Automated planning approaches for non-invasive cardiac valve replacement procedures from CT angiography

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Introduction

"A man's heart will grow stronger if he can learn from failure."

- Life

1.1 Cardiovascular system and diseases

Aortic root structure and disease

Structure

The heart is the engine of the circulatory system in the human body, and it pumps blood through the network of arteries, veins, and capillaries to transport oxygen and nutrients to the body and waste materials from the body (Hall 2015). The heart is constituted of the left heart (the left ventricle, the left atrium, the aortic valve and the mitral valve), and the right heart (the right ventricle, the right atrium, the tricuspid valve and the pulmonary valve)) as depicted in Figure 1.1.

The oxygen depleted blood flows from the venous system into the right atrium, descends into the right ventricle through the tricuspid valve. The tricuspid valve prevents the backflow of the blood into the right atrium. Through the contraction of the right ventricle it pushes the blood through the pulmonary valve into the pulmonary trunk, and the blood ends up in the lungs where it is recharged with oxygen. The pulmonary valve closes at the end of the contraction period of the right ventricle. Through the pulmonary veins, the oxygenated blood flows into the left atrium of the heart, and then through the mitral valve into the left ventricle. The mitral valve is closed when the left ventricle contracts. The contraction of the left ventricle pushes the blood into the arterial system through the opening of the aortic valve. As the left ventricle relaxes, the aortic valve closes due to the pressure from the aortic arch. During the cardiovascular cycle, the four valves function as one-way gates between the ventricles, the atria, the arterial system and the venous system.

The aortic root is the connecting part between the aorta and the left ventricle, defined by the sino-tubular ridge at the top and the bases of the valve leaflets at the bottom (Underwood et al. 2000). It is constituted of the following structures, which are also depicted in Figure 1.2: the sino-tubular junction is where the ascending aorta joins the Sinus of Valsalva (Ho 2009). The space between the valve leaflets and the bulb of the aortic wall is the aortic sinus, the attachment of the leaflet is the commissure, the area between the leaflets is the interleaflet triangle, and the aortic annulus is a ring constituted by three hinge points at the top of the aortic valve leaflets. Figure 1.3 shows an ex-vivo human aortic valve.

