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Automatic quantification of intravascular optical coherence tomography

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CHAPTER

5

Fully automated side branch detection in intravascular optical coherence tomography pullback runs

This chapter was adapted from:

**Fully automated side branch detection in intravascular optical coherence tomography
pullback runs**

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ABSTRACT

Side branches in the atherosclerotic lesion region are important as they highly influence the treatment strategy selection and optimization. Moreover, they are reliable landmarks for image registration. By providing high resolution delineation of coronary morphology, intravascular optical coherence tomography (IVOCT) has been increasingly used for side branch analysis. This paper presents a fully automated method to detect side branches in IVOCT images, which relies on precise segmentation of the imaging catheter, the protective sheath, the guide wire and the lumen. 25 in-vivo data sets were used for validation. The intraclass correlation coefficient between the algorithmic results and manual delineations for the imaging catheter, the protective sheath and the lumen contour positions was 0.997, 0.949 and 0.974, respectively. All the guide wires were detected correctly and the Dice's coefficient of the shadow regions behind the guide wire was 0.97. 94.0% of 82 side branches were detected with 5.0% false positives and the Dice's coefficient of the side branch size was 0.85. In conclusion, the presented method has been demonstrated to be accurate and robust for side branch analysis.

5.1 Introduction

Despite decades of progress in understanding the development of coronary artery disease (CAD), it remains the most common cause of death in the world. Nowadays, percutaneous coronary intervention (PCI) with stenting is widely performed to open narrowed coronary arteries and to restore the oxygen-rich blood supply to the myocardium. Bifurcation lesions, accounting for about 20% of the PCI cases and expecting to further increase, are continuous one of the most complex anatomic structures and remain a challenge for interventionalists. Without a single preferred approach, a bifurcation lesion should be analyzed prior to the PCI to plan the interventional strategy, because bifurcation stenting often suffers from higher risks of acute and chronic complications such as acute thrombosis or late restenosis [1-3]. Furthermore, a stent placed in the main branch may partially obstruct the blood flow to small side branches and impact the PCI outcome [4-6]. Medical imaging, like coronary angiography (CA) and intravascular ultrasound (IVUS), has been used for side branch analysis [7-11]. Current approaches require the combination of multiple imaging modalities to assess lesion characteristics, analyze the blood flow and optimize stent placement with respect to optimal stent selection, deployment and expansion since every modality has its limitations. For image registration in the same or different modalities, side branches are reliable landmarks [12, 13].

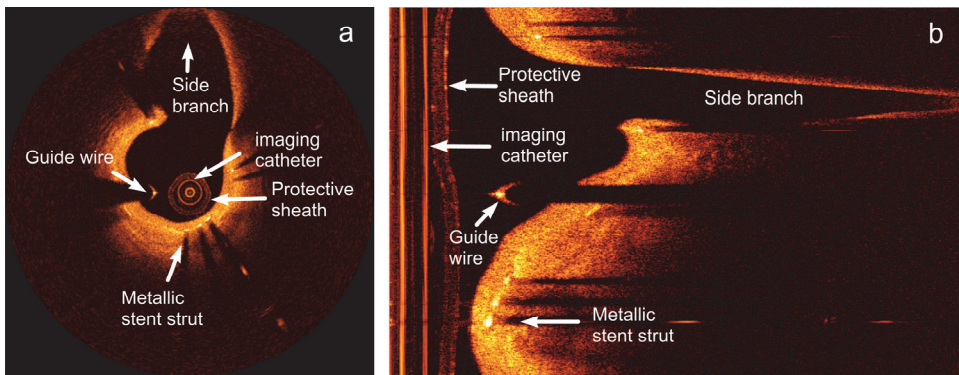


Figure 5-1. Two in-vivo IVOCT image examples. Figure (a) shows a Cartesian image, while figure (b) shows the corresponding polar image. In both images, a side branch, a guide wire, a metallic stent strut, the imaging catheter and the protective sheath are visible and annotated.

The continuous drive for optimal patient care demands precise delineation of the coronary vascular structures for accurate and reproducible quantifications. They can increase the understanding of CAD objectively and guide the intervention effectively, especially for patients with complex lesions. As a novel image modality, intravascular optical coherence tomography (IVOCT) has played a particular role in the setting of contemporary stenting by providing very high resolution ($<20\ \mu\text{m}$) intracoronary images. It utilizes a fiber optic catheter to emit near-infrared light toward samples and receive the back scattered signal. A protective sheath covers the fiber catheter when it is rotating and being pulled back through the vessel and a guide wire is usually applied to facilitate the placement of the imaging catheter. Figure 1 presents two typical IVOCT

images. Compared with IVUS, the current golden standard for assessing lesion situation, IVOCT is more accurate and reproducible for quantitative analysis in many fields [14-19]. It is becoming a routine modality to guide PCI and quantify clinically interesting features including side branches and has been used in image fusion to provide detailed plaque composition and lesion extent [20-22].

Currently, most of the side branch identification in IVOCT images is done manually. In this paper, we present a fully automated method to detect side branches in IVOCT pullback runs based on accurate segmentations of all the common components of typical IVOCT images. The details of the method are described in section 2, while the validation method and the empirical results are presented in section 3 and section 4. The discussion and the conclusions of the proposed methods are given in section 5 and section 6, respectively.

