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

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## **Summary and conclusions**



## 8.1 Summary

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In recent years, trans-catheter aortic valve replacement (TAVR), also known as Trans-catheter aortic valve implantation (TAVI), was demonstrated to have a low risk-benefit ratio as an alternative therapy for surgical aortic valve replacement (SAVR) in high risk elderly patients. During a TAVR procedure, the vascular access route and aortic root are not directly visible for the treating physician. Pre-operative imaging is necessary to evaluate the aorto-femoral vascular access and the aortic root. For vascular access, the vessel size and tortuosity are important parameters. For the aortic root, the size, the degree of calcification and the delivery direction are important parameters; these measurements can assist the cardiologist in selecting and delivering the appropriate prosthesis. Over-estimating or under-estimating the size of the vascular access and the aortic root can result in severe complications, such as peripheral arterial disease, aortic valve rupture, prosthesis migration and paravalvular regurgitation. This thesis focuses on the development and evaluation of fully automatic pre-operative planning methods for TAVR based on CT images. In addition, automatic pre-operative measurement of aorta dilatation is developed and validated.

To measure the size of the aorto-femoral vascular access in whole-body CTA imaging, at first the location of the access vessel needs to be identified manually, which can be time-consuming because of the long length and the high tortuosity of the vasculature. Chapter 2 describes a novel and fully automatic centerline extraction method of the vascular access from the left and right femoral arteries to the aortic root. First, the CTA Images were corrected for contrast inhomogeneity. Second, a wave propagation algorithm was developed to extract the aorta from an automatically detected anatomical landmark in the aortic arch towards the femoral arteries. Finally, the cost image resulting from a wave propagation algorithm was used to extract the centerlines using Dijkstra's algorithm. Based on visual inspection, the method succeeded in 91.7% of the patients with no need for user interaction. The average mean error compared with the manual reference standard was  $1.63 \pm 0.40$ mm. Based on this vessel localization, a fully automatic tool was developed that seamlessly integrates these measurements into the TAVR clinical workflow.

In Chapter 3, a fully automatic aorto-femoral vascular access segmentation framework was proposed for the pre-operative planning of trans-femoral aortic valve replacement. Its main component is the 3-dimensional deformable subdivision surface model fitting method. Two observers generated ground-truth contour data to benchmark the

automated method. The average Dice similarity indices between the automated segmentations and observer 1 for different vessel segments (left ilio-femoral artery, right ilio-femoral artery and the aorta) were all higher than 0.97; the Dice indices between the automatic measurements and the observer 2 were all higher than 0.95. The inter-observer variability was in the range of 0.95 to 0.97. Comparing the automated segmentation to observer 1, the mean error of the minimal diameter of the lumen in the ilio-femoral artery was  $0.32 \pm 0.49$  mm ( $p < 0.001$ ); In comparison to observer 2, the mean error was  $0.51 \pm 0.71$  mm ( $p < 0.001$ ). This demonstrates that the accuracy of the automated segmentations was in the same, clinically acceptable range as the inter-observer variability.

The difficulty of the aortic root segmentation in CTA image is its complex 3-dimensional geometrical structure. Manual segmentation is complex, time consuming and prone to variations between observers. In Chapter 4, a new method for automatic aortic root segmentation was introduced. The method was composed of 4 components: (1) the cardiac image was resampled for computational complexity reduction. The heart region was masked out by deformable subdivision surface model fitting.;(2) An atlas-based based method was used to segment the aortic root from the cardiac image. The most similar atlas to the patient anatomy was selected based on the similarity (the mutual information) between atlas and the patient's image.;(3) The segmentation result from the previous step was transferred to the whole body CTA image by affine registration; and (4) Refinement by deformable subdivision surface model fitting. The mean Dice index between the automatic segmentation and the reference standard was  $0.97 \pm 0.02$ . This novel framework reduced the time of registration, meanwhile delivering acceptable accuracy.

