Quantitative image analysis for planning of aortic valve replacement

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Chapter 1

Introduction and Outline
1.1 Abstract

Aortic stenosis is the most common and most frequent cause of sudden death among all valvular heart diseases. Symptomatic aortic stenosis is considered to be a fatal disease if left untreated. Aortic valve replacement is the mainstay of treatment of symptomatic aortic stenosis. Lately, various novel techniques have been introduced for aortic valve replacement, including transcatheter aortic valve implantation and minimally invasive aortic valve replacement. For both techniques, careful patient selection and preoperative planning play an important role in the successful deployment of the new prosthetic. Despite the progress made in preoperative planning, including standardized and automated planning, there still is need for further improvement. This chapter provides a basic overview of aortic valve anatomy and aortic stenosis, discusses the aortic valve replacement techniques, and reviews the current planning procedures and their limitations.
1.2 Aortic Valve Anatomy

The normal human heart contains four valves that are crucial for proper pump function. These are the mitral valve and tricuspid valve between the atria and the ventricles and the aortic valve and pulmonary valve between the ventricles and respectively the aorta and pulmonary artery (Figure 1.1). A normal, healthy aortic valve prevents the regurgitation of blood from the aorta into the left ventricle during diastole and allows sufficient blood flow from the left ventricle into the aorta during ventricular systole.

The aortic valve is located between the left ventricular outflow tract and the ascending aorta and has three main components: the annulus, cusps, and commissures. The normal aortic valve is a semilunar valve with three leaflets (tri-leaflet valve). It is surrounded by fibrous tissue forming a partial or complete valvular ring, or annulus. This annulus joins the fibrous skeleton of the heart that anchors and supports the valvular structures (Figure 1.2).

Figure 1.1: Schematic diagram showing the aortic valve with other heart valve and main heart arteries (Left) and aortic valve location within the heart (Right). (Reproduced from [1])

Figure 1.2: Schematic showing the aortic leaflets and other aortic root geometrical landmarks; sinus of valsalva, commissures, sinotubular junction, and annulus.
Chapter 1

1.3 Aortic Valve Stenosis

Aortic valve stenosis (or aortic stenosis, AS) is a condition when the heart’s aortic valve opening becomes narrower. This narrowing prevents the valve from opening completely, which reduces cardiac output and increases systolic left ventricular pressure. Aortic stenosis is the most common cause of sudden death among valvular heart diseases. AS is also the most common valvular heart disease in the elderly population, with a prevalence of 2–7% in patients older than 65 years [2–4]. In addition to AS, aortic valve insufficiency may occur, in which the valve fails to close completely and blood flow regurgitates in diastole. These abnormalities can be either pure or may be mixed, when both stenosis and regurgitation coexist, although usually either pathology dominates [5].

Causes of aortic valve stenosis include calcium buildup on the aortic valve leaflets (calcific aortic stenosis) [6,7], congenital aortic defects [8], and valve damage by rheumatic fever or endocarditis [8]. Calcification accounts for the overwhelming majority of aortic stenosis cases, affecting about 25% of the population older than 65 years [9](see Figure 1.3). The second most common cause is congenital bicuspid aortic stenosis (1–2% of newborns) [8]. Other less common conditions include rheumatic aortic stenosis and unicuspid aortic stenosis [10,11].

Aortic valve stenosis strongly increases cardiac workload. Thus, intrinsic mechanisms and responses of the autonomic nervous system cause increased frequency and contractility, aimed at restoring cardiac output and cardiac filling. This extra effort may weaken the left ventricle muscle as a consequence. The classic symptoms of aortic stenosis are angina, syncope, and heart failure. Angina is the prominent symptom in patients with severe aortic stenosis, occurring in two thirds of patients [13,14]. Sudden death is a feared manifestation of aortic stenosis, occurring in 3-5% of patients, but is rare in asymptomatic patients [15,16]. If the aortic stenosis is left untreated, the mortality of aortic stenosis once angina became manifested is 50% after 5 years, increasing to 50% in 3-year once syncope is manifested, and 50% in 2-years in the presence of congestive heart failure [17]. Therefore, symptomatic aortic stenosis is

![Figure 1.3: Calcified aortic valve before dissection during an aortic valve replacement surgery (Reproduced from [12]) (Left) and a computed tomography angiography image of the aortic root cross section showing hyperdense calcium deposits on the aortic leaflets (Right).](image-url)
considered to be a fatal disease if left untreated. The annual mortality in such individuals is estimated to be 25%, and average survival is only 2 to 3 years [18].