5.2 Methods

As Fig. 1 shows, a side branch appears as a cavity in the vessel tissue so it can be detected by analyzing the distance variation between the lumen center and the leading-edge of the intimal layer. To accomplish this, all the bright components inside the lumen have to be removed and the guide wire shadow cavity in the vessel wall should be fixed in the beginning. Therefore, polar IVOCT images are pre-processed in four steps: (1) first, the imaging catheter is segmented and removed, so it will not affect the next step; (2) the guide wire is detected by analyzing the intensity profile of every scan-line; (3) after guide wire masking, the protective sheath is segmented for image correction and masking purposes; and in the end (4) the lumen contour is detected for lumen center calculation and guide wire shadow fixing. After the pre-processing, polar IVOCT images are converted into the Cartesian coordinate system, so that the distance between the lumen center and the leading-edge of the intimal layer can be computed and analyzed for side branch detection. In Fig. 2, a flow chart illustrates the main steps of this methodology. Details of each step are discussed in the following paragraphs.

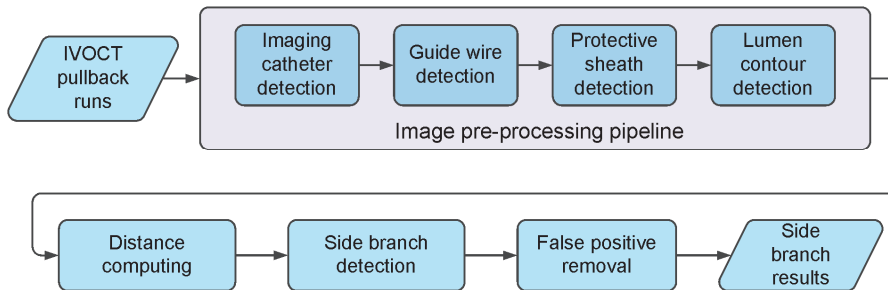


Figure 5-2. The flow chart of the presented side branch detection method.

5.2.1 Imaging catheter detection

As Fig. 1(b) shows, the imaging catheter appears as the rightmost bright vertical line in the polar IVOCT image and should be at a constant position in all frames in a pullback run. However, due to slight optical path length changes, the zero-point of a frame, also called Z-offset, can be different, which may lead to imaging catheter radius changes in a pullback run. As a result, the imaging catheter is segmented frame by frame. An extra complication is that the abluminal wall of the imaging catheter can be

blurred by the protective sheath attached to it or by bright (air bubble/blood) noise between the imaging catheter and the protective sheath. In contrast, the adluminal wall of the imaging catheter is always clear and can be used to define a region of interest (ROI) for the abluminal wall detection.

First, the image is converted into a binary image use a denoising threshold based on a percentile of its intensity histogram [23]. In this paper, it is the 80th percentile. Next, a vertical edge Prewitt compass operator is applied to generate a gradient image, followed by a normalizing operation on every scan-line. The normalized gradient in every column is multiplied by a coefficient based on the distance to the left boundary of the polar image, so that the imaging catheter has stronger weighted gradient value than other vertical lines. The coefficient equals to the column index divided by the image width. An example is presented in Fig. 3. To be more precise, the adluminal wall of the imaging catheter is first segmented and next, to its right, the abluminal wall is detected within a certain distance range. By analyzing their position variation in the pullback, outliers are replaced by interpolated results from neighboring frames. Finally, the imaging catheter and the image region to its left are masked so that the next processing will not be affected.

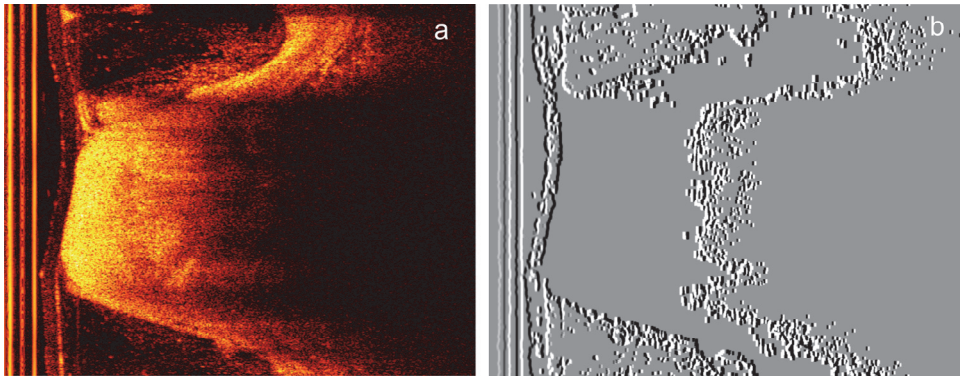


Figure 5-3. The imaging catheter and two other parallel vertical lines can be seen on the left of figure (a) and the corresponding distance weighted gradient image is given in figure (b). In figure (b), the adluminal wall of the imaging catheter is represented by negative values and the abluminal wall by positive values.