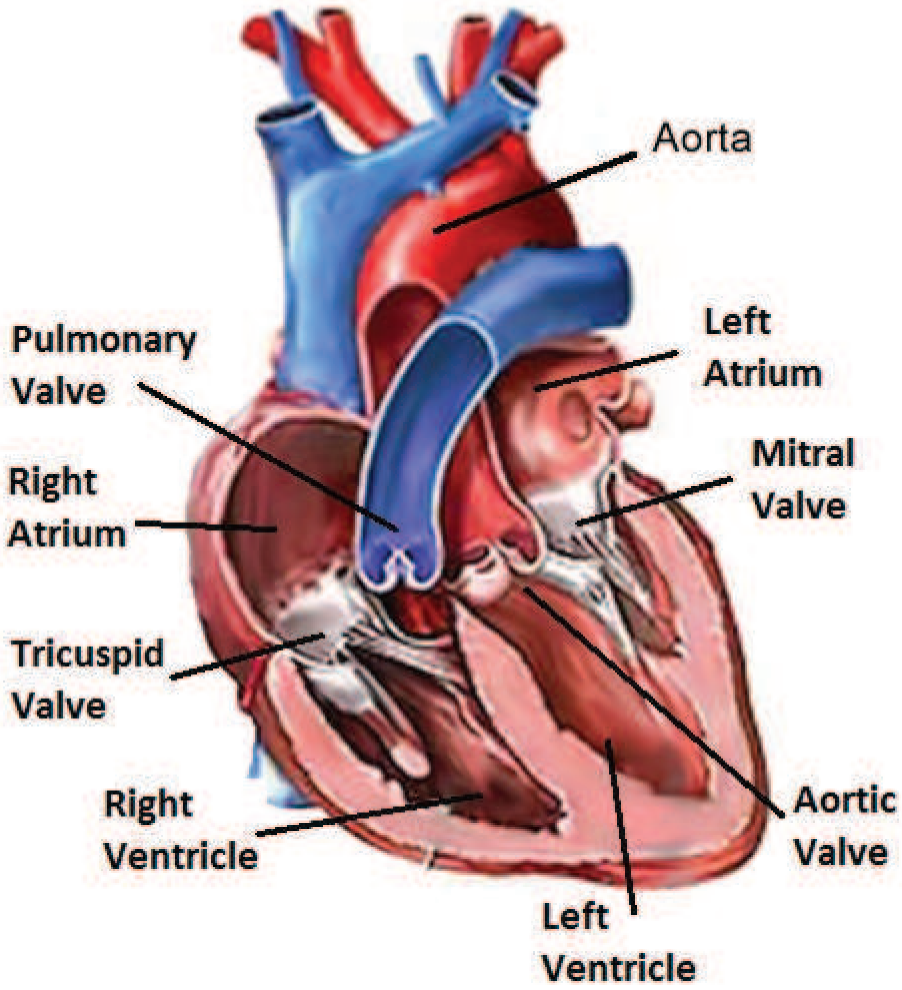

Figure 1.1 Heart anatomy (modified from source: https://upload.wikimedia.org/wikipedia/commons/e/ee/Aorta.jpg)

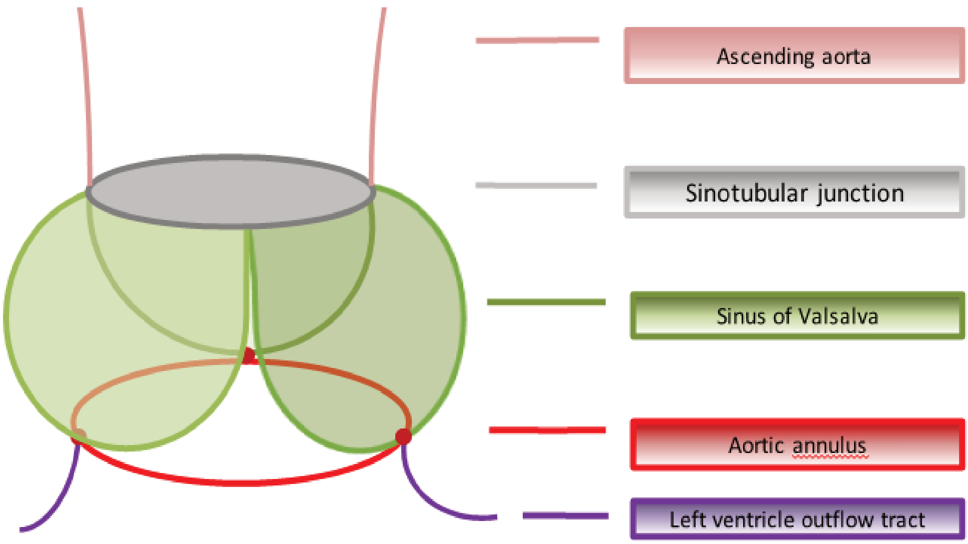

Figure 1.2. The aortic root connects the ascending aorta and the left ventricular outflow tract; the three important landmark locations of the aortic root are: the Sino tubular junction, sinus of Valsalva and the aortic annulus.

Figure 1.3 Aortic valve in human (author: CDC/Dr. Edwin P. Ewing, Jr.; source: https://commons.wikimedia.org/wiki/File:Aortic_stenosis_rheumatic,_gross_pathology_20G0014_lores.jpg?uselang=zh)

Aortic valve stenosis

The aortic valve usually constitutes of 3 leaflets, and acts as a one-way gate. During the systolic phase, the aortic valve opens, the blood is pumped from the left ventricle into the aorta thereby providing the blood supply to the whole body; during the diastolic phase, the aortic valve is closed, the left ventricle is filled again with blood from the left atrium, and the valve prevents the blood flowing back from the aorta into the left ventricle.

Over time, calcium may accumulate on the aortic valve. Subsequently, when there is heavy calcification on the aortic valve, it causes narrowing of the aortic valve, which is called aortic valve stenosis. Aortic valve stenosis results in incomplete opening and closing of the leaflets. During systole, the blood cannot be pumped out of the left ventricle easily; during diastole, the blood might leak back from the aorta into the left ventricle (Sawaya et al. 2012). This will cause a decrease in exercise capability in the patient, followed by syncope and potentially heart failure. As the third most prevalent cardiovascular disease in Europe and North America (Sawaya et al. 2012), it can cause around 50% death rate in the first two years after the onset of symptoms if left untreated (Carabello 2002).

Treatment options

Surgical aortic valve replacement (SAVR) used to be the principal therapeutic technique for aortic valve stenosis (Zajarias and Cribier 2009). Nevertheless, not all patients are suitable candidates for SAVR due to high surgical risk and multiple co-morbidities such as renal impairment and prior stroke (Achenbach et al. 2012).

