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The Role of Visualization, Force Feedback, and Augmented Reality in Minimally Invasive Heart Valve Repair

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Graduate Program in Biomedical Engineering
A thesis submitted in partial fulfillment of the requirements for the degree in Doctor of Philosophy
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THE ROLE OF VISUALIZATION, FORCE FEEDBACK, AND AUGMENTED
REALITY IN MINIMALLY INVASIVE HEART VALVE REPAIR

(Thesis format: Integrated Article)

by

Maria Elizabeth <u>Currie</u>

Biomedical Engineering Graduate Program

A thesis submitted in partial fulfillment
of the requirements for the degree of
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Abstract

New cardiovascular techniques have been developed to address the unique requirements of high risk, elderly, surgical patients with heart valve disease by avoiding both sternotomy and cardiopulmonary bypass. However, these techniques pose new challenges in visualization, force application, and intracardiac navigation. Force feedback and augmented reality (AR) can be applied to minimally invasive mitral valve repair and transcatheter aortic valve implantation (TAVI) techniques to potentially surmount these challenges.

Our study demonstrated shorter operative times with three dimensional (3D) visualization compared to two dimensional (2D) visualization; however, both experts and novices applied significantly more force to cardiac tissue during 3D robotics-assisted mitral valve annuloplasty than during conventional open mitral valve annuloplasty. This finding suggests that 3D visualization does not fully compensate for the absence of haptics, including force feedback, in robotics-assisted cardiac surgery. Subsequently, using an innovative robotics-assisted surgical system design, we determined that direct force feedback may improve both expert and trainee performance using robotics-assisted techniques. We determined that during robotics-assisted mitral valve annuloplasty the use of either visual or direct force feedback resulted in a significant decrease in forces applied to cardiac tissue when compared to robotics-assisted mitral valve annuloplasty without force feedback.

We presented NeoNav, an AR-enhanced echocardiograpy intracardiac guidance system for NeoChord off-pump mitral valve repair. Our study demonstrated superior tool navigation accuracy, significantly shorter navigation times, and reduced potential for injury with AR enhanced intracardiac navigation for off-pump transapical mitral valve repair with neochordae implantation. In addition, we applied the NeoNav system as a safe and inexpensive alternative imaging modality for TAVI guidance. We found that our proposed AR guidance system may achieve similar or better results than the current standard of care, contrast enhanced fluoroscopy, while eliminating the use of nephrotoxic contrast and ionizing radiation.

These results suggest that the addition of both force feedback and augmented reality image guidance can improve both surgical performance and safety during minimally invasive robotics-assisted and beating heart valve surgery, respectively.

Keywords

Co-Authorship Statement

Chapter 2 is adapted the following work:

• Currie ME, Trejos AL, Rayman R, Chu MWA, Patel R, Peters TM, Kiaii B. The role of three-dimensional visualization in robotics-assisted cardiac surgery. Proc SPIE 2012; 8316: 83160F1-10.

• Currie ME, Romsa J, Fox S, Vezina WC, Akincioglu C, Warrington JC, McClure RS, Stitt LW, Menkis AH, Boyd WD, Kiaii B. Long-term angiographic follow-up of robotics-assisted coronary artery revascularization. Ann Thorac Surg 2012;93:1426-1431.

• Currie ME, Trejos AL, Rayman R, Chu MWA, Patel R, Peters TM, Kiaii B. Evaluating the effect of three dimensional visualization on force application and performance time during robotics-assisted mitral valve repair. Innovations (Phila) 2013; 8(3): 199-205.

My contribution to this chapter involved (i) designing the surgical test bed, (ii) conducting experiments, and (iii) analyzing data. All authors participated in data acquisition and manuscript preparation.

Chapter 3 is adapted from the following work:

• M. E. Currie, A. L. Trejos, R. Rayman, M. W. A. Chu, R. Patel, T. M. Peters, B. Kiaii. The role of haptics in robotics-assisted mitral valve annuloplasty. Hamlyn Symposium on Medical Robotics, July 2012, London, England.

• Visual and Direct Haptic Feedback in Robotics-Assisted Cardiac Surgery. M. E. Currie, A. Talasaz, A. L. Trejos, R. Rayman, M. W. A. Chu, B. Kiaii, T. M. Peters, R. Patel. Minimally Invasive Robotic Association International Congress, September 2012, Boston, USA.

• M. E. Currie, A. Talasaz, A. L. Trejos, R. Rayman, M. W. A. Chu, B. Kiaii, R. Patel, T. M. Peters. The Role of Visual and Direct Haptics in Robotics-Assisted Mitral Valve Annuloplasty. Journal of Medical Robotics and Computer Assisted Surgery (Submitted).

This work involved collaboration with Dr. Ali Talasaz designed and wrote complex control algorithms and a safety system for the 7-DOF dual arm teleoperation system with force

feedback, Dr. Ana Luisa Trejos sensorized the da Vinci needle drivers used in the experimental work, Dr. Harman Bassan performed mechanical design of the grasping mechanism of the 7-DOF Haptic Wand, and with Simon Perreault helped with development of kinematics modeling of the 7-DOF Haptic Wand and the da Vinci needle driver instrument. Drs. R. Rayman and M. W. A. Chu performed the trials and contributed to preparation of the manuscript. Drs. B. Kiaii, R. Patel, and T. Peters supervised the experiments and presentations, and were involved in manuscript preparation. My contribution to this chapter involved (i) designing the surgical test bed (ii) conducting experiments and (iii) analyzing data.

Chapter 4 is adapted from the following work:

- Chu MW, Moore J, Peters T, Bainbridge D, McCarty D, Guiraudon GM, Wedlake C, Lang P, Rajchl M, Currie ME, Daly RC, Kiaii B. Augmented reality image guidance improves navigation for beating heart mitral valve repair. Innovations (Phila). 2012 Jul-Aug; 7(4): 274-81.
- Moore JT, Chu MW, Kiaii B, Bainbridge D, Guiraudon G, Wedlake C, Currie M, Rajchl M, Patel RV, Peters TM. A navigation platform for guidance of beating heart transapical mitral valve repair. IEEE Trans Biomed Eng. 2013 Apr; 60(4): 1034-40.

This work involved collaboration with Neochord, Inc. and Dr. Richard Daly who contributed to the design and use of the NeoChord device. It is important to note the significant contributions of the following individuals in the design and implementation of the NeoNav guidance system. Chris Wedlake wrote the programs for augmented reality tracking. John Moore constructed the magnetically tracked devices, tested their effectiveness, and organized the navigation trials with surgeons. My contribution to these manuscripts involved organizing and conducting experiments.

The remainder of the chapter is a summary of:

- Currie ME. NeoChord Progress Report. Safety and performance study of the NeoChord Suturing Device in subjects with degenerative mitral valve disease diagnosed with severe mitral regurgitation. NeoChord. September, 2013.

v

This report was submitted as part of an agreement with NeoChord, Inc.

Chapter 5 is adapted from the following work:

- McLeod AJ, Currie ME, Moore JT, et al. Phantom study of an ultrasound guidance system for transcatheter aortic valve implantation. Comput Med Imaging Graphics. 2014 Dec 15.
- Currie ME, McLeod AJ, Moore JT, Chu MWA, Patel R, Kiaii B, Peters T. Augmented Reality System for Ultrasound Guidance of Transcatheter Aortic Valve Implantation. Innovations (Phila). Accepted 2015.

My contribution to this chapter involved designing and conducting experiments and analyzing data.

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Table of Contents

List of Abbreviations and Terms

2D	Two-Dimensional
3D	Three-Dimensional
ANOVA	Analysis of Variance
AR	Augmented Reality
ASD	Atrial Septal Defect
CABG	Coronary Artety Bypass Graft
CT	Computed Tomography
DOF	Degree-of-freedom
ECG	Electrocardiogram
ED	End-diastole
EROA	Effective Regugitant Orifice Area
ES	End-systole
Haptics	Comprises kinesthetic, tactile, and proprioceptive information. Kinesthetic feedback provides position, force, and movement information and can be acquired using a force/torque sensor. Tactile feedback includes the sensation of vibration, shape, and texture. Proprioception provides the sense of position and movement of body segments.
LA	Left Atrium
LAD	Left Anterior Descending coronary artery
LV	Left Ventricle
MRI	Magnetic Resonance Imaging
MTS	Magnetic Tracking Systems
MV	Mitral Valve
MVA	Mitral Valve Annulus
OR	Operating Room
PISA	Proximal Isovelocity Surface Area
P_kV_{reg}	Peak Velocity of the Regurgitant Jet
PTFE	Polytetrafluoroethylene
RA	Right Atrium
RMS	Root Mean Squared
RV	Right Ventricle

TAVI	Transcatheter Aortic Valve Implantation
TEE	Transesophageal Echocardiography
TTE	Transthoracic Echocardiography
US	Ultrasound
V_a	Aliasing Velocity
VTK	Visualization Toolkit

Chapter 1

1   Introduction

Mitral valve regurgitation is the most common valvular heart disease affecting 2-6% of the general population [1]. However, in Canada, approximately 40% of patients with indications for mitral valve surgery receive no operation due to the perceived risk of conventional mitral valve surgery involving median sternotomy and cardiopulmonary bypass [2]. A large proportion of these patients are elderly with multiple comorbidities.

Similarly, degenerative calcific aortic valve stenosis has increased prevalence in the elderly and surgical aortic valve replacement is the only treatment for this heart valve disease [3-5]. Without aortic valve replacement, the one-year mortality of patients with severe symptomatic aortic stenosis is 30%–50% [5-7]. Nevertheless, many patients are denied surgery because of the perceived risk of conventional aortic valve replacement. Transcatheter aortic valve implantation (TAVI) has emerged as an effective alternative treatment to conventional aortic valve surgery in high risk surgical patients with multiple comorbidities [7]. Unfortunately, TAVI relies on the use of single-plane fluoroscopy and nephrotoxic contrast medium for valve deployment and the use of multiple contrast fluoroscopic images can increase a patient's risk of acute kidney injury [8-11]. In fact, the development of acute kidney injury is an independent predictor of prolonged hospital stay and impaired early survival following cardiac surgery [11-13].

Clearly, new cardiovascular techniques must be tailored to address the unique requirements of high risk, elderly, surgical patients with mitral valve regurgitation and aortic valve stenosis. This chapter will review mitral valve regurgitation, surgical techniques for mitral valve repair, and the challenges posed by innovation in surgical

mitral valve repair. In addition, these challenges will be compared and contrasted with those of TAVI for aortic valve stenosis.

1.1   Mitral Valve Anatomy

The mitral valve opens to permit the passage of oxygenated blood from the left atrium to the left ventricle during diastole. It closes to ensure efficient flow of oxygenated blood through the aortic valve during systole and to prevent backflow of blood into the left atrium during systolic ventricular contraction. Mitral valve regurgitation occurs when the anterior and posterior leaflets of the mitral valve fail to coapt or close normally during systole. This allows blood to leak back from the left ventricle to the left atrium during systole. Dysfunction of any part of the mitral valve apparatus may result in mitral valve regurgitation; therefore, a thorough knowledge of mitral valve anatomy is necessary for the understanding of both mitral valve pathology and surgical repair.

The mitral valve apparatus consists of the left ventricle, the mitral valve annulus, the anterior and posterior mitral valve leaflets, the chordae tendineae, and the anterolateral and posteromedial papillary muscles (Figure 1.1). The **left ventricle** both encloses and supports the mitral valve apparatus. The **mitral valve annulus** is divided into an anterior fibrous portion and a posterior muscular portion. The anterior portion is in continuity with the left coronary and noncoronary cusps of the aortic valve. It occupies one third of the mitral valve circumference. The anterior mitral valve annulus is separated from the posterior mitral valve annulus by the right and left fibrous trigones. The posterior portion of the annulus is in continuity with both the atrial and ventricular muscle. It occupies two thirds of the mitral valve circumference [14]. As the posterior annulus is primarily muscular and not fibrous, it is primarily affected by any enlargement or dilatation of the left ventricle. Critical cardiac structures also lie adjacent to the posterior mitral valve annulus. The circumflex coronary artery is adjacent to the left half of the posterior mitral

valve annulus. The coronary sinus is adjacent to the right half of the posterior mitral valve annulus. Dilatation of the mitral valve annulus may increase the distance between the anterior and posterior mitral valve leaflets, and, in turn may prevent leaflet **coaptation** or closure. This will result in mitral valve regurgitation.
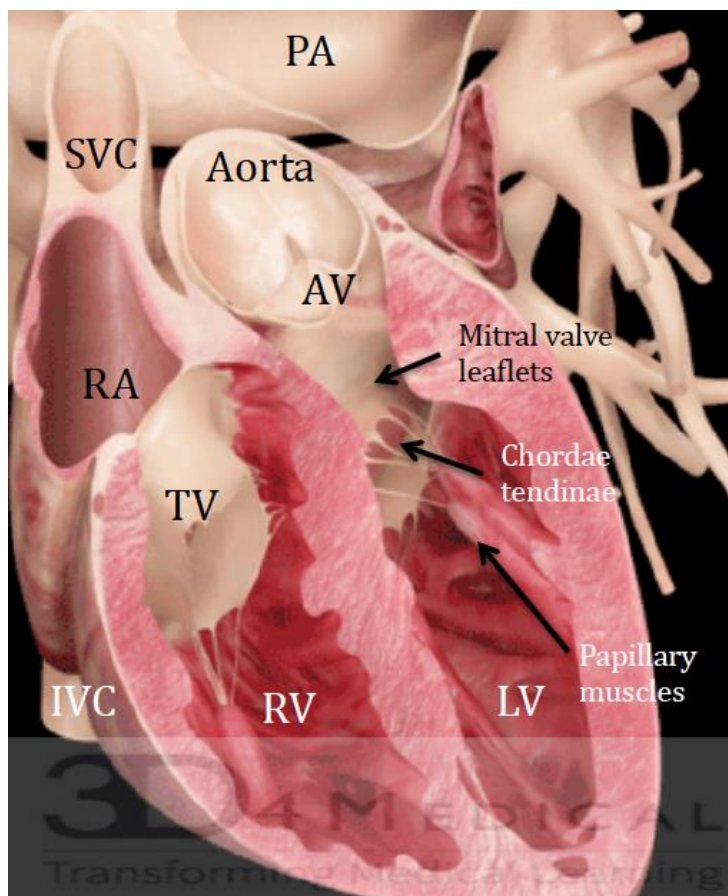
Figure 1.1: Cardiac anatomy with mitral valve apparatus. Adapted with permission from Heart Pro III, 3D4Medical.com, LLC. SVC: superior vena cava, RA: right atrium, IVC: inferior vena cava, TV: tricuspid valve, RV: right ventricle, PA: pulmonary artery, AV: aortic valve, LV: left ventricle.

The **anterior, or septal, leaflet** comprises anterior (A1), middle (A2), and posterior segments (A3). The posterior leaflet comprises anterolateral (P1), middle (P2), and posteromedial (P3) scallops (Figure 1.2) [15]. Although leaflets usually have three scallops, there can be as many as five or six on a leaflet. The anterior and posterior mitral valve leaflets are separated by anterolateral and posteromedial commissures. Failure of the anterior and posterior leaflets to coapt leads to mitral valve regurgitation. This may be secondary to any component of the mitral valve apparatus, as all these elements have an integral role in mitral valve leaflet motion and coaptation.

Three orders of **chordae tendineae** insert on the anterior and posterior valve leaflets [15]. First order chordae tendineae connect the free edge of the leaflets to the **anterolateral and posteromedial papillary muscles** and prevent the leaflet edges from **prolapse**, or displacement into the left atrium, during systole. The anterolateral papillary muscle is supplied by the left anterior descending artery and circumflex artery. The posteromedial papillary muscle is supplied by the right coronary artery or by the dominant circumflex artery in ten percent of the population [14]. Second order chordae tendineae insert on the ventricular surface of the leaflet. These thick chordae may attach the leaflet to two different papillary muscles or attach one papillary muscle to the ventricular wall. These chordae are required for optimal ventricular motion during systole. Third order, tertiary or basal, chordae tendineae are short and broad fibers that connect the ventricular surface of the leaflet to the ventricular wall [15]. In total, 15 to 32 major chordae tendineae trunks give rise to over one hundred individual chordeae that attach to the mitral valve leaflets. Elongation and rupture of the papillary muscles or chordae tendineae may also lead to mitral valve regurgitation as the corresponding leaflet segment may prolapse into the left atrium preventing normal leaflet coaptation.

The mitral valve orifice area varies between 5-11.4 cm^2 with an average area of 7.6 cm^2 [14]. This area increases in size throughout late systole into diastole and decreases in size during atrial contraction at the end of diastole. The annulus also varies in shape and position throughout the cardiac cycle. The mitral valve forms a hyperbolic paraboloid or saddle shape wherein the center of the anterior mitral valve leaflet is furthest away from the left ventricular apex. During systole, the posterior leaflet moves toward the anterior leaflet and the annulus moves 3-16 mm toward the left ventricular apex. During diastole, the posterior leaflet moves away from the anterior leaflet and the annulus moves away from the left ventricular apex and 2-4 mm into the left atrium. Changes in left ventricular function and shape may alter the normal size, shape, and motion of the mitral valve annulus through the cardiac cycle. This may also result in mitral valve regurgitation.
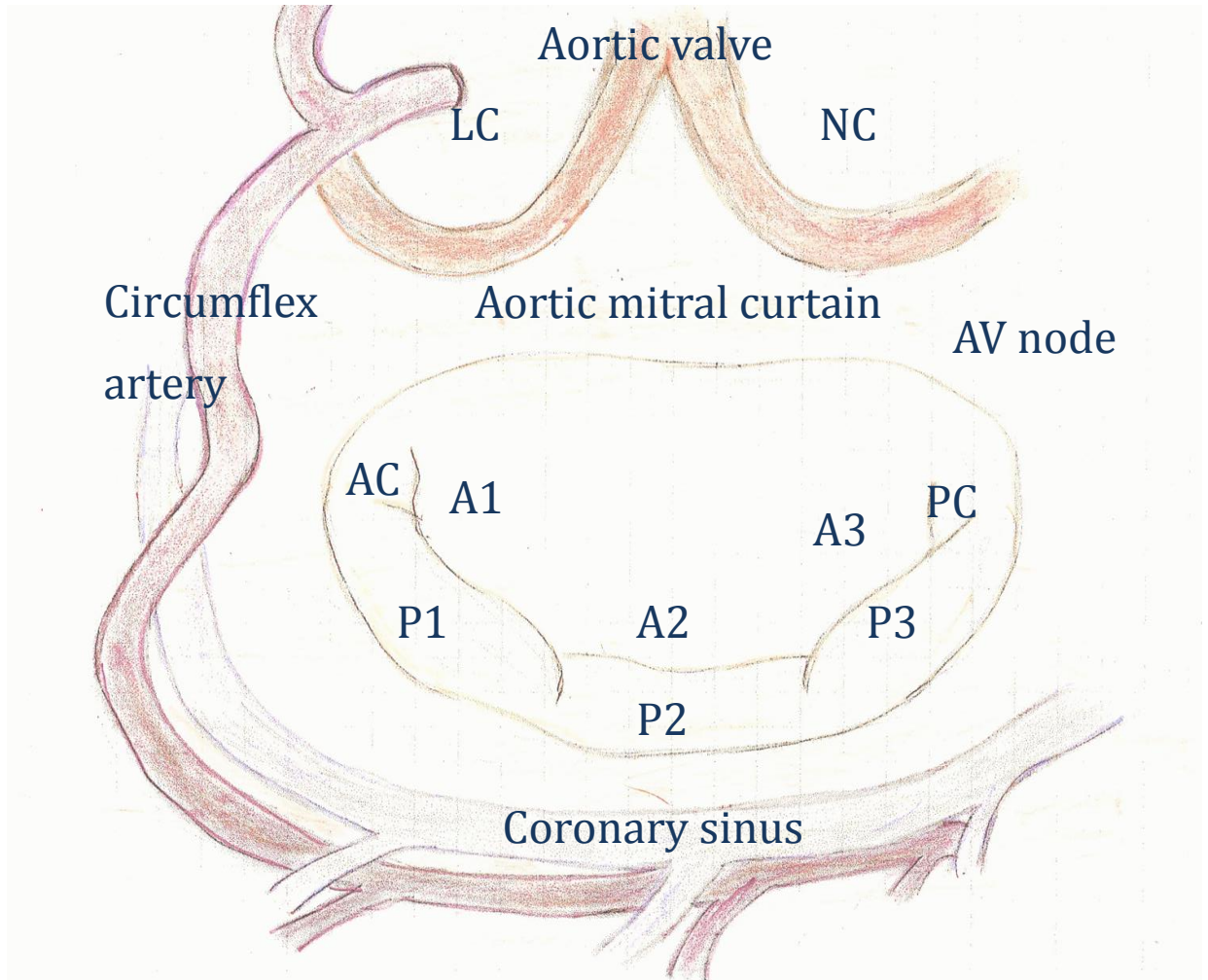
Figure 1.2: Mitral valve with surrounding critical anatomy. AC: anterior commissure, PC: posterior commissure, AV node: atrioventricular node, LC: left coronary sinus of aortic valve, NC: noncoronary sinus of aortic valve.

1.2   Classification of mitral valve regurgitation

Normal function of the mitral valve apparatus depends on the proper coordinated interaction of all of its components. Dysfunction of the left ventricle, the mitral valve annulus, the anterior and posterior mitral valve leaflets, the chordae tendineae, or the anterolateral and posteromedial papillary muscles will result in failure of the mitral valve leaflets to coapt during systole, or mitral valve regurgitation. Mitral valve regurgitation can be classified by the etiology, the location of the lesion, and the resulting valve dysfunction [16].

1.2.1   Mitral Valve Regurgitation Classified by Etiology

A thorough understanding of mitral valve etiology is required as it dictates disease prognosis, surgical treatment, and medical therapy. Firstly, the etiology of mitral valve regurgitation may be primary or secondary. Primary mitral valve regurgitation is the result of pathology involving the mitral valve leaflets or chordae; for example, rheumatic valve disease, infective endocarditis, or degenerative mitral valve regurgitation. Secondary mitral valve regurgitation is the result of pathology involving the myocardium, the muscular tissue of the heart, and as a result, affect valve function; for example, ischemic mitral valve regurgitation [16]. The underlying etiology of mitral valve regurgitation affects the disease prognosis and the medical and surgical management. These etiologies may result in lesions in one or multiple components of the mitral valve including the annulus, leaflets, commissures, papillary muscles, or left ventricle.

1.2.2   Mitral Valve Regurgitation Classified by Lesion Location

Certain lesions are characteristic of specific mitral valve regurgitation etiologies. For example, degenerative mitral valve regurgitation commonly results in excess leaflet tissue and thin chordae or chordal rupture. Rheumatic mitral valve regurgitation results in

leaflet and chordae thickening with commissure fusion. Infective endocarditis may result in chordal rupture and leaflet vegetations and perforations. Finally, ischemic mitral valve regurgitation may result in a dilated annulus, restricted or tethered chordae tendineae and leaflets, and displaced papillary muscles. Therefore, a thorough understanding of the lesions contributing to mitral valve regurgitation is essential for appropriate surgical planning.

1.2.3   Mitral Valve Regurgitation Classified by Function

To guide surgical planning, Carpentier developed a functional classification of mitral valve regurgitation based on leaflet motion [16]. Using this classification, the sum of effects from an etiology of mitral valve regurgitation on components of the mitral valve apparatus can be summarized based on the resulting leaflet motion. Type I mitral valve regurgitation has normal leaflet motion. Mitral valve regurgitation is due to lack of leaflet coaptation, annular dilatation from a dilated or ischemic left ventricle, or leaflet damage in the form of perforation, tear, or vegetation. Type II mitral valve regurgitation involves excessive leaflet motion or prolapse of a leaflet edge into the left atrium. This may be due to elongation or rupture of chordae tendineae or papillary muscles. The degree of prolapse can be measured using echocardiography. Type III mitral valve regurgitation involves the limitation or restriction of leaflet motion such that the leaflets do not coapt. This may be further classified into leaflet restriction during diastole (Type IIIa) or during systole (Type IIIb). Rheumatic mitral valve regurgitation typically results in Type IIIa valve dysfunction. Ischemic mitral valve regurgitation typically causes papillary muscle displacement and leaflet tethering that results in Type IIIb valve dysfunction [16].

1.3   Natural History of Mitral Valve Regurgitation

The natural history of mitral valve regurgitation depends on the etiology, the acuteness or chronicity of the disease, the severity of mitral valve regurgitation, and the patient's age and underlying comorbidities, particularly left ventricular dysfunction.

1.3.1   Natural History of Rheumatic Mitral Valve Regurgitation

Rheumatic fever remains a common cause of mitral valve regurgitation in developing countries; however, its incidence in Canada and the United States has greatly diminished [14, 17-20]. During the first episodes of rheumatic fever in childhood, patients may develop acute mitral valve regurgitation. This occurs as a result of annular dilatation and leaflet edema and prolapse with myocarditis or inflammation of cardiac muscle [14, 21, 22]. Those with posterior leaflet prolapse, not anterior leaflet prolapse, have a less favorable outcome and often require early surgical repair [22]. After remission of the acute process, myocarditis subsides and annular dilatation regresses leading to reversion of mitral valve regurgitation in some cases. However, in most cases, there is progressive leaflet thickening, fusion, prolapse, and chordae shortening or rupture leading to mitral valve regurgitation and stenosis [20]. It is unknown why rheumatic fever leads to valvular stenosis in some patients and pure regurgitation in others [18].

1.3.2   Natural History of Mitral Valve Regurgitation Secondary to Infective Endocarditis

Infective endocarditis is an uncommon cause of pure mitral valve regurgitation. It may occur on a previously abnormal mitral valve or pass from an infected aortic valve to the anterior leaflet of the mitral valve to produce perforation and mitral valve regurgitation. Further infection may cause destruction of both mitral valve cusps and chordae tendineae

[23]. Mortality for mitral valve regurgitation secondary to infective endocarditis is high and may be related to uncontrolled systemic infection [23].

1.3.3   Natural History of Ischemic Mitral Valve Regurgitation

Mitral valve regurgitation is a frequent complication of an acute myocardial infarction and has been detected in up to 39% of patients early after an infarction [24]. There are multiple mechanisms wherein ischemic heart disease may produce mitral valve regurgitation. Papillary muscle rupture, altered papillary muscle position and dynamics, annular dilatation and shape change, and left ventricular remodeling may all occur following a myocardial infarction; and they may all contribute to incomplete leaflet coaptation [14, 23, 24].

Papillary muscle rupture is a rare but potentially fatal complication of an acute myocardial infarction, occurring in 1-3% of patients following a myocardial infarction [24]. Rupture usually occurs two to seven days after myocardial infarction and accounts for approximately half of the acute mitral valve regurgitation in patients following a myocardial infarction. Patients develop acute mitral valve regurgitation with pulmonary edema and hypotension. Without urgent surgery, approximately 50 to 75% of these patients may die within 24 hours. Survival after partial papillary rupture is slightly better at more than 70% within the first 24 hours, and approximately 50% at one month [25]. They are then considered to have chronic mitral valve regurgitation.

Left ventricular systolic dysfunction and remodeling following myocardial ischemia may also produce mitral valve regurgitation. Incomplete mitral coaptation in the mitral valve regurgitation in the setting of left ventricular dysfunction and dilatation is called functional mitral valve regurgitation [26-28]. Ischemic mitral valve regurgitation is a

subset of functional mitral valve regurgitation and occurs in approximately 15% of patients with anterior wall involvement and up to 40% of patients with an inferior infarct [18, 29].

Following a myocardial infarction, left ventricular dysfunction leads to ventricular and mitral valve annulus dilatation. These increased dimensions require the mitral leaflets to cover more area prior to coaptation. Furthermore, remodeling of the left ventricle to a more spherical shape leads to loss of the saddle shape of the normal mitral valve annulus and lateral displacement of the posteromedial papillary muscle. This may increase the distance from the middle of the anterior annulus to the posteromedial papillary muscle tip and affect leaflet coaptation with systolic leaflet tethering [28, 30-33]. Therefore, mitral valve regurgitation occurs with failure of leaflet coaptation despite structurally normal mitral valve leaflets.

1.3.4   Natural History of Degenerative Mitral Valve Regurgitation

Degenerative mitral valve regurgitation encompasses a spectrum of connective tissue changes in the mitral valve apparatus that lead to mitral valve prolapse [34]. Mitral valve prolapse is a billowing of one or both leaflets into the left atrium during ventricular systole. Mitral valve prolapse may occur in younger patients as a result of fibroelastic connective tissue disorders, such as Barlow's mitral valve disease, or in older patients as a result of fibroelastic deficiency. Regardless of etiology, mitral valve prolapse may result in mitral valve regurgitation.

Barlow's mitral valve disease occurs as a result of the replacement of mitral valve leaflet collagen with dermatan sulfate, a glucosaminoglycan [24]. These leaflets may begin to prolapse into the left atrium during systole and fail to coapt. This places more strain on the attached chordae tendineae that, as a result, elongate. Ultimately, some chordae

tendineae rupture. This further exacerbates both mitral valve prolapse and mitral valve regurgitation. These histologic changes and severe valve redundancy are especially pronounced in younger patients. Barlow's mitral valve is characterized by myxomatous leaflet tissue with bileaflet prolapse and by dilatation of the valve annulus. Barlow's syndrome comprises prolapse of the posterior leaflet, chest pain, palpitations, syncope, and dyspnea [14].

Older patients with degenerative mitral valve regurgitation are more likely to have fibroelastic deficiency. This is characterized by abnormal connective tissue of the mitral valve resulting in weakening and rupture of the chordae tendineae [23, 34]. The chordae tendineae are one of the supporting structures of the mitral valve; therefore, their degeneration hinders valve closure and produces mitral valve regurgitation [35]. With degenerative mitral valve disease, the mitral valve leaflets and chordae tendineae become thin and pellucid. The most common cause of severe mitral valve regurgitation is rupture of the elongated chordae (Figure 1.3) [35]. Chordal rupture commonly occurs without any leaflet pathology. This results in unsupported leaflets and a flail leaflet tip. Posterior
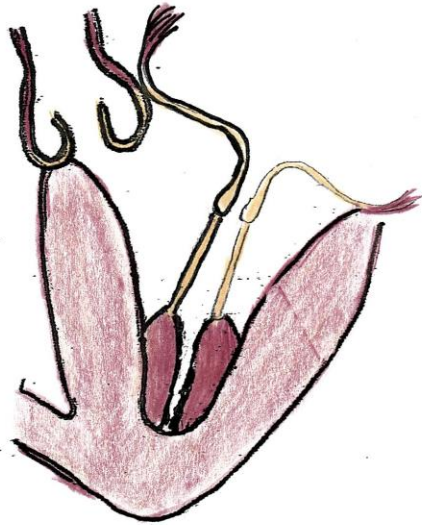
Annular Distension

Leaflet Perforation

Vegetations

Leaflet Tear

Figure 1.3: Etiology of Carpentier Type I Mitral Regurgitation with Normal Leaflet Motion.

Chordal Rupture
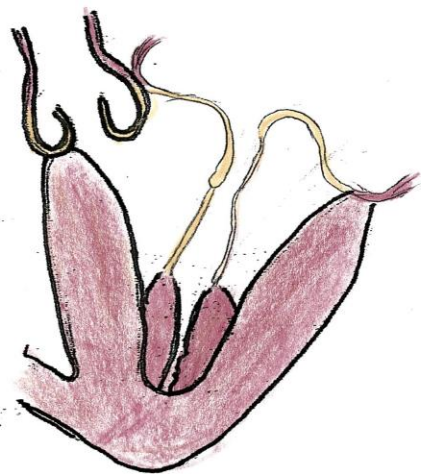
Chordal Elongation

Papillary Muscle Rupture

Papillary Muscle
Elongation

Figure 1.4: Etiology of Carpentier Type II Mitral Regurgitation with Leaflet Prolapse.

Commissure Fusion
Leaflet Thickening

Chordal Thickening
And Fusion
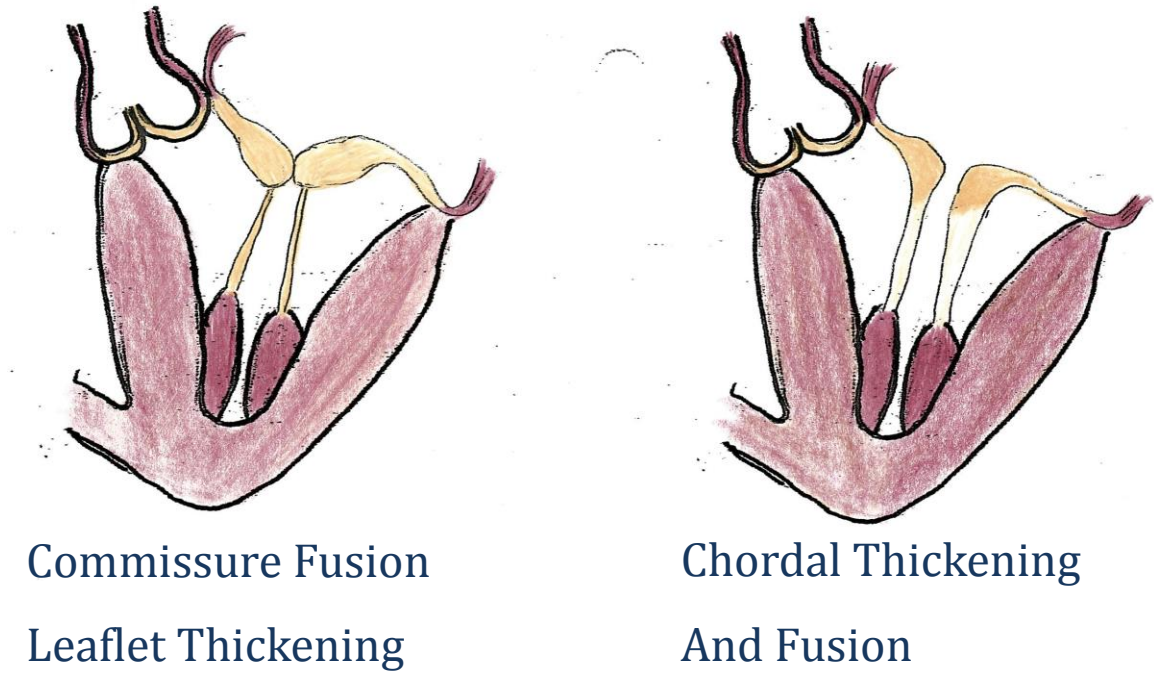
Figure 1.5: Etiology of Carpentier Type IIIa Mitral Regurgitation with Restricted Leaflet Motion During Diastole.

Myocardial Infarction

Ventricular Dilatation
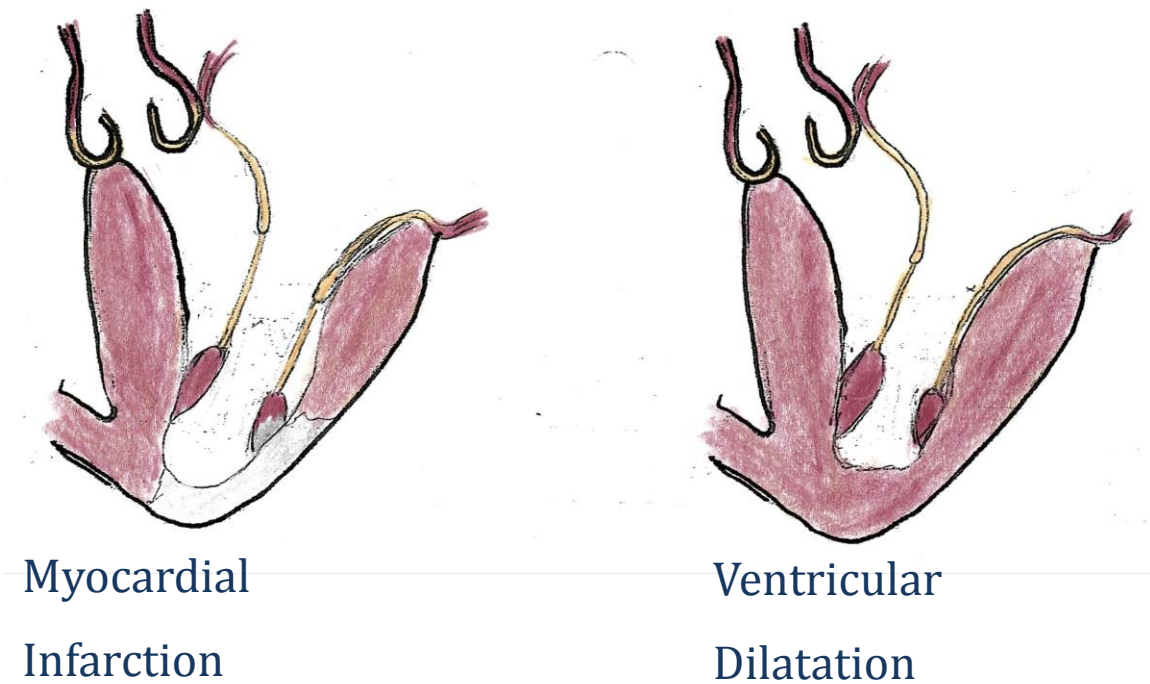
Figure 1.6: Etiology of Carpentier Type IIIb Mitral Regurgitation with Restricted Leaflet Motion During Systole.

chordal rupture is the most commonly seen etiology [18, 36]. Improper closure of the mitral valve leaflets is associated with volume overload and subsequent ventricular and atrial enlargement with dilatation of the mitral annulus, particularly along the posterior aspect of the valve. This leads to atrial fibrillation, heart failure and death [35].

Furthermore, mitral annular calcification may occur with or without degeneration and prolapse of the mitral leaflets [37]. This is usually the result of degenerative disease, seen more commonly in elderly patients, particularly women [17]. The annular calcification may be localized or more extensive with rigid bars up to 2 cm in thickness in the annulus and leaflets [14]. Calcification commonly extends from the posterior annulus

and displaces and immobilizes the posterior leaflet, stretching the attached chordae tendineae to produce mitral valve regurgitation. Ultimately, a rigid bar of calcium may surround the entire posterior annulus and, eventually, the entire mitral valve annulus. Further extension of calcium into the left ventricular septum may result in conduction defects[3]. Finally, systemic embolization of the calcium deposits may occur. Notably, the presence of mitral annular calcification appreciably adds to the complexity of any surgery on the mitral valve [38].

Isolated mitral valve prolapse occurs in 1% to 2.5% of the population and it is the most common cause of mitral valve regurgitation in patients undergoing mitral valve surgery [39-41]. However, not all patients with mitral valve prolapse progress to require surgery. The major predictor of cardiac mortality is moderate to severe mitral valve regurgitation, but only five to ten percent of patients with mitral valve prolapse develop severe mitral valve regurgitation, and rarely before the age of 50 [42, 43]. Severe mitral valve regurgitation due to flail leaflets has been reported to have a mortality of 6.3% per year [44]. The reported 10-year incidence of atrial fibrillation was 30% and the reported 10-year incidence of congestive heart failure was 63% [45]. At 10 years, 90% of patients with severe mitral valve regurgitation have died or undergone surgery [45].

1.3.5   Natural History of Acute Mitral Valve Regurgitation

Acute mitral valve regurgitation may result from partial or complete rupture of chordae tendineae secondary to ischemia, infective endocarditis, or trauma. Regurgitation into the left atrium increases left atrial pressure and reduces forward cardiac output. In patients with acute mitral valve regurgitation with normal or reduced left atrial compliance, a sudden increase in left atrial pressure initially elevates pulmonary vascular resistance and results in flash pulmonary edema [17, 46]. Patients experience acute decompensation with pulmonary congestion and hypoxia, or insufficient oxygen supply to tissue. In

addition, the fall in cardiac output through the aortic valve results in hypotension and cardiogenic shock. Finally, severe pulmonary venous hypertension may progress to right-sided heart failure.

1.3.6   Natural History of Chronic Mitral Valve Regurgitation

Chronic mitral valve regurgitation occurs when the gradual progression of mitral valve regurgitation leads to compensatory increases in left atrial and pulmonary venous compliance. Enlargement of the left atrium leads to further dilatation of the mitral valve annulus and worsening of mitral valve leaflet coaptation. In addition, atrial enlargement leads to atrial fibrillation. In one longitudinal study of patients with mitral valve regurgitation, the incidence of atrial fibrillation among those with severe mitral valve regurgitation was over five percent per year [35]. Patients in whom atrial fibrillation develops are at increased risk for adverse cardiovascular outcomes, including cerebral ischemia or stroke [47].

The left ventricle also adapts by increasing the left ventricular end-diastolic volume to maintain adequate forward output. Patients with mild to moderate mitral valve regurgitation may remain asymptomatic for many years. However, this higher preload eventually leads to left ventricular dilatation and spherical remodeling [48]. Therefore, left ventricular size increases as left ventricular contractility decreases.

After the initial compensatory phase, left ventricular systolic contractility becomes progressively impaired [49-51]. However, because the afterload is low as a result of ejection of part of the stroke volume into the low-pressure left atrium, the ejection fraction can be normal despite depressed systolic function [51-53]. Therefore, left ventricular end systolic volume is a better estimate of severity of mitral valve regurgitation than ejection fraction, end-diastolic volume, or end-diastolic pressure [54].

A lower afterload and increased preload allows the heart to compensate for chronic mitral valve regurgitation for many years before symptoms occur [17]. However, the rate of death from cardiovascular causes among asymptomatic patients with at least moderate mitral valve regurgitation exceeds three percent per year [35].

The advanced stage of left ventricular decompensation can result in irreversible left ventricle changes. However, as left ventricular dysfunction progresses, patients may exhibit symptoms of heart failure including dyspnea. Without intervention, the rate of death among symptomatic patients with at least moderate mitral valve regurgitation exceeds five percent [55-57].

1.4   Role of Imaging in Mitral Valve Regurgitation

The presence of symptoms is a crucial, but subjective determinant of mitral valve regurgitation severity; therefore, multiple cardiac imaging modalities are used to provide a more objective assessment. Cardiac imaging is used to determine the etiology, the severity, and the surgical timing and approach in patients with mitral valve regurgitation. The roles of transthoracic echocardiography, transesophageal echocardiography, cardiac angiography, and magnetic resonance imaging will be discussed.

1.4.1   Role of Transthoracic Echocardiography

Transthoracic echocardiographic (TTE) images are used to determine the etiology and severity of chronic primary mitral valve regurgitation. These images are two-dimensional and demonstrate the details of leaflet pathology. Firstly, the degree and location of mitral valve prolapse can be ascertained. Echocardiographic diagnosis of mitral valve prolapse requires prolapse of 2 mm or more above the annulus in the long-axis parasternal view [58, 59]. Furthermore, Doppler color flow imaging can identify the location and magnitude of the mitral regurgitant flow. Secondly, TTE can demonstrate

valve disruption or perforation from infective endocarditis, chordal rupture, and papillary muscle rupture. This is especially useful when there are no obvious signs of mitral valve regurgitation on physical examination; for example, in acute mitral valve regurgitation, when the rapid rise in left atrial pressure and fall in left ventricular pressure limit both the pressure gradient and the audible murmur in systole [24].

There is no single transthoracic echocardiographic parameter to quantify mitral valve regurgitation [60, 61]. Therefore, as stated in the 2003 American Society of Echocardiography's consensus statement on echocardiographic quantification of valvular regurgitation, it is essential to consider the entire echocardiographic image for an accurate assessment of valve severity [61]. This includes the assessment of mitral valve structure and the measurement of chamber dimensions, Doppler flow, Proximal Isovelocity Surface Area (PISA), and vena contracta width (Table 1.1) [61].

Structural abnormalities, such as an enlarged left atrium or left ventricle and the appearance of the mitral apparatus, can be used to assess the severity of mitral valve regurgitation. As previously mentioned, the onset of left ventricular dysfunction and presence of pulmonary artery hypertension both portend advanced mitral valve regurgitation and poor patient outcomes. Furthermore, increased preload and normal to decreased afterload in chronic mitral regurgitation enable left ventricular ejection fraction to remain above 60%, despite progressive valvular and ventricular dysfunction. Therefore, chamber volumes are used to determine a more accurate measure of left ventricular dysfunction [45]. Mild mitral regurgitation is usually associated with normal or near-normal left atrial size, left ventricular size, and intact mitral apparatus. Moderate mitral regurgitation is frequently associated with some degree of left atrial enlargement, normal or mildly dilated left ventricle, and varying degrees of mitral apparatus abnormalities. Severe chronic mitral regurgitation is usually associated with moderate to

severe left atrial enlargement and some degree of left ventricular dilatation. In addition, it is often associated with flail mitral leaflet, ruptured papillary muscle, or malcoaptation of the mitral leaflets [45].

