CHAPTER

6

Summary and conclusions

6.1 Summary and conclusions

For decades, coronary artery disease (CAD) has remained one of the leading causes of death worldwide despite the enormous progress in modern medical knowledge of diagnosing and treating. Atherosclerosis development in coronary arteries is the major pathophysiology of CAD which narrows the lumen volume and results in restricted oxygen-rich blood supply to myocardium. The CAD treatment includes lifestyle changes, medications and medical procedures. In 1977, the invention of balloon angioplasty by Andreas Grüntzig struck a prelude to the revolution of percutaneous coronary intervention (PCI) as a new revascularization method for CAD treatment. Undergone an evolution over the past few decades, PCI has been proven to be an effective and less costly medical procedure compared with surgeries such as coronary artery bypass grafting and regarded as one of the primary choices to treat the ischemic heart disease. Nowadays, stenting operation has been applied in most of the PCI procedures as one of the most remarkable improvements. Stent is a small medical device to support vessel wall after the angioplasty to overcome the risk of acute vessel closure. The first available stent was a bare metal stent (BMS) and later the drug-eluting stent (DES) was invented to overcome the risks of BMS such as in-stent neointimal hyperplasia. Both BMS and DES are permanent so that the stented vessel is caged by metal and late advanced vascular remodeling could no longer be applied. Therefore, bioresorbable vascular scaffold (BVS) was invented as a temporary device which can support the vessel after the implantation and slowly be absorbed by tissue during the follow up.

Continuous demand for optimal CAD diagnosis and treatment drives the evolution of medical imaging technologies. Before the invention of intravascular optical coherence tomography (IVOCT), many image modalities, including non-invasive ones like computed tomography (CT) and invasive ones like coronary angiography and intravascular ultrasound (IVUS), have been conventionally used during the research and clinical routine for CAD treatment. However, none of them have sufficient resolution to delineate fine structures such as thin fiber caps of vulnerable plaques or thin tissue coverage of stent struts. IVOCT is a new near-infrared light source based imaging technology which can acquire three-dimensional (3D) in-vivo images of vessels with a resolution of about 10 micrometers. The latest frequency-domain IVOCT imaging system has already dramatically improved the imaging speed and signal to noise ratio. Its unparalleled resolution makes it currently the only image modality for accurate stent analysis. The goal of this thesis was therefore to develop efficient and accurate algorithms to process IVOCT images for stent analysis and stenting optimization.

Stent analysis, for example the strut distribution, strut number, strut position and intra-strut angle, is highly interested as it has assisted the continuous improvements in stent manufacturing for such as better support to vessel well, flexibility for implantation and dosing of drug from DES. Furthermore, stent analysis is also increasingly used to improve the efficacy of stenting in PCI procedures by suggesting optimal stent size and proper stent expansion. Undersized stent or insufficient expansion can result in stent malapposition while stent deployment failure can cause incomplete lesion coverage. The risks include late neointimal hyperplasia and late stent malapposition. As a result, an accurate stent strut detection method in IVOCT could significantly reduce the risks of vessel revascularization. However, given the large number of the struts visible in a pullback run covering an entire stent length,

quantitative analysis is only feasible when the strut detection is carried out automatically. In **Chapter 2**, we presented a novel automated method to detect metallic stent struts in IVOCT pullback runs. As the metallic stent strut appears as a bright spot with a long, dark shadow behind it, the proposed algorithm analyzed the intensity distribution in every scan line to detect the candidate pixels that may belong to metallic struts. Next, strut shadow edges were detected and innovatively used as restrictions to remove the false candidate pixels and cluster the rest into candidate struts. Even if candidate pixel detection fails for a strut due to the thick tissue coverage or artifacts, this strut could be retrieved only based on its shadow edges. In the end, guide wires were removed and the strut center positions were computed. Validated with all 18001 struts in 10 in-vivo pullback runs with different image quality (high, median and low), 91% of malapposed struts, 93% of apposed struts and 94% of tissue-covered struts were detected with only 4% of false positives. With the validation results, the presented detection method demonstrated its possibility to be used for quantitative stent analysis.