Transcatheter aortic valve replacement

TAVR (transcatheter aortic valve replacement) or TAVI (transcatheter aortic valve implantation) is a minimally invasive procedure to replace the diseased valve by a valve prosthesis delivered through a catheter. In 2002, TAVR was successfully applied for the first time in humans (Cribier 2014). The minimal invasiveness of TAVR led to a lower risk-benefit ratio in these patients, which makes TAVR a potential alternative therapy to SAVR. Until 2015, more than 200,000 procedures were carried out in more than 65 countries around the world (Vahl, Kodali, and Leon 2016). With at least similar clinical effectiveness compared to SAVR in high-risk surgical patients, TAVR has been demonstrated to be safe (Mack et al. 2015).

The first choice of implantation route is trans-femoral, i.e. through the femoral artery. It is the most minimal invasive implantation route (Mack 2012). Trans-apical, trans-subclavian and trans-aorta routes are alternatives for implantation, if the trans-femoral route is not accessible because of vascular complications. The second most frequently used access route is trans-apical which has the advantage of a short access route from the apex through left ventricle to the aortic annulus (Mack 2012); however, this approach requires surgical assistance in the catherization lab because of the opening that has to be made in the chest wall. Trans-aortic access, as a new approach, has been proven to have a similar success rate compared to trans-apical access, posing an alternative choice for trans-apical access (Bapat et al. 2016; Lardizabal et al. 2013). Trans-subclavian access is the implantation through the left subclavian artery. However, compared to the femoral artery, the wall of the subclavian artery is more fragile. Thus trans-subclavian TAVR requires more operating skills during the procedure. As concluded by the study in (Bleiziffer et al. 2013), trans-subclavian TAVR "should be considered a valid option not only when the femoral approach is impossible but also when it is difficult, albeit feasible".

TF-TAVR devices

There are two kinds of devices: the self-expandable and the balloon-expandable system, both of them have been demonstrated and reported to be safe and effective (Abdel-Wahab et al. 2014).

For the trans-femoral TAVR (TF-TAVR) approach the physician makes a small incision in the leg so that the catheter can be guided from the groin into the iliac-femoral artery, the descending aorta and the aortic arch (Figure 1.4) into the aortic root. The artificial valve is installed onto the remote end of the catheter which is advanced by the physician into the calcific stenotic aortic valve. The artificial valve will be anchored carefully at the exact location of the old valve by balloon expansion or self-expansion (Davidson, Welt, and Eisenhauer 2011). The old valve is pushed into the wall.