5.2.2 Guide wire detection

The guide wire appears as a bright crescent followed by a dark shadow because it reflects all the light during the IVOCT scanning. It needs to be segmented in this method as it can negatively affect the protective sheath and lumen contour detection. Moreover, cavities in the vessel wall caused by guide wire shadows should be fixed before the side branches can be effectively detected. Figure 4(a) demonstrates the intensity profile of a scan-line passing through a guide wire. The guide wire contains the highest intensity of this scan-line. After the peak point, the intensity value of the shadow region is close to zero. In contrast, in a scan-line passing through vessel tissue, the sum of intensities behind the peak point occupies a bigger proportion of the whole intensity sum like Fig. 4(b) shows. Hence, the guide wire can be detected by analyzing the intensity profiles.

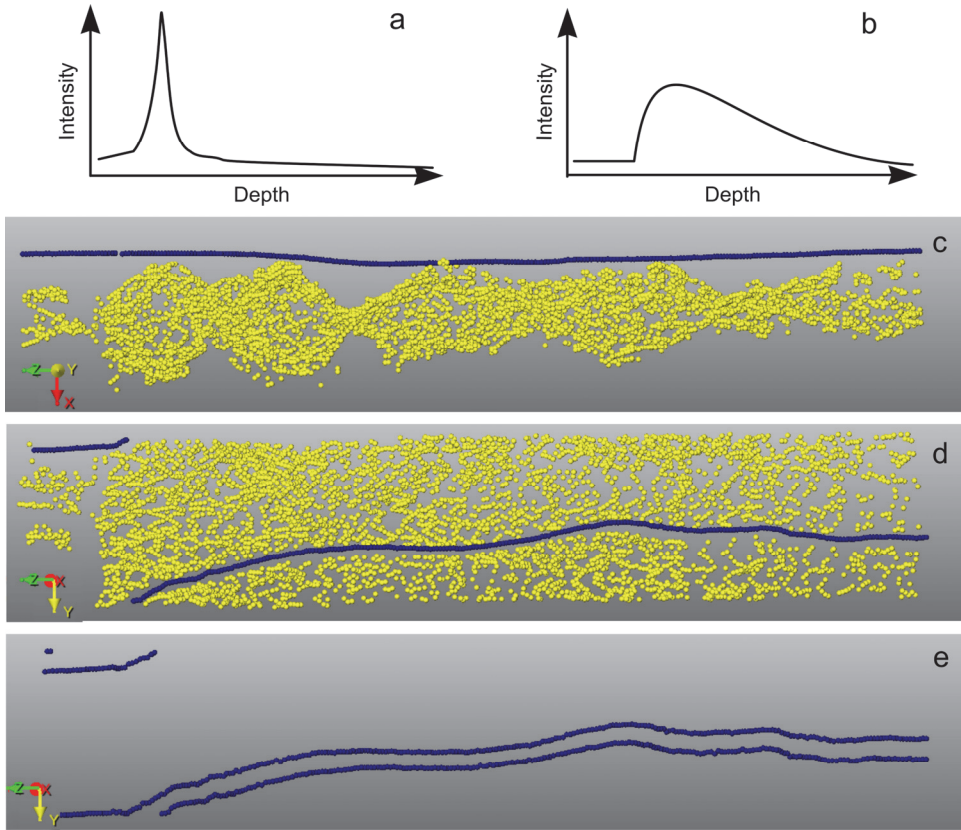


Figure 5-4. The Following imaging catheter removal, the intensity profile of a scan-line passing through a guide wire is given in figure (a) and passing through only tissue in figure (b). The candidate clusters (dots) detected in a polar pullback run are presented in two different viewpoints in figures (c) and (d). The yellow dots are noise like metallic struts and the blue dots indicate the guide wire which is continuous during the pullback run and located close to the imaging catheter. Figure (e) shows the shadow edges of the guide wire as blue dots.

The guide wire detection algorithm works as follows. First, for each scan-line, we detect its peak point (with maximum intensity value) and compute the proportion of the intensity sub-sum behind the peak point. If the proportion is lower than a threshold, this peak point may belong to a guide wire. In this research, this threshold is 0.75. These peak points are clustered into guide wire candidates frame by frame based on the distance as we have presented in [23]. As Figs. 4(c) and 4(d) present, the clustering results may contain false positives such as metallic stent struts, since they have a similar appearance as guide wires. In contrast to metallic struts and other noise, a guide wire is present in the all the frames of a pullback run. Moreover, its position does not change significantly between two adjacent frames and is usually close to the imaging catheter. To remove these, Dijkstra's algorithm [24] is used to detect the clusters which can be linked by the shortest path through the entire pullback. The cost function is the absolute position offset between two clusters from the adjacent frames. If multiple shortest paths were found, the one located closer to the imaging

catheter was selected. Based on the width of the cluster, the guide wire shadow edge positions can be detected as follow. First, a horizontal edge Prewitt compass operator is applied to the original polar image. Next, the guide wire shadow edges are detected by searching for the scan-line that has the strongest gradient sum within a certain distance from the initial top or bottom position of a guide wire cluster. The detected edges are given in Fig. 4(e).

5.2.3 Protective sheath detection

The protective sheath is a transparent tube-like cover which protects the imaging catheter from the vessel tissue. As Fig. 5(a) illustrates, the protective sheath usually appears as two bright parallel curved layers in the polar images because the image center is not the center of the protective sheath. Both the inner and outer layers have their own adluminal and abluminal wall. The protective sheath and the bright noise in it will be removed as they influence the lumen detection. Moreover, as the protective sheath has a fixed diameter, it is used for Z-offset correction [25]. The challenge lies in the complex image situations, as there could be bright noise between the imaging catheter and protective sheath, inside a protective sheath or between the protective sheath and vessel lumen as Figs. 5(b)–(d) show. Therefore, any of these four edges could be very unclear and should not be used alone for the segmentation.