Colour Doppler flow, illustrating the regurgitation of blood as a jet into the left atrium, is considered to be a qualitative or semi-quantitative measure of mitral valve regurgitation severity. A small jet occupying less than 20% of the left atrial area is graded as mild mitral valve regurgitation. A large jet occupying more than 40% of the left atrial area and extending into the pulmonary veins is graded as severe mitral valve regurgitation [62].

Proximal flow acceleration or proximal isovelocity surface area (PISA) is seen as a concentric series of hemispheric shells of alternating colors, each shell denoting an isovelocity of aliasing [62]. After the color jet crosses the mitral valve, the width of the jet increases. At a given aliasing velocity, the radius of PISA increases with increasing regurgitant volume. In the parasternal long-axis view, the narrowest portion of the regurgitant jet across the valve is defined as the vena contracta. Mild mitral regurgitation is usually associated with a vena contracta less than 0.3 cm, while severe mitral regurgitation is usually associated with a vena contracta of 0.7 cm or more [63, 64].

The effective regurgitant orifice area (EROA) can be calculated by dividing the flow rate through the regurgitant orifice, that is, the product of the surface area of the hemisphere ($2\pi r^2$) and aliasing velocity (V_a), by the peak velocity of the regurgitant jet ($P_k V_{reg}$): EROA = $(2\pi r^2 * V_a)/P_k V_{reg}$ [65]. Mild mitral regurgitation is associated with an EROA of less than less than 0.2 cm. Moderate mitral regurgitation is associated with an EROA of 0.2 to 0.39 cm. Severe mitral regurgitation is associated with an EROA of at least 0.4 cm [45].

Table 1.1: Mitral Regurgitation Severity Assessment by Echocardiography [66].

Measurement	Mild	Moderate	Severe
Regurgitant Volume (mL)	<30	30-60	>60
PISA radius (mm)	<4	4-10	>10
Vena Contracta (mm)	<3	4-6	>7

1.4.2   Role of Transesophageal Echocardiography

Whereas TTE is generally sufficient to determine the etiology and severity of mitral valve regurgitation, transesophageal echocardiography (TEE) provides excellent imaging of the mitral valve apparatus and may provide additional information. Firstly, TEE is indicated when two-dimensional TTE does not provide adequate information regarding the etiology and severity of mitral valve regurgitation. This is particularly important in cases of acute severe mitral valve regurgitation when neither physical examination nor TEE provide a clear diagnosis. As previously noted, acute mitral valve regurgitation may create early equalization of left atrial and ventricular pressures with only narrow eccentric jets that may not be readily seen with TTE. Secondly, TEE is especially useful in cases of mitral valve regurgitation due to infective endocarditis to visualize vegetations and to ascertain if additional adjacent cardiac structures are infected. Thirdly, TEE allows more precise quantitation of mitral valve regurgitation severity and provides more anatomical information for surgical planning and for determining the likelihood of successful valve repair. In particular, three-dimensional TEE provides an enhanced understanding of the mitral valve anatomy for surgical planning. Finally, following repair, an intraoperative transesophageal echocardiogram is used to determine the adequacy of repair. Even mild residual mitral valve regurgitation after repair increases the likelihood of later repair

failure necessitating reoperation. Therefore, recognizing any residual mitral valve regurgitation is critical and often an indication that the repair should be revised. Furthermore, any observed left ventricular inflow or outflow obstruction secondary to the repair should be rectified [67, 68].

However, as TEE is more invasive than TTE, it is not recommended for routine evaluation of patients with mitral valve regurgitation. Furthermore, TEE, which requires sedation, can downgrade the severity of mitral valve regurgitation [69]. Therefore, although TEE is helpful in examining leaflet anatomy it can be misleading due to the nonphysiological conditions under sedation.

1.4.3   Role of Cardiac Angiography

Although not as critical as echocardiography in diagnosis and surgical planning, angiography with a left ventriculogram will also demonstrate mitral valve regurgitation. Whereas Doppler interrogation of the mitral valve with echocardiography measures flow velocity, left ventriculography uses the density of contrast to estimate the amount of blood flow from the left ventricle to the left atrium with mitral valve regurgitation. Firstly, this can be used to estimate the severity of mitral valve regurgitation and left ventricular function. Secondly, any underlying coronary artery disease contributing to ischemic mitral valve regurgitation can be defined by coronary angiography. Thirdly, hemodynamic measurements from cardiac angiography can be used when there is a clinical discrepancy between symptomatic status and noninvasive testing. For example, a normal hemodynamic examination in a symptomatic patient with less than severe mitral valve regurgitation suggests a noncardiac cause for the symptoms. In patients with concomitant lung disease, a normal left atrial pressure and a large transpulmonary gradient suggest pulmonary hypertension due to lung disease rather than mitral valve disease [70]. Finally, all patients older than 40 years should undergo coronary

angiography to detect the presence of concomitant coronary artery disease for revascularization.

1.4.4 Role of Cardiac Magnetic Resonance Imaging

Cardiac magnetic resonance imaging may also be used to assess left and right ventricular volume and function if these values cannot be adequately assessed with TTE. However, this imaging modality is less helpful in establishing the etiology of mitral valve regurgitation [71-73].

1.5 Indications for Surgery in Patients with Mitral Valve Regurgitation

1.5.1 Rheumatic Mitral Valve Regurgitation

As previously mentioned, symptoms such as dyspnea, or shortness of breath, on exertion, orthopnea, or shortness of breath in the recumbent position, and declining exercise are the culmination of the pathophysiology of mitral valve regurgitation. The onset of symptoms may indicate changes in left ventricular function, left atrial compliance, increases in pulmonary artery pressure, and decreases right ventricular pressure. Therefore, once symptoms have occurred, the patient should be considered for mitral valve operation even if medication has led to improvement [23, 74, 75].

Mitral valve repair and mitral valve replacement with preservation of the subvalvular apparatus are the main surgical options for mitral valve regurgitation. As surgical results improve, the indications for surgery are broadening. Improved myocardial protection, cardiopulmonary bypass technology and minimally invasive incisions, coupled with enhanced intensive care unit support have all contributed to improved patient outcomes [14].

The Canadian Cardiovascular Society, the American Heart Association and the American College of Cardiology recommendations for surgical intervention in mitral valve regurgitation are assigned classes of support based on clinical evidence. A **Class I** indication denotes a condition for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective. Whereas, a **Class II** indication denotes a condition for which there is conflicting evidence and/or a divergence of opinion about the usefulness and efficacy of a procedure or treatment. Recommendations for which the weight of evidence is in favor of the usefulness and efficacy of a procedure or treatment are classified as **Class IIa**. Recommendations for which the usefulness and efficacy of a procedure or treatment are less well established by evidence are classified as **Class IIb** [23, 45, 69].

Prior to surgical management of mitral valve regurgitation, the indications for surgery, surgical timing, and operative approach must be carefully planned. Operative candidacy, timing, and surgical approach must take into consideration not only mitral valve regurgitation etiology and severity, but also patients' comorbidities including left ventricular dysfunction. The following section will outline the indications for surgery, surgical management, and surgical outcomes for rheumatic, acute ischemic, chronic ischemic, and degenerative mitral valve regurgitation.

1.5.2   Acute Ischemic Mitral Valve Regurgitation

Acute ischemic mitral valve regurgitation due to complete papillary muscle rupture is a rare but potentially fatal complication following a myocardial infarction. Only 25% of patients are expected to survive if treated nonsurgically. Clearly, acute ischemic mitral valve regurgitation accompanied by hemodynamic instability is a **Class I** indication for emergent mitral valve replacement [56, 69, 74, 76-79].

1.5.3   Chronic ischemic mitral valve regurgitation

The surgical management of chronic ischemic mitral valve regurgitation requires consideration of not only the etiology and severity of mitral regurgitation, but also the availability of valve repair and operative mortality risk. Furthermore, the literature does not offer strict guidelines for the surgical management of chronic ischemic mitral valve regurgitation.

Both the AHA and CCC state that revascularization alone may be sufficient to reverse less than moderate ischemic mitral valve regurgitation [23, 45]. However, no reported randomized trials have compared coronary revascularization alone versus coronary revascularization with mitral valve repair or replacement in patients with mild or moderate mitral regurgitation.

It is a **Class IIb** recommendation for patients with chronic **moderate** ischemic mitral valve regurgitation who are undergoing other cardiac surgery to undergo concomitant mitral valve surgery [23].   It is a **Class IIa** recommendation for patients with chronic **severe** ischemic mitral valve regurgitation who are undergoing other cardiac surgery to undergo concomitant mitral valve surgery [23]. It is a **Class IIb** recommendation for patients with chronic severe ischemic mitral valve regurgitation with symptoms of heart failure to undergo mitral valve surgery [23].

Chronic moderate to severe ischemic mitral regurgitation adds volume overload to a decompensated left ventricle and worsens prognosis in patients with ischemic heart disease. Small randomized controlled trials have demonstrated that mitral valve surgery reduces chamber size and improves peak oxygen consumption in chronic severe ischemic mitral valve regurgitation [57, 80-93]. However, there are sparse data that this surgery

prolongs life or even improves symptoms over an extended time [93-95]. In fact, there is accumulating evidence that in patients with severe functional ischemic mitral regurgitation and left ventricular ejection fraction less than 45%, long-term survival and functional status are not improved by adding mitral valve annuloplasty to coronary revascularization [86, 87, 91, 96-98].

1.5.4   Degenerative Mitral Valve Regurgitation

It is a **Class I** recommendation for patients with chronic severe degenerative mitral valve regurgitation, with or without symptoms of heart failure and a left ventricular ejection fraction greater than 30%, to undergo mitral valve surgery. Mitral repair is recommended over replacement if a successful and durable repair can be accomplished [23]. It is also a **Class I** recommendation for patients with chronic **severe** degenerative mitral valve regurgitation who are undergoing other cardiac surgery to undergo concomitant mitral valve repair or replacement [23]. It is also a **Class IIa** recommendation for patients with chronic **moderate** degenerative mitral valve regurgitation who are undergoing other cardiac surgery to undergo concomitant mitral valve repair or replacement [23].

 For asymptomatic patients, it is a **Class IIa** recommendation for patients with chronic **severe** degenerative mitral valve regurgitation and preserved left ventricular function to undergo mitral valve repair if the likelihood of successful repair is greater than 95% and the mortality rate is less than 1% [23]. It is also a **Class IIa** recommendation for asymptomatic patients with chronic **severe** degenerative mitral valve regurgitation, with preserved left ventricular function and recent onset atrial fibrillation or pulmonary hypertension, to undergo mitral valve surgery if a successful mitral valve repair is highly likely [23].

Excellent surgical outcomes in these patients are due to the low postoperative incidence of congestive heart failure. In fact, the survival of these patients at ten years is equivalent to that expected for a matched population [99-101]. There is recent evidence that asymptomatic patients have better long-term survival than symptomatic patients with the same risk of reoperation if low risk reparative surgery is possible. Furthermore, early surgery improves morbidity and long-term survival [41, 44, 102-108]. Therefore, delaying surgery may lead to the development of left ventricular dysfunction and impair long-term survival and quality of life [109-114].

When patients with chronic severe mitral regurgitation decompensate to the extent that their left ventricular ejection fraction is 30% or less, mitral valve surgery is recommended, but only as a **Class IIb** recommendation [23]. The onset of symptoms, ventricular dysfunction, and pulmonary hypertension all worsen prognosis for mitral valve regurgitation. Therefore, some advocate mitral valve repair in patients with chronic severe degenerative mitral valve disease prior to the onset of symptoms or physiologic sequelae. Reduction annuloplasty may be beneficial in these patients with operative mortality below 10% [115]; however, if mitral valve replacement is required, there is unlikely to be a benefit in symptoms or mortality [116-119].

1.6 Surgical Management of Mitral Valve Regurgitation

As previously stated, there is no proven therapy for the treatment of mitral valve regurgitation; and, in addition, mitral valve replacement with preservation of the subvalvular apparatus and mitral valve repair are the main surgical options. Surgical mitral valve replacement with either a biologic or mechanical prosthesis was the standard treatment for patients with mitral valve disease until effective techniques for valve repair were developed, reducing the risk of complications associated with prosthetic valves. Moreover, current mitral valve repair techniques are associated with lower rates of

operative mortality than mitral valve replacement (1-3% for valve repair versus 5-9% for valve replacement) [120-123]. Therefore, mitral valve repair represents the procedure of choice by current North American and European guidelines for treatment of degenerative mitral valve regurgitation [122, 124]. Certain mitral valve repair techniques can be employed for the treatment of ischemic and rheumatic mitral valve regurgitation; however, often due to the nature and extent of the mitral valve pathology, repair is not possible and the valve is replaced. Mitral valve replacement and repair techniques for specific valve etiologies and their outcomes will be reviewed in this section.

1.6.1   Mitral Valve Replacement

Prior to the onset of mitral valve repair procedures, surgical mitral valve replacement with either a biological or mechanical prosthesis was the standard treatment for patients with mitral valve disease. The first successful mitral valve mechanical prosthesis was developed by Starr and Edwards in 1961 [125]. Over a decade later, St. Jude Medical developed a bileaflet mechanical prosthesis that has remained similar in design and remains widely used today [126-129]. Although bioprosthetic valves were first developed in the 1950s, they did not become available commercially until 1970 [24, 130].

Rheumatic mitral valve regurgitation is a complex, progressive mitral valve disease that may result in concomitant mitral valve regurgitation and stenosis. Therefore, this disease is more suitable for mitral valve replacement because the durability of a repair is limited by disease progression with further thickening and calcification of leaflets and chordal fusion [131-133]. According to ACC/AHA guidelines, mitral valve repair for rheumatic mitral valve regurgitation should only be considered if a durable and successful repair is likely or if long-term anticoagulation for a prosthetic valve is not possible. Additionally, the Canadian Cardiovascular Society's recommended management of acute ischemic

mitral regurgitation is coronary artery revascularization followed by mitral valve replacement with preservation of the subvalvular apparatus [45].

The mitral valve may be approached through either a left or right atrial incision. As the mitral valve apparatus has an integral role in left ventricular contraction, its preservation during mitral valve surgery results in better left ventricular function postoperatively [134-145]. The anterior and posterior chordae tendineae may be preserved by splitting the anterior leaflet centrally and folding the anterior and posterior leaflets laterally prior to prosthesis insertion [146].

The mechanical or biologic prosthesis is sewn into place with pledgeted horizontal mattress sutures on the atrial or ventricular side. Excessive force should be avoided during placement of these annular sutures, as the tissue may be very friable and postoperative ventricular rupture should be avoided. Further care should be taken in avoiding the circumflex artery that is in close proximity to the mitral valve annulus.

1.6.2   Mitral Valve Repair

Prior to the development of the cardiopulmonary bypass machine, closed repair techniques for mitral valve regurgitation were performed by Bailey, Davila, Nichols, and their colleagues [147-149]. In 1957, Lillehei, Merendino, and Bruce and their colleagues were the first to report open repair of mitral valve regurgitation using cardiopulmonary bypass [150, 151]. In subsequent years, a number of surgeons have contributed technical advances in the repair of mitral regurgitation, particularly Carpentier, Duran, Frater, Reed, and their colleagues [152-155].

The goals of mitral valve repair for mitral regurgitation are: to restore physiological leaflet motion, to recreate leaflet coaptation or closure, and to stabilize the mitral annulus, correcting annular dilatation. Many techniques have been proposed to attain these goals

of mitral reconstruction. However, the technique and operative results of mitral valve repair are highly dependent on both the etiology of mitral valve regurgitation and the anatomy of the valvular apparatus.

1.6.2.1   Repair in Ischemic Mitral Valve Regurgitation

Mitral valve repair techniques may be employed in ischemic mitral valve regurgitation if only one papillary muscle head is ruptured or if both the papillary muscles and chordae tendineae are intact [156, 157]. Mitral valve repair for ischemic mitral valve regurgitation must restore the elements of the mitral valve apparatus that were distorted with left ventricular dilatation and remodeling [158]. These surgical interventions include: coronary revascularization, narrowing the mitral valve annulus, reducing the left ventricular volume and restoring the elliptical shape of the left ventricle from its distorted spherical shape.

In the presence of mild ischemic mitral valve regurgitation, coronary revascularization alone is sufficient. However, if there is at least moderate mitral valve regurgitation, coronary revasculization should be accompanied by concomitant mitral valve surgery, unless the patient has prohibitive operative risk [82, 159-161]. Conventional mitral valve repair is performed through a median sternotomy incision and requires aortic cross-clamping with cardiac arrest and cardiopulmonary bypass.

In order to narrow or to reduce the size of an enlarged mitral annulus and restore leaflet coaptation, an annuloplasty band or ring can be placed [162-165]. Flexible or rigid posterior annuloplasty bands and complete flexible, semi-rigid, rigid, flat, or shaped annuloplasty rings are all available for use. There is no large trial comparing the relative efficacy of these annuloplasty devices. The most important aspect of ring or band selection is to find a size and shape that adequately stabilizes the area between the trigone

of the anterior leaflet of the mitral valve [14]. Eight to twelve sutures deep mattress sutures are used to secure the annuloplasty band or ring. The sutures themselves serve to reinforce the mitral valve repair. For example, sutures at the commissures flatten and narrow the commissure to further annular dilation. Although these sutures reinforce the repair, they may injure cardiac muscle and adjacent cardiac structures. Possible complications during annuloplasty suturing include circumflex coronary artery compromise, atrioventricular dissociation, and dehiscence, or tearing, of the annuloplasty band or ring from the mitral valve annulus [166].

In addition, some recommend left ventricular volume reduction and restoration of the left ventricular elliptical shape. This surgery not only reduces the posterior mitral annulus, but also aims to exclude any noncontracting akinetic or dyskinetic ventricular muscle.

Other techniques used in repair of acute ischemic mitral valve regurgitation include: division of secondary chordae tendineae, and posterior mitral leaflet extension. Division or cutting of secondary chordae tendineae may be used to decrease leaflet tethering [167, 168]. Posterior mitral leaflet extension involves enlarging the posterior half of the posterior leaflet with pericardium [169]. These techniques are also commonly accompanied by mitral valve annuloplasty.

1.6.2.2   Repair in Degenerative Mitral Valve Regurgitation

The surgical techniques used for repair of degenerative mitral valve regurgitation are: posterior leaflet quadrangular resection with or without sliding plasty, triangular resection of the anterior leaflet, chordal transfer, chordal shortening, papillary muscle repositioning, edge to edge repair, and chordal replacement with artificial expanded polytetrafluoroethylene sutures [45].

Following median sternotomy and establishment of cardiopulmonary bypass, the mitral valve is exposed. Each element of the mitral valve apparatus is examined and areas of prolapse and regurgitation are identified. Normal chordae tendineae are distinguished from the abnormal or ruptured chordae. The middle segment of the posterior leaflet, P2, is the most commonly affected part of the valve in degenerative mitral valve disease [170]. The P2 portion of the posterior leaflet is severely prolapsed in approximately 80% of patients with mitral regurgitation. The most critical element in repair of P2 prolapse is to decrease the height of the posterior leaflet.

Several techniques have been developed to repair P2 prolapse. The most commonly used technique is resection of the redundant posterior leaflet tissue to reduce the height of the posterior leaflet and to eliminate mitral regurgitation. This can be accomplished with quadrangular resection with or without sliding plasty, when there is a more extensive leaflet segment prolapsing (Figure 1.5) [166]. A rectangular section of the prolapsed leaflet is excised. The resulting gap is bridged with interrupted nonabsorbable sutures from the base of the resected leaflet. Alternatively, with a sliding plasty, adjacent normal portions of the posterior leaflet are incised at their bases and moved centrally to obliterate the gap [24]. An annuloplasty band or ring is usually sutured in place to prevent further annular dilatation. In the case of bileaflet prolapse without anterior chordal pathology, posterior leaflet quadrangular resection and annuloplasty alone may be sufficient to resolve any mitral valve regurgitation [171]. Annular plication can be used in extensive posterior leaflet prolapse to reduce tension of the suture line of the reconstructed leaflet by imbricating the annulus back into the left atrium. In cases with short segments of redundant posterior leaflet, repair can be accomplished by completing a folding plasty. Folding plasty involves tacking the leading edge of the posterior leaflet to the underside of the leaflet at the annulus, decreasing the height by fifty percent [166].

Anterior leaflet pathology is more challenging and less often successful than posterior leaflet repair. For triangular resection of a prolapsed anterior leaflet, a triangular wedge, extending no more than one third of the diameter of the involved anterior leaflet, is resected [172, 173]. Finally, an annuloplasty band or ring is usually sutured in place to prevent further annular dilatation.

In addition, more technically challenging techniques have been developed for the resolution of anterior leaflet mitral valve prolapse. Chordal transfer involves excising the leaflet insertion of a normal intact chord from the posterior leaflet and attaching it to the anterior prolapsing sectorn [174]. Chordal shortening involves embedding the elongated anterior chordae tendineae in an incised papillary muscle [175, 176]. Papillary muscle repositioning was also developed to eliminate anterior leaflet prolapse. With A1 to A2 prolapse, the anterior head of the anterolateral papillary muscle can be repositioned. With A2 to A3 prolapse, the anterior head of the posteromedial papillary can be repositioned [177]. Finally, a simple technique for treatment of anterior leaflet prolapse was developed by Alferi and colleagues [178, 179]. This technique involves approximating the free edge of the anterior and posterior leaflets with one or two mattress sutures to create a double mitral valve orifice [180]. The resultant orifices should be at least 2 cm in diameter [181]. However, mitral valve stenosis is a possible complication of this technique if the resulting mitral valve orifices are too small. This technique can be used for anterior leaflet prolapse, bileaflet prolapse, posterior leaflet prolapse with severe annular calcification, or when other surgical repair techniques have failed [166].

More recently, polytetrafluoroethylene (PTFE) neochordae have been used to replace diseased chordae tendineae causing anterior or posterior mitral valve prolapse. These size 5-0 PTFE chords are used support the free edge of the prolapsing leaflet and to displace abnormal excess tissue into the ventricle, ensuring a good surface of coaptation

instead of resection of leaflet tissue [182, 183]. The neochordae are made short enough to displace the prolapsing segment into the left ventricle and to ensure a large surface of coaptation for the anterior leaflet while preventing anterior leaflet displacement in the outflow tract [166]. A double-armed suture is passed twice through the usually fibrous tip of the papillary muscle; each arm is then passed through the area of the leaflet where the native chordae are inserted and then tied.

This technique is associated with low operative mortality, high freedom from re-operation, and long-term survival similar to the general population [176, 182, 183]. Artificial chordae tendinae, or neochordae, do not shrink or break and become covered by an intimal tissue like native chordae [184]. Moreover, this technique is simple and reproducible [182]. Therefore, since 1985, implantation of artificial chordae tendineae has become a well established repair technique for the correction of both posterior and anterior leaflet prolapse with excellent postoperative outcomes [176, 182, 183].

The final step in contemporary repair of mitral valve regurgitation is the insertion of an annuloplasty band or ring. The aim of mitral valve annuloplasty is to restore a normal ratio between the annular size and leaflet surface area in order to restore the normal circumference and shape of the mitral valve to match the available leaflet tissue [185]. In addition, this technique may adjust the shape of the annulus to restore normal geometry. Undersized annuloplasty has been associated with left ventricular reverse remodeling and improvement of symptoms in the majority of patients. Several investigators have concluded that mitral valve annuloplasty as essential to a complete and long-lasting repair [170, 186].

If all this is satisfactory, the left atrium is closed and cardiopulmonary bypass is discontinued. At this point, competence of the valve is assessed by TEE and if more than mild regurgitation is present, the repair is revised or the mitral valve is replaced [187].

1.6.3   Outcomes of Mitral Valve Repair and Replacement

The decision to repair or replace the mitral valve for mitral regurgitation depends on the feasibility of a successful repair and the possibility of survival benefit if a repair is done. As previously indicated, not all cases of mitral valve regurgitation are amenable to valve repair and, therefore, mitral valve replacement is required. For example, rheumatic mitral valve regurgitation is more suitable for replacement than repair because the durability of any repair is limited by disease progression. Therefore, the ACC/AHA recommends repair of rheumatic mitral valve regurgitation only in patients with less advanced disease in whom a durable repair can be accomplished or in patients for whom a mechanical prosthesis cannot be used because of anticoagulation management concerns [80, 188]. Similarly, mitral valve repair may not be feasible in patients with acute ischemic mitral regurgitation with complete papillary muscle rupture and hemodynamic instability.

The benefits of performing mitral valve repair over mitral valve replacement with preservation of the subvalvular apparatus are unclear in patients with chronic **ischemic** mitral valve regurgitation [93-95]. No reported randomized controlled trials have compared mitral valve repair and mitral valve replacement in patients with severe ischemic mitral regurgitation, with or without concomitant coronary revasculization. In fact, current studies show the two surgical approaches provide equally poor results [189-192]. This may be due to the fact that the durability of any mitral valve repair is dependent on any progression of ventricular dilation [57, 80, 83-87, 89-91, 188, 189, 191]. As ischemic left ventricular remodeling is a progressive process, mitral valve repair with annuloplasty may recur as the left ventricle gradually dilates and impairs leaflet coaptation. In an effort to curb this remodeling, surgeons may undertake ventricular restoration surgery; however, the results of this surgery are limited [193-195].

On the other hand, repair of degenerative mitral disease limited to the posterior leaflet has superior mortality and morbidity results as compared to biological or mechanical mitral valve replacement. The reparability of ruptured posterior chordae should be 85% to 90% in degenerative disease [102]. In this case, the operative mortality is less than one percent and long-term survival is equivalent to that of age-matched general population with approximately 95% freedom from reoperation and greater than 80% freedom from recurrent moderate or severe regurgitation at 15 to 20 years after operation [124, 196-198]. Therefore, the AHA guidelines state that mitral valve replacement should not be performed for the treatment of chronic severe degenerative mitral valve regurgitation limited to less than one half of the posterior leaflet unless mitral valve repair has been attempted and was unsuccessful.

In summary, these repair techniques have demonstrated excellent outcomes with a high durability and high freedom from reoperation rate with minimal perioperative mortality. If successful, mitral valve repair enables better preservation of the subvalvular apparatus than mitral valve replacement and, in turn, improved postoperative left ventricular function. Furthermore, mitral valve repair avoids the risk associated with prosthetic heart valves including thromboembolism, anticoagulant related hemorrhage, and structural deterioration [199-101].

1.7   Emerging Challenges in Mitral Valve Repair

Despite these favorable outcomes, a lack of adherence to guidelines addressing the timely referral of patients with indications for mitral valve repair can be observed. Several studies have found that numerous patients with indications for surgery received no operation. For example, Toledano and colleagues [2] surveyed Canadian cardiologists and found nearly 40% of those cardiologists indicated that they delay surgical referral of an asymptomatic patient with severe mitral valve regurgitation until the ejection fraction

fell below 40% or symptoms occur. Furthermore, Mirabel and colleagues found that 49% of patients with symptomatic mitral valve regurgitation from the Euro Heart Survey were not referred for surgery due to advanced age, co-morbidities and a decreased ejection fraction [202].   Patients are either not referred for surgery or denied surgery due to the perceived risk of conventional mitral valve surgery involving median sternotomy for surgical access and cardiopulmonary bypass for exposure of the surgical site.

Median sternotomy is associated with postoperative infection, risk of blood transfusion, prolonged ventilation time, and pain, which may all increase recovery time and stay in hospital. Firstly, sternotomy site infection is the most common postoperative infection following cardiac surgery [203]. Sternotomy infections can range from a superficial skin infection to a deep sternal wound infection, or mediastinitis. Although the most serious wound infection, mediastinitis, has a reported incidence of 0.6-2.65% following cardiac surgery, the mortality rate associated with this infection is 14-23% [203]. Moreover, the proportion of cardiac surgery patients at increased risk of postoperative infection is increasing [204].   This patient population includes the obese, diabetic, elderly, patients with chronic obstructive pulmonary disease, and patients with a history of smoking or previous vascular surgery. All of these patient characteristics are reported as independent predictors of postoperative infections [203, 204].

Secondly, administration of blood products and prolonged ventilation times associated with sternotomy have both been linked to an increased risk of postoperative infections in cardiac surgery patients [203, 205-207]. One study reported that the risk of postoperative infection increases 30% for every day on mechanical ventilation [203]. In addition, patients treated with mechanical ventilation for over 48 hours have a 5.4 times higher risk for developing a severe postoperative infection, a four times higher risk for pneumonia, and a four times increased risk for postoperative sepsis [205].

Cardiopulmonary bypass is employed to remove blood from an arrested heart, to oxygenate the blood, and to maintain oxygenated blood circulation to the remainder of the body during cardiac surgery. Blood is removed through cannulas in the superior and inferior vena cava such that blood does not reach the right atrium. Additional blood is removed using cannulas that pass from the aortic root or through the right upper pulmonary vein into the left atrium and left ventricle. This blood is oxygenated by a membrane oxygenator in the cardiopulmonary pulmonary bypass machine [3]. The oxygenated blood passes to the ascending aorta beyond an aortic cross-clamp. In order to decrease the metabolic demand of the heart during cardiac surgery, the heart is cooled and arrested with a solution called cardioplegia. This solution is infused from the cardiopulmonary bypass machine to the aortic root and coronary arteries through a cardioplegia cannula placed below the aortic cross-clamp. In this way, mitral valve surgery can take place in an arrested, relatively bloodless heart while the remainder of the body is supplied with oxygenated blood.

However, cardiopulmonary bypass has been related to perioperative morbidity and mortality [208, 209]. This is because cardiopulmonary bypass is associated with a generalized systemic inflammatory response, cerebral dysfunction, myocardial depression, and hemodynamic instability [210-212]. The inflammatory response is believed to be caused by exposure of blood to abnormal shear forces from the cardiopulmonary bypass circuit pumps and its contact with the artificial surface of bypass circuit [213-215]. This trauma activates the coagulation and fibrinolytic systems [216] and, as a result, cytotoxic enzymes and inflammatory mediators are released [217, 218]. Therefore, the longer the duration of cardiopulmonary bypass, the longer the exposure to its detrimental effects. Several studies have shown a significant correlation between prolonged cardiopulmonary bypass time and postoperative blood loss and blood product transfusions [219-221], postoperative prolonged mechanical ventilation, pulmonary

edema, or acute respiratory distress syndrome [209, 222, 223], and renal dysfunction [224].

Furthermore, the use of cardiopulmonary bypass has been linked to permanent neurologic dysfunction and postoperative decreases cognition and motor abilities. Application of the aortic cross-clamp may dislodge aortic atheromatous plaque into the aortic arch and carotid arteries to the brain causing a stroke. In addition, decreases in pressure during cardiopulmonary bypass may cause brain ischemia, particularly in patients with narrowed carotid arteries. Artificial oxygenation, microemboli, tissue microaggregates, and gaseous microbubbles from the cardiopulmonary bypass circuit may also occlude the microvessels in the cerebral cortical region, leading to edema and stroke [209]. There is a correlation between prolonged cardiopulmonary bypass time and neurologic complications, such as stroke [225]. Elderly patients with multiple comorbidities are particularly vulnerable to cognitive deficits including stroke [212, 226-232].

Therefore, the two main challenges of conventional cardiac surgery are the sternotomy incision for surgical access and cardiopulmonary bypass for exposure of the surgical site. Both these procedures are associated with risk of longer recovery periods, which may not be as well tolerated in elderly patients with multiple co-morbidities. In Canada, the fastest growing population group is among seniors 65 years and over [233]. In addition, the fastest growth in the senior population is occurring among the most elderly, those seniors 80 years or older [234]. Within this group, cardiovascular disease is the leading cause of death [234]. Clearly, new cardiovascular techniques must be tailored to address the unique requirements of high risk, elderly, surgical patients with mitral valve disease.

1.8   New Surgical Techniques for Mitral Valve Repair

Minimally invasive mitral valve surgery encompasses a spectrum of new operative techniques that aim to minimize surgical trauma by reducing incision size [3].   In order to avoid sternotomy and use smaller incisions, innovative strategies for surgical site access have been developed, including hemisternotomy, minithoracotomy, and totally endoscopic access. Furthermore, these smaller incisions require advanced visualization systems and customized instruments for surgery and cardiopulmonary bypass. Fortunately, simultaneous advances in biomedical engineering have facilitated the use of minimally invasive access for mitral valve repair.

The ascending levels of minimally invasive cardiac surgery are defined in Table 1.2 [3].

Table 1.2: Levels of Ascent in Minimally Invasive Cardiac Surgery [3]

Level 1	Direct Vision	10-12 cm incisions
Level 2	Direct vision/Video Assisted	4-6 cm incisions
Level 3	Video-directed and Robotics-assisted	1.2-4 cm incisions
Level 4	Robotic (computer telemanipulation)	<1.2 cm port sites

Level 1 includes cardiac surgery, including mitral valve repair and replacement, under direct vision using a10-12 cm limited incision that is slightly smaller than the typical median sternotomy. Level 2 includes more complex surgery through a 4 to 6 cm mini incision that requires both direct and video assisted visualization. Level 3 includes surgery through a micro incision measuring 1.2 to 4 cm in size. This smaller incision requires either video or robotics assisted visualization and instrumentation. Finally, Level 4 includes surgery through port sites under 1.2 cm in size. These surgeries are performed using robotic computer telemanipulation [3]. The evolution of minimally

invasive mitral valve repair from Level 1 to Level 4 robotics-assisted mitral valve surgery
will be outlined in the next section.

1.8.1   Robotics-Assisted Mitral Valve Repair

The first minimally invasive mitral valve repair operations were performed under direct
vision in 1996 using ministernal or parasternal incisions [235-237]. Surgeons reported
low surgical mortality (1-3%), low morbidity, and shorter stay in hospital for patients
following these minimally invasive mitral valve repairs [235, 238, 239].

Concurrently, arterial and venous cannulation for cardiopulmonary bypass were modified
to accommodate minimally invasive valve surgery. Arterial access could be obtained via
femoral cannulation, direct aortic cannulation either through the incision, or right axillary
artery cannulation. Venous cannulation and drainage of the right atrium could be
established from direct access through the incision, from the right internal jugular vein, or
from the femoral vein.   Furthermore, a retrograde coronary sinus cardioplegia catheter
can be inserted directly into the right atrium through the incision for myocardial
preservation during cardiopulmonary bypass. Echocardographic guidance of both arterial
and venous cannulas is essential for safe and effective cardiopulmonary bypass using
minimally invasive access.

In order to accommodate aortic cross clamping for minimally invasive valve surgery, an
intra-aortic balloon occlusion and cardioplegia device called Port-access was developed
in 1996 [237, 239-241]. This device is advanced retrograde through the femoral artery
and positioned above the sinotubular junction under echocardiographic guidance. The
balloon is inflated to obstruct aortic blood flow and antegrade cardioplegia is given via
the catheter central lumen and a percutaneous retrograde cardioplegia is introduced via
the internal jugular vein preoperatively under echocardiographic guidance. Aortic

occlusion for minimally invasive valve surgery can also be completed using a standard cross-clamp placed through the incision or using a flexible-handle aortic clamp to increase exposure through the hemi-sternotomy.

Subsequently, Carpentier performed the first video assisted mitral valve repair through a minithoracotomy using hypothermic ventricular fibrillation [242]. Two-dimensional (2D) video-assistance was used for intracardiac visualization. From this experience, Carpentier concluded that 2D visualization was inadequate for detailed repairs [243]. However, other surgeons have successfully completed complex repairs including quadrangular resections, chordal transfers, and synthetic chordal replacements using only 2D visualization.

In 1997, the Aesop 3000 voice-activated camera robot (Intuitive Surgical, Inc., Sunnyvale, CA, USA) was used for minimally invasive videoscopic mitral valve repair. This device provides automatic vision control [244]. The surgeon directs the movement of the 2D endoscopic camera by voice activation and continues to operate with long instruments.

Performance of surgical tasks with 2D vision requires the use of indirect monocular cues to compensate for the lack of depth perception [245]. These cues include the relative position of instruments, anatomic structure size, shading of light and dark, and texture grading [246]. Therefore, performance of detailed skills such as intracorporeal suturing, tying, and fine dissection with 2D visualization requires practice and experience. Previous studies have suggested that because 3D visualization provides more binocular depth cues, depth perception with binocular 3D systems is superior to that achieved with monocular 2D systems [247, 248]. Furthermore, compared to 3D binocular vision, 2D performance with monocular vision affects the kinematics and pattern of human motions. 2D visualization increases movement time and lowers peak velocity. In addition, with 3D

vision, reach and grab tasks are performed faster than with 2D visualization [246, 248-251].

In 1997, minimally invasive mitral valve repair using time three-dimensional (3D) videoscopy was first reported [252]. Despite 3D visualization, simple reconstructions in a series of patients were significantly more difficult than those done through a sternotomy.

In June 1998, Carpentier and Mohr reported the first robotic mitral valve operations using the da Vinci surgical system (Intuitive Surgical, Inc., Sunnyvale, CA, USA) [253, 254]. The surgeon operates from a console through end-affecter instruments that are mounted on robotic arms inserted through port hole incisions in the thorax. These devices emulate human wrist motion with seven full degrees of freedom: x, y, z, pitch, yaw, rotation, and grasp. Additionally, arm insertion and rotation, as well as variable grip strength, give additional freedom to the operating wrist [254, 255]. Lange and associates in Munich were the first to perform a totally robotic mitral valve repair using the da Vinci surgical system [256].

1.8.2   Robotics-Assisted Mitral Valve Repair Outcomes

Currently, minimally invasive techniques, including robotics-assisted surgery, are used for simple to complex mitral valve repairs [255, 257]. Reported outcomes following minimally invasive mitral valve repair show no significant difference in overall mortality between minimally-invasive and conventional approaches. Specialized centres have reported thirty day operative mortality between 0.3% and 2% following robotics-assisted mitral valve repair.

Furthermore, favourable outcomes of patients undergoing cardiac surgery without sternotomy have been reported [238, 239, 258-270]. For example, reductions in mortality among high-risk patients and obese patients have been reported with minimally invasive

cardiac surgery as opposed to cardiac surgery with sternotomy [258]. In addition, patients undergoing minimally invasive cardiac surgery have reduced blood loss, reduced need for reoperation for bleeding, reduced pain, reduced ventilation time, and improved postoperative respiratory function [238, 239, 259-271]. Avoidance of sternotomy incision with minimally invasive techniques has also been reported to significantly decrease patients' postoperative length of stay in the hospital and the intensive care unit [259, 264, 266]. In one study, patients undergoing minimally invasive cardiac surgery had less than half the length of stay in hospital than patients who had undergone cardiac surgery with sternotomy [266]. These patients experience more rapid return to functional activity and higher levels of satisfaction. Furthermore, minimally invasive surgeries have been shown to decrease health care costs [238].

These results suggest that the potential benefits of minimally invasive cardiac surgery can be attained without compromising the proven efficacy of conventional approaches.

On the other hand, this may come at an expense of increased cardiopulmonary bypass time and longer cross-clamp and procedure times. Although these techniques employ small access incisions, they still require the use of aortic cross clamping and cardiopulmonary bypass.

Furthermore, these outcomes are generated from high-volume and single-center prospective cohort studies. A randomized, prospective trial comparing minimally invasive mitral valve repair to conventional mitral valve repair is required to adequately assess the relative risks and benefits of minimally invasive versus conventional mitral valve repair in patients with degenerative mitral regurgitation.

1.9 Challenges of Robotics-Assisted Mitral Valve Repair

Avoidance of sternotomy for minimally invasive mitral valve repair presents unique challenges for the surgeon. Acceptance of this technology has been limited as a result of the risk of intraoperative conversion to sternotomy, procedure complexity, steep learning curves, and prolonged cardiopulmonary bypass and operative times.

Due to new challenges in preoperative planning and limited surgical access, minimally invasive techniques are technically more demanding. Surgeons' learning curves for robotics-assisted coronary artery bypass grafting (CABG) and mitral valve repair have been reported. Novick et al. reported the learning curve for 90 beating heart robotics-assisted coronary artery bypass grafting (CABG) surgeries [272]. Operating time reduced from a mean of 537 ± 119 min in first quintile to 307 ± 56 min in last quintile. Chitwood reported lower rates of reoperation and failure of mitral valve repair in the last 200 of 300 patients [273]. Therefore, innovative training platforms for complex minimally invasive surgery, such as mitral valve repair, are of growing interest for surgery training programs.

Minimally invasive surgeries have the potential to be not only more complex, but also longer. Limited incision size, incomplete or inadequate exposure, and tissue manipulation using robotic or long- shafted instruments all have the potential to increase operative times. Increased operative times may be due to the use of indirect visualization through an endoscope and remote manipulation of tissue through a master-slave configuration [257]. In conventional or open heart surgery, sensory input is derived from both vision and haptic feedback [274, 275]. Haptics is the combination of kinesthetic, tactile, and proprioceptive information. Kinesthetic feedback provides position, force, and movement information and can be acquired using a force/torque sensor. Tactile feedback includes the sensation of vibration, shape, and texture. Proprioception provides the sense of

position and movement of body segments [276]. For a complete depiction of haptic interactions between surgical instruments and tissue, feedback from kinesthetics, tactile, and proprioception must be acquired [276-278].

During robotics-assisted surgery, the indirect manipulation of tissue through the master-slave configuration of the robotic system prevents realistic interaction forces between the surgeon, the therapeutic instruments, and the tissue [277]. This may be particularly deleterious in dexterous fine movements such as intracorporeal suturing and knot tying, which require accurate control of applied forces and instrument positions [277-279]. Without haptic feedback, insufficient forces might be applied when grasping tissue or sutures, resulting in loose knots [276, 277]. Conversely, excessive forces may be applied to tissue leading to increased trauma and damage to tissue. This is particularly important in robotics-assisted mitral valve repair, which requires fine motor skill to suture an annuloplasty band to the cardiac tissue surrounding the mitral valve annulus. Therefore, improved training methods and tissue manipulation with the addition of haptic feedback are both means of potentially decreasing minimally invasive operating times.

Furthermore, although robotics-assisted mitral valve repair avoids the use of sternotomy incision, aortic cross-clamping and cardiopulmonary bypass are required for access to the mitral valve. Therefore, compared to conventional surgery with sternotomy, minimally invasive surgeries have significantly longer cross-clamp, bypass, and operative times. Results from a multicentre phase II FDA trial of the da Vinci robotic system for mitral valve repair in 112 patients reported total operative, aortic cross-clamp, and cardiopulmonary bypass times were: 2.8 ± 0.1 hours, 1.3 ± 0.01 hours, and 2.1 ± 0.1 hours, respectively [255].   A further comparison of robotics-assisted mitral valve repair to conventional techniques with sternotomy reported significantly longer operative times (186 ± 61 versus 169 ± 59 minutes, p<0.01), cardiopulmonary bypass (142 ± 54 versus

102 ± 45 minutes, p<0.000), and cross-clamp times (74 ± 44 versus 64 ± 28 minutes, p <0.015) using robotics-assisted techniques [266]. Previous studies have shown prolonged cross-clamp and cardiopulmonary bypass time are independent predictors of mortality with a linear relationship between cross-clamp time and mortality rates [280].

Moreover, because cardiopulmonary bypass is associated with an increased risk of perioperative stroke and ischemia, particularly in an elderly population with multiple comorbidities, innovative minimally invasive techniques that avoid cardiopulmonary bypass and aortic cross-clamping are an area of growing interest. As a consequence of this challenge, minimally invasive techniques have been developed for beating heart surgery.

1.10   Beating Heart Mitral Valve Repair

Although robotics-assisted mitral valve repair avoids the use of sternotomy incision, aortic cross-clamping and cardiopulmonary bypass are required for access to the mitral valve. **Cardiopulmonary bypass is associated with an increased risk of perioperative stroke and ischemia, particularly in an elderly population with multiple comorbidities.** As a result of this challenge, there is renewed interest in minimally invasive beating heart mitral valve repair. In order to avoid aortic cross-clamping and cardiopulmonary bypass, minimally invasive techniques have been developed for beating heart surgery.

In fact, beating heart mitral valve repairs were first performed prior to the development of the cardiopulmonary bypass machine to repair mitral valve stenosis [281-286]. However, the development of the cardiopulmonary bypass machine enabled surgeons to perform more complex mitral valve repair [287]. More recently, beating heart mitral valve repair techniques have been developed for: edge-to-edge leaflet repair, leaflet ablation repair,

repair of leaflet coaptation, direct annuloplasty repair, indirect annuloplasty repair, subannular repair, and chordae tendineae replacement.

This chapter provides a description of beating heart mitral valve repair techniques, an evaluation of the published outcomes following the use of these techniques, and a discussion of the main challenges encountered in the implementation of these techniques.