1.4 Aortic Valve Replacement

Aortic valve replacement (AVR) is a procedure in which a patient’s aortic valve is replaced with an artificial heart valve. Current AVR approaches include open heart surgery via a full sternotomy, transcatheter aortic valve implantation, and minimally invasive AVR[19].

There are three basic types of artificial heart valves: mechanical valves, surgical tissue valves, and expandable tissue valves (see Figure 1.4). Although mechanical valves are lasting for more than 30 years and generally present a one-surgery solution [20], these valves cause an increased risk of coagulation. As a result, mechanical valve recipients must take anticoagulant drugs for the rest of their lives, making the patient more prone to bleeding [21].

![Figure 1.4: Different types of aortic prosthetic valves. (A) Bi-leaflet mechanical valve (St Jude); (B) Stented pericardial bio-prosthesis fixated with sutures (Carpentier-Edwards Magna); (C) bio-prosthesis expanded by a balloon (Edwards Sapien).](image)

Tissue valves are usually made from animal tissue, either animal heart valve tissue or animal pericardial tissue. The tissue is treated to prevent rejection and calcification. They come in two forms: surgical valves that are delivered through a conventional or minimal sternotomy and expandable valves that are delivered using catheters. Tissue valves typically last 10–15 years in less active patients [22], but wear out faster in younger patients [23]. When a tissue valve wears out and needs replacement, the person must undergo another valve replacement surgery. For this reason, younger patients are often recommended mechanical valves to prevent the increased risk (and inconvenience) of another valve replacement [23].

There are alternatives to animal tissue valves. In some cases, a homograft of human aortic valve can be implanted. The durability of homograft valves is comparable to that of porcine and bovine tissue valves. The so-called Ross procedure (pulmonary autograft) is another alternative procedure for AVR [24].
1.4.1 Open Heart Surgery (Full Sternotomy)

Full sternotomy is the most frequent approach used for conventional aortic valve replacement surgery [25,26]. In this approach, the incision is made by cutting through the sternum. Once the pericardium has been opened, the patient is put on cardiopulmonary bypass [26]. Afterward, a cut is made in the aorta and a cross-clamp applied. The surgeon removes the patient’s diseased aortic valve and a mechanical or tissue valve is put in place. Once the valve is in place and the aorta has been closed, the patient is taken off the heart-lung machine. Pacing wires are usually sewed to manually pace the heart in case any on-site complication occurs after surgery [27].

However, at least 30% of patients are not referred for AVR due to the estimated high risk based on advanced age or presence of various comorbidities [28]. For these high risk patients, transcatheter aortic valve implantation (TAVI) and minimally invasive aortic valve replacement (mini-AVR) are less invasive procedures.

1.4.2 Transcatheter Aortic Valve Implantation

Transcatheter aortic valve implantation (TAVI) offers help to patients who are too old for conventional aortic valve replacement operations. Since its introduction in 2002 it has spread swiftly: By the end of 2011, an estimated 40,000 transcatheter implantations had been done [29]. TAVI allows an aortic valve to be implanted using a catheter. The catheter is inserted into one of the large arteries or apex through a small incision. There are multiple approaches used in TAVI including transfemoral, transapical, transaortic (direct access), and subclavian approaches [30,31] (see Figure 1.6). Currently, transfemoral TAVI (TF-TAVI) is the predominant route of delivery. However, transapical TAVI (TA-TAVI) is considered to be a reliable and reproducible procedure in experienced hands [32].
TAVI is performed as follows [34–38]: an interventional cardiologist places a temporary pacemaker lead in the apex of the right ventricle for rapid pacing during deployment and places an angled pigtail catheter in the right coronary cusp. Based on the approach [36,39–41], the puncture site is used for inserting a guide wire, which is assisted by on-site X-ray angiography (XA) images. Once the guide wire crosses the native valve and reaches the apex of the left ventricle, the interventional cardiologist uses a multipurpose catheter that can be used to cross the native valve (See Figure 1.7).