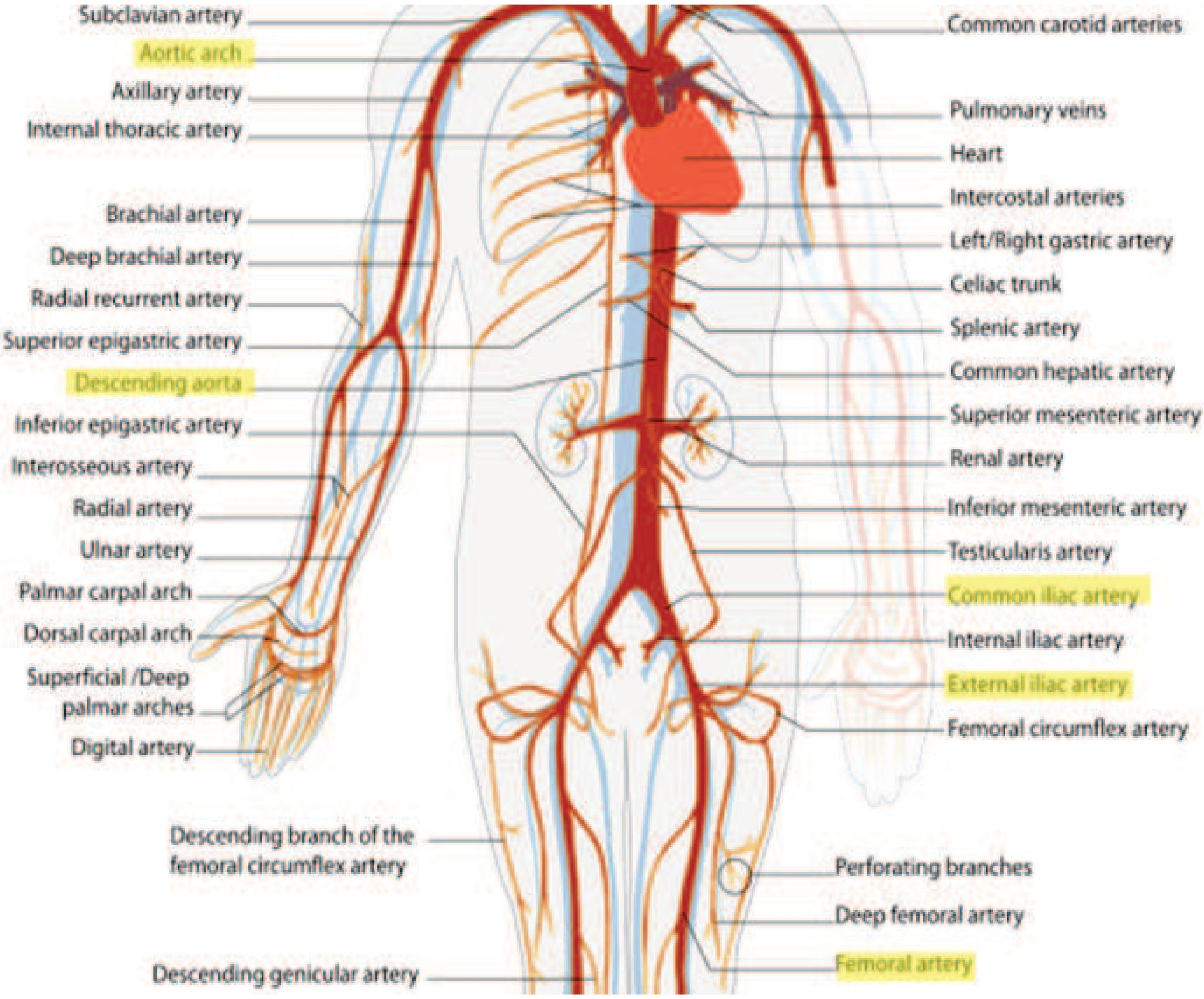

Figure 1.4 Vascular access to delivery prosthesis in TF-TAVR: femoral artery, external iliac artery, common iliac artery, descending aorta and aortic arch. (Source: https://commons.wikimedia.org/wiki/File:Arterial_System_en.svg)

Aorta structure and disease

Structure

Sofar, we have concentrated on the aortic valve stenosis. However, aortic dilatation is also a frequently occurring disease of the aorta.

The aorta is constituted of 4 parts: the ascending aorta, the aortic arch, the thoracic aorta and the abdominal aorta. The ascending aorta starts from the aortic root to the point defined by the pericardial reflection on the aorta. Next part is the aortic arch, which ends at the intervertebral disc. The thoracic aorta continues with the aortic arch and ends at the diaphragm. The aorta segment below the diaphragm is the abdominal aorta, which ends at the bifurcation to the iliac arteries. If the heart is denoted the primary pump of the circulatory system, then the aorta can be called the secondary pump because of its elasticity. It carries the blood with oxygen from the heart into the circulatory system and distributes it into all the tissues and organs of the body. Besides, in the ascending aorta and the aortic arch, there are the pressure-responsive receptors, which can help the aorta to influence the heart rate and systemic vascular resistance (Erbel et al. 2014a).