First, a ROI is set in the polar image for protective sheath detection. It starts from the abluminal wall of the imaging catheter and should contain the whole protective sheath, and as little vessel tissue as possible. In this study, the ROI width was calculated based on the image resolution. Within the ROI, the polar images are down sampled by a factor of four to reduce the computation time and to smooth the final boundary. Next, a vertical edge Prewitt compass operator is applied to represent the dark-to-bright edges by positive values and bright-to-dark edges by negative values. To enhance the abluminal wall of the outer layer, its gradient value is combined with the gradient values of the other three edges [26]. As all four edges are generally paralleled, their relative distances are stable. According to the image resolution and protective sheath size, the distance between two layers is about 14 pixels and the layer thickness is about 6 pixels. More formally, the original gradient value at point (x, y) is denoted as $g(x, y)$. The combined gradient value $f(x, y)$ is related to the sum of four points:

$$f(x, y) = G(x, y) - 0.5E_1 + E_2 - 0.5E_3 \quad (1)$$

with

$$G(x, y) = \begin{cases} g(x, y) & \text{in the ROI} \\ 0 & \text{others} \end{cases} \quad (2)$$

$$E_1 = \max_{i \in [-6, -3]} \{G(x + i, y)\} \quad (3)$$

$$E_2 = \min_{i \in [-20, -17]} \{G(x + i, y)\} \quad (4)$$

$$E_3 = \max_{i \in [-26, -23]} \{G(x + i, y)\} \quad (5)$$

Next, Dijkstra's algorithm is applied to detect the minimum cost path in the combined gradient image as the outer abluminal wall of the protective sheath. The cost function is $f(x, y)$. Examples are given in Figs. 5(a)–(d). Like Fig. 5(e), the detected contours are converted into the Cartesian coordinate system and then fitted

to circles using a least-squares method [27]. Because the diameter and the center of the protective sheath should not change much between the neighboring frames, a median filter is applied to remove outliers and replace them by interpolation. Figure 5(f) presents the center shifting and size changing of the protective sheath along the pullback run. The Z-offset is corrected according to the protective sheath diameter in every frame. Finally, the protective sheath is masked out before lumen detection.

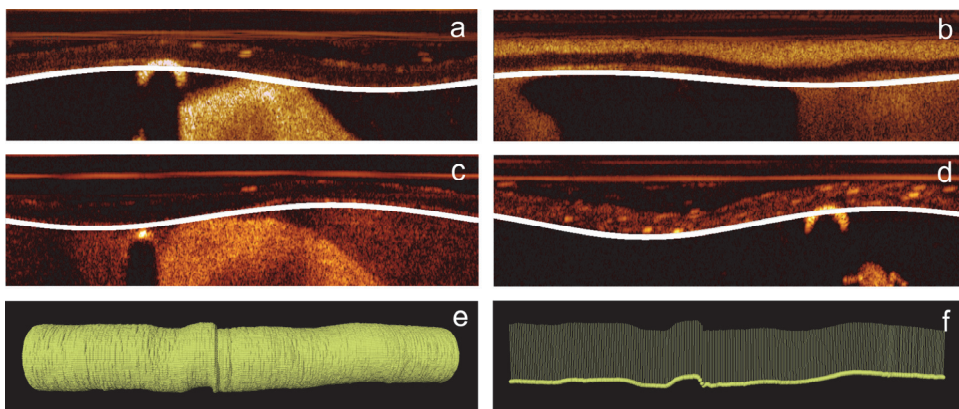


Figure 5-5. Figure (a) illustrates a normal protective sheath appearance. However, bright noise may exist between the imaging catheter and the protective sheath like figure (b), between the protective sheath and the lumen contour like figure (c) shows, or inside the protective sheath like figure (d). White curves indicate the detected protective sheath. A 3D visualization of the protective sheath contours in a Cartesian dataset is given in figure (e). The corresponding contour center (yellow dots) and the radii (yellow vectors) are presented in figure (f). In figures (e) and (f), the scale between the axial direction and longitudinal direction is about 1:10.

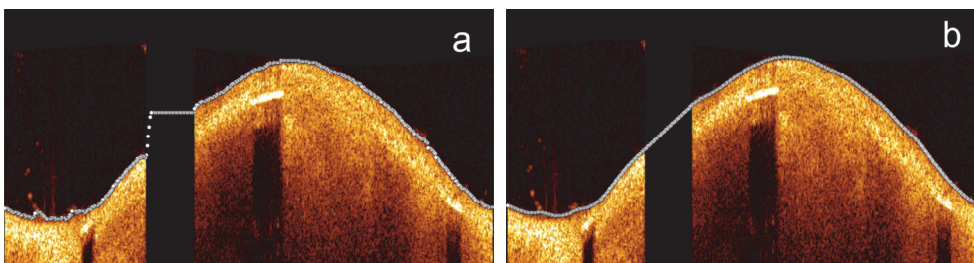


Figure 5-6. Figure (a) shows the originally detected lumen contour (white dots in each scan-line). The segment in front of the guide wire shadow does not fit the lumen trend. Using the guide wire width information, this part of the lumen contour is smoothly interpolated like figure (b) demonstrates.