Unlike metallic stents, BVS is commonly made of various polymers and has different appearance in IVOCT images. For accurate BVS strut analysis, IVOCT is currently the most suitable imaging technique due to its high resolution and the translucency of polymeric BVS struts. The internal composition of a BVS strut is homogeneous so that transmitted light can pass through it and backscattering originates from the difference in refractive index between the strut and its environment such as flush fluid or tissue. Therefore, BVS struts appear as bright boxes with black cores. Similar as metallic strut detection, BVS strut detection also could be used for stent analysis. Moreover, to track the bioresorption process of BVS, the strut area is also interested. Therefore, in **Chapter 3**, we presented an automated BVS strut detection method in IVOCT pullback runs to segment the black cores of BVS struts. Based on the strut location difference between baseline and follow-up datasets, the lumen contour was used to indicate different reliable regions of interest (ROI) for strut detection. This method detected short line segments belonging to black cores and then clustered them to generate smoothed black core contours. Validated with 6 in-vivo IVOCT pullback runs, including 3 baseline datasets and 3 follow-up datasets, this algorithm correctly detected 90.4% of 2183 baseline BVS struts and 96.6% of 2508 follow-up BVS struts with 3.0% and 0.8% false positives, respectively. BVS strut area was measured by the black core region and the performance was validated using Dice's coefficient. For baseline datasets, the Dice's coefficient between the ground truth and algorithmic results was 0.83 while in follow-up datasets, the Dice's coefficient is 0.85. The validation study showed that the new method can accurately detect BVS struts and measure their core areas which could be a useful tool for 3D reconstruction, tissue coverage thickness measurement, malapposition analysis, strut distribution and bioresorption assessment.

In addition to the stent type evolution, the impact of the stent design to the treatment outcome has gained increasing attentions. Existing stent design analysis mainly focuses on the two-dimensional (2D) information such as strut number, distribution or inter-angle in a single frame. However, it has been proved that stent cell structure could influence the stent support ability, expansion ability, flexibility, conformability, dosing distribution and side branch access. As it is naturally a 3D structure, the stent cell should be measured in 3D space. Both full stent cell size and maximum circular unsupported surface area (MCUSA) are currently used to evaluate stent influence to the vessel wall. In **Chapter 4**, we presented a semi-automated

method to measure the stent cell size, MCUSA and side branch access through stent cells. First, the 3D stent surface and stent cell contour were reconstructed from the detected struts for the stent cell surface segmentation and measurement. A 2D approximation of the stent cell surface was generated to detect and measure its MCUSA. In the end, the side branch access through a stent cell was computed based on the side branch surface and stent cell surface. This method was implemented using VTK toolkit with in-house developed modules and validated with a phantom dataset. The error of the algorithmic results for the 3D stent cell surface, 2D stent cell surface approximation, MCUSA and side branch access was 0.96 ± 0.64%, 0.98 ± 0.74%, 5.0 ± 5.2% and 8.9 ± 7.0%, respectively. The usability of this approach in clinical datasets was tested with 12 in-vivo IVOCT datasets from a one-year follow-up study. With the presented results, we concluded that the proposed method could be used to analyze the efficacy and performance of different stent designs to improve the outcome of PCI treatments.

In **Chapter 4,** stent covered side branches were detected for stent analysis. However, demands for uncovered side branch detection in the lesion region of a coronary artery have increased in the past decades, because the side branch location and size can suggest the optimal stent type, length, diameter, deployment position and operation plan before implanting a stent or during the diagnosis. This essential information can greatly impact the outcome of PCI treatment. Moreover, the side branch is also one of the most reliable landmarks used for image registration between baseline and follow-up datasets or multi-modality image fusion. Therefore, in **Chapter 5**, we presented a fully automated detection algorithm for both covered and uncovered side branches in IVOCT pullback runs. As side branches appear as cavities in the vessel tissue, they were detected by computing and analyzing the distance between the lumen center and the leading-edge of the intimal layer. To compute this distance, we need to remove all the bright components inside the lumen, fix the cavity caused by guide wire shadow and detect the lumen center. As a result, an image segmentation pipeline to segment the imaging catheter, protective sheath, guide wire and lumen was implemented. To validate the image segmentation pipeline and side branch detection method, 25 in-vivo IVOCT pullback runs from a two-year follow-up study were used. The image datasets were acquired with different pullback speed in different time periods and contain different types of stents or no stent at all. The intraclass correlation coefficient (ICC) of the imaging catheter radius, protective sheath radius and lumen contour position between the algorithmic results and ground truth was 0.997, 0.949 and 0.974, respectively. 100% of the guide wires were detected and the Dice's coefficient of the guide wire shadow region between the algorithmic results and ground truth was 0.97. In this chapter, only the side branches which are at least 0.8 mm in longitudinal direction and 8 degrees in the circumferential direction were included. The validation results show that 94.0% of 82 side branches were detected with less than 5.0% false positives. The Dice's coefficient of the angle region in circumferential direction between the ground truth and algorithmic results was 0.85. With the presented results, it is concluded that our image segmentation pipeline is accurate and robust enough for many advanced image processing algorithms that require the segmentations of these common components in IVOCT images. For example, it could be used to improve the robustness and accuracy of our strut detection methods. In **Chapter 2**, the metallic strut detection method should skip the bright imaging catheter because its high intensity value can influence the intensity profile analysis. In case there is bright air bubble noise in the protective sheath, it