1.10.1   Edge-to-Edge Repair

The edge-to-edge repair was first performed by Alfieri in 1991 for anterior leaflet prolapsed [190, 299, 300]. The procedure was first performed through a median sternotomy with cardiopulmonary bypass and cardiac arrest. Since that time, this technique has been successfully used in the **minimally invasive repair** of both degenerative and functional mitral regurgitation.

The Mitraclip (Evalve Inc, Redwood City, Calif; MitraClip Inc., Abbott Vascular, USA) device is a 4 mm wide cobalt-chromium clip housed in a catheter, and it is advanced through the femoral vein to the right atrium under 3D TEE and fluoroscopy guidance [94, 290, 291]. Trans-septal puncture is performed in the mid-superior and posterior aspect of the fossa ovalis. The clip is advanced through the left atrium to the left ventricle below and perpendicular to the line of coaptation. The leaflets are grasped by retraction of the clip and the leaflet edges clipped together when the device is closed. The clip can be reopened and repositioned if required. Also, a second or third clip may be added to improve the result. MitraClip has been implanted in over five thousand patients with degenerative and functional mitral regurgitation worldwide.

Although both the EVEREST I and EVEREST II trials have demonstrated the safety of MitraClip implantation, the efficacy of this device to repair mitral valve regurgitation is not clear cut [94, 290, 291]. The safety advantage of MitraClip over conventional mitral

valve repair is derived from a higher rate of transfusions with conventional mitral valve repair.

Both randomized controlled trials demonstrate that conventional mitral valve repair is more effective than MitraClip implantation at reducing mitral regurgitation. Despite these outcomes, patients in the MitraClip cohort reported better quality of life and symptomatic relief than conventional surgery patients. Therefore, MitraClip emerges as an option for those patients who are elderly higher risk surgical candidates in whom a decreased reduction in mitral regurgitation may afford a better quality of life following the procedure.

With this patient cohort in mind, the ACCESS-EU trial was initiated. ACCESS-EU is a prospective, observational study at 14 European centres [93]. Compared to the EVEREST trial patient cohort, patients enrolled in this study are older (mean age 74 ± 10 years), with more comorbidities, and depressed left ventricular function. The thirty day mortality in MitraClip patients was 2.3% and one year mortality 17.3%. Mitral valve regurgitation improved to grade 2 or less in 79% of 327 patients with matched echocardiographic data, and NYHA class to II or less in 72% of 343 patients with matched clinical data. At one year, the results from MitraClip patients are as follows: freedom from death was 82%, freedom from mitral valve regurgitation greater than 2+ was 79%, and freedom from mitral valve surgery was 94% [93].

Similarly, the MOBIUS Leaflet Repair System (Edwards Lifesciences Corp., USA) was developed to achieve an edge-to-edge repair; however, this system uses a suture secured by nitinol clips to create a double mitral valve orifice. The MOBIUS catheter is advanced through the femoral vein to the right atrium, and requires transeptal puncture to allow it to enter the left atrium. The mitral valve leaflets are grasped sequentially under transesophageal echocardiographic guidance. Following needle penetration of the

leaflets, the suture is exteriorized and fastened with a nitinol suture clip to create a double orifice. Although initial animal trials showed feasibility of this device, poor outcomes were reported in human trials [292, 293]. Insufficient tissue penetration of the suture and asymmetric deployment of the sutures led to unsuccessful deployment and limited device durability [292, 293].

The main limitations of edge-to-edge techniques are their limited applicability to mitral valve pathology and the lack of annuloplasty repair. Candidacy for the MitraClip is determined according to strict anatomical features including a flail segment width less than 1.5 cm and a regurgitant jet origin from within the central two-thirds of the line of leaflet coaptation [290]. Conventional edge-to-edge mitral valve repair can be applied to a larger number of patients because annuloplasty repair and other required procedures can be performed concurrently through a median sternotomy with cardiopulmonary bypass. Moreover, the addition of mitral valve annuloplasty is an important component of mitral valve repair and the absence of an annuloplasty band or ring has been associated with shorter durability in some studies [289, 294-296]. In the future, a combination of both percutaneous edge-to-edge leaflet repair and annuloplasty repair may expand the indications and improve efficacy and durability of these devices.

1.10.2   Leaflet Ablation

Radiofrequency ablation has been proposed as a treatment of mitral valve regurgitation. In myxomatous mitral valve regurgitation, redundant leaflet tissue prevents the valve from coapting during systole. Radiofrequency ablation generates thermal lesions by denaturing collagen and disrupting the tissue architecture. As a result, the leaflet size can be reduced and coaptation is improved. The Thermocool irrigation ablation electrode (Biosense Webster, Inc., Diamond Bar, California) is a radiofrequency ablation catheter that is advanced through the femoral artery to the left ventricle. Radiofrequency ablation

is delivered to the anterior leaflet of the mitral valve to induce scarring, fibrosis, and reduced leaflet motion [297].

At this time, there is little evidence of efficacy of this device. Only animal studies have been reported that require median sternotomy access to the mitral valve leaflets. Unfortunately, the resulting fibrosis is difficult to predict; therefore, there may be residual or worsening mitral valve regurgitation. Furthermore, damage to the leaflets and adjacent cardiac structures may be induced [297].

1.10.3 Direct Annuloplasty Repair

The aim of mitral valve annuloplasty is to restore a normal ratio between the annular size and leaflet surface area in order to increase the surface of coaptation [298]. In addition, this technique may adjust the shape of the annulus to restore normal geometry. Annuloplasty is usually performed after leaflet lesion correction. Different annuloplasty methods and devices are available. Typically, annuloplasty repair involves the implantation of a ring or band surrounding the mitral annulus that brings the leaflets together to facilitate coaptation. While several devices have been developed for minimally invasive direct annuloplasty repair, these technologies are at an early phase of development.

The Mitralign device (Mitralign Inc, Tewksbury, Mass, USA) is advanced through transfemoral arterial access to the left ventricle. Plegetted anchors connected by a suture are placed at the base of the posterior mitral valve leaflet along the posterior mitral valve annulus. The resulting purse-string suture is tightened to reduce the annular dimensions. The first human trial of this technique achieved success; however, no further results are reported [298].

Similarly, the AccuCinch (Guided Delivery Systems, Santa Clara, CA, USA) device is advanced transapically to the left ventricle where multiple anchors are deployed below the leaflets from commissure to commissure [298, 299]. The anchors are joined by a contracting wire, with the resulting cinching device being adjusted to reduce the annular dimensions. The first human trial of this technique achieved success [299]; however, no further results are reported.

Cardioband (ValtechCardio, OrYehuda, Israel) is advanced through a left mini-thoracotomy to the left atrium [300, 301]. The steerable device carrying a Dacron band and metallic anchors are advanced to the mitral valve under echocardiographic guidance. Next, up to fifteen metallic helical anchors are implanted in the base of the mitral valve annulus under echocardiographic guidance and tactile feedback. Once deployment of the implant is completed, the implant is disconnected from the delivery system and connected to an adjustment roller used to contract or expand the band under echocardiographic guidance. Once the desired contraction is obtained, the implant is released from the adjustment tool. The delivery system is removed through an 18F sheath in the left atrium and the access incision is closed using a purse string stitch. Animal trials of this device were successful off pump; however, human trials of this device require implantation on cardiopulmonary bypass [300, 301]. The annuloplasty band is adjusted under beating heart conditions. Therefore, although this technique is considered minimally invasive, all human trials have required cardiopulmonary bypass for implantation of the annuloplasty band.

1.10.4 Indirect Annuloplasty Repair

Due to the close location of the coronary sinus to the mitral valve annulus, devices have been developed for deployment in the coronary sinus to decrease the annular diameter by forcing the posterior annulus anteriorly and reducing the anterior-posterior dimension.

The MiCardia DYANA annuloplasty system (MiCardia Corp, Irvine, Calif) is a nitinol-based annuloplasty ring that decreases the anterior-posterior diameter of the mitral valve by radiofrequency ablation via detachable activation wires, under TEE guidance [302-306]. Without radiofrequency activation, it functions as a standard complete annuloplasty ring. The nitinol support is encapsulated in silicone and covered with a polyester cloth to allow for suture attachment. The annuloplasty ring is sutured to the mitral valve annulus under cardiopulmonary bypass, as in conventional surgery. The distal ends of activation wires are attached to the annuloplasty ring, and the proximal ends are attached to a radiofrequency generator. After surgical implantation of the annuloplasty ring, the proximal ends of the activation wires are passed through the atriotomy, the left atrium is closed, and the patient is weaned from cardiopulmonary bypass. The size of the annulus is adjusted using TEE guidance. Finally, the activation wires are disengaged and removed through the atriotomy suture line at the end of the procedure in all patients before closure of the sternum. Human implantation of this annulplasty ring has successful outcomes [306]; however, cardiopulmonary bypass is required for ring implantation.

The PS3 system (Ample Medical Inc, Foster City, CA, USA) deploys an anchor in the coronary sinus and attaches a cord traversing the left atrium to be anchored in the fossa ovalis [307, 308]. This tether is then tensioned to diminish the anterior-posterior dimension of the mitral annulus. In an unpublished report, the PS3 system was implanted in two patients before open heart surgery and then removed during the surgical procedure [307, 308]. Mitral valve regurgitation was significantly reduced by the device alone. No further trials have been reported.

The MONARC device (previously Viking device; Edwards Lifesciences, Irvine, California, USA) consists of proximal and distal self-expanding nitinol stents connected

by a strut [309]. The strut consists of a spring with an absorbable suture holding the spring in a partially open position. The device is advanced through the internal jugular vein to the coronary sinus.   After the coronary sinus diameters and length have been carefully measured before the procedure, the device is advanced into the coronary sinus in an introducer. The distal stent is deployed by extruding the device out of the introducer, and it becomes fixed in place by the radial force the stent applies on the coronary sinus wall. The remainder of the device is then deployed, with placement of the proximal stent in the proximal coronary sinus. Over a period of weeks, the suture dissolves, allowing the spring to compress between the fixed proximal and distal stents. Shortening the device reduces the anterior-posterior dimension of the mitral valve, thereby improving leaflet coaptation. As a result, the annulus size is reduced leading to a reduction in mitral regurgitation.

The first-generation MONARC device developed a fracture in the bridge segment that resulted in device separation during follow-up in 3 of 5 patients. Bridge separation did not cause adverse events but may have reduced the efficacy of the device. Therefore, a non-biodegradable suture was added to reinforce the bridge segment and reduce the likelihood of separation of the device following implantation. The human trial of this new device is reported in the EVOLUTION trial [309]. Despite the new design, device fracture continues to occur following MONARC implantation.

CARILLON Mitral Contour System (Cardiac Dimensions Inc., Kikland, Washington) uses two self-expanding nitinol hoop-shaped helical anchors connected by a nitinol bridge [310-312]. The device is advanced through the internal jugular vein to the coronary sinus. The distal anchor is deployed in the coronary sinus anchor, then manual tension is applied to the connecting wire and the proximal anchor is deployed, obtaining a shortening of the mitral annular dimension. The tension on the device can be adjusted

before the final release, with the degree of traction being guided by both fluoroscopic and echocardiographic assessments. Once tissue plication is optimized, the proximal anchor was deployed near the coronary sinus ostium. Despite reports of reverse left ventricular remodeling and significant clinical improvements following implantation, the safety of this device has yet to meet the standard of conventional mitral valve repair [310-312].

The Viacor device (Viacor, Inc., Wilmington, Massachusetts) is based on placing a multilumen delivery catheter through the right internal jugular vein into the coronary sinus, and then introducing one or more nitinol rods of different lengths and extensibility into the lumens to reshape the annulus [313-317]. The device consists of a composite nitinol (nickel titanium alloy) and stainless steel construct and is coated with medical-grade teflon and polyethylene plastic. In addition, this device is comprised of a substantially straight and rigid element that is connected to a flexible push rod to facilitate delivery. When passed through the internal lumen of a guiding catheter positioned in the coronary sinus, the rods maintain their straight shape. This exerts outward force on the mitral valve annulus resulting in anterior displacement of the posterior annulus and increases leaflet coaptation. The guide catheter and annuloplasty device are designed with radiopaque components to enable visualization under fluoroscopy. However, results from in-human trials were disappointing due to difficult device delivery and device fracture [316, 317].

Clearly, although initial animal trials of indirect annuloplasty devices were promising, human trials proved more challenging [316, 317]. There are several reasons for this discrepancy. In patients with chronic mitral valve regurgitation, the distance between the coronary sinus and the posterior mitral valve annulus increases with left ventricular remodeling; therefore, the effectiveness of the device is potentially decreased. Furthermore, the anatomic location of the coronary sinus does not consistently lie in

plane with the mitral valve annulus. In some patients, force is applied to the left atrial wall and not the mitral valve annulus; therefore, the annulus may continue to dilate, reducing device effectiveness.

Moreover, coronary arteries may lie between the mitral annulus and the coronary sinus. In fact, the diagonal or intermediate ramus coronary vessel crosses between the coronary sinus and the mitral valve annulus in 16% of patients; and the circumflex artery crosses between these two structures in 64-80% of patients [318-322]. Furthermore, the friable coronary sinus can be dissected with advancement of these devices. In addition, several studies have reported device fracture after implantation into the coronary sinus.

Finally, other limitations include significant mitral valve calcification, the presence of coronary sinus pacing leads, coronary venous branch point variability, coronary venous system size constraints as a risk for coronary sinus perforation, and structural mitral valve leaflet abnormalities. In addition, these devices may prevent future attempts at implanting cardiac resynchronization devices.

1.10.5 Subvalvular repair

Coapsys device (Myocor Inc, Minneapolis, Minn) employs a transventricular splint with pads on the anterior and posterior epicardial surfaces of the left ventricle connected by a subvalvular cord [323-336]. In an open chest, this device is placed on a beating heart under direct echocardiographic guidance. A suction cup-stabilized c-clamp with anterior and posterior locators is placed around the left ventricle. The posterior locator is positioned externally between the papillary muscle insertions, about 2 cm below the insertion of the posterior leaflet. The anterior locator is placed on the right ventricle side of the left anterior descending coronary artery, halfway down the longitudinal axis of the ventricle. Verification of these locations is determined by handheld epicardial

echocardiography. The jig guides a thin blunt-tipped needle through the left ventricle from one locator to the other. The needle is followed by the Coapsys cord. The Coapsys device, with pads attached to either end, is initially placed without tension. Sizing is then conducted under real-time colour flow Doppler imaging to quantify mitral valve regurgitation. Pads attached to each end of the splint are tightened to pull the ventricle into the region of the papillary muscles and also to move the posterior leaflet to better coapt with the anterior leaflet.

The i-Coapsys (Myocor Inc, Minneapolis, Minn) device performs the same role but can be delivered by transcatheter implantation system with fluoscopic guidance [336]. The device consists of two epicardial pads (anterior and posterior) connected by a load-bearing transventricular chord. Pericardial access is gained through a right anterolateral intercostal incision through which the device is advanced into the pericardial space. Three vacuum stabilized catheters are used to identify the appropriate anterior and posterior pad implantation sites and anterior and posterior pads are advanced under fluoroscopic guidance.

1.10.6 Chordae tendineae replacement

Replacement of the diseased chordae tendineae with PTFE neochordae for conventional repair of mitral valve regurgitation is associated with low operative mortality, high freedom from re-operation, and long-term survival similar to the general population [187, 193, 194]. The NeoChord DS1000 (NeoChord Inc., Eden Prairie, MN USA) was developed as an off-pump device that uses transapical access to deliver PTFE sutures to flail segments of the mitral valve [337-340]. This device is introduced into the left ventricle and left atrium through transapical access. Using the center thumb ring shaft (Figure 1.7), the surgeon opens the gripper at the distal end of the tool and then closes the gripper on the prolapsed portion of the mitral leaflet by releasing the thumb ring. Correct

leaflet capture is verified using a fiber-optic-based detection mechanism. After leaflet capture has been verified, a needle and an exchangeable cartridge for loading the NeoChord suture are installed within the tool. The needle is used to puncture the leaflet and a PTFE suture is pulled through the leaflet; then the tool is retracted outside the apex of the heart with both ends of the suture. The suture is fixed at the leaflet with a girth hitch knot, adjusted under Doppler ultrasound to ensure minimum mitral regurgitation and then secured at the apex using a pledget. Multiple neochordae are typically used to ensure optimal valvular function.
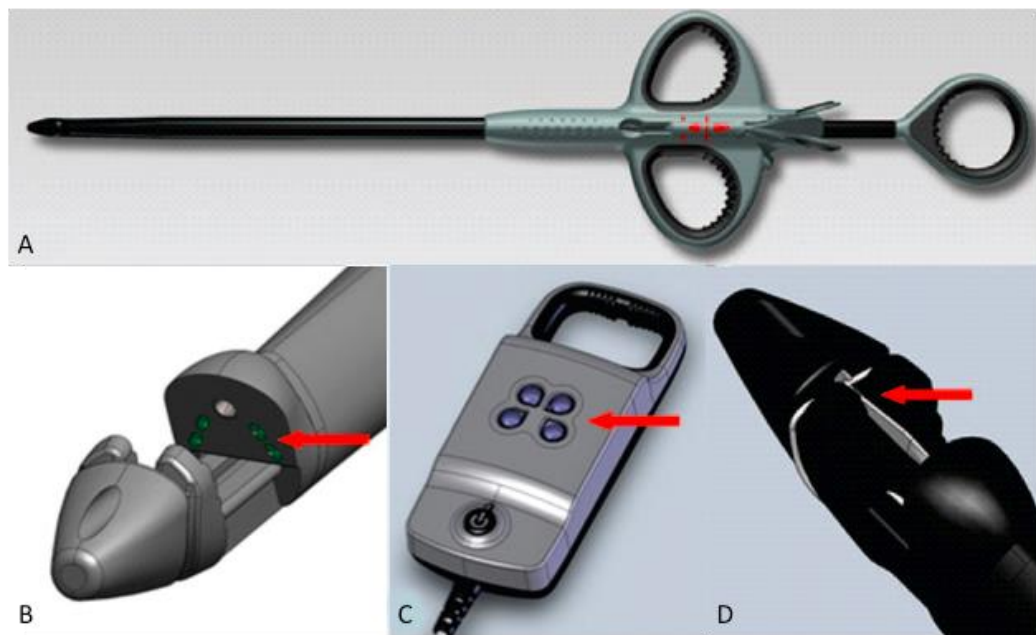
Figure 1.7: The NeoChord DS1000 (A) has the following features: A tip with expandable jaws to grasp the leaflet and 4 fiber-optic channels (B) each of which corresponds to an indicator light on the device monitor (C) to confirm proper leaflet capture. The needle (D) is also included in the device to deploy the suture after confirmation of leaflet capture [340].

After extensive acute and chronic animal studies throughout Europe, Canada, and the United States, the NeoChord is undergoing human trials for the repair of degenerative mitral valve regurgitation [337-340]. Initial results confirm the safety and efficacy of this surgical tool for mitral valve repair in patients with degenerative mitral valve regurgitation. However, the limited visualization during tool navigation to the mitral valve leaflets and neochord dehiscence, or tearing, from the mitral leaflet following deployment are ongoing challenges with this procedure.

1.11   Challenges of Beating Mitral Valve Repair

Beating heart cardiac surgery alone is technically challenging and requires superior visualization of cardiac structures; however, minimally invasive techniques are even more challenging due to the absence of direct vision.

Transcatheter valve techniques have been developed to enable beating heart mitral valve repair. Although these techniques have shown positive results in animal and human trials, beating heart mitral valve repair is **challenging due to the limitations of currently available medical imaging techniques**.

Mitral valve repair using beating heart minimally invasive procedures requires adequate visualization of the mitral valve apparatus and critical cardiac structures adjacent to the mitral valve. At this time, fluoroscopy and echocardiography are used for intraoperative guidance of beating heart mitral valve procedures.

Although fluoroscopy provides 2D imaging of these gross anatomical structures, their 3D context is lost [341].   Echocardiography lacks the spatial and temporal resolution to view intracardiac instruments and critical cardiac structures simultaneously; therefore, there is a risk of potential injury to intracardiac structures during instrument navigation.

For example, use of the NeoChord DS1000 tool relies exclusively on TEE guidance in the form of 2D single plane, biplane, and 3D imaging for tool navigation and neochordae deployment [342, 343]. The tool is identified in 2D biplane ultrasound (mitral valve commissural, midesophageal long-axis view), and navigated into the commissure of the mitral valve leaflets, while the surgeon and echocardiographer attempt to maintain tool tip, tool profile, and final target site in the ultrasound image planes at all times. Correct position and orientation of the grasping tool are then achieved using a 3D zoomed view. Returning to biplane ultrasound for higher temporal and spatial resolution, the prolapsing leaflet is grasped by the jaws of the NeoChord device.

A major challenge in navigating the NeoChord device to the mitral valve target region is that ultrasound imaging must simultaneously keep the target region (mitral valve line of coaptation) and the tool tip in view. While TEE has so far proven adequate for the final positioning of the tool and grasping the leaflet, there have been safety concerns relating to the navigation of the tool from the apex to the target mitral valve leaflet.

Echocardiography lacks the spatial and temporal resolution to view intracardiac instruments and critical cardiac structures simultaneously; therefore, there is a risk of potential injury to intracardiac structures during instrument navigation. TEE guidance is problematic since it is not always possible to maintain appropriate spatial and temporal resolution in 3D, and it is not always possible using 2D and 2D bi-plane views to simultaneously maintain both the tool tip and the target site in the field of view. Due to these navigation challenges, the tool can be caught in the subvalvar apparatus risking chordal rupture or leaflet perforation. **Clearly, novel imaging modalities are required for superior tool guidance and improved patient safety and outcomes.**

1.12   Aortic Valve Anatomy

The aortic valve opens to permit the passage of oxygenated blood from the left ventricle to the aorta and systemic circulation during systole. It closes to ensure efficient flow of oxygenated blood from the aortic root to the coronary arteries during diastole and to prevent backflow of blood into the left ventricle. The aortic root extends from the basal attatchment of the aortic valve leaflets within the left ventricle to the leaflet attachments at the sinotubular junction [344, 345]. The sinotubular junction is demarcated by the top attachments of the aortic valve leaflets and it forms an outlet of the aortic root into the ascending aorta [344, 345]. The sinus of Valsalva is the dilated portion of the aortic just above the aortic valve annulus from which the coronary arteries originate. The aortic valve comprises three leaflets, or cusps: the left coronary cusp, the right coronary cusp, and the noncoronary cusp. The left coronary artery originates from the aortic root above the left coronary cusp. The right coronary artery originates from the aortic root above the right coronary cusp.

1.13   Aortic Valve Stenosis Etiology and Classification

Aortic valve stenosis occurs when there is incomplete opening of the aortic valve orifice that obstructs the normal flow of blood from the left ventricle during systole. Thickening and fusion of aortic valve leaflets may occur secondary to degenerative calcification in tricuspid or bicuspid aortic valves or to rheumatic heart disease [3, 346].

1.13.1   Degenerative Aortic Valve Stenosis

The most common cause of aortic valve stenosis is degenerative calcification of the aortic valve leaflets. With aging, cumulative mechanical stress generates proliferative and inflammatory changes with lipid accumulation and calcium deposits on the leaflets making them thick and immobile [348-352]. As a result, they are prevented from opening

properly during systole. This generally culminates in septuagenarians and octogenarians. In fact, the prevalence of moderate to severe aortic valve stenosis in the population over the age of 75 is between 3-9 % [353].

Calcium may also deposit cephalad through the ascending aorta. As this process is similar to atherosclerosis, the risk factors for the development of degenerative calcific aortic valve stenosis also include elevated serum levels of low-density lipoprotein cholesterol, diabetes, smoking, and hypertension [351].

1.13.2   Bicuspid Aortic Valve Stenosis

Bicuspid aortic valves are more prone to developing calcified aortic valves. These valves have two fused leaflets that result in a bicuspid conformation, rather than the normal tricuspid aortic valve conformation. Bicuspid aortic valves are present in approximately 2% of the general population [354]. The bicuspid conformation induces more turbulent blood flow across the aortic valve; therefore, buildup of calcification becomes significant earlier and is seen in the fifth and sixth decades of life [355].

1.14   Rheumatic Aortic Valve Stenosis

Furthermore, rheumatic deposits on the aortic valve may also cause aortic valve stenosis. Rheumatic aortic valve disease is characterized by lymphocytic infiltration to the aortic valve leaflets. As a result, the leaflets become thickened with scarred and fused leaflet [356]. Rheumatic valve disease is rarely isolated to the aortic valve, as it commonly involves the mitral valve [357].

1.15   Natural history of aortic valve stenosis

The average area of the aortic valve orifice is 3-4 cm^2 [3]. As the aortic valve leaflets become thickened and fused, the left ventricular outflow tract is narrowed. Once the

aortic valve area decreases to below 1.5 cm^2, there is increased pressure and wall stress within the left ventricle [3, 346]. As a result, the left ventricle adapts by increasing wall thickness. This is called left ventricular hypertrophy. The hypertrophied left ventricle is less compliant during diastole and requires increased myocardial oxygen consumption. Furthermore, diastolic dysfunction and increased diastolic pressures compresses coronary arteries and decreases coronary flow to the left ventricle [358].

In summary, there is increased myocardial oxygen demand and decreased myocardial oxygen supply. Therefore, the heart is more susceptible to ischemic injury. At this point, patients with aortic valve stenosis may develop angina. In the late stages of severe aortic valve stenosis, the left ventricle gradually decompensates, resulting in heart failure. With progressive left ventricular outflow obstruction and left ventricular dysfunction, there is inadequate cardiac output to the systemic circulation. Patients develop symptoms of syncope, or loss of consciousness, from cerebral hypoperfusion [359]. Furthermore, as cardiac output declines, there is an increase in pulmonary congestion leading to pulmonary hypertension. Patients may present with dyspnea as a result of congestive heart failure [360].

Initially, patients may be asymptomatic for a long period of time; however, as the aortic valve narrowing becomes more hemodynamically significant and symptoms develop, prompt surgical intervention is required, as patient mortality increases dramatically [69]. The mean survival of patients with angina is five years. The mean survival of patients that present with syncope is three years, and the mean survival of patients who present with symptoms of congestive heart failure is less than one year [361].

1.16   Role of imaging in aortic valve stenosis

1.16.1   Role of Echocardiography

Echocardiography is the most common diagnostic tool for diagnosis and grading of aortic valve stenosis. Both TTE and TEE are used to diagnose and grade the severity of aortic valve stenosis, to diagnose any concomitant cardiac disease, and to evaluate ventricular function. Grading the severity of aortic valve stenosis is based primarily on echocardiographic measurements of pressure gradients across the aortic valve and peak jet velocity across the aortic valve, and on the calculation of aortic valve area [Table 1.3; 69]. As aortic valve stenosis is a progressive disease, the AHA recommends periodic TTE every five and two years for mild and moderate aortic valve stenosis, respectively [69].

Table 1.3: Aortic Valve Stenosis Severity Assessment by Echocardiography [3].

Measurement	Mild	Moderate	Severe
Aortic valve area (cm^2)	>1.5	1.0-1.5	<1.0
Mean pressure gradient (mmHg)	<25	25-40	>40
Peak jet velocity (m/s)	<3	3-4	>4

1.16.2   Role of Cardiac Angiography

Cardiac angiography is the gold standard for measuring the gradient across the aortic valve [3]. Therefore, cardiac angiography is used to determine both the severity of aortic valve stenosis and any concomitant coronary artery disease. Ventricular function and the presence of additional cardiac disease can also be elucidated from angiography.

1.16.3   Role of Computed Tomography (CT)

Although CT is not used routinely for diagnosis of aortic valve stenosis, it may be used for preoperative assessment of ascending aortic calcification prior to aortic valve surgery. The presence of extensive aortic calcification may preclude aortic cross clamping required for cardiopulmonary bypass. In addition, CT can be used to assess the caliber of the ascending aorta. A dilated ascending aorta that may be prone to dissection or rupture should be identified prior to aortic valve surgery for appropriate operative planning.

1.16.4   Role of Magnetic Resonance Imaging (MRI)

Similarly, MRI is not used routinely for diagnosis of aortic valve stenosis; however, it is an alternative noninvasive imaging modality for assessment of aortic valve stenosis [362]. Cardiac MRI uses a range of pulse sequences to assess structural heart disease, including aortic valve leaflet pathology and left ventricular hypertrophy [363-366].

1.17   Indications for surgery in aortic valve stenosis

Aortic valve replacement is the only definitive treatment for aortic valve stenosis. No effective medical therapy for aortic valve stenosis exists. As the onset of symptoms and ventricular dysfunction herald a dramatic increase in mortality, both symptom onset and left ventricular dysfunction are **Class I** indications for aortic valve replacement in patients with severe aortic valve stenosis [23]. It is also a **Class I** indication to replace the aortic valve in asymptomatic patients with severe aortic valve stenosis who require concomitant coronary revascularization or aortic surgery [69].

1.18   Surgical management of aortic valve stenosis

1.18.1   Aortic valve replacement

1.18.1.1   Aortic valve prostheses

Currently, mechanical or bioprosthetic aortic valve replacement is the only established treatment for aortic valve stenosis [3]. The first orthotopic mechanical prosthetic aortic valves were a ball and cage design; however, their poor hemodynamic performance prompted the development of tilting disc prosthetic aortic valves [3, 367, 368]. In 1977, St. Jude Medical developed a bileaflet tilting disc valve with a lower postoperative aortic gradient and a lower rate of thromboembolism than previously developed models [369-373]. This is the most commonly implanted type of mechanical prosthesis in the world [374].

There are several different types of bioprosthetic valves available: stented, homografts, stentless, and pulmonary autografts. Stented biologic prostheses are constructed from either porcine aortic valves or bovine pericardium fixed with glutaraldehyde to reduce calcium deposition and to antigenicity [375]. Over the years, the design of stented bioprosthetic valves has been ameliorated with newer fixation methods to reduce material fatigue and calcification and with thinner stents and lower profiles.

However, the stents, large sewing rings, and supporting structures of mechanical and stented bioprosthetic valves may impinge on the left ventricular outflow tract. In contrast, homografts, stentless valves, and pulmonary autografts are free of these support structures. Therefore, larger prostheses can be implanted to produce superior aortic valve hemodynamics. In fact, the first valve used for aortic valve replacement was an aortic homograft valve in the descending aorta [376, 377]. Subsequently, orthotopic aortic homograft implantation was completed using subcoronary placement [378-380].

Homograft valves can be obtained from donors whose beating hearts are not suitable for transplantation or from nonbeating heart donors and cryopreserved until use [3]. In addition to an excellent hemodynamic profile, aortic homografts have a low risk of thromboembolism and do not require anticoagulation and they have a low risk of valve infection. Unfortunately, these valves are also subject to structural deterioration that is directly related to donor age and inversely related to recipient age [3]. In addition, homograft availability is limited. Therefore, their use is usually reserved for challenging cases of aortic valve endocarditis or for younger patients requiring both aortic valve and root replacement who cannot be anticoagulated [381].

Pulmonary autografts were first implanted in the aortic position in 1967 [382]. They are the only autologous valve replacement option. In addition to an excellent hemodynamic profile, aortic homografts have a low risk of thromboembolism and do not require anticoagulation and they have a low risk of valve infection [383]. However, aortic valve replacement with a pulmonary homograft is technically demanding [3].

Stentless xenograft aortic valves were developed to offer the excellent hemodynamics of homografts and autografts, but with improved availability and lower cost [384-386]. However, implantation of stentless aortic valves is technically challenging and has the potential for increased operative risk and higher operative mortality stented aortic valve replacement [387]. Therefore, the use of stentless aortic bioprostheses is contentious.

1.18.1.2 Surgical procedure for aortic valve replacement

In conventional aortic valve replacement with a mechanical or stented bioprosthetic valve, the aortic valve is accessed though a midline sternotomy. The pericardium is opened and the patient is placed on cardiopulmonary bypass using an aortic cannula in the ascending aorta and a venous cannula through the right atrial appendage. The aorta is

cross-clamped and an aortotomy incision is made below the cross-clamp and approximately 1 cm above the takeoff of the right coronary artery. This is extended approximately three-quarters of the way around the aorta and the native aortic valve leaflets are excised along with any calcium. Braided 2-0 stitches are sutured in an interrupted mattress fashion around the annulus, then passed through the sewing ring of the prosthesis. The prosthetic valve is lowered into the annulus. After proper leaflet motion and coronary artery patency are assured, and the aortotomy is sutured closed.

1.18.2   Outcomes of aortic valve replacement

The mortality rate for isolated aortic valve replacement at both high and low volume centres, as reported by the Society of Thoracic Surgeons' is 3.2% [69]. The expected survival after aortic valve replacement is approximately 80 to 85% at five years, 65 to 75% at ten years, and 45 to 55% at fifteen years [388-390]. Longitudinal analysis demonstrates no difference in survival up to ten years between patients of the same age receiving mechanical and bioprosthetic valves [391]. However, at fifteen years, there is a survival benefit for patients with mechanical valves as bioprosthetic valves fail due to structural valve deterioration. In one trial, the fifteen year mortality was 79 and 66% for bioprosthetic and mechanical valves, respectively [392].

In the early follow-up period, anticoagulation related hemorrhage is the most common untoward event for mechanical valve prostheses. Thus, over the first ten years of follow-up there is a higher incidence of valve related complications in patients with mechanical prostheses as opposed to those with biologic valves [393]. Whereas from ten to twenty years following surgery, this ratio is reversed because of incidence of bioprosthetic valve failure. Furthermore, biological valves have a higher failure rate in younger patients. Burdon and colleagues found that after 15 years of follow up only a third of patients who had received a bioprosthesis for aortic valve replacement between the ages of 16–39

years remained free of structural valve deterioration, compared with more than 90% of those over 70 at the time of implantation [394]. These findings have been corroborated by others [395].

For this reason and to avoid the bleeding risks of anticoagulation, many surgeons have recommend a bioprosthetic aortic valve for patients age 70 and over. In patients younger than 60 years of age, most opt for a mechanical prosthesis based on prosthesis durability.

1.18.3   Challenges in aortic valve replacement

Conventional aortic valve replacement drastically improves the mortality of patients with symptomatic aortic stenosis. However, it requires sternotomy and cardiopulmonary bypass that are particularly detrimental in elderly or frail patient with comorbidities. Therefore, these high risk patients may not be offered surgery and managed conservatively with medical therapy. Unfortunately these patients have an extremely poor prognosis [396, 397].   Transcatheter aortic valve implantation (TAVI) has emerged as an therapeutic option for these high-risk patients [8, 398, 399].

1.18.4   TAVI

TAVI is a minimally invasive aortic valve replacement technique involves the delivery of a bioprosthetic valve within an expandable stent to the beating heart via a catheter. Guidewires and sheaths are placed through a vascular access site to reach the level of the aortic valve. TAVI access has been described through the left ventricular apex using a left anterior minithoracotomy incision, or through femoral, subclavian, axillary, and carotid arteries [400-402]. Some cases of ascending aortic access have also been reported. Balloon valvuloplasty may be performed to relieve the stenosis of the native aortic valve. The prosthesis is then guided up to the level of the aortic annulus and

implanted under rapid ventricular pacing to temporarily reduce cardiac output [403, 404]. The deployed valve relies on radial traction forces to remain within the native aortic annulus. This procedure was first reported in human patients in 2008 [405].

The Placement of AoRTic TraNscathetER Valve (PARTNER) trial has demonstrated significantly better survival in TAVI treatment compared to medical therapy in non-surgical patients up to five years postoperatively [8, 398]. However, the second arm of the PARTNER trial comparing TAVI treatment to high risk patients who underwent conventional aortic valve replacement found no significant difference in mortality and higher morbidity in the TAVI group [399].

Currently, there are many commercially available TAVI stent designs. The SAPIEN TM valve (Edwards Lifesciences, Irvine, CA,) and the CoreValve TM (Medtronic Inc., Minneapolis, MN) received Food and Drug administration approval for use. The JenaValve (JenaValve, Munich, Germany) was awarded CE mark in 2011. Medtronic's Engager valve, Boston Scientific's Lotus valve, St Jude Medical's Portico valve, and Direct Flow Medical's Direct Flow valve were awarded European CE mark in 2013. Symetis' AcurateTM valve (Symetis, Lausanne, Switzerland) was awarded European CE mark in 2014.

The SAPIEN bovine pericardial valve on a balloon-expandable stent, while the CoreValve is a porcine pericardial valve on a self-expanding nitinol frame. The JenaValve is a porcine root valve within a nitinol self-expanding stent. The Engager is a bovine pericardial valve on a self-expanding nitinol frame. The Lotus is a bovine pericardial valve on a nitinol frame that requires controlled mechanical expansion for deployment. The Portico valve is a bovine pericardial valve on a self-expanding nitinol frame. The Direct Flow valve is a bovine pericardial tissue valve mounted between two inflatable polyester rings that adapt to the native aortic annulus and the left-ventricular

outflow tract fill with contrast dye for optimal positioning under fluoroscopy. The Acurate valve is a porcine valve mounted within a self-expanding nitinol stent [406].

1.19   Emerging challenges in TAVI

As the use of TAVI has expanded, the risks and challenges associated with this technology have been reported. Postoperative mortality, stroke, and nephrotoxicity from contrast use have been reported [407]. Moreover, several additional postoperative complications have been reported that are directly linked to improper valve positioning and deployment. These include prosthetic valve embolism, coronary obstruction, heart block requiring permanent pacemaker, and paravalvular leak and secondary [407].

Optimal positioning and safe deployment of TAVI valved-stent is integral to the success of the procedure. The PARTNER Trials demonstrated a 30-day mortality of 3.4-5% for TAVI patients [8, 399]. The majority of these complications may be related to inadequate image guidance and suboptimal valve positioning. Implantation of the valved-stent too far above the aortic valve annulus may result in embolism of the valved-stent or coronary occlusion by the valved-stent; whereas, positioning the valved-stent too far below the aortic valve annulus may cause atrioventricular block requiring a permanent pacemaker or retrograde embolization [341]. Some cases of paravalvular leak may also be related to poor positioning of the stent with respect to calcium on the native leaets, which prevents the stent from deploying fully [27].

Currently, many imaging modalities may be used intraoperatively to guide valve deployment. However, most centres use fluoroscopy for positioning and deployment of the transcatheter valve. Ideal valve positioning depends on the type of valve being deployed. Ideally, the Edwards Sapien Valve rim should be positioned 2/3rd above and 1/3rd below the native aortic valvular annular plane. Whereas, the Medtronic CoreValve

rim should be placed 5-10 mm below the aortic valve annular plane.

Although single-plane fluoroscopy provides good visualization of guidewires, this imaging modality has several limitations. Fluoroscopic images are only able to display gross anatomic structures; therefore, to improve visualization, nephrotoxic contrast medium is required to obtain contrast-enhanced images. However, the use of multiple contrast fluoroscopic images can increase a patient's risk of acute kidney injury [401-404]. Many TAVI patients have underlying renal dysfunction and are therefore more vulnerable to acute kidney injury. The reported incidence of acute kidney injury following TAVI is between 12 and 57% [408, 409, 411, 412]. One registry of TAVI patients reported that up to 6.7% of patients required acute hemodialysis was required in the post-procedural period [413]. Furthermore, the development of acute kidney injury is an independent predictor of prolonged hospital stay and impaired early survival following cardiac surgery [411, 414, 415]. In fact, one study reported an 11.7% incidence of acute kidney injury following TAVI and a greater than four-fold increase in the risk of postoperative mortality among those patients [417]. Finally, fluoroscopic imaging exposes both patients and health care professionals to ionizing radiation.

As a result of these challenges, image guidance systems have been developed for TAVI that provide visualization of the critical structures within the aortic root and the valve stent prosthesis. For example, the DynaCT system is an intra-operative cone-beam CT overlaid onto a fluoroscopy image. The DynaCT C-arm system constructs a segmented aortic root from rotational angiography, and automatically detects landmarks, such as the coronary ostia [416-418]. The static segmented CT image is superimposed onto the real-time fluoroscopy image, to be employed to select an optimal C-arm angulation for fluoroscopy. Recent results from Kempfert et al. in 50 patients demonstrate a positional accuracy of the coronary ostia, as displayed on the fluoroscopy image, of 4.8mm [417].

Although this technique represents an improvement, the CT aortic root image remains static and does not allow for real-time intraoperative guidance. Furthermore, this system requires fluoroscopy and contrast dye therefore exposing both patients and health care professionals to ionizing radiation.

Others have proposed intraoperative MRI to guide TAVI placement [419, 420]. Although this technique avoids ionizing radiation, this imaging modality is not only very expensive, but also scarce. Furthermore, many TAVI valves and surgical tools required for the procedure are not MRI compatible [420].

TEE is an imaging modality that is currently used throughout both conventional and transcatheter aortic valve implantation. During TEE procedural guidance, both the 2D short axis and long axis views of the aortic valve are used individually or simultaneously to align and center the prosthesis. Live 3D images may also be used for prosthetic valve alignment. Following valve deployment, TEE is used to assess valve function and to identify any procedural complications including perivalvular leak or vascular injury [422]. In fact, TEE has been successfully utilized as an alternative primary imaging modality for TAVI guidance. In fact, a study by Bagur et al. [423] demonstrated similar results when using fluoroscopy and echocardiography as the primary intra-operative image guidance modality for TAVI. However, TEE alone has limited resolution and does not provide satisfactory imaging of the TAVI catheter [424].

Integrating AR with TEE would enable virtual representations of both the TAVI valved-stent and critical aortic valve anatomy to be registered to biplane TEE.

1.20   Thesis Statement, Objectives, and Hypothesis

Clearly, although minimally invasive and beating heart surgery provide both improved postoperative morbidity and quality of life, they are technically demanding and require

additional surgical training and expertise. My thesis is that innovative strategies developed by our research team in medical imaging, force feedback, and electromagnetic tracking can be applied to minimally invasive mitral valve repair and transcatheter aortic valve implantation techniques to surmount the current challenges in minimally invasive cardiac surgery and to make these techniques more facile and safe.

We have also developed a robotics-assisted surgical test bed with force reflection that can be used to determine the effect of stereoscopic visualization and force feedback on operative performances [425, 426]. This information can be applied to robotics-assisted mitral valve repair training systems for training and skill evaluation. In addition, we have developed an augmented reality enhanced TEE guidance system that can be used to facilitate more direct and safe intracardiac navigation during beating heart cardiac surgery [342, 343]. The working hypothesis for this work was that the addition of force feedback to robotics-assisted mitral valve repair and the addition of augmented reality to beating heart valve procedures would improve both the ease and safety of these techniques.

The primary objective of this thesis is to evaluate the usefulness of 3D visualization, force feedback, and augmented reality technologies to surgeons as they are applied in a clinical setting. Specifically, the aims of this thesis are:

1. To determine the effect of 3D stereoscopic vision on the amount of force applied to cardiac tissue during robotics-assisted cardiac surgery.
2. To determine the effects of force feedback on the amount of force applied to cardiac tissue during robotics-assisted cardiac surgery and to determine is these effects are consistent between novices and experts in robotics-assisted cardiac surgery.

3. To evaluate the use of an augmented reality guidance system for successful NeoChord navigation to the mitral valve annulus.

4. To determine what factors contribute to NeoChord suture dehiscence from the miral valve leaflet.

5. To apply the innovative augmented reality guidance system for valve implantation in transcatheter aortic valve replacement.

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Chapter 2

2 Evaluating the effect of three dimensional visualization on force application and performance time during robotics-assisted mitral valve repair

In this chapter, the effect of three-dimensional (3D) binocular (stereoscopic) and two-dimensional (2D) monocular visualization on robotics-assisted mitral valve annuloplasty versus conventional techniques is examined in an *ex vivo* animal model. In addition, these effects are compared between novices and experts in robotics-assisted cardiac surgery.

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- Currie ME, Romsa J, Fox S, Vezina WC, Akincioglu C, Warrington JC, McClure RS, Stitt LW, Menkis AH, Boyd WD, Kiaii B. Long-term angiographic follow-up of robotic-assisted coronary artery revascularization. Ann Thorac Surg 2012;93:1426-1431.

- Currie ME, Trejos AL, Rayman R, Chu MWA, Patel R, Peters TM, Kiaii B. Evaluating the effect of three dimensional visualization on force application and performance time during robotics-assisted mitral valve repair. Innovations (Phila) 2013; 8(3): 199-205.

My contribution to this chapter involved designing and conducting experiments and analyzing data.

2.1 Challenges of Robotics-Assisted Cardiac Surgery

Robotic surgical systems assist surgeons in performing minimally invasive procedures, through their provision of high-definition stereoscopic imaging and wristed suturing capability through smaller endoscopic ports. As a result of these engineering advances, the surgical robot reduces tremor at the instrument and increases surgeons' dexterity [1, 2]. However, robotic surgical systems present new and unique challenges resulting from the use of indirect visualization through an endoscope and remote manipulation of tissue through a master-slave configuration [3].