Disease

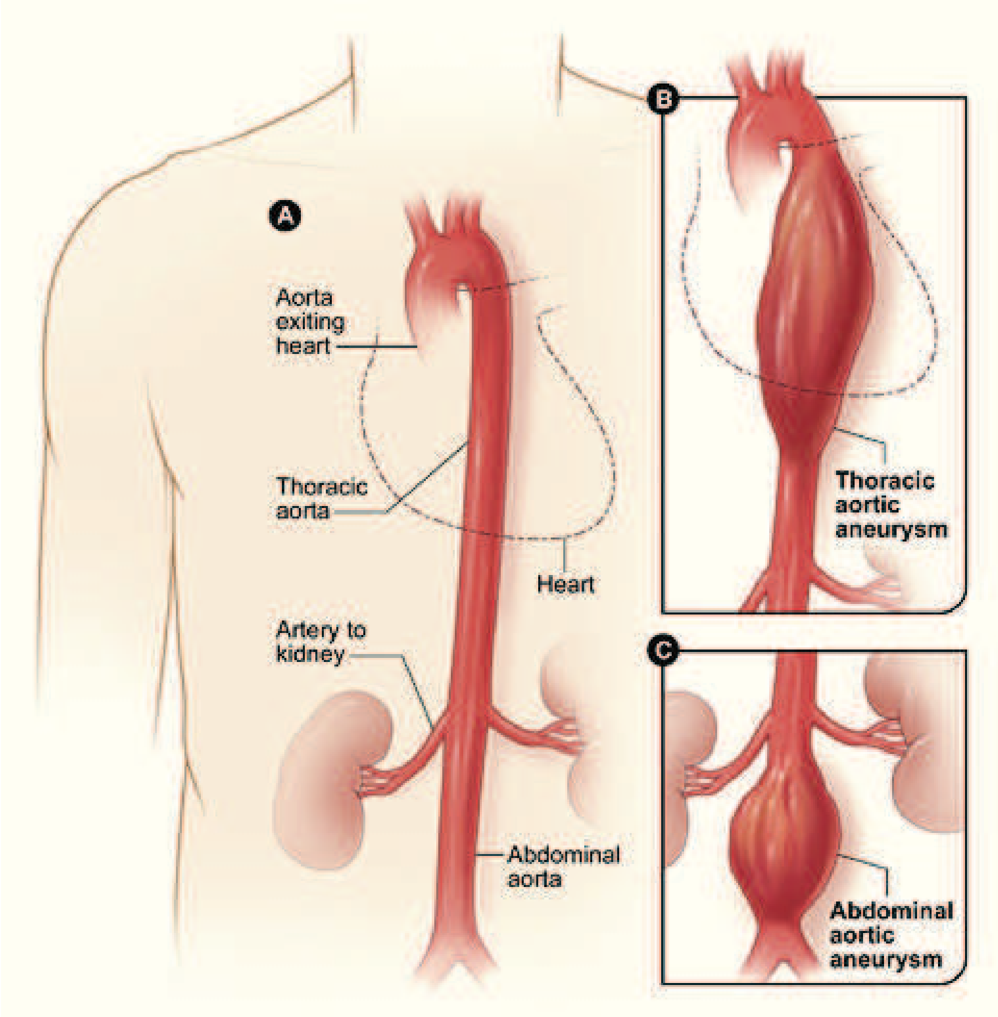

Figure 1.4 Thoracic and abdominal aorta aneurysm (author: National Institutes of Health; source: https://commons.wikimedia.org/wiki/File:Aortic_aneurysm.jpg?uselang=zh)

Aortic dilatation is a frequently occurring disease of the aorta. When the dilatation is larger than 1.5 times its normal size, it is called aortic aneurysm, which tends to further enlarge and rupture at some point in time (Mann et al. 2014). Figure 1.4 displays the thoracic and abdominal aortic aneurysms. According to the global assessment in (Sampson et al. 2014), the Global Burden of Disease 2010 study summarized that the aortic aneurysm mortality rate increased from 2.49 per 100,000 in 1990 to 2.78 per 100,000 in 2010 globally.

1.2 Challenges in TAVR procedure planning and aorta dilatation measurements

Computed tomography angiography for TAVR pre-operative planning

In contrast to SAVR, the aortic root is not visible during the TAVR procedure because of its minimal-invasiveness. To plan the access route and select the suitable prosthesis to be implanted into the aortic valve, imaging is necessary. The size, tortuosity, and calcification burden of the access route and the size, dimension, and calcification of the aortic valve are important parameters for TAVR.

Computed tomography (CT) is a technique that produces three-dimensional images by the combinations of X-ray projections from different angles and subsequent reconstruction. Computed Tomography Angiography (CTA) is the CT scanning of the body following the injection of a contrast agent into the blood vessel. With the contrast flowing inside the vessel, the lumen border becomes visible for the physician, and the presence of an aneurysm or stenosis of the vessel will become more apparent.

Furthermore, CTA allows the evaluation of the diameter and the extent of the calcification of the ilio-femoral arteries and the thoracic aorta. In addition, it is feasible to predict the optimal projection angulation for intra-operative X-ray. Figure 1.5 shows CTA images to estimate vascular access and aortic root during the per-operative planning of TAVR.

To check whether the patient is eligible for TF-TAVR and to select the sheath with appropriate size, the minimal luminal diameter (MLD) along the ilio-femoral artery is an important indication. The "Sheath outer diameter divided by the access-side vascular diameter", which is called Sheath-to-ilio-femoral artery ratio, is able to help to assess whether TF-TAVR is safe (Okuyama et al. 2015). Besides, the tortuosity and extent of calcification of the ilio-femoral artery access can influence the decision of the physician.