should be skipped as well. In **Chapter 3**, the performance of the BVS strut detection method is influenced by the accuracy of lumen contours which indicate the ROIs. The automated side branch detection method offers a new option for accurate 3D side branch analysis in IVOCT pullback runs to optimize the CAD treatment or for image registration.

6.2 Future works

According to the validation results demonstrated in this thesis, we can conclude that our goals in each chapter have been achieved to a certain degree. However, there is still plenty of room for further improvement of this work.

6.2.1 3D stent model

In **Chapter 2** and **3**, the stent strut detection relies on only 2D information in individual frames. Actually, a stent is usually formed by repeated structures called stent cells and can be presented as a 3D model. This pattern should globally match the stent strut distribution. The complexity, when using the stent model, is that different stents have different models and a stent structure could be distorted during the expansion because the hardness of tissue and plaques is different. Due to these reasons, stent pattern model is not used in this thesis. In future, stent pattern model could be used to supervise the stent strut detection. It can be fitted to the detected stent struts, and help to remove the false positives that locate in the wrong position or retrieve the false negative struts by checking the trend of each stent wire. For a new type of stent without existing model, a model could be manually defined based on the detected struts and later used to supervise future strut detection for the same type of stents. The stent pattern model can also help the 3D stent cell contour reconstruction in **Chapter 4** and improve the efficiency of the 3D stent cell analysis. Furthermore, the spiral information of the stent wire could be used to reconstruct the whole implanted stent skeleton automatically for visualization and further measurement.

6.2.2 IVOCT image improvements

Ideally, in IVOCT images, different tissue should be represented by different intensity values so that segmentations can be easily applied. However, we noticed that homogeneous tissue also has very different gray-scale in the same pullback run or even in the same frame. The main reasons for the non-uniform gray-scale include the distance between the imaging catheter and scanned sample, tissue coverage of the sample or the angle of incidence. Once an image correction model is set up, the intensity of IVOCT images can be unified and the segmentation and detection performance in **Chapter 2, 3** and **5** should be greatly improved. Better strut detection results also positively influence the stent cell analysis in **Chapter 4**.

Relative low longitudinal resolution of frequency-domain IVOCT images could hamper the quantitative analysis in IVOCT images. Both time-domain IVOCT and new super-high speed OCT catheter can increase the longitudinal resolution by reducing the slice distance which makes small side branch detection and side branch lumen smoothness possible in **Chapter 5**. Furthermore, the strut detection methods in **Chapter 2** and **3** also can benefit from the additional slices, because smaller slice distance suggests that when analyzing one frame, its neighboring frames could be

used as reliable references. All above can consequently help to generate more accurate stent surface and stent cell contours in **Chapter 4**.

6.2.3 Image registration

Despite IVOCT is one of the best image modality for intuitive visualization of fine coronary vascular structures as well as accurate and reproducible quantifications, every single modality has its drawbacks and is insufficient to provide all necessary information. The modern approach requires the combination of multiple imaging modalities to be able to assess the CAD situation. The main shortcoming of IVOCT is its limited penetration which cannot delineate deep structures such as plaques with thick coverage or side branch lumen wall. Eccentrically located imaging catheter in a big lumen could also cause image blurring or even missing in the region far away from the catheter. Besides, the longitudinal image acquired by IVOCT system does not contain the sensor travelling trajectory so that could not outline the original tortuosity of the artery. Multi-modality image registration could be a solution for this challenge. Compare with IVOCT, IVUS has lower resolution but much deeper penetration. If both IVUS and IVOCT images are acquired for the same vessel, these images can be co-registered based on the side branches detected in **Chapter 5**, and the IVUS image could provide the deep region information of the vessel. Moreover, the detected side branches can assist the registration between IVOCT and coronary angiography, CT or other image modalities, which will help us to reconstruct the real 3D tortuosity of vessels for IVOCT images. Image registration can lead to a comprehensive and objective understanding of coronary disease and guide the intervention effectively, especially for patients with complex lesions.