensorizing the Foresight™ ICE probe is not as trivial as the other ultrasound probes. It is unfortunate that, due to the hardware complexity and intricate nature of the ICE probe, Conavi Medical Inc. has since terminated the manufacture of this ICE probe and instead focus on a radial high-frequency IVUS imaging. While chapters 4 and 5 discuss the applications of Foresight™ ICE probe, but they are equally applicable to any other radial ultrasound probe. Chapter 6 discusses some of the ICE probes and advanced imaging techniques that have since become available in the market.
Chapter 3

Towards Vessel Navigation: Ultrasound-realistic, Dual-layered Vessel Phantom

Guidance systems proposed in this thesis are designed for micro invasive cardiac interventions. This chapter presents the methods to design an ultrasound-realistic vascular phantom which can serve as a first-step towards validation of a newly designed IGS aimed for cardiac interventions with a transfemoral approach.

This chapter is adapted from the following manuscript:


3.1 Introduction

Ultrasound phantoms are widely used in clinical training, pre-procedural planning, academic research methodologies, and industrial device design and testing. Vascular phantoms are extensively employed in many applications including training on ultrasound-based vascular access [148, 104], study of vascular blood flow dynamics using ultrasound Doppler [50], testing of intravascular catheters [43], as well as the design of image-guided systems for intravascular and cardiac interventional procedures [31, 198].

A wide range of vascular phantoms is described in the literature, from simple, tubular, wall-only vessels [120, 76] to complex, wall-less vascular phantoms surrounded by realistic tissue-mimicking material (TMM). Walled phantoms are easy to fabricate, often using solid
rubber-like materials, such as silicone, latex, and C-flex tubing, as vessel-mimicking materials (VMM). Walled phantoms usually have a rough lumen surface, high ultrasound attenuation coefficient and no TMM in the surroundings, causing them to have an unrealistic appearance in ultrasound and poor haptic response when interacting with an intra-lumenal device. On the other hand, wall-less phantoms are often fabricated by creating an absence of vessel wall and lumen in a block of TMM. A hollow vessel is created by placing a rigid lumen core and pulling it out once the TMM is set [148], a method that is suitable for simple to moderately complex vessel designs. Highly realistic and intricate vessel geometries can be achieved by constructing the vascular tree from a low-melting point material, surrounding it by a (higher melting point) TMM, and subsequently melting and removing the inner lumen material [130] along with elaborate, resource intensive and expensive procedures. Moreover, wall-less phantoms do not incorporate a layer to mimic the vessel wall, and hence lack realism when imaged by intravascular (IVUS) and intracardiac (ICE) ultrasound.

Gel-based materials are a popular choice of TMMs for wall-less phantoms. Agar [148, 163, 169] and gelatin [173] based gels have been employed due to their ready availability, but they lack the mechanical durability to maintain the integrity of complex structures. Polyvinyl alcohol cryogel (PVA-c) is another potential option, offering high strength, flexibility, and endurance of external pressures [191]. PVA-cryogel is a water-insoluble hydrogel prepared by mixing water-soluble PVA powder in distilled water over a controlled temperature. Mechanical and acoustic properties of PVA-c can be customized by controlling the number of freeze-thaw cycles (FTC) used in its preparation. A drawback to using PVA-c as a TMM is its sensitivity to heat. Melting the inner lumen material to create a hollow vessel becomes difficult as the heat may also affect the acoustic properties of PVA-c. A pull-out method is therefore preferred to create a hollow lumen when using PVA-c as a TMM.

The ideal characteristics of a phantom are dictated by its intended application. Low-cost phantoms are available in the literature for certain applications, including clinical training of ultrasound needle guidance and procedural training [148, 141, 83]. However, only a few phantom designs are also acceptable for intravascular or cardiac interventional research applications where both vessel and tissue-mimicking layers are required. An ideal phantom for such applications must also be hollow and haptically realistic to allow smooth flow of blood-mimicking fluid (BMF) and proper maneuvering of tools, catheters, and ultrasound probes. Ultrasound imaging of such a phantom should show the vessel wall distinctly, with liquid flowing inside and the TMM in the surroundings.

Human and animal vascular and surrounding anatomy is highly complex, and it is often difficult to combine all aspects in one phantom. Ultrasound images of any vessel, tissue or organ can vary significantly among different subjects and even within the same subject. Vessel
wall structures, consisting of tunica intima, media, and externa, have varying proportions of elastic tissue, smooth muscle fibers, and collagen fibrous tissue. The same vessel may have a different appearance under ultrasound as it passes through different regions. For example, the inferior vena cava (IVC) is a long vessel that travels through different anatomical regions of the body. Some parts of this vein located in the abdominal region may appear weakly reflective due to a small proportion of fibrous tissue in tunica externa, while other parts of the vessel that pass through the thoracic region may appear bright under ultrasound. Fig. 3.1 shows some of the variations in the ultrasound imaging of the IVC. Vascular phantom design, like any organ phantom, needs to be specific to the targeted region in the body. In this study, we focused on targeted image Fig. 3.1(b) or (d), likely to be acquired when a vessel is ensheathed by a fibrous membrane or surrounded by fatty tissues. Hence, all the design parameters are tailored towards such ultrasound appearance.

Figure 3.1: Conavi Foresight™ ultrasound imaging (ICE) of swine inferior vena cava (IVC) showing variations in the appearance of a vessel. Image (b) and (d) represent the targeted ultrasound imaging aimed in this study. The central dark/bright spot represent the inherent imaging probe artefact.
This study investigated the use of PVA-c containing a scattering agent to create a two-layered walled vascular phantom combining both VMM and TMM. We experimented with multiple FTCs as well as varying concentrations of scattering agent to obtain the desired ultrasound appearance (Fig. 3.1d) of the vascular phantom. The overall goal is to develop a simple, low-cost vascular phantom with both a vessel-mimicking layer and surrounding tissue-mimicking material, to obtain anatomically realistic ultrasound imaging, especially under IVUS and ICE.

### 3.2 Materials and Methods

The fabrication process for the vascular phantom involved two main stages: the construction of both vessel-mimicking and tissue-mimicking layers. Fig. 3.2 shows the various steps involved in these stages. A positive model of the required vessel wall was used to generate custom mould and container designs, which were 3D printed in polylactic acid (PLA) thermoplastic. PVA-c was used as a base medium for both vessel and TMMs. Commonly available talcum powder was used as a scattering agent to introduce speckle and backscatter in the vessel and background layer [192]. A solid vessel-mimicking layer was prepared prior to adding the tissue-mimicking material.

![Figure 3.2: Overall workflow for fabrication of two layered vascular phantom. Stage 1 involved preparation of vessel-mimicking material (VMM) by mixing polyvinyl alcohol cryogel (PVA-c) with talcum powder as scattering agent and subjecting to freeze-thaw cycles (FTCs). Stage 2 involved preparing and combining tissue-mimicking material (TMM) with solidified VMM. *Fig. 3.5, †Fig. 3.6, ‡Fig. 3.7](image)

Three successive vascular phantoms, A, B, and C, were built sequentially in an iterative
fashion, with various parameters for each being revised based on the outcomes of the imaging tests on the previous phantom. The aim was to develop a phantom with ultrasound images resembling those obtained from the target anatomy (Fig. 3.1d). At each iteration, the concentrations of the scattering agent were chosen based on the ultrasound images of the previous phantom. Initial estimates for these concentrations were made based on the expertise of the authors as well as an ongoing study in the lab regarding multiple scattering agents in PVA-c. Furthermore, the image contrast between the VMM and TMM layers was investigated by exploiting the change in acoustic impedance that followed the increased number of FTCs. In general, the acoustic impedance of PVA-c increases with the number of FTCs experienced during manufacture. Two PVA-c layers subject to different numbers of FTCs showed distinct appearances in ultrasound. Table 3.1 summarizes the differences in the three phantoms. Phantom A was made with PVA-c only, with a total of 4 and 2 FTCs for the VMM (vessel wall) and TMM, respectively. Phantom B introduced scattering agent in the TMM and employed a total of 6 and 2 FTCs for the VMM (vessel wall) and TMM. The final version (Phantom C) involved generating ultrasound image contrast based on different concentrations (2.5% and 0.05% w/w) of scattering agent in both the vessel and tissue-mimicking layers. Note that, after pouring the PVA-c material for the TMM and subjecting it to a number of FTCs, the VMM is also subject to these additional FTCs.

<table>
<thead>
<tr>
<th>Phantom</th>
<th>Scattering agent concentration</th>
<th>Difference in FTCs between VMM and TMM</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0%</td>
<td>2</td>
</tr>
<tr>
<td>B</td>
<td>0%</td>
<td>4</td>
</tr>
<tr>
<td>C</td>
<td>2.5%</td>
<td>1</td>
</tr>
</tbody>
</table>

**3.2.1 Mould and container design**

Transfemoral access is routinely employed to access targets during cardiac interventions. Surgical catheters, and in some cases an ultrasound probe (e.g. ICE) are inserted into the femoral vein, passed through the inferior vena cava (IVC) finally entering the right atrium of the heart. For the purpose of this study, we aim to replicate the geometry of the post-renal portion of the IVC as well as the renal bifurcations. Veins are thin-walled compared to arteries and can be difficult to mould. Typical measurements for wall thickness of vena cava, veins, aorta, and medium arteries are 1.5 mm, 0.5 mm, 2 mm and 1 mm, respectively [44]. However, these
anatomical dimensions of vessels are highly variable between subjects. The vena cava has the largest diameter lumen of any human vein, with an average diameter of 30 mm [44]. The IVC runs from the lower abdominal region to the right atrium in the heart, collecting de-oxygenated blood from multiple organs through tributaries. Along the length of IVC, the lumen diameter, wall thickness and its appearance in ultrasound can vary significantly depending on the surrounding organs and tissue, with the mean IVC diameter in the infra-renal region being around 20.3 mm [67]. Renal veins have an average diameter of 12±2 mm [177]. Renal veins are not usually orthogonal to the IVC, but instead have a wide range of infra-renal angles, with the IVC i.e. 15°–85° on the right side and 50°–90° on the left side, with an average of 45° and 78° with right and left infra-renal angle [81].

Vessel structures were modelled in SpaceClaim CAD software (2019 R3, ANSYS, Concord, USA) (Fig. 3.3). A straight vessel, with an inner diameter of 20 mm, representing the IVC, extended 100 mm below the bifurcations. The left renal vein was 33 mm long with a 12 mm inner diameter and placed at an angle of 45° with the IVC, while the right renal vein had a length of 37 mm, with an inner diameter of 16 mm and with infra-renal angle of 78°. The left renal vein sits 20 mm higher than the right. The targeted wall thickness for the phantom was 1.5 mm. However, to compensate for the shrinking of PVA during FTCs and the slightly oversized prints (sub-millimeter inaccuracy) produced by the 3D printer used in the process, the wall thickness in the CAD model was set to be 1.73 mm.

The vessel lumen was elongated to generate support structures for better handling. This inner core design was split into three core elements, with a collinear cylindrical joint, so they could be individually pulled out following the setting of the TMM (Fig. 3.3). A clam-shell mould was then designed by taking the negative of the core and vessel wall structures, followed by horizontally splitting the negative into cope (top half) and drag (bottom half) structures (Fig. 3.4). Screws were used to ensure tight closure of the mould. A sprue was made in the cope to allow insertion of fluid VMM through a syringe. Air vents with 2 mm diameter were also made at the top of the vessel and the end of the bifurcations to allow trapped air bubbles to escape from the mould as the VMM is inserted. A custom-made rectangular container (Fig. 3.4b) was designed for housing the block of tissue-mimicking layer, with separable top and bottom halves, and a space to hold the vessel core elements in the middle of the block.

Mould, core elements, and container were printed in low-cost PLA material using an Ultimaker S3 (Ultimaker, Geldermalsen, The Netherlands). The mould’s cope and drag were printed horizontally with the hollow lumen side facing up in order to achieve a smooth cylindrical surface without any support material attachments. Core insert elements were printed vertically for the same reason. 3D printed parts are shown in Fig. 3.5. After the printing, screw holes were tapped and a Luer lock was attached to the sprue to create an attachment point for
Figure 3.3: CAD model of vessels representing inferior vena cava (IVC) and renal veins. Extended core for support can be seen at the ends.

Figure 3.4: CAD model of (a) mould to be filled with vessel-mimicking material and core elements; (b) container to create a tissue-mimicking block.
3.2. Materials and Methods

the syringe. Core elements and the inner surface of the mould were gently smoothed with fine sandpaper to achieve a smooth, curved surface and to remove any irregularities.