As of 2017, multiple sizes of the prosthesis are available for patients with different aortic annulus sizes: Edwards Sapien XT 23mm for 18-22 mm diameter, Edwards Sapien XT 26mm for 21-25 mm diameter, Edwards Sapien XT 29mm for 24-27 mm diameter; Medtronic CoreValve 26mm for 20-23 mm diameter, Medtronic CoreValve 29mm for 23-27 mm diameter, and the Medtronic CoreValve 31mm for 26-29 mm diameter (Ho 2009). To select the prosthesis with appropriate size and delivery into aortic valve, the size measurement and the X-ray angulation prediction of aortic root are the important steps for TAVR. The X-ray angulation in which the tops of the aortic valve leaflets are on one-and-the-same line is crucial for delivering the prosthesis properly into the native valve.

Image-based measurements for TAVR procedure

For a proper preparation of a TAVR procedure, the following measurements would be helpful:

(1) Determine the access route by means of a definition of a centerline, the sizes of the vessels along the centerline and the tortuosity of the vessel;

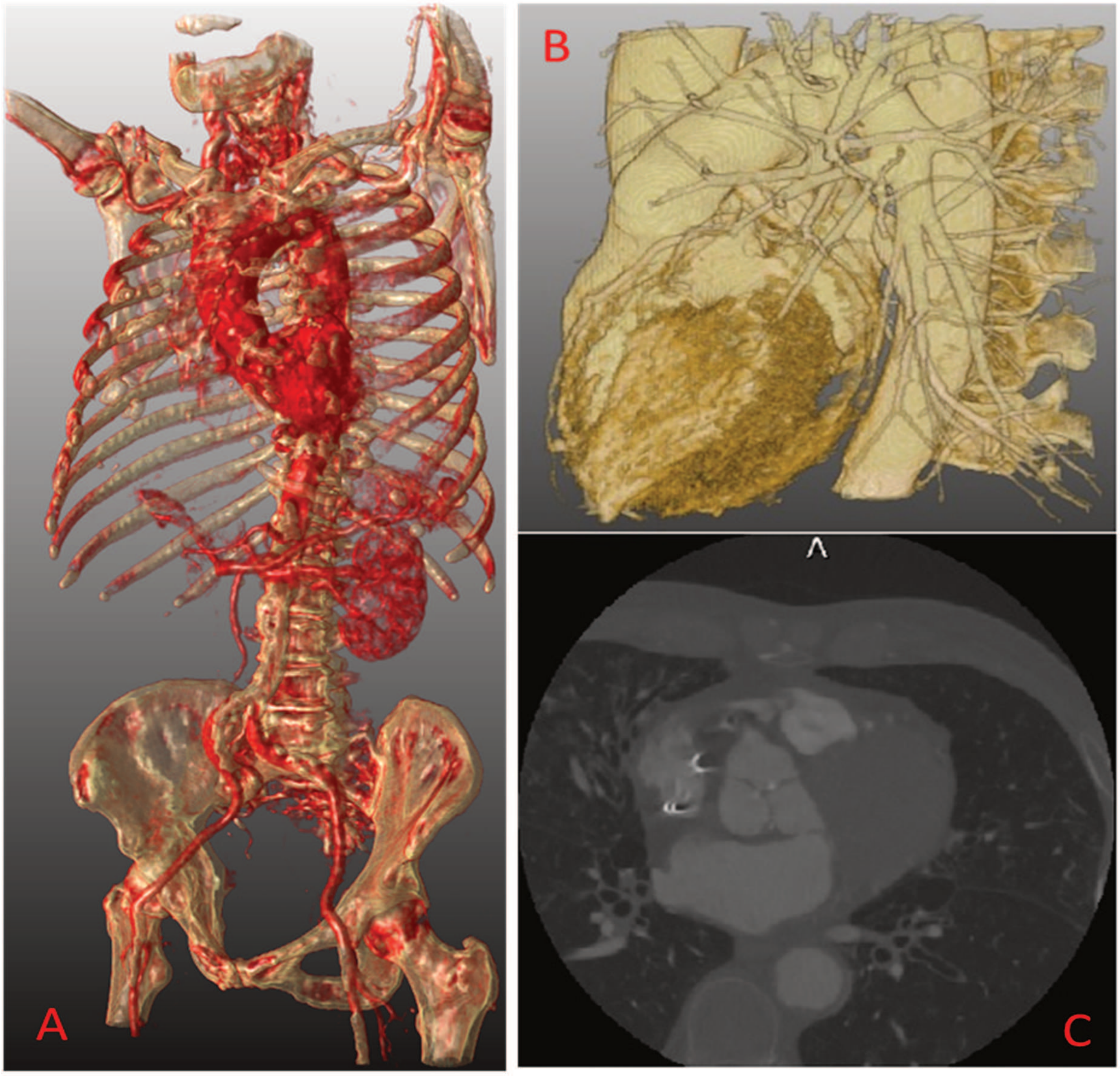

Figure 1.5 CT images for pre-operative TAVR planning: A. CTA image for vascular access, B & C. cardiac CTA image for aortic root: B. 3D view C. 2D view

(2) Cross-sectional diameter measurements, including minimal and maximal diameters, from multi-planar images;
(3) Calcium deposits along the aortic trajectory and the aortic root;
(4) Determination of the proper X-ray projection for optimal view of the aortic root.