Automatic sizing of the aortic annulus and determination of the optimal angulation of the C-arm X-ray projection are essential to select and deliver the appropriate prosthesis in the aortic valve for the TAVR procedure. In clinical practice, multi-planar reconstruction of the image data is required to manually measure the size and the dimension of the aortic annulus. In Chapter 5, we presented a fully automatic method to quantify the size parameters and the optimal projection curve of the aortic annulus. The method is based on the segmentation of the aortic annulus by atlas-based algorithm and the calculation of the annulus direction by principal component analysis. 26 patients were included in a retrospective validation study. The error of the automatic tool was assessed on the clinical parameters:  $0.1 \pm 0.4$  cm<sup>2</sup> for the area,  $0.1 \pm 0.5$  mm for the radius,  $0.7 \pm 2.3$  mm for the long-axis diameter,  $0.3 \pm 1.5$  mm for the short-axis diameter and  $1.8 \pm 5.5$  mm for the perimeter; the correlation coefficients

between the automatic measurements and the reference standard were 0.92 for the area, 0.91 for the radius, 0.85 for the long-axis diameter, 0.82 for the short-axis diameter and 0.82 for the perimeter (all  $p < 0.001$ ), respectively. The mean error of the optimal projection curves was  $6.4^\circ$  in the cranial/caudal (CRA/CAU) direction. For each patient, the average computation time was around 60 seconds, while it would take a physician about 600 seconds to manually quantify the aortic annulus. As such, the developed tool can provide accurate results, reducing analysis time and minimizing manual interaction.

Aortic valve calcium quantification plays an important role in the prognosis of coronary and cardiovascular disease. The extent of calcium is also correlated to the occurrence of paravalvular regurgitation after transcatheter aortic valve replacement. To detect and quantify the presence and extent of the aortic valve calcium, in Chapter 6, a fully automatic approach was developed. The calcium on the valve was segmented by thresholding after the segmentation of the aortic root and the reconstruction of the double-oblique view of the aortic valve. Finally, the calcium volume score was calculated. To validate the automated scores, 68 CTA data sets of patients with suspicion of having coronary artery disease, were used. The reference standard was the calcium volume score semi-automatically obtained by a cardiologist with a different, manual calcium annotation tool. The accuracy of our approach was assessed by comparing with this reference standard. The median difference was  $1.82 \text{ mm}^3$  (25th-75th percentile: 0 to  $5.08 \text{ mm}^3$ ), with a Spearman rank correlation coefficient of 0.81 ( $p < 0.001$ ). Bland-Altman analysis showed that the bias between the automatic and the reference standard was  $-1.1 \text{ mm}^3$  with limits of agreement between  $-16.2$  and  $+14.1 \text{ mm}^3$ . The specificity of our automatic approach was 82.4%; the sensitivity was 85.3%. The mean processing time was 90 seconds. In conclusion, we demonstrated that a new fully automatic approach for aortic valve calcium quantification is feasible.

The aorta is the main conduit for the blood in the human body and plays a key role in controlling the vascular resistance and heart rate. CT imaging is important in the diagnosis and pre-operative planning of patients with aortic disease. To be able to monitor aortic disease using CT, images from the same patient at different time points are required, as well as standardized measurement protocols and automated quantification tools to minimize systematic and random errors. In Chapter 7, we introduced an automatic aorta dilatation quantification framework. This framework works as follows: first, the thoracic aorta is segmented automatically from the baseline CTA image. Next, the follow-up image is automatically aligned to the baseline image by rigid and affine image registration. Subsequently,

with the segmented contour in the baseline CTA image as initial contour, the contour of the thoracic aorta in follow-up CTA image is extracted by deforming the baseline contour. Finally, the measurement positions along the thoracic aorta are manually defined, and the maximal diameters at these locations in the baseline and the follow-up images are calculated. In a validation study with CT data from 29 patients, the intraclass correlations of the maximal diameters were all higher than 0.90; the mean differences between the manual measurement and the automatic measurement at different landmarks were all lower than 2mm except at the mid aortic arch and the sinotubular junction.