![Core elements, Mould: cope and drag, Container: top and bottom](image)

Figure 3.5: Solid parts of phantom, 3D printed in poly-lactic acid (PLA) plastic material. From left to right: disassembled core elements with collinear cylindrical joints; cope and drag for the mould; bottom and top half of the custom container

3.2.2 PVA-c preparation

PVA-c was prepared using 10 % w/w PVA resin [106]. PVA crystals (Sigma Aldrich, molecular weight 146 000–186 000, 99 % + hydrolyzed) were mixed with distilled water. For one of the batches, the desired quantity of talc was thoroughly mixed with the water in the conical flask instead of mixing it with PVA prior to freezing, in order to create a more homogeneous mixture. The solution was stirred with an electronic stirrer (Fisher Scientific, Pittsburgh, USA) in a heating mantle (Glas Col, Terre Haute, USA). PVA-c was then set to cool at room temperature before use. 5 g of Diazolidinyl urea (>95 %) was added to increase the longevity and shelf life of the PVA-c but this step is not crucial to the construction of phantom and can be omitted.

3.2.3 Vessel-mimicking layer

The VMM was prepared by adding the desired percentage (see Table 3.1) of talcum powder, to previously prepared 10 % w/w PVA-c. A syringe was used to insert the VMM into the mould. To solidify the PVA-c vessel wall, the VMM-filled mould was subjected to initial FTCs in an environment chamber (TestEquity model 1007, Moorpark, USA). Each cycle involved instant freezing at −20 °C for 6 hours and slowly thawing to 15 °C for 10 hours under controlled conditions using an environment chamber. The mould was disassembled to obtain the solid vessel wall but the core elements were kept intact at this stage. Fig. 3.6a shows solidified vessel-mimicking layer after two FTCs.
Figure 3.6: (a) Vessel-mimicking material (VMM) after FTCs, still present inside mould. (b) Solidified VMM with core placed inside the custom container, before filling with tissue-mimicking material. The insert in the oblique bifurcation was printed with white PLA, the other inserts with black PLA.

3.2.4 Tissue-mimicking layer

The solidified vessel wall including core elements was correctly positioned and sandwiched between the walls of the 3D printed plastic container (Fig. 3.6b). The assembly was held together with metal screws. PVA-c was mixed with the desired ratio of talcum powder (see Table 3.1) to introduce acoustic backscattering and form the TMM. The TMM was poured into the container, covered with plastic wrap to avoid water sublimation due to direct air exposure, and subjected to two FTCs. Each cycle involved freezing at $-20\,^\circ\text{C}$ for 10 hours and slowly thawing to $15\,^\circ\text{C}$ for 12 hours. During the first cycle, the TMM fully adhered to the vessel-mimicking layer as it was solidifying. This attachment was expected as the direct result of cross-linking of PVA polymer chains [55, 203]. Once the phantom construction was complete (see Fig. 3.7), the core elements were readily extracted and no release agent was required.

3.2.5 Ultrasound imaging

The phantom was fully submerged in a water bath and scanned with the Conavi Foresight™ ICE probe. The probe was inserted inside the vessel lumen and moved along its length. Images were acquired at 12 MHz, and a $55^\circ - 70^\circ$ tilt angle, and an imaging depth of 5 cm and 8 cm radially. The phantom was padded with a silicone boundary as sound dampening material to remove any ringing artefact that could arise from the PVA-c to water boundary. Alternatively, time gain compensation (TGC) could be applied at the distal end of the radial image to suppress the signal and remove the appearance of phantom edges in the image. This adjustment was not
3.3. Results

(a) (b)

Figure 3.7: (a) Tissue-mimicking layer after freeze-thaw cycles, still present inside container. (b) Vascular phantom, with tissue and vessel-mimicking layers, accompanied by an optional silicone padding layer

essential for imaging the phantom, but it served to render the images in a more realistic manner and enable the observer to focus on the vessel of interest.

The ICE images obtained from the phantom were compared with those obtained from porcine experiments. Imaging experiments on Yorkshire swine, approximately 40 kg in weight, were performed under a protocol approved by Sunnybrook Research Institute’s Animal Care Committee.

3.2.6 Computed tomography (CT) imaging

A CT scan of the PVA-c phantoms was performed to validate the phantom design technique by quantifying their geometrical properties. O-arm (Medtronic, Dublin, Ireland) standard settings for the HD scan for a small head protocol (with 100 kVp, 20 mA and 250 mAs) were used. Reconstruction was performed on a Medtronic mobile station using their proprietary software. The lumen diameters for the three vessels mimicking IVC, left renal vein and right renal vein were measured, as well as the infra-renal angles for the bifurcations.

3.3 Results

The designed vascular phantoms exhibited mechanical strength and flexibility, and were able to endure external pressures and retain their shape after minor bending. In terms of haptics, the phantoms were slippery to the touch when placed in water, while the ultrasound probe and catheters were easily maneuvered inside the lumen. Conavi Foresight™ ICE probes were used to image these three phantoms. Imaging of phantom A (without scattering agent), depicted weak contrast between the vessel and tissue-mimicking layers. The vessel walls did not show
up brightly and there was minimal backscatter in the tissue-mimicking layer. Vessel bifurcations and the water-filled lumen could be seen clearly in the image. Fig. 3.8a shows the imaging of phantom A at a tilt angle of 56°, and radial depth of 5 cm, along with TGC to suppress the phantom edges. Note that the circular patterns in the middle of the image represent an artefact inherent to the ultrasound probe and should be ignored.

Phantom B (with a difference of four FTCs between the VMM and TMM, and the incorporation of scattering agent in TMM), was initially expected to have a sharper, brighter looking vessel wall because of the increased number of freeze-thaw cycles, but imaging showed otherwise. Fig. 3.8b shows a weak contrast between the two layers of the phantom, and the tissue-mimicking layer appears somewhat bright and heavily speckled in the ultrasound and appears unrealistic.

The final phantom (C, with 2.5% and 0.05% scattering agent in VMM and TMM respectively) produced bright reflections from the vessel wall and adequate speckle in the tissue-mimicking layer (Fig. 3.8c). Bifurcations could be seen properly as well. Figs. 3.9a and b show the ultrasound imaging of phantom at the depth of 80 mm without any TGC. Comparison with ICE images of the porcine IVC revealed Phantom C to be the most promising design. Fig. 3.9c and d compare our vascular phantom representing IVC and a swine IVC image, each acquired using different Conavi Foresight™ ICE probes. Relative contrast observed in the phantom images is evaluated against the targeted in-vivo animal IVC image. Ultrasound image of Phantom C (Fig. 3.9c) showed a tissue to vessel layer pixel intensity ratio of 1 : 1.9, as compared to the ratio of 1 : 1.7 observed in the swine IVC image (Fig. 3.9d).

A CT scan of one of the phantoms was used to measure the lumen diameter (see Fig. 3.10). An average of ten measurements across each vessel revealed a mean error of 1 mm, 0.9 mm and 0.7 mm for the IVC, left and right renal vein, respectively. The left infra-renal angle was measured at 43.8° compared to the CAD designed value of 45° and the right infra-renal angle was 77.5° as compared to the CAD designed 78°.

3.4 Discussion

In this study, the use of PVA-c was investigated to construct two-layered, walled, vascular phantoms. Talcum powder was used as a scattering agent and mixed with PVA-c to form vessels and TMMs. We designed a phantom with the geometry of IVC and renal bifurcations, imaged it using a Conavi Foresight™ intracardiac ultrasound probe and compared it with images obtained from a porcine IVC. We observe the contrast in ultrasound due to 1) varying acoustic properties of PVA-c related to the number of FTCs applied during the solidification process and 2) the brightness achieved by the scattering agent.
3.4. Discussion

Figure 3.8: Conavi Foresight™ intracardiac ultrasound (ICE) imaging of (a) phantom A, (b) phantom B and (c) phantom C, at a radial depth of 5 cm and with time gain compensation (TGC) to suppress the edges of phantom. Phantom A and B show weak reflections from the vessel-mimicking layer, while B depicts increased backscatter from tissue-mimicking material. Phantom C shows strong reflections from the vessel-mimicking layer. Concentric circles in the middle represent inherent imaging probe artefact.
Figure 3.9: Conavi Foresight™ ultrasound imaging (ICE) of Phantom C (a)(b) at a radial depth of 8 cm showing main vessels and bifurcations, (c) and with time gain compensation (TGC), showing strong reflections from the vessel-mimicking layer and adequate scattering in the tissue-mimicking material. (d) Swine inferior vena cava (IVC) imaged using Foresight™ ICE at a radial depth of 8 cm.
Figure 3.10: Cross-section of the CT scan of the phantom with average lumen diameter of the main vessel and bifurcations, and infra-renal angle measurements.

In-vivo ultrasound imaging of vasculature is highly variable as shown in Fig. 3.1. The phantom results are a representation of imaging observed in some parts of in-vivo imaging of human vasculature. Based on the ultrasound imaging of the three phantoms, recommended values for the varying parameters to acquire ultrasound images such as Fig. 3.1d are given in Table 3.2. Note that these values are specific for our designed phantom to obtain the target images. The scattering agent concentrations in the VMM and TMM may vary when aiming for other vessels or some other parts of IVC. The concentrations used in this study, along with the images (Fig. 3.8a, b and c) can nevertheless provide a good basis of a starting point to construct other similar vascular structures. This study focuses on a single application, and future work is required to consider an exhaustive range of scattering agent concentrations.

Table 3.2: Recommended values for talcum powder concentration in 10% w/w polyvinyl alcohol cryogel (PVA-c) to form vessel-mimicking material (VMM) and tissue-mimicking material (TMM), and the number of freeze-thaw cycles (FTCs), the VMM should be subjected to before adding TMM.

| Recommendations for targeted vascular phantom (representing part of inferior vena cava) |
|---------------------------------|-----------------|
| Talcum powder concentration     | TMM >2.5%       |
| VMM                             | VMM <0.1%       |
| Number of FTCs for vessel wall only | 2               |

Adding large quantities of talcum powder to prepared PVA-solution can cause minor clumping, and over-mixing introduces more air bubbles into the mixture. It is recommended that the scattering agent be added to distilled water during the PVA-solution preparation to achieve a
uniform, homogeneous mixture. Regardless of the stage at which talcum powder is added, the PVA-talcum mixture should not be allowed to sit for more than a few hours, otherwise the talcum will settle at the bottom making the mixture heterogeneous and will require further stirring. Stirring PVA-solution, especially before adding to an intricate vessel wall mould, can potentially introduce air bubbles into the fluid VMM. Fig. 3.6 shows that some portion of the vessel wall was lost due to the collection of air bubbles at the top. It is suggested that extra room in the vessel design be left at the top for air bubbles to rise and occupy this space. This extended portion of the vessel wall can be snipped after solidification of VMM.

The number of FTCs changes the mechanical and acoustic properties of PVA-c. According to [66], mechanical properties of PVA-c linearly vary with the increase in the number of FTCs. However, most curves of FTC-dependent properties achieve a plateau after four freeze-thaw cycles. As seen from phantom B image (Fig. 3.8b), a large difference in the number of FTCs did not drastically affect the contrast between the two layers. Scattering agents, on the other hand, seems to be more efficient at generating bright reflections and contrast in an ultrasound image. Nonetheless, a minimum of two FTCs are recommended for the inner, vessel-mimicking layer for better structural integrity of the phantom.

One of the limitations of our phantom is the homogeneity of the tissue-mimicking layer. Comparing phantom image (Fig. 3.9c) with the targeted swine IVC image (Fig. 3.9d), we observe several differences. The phantom image is plain, homogeneous in both layers and there is a sharp boundary between the vessel and surrounding tissue, while the animal image has random bright speckles in the surrounding tissue region. The swine IVC image is likely acquired when the vessel is close to a fatty region in the animal body, causing bright speckles in the surrounding tissue as well as brighter reflections from the vessel wall. It must also be kept in mind that the two images are taken using different ultrasound probes (Conavi’s Foresight™ ICE) and different parameters such as gain, frequency, and time-gain compensation. The center of all these images appears significantly different because of an absolute bright or dark circle, surrounded by concentric rings. These artefacts, inherent and unique to each Foresight™ ICE probe, are a result of near field noise in the ultrasound probe.

The technique was validated using a CT scan. CT imaging of the phantom showed that this is a promising method for reproducing moderately complex vessel geometries. Measurements of vessel lumen diameters from the CT, when compared to the targeted dimensions, report an overall error of 0.9 mm. An error of approximately 1° is observed between the targeted and measured infra-renal angles. We believe that these discrepancies are introduced by the non-rigid nature of PVA-c, which results in slight deformation of the phantom when compressed due to its weight. Note that the phantom lumen diameters were always less than the targeted values. This behavior is most likely caused by the fact that PVA-c tends to shrink when exposed
to air, and our phantoms were kept in an open environment for an hour before CT imaging. This attribute brings to lights a limitation for all PVA-c phantoms, that they required to be handled delicately. Particular attention must be paid when using and storing PVA-c, to ensure that it either submerged in water or maintained in a humid air-tight container.

