Quantitative image analysis for planning of aortic valve replacement
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Chapter 8

Summary & General Discussion
Chapter 8

8.1 Summary

In this thesis, several problems related to aortic valve replacement (AVR) procedures were addressed. We focused on their support by automating and standardizing planning of different AVR approaches. The main goal of this thesis was to introduce and develop novel segmentation and detection algorithms for Computed Tomography Angiography (CTA) images, to provide the clinicians with quantitative sizing parameters that standardize the planning process and reduce complications.

A variety of imaging modalities is capable of imaging the aorta. However, CTA has superior spatial resolution. High spatial resolution is mandatory for reproducible and accurate measurements and for accurate visualization of the coronary arteries, which is important for transcatheter aortic valve implantation (TAVI) measurements. CTA was used in most of the studies presented in this thesis. In postprocedural assessment, magnetic resonance imaging (MRI) can be used to assess the flow through the new prosthetic.

In chapter 2, we proposed a fully automated aortic root segmentation technique based on maximum likelihood classification of connected voxels and 3D normalized cut segmentation to detect the aortic root surface. The method was validated against manual delineations in twenty patients. Comparison of the proposed technique with manual segmentation showed that the accuracy is comparable to the manual interobserver variability.

In chapter 3, we presented a fully automated method for detecting landmarks in the aortic root that facilitates automated preprocedural sizing in TAVI patients. We utilized the developed techniques described in chapter 2 to segment the aortic root surface. The proposed method detected the sinotubular junction, the two coronary ostia, and the three valvular hinge points. This segmentation facilitated the calculation of TAVI sizing parameters such as the annulus to ostia distance, annulus radius, and annulus angle. Detection of landmarks and calculated sizing parameters showed high accuracy when compared with reference landmarks and sizing parameters.

Although we showed that our reported techniques were accurate at end-diastole, the measurements may be dependent on the selected part of the cardiac cycle. To study this potential dependence, we investigated the variation in annulus measurements during the cardiac cycle and determined if this variation is dependent on the amount of calcification at the annulus in chapter 4. We found that there is significant variation of annular anatomical and calcium measurements during the cardiac cycle. This dynamic variation was independent from the severity of the aorta calcification. Significant differences in annulus area were found between the most commonly used mid-systole and end-diastole phases.

We also studied the minimally invasive aortic valve replacement procedure, which is a different approach for replacement of the aortic valve. In chapter 5, we introduced support tools for minimally invasive aortic valve replacement surgery that automatically find the optimal incision location. We presented an algorithm that automatically determines the distance between intercostal spaces and the sinotubular junction that supports selection of the optimal incision location. The proposed
algorithm showed good accuracy for sinotubular detection compared to manual assessment. Visual inspection of the detected intercostal spaces also showed a high accuracy for 19 of 20 patients. The fourth intercostal space was found to be the closest to the sinotubular in 60% of the patients.

In chapter 6, we developed another mini-AVR planning prototype that calculates access angle and distance maps and visualizes these on the chest cage. This supports the surgeon in choosing the suitable incision location and approach. In this study we validated this prototype by associating quantitative image based measurements with on-site difficulty scores in patients who underwent the mini-AVR surgery. It was shown that the access angle is strongly associated with procedure complexity.

In chapter 7, image quality of non-contrast enhanced MRA (NC-MRA) is compared with contrast enhanced MRA (CE-MRA) of the thoracic aorta. We showed that the aortic root, ascending aorta, and distal descending aorta were significantly sharper delineated for NC-MRA compared to CE-MRA. Visual image quality scores were significantly better for NC-MRA compared to CE-MRA.

This thesis contributes to the aortic valve replacement and medical image analysis fields by introducing novel algorithms and tools for planning of AVR approaches. These planning tools can reduce some of the complications in valve replacement. All algorithms introduced in this thesis were validated and their clinical impact was shown. Further work should aim at a more interactive approach for the clinician. Our research will help improving future clinical practice, improving outcome of valve replacement and reducing costs.

8.2 Discussion and future perspectives

Aortic stenosis is a serious valvular heart disease when it is not treated. Aortic valve replacement is considered the most common solution for stenotic valves. Currently, catheter-based valve implantation and minimally invasive valve replacement are the standard replacement approaches used. The preprocedural planning of those approaches is important for proper patient, approach, and valve selection. Development of automatic preprocedural planning tools is strongly needed to standardize and facilitate the planning process. Our developed tools for TAVI and mini-AVR planning were presented and validated in this thesis. Despite our contribution to the automation and standardization of the planning of different AVR approaches described in this thesis, further effort is needed to introduce our developed technologies in the daily clinical practice. Such effort is linked to several challenges in the clinic, as discussed below.