5.2.4 Lumen contour detection

To compute the lumen center accurately, the lumen detection must follow the main vessel wall as much as possible, and pass over possible cavities like side branches or guide wire shadows. In this work, Dijkstra's algorithm is used with a side-step restriction. The cost matrix is the gradient image and the side step was limited to

10 pixels in accordance to the image size in this research to insure the minimum cost path passing over cavities. The side-step cost is 80. To avoid the strong gradient inside the tissue, first, all the intensity values above a given threshold are replaced by the constant value. The threshold is computed for each frame based on a fixed percentile of the intensity histogram, because even in the same pullback run, vessel tissue can have very different intensities in different frames. We have chosen the 85th percentile. After thresholding, the same Prewitt compass operator for vertical edges is applied to generate a gradient image as the cost matrix and the minimum cost path in this matrix is detected and defined as the lumen contour.

As the guide wire shadow in the lumen tissue region does not contain any edge information, the detected minimum cost path in this region could be wrong as shown in Fig. 6(a). This piece of lumen contour is located according to the guide wire width detected in section 2.2. It is replaced by linear interpolation in the polar coordinate system for smoothness as shown in Fig. 6(b), because the width of a guide wire usually is narrow when compared with that of the whole image. After converted into Cartesian coordinate system, the whole lumen contour looks natural. Along with the interpolated curve, the guide wire shadow cavity in the vessel tissue is fixed (filled) before the side branch detection.

5.2.5 Distance computing

A side branch can be detected by analyzing the distance variation between the lumen center and the leading edge of the intimal layer. A sharp increase in the distance indicates the possible existence of a side branch. Since very small side branches barely have clinical significance and cannot be used as reliable landmarks for image registration, we focus on side branches which are more than 8 degrees wide in the circumferential direction and continuous in at least 4 frames (about 0.8 mm). This is also the size restriction of the presented side branch detection method. First, the lumen center is determined. In case a detected main lumen area contains parts of a big side branch lumen as Fig. 7(a) shows, the center of the lumen contour would move to the side branch position, which results in a shorter distance than normal. To avoid this error, the main lumen region needs to be located. As the main vessel can be treated as a tube containing the imaging catheter, the maximum circle inside the lumen contour which contains the imaging catheter is defined as the main lumen region and its center is the lumen center. The lumen center is determined by using a distance transformation based method [5]. First, a binary image was generated from the detected lumen contour in which the lumen region was presented as 1 and the others as 0. Next, a distance transformation converted the binary image into another image where all nonzero pixels get a value which corresponds to the distance to the nearest lumen contour boundary. The center of the lumen is now identified by determining the maximum value in the distance transformation image. After detecting the lumen center, the distance to the intimal layer is computed every two degrees by looking for the first pixel having intensity value above the tissue threshold defined in section 2.4. If no tissue pixel is found, the search stops at the image border. Two examples are given in Figs. 7(b) and 7(c).