Quantification of acoustic properties of a phantom is highly significant, especially when the phantom is intended to be a direct substitute for a tissue – vessel, organ, etc. There is extensive literature available on the quantitative analysis of PVA-c, and its use in the construction of phantoms for biomedical applications. A summary can be found in [203]. Acoustic properties of PVA-c have been studied as a function of the number of freeze-thaw cycles. Surry et al. [191] concludes that while the speed of sound in PVA-c is comparable to that in human soft tissue (1540 m s\(^{-1}\)), the range of attenuation coefficient (0.075–0.28 dB cm\(^{-1}\) MHz\(^{-1}\)) does not correspond to the rule of thumb of 1 dB cm\(^{-1}\) MHz\(^{-1}\) for tissue. This means that PVA-c is not ideal to directly substitute for human tissue. Despite this issue, PVA-c has nevertheless been employed effectively for this purpose in numerous applications. The differences in attenuation can easily be compensated for by adjusting different parameters on an ultrasound machine such as frequency, gain, and TGC. Hence, while it would be useful, it is perhaps not absolutely necessary to match all acoustic properties of a phantom designed only for imaging. The speed of sound assumed by the ultrasound machines is that of an average soft tissue (1540 m s\(^{-1}\)), while the PVA-c phantoms are primarily composed of water (speed of sound = 1480 m s\(^{-1}\)). The difference in the speed of sounds may appear large, however, the resultant difference in the measured depths is quite small. As an example, let’s assume an ultrasound beam takes time \(t = 20 \mu\) sec to travel back from a surface at a certain speed of sound. The depth of this surface is given as:

\[
depth = \frac{\text{distance}}{2} = \frac{v \cdot t}{2} \tag{3.1}
\]

for \(v_{\text{tissue}} = 1540 \text{m s}^{-1} \rightarrow depth_{\text{tissue}} = 0.0154 \text{m} \tag{3.2}\)

for \(v_{\text{phantom}} = 1480 \text{m s}^{-1} \rightarrow depth_{\text{phantom}} = 0.0148 \text{m} \tag{3.3}\)

error in depth = \(\Delta d = 0.0006 \text{m} = 0.6 \text{mm} \tag{3.4}\)

The vascular phantoms described here were sturdy and easy to handle. The smooth surface of PVA-c makes it ideal for fabricating a vessel phantom compared to silicone or tube-based vessel phantoms, which have a tacky resistive surface. This characteristic allows for simulating intravascular procedures on a phantom with realistic imaging and haptic characteristics. The layered structure of the phantom presents an opportunity to make more complex, multi-layered arterial phantoms [43], using multiple doping agents or in different concentrations.
3.5 Conclusion

Vascular phantoms have been employed in many different medical applications. Their design, development and fabrication strategy strongly depend on the final purpose of the phantom. In this chapter, I presented a low-cost and repeatable methodology to build a hollow, walled vascular phantom, employing a simple method to obtain a replica of blood vessels, bridging the gap between walled and wall-less phantoms. Using only PVA-c and scattering agent, the ultrasound response of some parts of the IVC was satisfactorily replicated, clearly demonstrating the desired characteristics of a bright vessel wall, vessel bifurcations and weakly reflected TMM in the surroundings.
Chapter 4

Towards Vessel Navigation: Deep Learning-based ICE-Guidance System to Generate a Vascular Roadmap

In efforts to minimize the use of fluoroscopy in the interventional suite, we present an ultrasound-based IGS which uses tracked ICE imaging to generate a vascular roadmap, which can then be followed by tracked tools to navigate towards the heart. This chapter presents a user-friendly software platform and a phantom study to demonstrate the proposed clinical workflow.

This chapter is adapted from the following manuscripts:


4.1 Introduction

Advances in medical imaging, combined with miniaturized and flexible procedural tools, have allowed surgical procedures to be performed percutaneously using transcatheter-based approaches. These minimally invasive approaches have increased patient safety, decreased procedure time, and lowered complication rates [98]. Catheter-directed therapies inherently pro-
hibits a direct line-of-sight with the anatomy and the tools. Interventionalists rely heavily on image-guidance to navigate and position their tools to deliver therapy at the target region. Common imaging modalities used for transcatheter-based interventions include X-ray fluoroscopy, computed tomography (CT), magnetic resonance imaging (MRI), and intravascular (IVUS), intracardiac (ICE) or transesophageal (TEE) ultrasound (US).

Fluoroscopy is commonly used for minimally invasive procedures as it provides real-time, high contrast vascular images, by means of X-ray imaging with contrast enhancement. As mentioned in chapter 1, the radiation exposure produced by X-rays can be harmful to the patient, clinical staff, and medical trainees, even when used in conjunction with various shielding techniques.

Due to its high resolution and large field of view, pre-operative CT is a standard of care for vascular mapping and assessment of intravascular pathology [144]. However, CT imaging is typically used for diagnostic and pre-surgical planning, and is limited in its use for real-time procedural navigation. CT is also based on ionizing radiation and carries the same risks previously described for fluoroscopy. Furthermore, the surgery cannot be performed with the patient within the CT bore. In transcatheter procedures, there is an unmet need for safe, reliable, radiation-free and real-time image-guidance during vascular navigation.

In efforts to minimize radiation exposure in Cath labs, near-zero fluoro methods and no-fluoro procedural workflows have also been proposed in the literature [187, 209] to guide the catheters during an ablation procedure and perform transseptal puncture using ICE. Alternative imaging modalities such as MR, and US are also considered. Vascular navigation is fundamental to transcatheter cardiac interventions such as transcatheter aortic valve implantation (TAVI), caval-valve implantation, and mitral and tricuspid valve annuloplasty, repair and replacement surgeries [166]. Accurate representation of the vessel geometry is not only important for navigation towards the target site, but also for delivering the optimal therapy [145, 179]. Procedures such as angioplasty, stent placement, IVC filter placement all rely on vascular imaging to locate the pathological vessel region, select an appropriately sized device, and deploy the balloon or stent correctly.

Catheter-based US technologies such as intravascular US (IVUS) and intracardiac echo (ICE) are already indispensable components of Cath lab, assisting in the assessment of the disease and device placement. The recent introduction of optical US (OpUS) technology also shows the great potential for the use of catheter-based US for cardiovascular interventions [126]. US offers a radiation-free alternative for real-time image guidance. When combined with EM tracking technology, it offers the potential for a large-scale 3D US volume reconstruction, visualization of anatomy, as well as real-time tool tracking. For most transcatheter interventions, there are two interventional phases - navigation of tools towards the
4.1. Introduction

target site and positioning of tools to deliver the treatment. In the case of cardiac interventions, vascular navigation is an imperative prerequisite. Either transfemoral, transradial or transjugular access is required to guide the catheters towards the heart. Inferior vena cava (IVC) navigation, from the groin to the chest, is one of the most common techniques in cardiology and is traditionally guided by fluoroscopy. In this chapter, the targeted clinical application is the IVC navigation performed during transcatheter cardiovascular interventions.

We propose the use of tracked US as an alternative to CT-based vascular mapping and fluoro-guided tool navigation. Instead of using radiation-based imaging to navigate the tools, we propose the following procedural workflow: Prior to the intervention, a tracked, catheter-based US probe (such as ICE, IVUS, or OpUS) scans the desired vasculature and a virtual 3D roadmap is reconstructed (see concept diagram in figure 4.1). This vascular path can then be easily traversed by a tracked tool or guidewire. This workflow eliminates radiation exposure and the use of lead shielding. Such a system can also be used to make measurements of the vessel anatomy and intraluminal buildup. Ultrasound catheters including ICE and IVUS, as well as EM tracking technology are already an indispensable part of a Cath Lab and are used in electrophysiology procedures. The proposed ultrasound-based workflow has several advantages over the conventional fluoroscopic techniques. Apart from the lack of radiation and shielding, an US-based navigation system offers full 3D visualization of anatomy, and provides more information to the clinician. Furthermore, the use of EM tracking technology allows for tracked tools and catheters which can result in an engaged and informative experience for the clinicians. If images are presented to the clinicians in an appropriately intuitive manner, these features greatly reduce the cognitive load faced by the interventionalists and could potentially result in enhanced procedural outcome as well.

In this study, we utilized the Foresight™ ICE system as described in chapter 2. As a result, the ultrasound image produced is a 2D conical surface image lying in 3D space. One of the biggest advantages of using this probe for navigation is the ‘Forward-viewing’ feature which allows the clinicians to watch where they are going as they traverse the vessels, thus improving their experience and adding a layer of procedural safety. The use of ICE probe is not limited to navigation. For transcatheter cardiac interventions, the ultrasound can further facilitate the delivery of therapy or treatment. This study is geared towards the navigation of the inferior vena cava (IVC), it also has the potential to be applied to the navigation of other vessels as well. The IVC has many tributaries, but they need not to be navigated for cardiac procedures. The geometry of IVC is also comparatively simpler than its tributaries such as hepatic veins. Since the IVC passes through the entire length of the abdomen, its surrounding tissues and organs vary along the length. Thus, the appearance of the IVC in the ultrasound varies as well. Since all these physical and echogenic attributes of IVC are difficult to capture in one
phantom, for this first phantom study we demonstrate the concept on an ultrasound-realistic phantom representing the infrarenal portion of the IVC. The goal is to reconstruct a vascular roadmap without any radiation, safely navigate the guidewire through the vessel, and visualize the guiding catheters as they ascend towards the heart.

This chapter presents a pilot phantom study as a proof of concept to demonstrate the idea and feasibility of an US-based vascular navigation system for transcatheter interventions. A vascular phantom was scanned and reconstructed using a forward-looking radial ICE probe and EM tracking technology. Since vessel lumen segmentation is an important step during the process of vessel reconstruction as it dictates the overall accuracy, we employ deep-learning based methods to perform lumen segmentation from ICE imaging. The method details, open-source implementation, and phantom images are available online for reproducibility (https://github.com/hareem-nisar). The US-generated vessel model is validated against a CT-scan of the vessel phantom.

4.2 Materials and Methods

4.2.1 Data Acquisition

As described in chapter 3, a polyvinyl alcohol cryogel (PVA-C) vascular phantom was manufactured to imitate the infra-renal portion of the IVC [150]. The phantom generated realistic US imaging when scanned by an intravascular (IVUS) or intracardiac (ICE) US, thus displaying a vessel-mimicking layer, blood-mimicking fluid in the lumen, and a surrounding tissue-
4.2. Materials and Methods

In this study, a 10 Fr, forward-looking, Foresight™ ICE catheter was used to image the phantom. Its 3D conical images are projected on a conventional monitor screen as viewed from the apex of the cone and displayed as a circular image. A digital frame-grabber (DVI2USB 3.0, Epiphan Video, Ottawa, ON, Canada) was used to capture the projected ICE images, and the cone-angle information from the console. For US tracking, the ICE probe was rigidly instrumented with a 6 DoF magnetic pose sensor (Aurora, NDI, Waterloo, ON, Canada) and spatially calibrated using a point-to-line Procrustean approach [52, 149].

The vessel phantom was placed in a large water-bath at room-temperature (Fig. 4.2). The main vessel of the phantom was scanned using the tracked 12 MHz ICE probe at an imaging depth of 80 mm and imaging angle of 67°. Due to some hardware constraints in our configuration, we were only able to scan the central vessel of the phantom and not the branches (details in Discussion section). US images were acquired in real-time using screen-capture. The imaging and tracking data were then processed to reconstruct the surface representation of the vessel from the phantom. The data acquisition, vascular roadmap generation, and the user interface for navigation were all implemented as an open-source application using 3D Slicer [79]. The steps involved in the automatic generation of the 3D vascular roadmap include pre-processing to remove image artifacts, lumen segmentation from 2D images and reconstruction of the vessel based on the segmentations and tracking information.

Figure 4.2: Data acquisition setup - Ultrasound probe scans the vessel phantom present within the tracking space.
4.2.2 Pre-processing

The acquired screen-captures were cropped to remove any information outside of the US image. The bright reflections in the middle of the cropped US image represent an artifact inherent to the ICE probe (Fig. 4.3a). This artifact was minimized by using optimal display settings (third level 'wand' function) on the console, and later masking the central bright pixels in the image in our software. The time-gain compensation settings on the console were used to suppress the reflections from the phantom boundary and the container walls. A noise-removing filter (the “curve flow” filter) was applied to images to eliminate the interference from the EM tracker (Fig. 4.3b) while preserving the contours of the vessel boundary. This was a necessary step prior to performing image processing for lumen segmentation.

Figure 4.3: (a) Image data acquired using a frame-grabber as a 2D projection of the conical ultrasound. (b) Lumen segmentation (boundary) achieved using the initial seed (solid). (c) Conical reconstruction of the ultrasound image and the lumen segmentation.

4.2.3 Lumen Segmentation

Distinct from imaging using a hand-held percutaneous US transducer, the shape of the vessel wall can vary significantly for catheter-based US. Since the US catheters travel through the vasculature adhering close to the vessel wall, the wall does not always appear as a closed circle in the case of radial IVUS and ICE imaging. The first few millimeters of ICE imaging are corrupted by a ring artifact inherent to the radial ICE probe (Fig. 4.3a). As such, when the ICE catheter is clinging to the vessel wall, the reflection is interrupted close to the centre of the image (Fig. 4.3a) and the vessel boundary appears C-shaped. Therefore, in this study, a deep learning-based approach was used to segment the vessel lumen from the ICE images, minimizing the error/leakages caused by a discontinuous vessel boundary. We employ a pre-trained U-net model to perform the lumen segmentation from ICE images of the vessel phantom. For
4.2. Materials and Methods

clinical translation, the model was trained on in-vivo animal imaging data. The methods for training the model are given below.