8.2.1 TAVI

During the conduct of this thesis research, TAVI gained much popularity. As a result, multiple competing commercial and academic solutions were proposed that support TAVI planning by automatically segmenting and detecting aortic root landmarks [1–4]. However, we believe that the methods described in chapter 2 and 3 have several advantages. Thus, they aim at enhancing the functionality and the segmentation
accuracy, such that the clinician benefits from more reliable sizing measurements. Moreover, we validated our methods, and showed that the accuracy of the developed techniques is comparable to expert variations [5,6].

During the conduct of this thesis research, multiple limitations and challenges in the currently used approaches in the planning and execution of aortic valve replacement procedures have become apparent. As an example, paravalvular leakage is considered a less common postoperative complication lately. The introduction of Edwards Sapien 3 prosthetic with the outer skirt minimizes the leakage but it increases the permanent pacemaker implantation rates [7].

The normal aorta moves and deforms during the cardiac cycle to an extent that would be relevant for valve replacement procedures [8–11]. TAVI patients have increased stiffness, caused by calcium deposits, and this could affect the dynamic nature of the aortic annulus. Yet, in chapter 4 we also observed such dynamics in TAVI patients. It is well known that annulus measurements are assessed only at mid-systole or end-diastole [5,12,13]. Multiple postoperative complications are subject to over- or under-sizing of the aortic root such as aortic root rupture, left bundle branch block, and paravalvular leakage [11,14,15]. As we discussed in chapter 4, considering other cardiac cycle phases for analysis may help avoiding these complications.

The clinical value of dynamic aortic valve measurements fuels the need for automatic segmentation and detection algorithms. Such algorithms have to work reliably for all cardiac time phases in order to support accurate dynamic measurements over the cardiac cycle. We tested our algorithm on two different time phases (mid-systole and end-diastole). We found similar or superior accuracy of aortic root landmarks detection at end systole compared to the end diastole. Such similarity can be explained by the stenotic nature of the valve in the TAVI population, which translates to a narrower valve orifice at mid-systole, which looks similar to the end-diastolic closed valve.

Despite that our aortic root segmentation algorithm is validated only at end-systole and end-diastole, we believe that this algorithm can be extended to perform well in all cardiac cycle phases, especially for the TAVI patients. Our segmentation algorithm makes use of the closed valve during end-diastole, which forms a clear separation between the left ventricle outflow tract and the aortic root voxels. In order to apply the same algorithm at other cardiac cycle phases, this separation point can be copied from end-diastole phase to other time phases which missing it. Alternatively, the aortic radial function along the aorta centerline introduces a good feature that can be used to define the proximal end of the aortic root.

We utilized image data acquired using the conventional energy protocol during this thesis’s research. Lately, dual energy CT scans are well introduced in clinical practice [16,17]. Unfortunately, our segmentation and detection algorithms were not tested on images from dual energy CTA. We would expect accurate aortic segmentation. In a pilot study we found that calcium deposits were better defined and have less partial volume effects in dual energy scans than in conventional energy scans. This seems to relate to the higher signal-to-noise and contrast-to-noise ratio in dual energy CT scans.
We do therefore expect that dual energy may produce better segmentation and detection of landmarks for the TAVI preprocedural planning.

While aortic stenosis can be confirmed using 3D echocardiography, movement of the leaflets are frequently detected in 2D images [19]. We believe that dual energy CTA can introduce help for that purpose, permitting better segmentation of the leaflets in 4D. CTA is superior with its spatiotemporal resolution and the dual energy protocol provides good performance in patients with heavily calcified aortas. Dual energy CTA would therefore provide good measurements of aortic valve leaflet dynamics.

In the current state, our TAVI tool is functional and validated, but it misses a user-friendly interface. Also some other aspects are not optimized for its use in clinical practice. This requires a better analysis of the usability requirements.