To facilitate the workflow and minimize observer variabilities, these measurements should be provided in a preferably automated manner, with minimal user interactions.

Computed tomography for assessment of aorta dilatation

Apart from treatment planning for aortic valve implantation, CT angiography is highly recommended for the assessment of aortic dilatation applications. This makes computed tomography the modality of choice during the clinical examination and treatment of aortic disease.

For instance, the maximum aneurysmal diameter, when quantified in the multi-planar reconstructed image orthogonal to the centerline along the aorta, has higher accuracy and reproducibility than the axial axis diameter measurement (Ihara et al. 2013)(Dugas et al. 2012). Axial axis measurements can overestimate an aneurysm when the aneurysmal axis is not perpendicular to the axial slice (Dugas et al. 2012). In clinical practice, diameter measurement in standardized landmark locations can support the diagnosis. In Figure 1.6, different landmarks are explained.

Challenge of manual procedure

The measurement of the aortic diameter as defined in the guidelines requires the definition of a plane perpendicular to the centerline of the aorta. Such procedure should be facilitated by the use of a workstation, which allows multi-planar reconstructions, and the proper tools to provide landmark measurements.

In clinical routine, multiple scans (baseline and subsequent follow-up scans) of a particular patient need to be interpreted over time, which requires very precise repeat measurements at corresponding positions along the aorta. To minimize variabilities, automated registration techniques should become available. As such, in line with the challenges for TAVR procedure planning and aorta dilatation measurements, we can conclude that the automatization of manual measurement procedures will surely be able to simplyfy and standardize the work process, reduce the effort and time of the physicians, and decrease the inter- and intra-observer variabilities.

1.3 Thesis overview

The aim of this thesis is to develop image processing solutions that enable the fully automatic pre-operative planning of aorta-related procedures. Hence, the objectives of this thesis are as follows:

1. To fully automatically quantify the aorto-iliac vascular access route, including the aortic root by image processing methods in CTA.
2. To broaden the scope of automatic methods into the detection of aorta dilatation.
3. To integrate the automatic quantification methods into applications which allow manual interactions and the calculation of clinically relevant parameters.
4. To demonstrate the accuracy and feasibility of the fully automatic planning and quantification methods in different patient cohorts.

The thesis is further structure as follows:

Chapter 2 introduces a new, fully automatic approach to extract the centerlines of aorto-femoral arteries from CTA data sets. This approach can support the planning of transfemoral aortic valve replacement. CTA images acquired in two clinical centers were used to evaluate the accuracy and robustness of the approach.

Chapter 3 describes a novel, fully automatic technique for the segmentation of the aorto-iliac arteries in CTA images by the deformable