Training Data Collection

The Foresight™ ICE probe was used for ultrasound data acquisition, with the ICE images being acquired during experiments performed on Yorkshire swine, approximately 40 kg in weight, under a protocol approved by Sunnybrook Research Institute’s Animal Care Committee and provided to our research group by Conavi Medical Inc. The dataset comprised ICE images of the inferior vena cava (IVC) from two different animal subjects. The complete dataset included 88 2D images. 70 images were kept for training the network, 9 for validation, and 9 for final testing. Ground truth labels were generated by manually segmenting the IVC from the ICE images. The manual segmentations were corrected and verified by an experienced interventional radiologist at the London Health Sciences Centre (London, Canada).

Deep learning based segmentation

Our AI-based segmentation pipeline consists of many different steps as can be seen in figure 4.4. Our segmentation algorithm was entirely implemented using MONAI [10] - an open-source platform for implementing deep learning based solutions in the medical imaging and healthcare domain.

Our vessel lumen segmentation pipeline begins with a series of pre-processing steps to prepare the imaging dataset for the U-net architecture. The screen-captured ultrasound images are loaded, and a channel is added to represent the images in the channel-first format. Next, the image intensities are scaled to lie between 0 and 1. The 2D grayscale images are then cropped to acquire the central $300 \times 300$ pixels and resized to $256 \times 256$ images. Finally, random cropping is performed during network training to obtain samples of spatial size $96 \times 96$. This random sampling is computed at every epoch followed by data augmentation.

U-net architecture has been used in literature for medical image segmentation tasks, especially when the training dataset is small. In such a case, data augmentation can help generate variants of the training image and improve the output model. In our study, we performed data augmentation by randomly rotating the image by 90 degrees with a 0.5 probability. Since the vessel geometry is deformable, we also perform 2D elastic deformation using the bilinear interpolation method, control points spaced out by 10 pixels, a rotational range of 0.15 radians, and a scaling range of 0.05.

Our network uses a Residual UNet architecture [105], with 5 layers of 16, 32, 64, 128, and 256 channels respectively. Each of these layers is created using a residual unit with 2
Figure 4.4: Overall workflow for methods - Intracardiac ultrasound (ICE) imaging dataset is pre-processed and used to train a U-net model via the MONAI framework. Data augmentation is applied during network training. The segmentation labels generated by the U-net are processed to produce the final segmentation output.
convolutions and a residual connection. Convolutions are performed with stride 2 at every residual unit for up-sampling and down-sampling. The model was trained using batch sizes of 8, with batches being composed of 4 samples each taken from 2 different volumes per batch, using the Adam optimizer with learning rate 0.001 and a DICE score loss function \[108\]. The post-processing steps include keeping the largest connected island of the segmented regions, followed by hole filling based on the 8-pixel connectivity \[13\].

During training, the pipeline accuracy was estimated every 5 epochs by first segmenting the validation data images via the trained U-net model, followed by the post-processing steps. The resultant segmentations were compared to the ground truth labels. The segmentation accuracy was quantified using the DICE coefficient as a spatial overlap metric. The model with the highest accuracy is chosen as the final output model and saved for further testing.

**Segmentation evaluation**

We evaluate the accuracy of our segmentation algorithm, inclusive of a pre-trained U-net model, using our third ‘test’ dataset. The segmentation accuracy is quantified in terms of a DICE score.

### 4.2.4 Vessel Reconstruction

The Foresight\textsuperscript{TM} ICE probe generates forward-looking conical surface images. The images acquired by this device, and subsequently the lumen segmentation, were a version of the true US data projected onto a 2D disk. 2D lumen segmentations were subjected to 3D conversion to reconstruct true, conical segmentations (Fig. \[4.3c\]) using the radius and imaging angle information, available through the console. This reconstruction is governed by the equation:

\[
\begin{bmatrix}
    x_{3D} \\
    y_{3D} \\
    z_{3D}
\end{bmatrix} =
\begin{bmatrix}
    1 & 0 & -o_x \\
    0 & 1 & -o_y \\
    0 & 0 & \|(x_{2D}, y_{2D})\| \cdot \tan(90 - \phi)
\end{bmatrix}
\begin{bmatrix}
    x_{2D} \\
    y_{2D} \\
    1
\end{bmatrix}
\]  

(4.1)

where \((o_x, o_y)\) represents the center of the planar image or the apex of the conical image, and \(\phi\) represents the imaging angle of the cone-shaped image. Each segmentation was positioned and scaled to its correct shape and location in 3D space by applying US probe calibration and tracking information, producing a skeleton of the vessel (Fig. \[4.5h\]). The vessel skeleton was then processed to form a closed 3D surface representation using binary morphological closing, with an annulus kernel of size [60, 60] to fill the gaps between consecutive segments. For final smoothing of the reconstructed vessel, a Gaussian blur with a standard deviation of 3 was applied. The result represents the 3D model of the vessel scanned from our phantom.
Chapter 4. IGS for Vessel Navigation

(Fig. 4.5b), represented within the EM tracker’s coordinate system.

4.2.5 Validation

As described previously, vascular navigation is currently achieved using fluoroscopy or CT mapping. The vessel phantom was imaged using US, and the vessel was reconstructed and compared with X-ray and CT. Geometric accuracy of the US reconstructed vessel model was validated against the vessel segmented from the CT scan of the same phantom. The absolute surface-to-surface distance between the two models were computed after a rigid registration \[36\]. For vascular navigation, one of the clinically relevant goals is to know the overall alignment of the vessels in space. To evaluate the spatial alignment, we used DICE metrics which compares the spatial overlap between the reconstructed and CT vessel after CT-US registration was performed. False positive spatial region in the reconstructed US vessel is also an important metric and must be minimal to avoid the misrepresentation of the vessel. For many vascular procedures, the clinical objective is to avoid puncturing the vessels. In such cases, the boundary accuracy becomes important as well as the false positive regions. To evaluate the contours of the reconstructed vessel, we calculated the Hausdorff distance (HD) metrics \[193\]. Volumetric analysis was not performed as volume-based metrics are invariant to segmentation shape and boundary and thus can be misleading. As a visual validation, we demonstrate what US-based navigation may look like.

4.3 Results

4.3.1 Vessel Lumen Segmentation

The evaluation of our segmentation algorithm using the test dataset produced an average DICE score of 0.92. The DICE score for the individual nine test images can be seen in Table 4.1.

4.3.2 Vessel Reconstruction

The absolute distance between the US reconstructed vessel and the registered CT segmented vessel was computed and presented as a heatmap on the vessel surface in Fig. 4.5c. The average distance between the surface of the two models was 0.97±0.89 mm.

The spatial overlap between the registered US and CT models was evaluated using the Dice coefficient, sensitivity and specificity measures where
4.3. Results

<table>
<thead>
<tr>
<th>Test image #</th>
<th>DICE coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.97</td>
</tr>
<tr>
<td>2</td>
<td>0.96</td>
</tr>
<tr>
<td>3</td>
<td>0.88</td>
</tr>
<tr>
<td>4</td>
<td>0.9</td>
</tr>
<tr>
<td>5</td>
<td>0.91</td>
</tr>
<tr>
<td>6</td>
<td>0.92</td>
</tr>
<tr>
<td>7</td>
<td>0.92</td>
</tr>
<tr>
<td>8</td>
<td>0.92</td>
</tr>
<tr>
<td>9</td>
<td>0.92</td>
</tr>
<tr>
<td>Mean</td>
<td>0.92</td>
</tr>
</tbody>
</table>

Table 4.1: Quantitative evaluation of segmentation pipeline using the DICE coefficient of output labels corresponding to the testing dataset.

Figure 4.5: Image a) depicts the skeleton of the vessel comprised of spatially calibrated segmentations, Image b) depicts the ultrasound (US) reconstruction registered to the segmented CT scan of the phantom, and Image c) provides a visualization of the surface-to-surface distance analysis between the US and CT models.
The spatial distance between the two model boundaries was evaluated using the Hausdorff distance (HD). The geometric accuracy results are reported in Table 4.2. Comparison showed that the US model had 12.8% false negative and 0.69% false positive spatial overlap.

\[
\text{Dice} = \frac{\text{True positive overlap between CT and US vessels}}{\text{(num voxels CT vessel) } \times \text{ (num voxels US vessel)}}
\]  

(4.2)

<table>
<thead>
<tr>
<th>Spatial Overlap</th>
<th>Value</th>
<th>Hausdorff Distance (mm)</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DICE Coefficient</td>
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<td>Maximum</td>
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<tr>
<td>Sensitivity</td>
<td>0.75</td>
<td>Average</td>
<td>0.94</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.98</td>
<td>95%</td>
<td>2.58</td>
</tr>
</tbody>
</table>

Table 4.2: Summary of the metrics use to quantify the spatial overlap and boundary accuracy of the ultrasound reconstructed vessel compared to the vessel segmented from the CT scan of the phantom.

4.4 Discussion

In this study, we present a vascular reconstruction-based navigation system, which provides a safe and radiation-free method for guiding tools during transcatheter procedures. An EM-tracked ICE US probe was used to reconstruct the vascular path in a phantom, such that it can be visualized in a common coordinate system with a tracked guidewire for vessel navigation. The results indicate clinically acceptable results with an average error in terms of HD as 0.94 mm and a 2.58 mm confidence interval. During navigation, it is important to identify the vessel boundary and the regions outside the vessel lumen so as to not puncture or damage the vessel wall. Our results indicate that only 0.69% of the segmented region lies outside the ground truth provided by the CT scan of the phantom. The accuracy of the navigation system can be further enhanced by improving the tracking accuracy as discussed below.

The resulting error is a combination of many different errors in the system, such as EM tracking inaccuracies, propagation of calibration errors, US probe hardware constraints, registration errors, and relative motion of the phantom if any. One of the major limitations of our study is defined by the sensorizing the US probe and its calibration accuracy. This inaccuracy can be minimized by applying a manual offset correction for the imaging angle. The ICE probe used in this study has a small diameter of 3.3 mm, which required rigidly fixing the sensor on the outer sheath of the probe, farther away from the origin of the image. The rigid and outer positioning of sensor led to some hardware constraints resulting in our inability to turn and
guide the probe into the branches of the vessel. This limitation is strictly a characteristic of our experimental setup in this preliminary study using a Foresight™ ICE probe. The proposed idea can be extended to other radial ultrasound catheters as well. Ideally the tracking sensor should be integrated within the US catheter and pre-calibrated by the manufacturers to eliminate any limitation of maneuvering the US. For a clinical system, the EM sensor must be integrated inside the US catheter to achieve accuracy in tracking, freedom in motion and patient safety from an active element.

It should be noted that for vessel navigation based on solely on the center-line of the vessel may provide insufficient guidance for transcatheter interventions. Catheters - diagnostic ultrasound or therapeutic tools traverse the vessels by clinging on to the vessel boundary, therefore it is essential to acquire the true 3D representation of the vessel wall, in order to minimize iatrogenic complications and vessel wall punctures.

The vessel segmentation algorithm presented here is limited in its application, mainly due to the available training and evaluation datasets which represent very ideal patients with no intraluminal buildup like calcification or previously implanted devices like stents or pacemaker leads. We tested our algorithm on two pseudo-images (pixel intensities of the test images manually altered) with artifacts due to a stent and the presence of a wire within the vessel (Figure 4.6). Our algorithm is able to handle artifacts present near the vessel boundary and correctly segment the vessel lumen. However, the algorithm is not trained to ignore any intraluminal artifacts and fails to segment properly in the case of a wire. Future work can involve improving the accuracy of the existing segmentation algorithm by including a dataset with more varying vessel imaging. Another aspect will be to evaluate the performance of our segmentation pipeline in other vessels like the iliac and femoral vein, the aortic arch, and the superior vena cava.

Another limitation is the size of the US catheter. The US probe used in this study is a 10 Fr device which is large and less suitable for the arterial system, although it is usually not problematic for venous interventions. This is a limitation of the current technology (Foresight™ ICE probe by Conavi Medical Inc.) and ideally this device will be miniaturized by the manufacturers in the near future. The workflow presented in this chapter can potentially be adapted for intravascular ultrasound (IVUS) imaging where the catheter is much smaller. For example, the Novasight Hybrid (by Conavi Medical Inc.) is a combined IVUS-OCT imaging catheter with a size of 3.3 French [154].
Figure 4.6: Performance of our trained U-net model in the presence of an artifact due to a stent (top) and a lead (bottom) in the vessel.