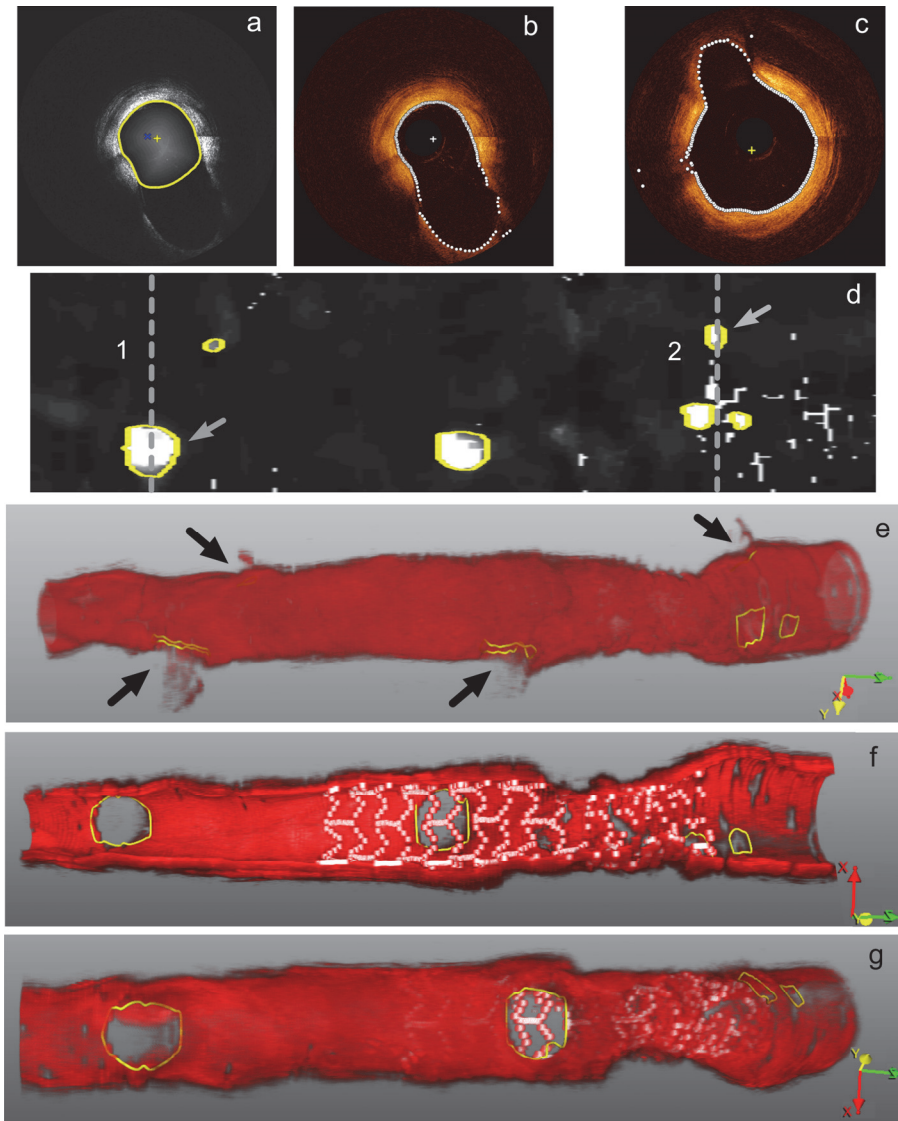


Figure 5-7. Figure (a) presents a detected lumen contour (yellow) containing part of a big side branch. The white overlay in the contour is the distance transformation result. The lumen center (yellow “+”) and the image center (blue “x”) are given as well. From the lumen center, the leading-edge of intimal layer is detected in all angles and the results are presented as white dots in figures (b) and (c). They show two cross-sections (vertical line 1 and 2) of figure (d). The distance matrix for this pullback run can be treated as a 2D image like figure (d) in which side branches are detected as yellow contours. Arrows indicate the side branches in figures (b) and (c). Figure (e) shows the corresponding 3D side branches (yellow contours). Arrows point to the opening of some side branches. Parts of side branch walls are visible. Figures (f) and (g) show the side branches in an opened vessel with the opposite view angles. To show side branches clearly, the viewing angles follow the side branch direction. The white dots are implanted bioresorbable stent struts.

5.2.6 Side branch detection

After the distance computation, we get a 2D matrix which contains the distance for all angles along the whole pullback run. The distances are normalized in each frame to unify different lumen sizes. While normalizing, the median distance in each frame is scaled to 1.0 and the other distances are scaled proportionally. By converting distances to intensities, the matrix can be treated as a 2D image as shown in Fig. 7(d) in which the side branches are represented by bright regions which have high intensity values and acceptable size. To detect these regions, the image is first smoothed and a 2D region growing method is applied to find all the connected pixels above a threshold. In this study, the threshold is set to 1.4. To filter out false positives caused by highly eccentric elliptical lumen contours, bright regions should contain at least one pixel whose intensity value is two times higher than the median value. Next, the regions which are too small according to the size restriction in section 2.5 are removed. The detection results are shown in Fig. 7(d). Finally, all these 2D results are transformed back to the original 3D IVOCT pullback runs based on the lumen centers and their distance to the lumen centers as Figs. 7(e)–(g) demonstrate.

5.2.7 False positive removal

The detected results could still contain false positives because black cavities in the vessel tissue are not always side branches. Because of the limited penetration capability of IVOCT, it may result in a cavity in the vessel wall when the imaging catheter touches the tissue as Fig. 8 illustrates. However, in this situation, the angle difference between the image center and the edges of this cavity is close to zero. Based on this feature, this type of false positives is easily removed.

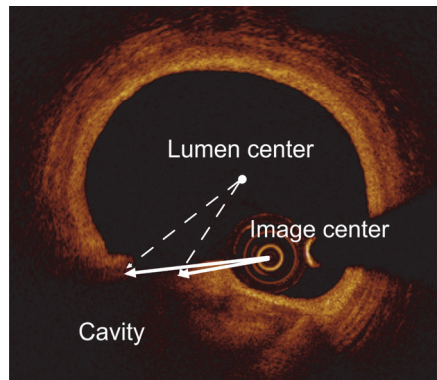


Figure 5-8. The false positive (based on the dashed lines) resulted from the tissue coverage over the imaging catheter. The angles from the image center to the side branch edges (between the solid lines) are almost the same.

If a pullback contains densely spaced incomplete apposed metallic stent struts, they could generate wide shadows in the vessel tissue and may lead to false positives. In a previous paper [23], we presented an automated method to detect metallic stent struts and their shadow regions. The stent strut and their shadow positions can be used for cross checking with the side branch candidates. A side branch candidate that is overlaid mainly with struts can be a false positive and should be removed.

5.3 Materials and validation method

The presented side branch detection method was developed using the MeVisLab toolbox 2.2.1 (MeVis Medical Solutions AG, Bremen, Germany) together with in-house developed C++ modules. A total of 25 random selected in-vivo IVOCT pullback runs were used to evaluate the presented method. All the images were acquired with a C7-XR OCT intravascular imaging system (St. Jude Medical, Westford, MA, USA) and the image resolution is $5.86 \mu\text{m} \times 5.86 \mu\text{m} \times 200 \mu\text{m}$. The pullback runs include baseline datasets and follow-up datasets at different time points. For 23 out of 25 datasets, each contains 271 frames (using a pullback speed of 20 mm/sec) while for the other 2 datasets, each contains 541 frames (using a pullback speed of 10 mm/sec). 19 datasets contain guide wires. 14 pullback runs contain metallic stents; 6 pullback runs have bioresorbable vascular scaffolds (BVS) and 5 others contain no stent or scaffold.