Taken together, this thesis presented several fully automatic algorithms for the pre-operative planning of TAVR procedures, including the sizing of the vascular access and the aortic root, the location definition of the aortic annulus, the determination of the optimal angulation of the C-arm X-ray projection and the quantification of the aortic valve calcium. Also, an algorithm for the automatic quantification of thoracic aorta dilatation was developed. For all these developments, a clinically acceptable accuracy was demonstrated against expert annotated reference standards, while significantly reducing analysis time and effort.

## **8.2 Future work**

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TAVR is an innovative cardiovascular intervention procedure developed in recent years. The successful planning of TAVR requires accurate and reproducible measurements of the vascular access and aortic root. As a high-resolution 3D modality, CT provides comprehensive visualization and precise quantification of aorto-femoral vascular access and aortic root.

In this thesis, fully automatic pre-operative planning by CT images is discussed and demonstrated to be accurate. However, the performed validation in the aortic root was limited: the size parameters of the annulus are quantified and validated, but no other landmark planes were validated. Although the annulus parameters are the most important ones for prosthesis selection, other landmark planes such as the sinotubular junction, the left ventricle outflow tract and the sinus of valsalva may provide additional useful information.

In the current study, only diastolic images were measured, while in clinical imaging the whole cardiac cycle can be useful. It is still under discussion which phases should be suitable for aortic annulus measurement and other landmark planes. A further limitation of this work is the fact that we could not investigate robustness of the presented approaches with



respect to all the main CT vendors. Images from multiple vendors has been included in our study, but there are still some vendors not tested. Therefore, future work may further complement the current study by focusing on other anatomical planes, images of multiple cardiac phases and on cross-vendor robustness.

Since the durability of the bioprosthetic valve is 10-20 years, pre-treated patients will have high possibility to receive "valve-in-valve" procedure. As it is risky for the patient to receive cardiac surgery twice, TAVR may provide a good alternative. In those cases, the previous bioprosthetic valve appears as a high intensity structure inside the aortic root in CT imaging. This will make the size measurement of the aortic annulus and other landmark planes difficult. In the future, it will be important to test whether our automatic algorithms for pre-operative planning can be generalized to "valve-in-valve" procedures. Apart from aortic valve replacement, it is important to also automate the pre-operative planning of other heart valves during trans-catheter valve replacement, such as the mitral valve, the pulmonary valve and the tricuspid valve. The minimal-invasive surgery of these valves has been implemented successfully just in recent years. There are still uncertainty and difficulty for the physicians without experience to do pre-operative planning. Especially, the mitral valve has a different anatomical structure than other valves, as it only has two leaflets while others have three. As such, an alternative segmentation and quantification approach of the other valves will be needed for the prosthesis selection and delivery for these valves.

This thesis focuses mainly on size measurements based on image segmentation. For pre-operative planning of TAVR, this quantification from anatomical perspective is important, but there are also other issues to consider to reduce complications.

Aortic regurgitation is one of the main factors which influence the final outcome of TAVR. It can be caused by unsuitable size, misplacement or incomplete expansion of the prosthesis during TAVR. Simulation of the prosthesis implantation procedure can help to predict the occurrence of aortic regurgitation post TAVR, and therefore has potential to improve the selection, placement and expansion of the prosthesis. Furthermore, the design of the prosthesis model can be improved by adjusting the mechanical parameters during simulation. The personalized aortic root models described in chapter 4 could also be used as input for such simulation models, which ultimately may lead to the reduction of the mortality rate of TAVR. Not only will the aortic valve, the simulation of trans-catheter replacement of other valves also be helpful.

As to the direct evaluation of aortic regurgitation in patient, Echocardiography plays an important role. Echocardiography can visualize the peri-TAVR hemodynamic change by multiple modalities such as Doppler and Transesophageal echocardiography, thus illustrating the mechanism of aortic regurgitation such as the under-expansion or misplacement of the prosthesis. The severity of aortic regurgitation can be quantified too and used to make clinical decisions. The combination of multiple image modalities will make TAVR a more trustable technique.