4.5 Conclusion

Transcatheter interventions provide a low-impact means of delivering therapy using miniaturized equipment and medical imaging technologies. Vascular navigation is a ubiquitous process as it is a prerequisite to reach the target organ or target site in another vessel. The current standard of care employs fluoroscopic techniques or the use of CT vascular mapping, both of which come at a cost of radiation exposure and wearing heavy, shielding aprons. Through this study, we aim to initiate a discussion on the merits of moving towards the use of ultrasound-based instead of radiation-based techniques for transcatheter and endovascular interventions. We present a proof of concept study to use catheter-based US technology, equipped with tracking sensors, to create a vascular roadmap. Results indicate that the geometric accuracy is comparable to that observed in CT mapping.
Chapter 5

Towards Tool Positioning: Localization of Regurgitation Site in Tricuspid Valves using ICE

Device positioning is a challenging task to be performed under 2D fluoroscopic and TEE imaging, especially in the case of tricuspid valve repair. In this chapter we design an IGS to facilitate the positioning of clips at the target/regurgitation site by pre-mapping information such as the annulus and the coaptation gap location in 3D space.

This chapter is adapted from the following manuscripts:


5.1 Introduction

Previously labeled as the forgotten valve, the tricuspid valve (TV) and its repair surgeries have gained prominence recently [75, 40, 207]. For the longest time, it was believed that “the TV is designed to be(come) incompetent” [96] and that the valve will heal itself after a left-sided surgery is performed [41]. Research and experience have shown otherwise. When left
untreated, even after mitral valve surgery, the TV can develop high-grade regurgitation disease [28,23]. Tricuspid valve regurgitation (TR) is the most common valvular disease in the right side of the heart, characterized by the backflow of blood from the right ventricle to the right atrium, and can be organic or functional in nature. Around 80% of the TR cases are functional and due to annulus dilation (diameter greater than 40 mm) and leaflet tethering caused by pressure overload [93]. The disease can vary in severity, which in turn dictates the type of surgical intervention performed on the patient. Tricuspid repair is preferred over replacement surgeries as the replacement interventions are associated with a high mortality rate [207]. It is also suggested that the TV repair can be safely performed simultaneously with a mitral valve repair intervention [94].

Currently, there are several devices and procedures approved for tricuspid valve repair. These repair techniques can be classified into two major categories – annuloplasty and coaptation devices. Ring annuloplasty, such as Cardioband (Edwards Lifesciences), is recommended in patients with early-stage TR. The leaflet repair is performed as a more generic procedure, and on a variety of TV anatomical configurations [133]. The common devices deployed for coaptation enhancement of TV include the Forma Spacer (Edwards Lifesciences), the TriCinch (4Tech Cardio), and edge-to-edge repair devices like the MitraClip (Abbott Vascular), TriClip (Abbott Vascular) and Pascal (Edwards Lifesciences) [89]. The edge-to-edge repair techniques are particularly successful in treating severe TR with the benefits of reducing the need for hospitalization as a result of heart failure [155].

Earlier success in TV repair include the use of the MitraClip on the TV to reduce the regurgitation by at least one grade [194,146]. Since then, a specialized tool called TriClip (Abbott Vascular, Santa Clara, California) has been developed as a safe and effective device for TV repair via the TRILUMINATE trial [147].

Leaflet repair via the TriClip is performed percutaneously via transfemoral access, and while a transjugular approach has also been developed, the transfemoral approach has shown superior performance [143]. The clip is deployed either using the triple-orifice technique or more commonly, using a bicuspidization method. In this latter technique, the clip is placed between the anterior and septal leaflets of the TV to achieve the best post-procedural outcomes [201]. Currently, this procedure is performed under general anesthesia, along with combined fluoroscopic and transesophageal echocardiographic (TEE) imaging. The tools are inserted into the right atrium and maneuvered carefully and iteratively using control knobs, fasteners, and levers to reach the TV in the right ventricle under image guidance [143]. Lebehn et al. [118] describe a protocol for TEE imaging during these various steps involved in the device positioning, where device positioning involves localizing the leaflet coaptation gap at the leaflet tips and the assessment of the regurgitation based on the vena contracta. This is followed by
the positioning of clip arms perpendicular to the coaptation gap - one of the most critical steps during a TV repair intervention. When describing the device positioning process, Nickenig et al. mention that “the catheter tip was manipulated (via the control knobs on the handles) in the right atrium until the clip was properly oriented perpendicular to the line of coaptation of the tricuspid valve leaflets” [147]. This step is similar to the mitral valve repair interventions where a closed clip is advanced to the site of the regurgitant jet under TEE guidance [181]. Device positioning using these steps is an established procedure for left-sided interventions, however, the same task becomes much more meticulous for right-sided cardiac interventions due to the constraint nature of the TEE.

The tricuspid valve and its interventions have been declared “TEE-unfriendly”. The TV is located anterior to the mitral valve, rendering it challenging to image using a TEE probe [165]. The large distance between the TEE probe and the TV, combined with the non-perpendicular alignment of the sub-valvular apparatus also makes the TEE imaging of the TV more demanding [199]. Quite often, the acquired TEE images of the TV are of suboptimal quality due to the presence of shadowing and complex TV anatomy. In such cases, it is recommended that the intracardiac echocardiography (ICE) be introduced into the procedural imaging [143]. ICE imaging can not only aid in the imaging of leaflets and tricuspid annulus but also guide the deployment of the tool correctly.

ICE ultrasound provides high-resolution imaging of cardiac structures, with several advantages over conventional TEE imaging. ICE imaging of the TV allows the anatomy to be viewed up close and provides clear and direct imaging of the sub-valvular apparatus. Unlike TEE, the insertion of an ICE probe can be performed under local anesthesia only and without the need for a specialized operator. ICE is also well tolerated by the patients. The major drawback of this technology is the high cost of each single-use probe, but it has the potential to offer a better cost/benefit ratio, by reducing the procedure times and length of post-op hospitalization in patients. ICE has made its mark in interventional cardiology for structural heart diseases and electrophysiology [21, 34, 74], and has also been a favorable choice for the interventional imaging of the tricuspid valve, where it may be utilized for discerning the annulus from the leaflets, and for guiding tool positioning and orientation [24]. In several studies, ICE is used in conjunction with fluoroscopy or TEE to guide the tools and repair the TV in both annuloplasty and edge-to-edge repair [115, 164, 174, 132, 78].

Image-guided systems (IGS) have helped simplify many interventions, as well as having made them safer and more reproducible [160]. In a meta-analysis comparing the efficacy of image-guided and standard cardiac resynchronization therapy in patients with heart failure, Jin et al. [99] demonstrated that a strategy of echocardiographic guidance was associated with improved outcomes compared with a routine strategy. IGS can greatly benefit TAVI procedure in
patients with complex and unusual anatomy, such as bicuspid aortic stenosis and situs inversus totalis [156]. As the push towards less-invasive cardiac therapies continues, image-guided intracardiac visualization has received clinical exposure, as it has the potential to improve the precision and outcome of surgical procedures [160].

To facilitate the positioning of a TriClip device, the identification and localization of coaptation gap is a crucial step, that can potentially be simplified by pre-mapping the 3D location of the coaptation gap prior to the device being positioned. This mapped location serves as an important landmark during the TriClip positioning stage. In ultrasound imaging, the neck of the regurgitant jet, as seen in the color Doppler, is called the vena contracta (VC) and it corresponds to the location of the coaptation gap. In this study we aim to map the coaptation gap by localizing the vena contracta in Doppler ICE imaging.

While there is currently no commercially available automatic VC and annulus detection system, several automatic VC quantification techniques have been published in the past for the assessment of mitral regurgitation using TEE [48] and TTE [204]. Sotaquira et al. [186] have developed an algorithm to automatically detect and quantify the shape of the effective regurgitant orifice area using 3D TEE, and Li et al. [119] have developed a rapid MV A tracking algorithm for use in the guidance of off-pump beating heart transapical mitral valve repair using 2D biplane TEE images. The eventual goal of these developments is the creation of an image-guided system (IGS) for cardiac interventions in order to provide more timely and accurate information to the interventionists.

To summarize the clinical need - TV repair interventions are challenging due to the anatomical complexity and lack of standard, reliable imaging protocols. A crucial step during these procedures is to align the device perpendicular to the coaptation gap or the site of the regurgitation. This step, along with others during the device positioning stage, is currently performed using suboptimal TEE imaging. ICE has been a suitable choice for imaging the tricuspid valve and its subapparatus as it allows one to view the tricuspid anatomy directly. ICE imaging, when used with an image-guidance system, holds the potential to provide more contextual information and facilitate the device positioning during edge-to-edge transcatheter TV repair interventions.

In order to assist the positioning of coaptation device at the site of regurgitation, we propose to use a tracked ICE probe with Doppler imaging to identify vena contracta from ultrasound images, and representing its location in 3D space. Tracked devices can then navigate to reach the targeted vena contracta. To the best of our knowledge, this chapter presents the first image-guidance system proposed for tricuspid valve interventions. We have presented out proof of concept study, performed on a simple silicone wall phantom at the 2022 SPIE Medical Imaging conference [77]. In this chapter, we present a guidance system which uses ICE imaging and EM
tracking technology to identify the site of regurgitation from a patient-specific tricuspid valve in a beating heart phantom. This system is developed on 3D Slicer and implemented as an open-source, one-click, 3D Slicer module. The module, as well as some test data along with a video demonstration, can be found at https://github.com/hareem-nisar/VC-localization.

5.2 Materials and Methods

5.2.1 Materials

In this study, we used a 10-French, forward-looking, and radial Foresight™ ICE probe along with the Hummingbird Console (Conavi Medical Inc., Toronto, Canada) to acquire ultrasound imaging of the valve. The Foresight™ ICE is unique as it provides radial ultrasound as well as Doppler imaging capabilities [60], thus enabling the direct visualization of the anatomy and the regurgitation during interventions.

To achieve magnetic tracking (MT) of the ultrasound, we utilized the Aurora Tabletop Field Generator (NDI, Waterloo, Canada) and a 6 DoF sensor to track the ICE probe in 3D space during data collection.

The LV Plus Simulator (Archetype Biomedical Inc., London, Canada) was used as a pulsatile heart phantom to simulate a ventricle and an atrial chamber. The phantom can be equipped with patient-specific valves, which includes the valve leaflets embedded in a silicone flange for support [38]. The details of the methods used in the modelling of TV are given in the next section. Three patient-specific valves were created using this technique.

5.2.2 TV modeling procedure

The negative mold of a silicone flange (11 cm in diameter, 3 mm thick) with patient modeled tricuspid valves [38] was created using an Ultimaker S5 3D Printer (Ultimaker, Utrecht, Netherlands) and printed using ToughPLA filament. Approximately 3 cm of the ends of 30 cm of dacron string were frayed to mimic chordae tendineae. A 50:50 by weight mixture of previously degassed (-0.8 atm at 1 min) Part A and Part B of Mold Star™ Eco Flex-003 was brushed on the TV valve mold leaflets. The Mold Star™ Eco Flex-003 was pigmented white with Silc-Pig Silicone Pigment to allow for easy visualization. The frayed ends of the dacron string were carefully placed onto the leaflets, with each leaflet being attached to two dacron strings. Once the dacron cordae tendineae were securely positioned, the leaflets were coated once more with the Mold Star™ Eco Flex-003 mixture. The silicone leaflets were allowed to cure for 30 min. To make the silicone flange surrounding the valve, a 50:50 by weight mixture of previously
degassed (-0.8 atm at 1 min) Part A and Part B of Mold Star™ Slow 15 was then poured into the mold. The silicone flange was allowed to cure at room temperature and pressure for 45 min prior to removal from the negative mold.

Figure 5.1: Three patient specific tricuspid valves modeled using silicone and darcon strings.

5.2.3 Data Collection

An EM tracking sensor was attached externally to a Foresight™ ICE probe using an adhesive. Prior to imaging, the ICE probe (in Doppler mode) was spatially calibrated using a point-to-line registration method [52, 149].

The pulsatile heart phantom was placed over the table-top MT field generator, set to a normal rhythm at 60 beats per minute. Pure talc powder was used as an ultrasound contrast agent to enhance Doppler imaging. The ICE probe, in Doppler mode, was positioned in multiple locations at which a regurgitant jet could be observed. The regurgitation was produced via the patient-specific, pathological tricuspid valves fitted inside the beating heart phantom. Three TVs (valves A, B, and C) were prepared and fitted consecutively to acquire data. It must be noted that valve C was a pediatric, infant valve which was comparatively smaller than valves A and B.

Images were acquired from the Hummingbird console display using a frame-grabber (Epiphain, Ottawa, Canada) at a rate of 15 frames/second. The data were recorded using the Plus Server to communicate ultrasound and tracking information to 3D Slicer. For each of the three valves, five datasets were acquired, with each containing at least 5 seconds of imaging and tracking information. These data were processed to localize the vena contracta in 3D from the tracked, Doppler imaging of pathological tricuspid valves in real-time.
5.2.4 Data Processing

The first step, to isolate the images with maximum regurgitation (Figure 5.3(a)), was performed semi-automatically by the user. The peak valvular regurgitation usually occurs somewhere during the systolic phase of the cardiac cycle. To identify the exact phase of peak regurgitation, the user scans the first few images in a dataset to manually identify the first image exhibiting the highest regurgitation, along with the number of subsequent US images to be selected from each cardiac cycle. Then, all the images present at the selected cardiac phase were automatically isolated by our customized Slicer module using the data acquisition-rate information from the frame-grabber and the beating rate selected of the heart phantom. These images were stored in a ‘Sequence’ in 3D Slicer.