One observer manually marked the imaging catheter, the guide wire region, the protective sheath contour and the lumen contour in one frame out of every 25 frames in each pullback. The boundaries of all side branches that are more than 8 degrees wide in the circumferential direction and continuous in at least 4 frames were marked. In total, 82 side branches were marked in 22 pullback runs and in the remaining 3 pullback runs, no visible side branches were found due to guide wire shadow blockage, massive residual blood noise or poor image quality. Therefore, they were excluded from the side branch detection validation. A second independent observer marked the ground truth in a subset containing 5 pullback runs. When marking the ground truth, in case a side branch was partly blocked by a guide wire shadow or residual blood, its boundary was estimated based on the 3D information and personal experience.

5.4 Results

The inter-observer agreements were measured using the intraclass correlation coefficient (ICC) and the Dice's coefficient. The ICC of the imaging catheter radius, the protective sheath radius and the lumen contour position between two observers were 0.983, 0.942 and 0.999. Here, the lumen contour positions were compared in radial direction from the image center in every 2 degrees. The distance between the protective sheath centers was 1.21 ± 0.57 pixels. The average Dice's coefficient between the corresponding guide wire shadow regions was 0.97 ± 0.02 . Both two observers agreed on all 15 side branches in the subset and the average Dice's coefficient of their angle regions were 0.92 ± 0.07 .

During the validation, the performance of the presented methods was measured using the ICC and the Dice's coefficient. Moreover, the radius error of the imaging catheter and protective sheath, the distance error of the protective sheath center and lumen contour were computed as well. Compared with the ground truth from the first and the second observer, the detected imaging catheter radii had an average error of -0.63 ± 1.13 and -0.93 ± 1.40 pixels. The corresponding ICC was 0.998 and 0.977. The detected protective sheath radii had an average error of 0.90 ± 0.67 and 1.05 ± 0.61 pixels while the corresponding ICC was 0.986 and 0.949. The average distance error of the protective sheath centers was 1.25 ± 0.79 and 1.15 ± 0.61 pixels. The average Dice's coefficient for guide wire region was 0.97 ± 0.03 and 0.97 ± 0.02 . The lumen contour distance error was computed in radial direction from the image center for every 2 degrees and the average error was -2.56 ± 12.21 and 1.49 ± 7.27 pixels. The ICC of the

lumen contour position was 0.940 and 0.974. Overall, 94.0% of 82 side branches were correctly detected with 4.9% of false positives, while in the subset, 93.3% of 15 side branches were detected with 6.7% false positives. The average Dice's coefficient of the angle region between the detected side branches and the ground truth from two observers was 0.85 ± 0.06 and 0.77 ± 0.07 , separately. Overall, 31 side branches were at least 1.0 mm in the longitudinal direction and had a maximum angle region of at least 60 degrees. These big side branches are more important than small side branches as they are solid bio-landmarks for image registration and essential for bifurcation lesion treatment. In the validation, 100% of these big side branches were successfully detected. A summary of the detailed inter-observer agreements and validation results are presented in Table 1.

Table 1. The similarity and difference among the ground truth (GT1) from the first observer, the ground truth (GT2) from the second observer and the algorithmic result (AR). For the imaging catheter radius (ICR), protective sheath radius (PSR) and lumen contour position (LM), the similarity is given as the intraclass correlation coefficient (ICC) and the difference is given as the average size difference (Diff) in pixels. The protective sheath center (PSC) position error is also measured by the average distance difference in pixels. The true positive rate (TP) and false positive rate (FP) are used for side branch (SB) detection performance. The overlaid region for the guide wire (GW) and SB is measured by the average Dice's coefficient (Dice)

Groups	ICR		GW region	PSR		PSC	Lumen		SB (%)		SB region
	ICC	Diff	Dice's	ICC	Diff	Diff	ICC	Diff	TP	FP	Dice's
GT1/GT2	0.983	-1.40	0.97	0.942	0.18	1.21	0.999	-0.13	100	0.0	0.92
GT1/AR	0.998	-0.63	0.97	0.986	0.90	1.25	0.940	-2.56	94.0	5.0	0.85
GT2/AR	0.977	0.93	0.97	0.949	1.05	1.05	0.974	1.49	94.0	5.1	0.77

5.5 Discussion

The performance of the presented side branch detection method depends heavily on the accuracy of the image segmentation in the pre-processing step. Moreover, segmentations of all the common components in IVOCT images are also important for many image processing and quantitative analyses. For example, imaging catheter detection is commonly required for lumen detection [28, 29] and metallic strut detection [23], because its high intensity is a negative influence. A guide wire could be mistakenly detected as a metallic strut due to its appearance [30, 31]. The protective sheath diameter can be used for Z-offset correction [25] as 1% change in the magnitude of the ideal Z-offset can result in a 12% to 14% error in area measurements, which may lead to misinterpretation [32]. Currently, only 38% of the peer-reviewed papers present correctly calibrated images [29]. Lumen contour detection is one of most common image segmentation steps and the published methods include Markov random field and wavelet transform analysis [28], fuzzy C means clustering and

wavelet transform [33], deformable spline models [34] and dynamic programming [35]. However, in many cases, only a light-weight and fast lumen contour estimation like our method is needed.