It is well established that in conventional or open surgery, sensory input is derived from both vision and haptic feedback [4, 5]. Haptics is the combination of kinesthetic, tactile, and proprioceptive information. Kinesthetic feedback provides position, force, and movement information and can be measured using a force/torque sensor. Tactile feedback includes the sensation of vibration, shape, and texture. Proprioception provides the sense of position and movement of body segments [6]. For a complete depiction of haptic interactions between surgical instruments and tissue kinesthetic, tactile, and proprioception feedback must be acquired [6-8].

During robotics-assisted surgery, the indirect manipulation of tissue through the master-slave configuration of the robotic system prevents realistic interaction forces between the surgeon, the therapeutic instruments, and the tissue [3]. This may be particularly deleterious in dexterous fine movements such as intracorporeal suturing and knot tying, which require accurate control of applied forces and instrument positions [6, 9-11].

Without haptic feedback, insufficient forces might be applied when grasping tissue or sutures, resulting in loose knots [3, 6]. Conversely, excessive forces may be applied to tissue leading to increased trauma and damage to tissue [3, 6]. This is particularly important in robotics-assisted mitral valve repair, which requires fine motor skill to suture an annuloplasty band to the cardiac tissue surrounding the mitral valve annulus. Without tactile and force information, surgeons must rely on visual cues to estimate the force being applied [4-6, 12].

2.2   Visualization in Robotics-Assisted Mitral Valve Repair

Two-dimensional (2D) visualization was used in the first minimally invasive mitral valve surgeries [13-15]. Performance of surgical tasks with 2D vision requires the use of indirect monocular cues to compensate for the lack of depth perception [16]. These cues include the relative position of instruments, anatomic structure size, shading of light and dark, and texture grading [17]. Therefore, performance of detailed skills such as intracorporeal suturing, tying, and fine dissection with 2D visualization requires practice and experience. Chitwood and colleagues [13-15] reported successful complex mitral valve repairs including quadrangular resections, sliding valvuloplasties, chordal transfers, and synthetic chordal replacements using 2D visualization.

However, others have suggested that 2D visualization was inadequate for detailed repairs [18]. Advanced surgical skills require fine-motor skills and depth perception. Minimizing tissue trauma while using these skills can ultimately affect patient outcome. As a result, fine-motor skills and depth perception may directly affect surgical performance, operative time, and morbidity.

Previous studies have suggested that because 3D visualization provides more binocular depth cues, depth perception with binocular 3D systems is superior to that achieved with monocular 2D systems [17, 19]. Furthermore, compared to 3D binocular vision, 2D performance with monocular vision affects the kinematics and pattern of human motions. 2D visualization increases movement time and lowers peak velocity. In addition, with 3D vision, reach and grab tasks are performed faster than with 2D visualization [17, 20-23].

Intuitive Surgical Incorporated, (Sunnyvale, CA) has developed the da Vinci surgical system with a very high quality three-dimensional (3D) stereoscopic visualization system to enhance the performance of robotics-assisted surgical procedures [8, 13, 24]. Throughout this chapter, stereoscopic and monoscopic visualization modes are referred to as 3D and 2D, respectively. While some have argued that the da Vinci's superior 3D visualization capabilities compensates for lack of haptic feedback, others assert that visualization alone cannot replace the value of force feedback.

The objective of the study outlined in this chapter is to determine the effect of three-dimensional visualization on the amount of force applied to mitral valve tissue and the time to perform *ex vivo* mitral valve annuloplasty using robotics-assisted and conventional techniques. In addition, our aim is to determine whether these effects are consistent between novices and experts in robotics-assisted cardiac surgery. Finally, to add further clinical relevance, we compare these results with those of conventional open mitral valve annuloplasty to examine differences in forces applied and times required to complete surgical tasks between robotics-assisted and conventional open surgery.

2.3   Mitral valve annuloplasty test-bed

A cardiac surgery test bed was constructed to measure forces applied by test subjects performing either conventional or robotics-assisted mitral valve annuloplasty. The tissue

test bed consisted of a porcine mitral valve mounted on a six-axis force/torque sensor (ATI Industrial Automation, Apex, NC) to measure applied forces in the x, y, and z directions (Figure 2.1). The porcine mitral valve annulus and attached leaflets were dissected from the porcine chordae tendinae attachments and left ventricle. A disc to mount the mitral valve on the force/torque sensor and expose the valve annulus and leaflets was designed and constructed using SolidWorks (Dessault Systèmes SolidWorks Corporation, Waltham, Massachusetts). The disc was printed from ABS*plus*™ production-grade thermoplastic (Dimension Incorporated, Eden Prairie, MN) using an Elite 3D printer (Dimension Incorporated, Eden Prairie, MN). The excised mitral valve was mounted between the two custom designed plates that firmly clamp the cardiac tissue along the outer edge of the annulus (Figure 2.1). Custom software was written in C++ to record forces applied to the porcine mitral valve and measured by the force/torque sensor every 1ms. Multiple studies have employed porcine mitral valves as a model of the human mitral valve for force modeling, pathology modeling, surgical techniques, surgical skills training and surgical outcomes [25-33]. In fact, a recent study compared the biomechanical properties of the human mitral valve to the porcine mitral valve and found that the annular and leaflet geometry of the porcine and human mitral valves are very close in dimensions; however, porcine mitral valves are more compliant than human valves [32].
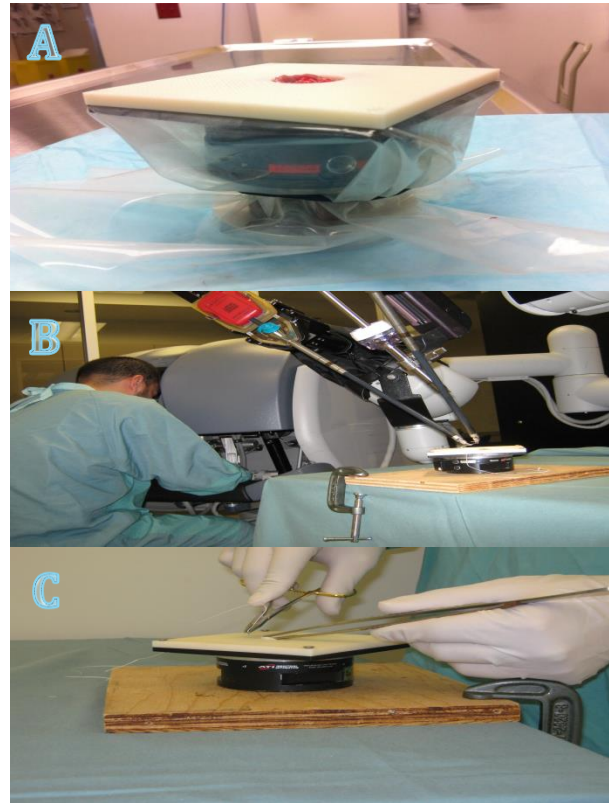
Figure 2.1: A, Mitral valve annuloplasty test bed. The tissue test bed consists of an excised porcine mitral valve mounted between two custom designed plates that firmly clamp the cardiac tissue along the outer edge of the annulus. The plates and valve are mounted on a six-axis force/torque sensor (ATI Industrial Automation, Apex, NC). B, Mitral valve annuloplasty test bed within the operative field of the da Vinci robot. C, Mitral valve annuloplasty test used for conventional valve repair.

2.4   Selection of Subjects

Following approval from the Western University Ethics Review Board, cardiac surgeons with experience in both conventional and robotics-assisted cardiac surgery, along with medical trainees with no experience in robotics-assisted surgery, were contacted to participate in this study. Nine study participants completed both conventional and robotics-assisted mitral valve annuloplasty trials. Three participants were surgeons with training in both conventional and robotics-assisted cardiac surgery, while six were trainees with no experience in robotics-assisted procedures. The three expert participants had each completed over five hundred robotics-assisted cardiac operations as part of their specialized training and surgical practice prior to the study. One of the three experts was left handed. The novice group consisted of cardiac surgery residents from postgraduate year one to postgraduate year six. None of the residents had completed a robotics-assisted cardiac surgery prior to the study. However, all residents had experience in conventional suturing and knot tying in cardiac surgery. One of the six trainees was left handed. All other participants were right handed.

2.5   Assessment of forces and time required for conventional mitral valve annuloplasty tasks

Study subjects completed conventional mitral valve annuloplasty within the mitral valve annuloplasty test bed. Each subject passed sixteen 75 cm 2-0 (V-5) Ethibond sutures (Ethicon Incorporated, Somerville, NJ) through the porcine mitral valve annulus in a transverse mattress fashion at predetermined points using the same six inch Crile-Wood needle driver and eight inch DeBakey tissue forceps (Pilling, Canada Teleflex Medical, Markham, ON). The sutures were then passed through a Cosgrove-Edwards flexible annuloplasty band (Edwards Lifesciences Corporation, Irvine, CA) and tied in place. The entire stitch length was not pulled through the annulus. Force and time were recorded; 1.

from contact of the needle with the mitral valve annulus to complete withdrawal of the needle from the mitral valve annlulus, 2; from contact of the needle to the annuloplasty band to complete withdrawal of the needle from the annuloplasty band, and 3; from initiating the first loop for tying two forehand surgeon's knots and one backhand knot to tightening the last knot before the surgeon removed their instruments from the suture. There was no surgical assistant for any of the trials. All surgeons completed suture placement at standardized demarcated points along the posterior annulus of the mitral valve.

2.6   Assessment of Forces and Time Required for Robotics-Assisted Mitral Valve Annuloplasty with 2D and 3D Visualization

Mitral valve annuloplasty was completed by study subjects as described above, using robotics-assisted techniques and the da Vinci Surgical System (Intuitive Surgical Incorporated, Sunnyvale, CA). The da Vinci was randomly switched between 2D and 3D visualization modes. Eight sutures and four ties were completed by study subjects for both 2D and 3D visualization modes. The forces applied by the study subjects during three different force actions (inserting the needle into the mitral valve annulus, inserting the needle into the annuloplasty band, and suture tying) were measured by the force/torque sensor and recorded by the customized software. In addition, the time taken to execute three instrument ties was recorded. The maximum force measurement acquired by the force/torque sensor during each suturing or tying task was recorded for each surgeon. The average of these maximum forces was calculated for experts and novices using 2D visualization, 3D visualization, or conventional techniques.

2.7   Statistical Analysis

All statistical analyses were performed using SPSS (International Business Machines Corporation, Armonk, NY). Univariate analysis of variance was employed to compare force and time measurements completed by subjects using conventional mitral valve annuloplasty and robotics-assisted mitral valve annuloplasty with either 2D or 3D visualization. Continuous variables are expressed as mean with standard deviation (SD). A p value < 0.05 was considered statistically significant.

2.8   Results

2.8.1   Assessment of Time Required for Robotics-Assisted Mitral Valve Annuloplasty with 2D and 3D Visualization

The mean time required to suture the mitral valve annulus using 3D visualization was significantly less than that required to suture the mitral valve annulus using 2D vision ($p < 0.001$, Table 2.1). This finding was consistent between experts and novices ($p = 0.5$). In addition, there was no significant difference in suture times between experts and novices

Table 2.1: Comparison of the time required by experts and novices during robotics-assisted *ex vivo* mitral valve annuloplasty with 2D and 3D visualization and with robotics-assisted and conventional surgical techniques.

Measurement	2D	3D	*p* value	Robotics-assisted surgery with 3D visualization	Conventional surgery	*p* value
Mitral valve suture time (s)						
Expert	49.4 ± 4.1	25 ± 3.2	<0.001	25 ± 3.2	12.4 ± 1.8	<0.001
Novice	45 ± 2	26.8 ± 1.9	<0.001	26.8 ± 1.9	19.4 ± 1.4	<0.001
Expert versus Novice (*p* value)			0.8			0.004
Mitral valve tie time (s)						
Expert	105 ± 15.2	63.5 ± 11.2	<0.001	63.5 ± 11.1	17.6 ± 8.2	<0.001
Novice	145.5 ± 9.5	97.7 ± 9.5	<0.001	97.7 ± 9.5	19.3 ± 6.4	<0.001
Expert versus Novice (*p* value)			0.03			0.002

with either 2D or 3D visualization ($p = 0.8$). Similarly, the mean time required to tie a suture to the mitral valve annulus using 3D visualization was significantly less than the mean time required to tie using 2D vision ($p < 0.001$, Table 2.1). This finding was consistent between experts and novices ($p = 0.9$). However, experts required significantly less time than novices to tie sutures using either 2D or 3D visualization ($p = 0.03$).

2.8.2 Assessment of Time Required for Mitral Valve Annuloplasty with Robotics-Assisted and Conventional Cardiac Surgery Techniques

The time required to complete suturing and tying tasks during *ex vivo* mitral valve annuloplasty using conventional techniques was compared to that required to complete these tasks using robotics-assisted techniques with 3D visualization. The mean time required to suture the mitral valve annulus using conventional surgical technique was significantly less than that needed to suture using robotics-assisted assistance and 3D vision (p < 0.001, Table 2.2). This finding was consistent between both experts and novices (p = 0.1). However, experts required significantly less time than novices to suture using either 3D visualization or conventional surgical technique (p = 0.004).

The mean time required to tie a suture to the mitral valve annulus using conventional surgical techniques was significantly less than that needed to perform the same task using robotics-assisted techniques with 3D vision ($p < 0.001$, Table 2.2). This finding was consistent between both experts and novices ($p = 0.1$). However, experts required significantly less time than novices to tie sutures using either robotics-assisted techniques with 3D vision or conventional surgical technique ($p = 0.002$).

2.8.3 Assessment of Forces Applied During Robotics-Assisted Mitral Valve Annuloplasty with 2D and 3D Visualization

Mean forces applied by the study subjects were measured and recorded during three different force actions: 1. Inserting the needle into the mitral valve annulus, 2. Inserting the needle into the annuloplasty band, and 3. Suture tying. The mean maximum force applied during suturing of the mitral valve annulus using 3D visualization was significantly less than that applied to suture using 2D vision in experts; however, there was no significant difference in the mean maximum force applied by novices using either

Table 2.2: Comparison of the force applied by experts and novices during robotics-assisted *ex vivo* mitral valve annuloplasty with 2D and 3D visualization and with robotics-assisted and conventional surgical techniques.

Measurement	2D	3D	*p* value	Robotics-assisted surgery with 3D visualization	Conventional surgery	*p* value
Mitral valve annulus force (N)						
Expert	4.6 ± 1.2	5.1 ± 0.9	0.7	5.1 ± 0.8	2.6 ± 0.5	<0.001
Novice	6.8 ± 0.6	4.8 ± 0.6	0.1	4.8 ± 0.6	2.8 ± 0.4	0.06
Expert versus Novice (*p* value)			0.5			0.9
Annulopasty band force (N)						
Expert	4.5 ± 0.5	4.2 ± 0.4	0.7	4.2 ± 0.4	1.6 ± 0.3	<0.001
Novice	4.8 ± 0.4	4.3 ± 0.4	0.7	4.3 ± 0.4	1.9 ± 0.3	<0.001
Expert versus Novice (*p* value)			0.8			0.6
Suture tie force (N)						
Expert	5.8 ± 1.9	4.1 ± 1.5	0.006	4.1 ± 1.5	2.9 ± 1.2	0.02
Novice	13.9 ± 1.3	11.5 ± 1.3	0.6	11.5 ± 1.3	3.6 ± 0.9	<0.001
Expert versus Novice (*p* value)			0.001			<0.001

3D or 2D visualization (Table 2.2). This finding was consistent between both experts and novices ($p = 0.3$).   In addition, there was no significant difference in force applied by experts or novices using 2D or 3D visualization ($p = 0.5$).

There was no significant difference in the mean maximum force applied to mitral valve tissue during suturing of the mitral valve annuloplasty band with either 3D visualization or 2D visualization (Table 2.2). This finding was consistent between both experts and novices ($p = 0.8$). In addition, there was no significant difference in force applied by experts or novices using 2D or 3D visualization ($p = 0.8$).

Finally, the mean maximum force applied during suture tying using 3D visualization was significantly less than the mean maximum force applied using 2D vision in experts ($p = 0.006$). However, there was no significant difference in the mean maximum force applied by novices using either 3D or 2D visualization (Table 2.2). In addition, experts applied significantly less force than novices during suture tying using either 2D or 3D visualization ($p = 0.001$).

2.8.4   Assessment of Forces Applied During Mitral Valve Annuloplasty with Robotics-Assisted and Conventional Cardiac Surgery Techniques

The mean maximum force applied when suturing the mitral valve annulus using the conventional surgical technique was significantly less than the mean force applied to the suture using robotics-assisted techniques with 3D vision (Table 2.2). This finding was consistent between both experts and novices ($p = 0.5$). In addition, there was no significant difference in the force applied by experts or novices using robotics-assisted techniques with 3D vision or conventional techniques ($p = 0.9$).

The mean maximum force applied when suturing the mitral valve annuloplasty band during conventional surgery was significantly less than the mean suturing force applied during robotics-assisted techniques with 3D vision (Table 2.2). This finding was consistent between both experts and novices ($p = 0.6$). In addition, there was no significant difference in the force applied by experts or novices using robotics-assisted techniques with 3D vision or conventional techniques ($p = 0.6$).

The mean maximum force applied when tying the suture to the mitral valve annulus using the conventional surgical approach was significantly less than that applied to the suture using robotics-assisted techniques with 3D vision (Table 2.2). Experts applied significantly less force than novices using either robotics-assisted techniques with 3D vision or conventional techniques ($p < 0.001$). However, the decrease in force applied to cardiac tissue was significantly greater in novices compared to experts ($p = 0.001$).

2.9   Discussion

Our results suggest that, when comparing 2D and 3D visualization when performing the use of the latter mode results in significantly shorter robotics-assisted suturing and tying times. In addition, both experts and novices had significantly shorter suturing and suture tying times with 3D compared to 2D visualization. This is consistent with previous studies that demonstrate that 3D visualization is associated with shorter movement times and higher movement velocities than 2D visualization [16, 20-22]. In addition, binocular, 3D visualization provides more depth cues than monocular 2D visualization [16, 19]. As a result, performance of surgical tasks with 2D vision requires the use of indirect monocular cues to compensate for the lack of depth perception [16]. These cues include the relative position of instruments, anatomic structure size, shading of light and dark, and texture grading [17]. There is no significant difference in the amount of time required by novices or experts to suture using robotics-assisted techniques on the da Vinci surgical

system. This point illustrates how intuitive the da Vinci system is for novice surgeons to conduct suturing. However, robotics-assisted suture tying is a more complex task and novices required significantly more time than experts to complete this task. Therefore, performance of detailed skills such as intracorporeal suturing, tying, and fine dissection with 2D visualization requires practice and experience.

Previous studies have illustrated the improvement in operative performance times by surgeons with increased experience [34, 35]. One center reported a 95% decrease in operative times each time the case number for a surgeon doubled [36]. Although learning curves differ between centers, this is reflected in the faster tying times for experts, who have completed over five hundred robotics-assisted procedures, versus novices. As our results show, on average, experts sutured each stitch 12.6 seconds faster and tied each knot 45.9 seconds faster with conventional techniques versus robotics-assisted techniques with 3D vision. Moreover, on average, novices sutured each stitch 4.4 seconds faster and tied each knot 78.4 seconds faster with conventional techniques versus robotics-assisted techniques with 3D vision.

On an annuloplasty band with ten double-armed stitches, the above results translate to a mean difference between conventional and robotics-assisted techniques with 3D vision for suturing and tying of 11.9 minutes in experts and 14.5 minutes in novices.

Our data also show that suture time with conventional open surgery required significantly less time than that required when employing a robotics-assisted procedure, with either 2D or 3D visualization. Therefore, although the da Vinci surgical system provides true stereoscopic vision, there are other effects associated with the robotics-assisted approach that still create an increase in the task completion time. This conclusion is consistent with previous clinical studies that have reported longer operative times in robotics-assisted surgeries compared to conventional or open surgeries [37-39].

Although previous studies have demonstrated superior performance curves and operative efficiency with 3D visualization, no previous studies have examined the effect of 3D visualization on force application on surgical tissue. These data suggest that there is no significant difference in the maximum force applied by novices to the mitral valve during insertion of needle in the annulus, insertion of needle in the annuloplasty band, or during suture tying using either 2D or 3D visualization. However, there is a significant decrease in the force applied by experts to the mitral valve tissue during suture tying with 3D visualization versus the corresponding forces with 2D visualization. Experts' mean maximum forces were also more consistent with 3D visualization, reflected as a smaller SE. In addition, novices consistently applied significantly more force to the mitral valve tissue than experts using 2D or 3D visualization. One possible explanation for this is that novices are less perceptive of visual cues to indicate the force applied to tissue. They may not have adapted to the lack of haptic feedback, while experts have more experience using visual cues to guide the force applied to tissue.

The force applied to cardiac tissue by novices was consistently greater than that applied by experts, particularly during suture tying. Previous studies employing porcine tissue have reported visible tissue damage with the application of an 11 N force over an area of 2.4 cm² [40]. In this study, novices applied potentially damaging forces to cardiac tissue using robotics-assisted techniques without force feedback. This suggests that force feedback may be particularly useful to novices employing robotics-assisted techniques. Moreover, force application could potentially be used as a measure of surgical performance or expertise in evaluating trainees on robotics-assisted procedures; however, further validity testing is required to support such a hypothesis.

This study and others have demonstrated shorter operative times with 3D visualization; however, despite high quality binocular images, both experts and novices applied

significantly more force to cardiac tissue during 3D robotics-assisted mitral valve annuloplasty than during conventional open mitral valve annuloplasty. The highest forces applied by experts were still less than the force required to inflict any damage on the cardiac tissue; however, novices applied potentially damaging force to the cardiac tissue using robotics-assisted techniques without haptic feedback. This finding suggests that 3D visualization does not fully compensate for the absence of haptic feedback in robotics-assisted cardiac surgery, particularly in novices. Therefore, although 3D visualization may provide more information regarding object depth to facilitate complex tissue grasping, 3D visualization may not provide adequate visual cues to reflect the force applied to cardiac tissue. We have demonstrated that although robotics-assisted mitral valve repair provides many benefits to the patient, this technique poses further challenges to the surgeon and surgical trainee. Robotics-assisted surgical tasks require additional time and may apply potentially damaging forces to cardiac tissue, a factor that is more prominent in novice surgeons. A simulation system providing force feedback may improve both expert and trainee performance using robotics-assisted techniques. We plan to test this hypothesis in future studies. Our results demonstrate that robotics-assisted mitral valve repair requires more time and surgeons apply more force to cardiac tissue using robotics-assisted techniques compared to conventional mitral valve repair. Conventional or open mitral valve repair is technically challenging and investigators have reported the improvement in trainee performance following simulation training for open or conventional mitral valve surgery [33].

Due to this repeated measures study design, results may have been limited by subject fatigue after several trials, carry over effects from one technique to the next, and the order of technique presentation. To minimize these effects, the order of trials with 2D and 3D visualization was randomized for each subject. In addition, the accuracy of suturing and quality of suture tying by novice study subjects was not assessed in this trial.

Furthermore, our sample size was limited by the number of experts in robotics-assisted cardiac surgery. If we had included more participants to increase the power of the study, we may have been able to detect a significant decrease in the amount of force applied to cardiac tissue with 3D visualization. We plan to address this limitation in future work.

In conclusion, although 3D visualization increases the control and consistency of the interaction forces on cardiac tissue, it does not prevent the application of damaging forces. The implication of these findings is that to achieve better control of the interaction forces on cardiac tissue haptics, including force feedback, may be required.

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Chapter 3

3   The Role of Visual and Direct Force Feedback in Robotics-Assisted Mitral Valve Annuloplasty

Robotics-assisted cardiac surgery involves the indirect manipulation of cardiac tissue and prevents realistic interaction forces among the surgeon, the instruments, and the tissue [1]. This absence of haptic feedback may be detrimental, as excessive forces may be applied to cardiac tissue leading to increased trauma and damage to tissue during suturing and tying [1, 2]. Minimizing tissue trauma during robotics-assisted surgery can ultimately affect patient outcome.

A force feedback-enabled master-slave surgical system was constructed to provide both visual and direct force feedback to the surgeon during robotics-assisted cardiac surgery with three-dimensional visualization. This novel robotics system was used to measure the amount of force applied to cardiac tissue during *ex vivo* mitral valve annuloplasty repair.

This chapter outlines the effect of both direct force feedback and visual force feedback on the amount of force applied to mitral valve tissue during *ex vivo* mitral valve annuloplasty using robotics-assisted techniques.

This chapter is adapted from the following work:

- M. E. Currie, A. L. Trejos, R. Rayman, M. W. A. Chu, R. Patel, T. M. Peters, B. Kiaii. The role of haptics in robotics-assisted mitral valve annuloplasty. Hamlyn Symposium on Medical Robotics, July 2012, London, England.

- Visual and Direct Haptic Feedback in Robotics-Assisted Cardiac Surgery. M. E. Currie, A. Talasaz, A. L. Trejos, R. Rayman, M. W. A. Chu, B. Kiaii, T. M. Peters, R. Patel.   Minimally Invasive Robotic Association International Congress, September 2012, Boston, USA.
- M. E. Currie, A. Talasaz, A. L. Trejos, R. Rayman, M. W. A. Chu, B. Kiaii, R. Patel, T. M. Peters. The Role of Visual and Direct Haptics in Robotics-Assisted Mitral Valve Annuloplasty. *Journal of Medical Robotics and Computer Assisted Surgery* (Submitted)

My contribution to this chapter involved designing and conducting experiments and analyzing data.

3.1   Introduction

Haptics is the combination of kinesthetic, tactile, and proprioceptive information. Kinesthetic feedback provides position, force, and movement information and can be measured using a force/torque sensor. Tactile feedback includes the sensation of vibration, shape, and texture. Proprioception provides the sense of position and movement of body segments [1]. For a complete depiction of haptic interactions between surgical instruments and tissue, kinesthetic, tactile, and proprioception feedback must be acquired [1-3].

During robotics-assisted surgery, the indirect manipulation of tissue through the master–slave configuration of the robotic system prevents realistic interaction forces among the surgeon, the therapeutic instruments, and the tissue [4]. This absence of haptic feedback may be detrimental in dexterous fine movements such as intracorporeal suturing and knot tying, which require accurate control of applied forces and instrument positions [1, 5–7]. Furthermore, without haptic feedback, insufficient forces might be applied when grasping tissue or sutures, resulting in loose knots [1, 4]. Conversely, excessive forces

may be applied to tissue leading to increased trauma and damage [1, 4]. This is particularly important in robotics-assisted mitral valve repair, which requires fine motor skill to suture an annuloplasty band to the cardiac tissue surrounding the mitral valve annulus. Without tactile and force information, surgeons must rely on visual cues to estimate the force being applied [1, 8–10]. Advanced surgical skills require not only fine motor skills but also depth perception. Minimizing tissue trauma while performing surgery may ultimately affect surgical performance, operative time, and morbidity.

In the currently used minimally invasive surgical robotic system (the da Vinci from Intuitive Surgical Inc.), the master–slave configuration and the absence of haptic feedback prevent the transmission of tool–tissue interaction forces to the surgeon [11]. Some have argued that the da Vinci's superior three-dimensional (3D) visualization capabilities compensate for lack of haptic feedback, others assert that visualization alone cannot replace the value of haptic feedback [12].

In fact, we have previously found that despite high-quality binocular images, both the experts and the novices applied significantly more force to the cardiac tissue during 3D robotics-assisted mitral valve annuloplasty than during conventional open mitral valve annuloplasty. This finding suggests that 3D visualization does not fully compensate for the absence of haptic feedback in robotics-assisted cardiac surgery [13]. Furthermore, although a complete depiction of haptic interactions has not been integrated into robotics-assisted surgical systems, other researchers have investigated the potential benefits of the addition of either direct force feedback or visual force feedback into robotics-assisted surgical systems [14–18].

Direct force feedback involves the kinesthetic perception of reflected weight and resistance to motion by muscles, tendons and joint sensory receptors [19]. For example,

Wagner and colleagues found that direct force feedback for a minimally invasive cannulation task using endoscopic visualization reduces applied forces [14]. Another study by Wagner and colleagues examined the effects of direct force feedback on blunt dissection of an artery in a synthetic model using endoscopic visualization [15]. The absence of direct force feedback increased the average force magnitude applied to the tissue by at least fifty percent, increased the peak force magnitude by at least 100%, and increased the number of errors that damage tissue by over a factor of three. Kazi and colleagues also showed that using direct force feedback during minimally invasive catheter insertion into a vessel could lower the magnitude of the force applied to tissue during a procedure [16].

Visual force feedback involves sensory substitution and provides force feedback by using size and/or color to represent the magnitude of forces applied by a surgical instrument [12]. For example, Reiley and colleagues examined the effects of visual force feedback during surgical knot tying using a modified da Vinci robotic system equipped with force-sensing instrument tips [17]. They found no differences in measured performance parameters between robotics-assisted knot ties executed with and without visual force feedback among surgeons with robotics-assisted surgical experience. However, visual force feedback was associated with lower suture breakage rates, peak applied forces, and standard deviations of applied forces among surgeons without robotics-assisted surgery experience. These results suggested that visual force feedback primarily benefits novice robotics-assisted surgeons. Finally, Tholey and colleagues developed an automated laparoscopic grasper with both direct force and visual feedback to help surgeons differentiate tissue stiffness [18]. These investigators found that the addition of both visual and direct force feedback led to better tissue stiffness characterization than either visual or direct force feedback alone.

Despite this evidence for the benefits of direct force or visual force feedback in robotics-assisted and laparoscopic surgery, many robotics-assisted mitral valve repair surgeries are performed in the absence of any haptic feedback with excellent results [20–24]. Furthermore, some have suggested that the addition of additional stimuli during task learning made the process more difficult, as novice trainees may have less attentional resources to attend to force feedback while learning a skill [25].

Therefore, the objective of this study is to determine the effect of both direct force feedback and visual force feedback on the amount of force applied to mitral valve tissue during *ex vivo* mitral valve annuloplasty using robotics-assisted techniques. In addition, our aim is to determine whether these effects are consistent between novices and experts in robotics-assisted cardiac surgery. We expect that the addition of either direct or visual force feedback will decrease the magnitude of force applied to cardiac tissue during robotics-assisted mitral valve annuloplasty. Furthermore, we expect that these differences will be more pronounced in novices, as they have less experience using visual cues to estimate the amount of force applied to tissue during robotics-assisted cardiac surgery.

3.2   Materials and Methods

3.2.1 Mitral valve annuloplasty test-bed

A cardiac surgery test bed was developed to measure forces applied by test subjects performing robotics-assisted mitral valve annuloplasty. The tissue test bed consisted of a porcine mitral valve mounted on a six-axis force/torque sensor (ATI Industrial Automation, Apex, NC) to measure applied forces in the x, y, and z directions (Figure 3.1). The porcine mitral valve annulus and attached leaflets were dissected from the porcine chordae tendineae attachments and left ventricle. A disc to mount the mitral valve

on the force/torque sensor and expose the valve annulus and leaflets was designed and constructed using SolidWorks (Dessault Systèmes SolidWorks Corporation, Waltham, Massachusetts). The disc was printed from ABS*plus*™ production-grade thermoplastic (Dimension Incorporated, Eden Prairie, MN) using an Elite 3D printer (Dimension Incorporated, Eden Prairie, MN). The excised mitral valve was mounted between the two custom designed plates that firmly clamp the cardiac tissue along the outer edge of the annulus (Figure 3.1). Custom software was written in C++ to record forces applied to the porcine mitral valve and measured by the force/torque sensor every 1ms.

Figure 3.1: Mitral valve annuloplasty test bed. The tissue test bed consists of an excised porcine mitral valve mounted between two custom designed plates that firmly clamp the cardiac tissue along the outer edge of the annulus. The plates and valve are mounted on a six-axis force/torque sensor (ATI Industrial Automation, Apex, NC).
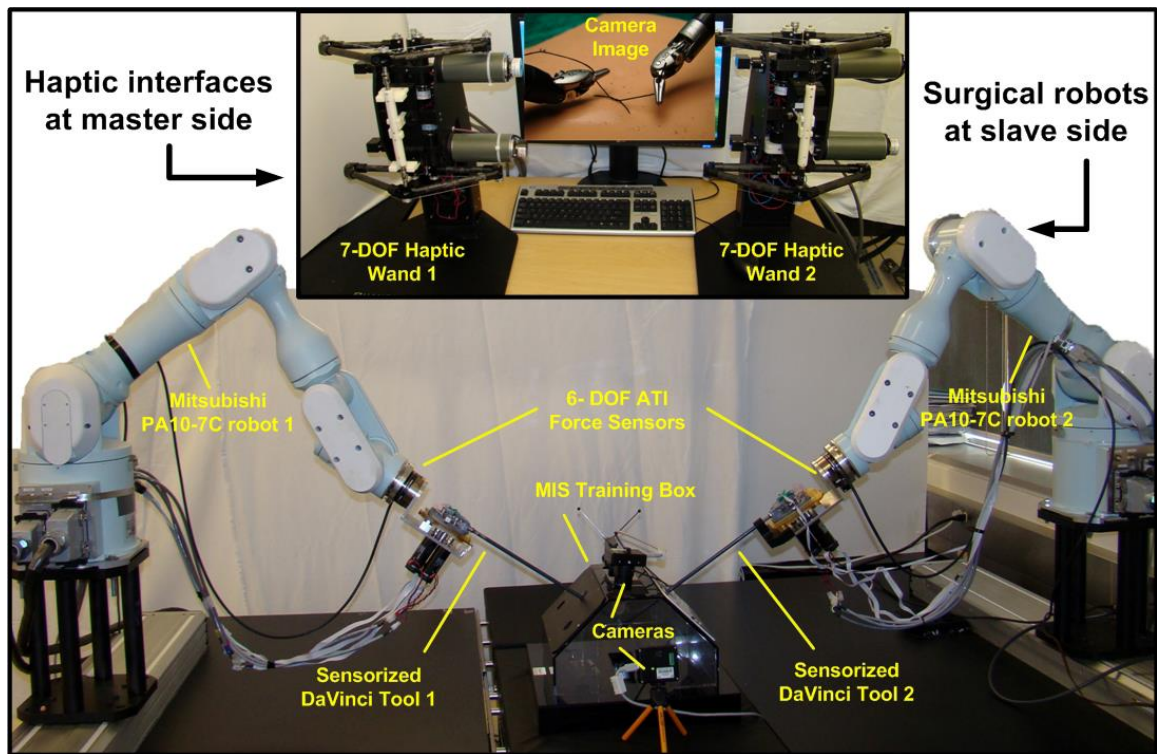
3.2.2 Force feedback-enabled robotic surgery system

The force feedback-enabled master-slave surgical system used for trials is shown in Figures 3.2 and 3.3. This setup consists of two Mitsubishi PA10-7C robots as the slave system controlled remotely over a dedicated network through two customized Quanser Haptic Wands as the master interface [2]. The structure of the Haptic Wand, its

workspace and force reflection capability have been described in a previous publication [3]. Stereoscopic visualization was provided by a zero-degree endoscope (Intuitive Surgical, Sunnyvale, CA) and a ProView XL50 head-mounted display (Kaiser Electro-Optics Inc, Carlsbad, CA).

3.2.3   Selection of subjects

Following approval from the Western University Ethics Review Board, three cardiac surgeons with experience in both conventional and robotics-assisted cardiac surgery, along with nine students with no experience in robotics-assisted surgery, agreed to participate in this study. Prior to the study, the three expert participants had each completed over 500 robotics-assisted cardiac operations as part of their specialized training and surgical practice. One of the three experts was left-handed. The novice group consisted of students and trainees with no previous experience in robotics-assisted surgery. Two of the nine trainees were left-handed. All other participants were right-handed.

Figure 3.2: Force feedback-enabled robotics-assisted surgery system with sensorized DaVinci instruments mounted on Mitsubishi robotic arms [19].
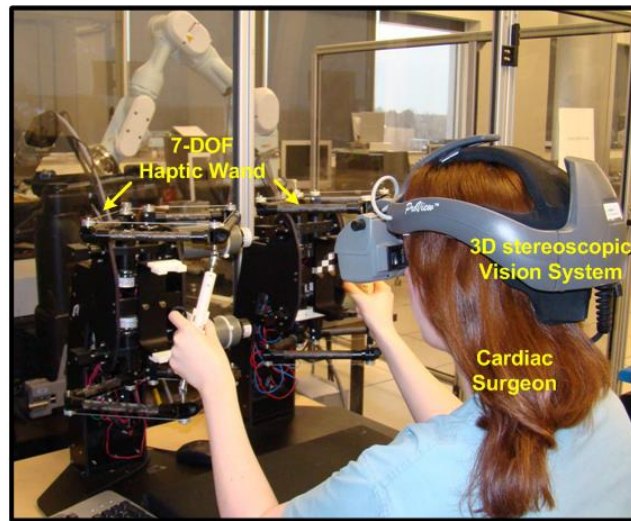
a) Haptic interfaces at the master side
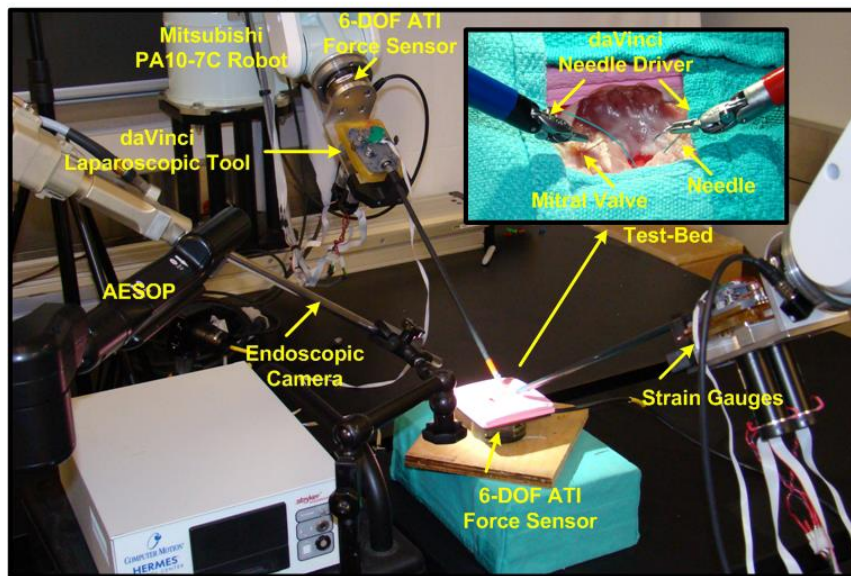
b) Surgical robots at the slave side

Figure 3.3: Experimental test bed for force feedback-enabled robotics-assisted mitral valve annuloplasty showing both the master control side (a) and the robotic slave side (b) [19].

3.2.4 Assessment of forces applied during robotics-assisted mitral valve annuloplasty tasks

Study subjects completed robotics-assisted mitral valve annuloplasty within the mitral valve annuloplasty test bed (Figure 3.3). The tasks used for measurement of time and force involved pulling the suture through the annuloplasty band and tightening the stitch holding the annuloplasty band to the mitral valve annulus.

For force measurement during suturing, two double-armed 75 cm 2-0 (V-5) Ethibond sutures (Ethicon Incorporated, Somerville, NJ) were passed through the porcine mitral valve annulus at predetermined points. The sutures were then passed through a Cosgrove-Edwards flexible annuloplasty band (Edwards Lifesciences Corporation, Irvine, CA) in a horizontal mattress fashion. The force required to pull each stitch a distance of 8 cm from the annuloplasty band was recorded. This was repeated four times, once for each end of two double-armed sutures, that is, a suture with a needle attached at each end. Next, the force required for study subjects to tighten two surgical knots and to secure the annuloplasty band to the mitral valve annulus was recorded. Subjects performed tasks with or without force feedback.

Force feedback was provided as visual force feedback, direct force feedback, or both visual and direct force feedback. Three levels were considered for both direct and visual force feedback. Direct force feedback was provided at the same, half, or double the intensity of the actual force applied to tissue. The main objective of showing visual force feedback in different levels was to assure the user that the force being applied on the tissue was safe and that there was sufficient force to tie a secure knot (Figure 3.4). Both colour and size denoted the magnitude of force applied by both the right and left arms. Green denoted the range of force below the threshold required for a tight knot, which was less than 4 N. Yellow denoted the range sufficient for a tight knot, which was between 4

N and 6 N. Red denoted force that could damage the tissue or break the suture, which was greater than 6 N [19]. In order to prevent sliding between the grippers and the suture when the subject tightened the suture knot, the grippers were commanded to maintain a 2 N grasping force with the grippers closed.

The order in which force feedback was presented was randomized. Randomization was performed by a statistical program (Design Expert®, Stat-Ease, Inc., Minneapolis, MN). Throughout all trials, all actions of the surgical instruments were captured on video and the positions of the master (Haptic Wand, Quanser, Inc., Markham, ON) and the slave robot were also recorded. All test subjects completed suture placement at standardized demarcated points along the posterior annulus of the mitral valve. There was no surgical assistant for any of the trials.

Figure 3.4: Visual force feedback, as shown to subjects. This figure shows the visual force feedback for the left surgical arm. Both colour and size denote the magnitude of the force applied by both the right and left arms. Green denotes the range of force/tension below the threshold required for a tight knot (under 4N). Yellow denotes the range sufficient for a tight knot (4-6 N). Red denotes force that may damage the tissue or break the suture (above 6N).

3.2.5 Statistical Analysis

Statistical analysis was performed using a multi-level linear regression model for this repeated-measures study design. Analysis of variance was employed to compare force measurements completed by subjects using robotics-assisted mitral valve annuloplasty with or without force feedback. The three options for providing force feedback included visual force feedback, direct force feedback, and both visual and direct force feedback. All statistical analyses were performed using RStudio (RStudio, Inc., Boston, MA). Continuous variables were expressed as the mean and standard deviation (SD). For purposes of data analysis, a *p* value of less than 0.05 was considered statistically significant.

3.3 Results

3.3.1 Amount of maximum force applied during suturing by novices and experts during robotics-assisted *ex vivo* mitral valve annuloplasty

Figure 3.5 illustrates the variability in the maximum force (N) applied to mitral valve tissue by novices and experts during four trials of robotics-assisted suturing. Novices are Subjects 1–9 and experts are Subjects 10–12.
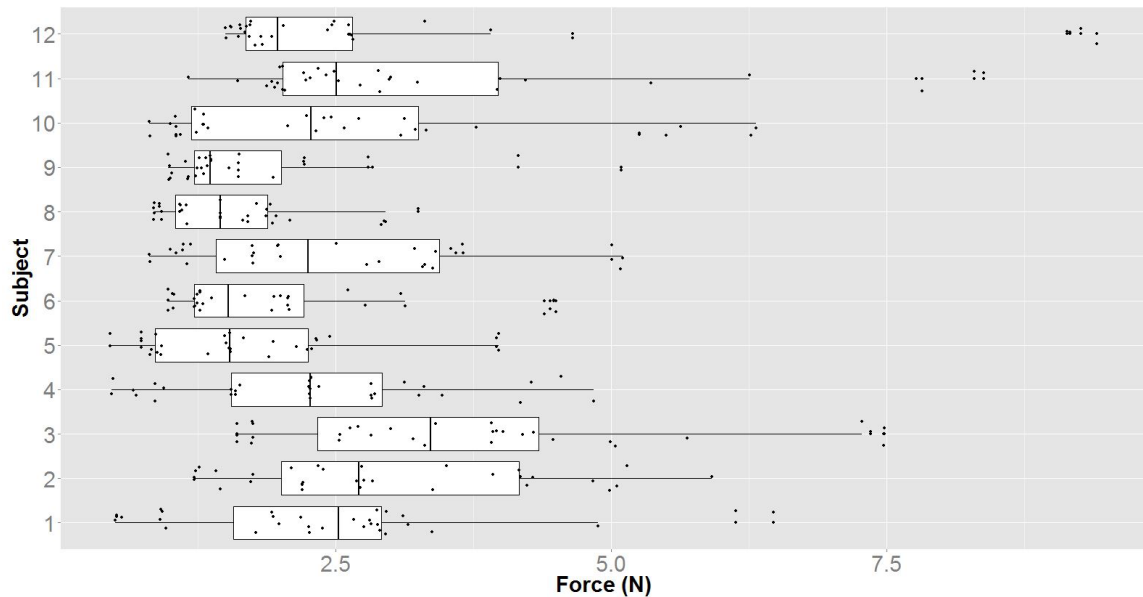
The dependent variable, maximum force applied to cardiac tissue, was right or positively skewed. Therefore, a logarithmic transformation of maximum force score was applied to the data to bring the outlying data closer to the center in order to achieve a normal distribution for further statistical analysis.