This sequence of peak-regurgitant Doppler ultrasound images was then processed to remove all the grayscale, B-mode information from all the images. Since the objective is to isolate the vena contracta, the non-regurgitant blood flow (depicted in cool colors) was also removed from the images by suppressing the pixels with blue channel information. It must be noted that the quality of the regurgitant jet from individual cardiac cycles can sometimes be suboptimal. Therefore, to acquire an adequate jet image, all the images in the sequence were compounded together into one resultant image with the regurgitant flow (Figure 5.3(c)). This step was achieved by using the maximum intensity projection (MIP) principle. In doing so, the most yellow pixel or the highest velocity information is retained in the resultant image.

The resultant combined Doppler image contained the complete regurgitant jet, depicting
blood flowing backward from the ventricle to the atrial chamber (Figure 5.3(c)), and was converted to grayscale for further processing. The image was subjected to a binary threshold at an intensity of 150 to segment the brighter pixels representing the higher velocities in the regurgitant jet. For valve C, this threshold was set to 130 to accommodate the flow through a smaller, infant valve.

The next step was to identify the axis of the regurgitant jet. The segmented region was subjected to principal component analysis (PCA) to identify the major and minor axis of the jet, as well the principal moments. This information was used to transform the segmented region to lie along the major axis (Figure 5.4(b)). The noise was removed by retaining only the largest connected island within the segmented region which was representative of the atrial regurgitant jet.

From the transformed regurgitant jet, our proposed algorithm then identified the location of the vena contracta. At each point along the major axis, the height of the segmentation was
measured, and the point with the minimum height was recorded. This minimum height was estimated as the vena contracta width (VCW), while the midpoint along the VCW was noted as the transformed vena contracta location. The inverse transformation from the PCA was applied to retrieve the original coordinates for the location of vena contracta in the US image. Figure 5.4 shows the VCW on the segmented jet region and the vena contracta location placed on a 2D ICE image.

The Foresight™ ICE images are conical in nature, and lie in 3D space. The ICE image displayed on the console is a projection of the conical surface image along the height-axis. As such, the location of vena contracta on 2D images is not accurate and lacks the third dimension. Using the imaging angle information provided on the console screen, the location of the VC with respect to the true 3D image is calculated. The details of this conversion can be found in Nisar et al. [149]. Finally, the ICE probe calibration information, and the probe location transform provided by the EM tracking system, were applied to acquire the location of the VC in 3D space (Figure 5.4(d)). This location represents the origin of the regurgitation in the tricuspid valve, which occurs most often at the coaptation gap.

5.2.5 Validation

Prior to data collection for each valve, the ground truth VC and annulus were identified for validation. A pre-tracked and pre-calibrated needle was used to identify the VC in 3D tracking space, where the tip of the needle, and the orientation of the needle shaft, are tracked. The position of the ground truth of the VC was obtained by visually identifying and manually tracing the periphery of the regurgitant orifice using the tracked needle tip. The points were used to construct a 3D model of the ground truth vena contracta. Similarly, the outline of the annulus points were marked, and the model was constructed. The VC point locations detected by the algorithm were compared to the manually isolated ground truth VC model by estimating the closest distance between them.

5.3 Results

For each of the valves, the distance between the ground truth VC model and the ICE-derived vena contracta locations were computed. The distance error for all the datasets can be seen in Figure 5.5. As can be seen by the three tall peaks in the graph, there is one outlier case for each valve where the error is unacceptable. The outliers were a result of insufficient Doppler imaging as captured by the framegrabber. Across the three valves and excluding the three outliers, the average distance error between the detected VC and the ground truth model is
1.22 ±2 mm.

Figure 5.5: Error bars representing the minimum distance between the algorithm-detected vena contracta location and the ground truth model. For each of the valves, one high error bar can be seen as an outlier.

Qualitatively, the position of the ground truth vena contracta, corresponding to the coaptation gap, can be seen as an irregular shaped body in yellow in Figure 5.6. The manually identified annulus ring is also represented to provide contextual information. The three high-error points can be seen near to the annulus in 3D, which is a clear indication that these points are incorrect and outliers. For valve A and B, the detected VC locations are close to the ground truth. The highest error was recorded in a dataset for valve C at 5.8 mm.

5.4 Discussion

During interventions, clinicians rely on anatomical landmarks to guide and align the tools properly. Traditionally the identification of landmarks and the positioning of tools takes place simultaneously, thus making the procedure intricate and demanding. Pre-mapping these landmarks can simplify these procedures by providing more information to the clinician while they position the devices. In this study, we present a method to semi-automatically extract the location of vena contracta, a clinically relevant landmark, from ultrasound images and represent it in 3D space. ICE imaging is used to generate 3D models of important anatomical features to potentially enhance the spatial awareness of the interventionalist, as well as give information about the relative positioning of the procedural tools with the cardiac anatomy. Moreover the
5.4. Discussion

Figure 5.6: A qualitative analysis of the results showing the ICE-derived vena contracta locations as points and the ground truth vena contracta as a model (in yellow). A pre-mapped annulus model and vena contracta location in a tracked environment can provide more contextual landmarks for device positioning.

Presence of ICE allows the clinicians to acquire up-close live ultrasound imaging as the procedure is being performed. Since ICE probes can be manipulated to acquire non-traditional anatomical views, the technique presented in this chapter can be particularly useful during complicated TV edge-to-edge repairs, where the clip has to be positioned at more challenging positions such as at the posteroseptal and anterioposterior commissures[37].

The results from this study indicate that the designed 3D Slicer module can reliably localize the VC in most cases. Literature suggests that for cardiac interventions an error margin of up to 5 mm is acceptable [122]. In comparison, our average error of 1.22 ±2 mm is appropriate for this early-stage study. It should also be noted that the ground truth established in these experiments should be considered as a “bronze” standard as it was manually identified by visual characterization of the coaptation gap. Hence it is susceptible to both human error and subjectivity.

A major limitation of this study is the presence of the outliers when the algorithm is unable to identify the VC accurately and instead the VC is localized near the annulus. In a use case, an outlier can be easily identified when the detected VC was positioned too close to the TV annulus. Outliers indicate that the valve should be reimaged and processed by the algorithm again. We suspect these outliers to be a result of the lower frame rate used in the study, which meant that the regurgitation was not captured in the imaging data. During the experiments, it was observed that the recorded data in Slicer lacked some of the imaging frames showing high regurgitation on the Hummingbird console screen. The frame grabber was operating at a rate of 15 frames per second and in some cases missed capturing the image frame with the maximum regurgitation. To record the complete regurgitant Doppler imaging, we recommend using a frame grabber with a higher frame rate. Ideally, the imaging data should be transmitted
directly from the ultrasound machine but this infrastructure is not yet available in most clinical consoles, including the Hummingbird console used in this study.

A consideration while imaging the valve would be to use a narrower field of view for Doppler imaging to optimize and focus in the direction of the regurgitant jet. This simple factor can greatly enhance the overall efficiency of the designed algorithm.

Besides the VC, the annular ring of the tricuspid valve is another important landmark during TV interventions. In this study we manually identified the annulus ring, however, the procedures can benefit from automated ultrasound-based techniques to identify the TV annulus in 3D space. Future work can involve implementation of the existing methods in the literature that can extract and model the annulus from ultrasound. Li et al. [119] present a method for tracking the mitral valve annulus and it can potentially be adapted for TV annulus modeling as well.

Since the valves used in this study are modeled after real patient-specific TV, there is room for collecting more and complex tricuspid regurgitation cases. The valve modeling technique and the beating heart phantom allow mimicking realistic conditions, reducing the need for in-vivo testing at such an early stage of the study. With a variety of TV models, the algorithm can be made more robust by testing and modifying it to accommodate more versatile patient cases. It should be noted that the beating heart phantom used in this study also has a few limitations including fixed contractility and missing soft tissue representation in the atrial chamber. These factors do not directly affect this study but it would be ideal to address these limitations for the design of cardiac IGS in the future.

Future work can involve making the Slicer module more robust and suitable for even more complex tricuspid valve pathologies. The ultrasound guidance approach can also be enhanced with the emerging 4D ICE technology, like VeriSight Pro (Philips) and NuVision (Biosense Webster), which provides improved imaging of the subvalvular apparatus during transcatheter TV repair.

5.5 Conclusion

Tricuspid valve interventions and related technology are evolving as more cases are being performed with imaging being a major challenge in them. A suitable alternative to the existing TEE-based workflows is to employ ICE imaging to visualize the anatomy. In this chapter, we presented a method to provide more contextual information to the interventionalists during the TV repair procedures to reduce the regurgitation. A tracked ICE probe can be used to localize and pre-map significant landmarks in order to assist the meticulous task of device positioning during TV repair. Image guidance systems with mapping technology have successfully sim-
plified complex cardiac procedures like ablation therapy [183]. This study is one step towards using image guidance for tricuspid valve interventions to potentially streamline the challenging TV repair procedures.
Chapter 6

Conclusions

Transcatheter interventions are rapidly becoming a standard of care for structural cardiac diseases. These micro-invasive procedures are known to improve patient safety, decrease recovery time and enhance procedural outcomes. However, due to the percutaneous nature of these procedures, there is a lack of direct line of sight with the anatomy and the tools. To provide “eyes looking into the heart”, imaging techniques such as fluoroscopy and echocardiography are routinely used during transcatheter procedures. In recent years, emphasis is placed on the reduction of harmful x-rays in the operating room to not only enhance patient safety but also protect the medical team from radiation exposure. Interventionalists are currently required to wear heavy lead shielding equipment to minimize x-ray exposure, which often leads to severe neck and back pain and spinal issues, collectively called “interventionalist’s disc disease”. Intracardiac echocardiography (ICE) imaging is a safe and non-ionizing technique for real-time soft tissue visualization. In 2017, Conavi Medical Inc. introduced a novel forward-looking ICE probe with progressive 3D and Doppler capabilities which opened new doors of possibilities for ultrasound-guided cardiac interventions. In this thesis I addressed the challenge of radiation exposure during transcatheter interventions by providing alternative ICE-guidance systems augmented with advanced tracking technology.

6.1 Thesis Contributions

Foresight ICE is a novel ultrasound technology that utilizes a single-element rotating transducer element, capable of tilting at a user-specified angle and thus able to generate a forward-looking 2D conical surface image lying in 3D space. We thus refer to this unique configuration as 2.5D. With the clinical motivation to minimize fluoroscopy by introducing US-based IGS, in this thesis, we explored two different clinical applications of radial ICE imaging – an IGS for transfemoral vessel navigation and a guidance system to assist clip positioning during tricus-
pid valve repair interventions. Both the applications represent an advanced image guidance system where an ICE probe is augmented with electromagnetic tracking technology; therefore it is imperative that we achieve accurate ICE probe tracking before designing the application-specific IGS. As such, the first research objective was to prepare the Foresight ICE probe to be used in an IGS which required that the imaging frames are characterized as well as the probe is calibrated both spatially and temporally. Chapter 2 provides a detailed analysis of the characteristics of the imaging acquired via the Foresight ICE probe on a Hummingbird console such as the image geometry, orientation, and display size. The chapter serves as a guide for anyone looking to integrate Foresight ICE in an IGS or aiming to characterize another radial ultrasound probe. It must be noted that the imaging data is acquired as a screenshot of the Hummingbird console screen showing circular 2D projections of the conical ICE image. For a true representation of the ICE image in an IGS, the image must be converted from a 2D circular to a 3D conical shape. Since the 2.5D configuration is novel and unique, we have developed three visualization techniques to view the conical ICE in a 3D environment such as the 3D Slicer software including volume reconstruction and rendering, real-time texture mapping on a conical surface, and offline conical volume reconstructions from raw DICOM data.

Magnetically tracked ICE probe is also spatially calibrated using a point to line registration technique. Characterization of the calibration methods showed that when the sheath is bent, there is an intrinsic rotation between the external sheath and the inner probe layers, resulting in inaccurate calibration and tracking of the ICE probe. An important conclusion is that the probe motion must be limited to linear movements when the tracking sensor is attached to the outer sheath. The temporal calibration technique showed that the time lag between the ultrasound and tracking system is minimal and can be ignored for most applications.