8.2.2 Mini-AVR

The selection of the optimal incision location is one of the most important aspects of a successful mini-AVR, since insufficient annulus exposure may lead to incision extension or conversion to full sternotomy. In chapter 5, we showed that the fourth intercostal space is the optimal incision location for mini-AVR in terms of distance to the sinotubular junction [20]. However, the second intercostal space is the most used incision location for right anterior minithoracotomy, as reported in multiple studies [21]. These results invited further investigation of distance measurements at other chest locations and access angle measurements as a probable access difficulty predictor. In chapter 6, a novel mini-AVR tool was developed that combines 3D imaging with these quantitative planning measures for mini-AVR. This tool allows automatic measurements of access angle, access distance, and additional aortic annulus dimensions.

Access angle was found to be a good predictor for difficulty of annulus access for mini-AVR surgery. We established an access angle threshold that can be used to expect difficult cases with high sensitivity and specificity. Against our expectation, access distance was not associated with the complexity of the procedure. We concluded that the closest intercostal space found, the fourth intercostal space, does not provide the optimal view of the aortic annulus because of its access angle. It was also shown that older patients were easier to operate and required shorter operation time. This can be explained by the fact that older patients have a larger aortic annulus [22] and smaller access angle, probably due to the increased vessel tortuosity that is common in the elderly [23,24].

One of the concerns could have been that the anatomical structures are differently positioned and oriented between CT imaging and surgery. These differences can be expected because the scan is acquired in a breath-hold setting, while the lungs are not expanded during surgery. Moreover, the heart is arrested during surgery. However, while this may affect distance measurements, it is unlikely to influence the more important access angle measurements, because the aortic root axis is not significantly changing due to breathing or beating.
Surgeons in training spend long periods on learning and practicing minimal invasive valve replacement approaches [25,26]. Our tools may help reducing the training time of new trainees doing AVRs in the wetlab, because surgeons can get impression of the location of the aortic root during surgery by investigating the 3D visualization and the supplied measurements using the tool.

Unlike for the above TAVI methods, the mini-AVR tool was developed up to the production level. To establish the true value of this quantitative and 3D visual planning tool, a prospective study should be performed on the association of the parameters with peri- and post-procedural complications. Also, the effects of the use of this tool on decision-making in surgery and on outcome should be determined. This could be achieved by inviting multiple surgeons with different experience (based on years of practice), asking them to decide which approach to pursue given the CTA images with and without the mini-AVR planning tool.

### 8.2.3 MRA

Contrast enhanced MRA (CE-MRA) is sensitive to artifacts and contrast administration is costly and requires venous access. Non-contrast enhanced 3D Navigator-gated Balanced Steady State Free Precession MRA (NC-MRA) has been suggested as a promising alternative. In chapter 7, we compared the objective and subjective image quality of NC-MRA and CE-MRA along the entire thoracic aorta. The results showed that image quality of the 3D NC-MRA was superior or comparable to 3D CE-MRA along the entire thoracic aorta as determined by both quantitative and qualitative quality assessments. This supports the standard use of NC-MRA in clinical practice for assessment of thoracic aortic pathology. Worth mentioning is that in our center, the results of this study already changed the protocol and NC-MRA is currently the imaging modality of choice for evaluation of aortic root and ascending aorta pathology. Additional studies are needed to determine disease specific strengths and weaknesses of NC-MRA.

MRA scans for patients undergoing AVR surgery is very challenging, as usually those patients have high heart rates (>90). This in turn adds extra burden as longer times are needed to acquire and reconstruct 4D scans. However, recently new and robust MRI acquisition and acceleration techniques have been developed. MR sequences based on self-gated and retrospective triggering acquisitions are examples of this [27].

TAVI postprocedural assessment can benefit from 4D Phase Contrast MRI, which enables blood flow measurement along the cardiac cycle. This would help in checking for proper valve deployment and normal aortic flow recovery. Use of PC-MRI rather than Doppler echocardiography would also allow standardization of paravalvular leakage assessment. However, further research should be done regarding the feasibility of scanning the aortic root with the new valve, since the prosthetic titanium stent may alter the quality of the scan.

### 8.2.4 Concluding remarks

We developed tools that support different AVR approaches by automating and standardizing their planning. We expect that our research will reduce complications in
TAVI that relate to suboptimal valve selection. In addition, our work will reduce the time spent by radiologists analyzing medical images for TAVI candidate patients and standardize their planning process. This is the case because of the automated and therefore reproducible computer algorithms. The mini-AVR tool will benefit the surgeon by supporting the choice for the type of minimally invasive approach. Further improvement and validation of the reported image analysis techniques is necessary for the introduction into daily clinical practice.

8.3 References