The valvuloplasty balloon is then placed in the middle of the annulus and inflated under rapid pacing (180-200 beats/min when the systolic pressure drops below 50 mm
Hg (pulse pressure <10 mm Hg)). Subsequently, the valve prosthesis is placed coaxially to the annulus and the position of the prosthesis can be manipulated by placing tension on the wire, by rotating or deflecting the flexed catheter system. Final positioning of the prosthesis is done under rapid pacing. It is required for the implantation of the balloon-expandable prosthesis, in order to decrease the pulse pressure and forward flow during the valvuloplasty and valve deployment [32]. After implantation, the position of the valve is confirmed using X-ray Angiography (XA) and the blood flow and absence of regurgitation are checked using 3D color Doppler [35,43] or phase contrast MRI.

1.4.3 Minimally Invasive Aortic Valve Replacement

Minimally invasive aortic valve replacement (mini-AVR) was introduced during the past decade. This development was possible following improved surgical techniques, which created room for less and minimal invasive access. Mini-AVR can be regarded as a conceptual approach of aortic valve replacement techniques rather than one single approach. Mini-AVR refers to a small chest wall incision that does not include the conventional full sternotomy. Compared with conventional surgery, mini-AVR was shown to reduce postoperative mortality and morbidity, including blood loss and postoperative pain. In addition, patients recover faster, requiring less rehabilitation resources with shorter admission time. This contributes to reducing the risk of wound infection and consequently to cost reduction [44–48].

A broad range of mini-AVR procedures has been described, all with the aim of minimizing the degree of surgical intrusiveness [49–52]. The most common minimally invasive approach is the partial upper ministernotomy (MS), followed by the right anterior minithoracotomy (RT) [53]. MS is performed through a vertical incision through skin and sternum and completed by a transverse sternal incision [54]. RT is performed through a 5 to 6 cm skin incision at the level of the second or third intercostal space, starting from the border of the sternum toward the lateral right side [55]. The decision to select one of the mini-AVR approaches largely depends on the clinical characteristics of the patient and the experience of the operator and center [49,52].

![Figure 1.8: Schematic drawing showing chest cage ribs and the intercostal spaces with dashed lines representing incisions of minimally invasive aortic valve replacement approaches: ministernotomy (left) and right anterior minithoracotomy (right).](image)
The general steps of the mini-AVR are as follows: The patient is placed in the supine position, as for a standard conventional median sternotomy. A 5-6 cm skin incision is made. Only for the MS approach, a partial median sternotomy is performed. A chest retractor is used to keep the sternum incision open during surgery and expand visual access. The pericardium is then entered through a vertical incision. Traction sutures are performed to improve exposure. Arterial cannulation is done through the ascending aorta and venous cannulation is achieved through the right atrium. Next, cardiopulmonary bypass is started by a right superior pulmonary vent line. After the heart is emptied, an aortic cross-clamp is applied through the main incision, after which the heart is arrested. AVR is performed similar to a standard median sternotomy. The sternotomy is closed with stainless steel wires and the soft tissue is closed with absorbable suture [56,57].

Figure 1.9: Schematic drawing showing the relatively small incision for right anterior minithoracotomy (Left). Image captured during a conventional aortic valve replacement showing Aortic annulus encircled with interrupted mattress sutures (Right) (Reproduced from [58]).

1.5 Complications Associated with AVR

1.5.1 TAVI

Various TAVI complications have been indicated [38,59,60]. These complications can be categorized according to the access and delivery, positioning and deployment, and other complications.