Since transcatheter interventions are invasive in nature, we must design the initial IGS on a realistic phantom first. The third chapter aims at designing an ultrasound-realistic vessel phantom that mimics the ultrasound of an inferior vena cava upon ICE imaging. Since the ICE imaging is intravascular and shows the vessel structures up close, we designed a vessel phantom that contained a hollow vessel lumen, a reflective vessel wall, and a weakly-reflective surrounding tissue. We tried different concentrations of talcum powder as an additive to PVA-c to obtain the desired ultrasound contrast in the ICE imaging of the phantom. This chapter shows ultrasound imaging of PVA-c with different talcum powder concentrations which can be helpful to researchers designing their own vessel phantom for a different part of the body. The resultant phantom was quite useful for our vessel reconstruction study (chapter 4) summarized below.

Navigating the vessels, or the inferior vena cava in the case of a transfemoral approach of the intervention is an obligatory part of transcatheter cardiac interventions. In efforts of
minimizing the use of fluoroscopy, we proposed and demonstrated an US-guided workflow where the vascular roadmap is reconstructed using magnetically tracked ICE imaging, which is then traversed by tracked tools to reach the target organ. Vessel segmentation is a ubiquitous step during the vessel reconstruction process which should ideally be both real-time and accurate. Therefore, we implemented a deep learning algorithm to perform the vessel reconstruction through a U-net model pre-trained on ICE imaging of swine inferior vena cava. This proposed IGS is designed as an open-source and user-friendly 3D Slicer module that can easily be accessed and used by the medical imaging community. Although the vessel reconstruction accuracy is only validated on a phantom, the module is ready for in-vivo testing as the algorithm is trained to segment vessels from animal imaging. This study provides a basic structure and software necessary for fluoro-free, ultrasound-guided vessel navigation. It should be noted that the proposed IGS works best with radial, side-looking ICE imaging as compared to the phased-array ICE probes that do not show the entire cross-section of the vessel. According to the clinicians with whom we collaborated, the accuracy constraints for navigation purposes are flexible. This system can also be adapted for mapping the vascular path during endovascular and abdominal procedures where multiple vessels and their branches must be traversed to reach the target site.

Transcatheter procedures are demanding for the clinicians due to the lack of direct line of sight with the tools and the anatomy. The invisible tool phenomenon in percutaneous interventions leads to challenging visualization of tool tip in real time. The task of viewing the anatomy is often performed by TEE ultrasound imaging, however tricuspid valve and its sub-apparatus are TEE-unfriendly and often require ICE imaging instead. During the repair procedure for tricuspid valve regurgitation, the positioning the tool tip at the target site (i.e., the coaptation gap between the leaflets) while simultaneously visualizing the tool and the anatomy can be cumbersome. In chapter 5, we present the first known IGS to assist tricuspid valve repair interventions by using tracked ICE imaging to pre-map the target site in 3D space. Tracked tools can then be maneuvered easily to reach and position at the desired target location without having to simultaneously image the valve leaflets. We hypothesize that showing the coaptation gap as well as the annulus geometry in 3D space will enhance the spatial awareness of the interventionalist, and thus reduce their cognitive load. The availability of tracked ICE imaging will also enable real-time, up-close visualization of the TV and its sub-apparatus resulting in enhanced procedural outcomes.
6.2 The New ICE Age

In the last five years (2017 – 2022) ICE technology has taken some major leaps and advanced from 2D imaging to live 3D echo imaging and 4D color Doppler imaging. Table 6.1 shows the comparison and testimonials from clinicians on the latest 4D ICE probes including Philips Verisight Pro [14], Siemens ACUSON AcuNAv Volume ICE [2] and Biosense Webster Nu-Vision ICE catheter [11]. The recent uprise of awareness in tricuspid valve interventions has also brought ICE imaging into the spotlight as TEE cannot be used in many patients due to anatomical constraints or TEE contraindications. Hagemeyer et al. [91] call this era “The New ICE Age” where ICE imaging has the potential to replace TEE imaging for many procedures in interventional cardiology. ICE can now provide real-time volumetric imaging similar to TEE and enhanced patient safety by eliminating the risks associated with TEE and general anesthesia. However, the ICE probes are currently designed for one-time use and thus increase the operation cost. On the other hand, ICE imaging reduces the length of hospital stay and costs associated with administering general anesthesia. Therefore, the cost-to-benefit ratio is still under debate, and thorough clinical studies need to be performed before we can assess the true economic impact of ICE. A brief comparison of the pros and cons of the use of ICE imaging is provided in figure 6.1.

<table>
<thead>
<tr>
<th>Advantages of ICE</th>
<th>Disadvantages of ICE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safer procedures.</td>
<td>High cost of the catheter.</td>
</tr>
<tr>
<td>Provides suitable echo when the patient is TEE contraindicated.</td>
<td>Extra vessel access required.</td>
</tr>
<tr>
<td>Imaging of anatomy where TEE views are restricted.</td>
<td>Probe motion during the intervention.</td>
</tr>
<tr>
<td>No acoustic shadowing from therapeutic tools or implant devices</td>
<td>Needs a learning curve.</td>
</tr>
<tr>
<td>Potentially reduced operating time.</td>
<td></td>
</tr>
<tr>
<td>No general anesthesia required.</td>
<td></td>
</tr>
<tr>
<td>Unaffected hemodynamics.</td>
<td></td>
</tr>
</tbody>
</table>

Figure 6.1: Advantages and disadvantages of intracardiac ultrasound (ICE) imaging
<table>
<thead>
<tr>
<th>Product Name</th>
<th>Verisight Pro</th>
<th>Acunav Volume ICE</th>
<th>NuVision</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manufacturer</td>
<td>Philips</td>
<td>Siemens</td>
<td>Biosense Webster</td>
</tr>
<tr>
<td>4D imaging</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>4D color Doppler</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Spectral Doppler</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Transducer</td>
<td>xMatrix</td>
<td>Multi-element 2D phased array</td>
<td>Multi-element 2D phased array</td>
</tr>
<tr>
<td>Catheter size</td>
<td>9 F</td>
<td>12.5 F</td>
<td>10 F</td>
</tr>
<tr>
<td>Working length</td>
<td>90 cm</td>
<td>90 cm</td>
<td></td>
</tr>
<tr>
<td>Frequency</td>
<td>4-10 MHz</td>
<td>4-10 MHz</td>
<td>4-10 MHz</td>
</tr>
<tr>
<td>Imaging sector</td>
<td>90</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>Imaging view</td>
<td>90° x 90°</td>
<td>90° x 50°</td>
<td>90° x 90°</td>
</tr>
<tr>
<td>Additional information</td>
<td>Deflection range 120 degrees</td>
<td>40 volumes per second in 4D B-mode and 20 vps in 4D color mode; joystick control design</td>
<td>Number of elements: 840; 2cm distal tip length</td>
</tr>
</tbody>
</table>
**Comments from clinicians**

<table>
<thead>
<tr>
<th>Comments</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>“The next generation 4-D ICE technology... facilitates the performance of left atrial appendage closure under moderate sedation, making the procedure accessible to many patients who are not good candidates for general anesthesia. It also provides excellent imaging of the tricuspid valve, allowing of a more effective transcatheter treatment of tricuspid regurgitation”</td>
<td>[7]</td>
</tr>
<tr>
<td>– Dr. Mohamad Adnan Alkhouli (Interventional cardiologist, Mayo Clinic, Rochester)</td>
<td></td>
</tr>
<tr>
<td>“Shorter articulation length of the distal tip enables me to get closer to the anatomy of interest, especially for left heart procedures. This means better imaging outcomes and better care for my patients.”</td>
<td>[12]</td>
</tr>
<tr>
<td>– Dr. Carlos Sanchez (Interventional Cardiologist of Advanced Structural Heart Disease, OhioHealth Riverside Methodist Hospital)</td>
<td></td>
</tr>
<tr>
<td>“With the NuVision ICE Catheter I can view complex intracardiac structures from an entirely new perspective, providing a more accurate picture of cardiac function compared to traditional TEE or 2D ICE”</td>
<td>[9]</td>
</tr>
<tr>
<td>– Dr. Azeem Latib (Director of Interventional Cardiology and Structural Heart Program Interventions, Montefiore Medical Center, New York)</td>
<td></td>
</tr>
</tbody>
</table>

Table 6.1: Comparison of 4D intracardiac echocardiography (ICE) probes commercially available in 2022.
6.3 Future Directions

Transcatheter interventions initiated the use of IGS in cardiology by the uptake of CARTO system to remedy atrial fibrillation. Electrophysiology labs are equipped with electromagnetic tracking technology and utilize ICE imaging for mapping the cardiac structures in real-time. In the future, we suspect similar systems to be adapted by the hospitals for structural heart repair as well. Live 3D ICE imaging is an attractive imaging modality and has opened up new possibilities in the field of interventional cardiology. While the forward-looking Foresight ICE probe may have been suspended by the manufacturer, the work in this thesis is still applicable to any radial US imaging modality. The IGS designed in this thesis for navigation and positioning tasks are in their early stages and require further improvements before they can be moved towards clinical testing.

The vessel reconstruction IGS involves two major steps – vessel lumen segmentation and vessel surface reconstruction. The segmentation algorithm can further benefit from retraining with a larger and versatile imaging dataset containing complex and pathological vessel cases as well. Doing so will ensure a more robust algorithm and result in a more accurate vessel reconstruction. The vessel reconstruction step is currently implemented in Python language as part of a 3D Slicer module. For clinical feasibility, the vessel reconstruction process must be near real-time, and a stand-alone program in a lower-level language is likely to reduce this reconstruction time. Other options such as GPU implementation and asynchronous programming can also be explored to decrease the processing time. If another radial and non-conical ICE probe is to be used, the processing will surely be more timely as the algorithm would not be required to perform the 2D to 3D (or rather 2.5D) conversion of the vessel segmentations. The next steps should involve in-vivo testing of the designed IGS starting with the vessel reconstruction of the inferior vena cava, aortic arch, and the vena cava tributaries in the abdominal region. Vessel reconstruction is only an instrument to perform fluoro-free tool navigation. The usefulness of the proposed IGS must be evaluated through a user study where vessels are navigated by tracked tools using the ICE-reconstructed vascular roadmap. The results of this user study based on the clinicians’ feedback will determine the efficiency of the IGS and whether it enhances the procedural outcomes.

There are numerous clinical applications and opportunities of research that can benefit from IGSs employing an ICE probe. As described earlier, ICE imaging is already an essential part of some cardiac interventions and with the advent of 4D imaging feature, ICE holds the potential to replace TEE imaging in many procedures. The navigation task can benefit from 3D live ultrasound imaging, allowing to stitch volumes together based on image intensities as well. Tool positioning, especially for right-sided procedures, can also greatly benefit from
the 4D imaging feature by providing more, intuitive information to the interventionalist and visualizing the tool tip in relation to the anatomy in real time.

One of the hurdles we foresee in the clinical uptake of ICE-guided systems is the economic resources. An ICE probe will be more affordable and attractive to the hospital administration if the probe were reusable, at least multiple times. 4D ICE technology holds the potential to make transcatheter procedures much safer and more efficient. ICE probes can be made reusable either by introducing advanced sterilization techniques or designing low-cost sheathes to envelop the ICE probe prior to insertion into the body. Another trajectory is in regards to the clinical adaptation of EM tracking systems which will allow for advanced IGS. The industry should prepare to integrate EM tracking sensors into the common surgical/procedural tools either by providing pre-tracked and calibrated tools or by redesigning the tool geometry to accommodate sensor placement if a user wishes to do so. In order to see the benefits of IGS and its impact on patients’ health and safety, the industry must work alongside academia to make the translation of technology more seamless and rapid.
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[121] Marian C Limacher, Pamela S Douglas, Guido Germano, Warren K Laskey, Bruce D Lindsay, Marlene H Mcketty, Mary E Moore, Jeanny K Park, Florence M Prigent, Mary N Walsh, James S Forrester, David P Faxon, John D Fisher, Raymond J Gibbons,


Appendix A

Codes for ICE Visualization

A.1 Code for Conical Volume Reconstruction From a 2D Image

```python
# #
# #
#------ Slicer function for Conical Image Reconstruction ----#
# # #
import slicer.util
import numpy as np
import math

def reconstruction(self, inputVolume, outputVolume, anglePhi):  # both volumes are scalar.
    phi = float(anglePhi)

    imgArr = slicer.util.arrayFromVolume(inputVolume)
    imgArr = np.squeeze(imgArr)
    Row, Col = imgArr.shape

    #Defining the origin/apex of the cone as the middle point of the image.
    origin = ((int(Row/2), int(Col/2)))
    edge = ((Row, Col))
```

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#Calculating the maximum value of z based on the max displacement of the image from the center
# i.e from the middle of the image (cone apex) to the corner of the image.
max_d = math.sqrt(sum((edge - origin)**2 for edge, origin in zip(edge, origin)))
max_z = max_d*math.tan(math.radians(90-phi))

#making an empty volume (choose an appropriate value of z)
vol = np.zeros((int(max_z+1), Row, Col), dtype=np.uint16)

#reconstruction: keeping x-axis and y-axis as same,
calculation a height for each pixel value and populating volume
#origin(at apex) stays where it is, peripherals moved along z-axis.
result = np.where(imgArr) #get index of all voxels, for label map
replace imgArr==1
X = result[0] #row
Y = result[1] #col
D = np.sqrt((X-origin[0])**2 + (Y-origin[1])**2) # 6.6 us for X= np.zeros(200)
Z = D*math.tan(math.radians(90-phi))
Z = Z.astype(int)
vol[Z,X, Y] = imgArr[X,Y]