The mean maximum force applied to cardiac tissue by experts (n = 3) and novices (n = 9) during suturing for all trials was 3.02 ± 2.12 N and 2.33 ± 1.39 N, respectively. There appeared to be a trend toward higher force applied by experts; however, this difference

was not statistically significant (p = 0.1609; Figure 3.6). This was likely due to the low number of experts included in the study.

Interestingly, the mean amount of force applied by both experts and novices gradually decreased after each trial. The mean amount of force applied by experts and novices during suturing for the first, second, third, and fourth trials were 2.86 ± 1.80 N, 2.57 ± 1.68 N, 2.35 ± 1.52 N, and 2.23 ± 1.48 N, respectively (Figure 3.7). In fact, there was a statistically significant decrease in the mean amount of force applied between the first and fourth trials (p = 0.0019). This also held true for novices alone, indicating a learning curve. The mean amount of force applied by novices alone during suturing for the first, second, third, and fourth trials were 2.64 ± 1.59 N, 2.37 ± 1.41 N, 2.21 ± 1.29 N, and 2.09 ± 1.22 N, respectively (p = 0.0009, Figure 3.8).
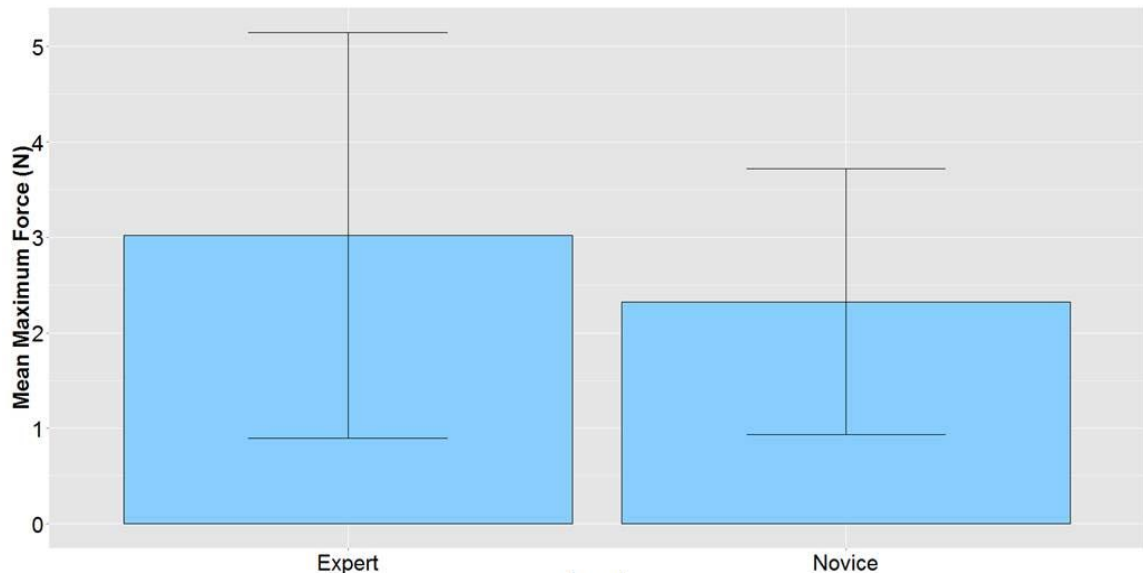

Figure 3.5: Variability in maximum force (N) applied to mitral valve tissue by novices and experts during robotics-assisted suturing.

The dependent variable, maximum force applied to cardiac tissue, was right or positively skewed. Therefore, a logarithmic transformation of maximum force score was applied to the data to bring the outlying data closer to the center in order to achieve a normal distribution for further statistical analysis.

The mean maximum force applied to cardiac tissue by experts (n = 3) and novices (n = 9) during suturing for all trials was 3.02 ± 0.22 N and 2.33 ± 0.08 N, respectively. This is not significantly different (p = 0.1609; Figure 3.5). In fact, there appeared to be a trend toward higher force applied by experts; however, likely to due to the low number of experts included in the study, this difference was not statistically significant.
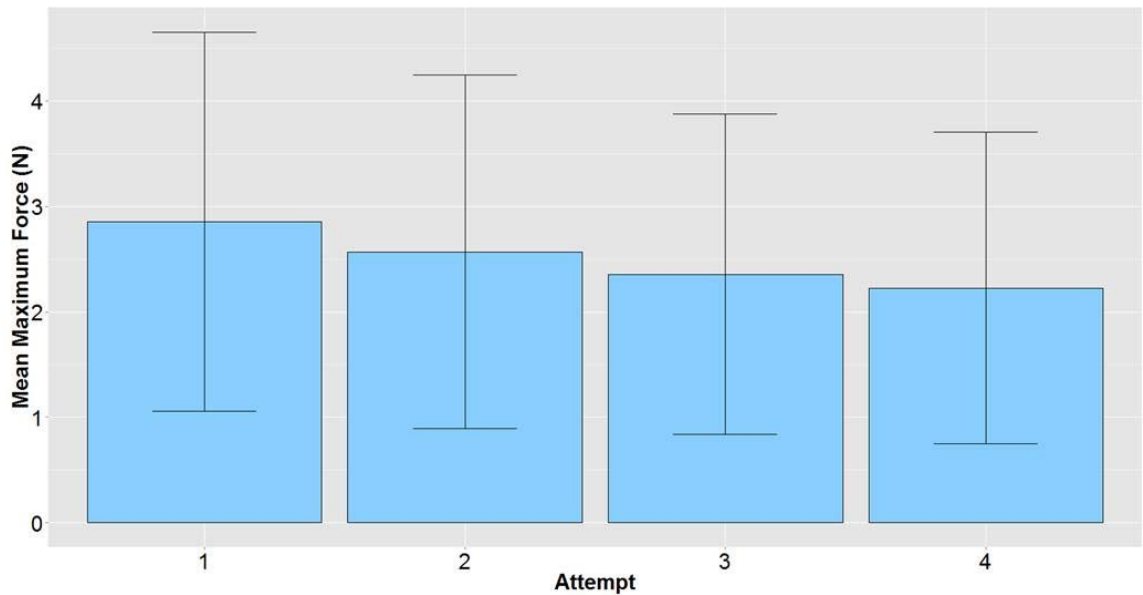
Interestingly, the mean amount of force applied by both experts and novices gradually decreased after each trial. The mean amount of force applied by experts and novices during suturing for the first, second, third, and fourth trials were 2.86 ± 0.18 N, 2.57 ± 0.17 N, 2.35 ± 0.15 N, and 2.23 ± 0.15 N, respectively. This also held true for novices alone, indicating a learning curve. The mean amount of force applied by novices alone during suturing for the first, second, third, and fourth trials were 2.64 ± 0.19 N, 2.37 ± 0.17 N, 2.21 ± 0.15 N, and 2.09 ± 0.14 N, respectively.
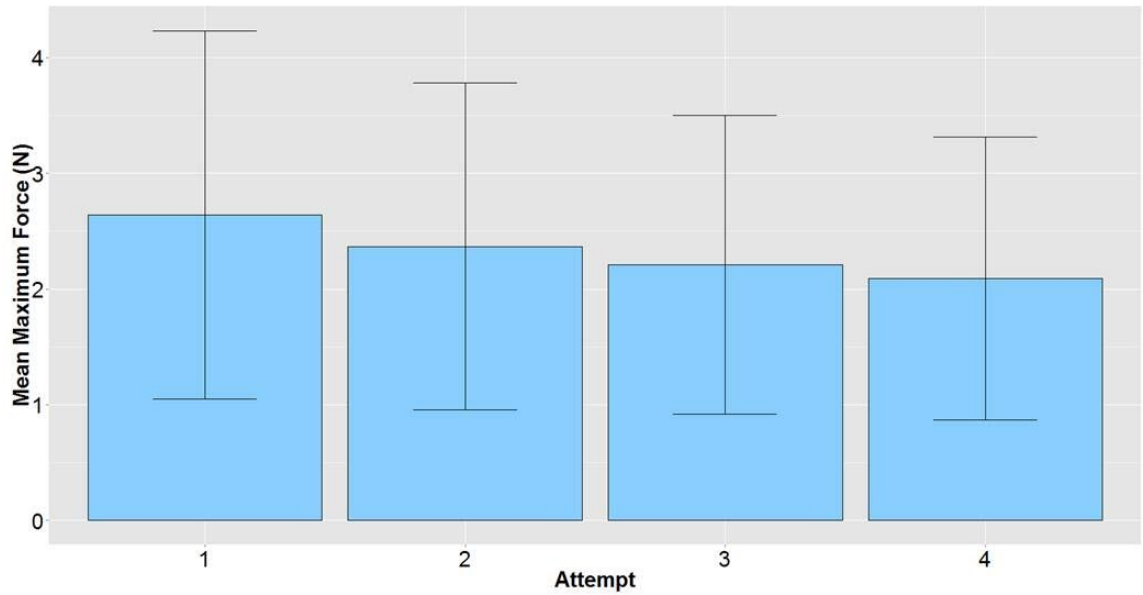
Figure 3.6: Mean maximum force applied to mitral valve tissue by experts (n = 3) and novices (n = 9) during robotics-assisted mitral valve annuloplasty suturing. There was no statistically significant difference in the mean maximum force applied to mitral valve tissue by experts (n = 3) and novices during robotics-assisted suturing (n = 9; p = 0.1609).

3.3.2 The effect of visual force feedback on the amount of force applied during suturing by novices during robotics-assisted *ex vivo* mitral valve annuloplasty
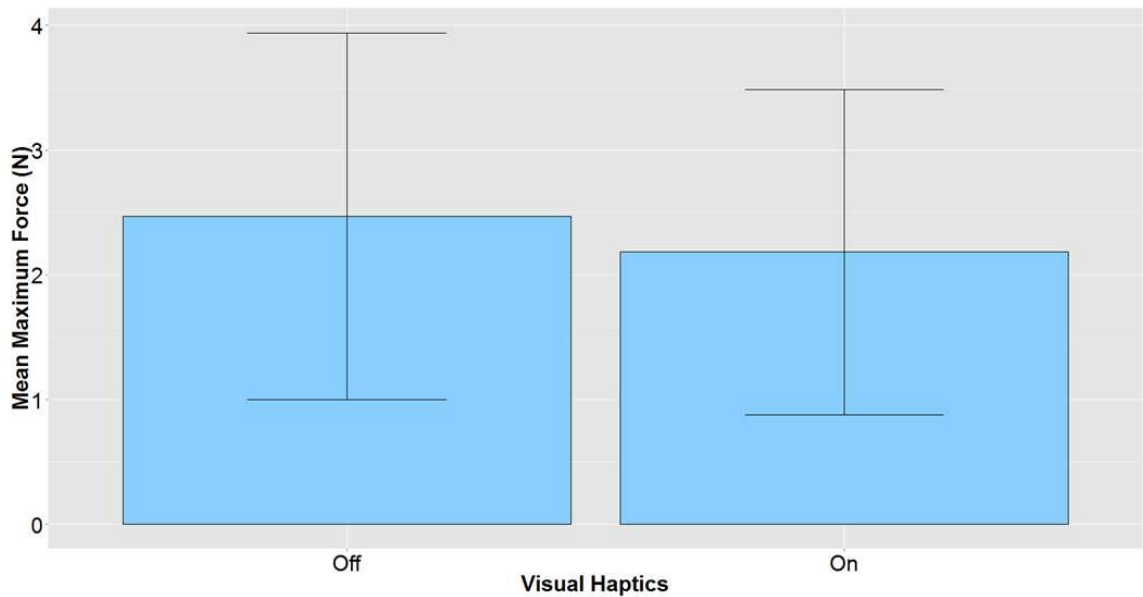
The mean maximum force applied to cardiac tissue by novices with visual force feedback (2.18 ± 1.30 N) was significantly lower than the mean maximum force applied to cardiac tissue by subjects without visual feedback (2.47 ± 1.47; $p = 0.018$; Figure 3.9).

Figure 3.7: Mean maximum force applied to mitral valve tissue by experts (n = 3) and novices (n = 9) during robotics-assisted mitral valve annuloplasty suturing decreases from the first to the fourth trial. The decrease in the mean amount of force applied between the first and fourth trials was statistically significant (p = 0.0019).

Figure 3.8: Mean maximum force applied to mitral valve tissue by and novices (n = 9) during robotics-assisted mitral valve annuloplasty suturing decreases from the first to the fourth trial. The decrease in the mean amount of force applied between the first and fourth trials was statistically significant (p = 0.0009).
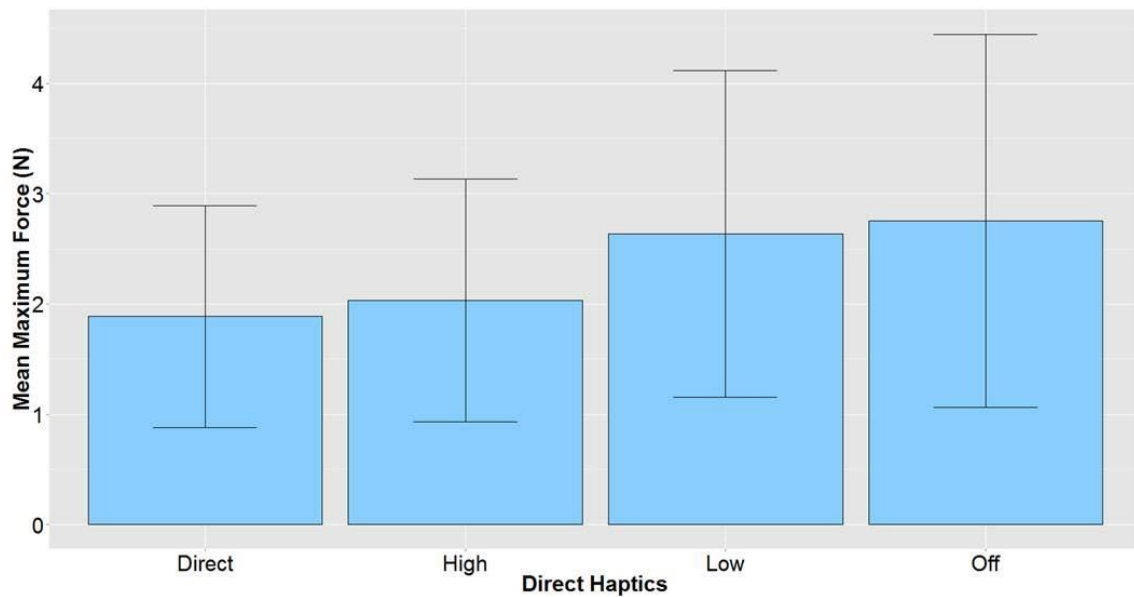
Figure 3.9: The mean maximum force applied to mitral valve tissue by novices with and without visual force feedback during robotics-assisted mitral valve annuloplasty suturing was significantly lower than the mean maximum force applied to cardiac tissue by subjects without visual feedback during robotics-assisted suturing (p = 0.018).

3.3.3 The effect of direct force feedback on the amount of force applied during suturing by novices during robotics-assisted *ex vivo* mitral valve annuloplasty

The mean maximum force applied to mitral valve tissue by novices with direct force feedback at the same, double, or half of the intensity of the actual force applied to tissue was 1.89 ± 1.01 N, 2.03 ± 1.10 N, and 2.63 ± 1.48 N, respectively. This is significantly lower than the mean maximum force applied to cardiac tissue by subjects without direct force feedback (2.75 ± 1.69 N; $p = 0.001$; Figure 3.10). Furthermore, the mean maximum force applied to mitral valve tissue with double the intensity of the actual force

applied to tissue was significantly lower than the mean maximum force applied to mitral valve tissue with half the intensity of actual force ($p = 0.0028$; Figure 3.10). Direct force feedback denotes the same intensity of force applied to tissue is transmitted back to the subject. High force feedback denotes that double the intensity of the actual force applied to tissue is transmitted back to the subject. Low force feedback denotes that half the intensity of actual force applied to tissue is transmitted back to the subject.

Figure 3.10: Main effects of different levels of direct force feedback on mean maximum force applied to mitral valve tissue by novices during robotics-assisted mitral valve annuloplasty suturing. The mean maximum force applied to mitral valve tissue by novices with direct force feedback at the same (Direct), double (High), or half (Low) the intensity of the actual force applied to tissue was significantly lower than the mean maximum force applied to cardiac tissue by subjects without direct force feedback (Off, p = 0.001).

3.3.4 The effect of combined visual and direct force feedback on the amount of force applied during suturing by novices during robotics-assisted *ex vivo* mitral valve annuloplasty

The groups examined all had 3D visualization with visual force feedback (ON) or without visual force feedback (OFF), and with or without (OFF) direct force feedback (Table 3.1). When compared to no force feedback, the addition of either visual force feedback, direct force feedback, or both visual and direct force feedback decreased the maximum force applied to mitral valve tissue during robotics-assisted *ex vivo* mitral valve annuloplasty ($p<0.05$; Figure 3.11). The lowest maximum force applied was seen with the addition of direct force feedback alone (1.62 ± 0.86 N) compared to no force feedback (3.34 ± 1.93 N; $p<0.0001$). The addition of both visual and high direct force feedback (1.68 ± 0.99 N) also significantly decreased the amount of maximum force applied to cardiac tissue when compared to no force feedback ($p<0.0001$). Both groups decreased the mean maximum force applied to mitral valve tissue by approximately 0.7 N. The addition of visual force feedback alone decreased the mean maximum force applied to mitral valve tissue by 0.5 N ($p = 0.0001$).

It is also interesting to note that damaging forces above 6N were only applied when no force feedback was provided. The addition of any force feedback prevented the application of any damaging forces above 6 N. However, the combination of both visual and direct force feedback did not result in an additive decrease in the amount force applied to cardiac tissue (Figure 3.12).

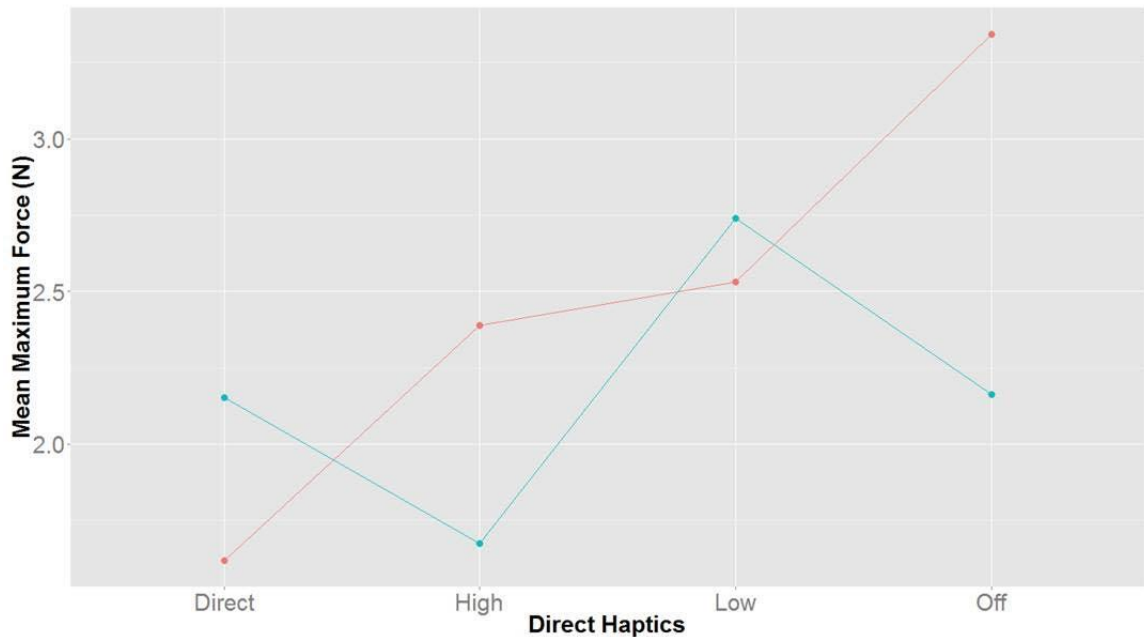**Table 3.1.** **The amount of force (N) ± SD applied during suturing by novices during robotics-assisted *ex vivo* mitral valve annuloplasty.**

| | Visual Force Feedback | |
| Direct Force Feedback | Force (N) ± SD | |
	OFF	ON
OFF	3.34 ± 1.93	2.16 ± 1.67
LOW	2.53 ± 1.26	2.74 ± 1.68
HIGH	2.39 ± 1.10	1.68 ± 0.99
DIRECT	1.62 ± 0.86	2.15 ± 1.08
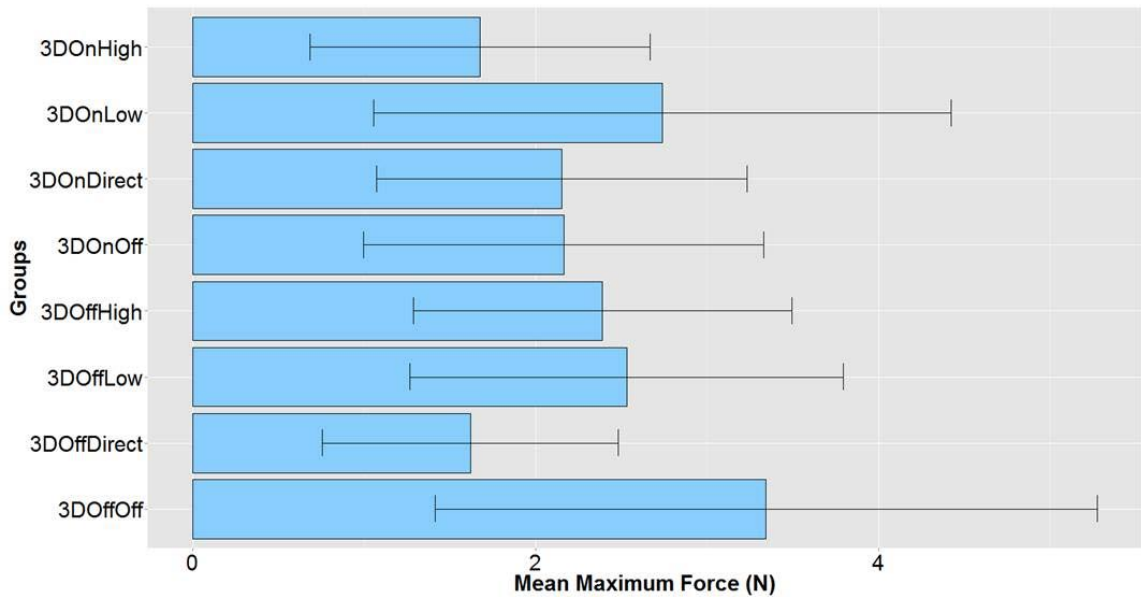
Figure 3.11: Mean maximum force applied to mitral valve tissue subjects with and without visual and direct force feedback during robotics-assisted mitral valve annuloplasty suturing. When compared to no force feedback, the addition of either visual force feedback, direct force feedback, or both visual and direct force feedback decreased the maximum force applied to mitral valve tissue (p<0.05). The lowest maximum force applied was seen with the addition of direct force feedback alone compared to no force feedback (p<0.0001). Each point represents the force applied for one trial.

Figure 3.12: Mean maximum force applied to mitral valve tissue subjects with visual force feedback (green) and without visual force feedback (red) in combination with or without direct force feedback during robotics-assisted mitral valve annuloplasty suturing.

3.3.5 Amount of maximum force applied during tying by novices and experts during robotics-assisted *ex vivo* mitral valve annuloplasty

Figure 3.13 illustrates the variability in the maximum force (N) applied to mitral valve tissue by novices and experts during robotics-assisted tying. Novices are Subjects 1–9 and experts are Subjects 10–12.
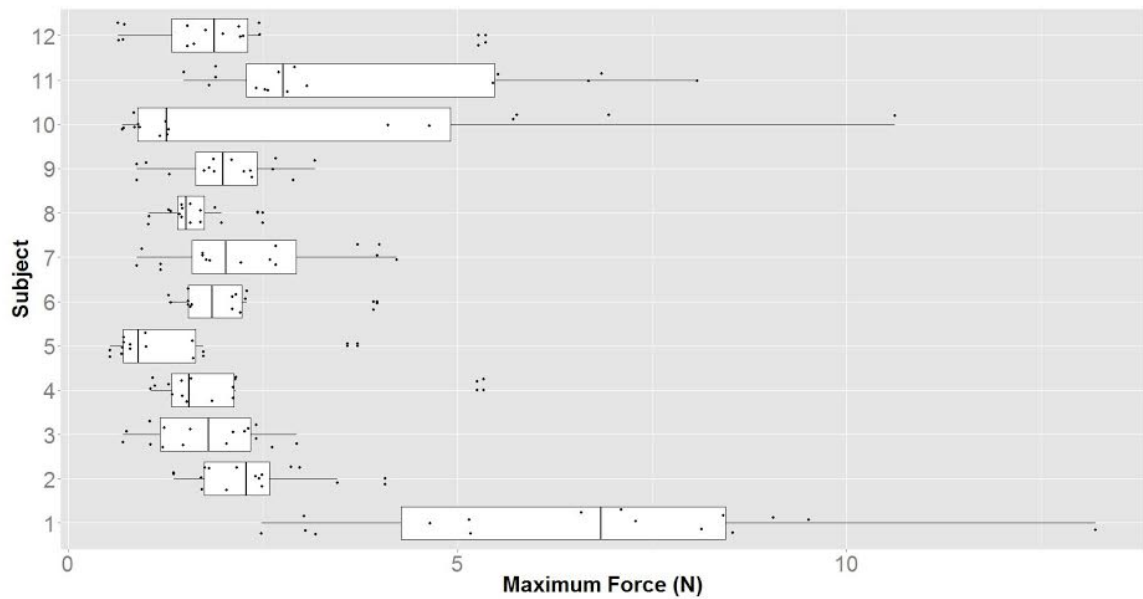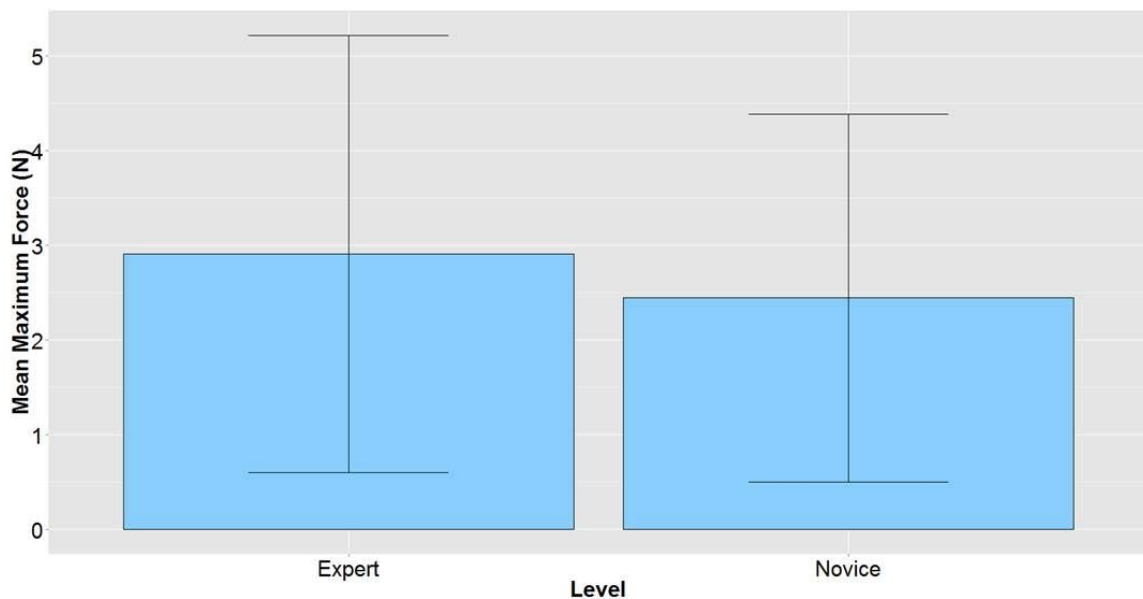
Figure 3.13: Variability in maximum force (N) applied to mitral valve tissue by novices and experts during robotics-assisted tying.

The dependent variable, maximum force applied to cardiac tissue, was right or positively skewed. Therefore, a logarithmic transformation of maximum force score was applied to the data to bring the outlying data closer to the center in order to achieve a normal distribution for further statistical analysis.

The mean maximum force applied to cardiac tissue by experts (n = 3) and novices (n = 9) during tying for all trials was 2.91 ± 2.31 N and 2.44 ± 1.94 N, respectively. There appeared to be a trend toward higher force applied by experts; however, likely due to the low number of experts included in the study, this difference was not statistically significant ($p = 0.72$; Figure 3.14).

Interestingly, the mean amount of force applied by both experts and novices gradually decreased after each trial. The mean amount of force applied by experts and novices

during tying for the first and second trials were 2.71 ± 2.29 N and 2.41 ± 1.77 N, respectively. Nevertheless, this decrease was not statistically significant ($p = 0.1635$). This decrease was also seen in novices alone. The mean amount of force applied by novices alone during tying for the first and second trials were 2.57 ± 2.16 N and 2.32 ± 1.70 N, respectively. However, the decrease was not statistically significant ($p = 0.3331$).

Figure 3.14: Mean maximum force applied to mitral valve tissue by experts (n = 3) and novices (n = 9) during robotics-assisted mitral valve annuloplasty tying

3.3.6 The effect of visual force feedback on the amount of force applied during tying by novices during robotics-assisted *ex vivo* mitral valve annuloplasty

The mean maximum force applied to cardiac tissue by novices with visual force feedback (2.35 ± 1.79 N) was not significantly different from the mean maximum force applied to

cardiac tissue by subjects without visual feedback (2.54 ± 2.10; p = 0.53; Figure 3.15).
When the results from both experts and novices were combined, the mean maximum
force applied to mitral valve tissue by all subjects with visual force feedback (2.48 ± 1.99
N) was also not significantly different from the mean maximum force applied to cardiac
tissue by subjects without visual feedback (2.64 ± 2.10; p = 0.47; Figure 3.16).
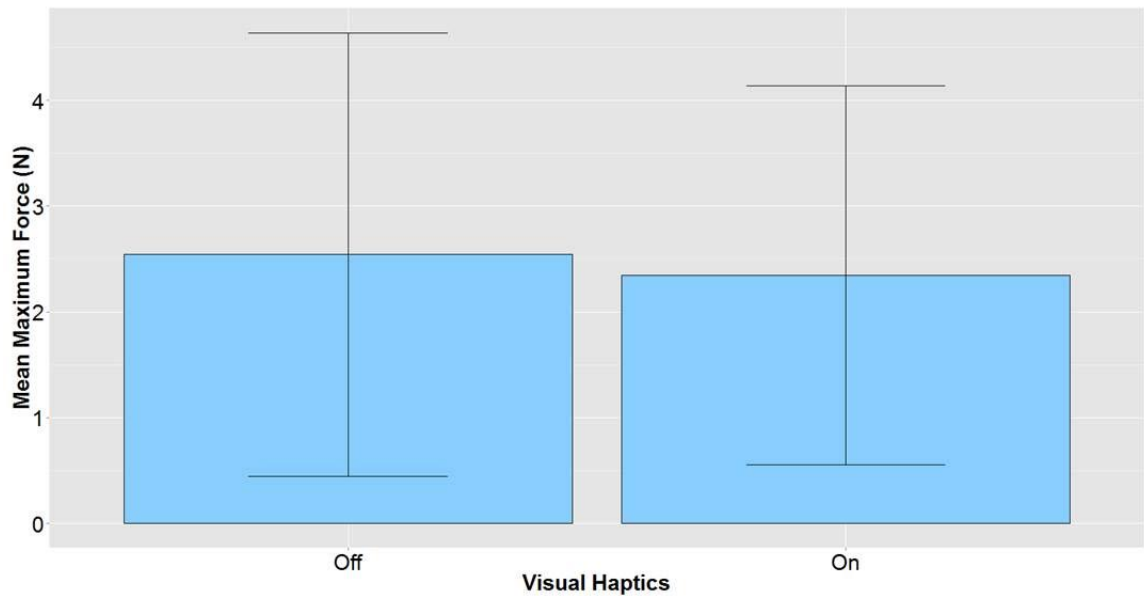
**Figure 3.15: Mean maximum force applied to mitral valve tissue by novices with
and without visual force feedback during robotics-assisted mitral valve annuloplasty
tying (p = 0.53).**

Figure 3.16: The mean maximum force applied to mitral valve tissue by novices and experts with and without visual force feedback during robotics-assisted tying was not significantly different (p = 0.47).
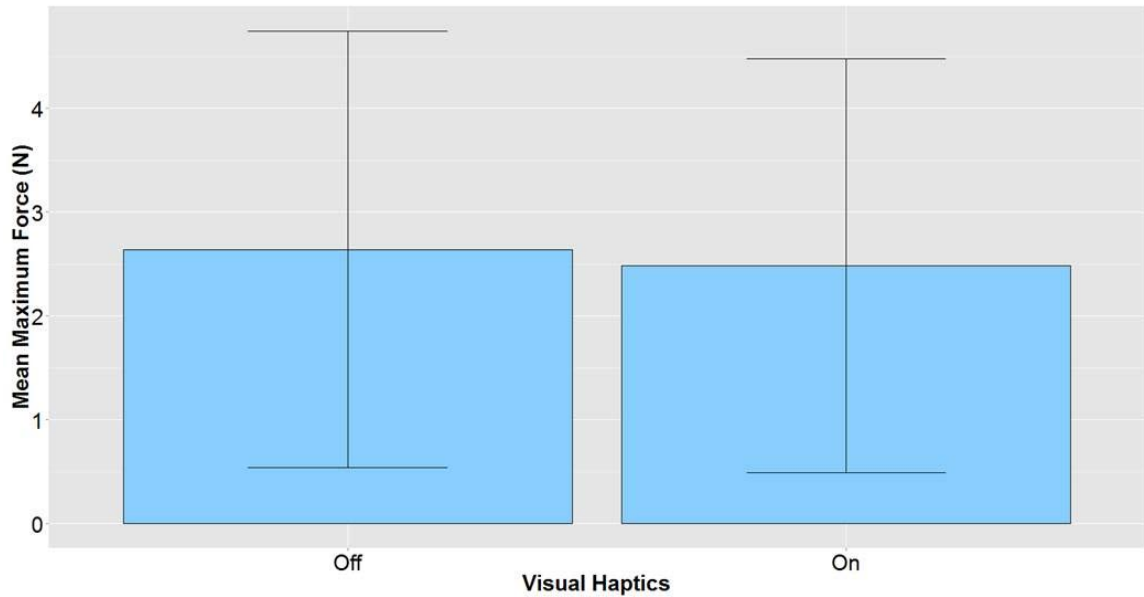
3.3.7 The effect of direct force feedback on the amount of force applied during tying by novices during robotics-assisted *ex vivo* mitral valve annuloplasty

The mean maximum force applied to mitral valve tissue by novices with direct force feedback at same, double, or half the intensity of the actual force applied to tissue was 2.12 ± 1.30 N, 2.68 ± 2.06 N, and 2.14 ± 1.01 N, respectively. This is not significantly different from the mean maximum force applied to cardiac tissue by subjects without direct force feedback (2.83 ± 2.84 N; $p = 0.99$; Figure 3.17). When the results from both experts and novices were combined, the mean maximum force applied to mitral valve tissue by all subjects with direct force feedback at same, double, or half the intensity of the actual force applied to tissue was 2.02 ± 1.18 N, 2.70 ± 1.95 N, and 2.43 ± 1.62 N,

respectively. This is also not significantly different from the mean maximum force applied to cardiac tissue by all subjects without direct force feedback (3.09 ± 2.92 N; p = 0.44; Figure 3.18).
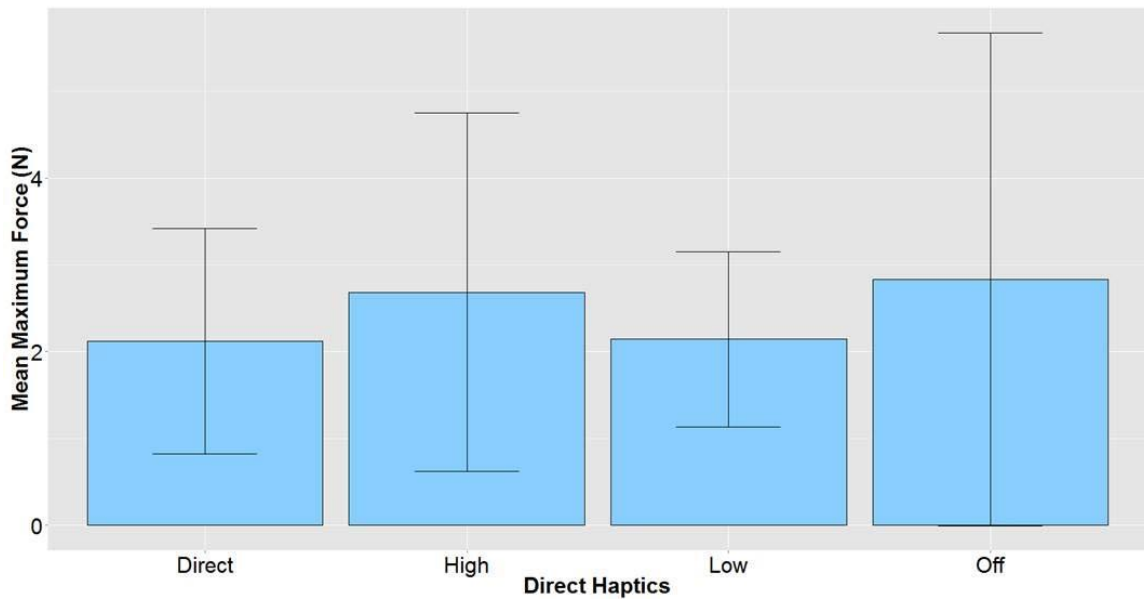
Figure 3.17: The mean maximum force applied to cardiac tissue by novices with and without different levels of direct force feedback during robotics-assisted tying was not significantly different (p = 0.99).

Figure 3.18: The mean maximum force applied to cardiac tissue by novices and experts with and without different levels of direct force feedback during robotics-assisted tying was not significantly different (p = 0.44).

3.3.8 The effect of combined visual and direct force feedback on the amount of force applied during tying by novices during robotics-assisted *ex vivo* mitral valve annuloplasty
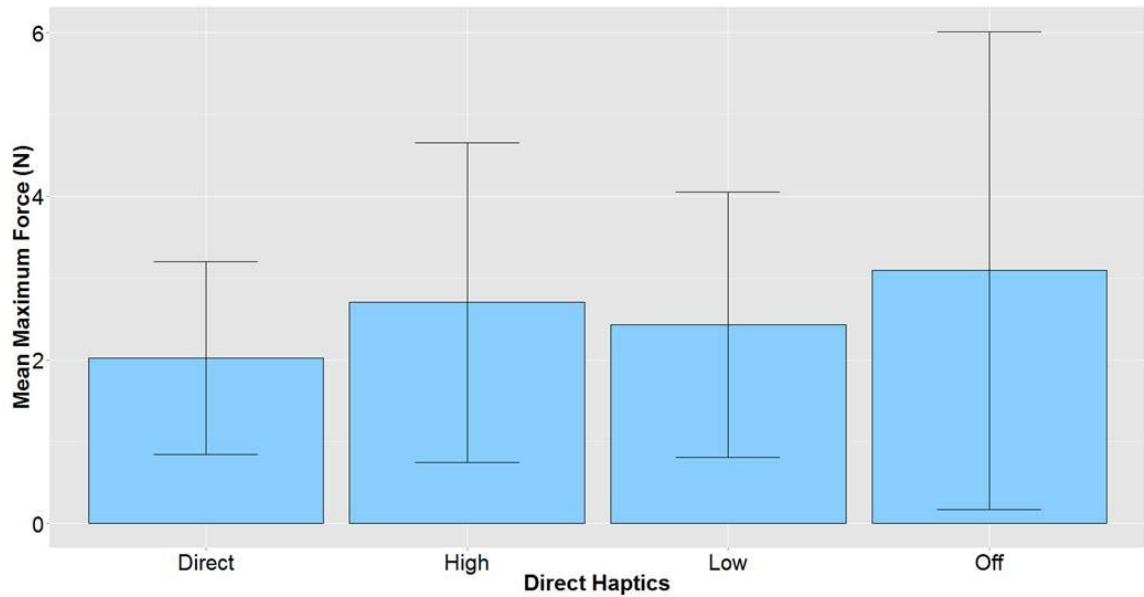
The effect of direct and visual force feedback on the amount of force applied during tying by novices (Table 3.2) and both experts and novices (Table 3.3) are summarized below. When compared to no force feedback, the addition of either visual force feedback, direct force feedback, or both visual and direct force feedback did not significantly decrease the maximum force applied to mitral valve tissue during robotics-assisted *ex vivo* mitral valve annuloplasty in either novices alone ($p = 0.16$; Figure 3.19) or novices and experts combined ($p = 0.19$; Figure 3.20).

Table 3.2. **The amount of force (N) ± SD applied during tying by novices during robotics-assisted *ex vivo* mitral valve annuloplasty.**

Direct Force Feedback	Visual Force Feedback	
	Force (N) ± SD	
	OFF	ON
OFF	3.39 ± 3.17	2.27 ± 2.43
LOW	2.13 ± 1.09	2.16 ± 0.95
HIGH	2.57 ± 1.83	2.79 ± 2.32
DIRECT	2.08 ± 1.61	2.16 ± 0.94

Table 3.3. The amount of force (N) ± SD applied during tying by novices and experts during robotics-assisted *ex vivo* mitral valve annuloplasty.

Direct Force Feedback	Visual Force Feedback	
	Force (N) ± SD	
	OFF	ON
OFF	3.23 ± 2.90	2.95 ± 2.99
LOW	2.35 ± 1.91	2.51 ± 1.30
HIGH	2.96 ± 1.81	2.44 ± 2.10
DIRECT	2.02 ± 1.41	2.03 ± 0.93
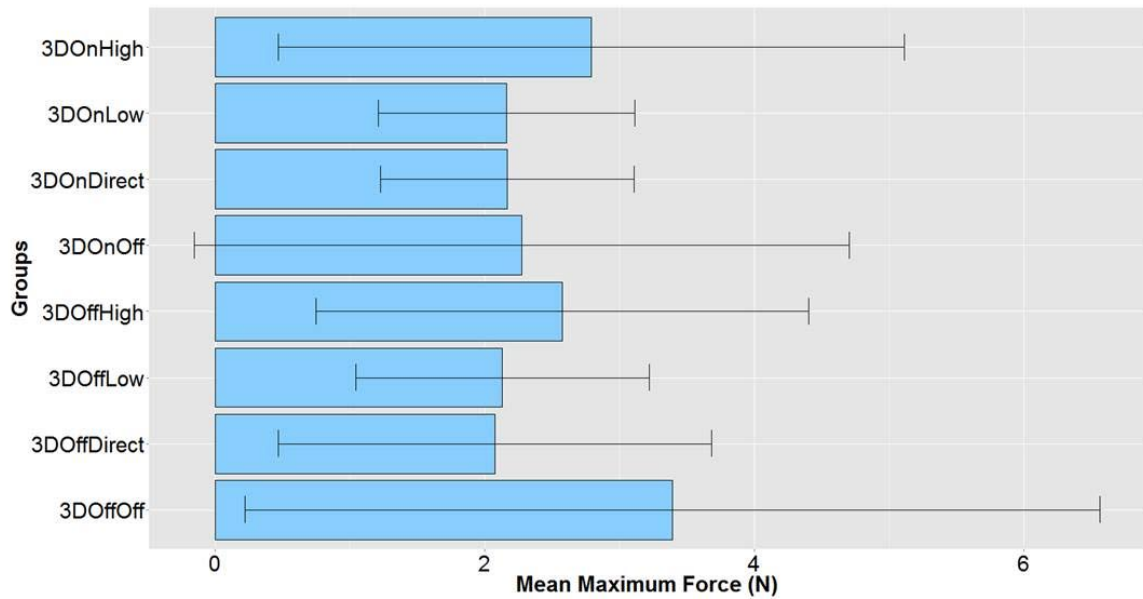
Figure 3.19: When compared to no force feedback, the addition of either visual force feedback, direct force feedback, or both visual and direct force feedback did not significantly decrease the maximum force applied to mitral valve tissue during robotics-assisted tying by novices (p = 0.16). Each point represents the force applied for one trial.
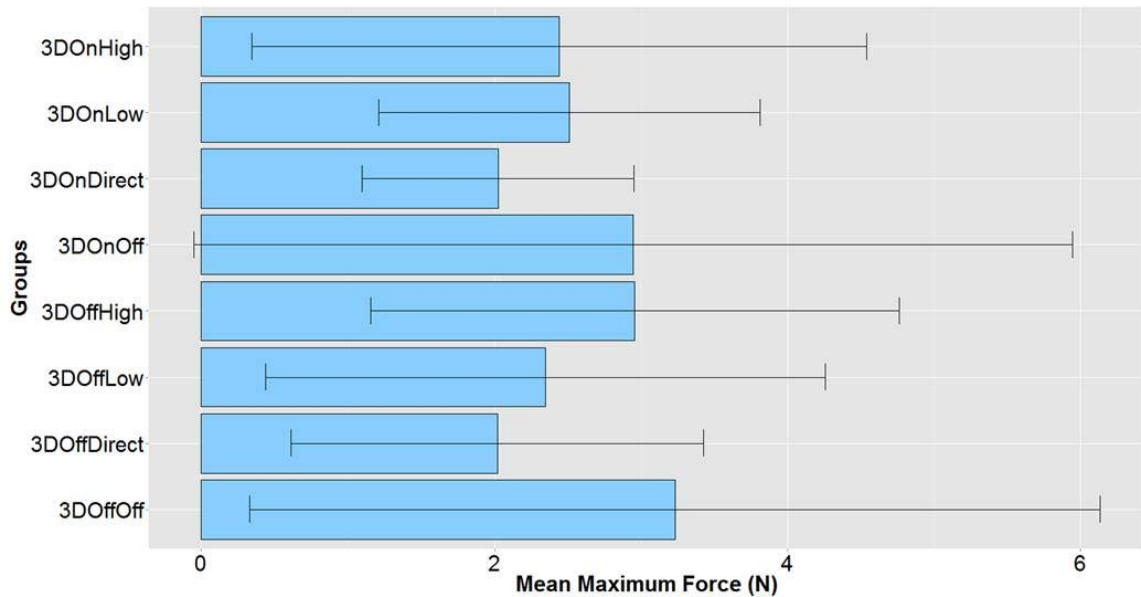
Figure 3.20: When compared to no force feedback, the addition of either visual force feedback, direct force feedback, or both visual and direct force feedback did not significantly decrease the maximum force applied to mitral valve tissue during robotics-assisted tying by novices and experts combined (p = 0.19). Each point represents the force applied for one trial.