Access related complications include arterial injury, which is common in the transfemoral approach. This is due to the relatively large diameter of the delivery catheter as compared to the smaller stenotic arteries. Such complications also include trauma during catheter insertion [61]. Stroke is another serious access complication, which may occur due to calcific embolism from the aortic valve or repeated or overly aggressive valvuloplasty [62,63]. Apical access is associated with some risks such as lung injury, pleural bleeding, respiratory compromise, and prolonged ventilation [64].

Deployment complications due to improper positioning may lead to prosthetic migration towards the aorta or left ventricle. Also, extending the valve in the left ventricle outflow tract may lead to mitral insufficiency [60,65]. Coronary obstruction
may occur if the prosthetic is positioned at the level of one of the coronary ostia [66]. Paravalvular leakage mainly takes place because of inserting a prosthetic with a diameter smaller than the annulus diameter [67]. In contrast, strong application of aortic balloon valvuloplasty may lead to annular or root rupture [68]. Cardiac perforation and cardiac block were also reported as on-site TAVI complications [60].

Post procedural complications include acute renal failure, structural heart failure, and arrhythmia [69].

Figure 1.10: (Top) X-ray angiography images for the aortic root and ascending aorta after transcatheter aortic valve implantation showing occlusion of right coronary artery (Left) successful implantation with no obstructions (Right) (Reproduced from [70]). (Bottom) Colored Doppler images for the aortic valve cross-section showing the paravalvular regurgitation (Reproduced from [71]).

1.5.2 Mini-AVR

Outcome of mini-AVR has improved due to recent technical advancements [50,72]. Yet, several complications remain. One of the main complications is a poor annulus exposure. This may lead to the conversion to full sternotomy (conventional aortic valve replacement), doubling the operative time in the case of late conversion [44]. Depending on center experience, this occurs in 0.8% to 8.0%, with 3-4% in most studies [56]. Apart from poor annulus exposure, also bleeding (from the right ventricle, aortotomy, or mammary vessels), and low cardiac output are reasons for conversion [51,55]. Also suboptimal chest wall reconstruction is another risk which may be associated with partial sternotomies or thoracotomies [57]. These risks in mini-AVR
may promote TAVI as a first choice for AVR. Yet, such complications can be minimized by a controlled and strictly protocol-driven procedure [73].

**1.6 Aortic Valve Replacement Planning**

**1.6.1 Computed Tomography Angiography**

Three dimensional imaging, especially computed tomography (CT), is used for patient selection. This provides a thorough and detailed overview of the anatomy and determines the aspects that may introduce on-site complications during AVR. Computed tomography angiography (CTA) is a technique that is used to visualize arterial and venous vessels by means of contrast media. CTA is considered as the gold standard imaging for planning of aortic valve replacement procedures and interventions [74].

CT is superior over the other imaging modalities, because it features high speed imaging, wide field-of-view, good spatial and temporal resolution, long and detailed z-axis coverage, and multiplanar reconstruction capabilities. These advantages facilitate a three dimensional comprehensive assessment of the cardiac anatomy with high spatiotemporal resolutions. However, CTA has some limitations, such as the radiation exposure and the usage of contrast agents, which forms a potential risk for patients with renal deficiency.

The electrocardiogram (ECG) is of great importance for cardiac CTA imaging. ECG is used to gate the CTA acquisition and label acquired image volumes at specific cardiac cycle phases, e.g. mid-systole and end-diastole. One of the common challenges in aortic stenosis patients is the difficulty of performing CTA acquisitions because of the high heart rate. To overcome this issue, beta-blockers are administered to reduce the heart rate to less than 65-70 beats per minute and to stabilize the cardiac rhythm for proper acquisitions [75].