#Update the volume(data) in the volume node with new array
slicer.util.updateVolumeFromArray(outputVolume, vol)

# -- Optional Volume Rendering --- #
volumeNode = outputVolume
slicer.util.updateVolumeFromArray(volumeNode, vol)
volRenLogic = slicer.modules.volumerendering.logic()
volRenWidget = slicer.modules.volumerendering.widgetRepresentation()
displayNode = volRenLogic.CreateDefaultVolumeRenderingNodes(volumeNode)
volumePropertyNode = displayNode.GetVolumePropertyNode()
volumePropertyNodeWidget = slicer.util.findChild(volRenWidget, 'VolumePropertyNodeWidget')
volumePropertyNodeWidget.setMRMLVolumePropertyNode(volumePropertyNode)

return outputVolume

A.2 Code for Texture Mapping an Image to a Cone Model

#
#------ VTK-based, Slicer function for Texture Mapping ------#
#
import vtk, math

def textureMap(self, inputVolumeNode, anglePhi):
    dim = inputVolumeNode.GetImageData().GetDimensions()
    radius = int(dim[0]/2)
    height = radius*(math.tan(math.radians(90-anglePhi)))

    print("Texture Mapping function")
    print("Cone Angle is ", anglePhi, " Radius is ", radius, " and Height is ", height)

    ##create a VTK coneSource / conical plane
    self.coneSource = vtk.vtkConeSource()
    self.coneSource.SetHeight(height)
    self.coneSource.SetRadius(radius)
    self.coneSource.SetResolution(100)

    #Center of the vtkConeSource is halfway up the height axis.
    #Actual origin should be at the apex of the cone/middle of circle
    self.coneSource.SetCenter(radius, radius, height/2)
    self.coneSource.CappingOff()
self.coneSource.SetAngle(anglePhi)

#This part defines the axis: the line drawn from the center of the
base up towards the apex/vertex.
self.coneSource.SetDirection(0,0,-1) #-z axis
self.coneSource.Update()

#Set the input image as teh texture
self.texture = vtk.vtkTexture()
sel.texteure.SetInputConnection(inputVolumeNode.
GetImageDataConnection())

#Set the cone source as the plane to be texture mapped
self.texturePlane = vtk.vtkTextureMapToPlane()
sel.texteurePlane.SetInputConnection(self.coneSource.GetOutputPort
())

#By default, the plane is centered at the origin and perpendicular
to the z-axis,
#with width and height of length 1 and resolutions set to 1.
#Match the origin to the corner off of the cone and set two points
at the other corners
self.texturePlane.SetOrigin( 0, 0, 0)
sel.texteurePlane.SetPoint1( 2*radius, 0, 0)
sel.texteurePlane.SetPoint2( 0, 2*radius, 0)

self.model = None
if self.model is None:
    ##creating a new model in Slicer and set display properties
    self.model = slicer.modules.models.logic().AddModel(self.
texturePlane.GetOutputPort())
sel.model.SetName("Cone_Model")
sel.modelDisp = sel.model.GetDisplayNode()
sel.modelDisp.SetAmbient(1)
sel.modelDisp.SetDiffuse(1)
sel.modelDisp.SetSpecular(1)
```python
self.modelDisp.SetPower(1)
self.modelDisp.SetFrontfaceCulling(0)
self.modelDisp.SetBackfaceCulling(0)

# Apply texture image to the plane (cone)
self.modelDisp.SetTextureImageDataConnection(inputVolumeNode.GetImageDataConnection())

return self.model

A.3 Code for Volume Reconstruction from a DICOM file

# #
# 
#------ Slicer function for Image Reconstruction from DICOM --#
# # #

import scipy
import pydicom
import numpy as np
import math

def dicomReconstruction(self, filePath, outputVolumeNode, interpFactor, interpEnabled):
    #fname = 'C:/Users/haree/Desktop/2.25.110163955407302945943070993686554932643.570.dcm'
    fname = filePath
    ds = pydicom.dcmread(fname)
    img = ds.pixel_array  # numpy array with pixel data
    [row, col] = img.shape  # [TH, R]
    R = img.shape[1]  # or R = cols, (representing each echo along radius R)
    TH = img.shape[0]  # or TH = rows (representing each theta)

    # Reading DICOM tags and extracting data
```
phi = ds[0x15, 0x1000].value #float
theta_en = ds[0x15, 0x1004].value #list #encoded [3,8... 1021]
numFrames = ds[0x28, 0x0008].value # pydicom.valuerep.IS
rows = ds[0x28, 0x0010].value #int (THETA)
cols = ds[0x28, 0x0011].value #int (along RADIUS)
spacing = ds[0x28, 0x0030].value #pydicom.multival.MultiValue
TH_spacing= float(ds.PixelSpacing[0]) #float
R_spacing = float(ds.PixelSpacing[1]) #float
theta = theta_en/1024*360 # decoded theta values in degrees

#------------------ interpolating
--------------------------------------------------------
if interpEnabled:
    print("DCM shape before interpolation:␣",np.shape(img), np.shape(theta), R, TH)
    rows2add = int(interpFactor) - 1
    [img, theta] = self.interpImage(img, theta, rows2add) #function to interpolate img data before reconstruction
    R = img.shape[1] # or R = cols
    TH = img.shape[0] # or TH = rows
    print("DCM shape after interpolation:␣",np.shape(img), np.shape(theta), R, TH)
#
#-------------------------

#needed for spacing later
maxC, minC = 0, 2000

# Min size requirement of 3D volume is based on simple geometry (see diagram)
[volx, voly, volz] = [2*R*math.sin(math.radians(phi)), 2*R*math.sin(math.radians(phi)), R*math.cos(math.radians(phi))]
vol = np.zeros((int(volx), int(voly), int(volz)), dtype=np.uint16)

[ox, oy, oz] = [round(volx/2), round(voly/2), 0]
vector = np.arange(0, TH)
sample = np.arange(0, R)

for v in vector:
  # getting polar angle theta for each vector
  th = theta[v]
  for s in sample:
    r = s*R_spacing # radial position for each sample
    # convert to cartesian
    a = r*math.sin(math.radians(phi))*math.cos(math.radians(th))
    b = r*math.sin(math.radians(phi))*math.sin(math.radians(th))
    c = r*math.cos(math.radians(phi))

    # scaling by 80 (optimum number) to avoid overlapping or maybe FOV?
    a = int(round(a*80) + ox)
    b = int(round(b*80) + oy)
    c = int(round(c*80) + oz)

    # dicom image to volume pixel mapping
    vol[a,b,c] = img[v, s]

    if maxC<c:
      maxC = c
    if minC>c:
      minC = c

sp = R*R_spacing*10*math.cos(math.radians(phi))/(maxC-minC)

# update the volume(data) in the volume node with new array
slicer.util.updateVolumeFromArray(outputVolumeNode, vol)
outputVolumeNode.SetSpacing((sp,sp,sp)) # setting spacing using cone geometry to ensure the radial length remains the same
outputVolumeNode.SetOrigin((0,0,0))
# now perform volume rendering through Slicer module
return outputVolumeNode

def interpImage(self, img, th, numRows):
    
    #-------------------INTERPOLATING THETA VALUES -------------------
    #
    #Getting theta information from the original data, duplicating the
    #last row, and then upsampling theta array

    TH = img.shape[0]
    # th = decoded theta values in degrees
    #2. Adding last row = first row (so that interpolation is on a
    #closed loop)
    th = np.append(th, [th[0]+360])
    TH += 1  #adding one to the total number of vectors TH=th.shape[0]

    # 3. Upsampling theta values
    intrp_func = interpolate.interp1d(np.array(range(TH)), th, kind='linear', axis=0)
    R2add = numRows #e.g. 15 ROWS or VECTORS TO BE ADDED IN BETWEEN TWO
    # VECTORS
    new_row = np.linspace(0, TH-1, R2add*(TH-1)+TH)
    intrp_th = np.array(intrp_func(new_row))
    TH = intrp_th.shape[0]

    # making sure that all theta values are under 360 (interpolation at
    #the end)
    for i in range(TH-1-R2add , TH):#intrp_th[-(R2add+1):]:
        if intrp_th[i]>=360:
            intrp_th[i] -= 360
        #end if
    #end for

    #
    #--------------------- INTERPOLATING IMAGE
# Before using interpolation on the rectangle image, copying the first vector as an additional last vector
# because of cone geometry or loop - first and the last vector will coincide now.

# Copy last row to end
img = np.concatenate((img, np.expand_dims(img[1,:], axis=0)), axis =0)
TH = img.shape[0]

# Upsampling - there is a duplicated last row which we will ignore in reconstruction
intrp_func = interpolate.interp1d(np.array(range(TH)), img, kind='linear', axis=0)

# ROWS or VECTORS TO BE ADDED IN BETWEEN TWO VECTORS (must be same as before)
new_row = np.linspace(0, TH-1, R2add*(TH-1)+TH)
intrp_img = np.array(intrp_func(new_row))
TH = intrp_img.shape[0]

return intrp_img, intrp_th
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Aug 2022

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Take Home Figure (fig 8) on page 437

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Curriculum Vitae

Name: Hareem Nisar

Post-Secondary Education and Degrees:
- National University of Sciences and Technology, Pakistan
- Bachelors in Electrical Engineering
- 2012 - 2016

Honours and Awards:
- Western Graduate Research Scholarship
- 2017-2022

Related Work Experience:
- Teaching Assistant
- The University of Western Ontario
- 2017 - 2022

Journal Publications:


172
Conference Proceedings:


International Conference Presentations:

**CARS 2022 Oral Presentation - Tokyo, Japan**
- Presented a 10 minute talk titled “3D localization of vena contracta using Doppler ICE imaging in tricuspid valve interventions”

**SPIE 2022 Poster and Pitch Presentation - Virtual**
- Presented a poster and pitch titled “Towards ultrasound-based navigation: Deep learning based IVC lumen segmentation from intracardiac echocardiography”

**CARS 2020 Oral Presentation - Virtual**
- Presented a 10 minute virtual talk titled “A simple, realistic walled phantom for intravascular and intracardiac applications”

**SPIE 2019 Poster Presentation - San Diego, USA**
- Presented a poster titled “Ultrasound calibration for unique 2.5D Conavi images”
- Cum Laude Conference Poster Award and Cash Prize

Local Conference Presentations and Event Participation

**ImNO Education Challenge 2022 - Virtual**
- Audience Choice Award for the presentation of a talk titled “Why do we see colors?” to middle-school students

**Imaging Network Ontario 2022 - Virtual**
- Chairing and judging multiple sessions during the conference
- Pitch presentation titled “Deep learning based vessel segmentation from ICE imaging”
• Oral presentation titled “Fluoro-free, ultrasound-based navigation system for cardiac interventions”

**London Imaging Discovery Day 2019 - London, Canada**
• Oral presentation titled “Calibration of unique 2.5D conical ultrasound images”

**3 Minute Thesis Competition 2019 - London, Canada**
• Western top 20 finalist: “Eyes for your heart”

**London Health Research Day 2019 - London, Canada**
• Poster presentation titled “Ultrasound calibration for unique 2.5D conical images”

**London Imaging Discovery Day 2018 - London, Canada**
• Poster presentation titled “Image guidance for MitraClip procedures for tricuspid valve regurgitation”

**Western University Health and Research Conference 2018 - London, Canada**
• Keynote speaker: VAAST lab research overview

**Supervisory Experience**

**Djalal Fakim**
Supervised and assisted Djalal in conducting a research project on the development of an image-guidance system for tricuspid valve repair, which resulted in him presenting his work at an SPIE conference and paved way for an IJCARS journal publication as well.

**Humayoun Akhunzada**
Supervised Humayoun in a research task of establishing manual ground truth for ultrasound vessel segmentation, resulting in an SPIE conference proceeding.

**Maya Bielecki**
Assisted in the supervision and mentoring of Maya for her undergraduate summer project on the development of a VTK-based algorithm where a 2D circular ultrasound image is mapped on to a 3D conical surface to enhance the image visualization of intracardiac echo images acquired via Foresight ICE probe.

**Leadership and Volunteer experience**
• Secretary General for IEEE –Women in Engineering, London Chapter, 2018-2022
• Volunteer public speaker for the Heart and Stroke Foundation 2018-2020
• Volunteer organizer for the Pen Pal Program, Engineers Without Borders –Gender Equity, London, ON, 2020-2021
• Treasurer for IEEE Engineering in Medicine and Biology Society at Western University 2017-2018
• Facilitated the Imaging Day for Western Engineering Summer Academy 2018
• Numerous demonstrations and presentations for Canadian Medical Hall of Fame Discovery Days 2017-2020
• Numerous demonstrations and presentations for Canadian Medical Hall of Fame School Museums 2017-2020