As the adluminal wall of an imaging catheter is clearer and more reliable than the abluminal wall, the firstly detected adluminal wall indicated an accurate ROI for the following abluminal wall detection. According to the validation results, the detected imaging catheter radii had an average error of less than 1 pixel. The error was mainly caused by the bright air bubble, blood noise or attached protective sheath which blurred the abluminal wall. The errors caused by these artifacts were mostly corrected by the median filter because they normally did not affect the majority of a pullback run.

All the guide wires were detected with no false positions. The Dice's index between the detected guide wire region and the ground truth was 0.97. The presented method searched for guide wire shadow edges for lumen fixing but a guide wire shadow edge could be blocked by metallic struts, so that the guide wire width may be overestimated. A similar situation was when a guide wire shadow region is overlaid with side branches. However, the searching depth limitation prevents the overestimation goes too far. A limitation is that only one guide wire can be detected automatically in a pullback run. A-priori knowledge of guide wire number is needed to detect additional guide wires.

The radius error and the center position error of the detected protective sheath are both about 1 pixel, which ensures accurate Z-offset correction in IVOCT images. Combining all four edges of the protective sheath greatly prevents the segmentation from being affected by complex noise around the protective sheath. Furthermore, circle fitting overcomes local distortions and the radius filter can remove outliers in the whole pullback.

In the radial direction, the detected lumen contour had an average distance error about 3 pixels. Most of the large differences between the algorithmic results and the ground truth occurs when side branches or part of a large lumen were invisible due to the limited penetration depth of IVOCT. Since we set a side-step limitation for the dynamic programming method, it returned a relatively smooth lumen contour which skipped sharp peaks and cavities. The ground truth was drawn based on personal experience which could be different. Some errors also resulted from the bright noise inside the lumen such as thrombi and malapposed struts, especially when they were located close to the real lumen boundary. In these cases, the detected lumen contour followed the leading edge of the bright noise instead of the lumen.

With the foregoing precise pre-processing steps, our method successfully detected 94.0% of 82 side branches including all the big side branches with less than 5% false positives. The Dice's index of the side branch angle size is 0.85. The side branch boundary was detected based on the distance change which is highly reproducible. The biggest side branch size errors were caused by the guide wire shadows. When a side branch was partly blocked by a guide wire, the detected side branch would be incomplete due to the guide wire shadow fixing. In contrast, the observers included these areas when they draw the side branch boundaries, so that the ground truth contained the shadow blocked region which resulted in a difference with the algorithmic results. However, these guide wire blocked side branches can still be used as landmarks or awareness of the existence of side branches, but their size is no

reliable for assessment. The other side branch results could be used for precise measurement.

In case the detection result is inaccurate, our prototype system provides a user interface for correction. All the detected side branches are indexed so the user can select or delete any side branch contour. As the 3D contour is generated from side branch edge points in each cross-sectional frame, the corresponding adjustment will be done in the 2D images. After modifying or adding the 2D side branch edge points, a new 3D side branch contour can be generated.

The presented side branch method also has limitations. It depends on the cavity detection in the tissue, but the guide wire, residual blood, plaque rupture, thrombus and calcified nodule also cause cavities and only the guide wire shadows were fixed. In the algorithmic results, we found 60% of the false positives were caused by the residual blood shadow. The remaining 40% of the false positives resulted from the shadows due to air bubbles in the protective sheath. Furthermore, using only distance based detection could also fail to detect some side branches, especially when a stent was present, because the malapposed struts and the tissue coverage may seal side branches. Two of five false negatives in the validation results were almost sealed by dense malapposed struts and very thick tissue coverage. The third false negative was caused by the guide wire shadow which covered the majority of this side branch. Another missed side branch was narrow and almost perpendicular to the scan line from the lumen center, so that the distance between lumen center and the leading-edge of intimal layer did not reveal the existence of this side branch. The last false positive was a tiny side branch on a very big main vessel lumen. Only in one frame, it was 8 degrees wide in circumferential direction. After the normalization, this side branch area shrank and later was removed mistakenly. Poor image quality including residual blood or other artifacts in the side branch area could affect the detection performance as well.

5.6 Conclusion and future work

As IVOCT contributes to clinical researchers and cardiologists by providing a better understanding of the in-vivo artery situation, there are increasing demands of side branch analysis in IVOCT images. In this paper, we presented a fully automated side branch detection method in IVOCT pullback runs based on an image segmentation pipeline including the imaging catheter, the protective sheath, the guide wire and the lumen. The validation showed a good agreement between the algorithmic results and the ground truth which suggested that this method could be used to indicate side branches and assist image registration. The accuracy of the image segmentation for pre-processing also implied that the segmentation results of all the common components in IVOCT images may contribute to accurate IVOCT Z-offset correction, stent strut detection, 3D visualization and many other quantitative analysis applications.

In future, we would like to improve the detection method by adding new false positive filters, using pullback runs acquired with a higher frame rate and utilizing extra information including longitudinal cross-sectional IVOCT images.

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