**1.6.2 Sizing Parameters**

For TAVI, patient eligibility is assured when a patient candidate satisfies three main criteria: severe symptomatic AS, high or prohibitive surgical risk, and absence of contraindications to TAVI [76]. CTA imaging is crucial for planning of the aortic valve replacement. The size of the aortic annulus, the degree and location of the aortic root calcification are general preoperative planning measures that make use of CTA images.

In addition to the aortic annulus dimensions, distance between the aortic annulus and the right and left ostium is considered one of the important TAVI preoperative planning measures. Diameters of sinus of valsalva and sinotubular junction are important for a specific kind of prosthetic (Core Valve) [77].
Figure 1.11: Aortic root sizing parameters shown on a segmented aortic surface where the left ventricle outflow tract voxels were excluded; Aortic annulus is shown in red, Annulus to right ostium distance is shown in blue, and annulus to left ostium distance is shown in green.

Figure 1.12: Annulus measurements are performed on computed tomography angiography images, (Left) A drawn polygon representing the annulus area. (Right) Two lines drawn representing the annulus minimum and maximum diameters.

For mini-AVR, preoperatively planning is considered crucial and the selection of the optimal location of the incision is one of the most important aspects of a successful valve replacement [46,78]. Preoperative planning of patients eligible for mini-AVR is done by evaluating CTA images. Distance from the ascending aorta to the sternum was reported as an important measure to choose the approach. The diameter of the aortic valve annulus, the length of the ascending aorta, and the calcifications of the aortic valve and the ascending aorta have been suggested as effective preoperative measures [78,79]. Visualization of the aortic root, ascending aorta, chest cage ribs, and calcification provide an overview of the anatomy. For mini-AVR procedures this is especially important since the aortic root is less exposed compared to conventional full sternotomy.
1.7 Current Limitations

For TAVI interventions, standardized and fully automated sizing of the aortic root dimensions would significantly improve and facilitate patient and prosthetic selection [80]. However, imaging and automated image analysis support is lagging the recent advancements in valve replacements technology. Despite the growth of the number of mini-AVR surgeries performed annually, planning and surgery guidance is still not well established. Currently, 2D CTA visualization is used to support surgeon preparation preoperatively to estimate difficulties caused by access and viewing limitations and this is not as efficient as 3D CTA based planning measurements. Moreover, automated and standardized quantitative planning tools need to be developed for mini-AVR.
1.8 Thesis Outline

The research presented in this thesis focuses on image analysis support for aortic valve implantation and replacement. We developed Computer Tomography Angiography (CTA) image segmentation and detection algorithms that provide clinicians with quantitative data on distances and dimensions relevant for planning of valve replacement. CTA was used in most of the studies presented in this thesis, since it allows a higher resolution and more anatomical detail than other imaging modalities.

Chapter 2 shows the application and validation of the normalized cut technique for fully automatic segmentation of the aortic root in CTA images, a procedure that facilitates aortic root sizing. Chapter 3 focuses on the detection of aortic root landmarks to automate the sizing of the aortic root as part of the preprocedural planning for transcatheter aortic valve implantation (TAVI) patients. In chapter 4, we study the dynamics of the aortic annulus by evaluating the annular dimensions using 4D CTA specifically for the TAVI population.

In chapter 5, we propose and validate an automated algorithm that segments and detects the chest intercostal spaces and the aortic sinotubular junction for the purpose of evaluating the closest incision location for minimally invasive aortic valve replacement surgeries (mini-AVR). In chapter 6, a clinical feasibility study is presented that validates our proposed mini-AVR planning tool retrospectively by analyzing patients who underwent the mini-AVR surgery and comparing their on-site difficulty scores with quantitative measurements.

Chapter 7 reports the comparison results between 3D navigator-gated balanced Steady State Free Precession MRA (NC-MRA) and 3D Contrast Enhanced MRA (CE-MRA) of the thoracic aorta image quality by evaluating a quantitative and qualitative assessed vessel. This thesis ends with a general discussion and the future perspectives in Chapter 8.
1.9 References


[33] Bellin Health Systems, “Transcatheter Aortic Valve Replacement (TAVR).”


Introduction and outline