Furthermore, the combination of both visual and direct force feedback did not result in an additive decrease in the amount force applied to cardiac tissue (Tables 3.2, 3.3, and Figure 3.21).
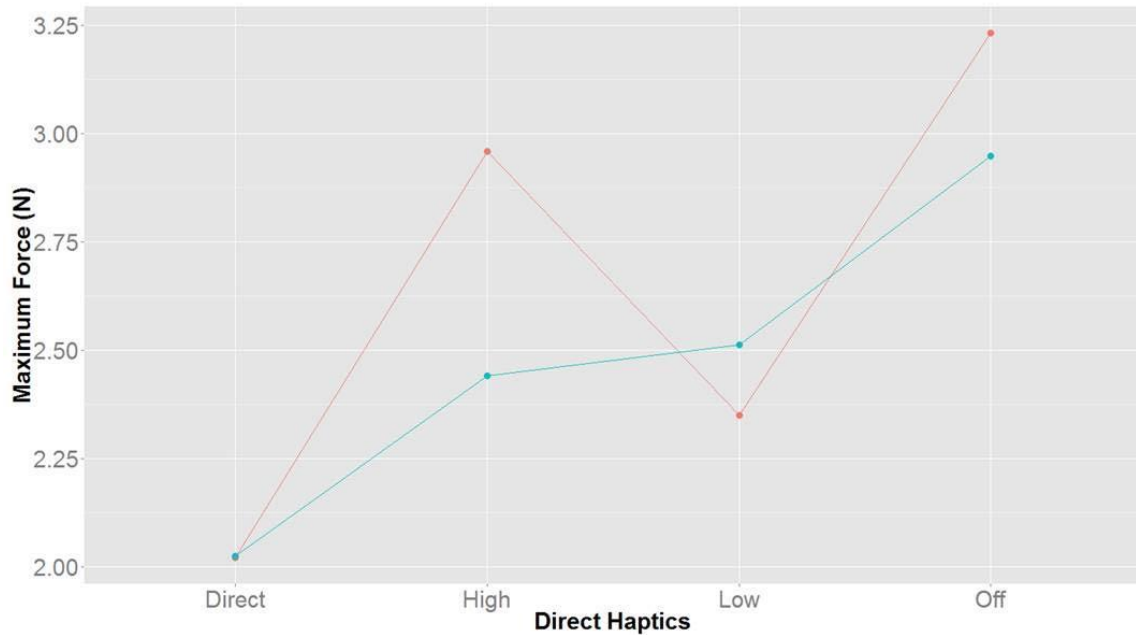
Figure 3.21: Mean maximum force applied to mitral valve tissue by both experts and novices with visual force feedback (green) and without visual feedback (red) in combination with or without direct force feedback during robotics-assisted mitral valve annuloplasty tying.

3.4 Discussion

The objective of this study was to determine the effect of both direct force feedback and visual force feedback on the amount of force applied to mitral valve tissue during *ex vivo* mitral valve annuloplasty using robotics-assisted techniques.

Previous studies using noncardiac robotics-assisted surgical models have found that force feedback [14, 15] and graphical displays of applied forces [16] could lower the magnitude of the force applied to tissue and increase the overall performance mostly for novice surgeons, respectively. In this robotics-assisted model of *ex vivo* mitral valve

annuloplasty, we found that significantly less force was applied to cardiac tissue when all modes of force feedback were provided to the study subjects. In particular, the use of direct force feedback during robotics-assisted mitral valve annuloplasty resulted in a greater decrease in forces applied to cardiac tissue when compared to visual force feedback. These results suggest that when comparing robotics-assisted mitral valve annuloplasty with and without force feedback, use of the former mode results in significantly less force applied to cardiac tissue during robotics-assisted suturing. Previous work by Tholey, *et al*. [18] found that using both visual and force feedback led to better tissue characterization compared to each individual method. However, we found that the addition of both visual and direct force feedback did not reduce the amount of force applied to mitral valve tissue in an additive fashion. This may reflect subjects' preference for one mode over the other. During trials, the results suggest that subjects followed the feedback from either direct or visual force feedback, but not both at the same time.

For the suture used, 4 N is sufficient to have a secure knot. If a subject applies forces greater than 6 N, he or she could damage the tissue or break the suture; therefore, this was set as the threshold of the red zone [19]. Previous studies of porcine tissue have reported visible tissue damage with the application of an 11 N force over an area of 2.4 cm^2 [1]. During the tying task, even without force feedback, no damaging forces were applied to the cardiac tissue. The addition of either visual or direct force feedback did not significantly decrease the amount of force applied to cardiac tissue.

In addition, our aim was to determine whether these effects are consistent between novices and experts in robotics-assisted cardiac surgery. Although there appeared to be a trend toward higher force applied by experts, this difference was not statistically significant. This refutes previous findings [26] and is most likely due to the low number

of experts included in the study. Unfortunately, there are a limited number of surgeons with expertise in robotics-assisted cardiac surgery; therefore, a larger number could not be recruited for this study. Furthermore, it could also be argued that the robotics-assisted cardiac surgery test bed doesn't fully measure tissue forces, as some forces would be absorbed by the cardiac tissue itself and not detected by the sensor below.

Importantly, the mean amount of force applied by both experts and novices gradually decreased after each trial. This suggests that, with practice on robotics-assisted surgical systems, less damaging force may be applied to cardiac tissue.

The implication of these findings is that in order to achieve better control of interaction forces on cardiac tissue during robotics-assisted mitral valve annuloplasty suturing, force feedback may be required. Furthermore, direct force feedback has a significantly greater impact on force applied than visual force feedback.

Force feedback has also been used to develop training simulators by some researchers [27-30]. Judkins, *et al*. [30] showed that using force feedback for training in MIS could cause novice surgeons to apply less force when performing surgery using the da Vinci surgical system in the absence of force feedback.

In conclusion, we have shown that in order to achieve better control of interaction forces on cardiac tissue during robotics-assisted mitral valve annuloplasty suturing, force feedback may be required. Direct force feedback may have a significantly greater impact on force applied than visual force feedback. In addition, this force feedback-enabled robotics-assisted surgical system can be used to effectively train novices in mitral valve annuloplasty and to apply force feedback for safer and improved surgical performances.

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Chapter 4

4 Evaluating Performance and Improving Safety of a Novel Tool for Beating Heart Mitral Valve Repair

New cardiovascular techniques for beating heart mitral valve repair using minimally invasive access avoid the risks associated with cardiopulmonary bypass; however, intra-cardiac visualization is challenging due to the limitations of currently available medical imaging techniques.   As a result, novel imaging modalities are required for superior tool guidance and improved patient safety and outcomes. One such guidance tool is augmented reality. Augmented reality (AR) refers to the integration of 'real-world' images, for example from video, endoscopic, or ultrasound, with a computer generated model [1, 2]. This may be used to add useful information to an image-guided surgical procedure. Recently, a variety of AR systems have been developed for intracardiac surgery [3, 4]. The following chapter will outline the application of a novel AR guidance system for the minimally invasive mitral valve repair on a beating heart.

This chapter is adapted from the following work:

- Chu MW, Moore J, Peters T, Bainbridge D, McCarty D, Guiraudon GM, Wedlake C, Lang P, Rajchl M, Currie ME, Daly RC, Kiaii B. Augmented reality image guidance improves navigation for beating heart mitral valve repair. *Innovations (Phila)*. 2012 Jul-Aug; 7(4): 274-81.

- Moore JT, Chu MW, Kiaii B, Bainbridge D, Guiraudon G, Wedlake C, Currie M, Rajchl M, Patel RV, Peters TM. A navigation platform for guidance of beating heart transapical mitral valve repair. *IEEE Trans Biomed Eng*. 2013 Apr; 60(4): 1034-40.

My contribution to these manuscripts involved organizing and conducting experiments.

- Currie ME. NeoChord Progress Report. Safety and performance study of the NeoChord Suturing Device in subjects with degenerative mitral valve disease diagnosed with severe mitral regurgitation. NeoChord. September, 2013.

My contribution to this report involved designing and conducting experiments and analyzing data.

4.1 Introduction

Conventional mitral valve repair requires aortic cross-clamping and cardiopulmonary bypass to remove blood from an arrested heart, to oxygenate the blood, and to maintain oxygenated blood circulation to the remainder of the body during cardiac surgery. However, cardiopulmonary bypass itself has been related to perioperative morbidity and mortality [5, 6] including postoperative blood loss and blood product transfusions [7-9], postoperative prolonged mechanical ventilation, pulmonary edema, or acute respiratory distress syndrome [6, 10, 11], and renal dysfunction [12]. Furthermore, the use of cardiopulmonary bypass has been linked to permanent neurologic dysfunction and postoperative decreases in cognition and motor abilities [13]. Elderly patients with multiple comorbidities are particularly vulnerable to cognitive deficits including stroke [14-20]. Therefore, a large proportion of elderly patients with multiple comorbidities and severe symptomatic mitral valve regurgitation are not referred for surgical repair. Clearly, new cardiovascular techniques must be tailored to address the unique requirements of high risk, elderly, surgical patients with mitral valve regurgitation.

In order to avoid aortic cross-clamping and cardiopulmonary bypass, many novel

transcatheter valve techniques have been developed to enable beating heart mitral valve repair [21-31]. Emerging transcatheter valve therapies have introduced various mitral valve repair strategies on the beating heart, including edge-to-edge repair [22-24], coronary sinus cerclage [25, 26], transcatheter annuloplasty [28], and neochordal reconstruction [27, 29, 30, 32]. For example, the NeoChord DS1000 (NeoChord Inc., Eden Prairie, MN USA) is an off-pump device that uses transapical access to deliver expanded polytetrafluoroethylene (ePTFE) neochordae to flail segments of the mitral valve [29, 30, 32].

Although these experimental techniques avoid the deleterious effects of cardiopulmonary bypass, they continue to be hampered by limited intraoperative visualization and suboptimal procedural accuracy. At present, fluoroscopy and/or echocardiography are used for intraoperative guidance of these new beating heart mitral valve procedures. Intraoperative TEE provides good real-time visualization of mitral valve anatomy but provides inadequate navigation and guidance of surgical tools. Intraoperative fluoroscopy with and without contrast provides reasonable visualization of surgical tools, but often lacks three-dimensional context with only gross anatomic structures visible. As a result, current imaging modalities provide limited intracardiac views that make transcatheter manipulation of the mitral valve challenging and can result in prolonged procedural times, additional device deployments, excessive radiation exposure, and most importantly, increased complication rates [32, 33]. Although many advances have occurred in transcatheter valve therapy designs, there remains great dependence on current imaging modalities and their known limitations [33]. Therefore, although these techniques have shown positive results in animal and human trials, beating heart valve implantation and repair is challenging due to the limitations of currently available medical imaging techniques.

The NeoChord DS1000 is introduced into the left ventricle and left atrium through transapical access. Using the center thumb ring shaft (Figure 4.1), the surgeon opens the gripper at the distal end of the tool and then closes the gripper on the prolapsed portion of the mitral leaflet by releasing the thumb ring. Correct leaflet capture is verified using a fiber-optic-based detection mechanism. After leaflet capture has been verified, a needle and an exchangeable cartridge for loading the neochord suture are installed within the tool. The needle is used to puncture the leaflet and an ePTFE suture is pulled through the leaflet and the tool is retracted exterior to the apex of the heart with both ends of the suture. The suture is fixed at the leaflet with a girth hitch knot, adjusted under Doppler ultrasound to ensure minimum mitral regurgitation and then secured at the apex using a pledget. Multiple neochordae are typically used to ensure optimal valvular function.

Use of the NeoChord DS1000 tool relies exclusively on TEE guidance in the form of 2D single plane, biplane, and 3D imaging for tool navigation and neochordae deployment [29]. The tool is identified in 2D biplane ultrasound (mitral valve commissural, midesophageal long-axis view), and navigated into the commissure of the mitral valve leaflets, while the surgeon and echocardiographer attempt to maintain tool tip, tool profile, and final target site in the ultrasound image planes at all times. Correct position and orientation of the grasping tool are then achieved using a 3D zoomed view. Returning to biplane ultrasound for higher temporal and spatial resolution, the prolapsing leaflet is grasped by the jaws of the NeoChord device.
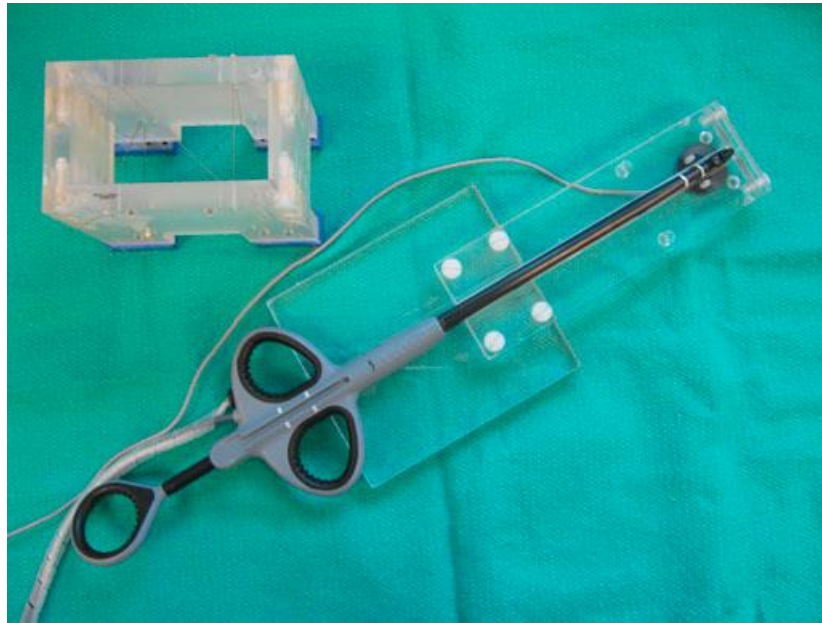
Figure 4.1: Z-bar calibration block (top left) and NeoChord calibration block holding the DS1000 device.

After extensive acute and chronic animal studies throughout Europe, Canada, and the United States, the NeoChord is undergoing human trials for the repair of degenerative mitral valve regurgitation [29-31]. Initial results confirm the safety and efficacy of this surgical tool for mitral valve repair in patients with degenerative mitral valve regurgitation. In fact, analysis of initial echocardiographic parameters following NeoChord placement revealed a trend towards improved left ventricular dimensions following the procedure. These results from the Transapical Artificial Chordae Tendineae (TACT) study in Europe (Tables 4.1, 4.2). Nevertheless, limited data at this time preclude any firm conclusions regarding the efficacy of the NeoChord tool.

Table 4.1. Comparison to baseline data in all patients with data from TACT:

Matched data from TACT patient trials following paired two-tailed t-test.

	N	Mean ± SD	Paired Difference from Baseline 95% Confidence Interval	p
Left Ventricular Diastolic Diameter (cm)				
Baseline	15	4.9 ± 0.82		
Discharge	15	4.45 ± 0.84	0.21, 0.69	0.001
30-day	13	4.54 ± 0.60	-0.27, 0.83	0.29
6-month	8	4.26 ± 0.72	-0.36, 1.15	0.26
Left Ventricular Systolic Diameter (cm)				
Baseline	15	3.1 ± 0.81		
Discharge	15	3.64 ± 0.42	-0.33, 0.51	0.66
30-day	13	2.93 ± 0.52	-0.41, 0.60	0.70
6-month	8	2.84 ± 0.66	-1.0, 1.05	0.95
End Diastolic Volume (Teicholz formula, mL)				
Baseline	15	117.2 ± 45.92		
Discharge	15	94.66 ± 43.56	9.63, 35.5	0.002
30-day	13	96.62 ± 29.02	-10.05, 42.30	0.20
6-month	8	84.42 ± 33.62	-13.11, 56.21	0.19
End Systolic Volume (Teicholz formula, mL)				
Baseline	15	41.79 ± 27.42		
Discharge	15	38.31 ± 22.13	-10.38, 17.35	0.60
30-day	13	34.64 ± 14.10	-9.72, 18.98	0.50
6-month	8	32.94 ± 18.21	-28.16, 31.39	0.90

Table 4.2: Comparison to discharge data in all patients with data from TACT:

Matched data from TACT patient trials following paired two-tailed t-test.

	N	Mean ± SD	Paired Difference from Discharge 95% Confidence Interval	p
Left Ventricular Diastolic Diameter (cm)				
Discharge	21	4.51 ± 0.74		
30-day	21	4.56 ± 0.53	-0.34, 0.23	0.71
6-month	11	4.40 ± 0.66	-0.09, 0.47	0.16
Left Ventricular Systolic Diameter (cm)				
Discharge	21	3.08 ± 0.66		
30-day	21	2.96 ± 0.53	-0.19, 0.42	0.43
6-month	11	2.77 ± 0.65	0.08, 0.82	0.02
End Diastolic Volume (Teicholz formula, mL)				
Discharge	21	96.57 ± 38.42		
30-day	21	97.37 ± 25.91	-15.73, 14.13	0.91
6-month	11	90.44 ± 30.99	-3.81, 21.60	0.15
End Systolic Volume (Teicholz formula, mL)				
Discharge	21	39.83 ± 20.48		
30-day	21	35.48 ± 14.33	-4.89, 13.59	0.34
6-month	11	31.25 ± 18.30	1.04, 23.2	0.04

Furthermore, the limited visualization during tool navigation and neochord dehiscence, or tearing, from the mitral leaflet following deployment are ongoing challenges with this procedure. This chapter outlines the development and use of a novel image guidance system for safer NeoChord tool navigation and identifies factors in neochord deployment that may prevent neochord dehiscence.

4.2   A Navigation Platform for Guidance of Beating Heart Transapical Mitral Valve Repair

4.2.1 Motivation

A major challenge in navigating the NeoChord device to the mitral valve target region is that ultrasound imaging must simultaneously keep the target region (mitral valve line of coaptation) and the tool tip in view. While TEE has so far proven adequate for the final positioning of the tool and grasping the leaflet, there have been safety concerns relating to the navigation of the tool from the apex to the target mitral valve leaflet. Echocardiography lacks the spatial and temporal resolution to view intracardiac instruments and critical cardiac structures simultaneously; therefore, there is a risk of potential injury to intracardiac structures during instrument navigation.   TEE guidance is problematic since it is not always possible to maintain appropriate spatial and temporal resolution in 3D, and it is not always possible using 2D and 2D bi-plane views to simultaneously maintain both the tool tip and the target site in the field of view. The use of 2D ultrasound also makes it difficult to ensure that the tool tip itself is visualized, rather than an arbitrary cross section of the tool shaft that happens to be transecting the US plane. Due to these navigation challenges, the tool can be caught in the subvalvar apparatus risking chordal rupture or leaflet perforation. Current clinical practice involves the use of highly trained surgical proctors who are expert in the use of this device.

To overcome this challenge and to improve the overall safety of the navigation process, we have evaluated the efficacy of employing an AR technique capable of providing a robust 3D context for TEE image data [8]. We have adapted a visualization environment that uses tracking technology to locate both the tool and the TEE probe in 3D space, making it possible to represent the real-time ultrasound images with virtual geometric models of both devices and interactively defined anatomy within a common coordinate

system (Figure 4.2) defined by the Aurora (Northern Digital, Waterloo, Canada) magnetic tracking system. In this real-time environment, the surgeon can easily and intuitively identify the tool, surgical targets, and high-risk areas, and view tool trajectories and orientations.
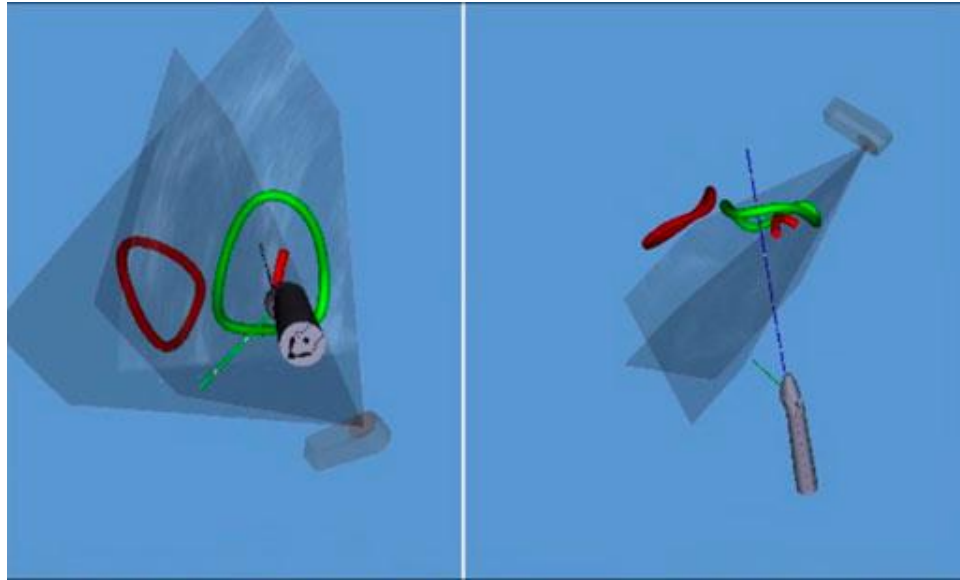
Figure 4.2: Real-time ultrasound image data integrated with geometric models representing aortic and mitral valve annuli (red and green, respectively), and tracked models of the NeoChord DS1000 and TEE probe.

This study is a proof-of-concept validation from two animal studies involving six cardiac surgeons. The purpose of this study was to compare navigation of the NeoChord DS1000 in a porcine heart using either TEE guidance alone or TEE with the AR guidance system.

4.2.2   Methods

4.2.2.1   Augmented Echocardiography

Virtual geometric models of each device were created in VTK (Visualization Toolkit, Kitware Inc.). VTK is an open-source, freely available software library of computer graphics and visualization algorithms for image processing and visualization [9]. The geometric representation of the TEE probe includes video image planes that can render real-time digital video capture of the dual ultrasound planes provided by the iE33 ultrasound device (Philips, Inc.). Real-time monitoring of rotation angles and depth settings makes it possible to properly represent the scale and orientation of the image planes in 3D. The geometric model of the NeoChord tool consists of the tip region only. Axes with 10 mm markings were projected from this virtual representation, indicating the forward trajectory of the tool and the direction of the opening jaws (Figure 4.2). This greatly facilitated the surgeons' ability to plan their tool trajectory toward the desired target site.

Magnetic tracking sensors are integrated into the tool and TEE probe, and appropriately calibrated, allowing geometric models of the tool and probe to be represented in the tracker coordinate reference frame. A six degrees of freedom (DOF) sensor was rigidly attached externally on the TEE probe of the Philips iE33 ultrasound (Figure 4.3).

Figure 4.3: NeoChord DS1000 outfitted with tracking sensors (left) and TEE probe with sensor on back (right and insert, top right). Devices rest on the NDI Aurora tabletop magnetic field generator.

Since the tip of the NeoChord device can open by over 20 mm (Figure 4.4), we required two tracked sensors to represent its real-time geometry. A 6DOF sensor was placed near the distal end of the fixed tool shaft to represent the pose of the tool as a whole, and a 5DOF sensor was incorporated in the thumb ring shaft that controls the opening and closing of the distal tip that is used to grasp the flail mitral valve leaflet. The Euclidean distance between these two sensors was measured with the gripper closed. Subsequently, any increase in this distance could be used to accurately represent the opening of the distal end of the tool.
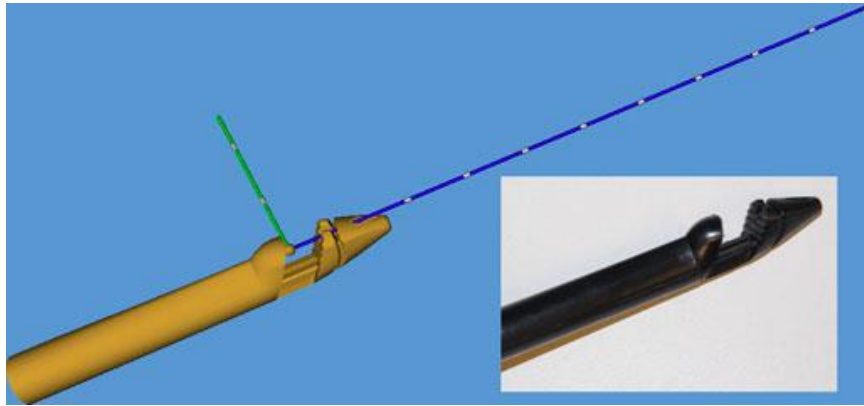
Figure 4.4: Geometric model of the open NeoChord tool, with trajectory axes. Insert: photograph of the device.

The 6DOF sensor representing the rigid portion of the tool was calibrated using a custom-built tracked calibration block designed to hold the NeoChord tool in a precise configuration (Figure 4.1). Using a CT image of the calibration block with a NeoChord tool attached, we were able to precisely define the tool and gripper geometry relative to the calibration block, making the calibration of the NeoChord tools a trivial task. The tracked TEE probe was calibrated using a Z-bar phantom [34]. A Z-bar calibration phantom comprises line fiducials in a known geometry. Homologous points in both the phantom and the image coordinate space from different tracked probe positions are obtained and used to determine the transformation matrix mapping the ultrasound imaging coordinate system to the coordinate system defined by the tracking tool [34].

A valuable corollary to tracking the 2D ultrasound image data in 3D space is the ability to define anatomy of interest such as the target location (mitral valve line of coaptation), and regions to be avoided (mitral valve annulus and aortic valve annulus) for contextual

purposes. For this application only the mitral and aortic valve annuli are required to safely complete the tool navigation task. These features are identified using tracked biplane ultrasound image data: four points defining the annular ring of each structure are defined in the image data and using these points, we define tubular splines and render them in the 3D scene in VTK (Figure 4.5). All features are identified in midsystole, since the mitral valve annular ring is closest to the apex at this point in the cardiac cycle. This in effect provides an indicator of the first danger zone to be avoided as the tool is moved into the left ventricle from the apex.

Figure 4.5: (Left) Intraoperatively defined anatomy (mitral valve annulus). (Right) Planning entry trajectory in the operating room.

Much of the difficulty associated with navigating the NeoChord device inside the beating heart stems from the use of intrinsically 2D image data to perform a 3D task. To address this limitation, our visualization platform consists of two views: a "bullseye" view as

seen from the apex of the heart toward the mitral valve annulus, and a side view orthogonal to the bullseye view, showing the mitral valve annulus and aortic valve annulus in profile (Figure 4.2). With these two views, in concert with the tool trajectory axis, the surgeon is able to quickly and intuitively orient the device for a direct line path from the apex to the target region, safely avoiding the annular ring and valve apparatus. In addition, the side view provides a graphical representation of the tool tip distance to the mitral valve annular plane, ensuring that the tool tip avoids becoming caught under the valve leaflet apparatus, or passing too deeply into the left atrium.

These views have the added benefit of simplifying the task of the echocardiographer who is otherwise required to maintain both the tool tip and mitral valve annulus in the image plane at all times. However, during the navigation task it is not uncommon for the ultrasound image plane to obstruct the surgeon's view of the tracked geometric models. In such circumstances, a balance must be struck between providing the surgeon with an unobstructed view (by adjusting the transparency of the ultrasound image data) and allowing the echocardiographer to ensure the accuracy of the geometric models relative to the real-time ultrasound data.

4.2.2.2   Integration Into OR Workflow

Our AR guidance system is designed to assist the surgeon with three related navigation tasks: planning the left ventricular apical access point and initial trajectory, maintaining a safe and direct entry through the mitral valve commisure into the left atrium, and establishing the correct tool orientation at the line of coaptation so that the NeoChord DS1000 device can grasp the flail leaflet. To achieve this, prior to making the apical entry incision, the echocardiographer identifies a minimal number of tie points along the pertinent anatomy (aortic valve annulus, mitral valve annulus, and line of coaptation) to represent this anatomy in our augmented ultrasound space. Next, the surgeon uses the

trajectory projection of the NeoChord DS1000 tool to plan the optimal entry point and orientation (Figure 4.5). After apical access, the surgeon simply orients and points the tool trajectory toward the desired target site and advances the tool, monitoring the geometric model representations as seen on the real-time ultrasound image data. By overlaying the geometric models on the real ultrasound image data, the surgeon is able to assess the accuracy and reliability of these representations in real time. If the features have moved, for example due to the introduction of the NeoChord tool, they can be redefined before proceeding. In future iterations, we plan to provide the surgeon with a view of the geometric models only, while the echocardiographer will have a separate monitor that includes the tracked ultrasound image data as well. Once at the desired target location, the procedure returns to the standard workflow, with the navigation task completed.

The technology associated with the AR navigation system can be easily integrated into the operating room. The Aurora tabletop magnetic field generator is specifically designed to work in the presence of various sources of metal. It has a large field of view, and easily fits on top of the OR table. Sensors attached to the TEE probe and surgical tools should not impede normal OR workflow. Furthermore, the cost associated with this technology is not prohibitive for most institutions.

4.2.2.3   Proof of Concept: Animal Study

Two porcine animal studies were performed to provide a proof-of-concept validation for the AR navigation system. All procedures were performed in compliance with standards of the Animal Use Subcommittee of Western University, London, ON, Canada.

A total of six cardiovascular surgeons participated in the study, performing the neochordae image navigation tasks a total of 12 times with and without AR imaging

guidance in two porcine models. All animals underwent general anesthesia with single-lumen endotracheal tube intubation and monitoring using a right internal jugular venous line, femoral arterial line, three-lead electrocardiography, oxygen saturation probe, and end-tidal carbon dioxide monitoring. A lower hemisternotomy was performed, and pericardial retention sutures were placed to expose the left ventricular apex. Two plegetted 2-0 Prolene purse-string sutures were placed around the left ventricular apex with Rummel tourniquets to secure the apical puncture site. The NeoChord DS1000 device was introduced into left ventricular apex. The surgeon then used TEE guidance alone or AR imaging guidance to navigate the tool from the left ventricular apex across the mitral valve orifice to face the open tool jaw toward the predetermined intended mitral valve leaflet segment. After the image guidance study, the targeted mitral valve leaflet segment was grasped by the jaws of the device. Correct leaflet capture was verified using the fiber optic Y based detection mechanism that is integrated into the NeoChord DS1000 tool. After leaflet capture was verified, an ePTFE suture was pulled through the leaflet and the tool was retracted out the left ventricular apex with both ends of the suture. The suture was fixed at the leaflet with a girth hitch knot, adjusted under real-time TEE guidance to the appropriate length, and then secured at the apex using a pledget.

The primary goal of these studies was to compare navigation of the tool from apex to target region with and without AR assistance. In random order, the surgeons were asked to navigate the NeoChord tool from a starting point near the apex, up through the mitral valve line of coaptation, situating the distal end of the tool in the left atrium. The NeoChord tool location was recorded every 0.5 seconds for all navigation attempts. Four metrics were used to assess the navigation task including (i) the total length the tool path followed; (ii) the distance error from tool locations to a direct line drawn from apex to final destination in the coaptation line; (iii) total task completion time; and finally, (iv)

the tool path data used to identify points of potential injury to neighboring intracardiac structures.

The echocardiographer determined the successful end point of the task by identification of the tool facing the appropriate mitral valve leaflet segment, as indicated by the 3D short axis TEE. In cases where the surgeon had to return to the apical region to reorient themselves, the attempt was defined as a fail and the task was started over.

4.2.2.4 Statistical Analysis

For purposes of data analysis, continuous variables were expressed as a mean +/- standard deviation and categorical variables were expressed as percentages.

Statistical analysis was performed using paired t-test and Fisher exact test for dichotomous variables and a p-value of ≤ 0.05 was considered statistically significant.

4.2.3 Results

Successful tool navigation from left ventricular apex to mitral valve leaflet was achieved in 12 (100%) of 12 and 9 (75%) of 12 (P = 0.2) attempts with AR imaging and TEE alone, respectively. The AR imaging guidance demonstrated significantly shorter distance errors from midline, total navigation times, and total path lengths traveled compared with TEE navigation alone (Table 4.3).

Table 4.3: Navigation data in TEE-guided attempts (n = 12) and AR-guided attempts (n = 12)

Navigation Data	TEE Alone	AR Guidance	P
Distance errors from midline, mm	16.8 ± 10.9	5.2 ± 2.4	0.003

Total navigation times from left ventricular apex to mitral valve leaflet, s	92.0 ± 84.5	16.7 ± 8.0	0.004
Total path length, mm	1128.9 ± 931.1	225.2 ± 120.3	0.003

The AR imaging guidance allowed for more accurate tool navigation from left ventricular apex to the mitral valve leaflet with greater than threefold reduction in distance error from the intended midline trajectory ($P = 0.003$) and greater than fourfold reduction in total tracked tool path lengths before reaching the intended mitral valve leaflet target ($P = 0.003$) when compared with TEE guidance alone. The total navigation times for the tool within the left ventricle was reduced fivefold with AR imaging compared with TEE alone ($P = 0.004$). Figures 4.6 and 4.7 demonstrate the striking differences in the magnetically tracked tool paths taken by each surgeon (each surgeon represents a different color) when using TEE guidance alone versus AR imaging guidance.
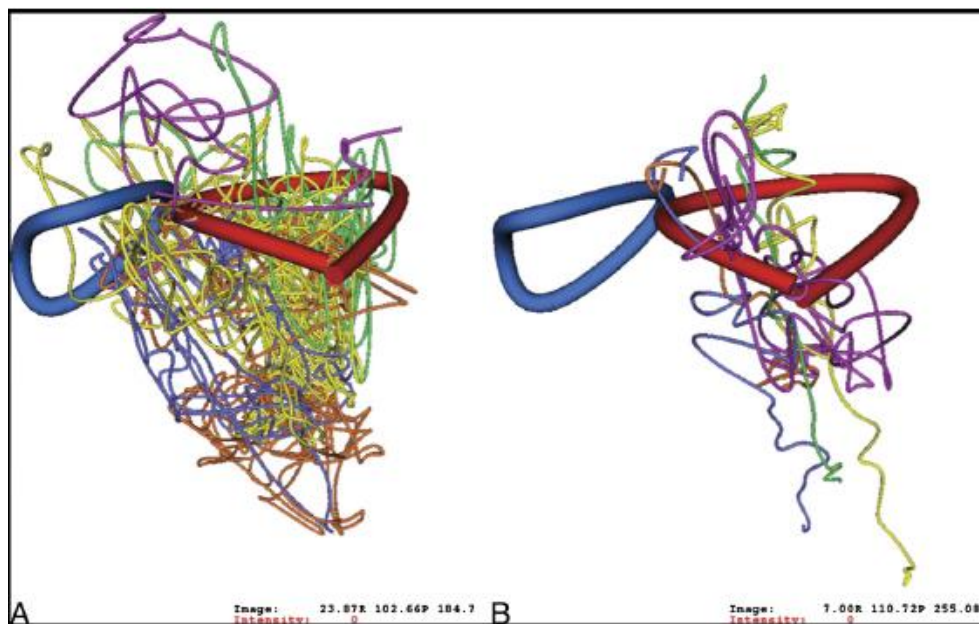
FIGURE 4.6: Tracked tool paths demonstrating guidance with TEE alone (A) versus AR imaging (B) from experiment day 1. Each colored line represents a different surgeon trial, and the mitral (red) and aortic (blue) annuli are represented.
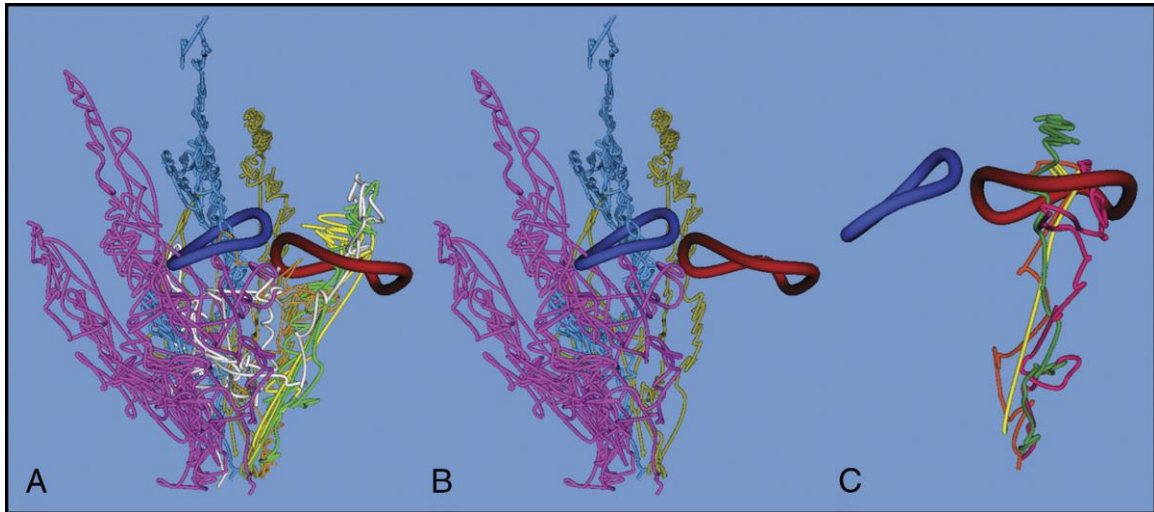
FIGURE 4.7: Tracked tool paths demonstrating guidance with TEE alone (A) versus AR imaging (C) from experiment day 2. B, Three failed navigations with TEE alone. Each colored line represents a different surgeon trial, and the mitral (red) and aortic (blue) annuli are represented.

We also analyzed these results by individual surgeon study, and Figure 4.8 demonstrates that even a surgeon with multiple NeoChord DS1000 human implants (one of the original inventors) can derive significantly improved tool navigation accuracy with AR guidance versus TEE alone.
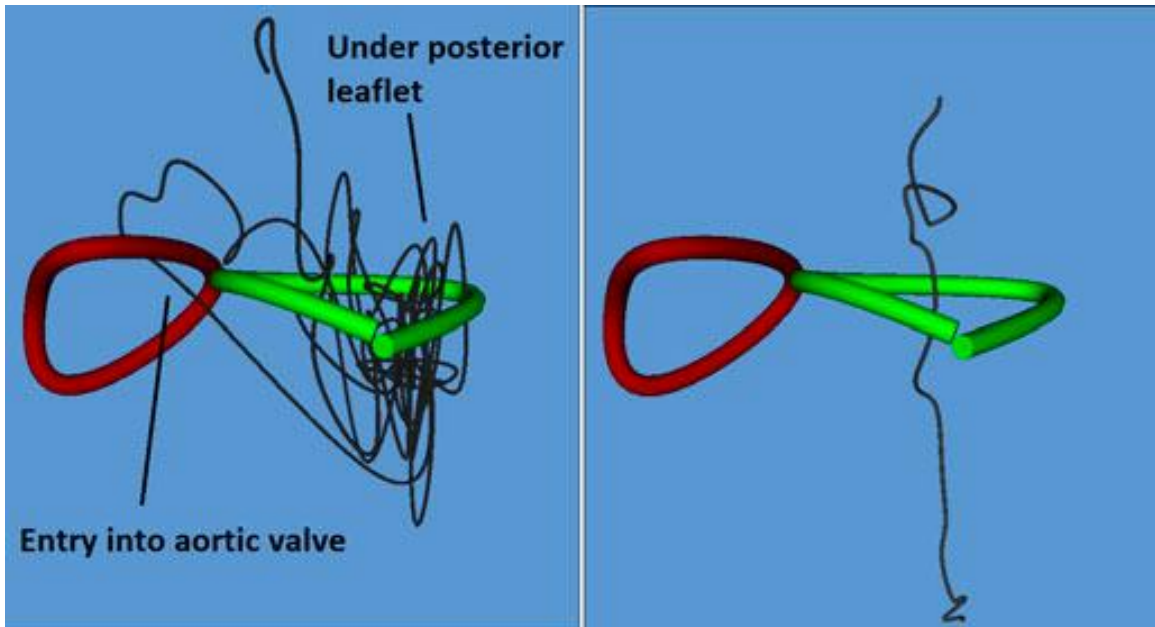
FIGURE 4.8: Tracked tool paths of the most experienced surgeon with the NeoChord DS1000 tool, with TEE guidance alone (A) and AR guidance (B). Note the entry into the left ventricular outflow tract (LVOT) and aortic valve and getting caught under the posterior mitral valve leaflet (A) and the direct path taken with augmented image guidance (B).

Although tool navigation accuracy is paramount, equally important is patient safety and prevention of iatrogenic injury to the aortic valve, anterior and posterior leaflets, left ventricular free wall, and left atrial roof.

Table 4.4 demonstrates the number of times the tool traversed other intracardiac structures with TEE guidance alone versus AR imaging guidance. In total, there were 78

instances of potential injury using TEE alone compared with only 2 in the trials using the AR imaging guidance system, resulting in an approximate 40-fold decrease in risk of possible injurious events (P = 0.008).

Table 4.4: Potential injury to other intracardiac structures

Intracardiac Structures	TEE Alone	AR Guidance	P
Aortic valve	34	0	
Anterior leaflet mitral valve	20	0	
Posterior leaflet mitral valve, Left ventricular free wall	15	2	
Left atrial roof	6	0	
Failed navigation	3	0	
Total	78	2	0.008

When comparing navigation outcomes between novices and experts (Table 4.5, Figure 4.9), there were no statistically significant differences between the two groups. However, the confidence intervals narrow significantly with AR imaging versus TEE imaging alone, suggesting that AR imaging improves the reproducibility of the procedure and may help novice surgeons to more expeditiously overcome the steep learning curve associated with navigating the NeoChord DS1000 tool (Figure 4.9).