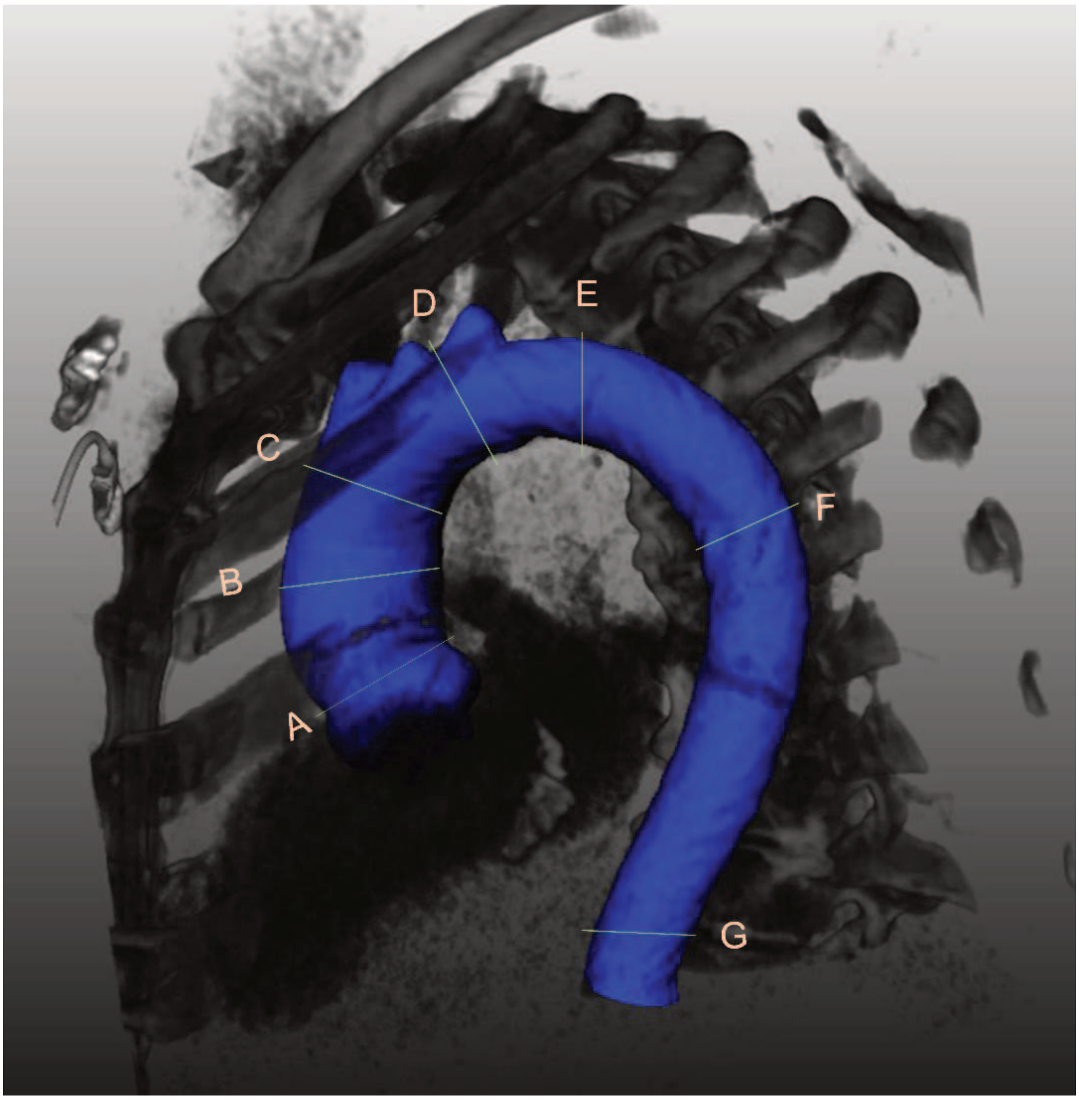

Figure 1.6 Landmark positions along the thoracic aorta: from the aortic root to the diaphragm, line A to G represent the following landmarks in different parts of the aorta. In the aortic root: A the sinuses of Valsalva and B the sino-tubular junction; the ascending aorta: C the mid ascending aorta; the aortic arch: D the proximal aortic arch and E the mid aortic arch; the thoracic aorta: F proximal descending thoracic aorta and G the mid descending aorta (Erbel et al. 2014a).

subdivision surface model fitting method. The accuracy of the lumen border, clinical parameters including minimal luminal diameter and area were demonstrated. In our opinion, this is the first method that allows the fully automatic detection of the aortic-femoral vascular access route in CTA images.

Chapter 4 presents a novel, fully automatic segmentation framework of the aortic root in the whole-body CTA image by combining the atlas-based segmentation algorithm and deformable subdivision surface model fitting method. This framework reduces the computational cost of atlas-based segmentation algorithm and was demonstrated to be accurate by comparing the overlap of the automatic segmentation results to a reference standard by an experienced expert.

Chapter 5 evaluates a fully automatic quantification approach of aortic annulus in CTA images. The quantification approach can detect the sizing parameters of the aortic annulus, and also predicts the optimal X-ray projection curves. The automatic results were demonstrated against semi-automatic and manual results from a radiologist experienced in cardiovascular imaging.

Chapter 6 introduces a novel method for fully automatic volume quantification of aortic valve calcium in coronary CTA images. The method was evaluated in patients with calcified and non-calcified aortic valves. Aortic valve calcium volume has been proven to have a prognostic value for cardiovascular disease. The automatic method can reduce the effort of the physicians, while it increases the reproducibility of the results.

Chapter 7 presents a new automatic workflow which supports the detection of the dilatation of the aorta based on segmenting and aligning the aorta in baseline and follow-up periods. The change of the diameter along the centerline can be calculated automatically for the physicians. The workflow was demonstrated by comparing the automatic results to manual measurement generated from the experienced cardiovascular radiologist

Chapter 8 summarizes and discusses the results presented in this thesis.