Table 4.5: Differences in tool navigation between novice and expert surgeons

Navigation	TEE Alone	AR Guidance
Distance errors from midline, mm		
Novice	25.12 ± 11.84	4.53 ± 2.00
Expert	10.85 ± 5.17	5.96 ± 2.64
P	0.43	0.02
Navigation time from Left ventricular apex to mitral valve leaflet, s		
Novice	110.4 ± 72.78	18.83 ± 2.84
Expert	78.86 ± 95.28	14.79 ± 10.11
P	0.53	0.55
Total path length, mm		
Novice	1337.13 ± 886.45	216.00 ± 20.68
Expert	980.08 ± 1001.85	228.35 ± 162.28
P	0.53	0.90
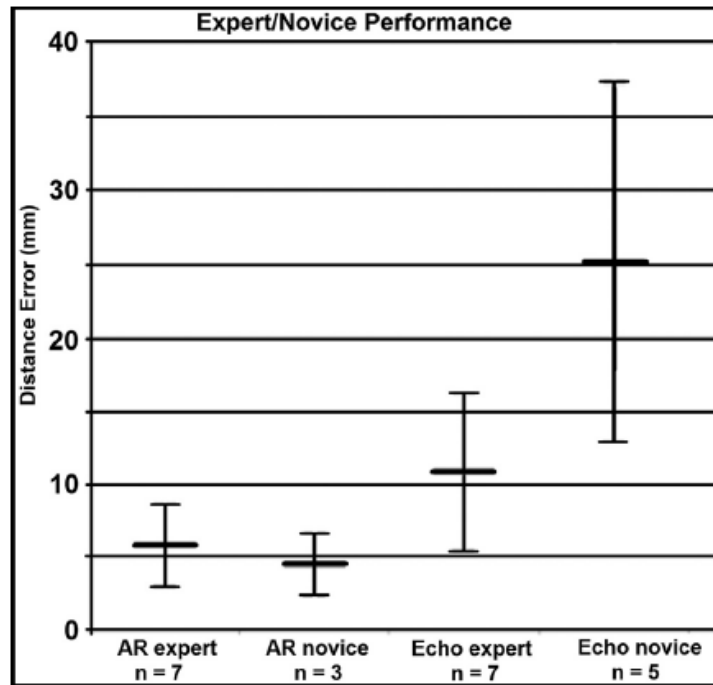
FIGURE 4.9: Data graph demonstrating the distance errors from the intended midline trajectory comparing expert with novice study results. Although there are no statistically significant differences between the experts and novices, the confidence intervals narrow significantly with AR guidance, suggesting that it may improve the reproducibility of tool navigation and reduce the learning curve for novice surgeons.

4.2.4   Discussion

4.2.4.1   Advantages of AR Guidance

A variety of AR imaging guidance systems have been developed to facilitate intracardiac beating heart surgery [3, 33-36]. We believe that our AR imaging platform demonstrated proof-of-concept with a robust three-dimensional context to enhance the TEE image guidance for beating heart mitral valve repair with the NeoChord DS1000

device. In this realtime environment, the surgeon easily and intuitively identified the surgical tool, relevant intracardiac anatomy, high-risk areas, and tool trajectories and orientations.

Our results demonstrated that tool guidance from the left ventricular apex to the mitral valve leaflet target was always successful with AR guidance, and more importantly, tool navigation was much more accurate (more than threefold to fourfold) with significantly reduced total navigation times (more than fivefold shorter). We also demonstrated a dramatic reduction in the incidence of tool misguidance (and potential injury) into adjacent cardiac structures, such as the aortic valve or anterior leaflet of the mitral valve, thus enhancing patient safety with AR imaging. For example, with TEE guidance alone, the aortic valve was crossed with the tool in nearly all trials, whereas with AR guidance, the aortic valve was never touched at all.

These studies also demonstrated the relatively poor tracking ability of two-dimensional echocardiography. Isolated three-dimensional TEE can be used for tracking tools in small spaces; however, it has a significant real-time delay and is often limited in the volume that it can display. As a result, three-dimensional TEE does not easily allow tracking of tools over long distances greater than 5 to 6 cm and cannot predict the optimal tool path for instrument navigation.

When we examined the results by level of expertise, unfortunately, we had too small of a sample size to demonstrate any significant differences. Nonetheless, the confidence intervals of the tool accuracy measurements (distances from intended midline trajectory) were much narrower with AR imaging guidance than TEE alone, suggesting that AR imaging guidance may help improve the reproducibility of results in novice surgeons and shorten the procedural learning curve. In addition, we believe that the AR imaging platform can still provide beneficial guidance to experts as well. Figure 4.8 demonstrates

the superior tool navigation paths with AR imaging compared with TEE alone performed by a surgeon experienced in numerous human implants with the NeoChord DS1000 device.

Overall, we believe that AR imaging guidance will shorten procedure times and significantly improve the safety of beating heart mitral valve repair with the NeoChord DS1000 device in both novices and experts. In addition, we believe that the improved image guidance provided by this AR navigation system could be easily adapted to other beating heart procedures.

The infrastructure costs of most currently available intraoperative image guidance systems, including Dyna computed tomography, magnetic resonance imaging, and hybrid operating rooms, are in excess of several millions of dollars [33]. Our AR imaging guidance platform is much more cost-effective, with the magnetic tracking system retailing for approximately $18,000 USD and $250 USD for each single-use sensor. In addition, the AR system is portable, avoids irradiation, and does not impede normal operating room workflow.

Beating heart mitral valve repair procedures, transcatheter aortic valve implantation, and atrial and ventricular septal defect device closure all rely on limited intraprocedural visualization that could be enhanced with this AR guidance system. Minimally invasive on-pump procedures, such as mini-thoracotomy mitral and aortic valve procedures, may also benefit from this assisted guidance to accurately place peripheral inserted cannulas centrally.

4.2.4.2   Study Limitations

Limitations in our study include the relatively small sample size, the porcine model, and misregistration errors related to aortic valve and mitral valve annular movement.

While this image guidance system provides sufficient accuracy for the procedure, it took up to 20 min to define the aortic valve annulus, mitral valve annulus, and line of coaptation in systole for these porcine studies. While the line of coaptation was particularly difficult to identify in healthy porcine hearts, we believe this feature to be much easier to define in humans, particularly when a prolapsed or flailing leaflet is present.

4.2.4.3   Summary

In summary, this proof-of-concept study demonstrated superior tool navigation accuracy, significantly shorter navigation times, and reduced potential for injury with AR enhanced intracardiac TEE navigation for off-pump transapical mitral valve repair with neochordae implantation.

4.3   Predictors of Surgical Success in Beating Heart Mitral Valve Repair with Artificial Chordae

4.3.1   Motivation

The NeoChord device is currently undergoing human trials for the repair of degenerative mitral valve regurgitation. Initial results confirm the safety and efficacy of this surgical tool for mitral valve repair [29-31]; however, clinical observations made during the conduct of the TACT study in Europe have highlighted key challenges with the procedure. One challenge is Neochord suture dehiscence, or tearing, from the mitral valve leaflet following suture deployment.

The length of the neochord sutures is adjusted from outside of the left ventricular apex using echocardiographic guidance. The left ventricular apex is used as the tethering point for neochords placed by the NeoChord tool. This is not physiologic. As previously described, natural chordae tendineae insert on the anterolateral and posteromedial papillary muscles. Therefore, apical tethering of the neochordae may affect the dynamic relationship between the mitral valve leaflets and chordae. For example, a previous study reported that the variation in chordae tendineae length between systole and diastole is greater at the apex compared to the papillary muscles [37]. This may contribute to increased risk of prolapse or tearing of the repaired mitral leaflet when chordae are attached to the left ventricular apex. In fact, recent results in the TACT study would suggest a posterolateral left ventricular access site has yielded improved acute results.

Furthermore, the NeoChord suture insertion site on the anterior or posterior leaflet may also affect risk of suture dehiscence. In the normal mitral valve, the posterior leaflet and chordae are subject to much lower levels of tensile stress than the anterior leaflet and chordae. Following neochord repair, there is an even higher stress concentration at the site of suture insertion, particularly at the suture close to the A2/P2 region.

The purpose of this study was to determine if there was a difference in the amount of force required for suture dehiscence when comparing different suture insertion and tethering sites. This information may indicate what factors in NeoChord suture placement determine successful NeoChord suture deployment on the mitral valve leaflet without suture dehiscence.

4.3.2 Methods

4.3.2.1   *Ex vivo* Porcine NeoChord Suture Deployment

Porcine hearts were obtained from a local abattoir. The approximate mass of the hearts was 1 kg. Only porcine hearts of similar size with intact mitral valve apparatus were selected for the study. The left atrium was transected from the porcine heart.

The NeoChord DS-1000 was used to deploy a 2-0 ePTFE suture (CV-4, W. L. Gore & Associates, Inc., Flagstaff, Arizona) at the anterior or posterior mitral valve leaflet of the porcine heart. All sutures were deployed at the A2 or P2 location approximately 3 mm from the leading edge of the leaflet. The order of NeoChord deployment to the anterior and posterior locations was randomized. Each NeoChord suture was passed through either the apex or the base of a papillary muscle. The order of NeoChord suture tethering to the apex or papillary muscle was randomized using Design-Expert statistical software (Stat-Ease, Inc., Minneapolis, MN).

Following *ex vivo* NeoChord suture deployment in a porcine heart, the suture was placed between a custom plate and the surface of a nano force-torque sensor. The force required for NeoChord suture dehiscence was measured using this nano force-torque sensor (ATI Industrial Automation, Apex, NC) mounted on a linear stage. The tethered NeoChord suture was retracted by the linear stage at a rate of 2 mm/s. The maximum net force required for NeoChord suture dehiscence from the leaflet was recorded. From this data, a threshold of net maximum force required for chordal dehiscence was calculated and related to the location of NeoChord deployment and tethering.

Next, the amount of force on the NeoChord suture between systole and diastole was measured *in vivo* in a porcine model. Following *in vivo* NeoChord suture deployment at P2 in a porcine heart, the suture was passed through the apex of the left ventricle and

placed between a custom plate and the surface of a nano force-torque sensor mounted on a linear stage. The tethered NeoChord suture was retracted by the linear stage at a rate of 2 mm/s until the suture was taught during systole. The forces on the NeoChord suture were recorded firstly during systole, when the suture is taught and forces are highest [38], and secondly during diastole, when the suture is lax and forces are lowest.

4.3.2.2   Statistical Analysis

There were four groups for this study: A2 to apex, A2 to anterolateral papillary muscle, P2 to apex, and P2 to posteromedial papillary muscle. The number of trials required for each group was determined by the resource equation, as this method does not require estimates of the effect size or standard deviation. Six trials per group were calculated as an acceptable number each of the four groups to be tested. Nevertheless, 22 trials were completed for each of the four groups.

Continuous variables were expressed as a mean $\pm$ standard deviation (SD), and categorical variables were expressed as percentages. The Shapiro-Wilk test for normality was performed on all four dehiscence trial data sets and confirmed a $p \geq 0.05$ for each data set, indicating a normal distribution. Statistical analysis was performed using two-tailed paired t-test with bootstrapping and a value of 0.05 was considered statistically significant.

4.3.3 Results

The mean maximum force required for NeoChord suture dehiscence from the anterior mitral valve leaflet to the apex (5.09 ± 0.36 N) was significantly lower than the mean maximum force required for NeoChord suture dehiscence from the anterior mitral valve

leaflet to the anterolateral papillary muscle (10.01 ± 0.95 N, Table 4.6).

The mean maximum force required for NeoChord suture dehiscence from the posterior mitral valve leaflet to the apex (4.07 ± 0.41 N) was significantly lower than the mean maximum force required for NeoChord suture dehiscence from the posterior mitral valve leaflet to the posteromedial papillary muscle (7.21 ± 0.77 N, Table 4.6).

The mean maximum force required for NeoChord suture dehiscence from the posterior mitral valve leaflet to the apex (4.07 ± 0.41 N) was lower than the mean maximum force required for NeoChord suture dehiscence from the anterior mitral valve leaflet to the apex (5.09 ± 0.36 N, Table 4.7). However, this difference was not statistically significant.

The mean maximum force required for NeoChord suture dehiscence from the posterior mitral valve leaflet to the posteromedial papillary muscle (7.21 ± 0.77 N) was significantly lower than the mean maximum force required for NeoChord suture dehiscence from the posterior mitral valve leaflet to the posteromedial papillary muscle (10.01 ± 0.95 N, Table 4.7).

The mean force measured from the NeoChord suture *in vivo* during systole was 0.151 ± 0.005 N. The range between of force measured from the NeoChord suture was 0.016 to 0.285 N during systole.

Table 4.6: Mean maximum force (N) required for neochord suture dehiscence for different attachment and tethering locations

Neochord Suture Attachment and Tethering Locations	Number of trials	Maximum Force (N) Mean ± SD
Anterior Leaflet to Apex	22	5.09 ± 0.36
Anterior Leaflet to Anterolateral Papillary Muscle	22	10.01 ± 0.95
Posterior Leaflet to Apex	22	4.07 ± 0.41
Posterior Leaflet to Posteromedial Papillary Muscle	22	7.21 ± 0.77

Table 4.7: Comparison of mean maximum force (N) required for neochord suture dehiscence for different attachment and tethering locations

Comparison	Paired difference Mean ± SD	95% Confidence Interval	Significance (p-value)
Anterior Leaflet to Apex – Anterior Leaflet to Anterolateral Papillary Muscle	-4.92 ± 1.03	-7.06, -2.78	<0.001
Posterior Leaflet to Apex – Posterior Leaflet to Posteromedial Papillary Muscle	-3.14 ± 0.74	-4.67, -1.60	<0.001
Anterior Leaflet to Apex – Posterior Leaflet to Apex Anterior Leaflet to	1.02 ± 0.59	-0.21, 2.25	0.1
Anterolateral Papillary Muscle– Posterior Leaflet to Posteromedial Papillary Muscle	2.80 ± 1.06	0.61, 5.00	0.02

4.3.4 Discussion

Initial results from the TACT trial of beating heart NeoChord repair in patients with mitral valve regurgitation revealed favourable outcomes. However, one complication of NeoChord suture placement is postoperative suture dehiscence, or tearing, from the mitral valve leaflet. NeoChord sutures are synthetic, nonabsorbable monofilament sutures made of ePTFE and they are more extensible than natural chordae tendineae. Whereas, natural chordae tendineae are extensible and may change up to 10-15% in length when higher load levels are applied, ePTFE sutures may change less than 2% under the application of higher loads [38]. Furthermore, once stretched, ePTFE does not have the ability of natural chordae tendineae to return to the original length. These differences may alter the conditions and forces on the mitral valve leaflets following NeoChord suture placement. The purpose of this study was to determine if there was a difference in the amount of force required for NeoChord suture dehiscence from the mitral valve leaflet when comparing different suture insertion and tethering sites.

We found that the mean maximum force required for NeoChord suture dehiscence from the anterior or posterior mitral valve leaflet to the apex was significantly lower than the mean maximum force required for NeoChord suture dehiscence from the anterior or posterior mitral valve leaflet to the anterolateral or posteromedial papillary muscle, respectively. Furthermore, the mean maximum force required for NeoChord suture dehiscence from the posterior mitral valve leaflet was lower than the mean maximum force required for NeoChord suture dehiscence from the anterior mitral valve leaflet. Therefore, there may be a lower threshold of force required for dehiscence when NeoChord sutures from either mitral valve leaflet are tethered at the left ventricular apex. NeoChord sutures inserted in the posterior mitral valve leaflet may be more vulnerable to dehiscence. Our results data follow from previous studies that found that in the normal

mitral valve, the posterior mitral valve leaflet is subject to much lower levels of tensile stress than the anterior leaflet. Therefore, tissues of the posterior mitral valve leaflet may be more vulnerable to the application of force through NeoChord sutures.

In addition, previous studies have found that the area of ePTFE suture attachment to the leaflet had higher stress concentrations, particularly at the suture closest to the midline. Therefore, differences in locations within the mitral valve leaflets may also play a role in NeoChord suture dehiscence. For example, NeoChord sutures placed closer to the leading edge or the midline (P2) of the mitral valve leaflet may dehisce more readily than NeoChord sutures placed further from the leading edge or the midline of the mitral valve leaflet. The force required for NeoChord suture dehiscence from locations within the anterior and posterior mitral valve leaflets including different A1, A3, P1, P3 segments and different distances from the leaflet edge were not explored in this study.

The mean force measured from the NeoChord suture *in vivo* during systole was much lower than the force required for dehiscence measured *ex vivo*. Therefore, the location of NeoChord suture placement and tethering is not the only factor that affects NeoChord suture dehiscence. Potential additional factors they may contribute to NeoChord suture dehiscence include individual patient and mitral valve characteristics. For example, a NeoChord suture in a thin myxomatous mitral valve leaflet would be more likely to dehisce than a NeoChord suture in a thickened rheumatic mitral valve leaflet. Therefore, as part of this study, the preoperative, intraoperative, and postoperative patient data and ultrasound images from patients who have undergone mitral valve repair using the NeoChord were requested from NeoChord, Inc. We had originally intended to correlate porcine *ex vivo* data with patient TEE data from the TACT trial. However, patient data was not available from the study centres across Europe and a standard TEE protocol was

not employed at all TACT study centres. Consequently, the requisite three-dimensional TEE volumes were not obtained for analysis.

 Despite the limitations of this study, we were able to ascertain one potential influence on NeoChord suture dehiscence. Although the location of NeoChord suture placement and tethering may not be the only contributor to suture dehiscence, careful consideration of this factor when placing NeoChord sutures may prevent suture dehiscence in mitral valve leaflets, particularly in patients more vulnerable to this unfortunate complication.

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Chapter 5

5   Augmented Reality System for Ultrasound Guidance of Transcatheter Aortic Valve Implantation

Transcatheter aortic valve implantation (TAVI) relies on fluoroscopy and nephrotoxic contrast medium for valve deployment. We propose an alternative guidance system using augmented reality (AR) and transesophogeal echocardiography (TEE) to guide TAVI deployment. The goals of this study were to determine how consistently the aortic valve annulus is defined from TEE using different aortic valve landmarks, and to compare AR guidance to fluoroscopic guidance of TAVI deployment in an aortic root model. We found that aortic valve commissures can be identified more reliably than cuspal nadirs from TEE. Furthermore, the AR guidance system achieved similar deployment accuracy to fluoroscopy while eliminating the use and consequences of nephrotoxic contrast and radiation.

My contribution to this chapter involved designing and conducting experiments and analyzing data.

5.1   Introduction

Transcatheter aortic valve implantation (TAVI) is a growing technology that provides an alternative surgical option for patients with severe aortic stenosis [1, 2]. Optimal positioning and safe deployment of TAVI valved-stent is integral to the success of the procedure. Implantation of the valved-stent too far above the aortic valve annulus may result in its embolism or coronary occlusion by the valved-stent; whereas, positioning the valved-stent too far below the aortic valve annulus may cause atrioventricular block requiring a permanent pacemaker or retrograde embolization [3].

Navigation and deployment of the valved-stent during TAVI relies largely on single-plane fluoroscopy; however, this imaging modality has several limitations. Fluoroscopic images are only able to display gross anatomic structures; therefore, to improve visualization, nephrotoxic contrast medium is required to obtain contrast-enhanced images. However, the use of multiple contrast fluoroscopic images can increase a patient's risk of acute kidney injury [4-7]. Many TAVI patients have underlying renal dysfunction and are therefore more vulnerable to acute kidney injury. The reported incidence of acute kidney injury following TAVI is between 12 and 57% [4-5, 7-8]. One registry of TAVI patients reported that up to 6.7% of patients required acute hemodialysis was required in the post-procedural period [9]. Furthermore, the development of acute kidney injury is an independent predictor of prolonged hospital stay and impaired early survival following cardiac surgery [7, 10, 11]. In fact, one study reported an 11.7% incidence of acute kidney injury following TAVI and a greater than four-fold increase in

the risk of postoperative mortality among those patients [7]. Finally, fluoroscopic imaging exposes both patients and health care professionals to ionizing radiation.

Transesophageal echocardiography (TEE) has been successfully employed as an alternative primary imaging modality for TAVI guidance, albeit in a limited number of centres. However, TEE alone has limited resolution and does not provide satisfactory imaging of the TAVI catheter [12, 13]. Integrating AR with TEE would enable virtual representations of both the TAVI valved-stent and critical aortic valve anatomy to be registered to biplane TEE. In fact, previous work using AR and TEE for beating heart mitral valve repair has found that simply defining the valve annuli from tracked TEE is sufficient for image guidance [14, 15]. This eliminates the need for complex preoperative models and registrations with associated errors [16, 17].

We have adapted this AR and TEE guidance system for TAVI deployment. The location of the magnetically tracked TAVI catheter and TEE in 3D space along with interactively defined aortic valve anatomy can be represented by virtual geometric models and overlaid onto real time TEE images, all within a common coordinate system. This enables the surgeon to assess the accuracy and reliability of the geometric models as compared to the underlying real ultrasound image data. Furthermore, augmenting the real-time TEE image data with virtual models of the critical anatomy required for accurate TAVI deployment may facilitate TAVI deployment that achieves similar deployment accuracy to the current standard of care, fluoroscopy, while eliminating the use of nephrotoxic contrast and ionizing radiation. The accuracy of TAVI deployment using this AR guidance system depends on the accuracy of the magnetic tracking system and on the accuracy of the location of the aortic valve annulus defined from TEE.

The goals of this study were to determine how consistently the aortic valve annulus is defined from TEE using different aortic valve landmarks, and to compare AR guidance to fluoroscopic guidance of TAVI valved-stent deployment in an aortic root model.

5.2   Methods

5.2.1   AR Guidance System Design

This guidance system was designed to assist the surgeon to establish the correct location for deployment of the TAVI valved-stent within the aortic annulus without using fluoroscopy. To accomplish this goal, real-time TEE images were augmented with the location of the magnetically tracked valved-stent and intra-operatively defined aortic valve anatomy.

Real-time tracking of the TEE and TAVI catheter was accomplished using the Aurora tabletop magnetic tracking system (Northern Digital, Waterloo, Ontario). A six degree of freedom (DOF) magnetic tracking sensor was attached to the Ascendra TAVI catheter (Edwards Life Sciences, Irvine, California) and integrated into a custom made cap that attaches to the x7-2t TEE probe (Philips Healthcare, Andover, Massachusetts). Virtual geometric models of the TEE probe and the TAVI valved-stent were created in VTK (Visualization Toolkit, Kitware Inc., Clifton Park, New York). The geometric representation of the TEE probe included video image planes that rendered real-time digital video capture of the TEE. The tracked TEE probe was calibrated using a standard Z-bar calibration technique [18]. Once the valve was crimped on to the catheter, a calibration was performed using a custom-built tracked calibration block designed to hold the catheter shaft and valve in a precise configuration (Figure 5.1). This allowed the crimped prosthetic valve to be magnetically tracked.
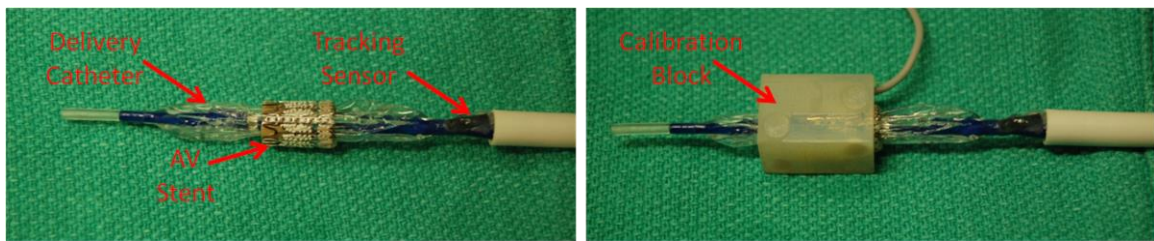
Figure 5.1: Calibration block for magnetic tracking of the transcatheter aortic valve on the catheter.

5.2.2   Surgical Workflow

Incorporation of this system into the operating room first involved identification of aortic valve landmarks from biplane TEE images. Our intention is for this task to be completed by the echocardiographer during rapid pacing prior to advancement of the TAVI catheter. Rapid pacing is routinely performed at this point in the procedure to test the leads. Based on the identification of clear aortic valve landmarks, virtual geometric models of the aortic annulus were displayed in the AR guidance system. Using the location of aortic annulus models superimposed on the live biplane TEE, the surgeon determined the ideal valved-stent deployment depth relative to the aortic valve annulus. The target deployment depth marks the ideal distance from an aortic valve landmark at which the leading edge of the valved-stent should be deployed. During navigation of the valved-stent to the target deployment depth or target depth, the remaining distance from the catheter to this plane was displayed numerically and the target plane changed color to indicate when the target deployment depth was reached (Figure 5.2).
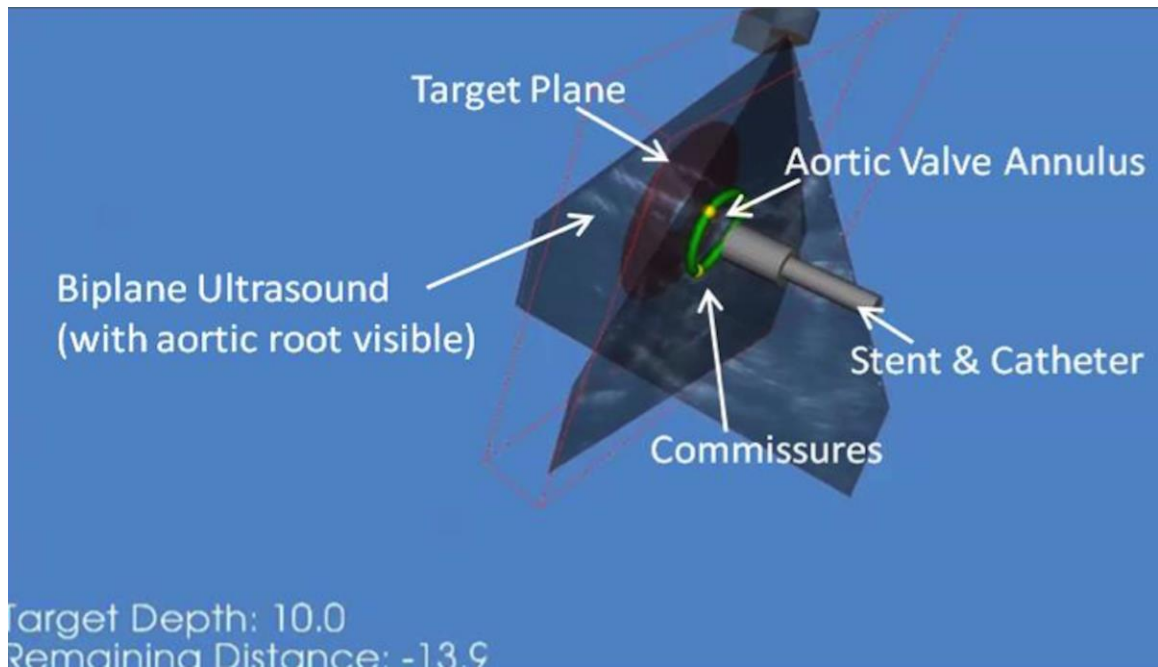
Figure 5.2: AR guidance system showing the catheter approach the target deployment depth (5.0 mm) marked by target plane. As the catheter reaches the target deployment depth, the target plane changes from red to green.

5.2.3 Localization of Aortic Valve Landmarks from Human Three Dimensional TEE Images

Defining the aortic valve annulus can be challenging, and it is essential that the landmarks used to delineate the valve annulus be well defined with minimal variability in identification. Aortic valve commissures and aortic valve cuspal nadirs were used as potential landmarks to define the aortic valve from TEE. Commissures of the aortic valve are stationary hinge points; therefore, the guidance system may use these points to determine the ideal valved-stent deployment depth. The nadirs of the aortic valve cusps have also been used as landmarks for determining the ideal fluoroscopic angle for TAVI deployment [19-25].

To assess the interoperator variability in identifying these landmarks, three subjects identified three commissures and three cuspal nadirs in ten full volume TEE images of the aortic root in diastole (Figure 5.3). The images provided were consistent with standard intraoperative TEE imaging (Figure 5.4). Furthermore, they provided a view similar to that of rapid pacing. To assess intraoperator variability, a cardiac surgery resident repeated the identification of aortic valve landmarks on ten volumes five times, each on separate days.

Feature localization error was calculated from the average overall standard deviation in commissure and nadir localization. The standard deviation in commissure and nadir localization in the direction parallel to the aortic annular plane was used as the in plane error. The standard deviation in commissure and nadir localization in the direction perpendicular to the aortic annular plane was used as the out of plane error.
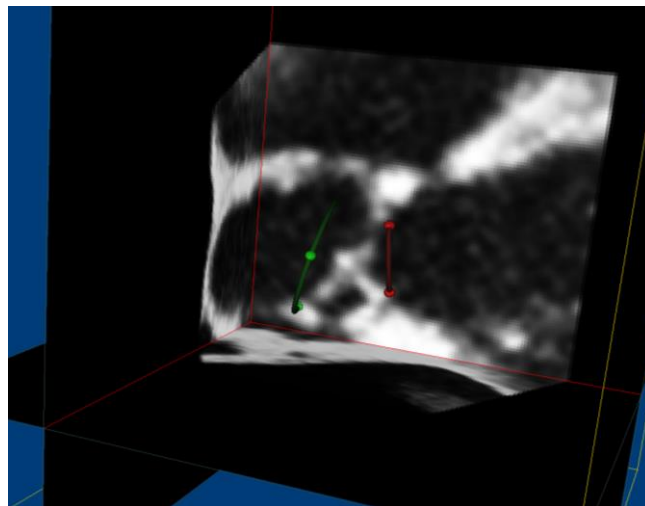
Figure 5.3: Human full volume cardiac images with aortic commissures labeled green and aortic cuspal nadirs labeled red.
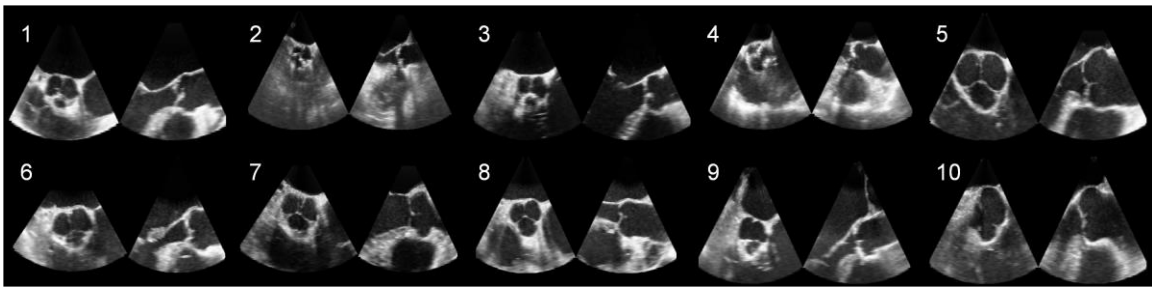
Figure 5.4: Long and short axis views from all 10 volumes used for the intraoperator variability experiment. Image quality is typical for diagnostic volumes.

## 5.2.4　Intraoperative Localization using Aortic Annulus Model

To assess the intraoperator variability in identifying the aortic commissures during TAVI deployment, a single subject identified the three commissures from a live TEE image of an aortic root model. This was repeated ten times by the same subject. The Euclidean distance from mean location of each identified commissure was measured. The feature localization error was calculated from the overall, in- plane, and out- of- plane standard deviation.

5.2.5　TAVI Deployment with Fluoroscopic or AR guidance

5.2.5.1　Aortic Root Model

To compare AR guidance of TAVI valved-stent deployment to fluoroscopic guidance, a model of the aortic root was used. This model consisted of a left ventricle, an atrial reservoir, a mitral valve, an aortic valve, and an actuator system. The ventricle had an apical access port for transapical TAVI. The model was constructed from soft silicone (Shore A 30 durometer). Water was used to simulate blood, and the inner diameter across the aortic valve was 23 mm at the commissures. Experiments were performed in a

static model to simulate rapid pacing (Figure 5.5). A static model of the aortic root was chosen for this experiment in order to maintain consistent distances between anatomic landmarks and a consistent aortic valve diameter for each trial.
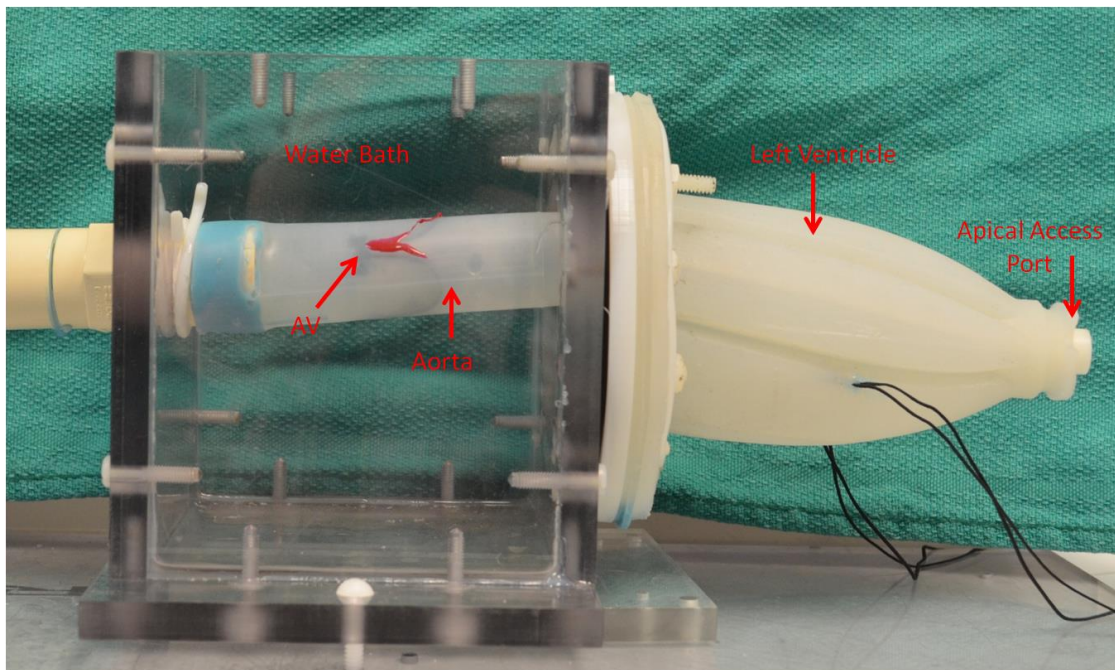
Figure 5.5: Static silicone cardiac model with aortic and mitral valves. Aortic valve (AV).

5.2.5.2   Surrogate TAVI Stent

As the balloon-inflated TAVI valved-stents are single use, a surrogate stent was used for the experiments, permitting a larger number of trials to be performed without consuming valuable valved-stents. The surrogate stent was made from an elastic material with radiopaque markers simulating the struts of the stent, and had a similar appearance in

both fluoroscopy and TEE to an actual valved-stent (Figure 5.6). The surrogate stent was reused without significant wear and collapsed as soon as the balloon was deflated. For this reason, all measurements were acquired while the balloon was still inflated.
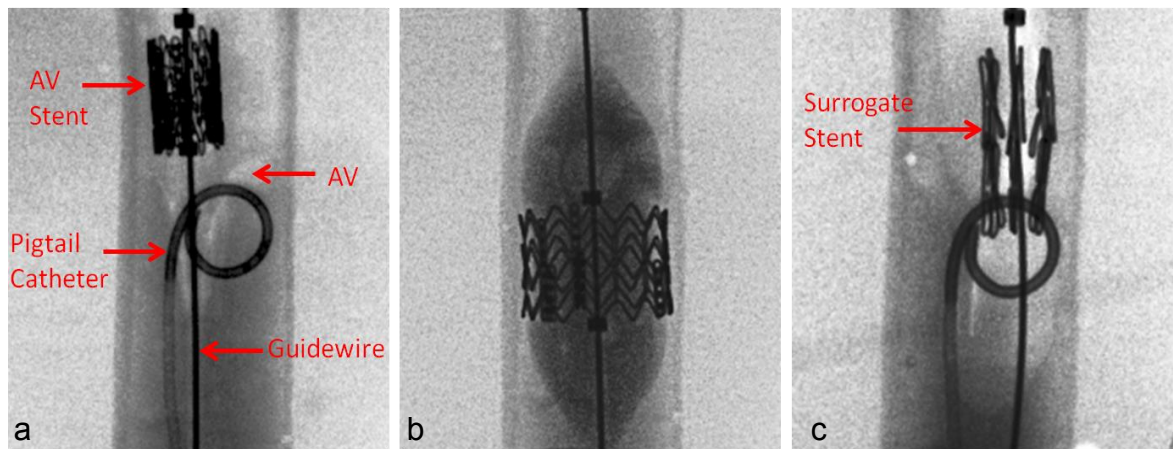
Figure 5.6:Transcatheter aortic valve (a) deployed using fluoroscopy (b). Surrogate transcatheter aortic valve shown under fluoroscopy (c).

5.2.5.3   Fluoroscopic TAVI Guidance

A cardiac surgery resident deployed the surrogate TAVI valved-stent ten times in the aortic root model using each of the two guidance systems.   For conventional contrast-enhanced fluoroscopic guidance, a qualitative target was used to guide the target deployment depth. The subject strived to achieve a consistent deployment depth.   First, a guide wire was inserted through the apex and passed through the ventricle and aortic valve, terminating in the aortic reservoir. A pigtail catheter was deployed through the aortic reservoir and rested under one of the aortic cusps. The valved-stent delivery catheter was inserted onto the guidewire and into the left ventricle of the model. Prior to

each trial, contrast was injected into the aortic root so that the valve, including commissures and nadir were visible in the fluoroscopic image. The valved-stent was positioned using fluoroscopic video so that it appeared that half the valved-stent lay on either side of the valve (Figure 5.6). Before deployment, the pigtail catheter was withdrawn to ensure that it would not become caged by the valved-stent. As the current standard of care is to deploy the valved-stent using the fluoroscopy images qualitatively without any quantitative target, it is difficult to give an exact deployment error or location for ideal deployment. In this experiment, the user was instructed to strive to achieve consistent deployment in all ten trials.

After each deployment, a camera assembly was positioned over the aortic root model to photograph the valved-stent inside the aorta from a fixed position. A reference checkerboard was mounted beside the aorta at the same depth as the two commissures visible from the camera's position. The distance between the commissure plane and the furthest visible stent strut was measured from photographs acquired immediately after deployment (Figure 5.7). The variability of target deployment depths gave an estimate of the minimum error achieved in fluoroscopic guidance.
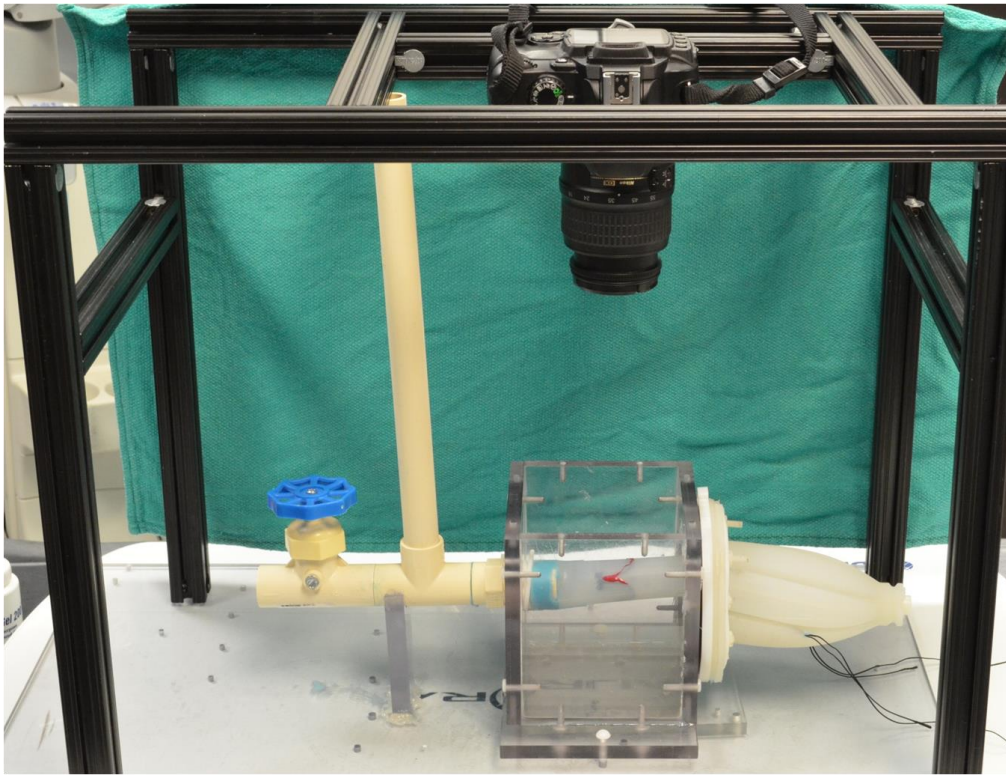
Figure 5.7:Camera jig for measurement of true distance of deployed transcatheter aortic valve from the aortic valve commissures.

5.2.5.4   AR TAVI Guidance

For AR guidance of TAVI deployment, a target depth 5 mm beyond the commissural plane was used. As in fluoroscopy, a guidewire was passed through the aortic valve. The surrogate stent was placed on the modified valved-stent delivery catheter and the position of the stent was determined using the calibration block. After the delivery catheter was inserted into the left ventricle, all three aortic commissures were identified in the TEE image. The target plane was created 5 mm behind the commissural plane, and the valved-stent was deployed at this location using the AR guidance system. In practice, the target deployment depth would depend on the patient's anatomy and the profile of the

prosthetic valved-stent to ensure the coronary ostia are not obstructed by the valved-stent. The aortic valve and stent calibration were repeated for each trial so that variability in these steps was included in the stent deployment.

After each deployment, the camera was positioned over the aortic root model to photograph the stent as previously described for fluoroscopic guidance. In addition to the photographic measurements, the target deployment depth reported by the AR system was also recorded.

5.3   Results

5.3.1   Comparison of Aortic Valve Commissure and Aortic Cuspal Nadir Localization Error

Errors in localizing commissures and nadirs from full volume human cardiac TEE images were compared. The error in feature-based localization was calculated using an unbiased estimate of variance of feature positions. Feature localization error was reported for every image and for the entire dataset and was broken down into both the in-plane and out-of-plane directions. In-plane errors indicate how difficult the feature was to localize on the valve plane. Out-of-plane errors indicate difficulty in finding the depth of the valve. While both errors contribute to deployment error, out-of-plane errors are more serious because achieving the correct depth is critical.

In examining interoperator variability, we found that the overall error for commissure localization was 2.2 mm. The errors in commissure and nadir localizations are shown in Table 5.1, where the in-plane commissure localization error was 1.4 mm, and the out-of-plane commissure localization error was 1.7 mm. The overall error for aortic valve cuspal nadir localization was 3.8 mm. The nadir localization error was 3.4 mm in-plane, and 1.5 mm out-of-plane.

Table 5.1. Interobserver feature localization error for each point. Error was calculated using the standard deviation of commissure and nadir positions in full volume TEE cardiac images.

Trial	1	2	3	4	5	6	7	8	9	10	Overall Error
Commissures	2.5	3.7	1.6	2.1	1.6	2.0	1.4	1.4	2.2	3.8	2.2
in-plane	1.9	3.2	0.8	1.4	1.1	0.7	0.9	0.8	1.3	1.7	1.4
out-of-plane	1.7	1.8	1.4	1.6	1.1	1.9	1.1	1.2	1.8	3.4	1.7
Nadir	2.3	3.5	3.0	5.2	5.2	4.1	3.4	2.9	4.2	4.2	3.8
in-plane	2.0	3.4	2.9	4.8	5.0	3.6	3.0	2.7	2.9	4.0	3.4
out-of-plane	1.1	0.8	1.0	1.8	1.3	2.1	1.4	1.2	3.0	1.1	1.5

For intra-operator variability, the overall error for commissure localization was 2.2 mm. The individual errors in commissure and nadir localizations are shown in Table 5.2. The in-plane commissure localization and out-of-plane commissure localization errors were 1.2 mm and 1.9 mm respectively. The overall error for aortic valve cuspal nadir localization was 4.7 mm, with in-plane nadir and out of plane errors being 4.2 mm and 2.1 mm respectively. The largest error of 3.8 mm for commissures and 8.2 mm for nadir

occurred in image two, which had the worst image quality in the dataset.

Table 5.2. Intraobserver feature localization error for each point. Error was calculated using of the standard deviation of commissure and nadir positions in full volume TEE cardiac images.

Trial	1	2	3	4	5	6	7	8	9	10	Overall Error
Commissures	1.4	3.8	2.3	1.7	2.6	1.9	1.9	1.3	2.3	2.1	2.2
in-plane	0.8	2.1	0.9	1.2	1.0	0.7	0.7	0.9	0.9	1.8	1.2
out-of-plane	1.1	3.2	2.1	1.2	2.4	1.8	1.8	1.0	2.1	1.0	1.9
Nadir	2.8	8.2	2.6	5.4	5.6	3.7	3.8	3.2	4.7	3.7	4.7
in-plane	2.6	6.5	2.5	5.0	5.4	3.3	3.6	3.1	4.2	3.6	4.2
out-of-plane	0.9	5.0	0.8	2.0	1.3	1.8	1.2	0.9	2.3	0.8	2.1

5.3.2 Localization of Aortic Valve Commissures from Live TEE Biplane Images in an Aortic Root Model

To examine the intraoperator localization error for identification of aortic valve commissures during the TAVI procedure, live biplane TEE images of the aortic root

model were used. Only commissures were considered for this experiment, as their localization was more consistent. The overall commissure localization error was 2.0 mm. Both the in-plane and out-of-plane commissure localization errors were 1.4 mm. The individual errors in commissure localizations are shown in Figure 5.8.
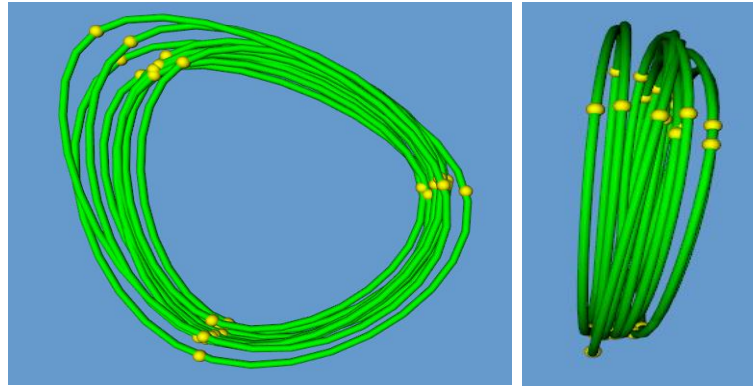
Figure 5.8: Short (left) and long (right) axis views of the ten live biplane definitions of the aortic valve.

5.3.3   TAVI deployment with Fluoroscopic or AR guidance

The TAVI deployment depths using either fluoroscopic or AR guidance systems are shown in Table 5.3. Fluoroscopic guidance of TAVI deployment achieved an average deployment depth of 6.3 ± 3.4 mm (mean $\pm$ standard deviation) for ten deployment trials.

AR guidance of TAVI deployment resulted in a deployment depth of 7.0 ± 2.9 mm as recorded by the photographic measurements, while the AR system reported a mean deployment depth of 5.03 ± 0.03 mm. Therefore, the stent was deployed an average 2 mm beyond the target depth displayed by the AR guidance system (5.0 mm). The variability in deployment depth was 2.9 mm. The root mean square (RMS) error of deployment using AR guidance was 3.4 mm. This error takes into account the variability

in both the deployment depth and the distance from the intended target, A comparison of deployment depths using either AR or fluoroscopic guidance is shown in Figure 5.8. The overlapping lines showing standard deviation reveal that both methods have a comparable accuracy in deployment depth. In addition, the standard deviation of deployment was slightly smaller using the AR guidance system indicating improved precision of deployment. Therefore, our proposed AR guidance system may achieve similar or better results than contrast enhanced fluoroscopy while eliminating the use of nephrotoxic contrast and ionizing radiation.
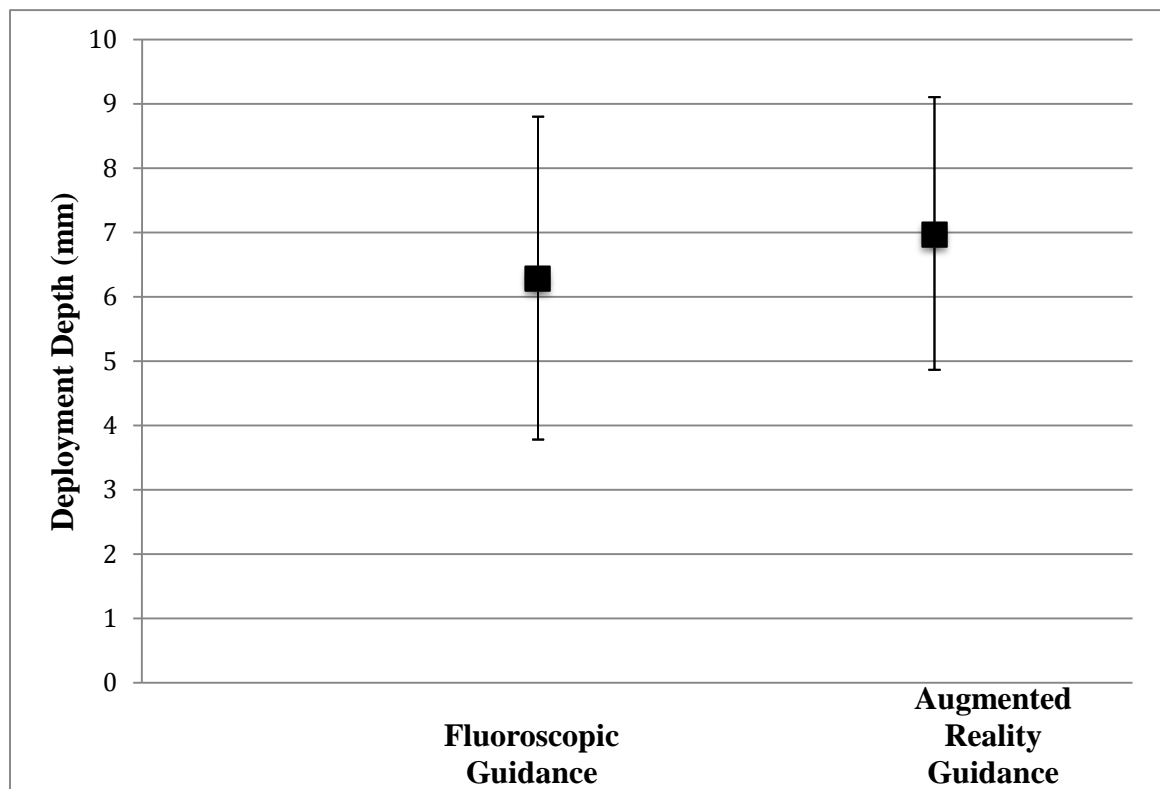
Figure 5.9: Mean distance of the transcatheter aortic valve from the commissures

following deployment with either fluoroscopic or AR guidance.

The TAVI deployment depths using either fluoroscopic or AR guidance systems are shown in both Table 5.3 and Figure 5.9. Fluoroscopic guidance of TAVI deployment achieved an average deployment depth of 6.3 ± 3.4 mm for ten deployment trials while the AR guidance of TAVI deployment resulted in a deployment depth of 7.0 ± 2.9 mm. While the AR guidance system had slightly better precision in our experiments this difference was not statistically significant. As fluoroscopic deployment was performed using live video without a quantitative target, only the precision could be assessed of this guidance system could be assessed. However, the AR guidance system had a specified target at 5 mm superior to the AV annulus. The RMS error of deployment using AR guidance was 3.4 mm. This error measures the overall accuracy of the system and takes into account both precision and bias in deployment depths. These results suggest that the errors associated with using AR guidance are within the variability in deployment depth that occurs with conventional contrast enhanced fluoroscopy.

Table 5.3. Deployment depths (distance from commissures to leading edge of TAVI valved-stent) achieved using each of the guidance systems. The overall mean and standard deviation (SD) of the deployment depths are summarized in the last column. The differences in the mean and variance of the deployment depth were not statistically significant.

Trial	1	2	3	4	5	6	7	8	9	10	Overall Mean (SD)
Fluoroscopy	7.0	1.3	0.6	6.0	9.3	11.1	7.3	9.4	6.0	4.9	6.3 (2.5)
AR	9.8	7.8	3.0	7.7	6.8	6.6	7.9	10.0	9.2	0.8	7.0 (2.1)

The actual deployment of the TAVI valve under both fluoroscopic and AR guidance was very fast, taking approximately a minute to complete under both guidance platforms. The TAVI procedure did require a more elaborate setup including, calibrating the TAVI valve and starting the guidance software. In addition, the valve commissures were manually defined from TEE before each deployment. While this would be performed before the TAVI catheter enters the heart, it may contribute slightly to longer procedure time. We observed a median time between trials of 8 minutes for the fluoroscopic guidance and 18 minutes for the AR system. This time included everything from resetting the experiments to taking photographs for measuring valve position. The extra 10 minutes required for the AR system were mostly due to the more elaborate setup required. In a clinical context, an extra 10 minutes of preparation in the OR before the procedure would not impede current workflow.

5.4   Discussion

Adequate and safe deployment of TAVI valved-stents is integral to the success of the procedure. The 2013 Society of Thoracic Surgeons Guidelines recommends intraoperative fluoroscopy as the standard of care for guidance of TAVI deployment [21]. However, fluoroscopy necessitates the use of nephrotoxic contrast medium, which is of concern in the TAVI patient cohort, as many are elderly, high-risk surgical patients with underlying renal dysfunction. The incidence of acute kidney injury following TAVI is reported as high as over 50% [4-5, 7-8]. Furthermore, the development of acute kidney injury is an independent predictor of postoperative mortality [7].

This study presents a TEE and AR guidance system for TAVI placement to visualize both the TAVI valved-stent and the critical aortic anatomy without exposure to contrast medium and ionizing radiation.

There have been several alternatives to single plane fluoroscopy that aim to improve valved-stent placement and reduce or eliminate the use of nephrotoxic contrast and ionizing radiation, including rotational angiography, magnetic resonance imaging (MRI), and TEE guidance.

In rotational angiography, an intraoperative cone beam computer tomography (CT) volume is acquired by rotating the C-arm around the patient during rapid ventricular pacing. This reduces the amount of contrast delivered and also minimizes motion artifacts. Subsequently, the image volume generated can be superimposed on the real-time fluoroscopic image to provide more anatomical context for aortic valved-stent implantation and to select the ideal fluoroscopic imaging plane. The optimal C-arm angle for TAVI deployment occurs when the nadir of all three aortic cusps are aligned, suggesting the aortic root is perpendicular to the imaging beam [19-25]. It has previously been shown that use of an optimal C-arm angle for TAVI deployment is associated with decreased rates of postprocedural paravalvular leak and reduces the number of contrast enhanced images [16]. Nevertheless, this image guidance technique employs fluoroscopic guidance that exposes the patient to both nephrotoxic contrast medium and ionizing radiation. Increased use of contrast medium results in increased risk of renal dysfunction [4-6].

Other investigators have used intraoperative MRI to guide placement of the valved-stent, resulting in successful implantation in animal studies [27]. Although this technique eliminates radiation and contrast medium exposure to the patients, such intraoperative 3D imaging is not widely available and is very expensive [28].

In comparison to cone-beam CT and MRI based imaging systems, TEE provides a more attractive modality for image guidance and does not require nephrotoxic contrast agents or ionizing radiation. In addition, TEE is already an integral part of the pre-, intra-, and postoperative valve assessment in both conventional aortic valve surgery and TAVI [29, 30]. Investigators have previously proposed the use of three dimensional (3D) TEE for TAVI guidance; however, visualization of both the aortic valve and TAVI valved-stent would not be possible given the limited spatial and temporal resolution of 3D TEE [30, 31]. Intraoperative guidance using only TEE and TEE with fluoroscopy but without contrast agents has been previously reported [12, 13]. However, TEE does not provide satisfactory imaging of the catheter or surrounding tissue due to the highly reflective surface of the catheter and resulting shadowing artifacts [12, 13]. For this reason, TEE has been proposed as a bridging modality allowing preoperative models to be registered into the intraoperative environment. Lang et al. [3], proposed using TEE to register preoperative CT models to fluoroscopy to improve image guidance without requiring rotational angiography. Luo *et al.* [17] proposed a system using magnetic tracking of the TEE and catheter to eliminate the need for fluoroscopy entirely. In this system, a preoperative model of the aortic root was registered to the tracked TEE. The tracked catheter could then be visualized in relation to the aortic model so that the valved-stent could be deployed at the desired depth. One challenge of these techniques is that the registration between TEE and preoperative CT is difficult resulting in a target registration error of 5.9 ± 3.2 mm and 3.3 ± 1.6 mm, respectively. In addition, both of these methods used a manual segmentation of the aorta from preoperative CT which is time consuming and difficult to integrate into clinical workflow.

We have also used magnetic tracking systems to display both real-time TEE data with virtual representations of the cardiovascular anatomy and surgical tools in an AR guidance system. Through the use of this guidance system for mitral valve repair, we

found that simply defining the valve annuli from tracked TEE was sufficient for image guidance and eliminated the need for complex preoperative models and registrations with associated errors [14, 15]. Using this guidance system, the surgeon can easily and intuitively identify the tool, surgical targets, and high-risk areas.

The accuracy of TAVI deployment using this AR guidance system depends on the accuracy of the magnetic tracking system and on the accuracy of the location of the aortic valve annulus defined from TEE. The latter depends on the operator's ability to consistently identify aortic valve landmarks. The first objective of this study was to determine how consistently the aortic valve annulus could be defined from either full volume TEE images or live biplane TEE images. We have shown that the aortic valve commissures can be identified more reliably than aortic valve cuspal nadirs from 3D full volume TEE images obtained from patients with aortic valve stenosis. Furthermore, there was a low variability in the identification of aortic valve commissures from an aortic valve root model intraoperatively.

The second objective of this study was to compare the accuracy of TAVI deployment using an AR guidance system to the accuracy of the current standard of care, fluoroscopy. In fluoroscopy, the error in deployment is generally determined by the visual appearance of the valve and its location with respect to gross anatomic structures. New fluoroscopic based image guidance systems with CT image overlays report the error in overlay between their own model and real time fluoroscopy. While not the same as a true targeting error, these studies provide a baseline for clinically acceptable errors. For example, the error in overlay of DynaCT on real-time fluoroscopy has been reported between 1.9±1.5 mm and 3.9±3.1 mm [16, 32]. Generally, errors in positioning less than 5 mm are clinically accepted.

We have shown that this guidance system may achieve similar or better deployment

results than contrast enhanced fluoroscopy while eliminating the use of nephrotoxic contrast and ionizing radiation. In the aortic root model study, the errors reported by the guidance system were very low, with a standard deviation of 2.9 mm from the desired deployment location indicating that good valved-stent positioning could be achieved using the AR system.

This AR guidance system for TAVI can be easily integrated into the operating room. The portable magnetic field generator is designed to fit on top of an operating room table and to work effectively in the presence of various metals. The customized cap with magnetic sensors for the TEE probe has been approved for use in humans by Health Canada. Addition of single use magnetic sensors to the deployment catheter for TAVI valves should not impede the usual operative flow due to their small size. Furthermore, the cost associated with this technology is not prohibitive for most institutions. The magnetic tracking system retails for approximately $18 000 USD and each single use sensor is $250 USD [3]. This is less than the infrastructure costs of most currently available intraoperative image guidance systems including Dyna CT, MRI and hybrid operating rooms.

The first limitation of this study was the use of a single TAVI catheter model for transapical deployment only. We plan to expand this system to include the use of additional transcatheter TAVI models.

The second limitation of this study is that it may not be applicable to the use of local anesthesia for transcatheter valve implantation. Studies have reported the use of sedation and local anesthetic for transfemoral aortic valve implantation in patients who are considered too high risk for a general anesthetic. Nonrandomized trials have shown several potential benefits of this approach including less patient hemodynamic instability, shorter procedure duration and shorter stay in hospital compared to patients who

underwent general anesthesia [33-35]. TEE may be used for TAVI with conscious sedation and local anesthetic [36-37]; however, TEE was not used in most studies reporting the benefits of TAVI under local anesthetic due to its potential for increased nociceptive stimulation [34, 37].

The third limitation of this study is the use of a rigidly defined aortic annulus from an aortic root model at the time of the procedure. Uniformity in anatomic landmarks and distances was particularly important for this trial because these distances were used to determine localization errors associated with the guidance system, while eliminating errors that may be associated with variation in anatomic features between hearts if an animal model were used. However, in the future, we hope to integrate real-time updates on the location of the aortic valve annulus using feature-based registration in a beating heart animal model. Further animal trials will be necessary to evaluate the safety and efficacy of this device prior to its implementation in the cardiac surgery operating room.

In conclusion, this study reveals that aortic valve commissures can be identified more reliably than aortic valve cuspal nadirs from TEE images and that our proposed AR guidance system may achieve similar or better results than contrast enhanced fluoroscopy while eliminating the use of nephrotoxic contrast and ionizing radiation.

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Chapter 6

6   Closing Remarks

Both mitral valve regurgitation and aortic valve stenosis are increasing in prevalence. In fact, they are the most common valvular heart diseases in the world [1-4]. Mitral valve repair and aortic valve replacement are the main surgical options for mitral valve regurgitation and aortic valve stenosis, respectively. Both mitral valve repair and aortic valve replacement demonstrate excellent outcomes [5-14].

However, despite these favorable outcomes, many elderly patients with indications for valve surgery receive no operation [15-16]. Patients are either not referred for surgery or denied surgery due to the perceived risk of conventional valve surgery involving median sternotomy for surgical access and cardiopulmonary bypass for exposure of the surgical site [15-16]. Both procedures are associated with risk of longer recovery periods, which may not be as well tolerated in elderly patients with multiple co-morbidities. Consequently, new cardiovascular techniques must be tailored to address the unique requirements of high risk, elderly, surgical patients with heart valve disease. These techniques must overcome the two main challenges of conventional cardiac surgery: sternotomy incision for surgical access and cardiopulmonary bypass for exposure of the surgical site.

6.1   Robotics-assisted minimally invasive mitral valve repair and challenges

Minimally invasive cardiac surgery encompasses a spectrum of new operative techniques that aim to minimize surgical trauma by avoiding sternotomy and reducing incision size [3]. These smaller incisions require advanced visualization systems and customized

instruments for surgery, but the surgery is dependent on cardiopulmonary bypass.

Simultaneous advances in biomedical engineering have facilitated the use of minimally invasive access for mitral valve repair. Furthermore, favorable outcomes of patients undergoing minimally invasive techniques, including robotics-assisted mitral valve repair, have been reported. For example, reduced mortality in high risk patients, reduced blood loss, reduced need for reoperation for bleeding, reduced pain, reduced ventilation time, improved postoperative respiratory function, decreased patients post operative stay in hospital and ICU, more rapid return to functional activity, increased levels of satisfaction, reduction in health care costs [17-21].

However, robotics-assisted mitral valve repair does have unique challenges. In conventional or open surgery, sensory input is derived from both vision and haptic feedback [22, 23]. For a complete depiction of haptic interactions between surgical instruments and tissue kinesthetic, tactile, and proprioception feedback must be acquired [24-26]. The currently used minimally invasive surgical robotic system, the da Vinci® from Intuitive Surgical Inc., was developed with a very high quality three-dimensional (3D) stereoscopic visualization system to enhance the performance of robotics-assisted surgical procedures [27-29]. However, the master-slave configuration and the absence of haptic feedback of the da Vinci system prevent the transmission of tool-tissue interaction forces to the surgeon [3]. This may be particularly deleterious in dexterous fine movements such as intracorporeal suturing and knot tying, which require accurate control of applied forces and instrument positions. Without haptic feedback, excessive forces may be applied to tissue leading to increased trauma and damage to tissue [3, 24]. This could be particularly important in robotics-assisted mitral valve repair, which requires fine motor skills to suture an annuloplasty band to the cardiac tissue along the mitral valve annulus. Without tactile and force information, surgeons must rely on visual cues

to estimate the force being applied [22-24, 30].

In addition to absence of haptic feedback, robotic-assisted minimally invasive techniques are technically more challenging and report steep learning curves of surgeons [31, 32]. Furthermore, compared to conventional surgery, minimally invasive surgeries have more prolonged cardiopulmonary bypass, cross-clamp and operative times [33-35].

To address these challenges, we propose that improved training methods and reduced operative time in robotics-assisted minimally invasive procedures can potentially be achieved by improving sensory input from both visualization and tissue manipulation with the addition of force feedback. We also propose the examination and development of an enhanced imaging modality that can provide superior tool guidance for the performance of robotics-assisted minimally invasive techniques for beating heart surgery. With this enhanced modality, avoidance of cardiopulmonary bypass and aortic cross-clamping can potentially be achieved and improved patient safety and outcomes can be attained during robotics-assisted minimally invasive beating heart surgery.

6.2   3D Visualization

Firstly, we examined the effect of three-dimensional visualization on the amount of force applied to mitral valve tissue and the time to perform *ex vivo* mitral valve annuloplasty using robotics-assisted and conventional techniques. In addition, we determined whether these effects are consistent between novices and experts in robotics-assisted cardiac surgery. Finally, to add further clinical relevance, we compared these results with those of conventional open mitral valve annuloplasty to examine differences in forces applied and times required to complete surgical tasks between robotics-assisted and conventional open surgery.

This study demonstrated that although 3D visualization may provide more information

regarding object depth to facilitate complex tissue grasping, 3D visualization may not provide adequate visual cues to reflect the force applied to cardiac tissue. Despite high quality binocular images, both experts and novices applied significantly more force to cardiac tissue during 3D robotics-assisted mitral valve annuloplasty than during conventional open mitral valve annuloplasty.   The highest forces applied by experts were still less than the force required to inflict any damage on the cardiac tissue; however, novices applied potentially damaging force to the cardiac tissue using robotics-assisted techniques. This finding suggests that 3D visualization does not fully compensate for the absence of haptic feedback in robotics-assisted cardiac surgery, particularly for novices.

Furthermore, these findings imply that haptic feedback may be required to achieve better control of the interaction forces on cardiac tissue.

6.3   Force feedback

Secondly, our objective was to determine the effects of force feedback on the amount of force applied to cardiac tissue during robotics-assisted cardiac surgery and to determine if these effects are consistent between novices and experts in robotics-assisted cardiac surgery. Our results show that consistently less force was applied to cardiac tissue when all modes of force feedback were used. In particular, the use of direct force feedback during robotics-assisted mitral valve annuloplasty resulted in a greater decrease in forces applied to cardiac tissue when compared to visual force feedback alone. There was no significant difference in the amount of force applied to mitral valve tissue between experts and novices. Therefore, in order to achieve better control of interaction forces on cardiac tissue during robotics-assisted mitral valve annuloplasty, direct or visual force feedback may be required.

6.4   NeoNav: An Augmented Reality Guidance System

Thirdly, we evaluated the use of an augmented reality (AR) guidance system for minimally invasive beating heart surgery. This is an emerging field of transcatheter mitral valve repair that avoids the risks of cardiopulmonary bypass and cross-clamp used in conventional surgery, and it potentially offers hopes of beating heart mitral valve reconstruction. However, concerns relating to the navigation of the tool from the apex to the target mitral valve leaflet have been raised.

The NeoChord DS-1000 (NeoChord, Minnetonka, MN) is a device capable of performing off-pump, mitral valve repair for certain forms of degenerative mitral valve disease [36]. Currently, this procedure relies exclusively on transesophageal echocardiography (TEE) guidance. Due to the navigational challenges of TEE, the tool can be caught in the

subvalvar apparatus risking chordal rupture or leaflet perforation [37, 38]. Current clinical practice involves the use of highly trained surgical proctors who are expert in the use of this device.

To improve the overall safety of the navigation process in the NeoChord procedure, we have evaluated the efficacy of employing an AR technique capable of providing a robust 3D context for TEE image data. In this real-time environment, the surgeon can easily and intuitively identify the tool, surgical targets, and high-risk areas, and view tool trajectories and orientations.

6.5   AR Guidance for Transcatheter Aortic Valve Implantation

Finally, we designed a study to determine how consistently the aortic valve annulus is

defined from TEE using different aortic valve landmarks, and to compare AR guidance to fluoroscopic guidance of transcatheter aortic valve implantation (TAVI) deployment in an aortic root model. TAVI is a growing technology that provides an alternative surgical option for patients with aortic stenosis. Navigation and deployment of the valve during TAVI relies largely on single-plane fluoroscopy, which has several limitations [38].

We have adapted the NeoNav guidance system for TAVI deployment to achieve similar deployment accuracy to the current standard of care, while eliminating the use of nephrotoxic contrast and ionizing radiation used in fluoroscopy. TEE is essential for accessing valve function in both conventional aortic valve surgery and TAVI.

Through the use of the AR guidance system, we simply defined the valve annulus from tracked TEE for image guidance and eliminated the need for complex preoperative models and registrations with associated errors. Using this guidance system, the surgeon can easily and intuitively identify the tool, surgical targets, and high-risk areas. We have shown that the aortic valve commissures can be identified more reliably than aortic valve leaflet nadirs from 3D full volume TEE images obtained from patients with aortic valve stenosis. Furthermore, there was a low variability in the identification of aortic valve commissures from an aortic valve root model intraoperatively. In the aortic root model study, the errors reported by the guidance system were very low.

In conclusion, the following findings are the results of our primary objectives to evaluate the usefulness of three-dimensional visualization, force feedback, and AR technologies to surgeons as they are applied in a clinical settings:

- We determined that although 3D visualization may provide more information regarding object depth to facilitate complex tissue grasping during robotics-assisted minimally invasive surgery, 3D visualization may not provide adequate visual cues

to reflect the force applied to cardiac tissue. This suggests that 3D visualization does not fully compensate for the absence of haptic feedback in robotics-assisted cardiac surgery.

- We determined that novices applied potentially damaging force to the cardiac tissue using robotics-assisted techniques; and, therefore, we propose that a simulation system providing force feedback may improve both expert and trainee performance using robotics-assisted techniques.

- We learned that the addition of either direct or visual force feedback significantly decreased the amount of force applied to cardiac tissue during robotics-assisted mitral valve annuloplasty.

- We presented NeoNav, AR-enhanced echocardiograpy intracardiac navigation for the NeoChord off pump mitral valve repair procedure. Using ultrasound guidance alone compared to AR navigation, six cardiac surgeons used the NeoChord device to navigate the tool from entry at the apex of the heart to a point at the line of coaptation in the MV. Tracked path results clearly show improved safety and time using AR navigation.

- We proposed our NeoNav integrated AR and TEE as a safe and inexpensive alternative imaging modality for TAVI guidance. Through the use of the NeoNav guidance system for mitral valve repair, we simply defined the valve annuli from tracked TEE for image guidance and eliminated the need for complex preoperative models and registrations with associated errors. Using this guidance system, the surgeon can easily and intuitively identify the tool, surgical targets, and high-risk areas.

6.6   Future Directions

With a rapidly expanding elderly population, the complexity of cardiac surgery continues

to evolve. Innovative strategies to treat pathology and also improve quality of life in this high risk population are in high demand. Minimally invasive and beating heart surgery provide both improved postoperative morbidity and quality of life; however, they are technically demanding and require additional surgical training and expertise. Therefore, these techniques are limited to few centres with specialized cardiac surgeons. This thesis has proposed innovative strategies to make these technologies more facile and safe. Hopefully, these force feedback and AR guidance systems will be utilized by cardiac surgeons so that robotics-assisted and beating heart mitral valve repair may be available to a broader population. Furthermore, the use of both force feedback and AR guidance may be applied to additional minimally invasive techniques in cardiac surgery including the MitraClip and other beating heart valve procedures in development.

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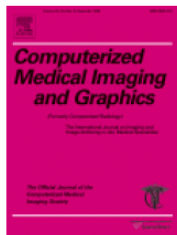
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Curriculum Vitae

MARIA ELIZABETH CURRIE MD

Cardiac Surgery Resident
Postgraduate Year Six
Division of Cardiac Surgery
Western University

PhD Candidate
Department of Biomedical Engineering
Western University

EDUCATION

2010 - present PhD, Biomedical Engineering, Western University, London, ON, in progress; 2010-2015.

        Thesis supervisors: B. Kiaii M. D., FRCSC; R. Patel Ph.D., P.Eng.; T. Peters Ph.D., FCCPM

        Clinical Investigator Program, Royal College of Physicians and Surgeons of Canada, Western University, London, ON, in progress; 2010-2013.

2008 - present Cardiac Surgery Residency, Western University, London, ON, in progress; 2008-2016

2004-2008   Medical Doctor, Dalhousie University Medical School, Halifax, NS, June, 2008.

        Bachelor of Science (Medicine), Surgery Research, Dalhousie University Medical School, June, 2008.

Thesis supervisors: G. M. Hirsch M. D. FRCSC and T. D. G. Lee Ph.D.

2000-2004 Bachelor of Science, Honours in Microbiology and Immunology,

Dalhousie University, Halifax, NS, May 2004.

Thesis supervisors: G. M. Hirsch M. D. FRCSC and T. D. G. Lee Ph.D.

PUBLICATIONS/PRESENTATIONS

Publications –

McLeod AJ, Currie ME, Moore JT, Bainbridge D, Kiaii B, Chu MW, Peters TM. Phantom study of an ultrasound guidance system for transcatheter aortic valve implantation. Comput Med Imaging Graph. 2014 Dec 15. [Epub ahead of print]

Pepe DL, Anantha RV, Currie ME, McCormick JK, Mele T, Chu MW. Recalcitrant prosthetic valve endocarditis requiring repeated reconstruction: running out of options.
Can J Cardiol. 2014 Dec;30(12):1732.e5-8.

Ouzounian M, Currie ME, Buth KJ, Yip AM, Hassan A, Hirsch GM. Myocardium at risk is associated with adverse clinical events in women but not in men, after coronary artery bypass grafting. Can J Cardiol. 2014 Jul;30(7):808-13.

Currie ME, Trejos AL, Rayman R, Chu MW, Patel R, Peters T, Kiaii BB. Evaluating the effect of three-dimensional visualization on force application and performance time during robotics-assisted mitral valve repair. Innovations (Phila). 2013 May-Jun;8(3):199-205.

Verma S, Yanagawa B, Kalra S, Ruel M, Peterson MD, Yamashita MH, Fagan A, Currie ME, White CW, Wai Sang SL, Rosu C, Singh S, Mewhort H, Gupta N, Fedak PW. Knowledge, attitudes, and practice patterns in surgical management of bicuspid aortopathy: a survey of 100 cardiac surgeons. J Thorac Cardiovasc Surg. 2013 Nov;146(5):1033-1040

Moore JT, Chu MW, Kiaii B, Bainbridge D, Guiraudon G, Wedlake C, Currie ME, Rajchl M, Patel RV, Peters TM. A navigation platform for guidance of beating heart transapical mitral valve repair. IEEE Trans Biomed Eng. 2013 Apr;60(4):1034-40.

Currie ME, Fox SA, Greer-Bayramoglu RJ, Fortin AJ, Chu MW. Can internal thoracic arteries be used for both coronary artery bypass and breast reconstruction? Interact Cardiovasc Thorac Surg. 2012 Nov;15(5):811-5.

Chu MWA, Moore JT, Peters TM, Bainbridge D, McCarty D, Guiraudon G, Wedlake C, Lang P, Rajchl M, <u>Currie ME</u>, Daly R, Kiaii B. Augmented reality echocardiographic navigation and guidance for beating heart transapical mitral valve repair. Innovations (Phila). 2012 Jul-Aug;7(4):274-81

<u>Currie ME</u>, Romsa J, Fox S, Vezina WC, Akincioglu C, Warrington JC, McClure RS, Stitt LW, Menkis AH, Boyd WD, Kiaii B. Long-term angiographic follow-up of robotic-assisted coronary artery revascularization. Ann Thorac Surg 2012;93:1426-1431.

<u>Currie ME,</u> Trejos AL, Rayman R, Chu MWA, Patel R, Peters TM, Kiaii B. The role of three-dimensional visualization in robotics-assisted cardiac surgery. Proc SPIE 2012; 8316: 83160F1-10.

Currie ME, Trejos AL, Rayman R, Chu MWA, Patel RV, PetersTM, Kiaii B. Measurement of forces applied by the DaVinci Robot During *ex vivo* robotics-assisted porcine mitral valve annuloplasty. Can J Cardiol. 27 (5), S283.

Buth KJ, <u>Currie ME</u>, Yip AM, Hirsch GM. Extent of Myocardium at Risk in Women, but not in Men, is associated with Major Adverse Cardiac Events following Coronary Artery Bypass Grafting. Circ Cardiovasc Qual Outcomes. 2011; 4: AP186.

<u>Currie ME</u>, Yip AM, Buth KJ, Fraser JD, Love MP, Kirkland SA, Hirsch GM. Higher in-hospital mortality among women after coronary artery byass grafting not explained by preoperative angiograghic findings. Canadian Journal of Cardiology. 24 (2008): Suppl SE.

<u>Currie ME</u>, Zaki AM, Nejat S, Hirsch GM, Lee TDG. Immunologic targets in the etiology of allograft vasculopathy: endothelium versus media, Transplant Immunology. 19 (2008), 120–126.

Recently Submitted Publications—

Currie ME, McLeod AJ, Moore JT, Bainbridge D, Kiaii BB, Chu MW, Peters TM. Augmented

Reality System for Ultrasound Guidance of Transcatheter Aortic Valve Implantation. Innovations

(Phila).

Presentations--
Augmented Reality System for Ultrasound Guidance of Transcatheter Aortic Valve Replacement. <u>M. E. Currie</u>, A. J. McLeod, R. Patel, T. M. Peters, B. Kiaii. American Association for Thoracic Surgery Annual Meeting, April, 2015, Seattle, USA.

Augmented Reality System for Ultrasound Guidance of Transcatheter Aortic Valve Implantation. <u>M. E. Currie</u>, A. J. McLeod, J. T. Moore, M. W. A. Chu, R. Patel, B. Kiaii,

T. M. Peters. International Society for Minimally Invasive Surgery Annual Scientific Meeting, June 2014, Boston, USA.

NeoNav: Augmented reality echocardiographic navigation and guidance for beating heart mitral valve repair. M. E. Currie, A. J. McLeod, J. T. Moore, M. W. A. Chu, R. Patel, B. Kiaii, T. M. Peters. Canadian Cardiovascular Congress, October 2013, Montreal, QC.

Visual and Direct Haptic Feedback in Robotics-Assisted Cardiac Surgery. M.E. Currie, A. Talasaz, A. L. Trejos, R. Rayman, M. W. A. Chu, B. Kiaii, T. M. Peters, R. Patel. Minimally Invasive Robotic Association International Congress, September, 2012, Boston, USA.

The role of haptics in robotics-assisted mitral valve annuloplasty. M. E. Currie, A. L. Trejos, R. Rayman, M. W. A. Chu, R. Patel, T. M. Peters, B. Kiaii. Hamlyn Symposium on Medical Robotics, July, 2012, London, England.

A navigation platform for guidance of beating heart transapical mitral valve repair. M. E. Currie, J. T. Moore, M. W. A. Chu, B. Kiaii, D. Bainbridge, G. Guiraudon, C. Wedlake, M. Rajchl, T. M. Peters. International Workshop on Cardiac Tissue Characterization and Image-based models, June, 2012, Toronto, ON.

The role of three-dimensional visualization in robotics-assisted cardiac surgery. M. E. Currie, A. L. Trejos, R. Rayman, M. W. A. Chu, R. Patel, T. M. Peters, B. Kiaii. International Society of Photonics and Optics Medical Imaging Conference, February, 2012, San Diego, CA, USA.

The Role of Haptics and Three-Dimensional Visualization in *Ex Vivo* Mitral Valve Annuloplasty. M. E. Currie, A. L. Trejos, R. Rayman, M. W. A. Chu, R. Patel, T. M. Peters, B. Kiaii. Canadian Cardiovascular Congress, October, 2011, Vancouver, British Columbia.

The Role of Haptics and Three-Dimensional Visualization in Robotics Assisted Mitral Valve Annuloplasty. M. E. Currie, A. L. Trejos, R. Rayman, M. W. A. Chu, R. Patel, T. M. Peters, B. Kiaii. Clinician Investigator Trainee Association of Canada Annual Meeting, September, 2011 Ottawa, Ontario.

The Role of Haptics and Three-Dimensional Visualization in Robotics Assisted Cardiac Surgery. M. E. Currie, A. L. Trejos, R. Rayman, M. W. A. Chu, R. Patel, T. M. Peters, B. Kiaii. Dr. Robert Zhong Department of Surgery Research Day, Western University, London, Ontario, June, 2011

The Role of Three-Dimensional Visualization in Robotics-Assisted Cardiac Surgery. M. E. Currie, A. L. Trejos, R. Rayman, M. W. A. Chu, R. Patel, T. M. Peters, B. Kiaii. London Imaging Discovery, London, Ontario, June 2011.

The Role of Haptics and Three-Dimensional Visualization in Robotics Assisted Cardiac Surgery. M. E. Currie, A. L. Trejos, R. Rayman, M. W. A. Chu, R. Patel, T. M. Peters, B. Kiaii. International Society for Minimally Invasive Surgery Annual Scientific Meeting, Washington, D. C., June, 2011

The Role of Three-Dimensional Visualization in Robotics-Assisted Cardiac Surgery. M. E. Currie, A. L. Trejos, R. Rayman, M. W. A. Chu, R. Patel, T. M. Peters, B. Kiaii. Minimally Invasive Robotic Association International Congress, Athens, Greece, May, 2011

Forces Applied by the Da Vinci Robot During *Ex Vivo* Robotics-Assisted Mitral Valve Annuloplasty. M. E. Currie, A. L. Trejos, R. Rayman, M. W. A. Chu, R. Patel, T. M. Peters, B. Kiaii. Margaret Moffat Research Day, Western University, London, Ontario, March, 2011.

Measurement of Forces Applied by the da Vinci Robot During *Ex Vivo* Robotics-Assisted Procine Mitral Valve Annuloplasty. M. E. Currie, A. L. Trejos, R. Rayman, M. W. A. Chu, R. Patel, T. M. Peters, B. Kiaii. Canadian Winter Cardiac Team Meeting, Mont Tremblant, Quebec, February, 2011. (Resident Research Presentation Award)

Conduit Patency Rates Following Robotics Assisted Coronary Artery Bypass Surgery. M. E. Currie, B Kiaii, J Romsa, WD Boyd, RS McClure, C Akincioglu, W Vezina, J-L Urbain, S Fox, A Sousa, Canadian Cardiovascular Society, Montreal, Quebec, October, 2010.

Long-term follow-up of robotic-assisted surgical revascularization with CT angiography. M. E. Currie, B Kiaii, J Romsa, WD Boyd, RS McClure, C Akincioglu, W Vezina, J-L Urbain, S Fox, A Sousa, Annual Scientific Meeting, International Society for Minimally Invasive Cardiothoracic Surgery, Germany, June, 2010.

Extent of Myocardium at Risk in Women, but not in Men, is Associated with Major Adverse Cardiac Events following Coronary Artery Bypass Grafting. K. J. Buth, M. E. Currie, A. M. Yip, and G. M. Hirsch American Heart Association Quality of Care and Outcomes Research in Cardiovascular Disease and Stroke 2010 Scientific Sessions, Washington, D.C., May, 2010.

Long-term follow-up of robotic-assisted surgical revascularization with CT angiography. M. E. Currie, B Kiaii, J Romsa, WD Boyd, RS McClure, C Akincioglu, W Vezina, J-L Urbain, S Fox, A Sousa, Annual Canadian Winter Cardiac Team Meeting, Mont Tremblant, Quebec, February, 2010.

Robotic Assisted Redo Minimally Invasive Coronary Artery Bypass: A Case Report. M. E. Currie, C Adams, S McClure, A Goela, I Ross, K Sridhar, B Kiaii, Annual Canadian Winter Cardiac Team Meeting, Mont Tremblant, Quebec, February, 2009.

Higher in-hospital mortality among women after coronary artery byass grafting not explained by preoperative angiograghic findings. M. E. Currie, A. M. Yip, K. J. Buth, J. D. Fraser, M. P. Love, S. A. Kirkland, and G. M. Hirsch, Canadian Cardiovascular Society, Toronto, Ontario, October, 2008.

Intima versus media in allograft vasculopathy. M. E. Currie, G. M. Hirsch, Timothy D. G. Lee. Canadian Society for Immunology, Halifax, Nova Scotia, June, 2006.

RESEARCH EXPERIENCE

Robotics-Assisted and Minimally Invasive Cardiovascular Surgery –

London Health Sciences Centre, Division of Cardiac Surgery, London, Ontario

- Determining the role of haptics and three-dimensional visualization in robotics-assisted mitral valve repair

- Assessed the long-term patency rate of bypass conduits and patients' clinical outcomes following Endoscopic atraumatic coronary artery bypass (Endo-ACAB) surgery.

Cardiovascular Surgery –

Queen Elizabeth Health Sciences Centre, Division of Cardiac Surgery, Maritime Heart

Centre, Halifax, Nova Scotia

- Investigated sex differences in preoperative angiographic findings and the subsequent number and type of bypass grafts used in coronary artery bypass grafting. Determined the impact of these differences on short and long-term outcomes including mortality,

morbidity, and readmission to hospital. Presented project at the Canadian Cardiovascular Congress (2008) and the Division of Cardiac Surgery Clinical Research meeting (2007).

Cardiac Transplantation –

Dalhousie University Medical School, Transplantation Laboratory, Departments of

Microbiology & Immunology and Surgery, Halifax, Nova Scotia

- Developed a chimeric animal model for the study of cardiac transplant rejection (2004-2005). Investigated the impact of damage to blood vessel endothelium versus media in the progression of chronic cardiac transplant rejection (2006-2007).   Presented project at Canadian Society for Immunology Annual Meeting (2006), Dalhousie Medical Student Research Day (2006), and Undergraduate Health Sciences Student Research Day (2007).

- Examined the role of CD8+ T cells and cytotoxic T cell effector mechanisms in the progression of chronic cardiac transplant rejection in vitro (2001-2002) and in a mouse aortic interposition model (2003-2004).

AWARDS/ACHEIVEMENTS

2010	**Presentation Award,** Residents' Research Competition, **Annual Canadian Winter Cardiac Team Meeting**
2004-2006	**Leo Alexander Studentship in Cardiovascular Research**, Dalhousie Medical Research Foundation
2005	**Presentation Award,** Medical Student Research Day, Dalhousie University
2004-2005	**Faculty of Medicine Award**, Dalhousie University
2000-2004	**Chancellor's Scholarship**, Dalhousie University
	Canadian Millennium Excellence Award: Leadership, Innovation, & Service
2003-2004	**Scholastic Achievement Key Award**, Alpha Gamma Delta Foundation
2003	**Harriett Fox Grant Scholarship**, Alpha Gamma Delta Foundation

2001-2004	**NSERC Undergraduate Student Summer Research Award**
	Dean's List, Faculty of Science, Dalhousie University
2000-2001	**Women's Division Alumnae Association Scholarship,** Dalhousie University
	Canadian Merit Scholarship Foundation Regional Award: Leadership, Character, and Service
2000	**Queen Elizabeth II Medal**
	Alumnae Award for Excellence in Science
	Millennium Award for Environmental Action

PROFESSIONAL SOCIETIES

2010-present	Clinician Investigator Trainee Association of Canada
2009-present	The International Society for Minimally Invasive Cardiothoracic Surgery
2008-present	Canadian Cardiovascular Society
	Cardiothoracic Surgery Network
	Ontario Medical Association
	Canadian Medical Association
	Association of Women Surgeons
2006-present	Federation of Medical Women of Canada
2004-2008	Doctors Nova Scotia
2006-2007	Canadian Society for Immunology
2000- present	Millennium Scholarship Network

2004-2008	Doctors Nova Scotia
2006-2007	Canadian Society for Immunology
2000- present	Millennium Scholarship Network

COMMITTEES AND PROFESSIONAL ACTIVITIES

2013, July-present	**Chief Resident**, Division of Cardiac Surgery, Western University
2009-present	**Postgraduate Education Committee,** Resident representative
2009-present	**Western University, Division of Cardiac Surgery Residency Selection Committee**, Resident representative
2006-2008	**Federation of Medical Women of Canada,** Dalhousie University Co-Chair and Medical Student Representative
2004	**Dalhousie University Selection Committee for University Registrar**, Student Body Representative
2003-2004	**Dalhousie Scholarship Appeals Committee**, Student Body Representative
2003-2004	**Dalhousie Scholarship Advisory Committee**, Student Body Representative
2003-2004	**Dalhousie Science Society**, Executive Council
2001-2004	**Society of Immunology & Microbiology**, Student Representative

REFERENCES

Bob Kiaii, MD, FRCSC
Hospital Chief, Cardiac Surgical Unit, London Health Sciences Centre
Associate Professor, Schulich School of Medicine and Dentistry, Western University

Dr. Michael W. A. Chu, MD, MEd, FRCSC
Cardiac Surgery Consultant, Cardiac Surgical Unit, London Health Sciences Centre
Assistant Professor, Schulich School of Medicine and Dentistry, Western University

Rajni Patel, Ph.D., P.Eng
Director of Engineering, Canadian Surgical Technologies & Advanced Robotics
London Health Sciences Centre, University Hospital

Dr. Terry Peters, Ph.D., P.Eng
Professor, Biomedical Engineering, Western University
Scientist, Imaging Research Laboratories, Robarts Research Institute

Greg Hirsch, MD, FRCSC
Chief, Division of Cardiac Surgery
QEII Health Sciences Centre

Timothy D. G. Lee, Ph. D.
Director of the Atlantic Centre for Transplantation Research
Professor, Department of Microbiology and Immunology,
Department of Surgery, Department of Pathology
Dalhousie University