12 Interpretation of Optical Coherence Tomography: Quantitative Measurement

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Obtaining of good-quality image is essential to make accurate measurements. The image should be correctly calibrated for z-offset, the zero-point setting of the system before measurements. The definition of lesion, reference, and stented segment from the Journal of American College of Cardiology intravascular ultrasound (IVUS) consensus document has been adopted for optical coherence tomography (OCT) [1]. For standardization of OCT measurement, expert review documents and consensus standards have been published previously [2–4]. Studies regarding the accuracy and the reproducibility of qualitative and quantitative OCT measurements have been published previously [5–7].

12.1 Border Identification

The borders of the lumen, external elastic membrane (EEM), internal elastic membrane (IEM), plaque, and stent could be demarcated in OCT cross-sectional images similar to IVUS. In normal vessel without any plaque, OCT may discriminate IEM which is defined as the border between the intima and media and EEM which is defined as the border between the media and the adventitia. Measurements that EEM uses are likely closer to those of IVUS, whereas IEM measurements that use the IEM more closely approximate the pathologic definition of atherosclerosis as a disease of the intima. However, because of low penetration depth and rapid attenuation of its signal, OCT could not visualize IEM or EEM border in most diseased segments. The border measurements should not be made in cross-sectional images that contain artifacts that obscure a significant portion (>90°) of the image or over regions that contain side branches. The differences between OCT and IVUS measurements were demonstrated in Table 12.1 and Fig. 12.1.

12.2 Lesion Assessment

12.2.1 Reference Segment

Reference Assessment *Proximal or distal reference* is defined as the sites with the largest lumen proximal or distal to a stenosis within the same

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Table 12.1 Comparison of major quantitative measurements between optical coherence tomography and intravascular ultrasound

	OCT	IVUS
Lesion		
Lumen area	+	+
Vessel area	−/+	+
Plaque burden	−/+	+
Area stenosis	+	+
Stent		
Stent area	+	+
Vessel remodeling	−/+	+

IVUS intravascular ultrasound; *OCT* optical coherence tomography

segment with no major intervening branches (usually within 10 mm of the stenosis).

Reference Lumen and EEM Assessment *Proximal or distal mean reference lumen diameter* is the mean value of the shortest and the longest lumen diameter through the center of mass of the lumen at proximal or distal reference site. *Proximal or distal mean reference EEM diameter* is the mean value of the shortest and the longest EEM diameter through the center of mass of the lumen at proximal or distal reference site.

Average reference lumen diameter is the average value of mean lumen diameter at the proximal and distal reference sites. *Average reference EEM diameter* is the average value of mean EEM diameter at the proximal and distal reference sites. Both average reference lumen diameter and average reference EEM diameter are useful parameters for stent sizing during PCI.

Average reference EEM CSA, which is a useful parameter for evaluation of lesion severity in terms of stenosis, is the average value of EEM CSA at the proximal and distal reference sites.

Recent in the OPINION study, which had a randomized controlled design to compare the benefit of OCT guidance with IVUS guidance during percutaneous coronary intervention (PCI), OCT reference site was defined as the most normal-looking site with free of lipidic plaque (defined as signal-poor region with diffuse border) at a cross-section adjacent to the target lesion [8]. In other randomized controlled study, the ILUMIEN III: OPTIMIZE PCI study comparing OCT guidance, IVUS guidance, or angiography-guided stent implantation, proximal and distal reference mean EEM diameters and the smaller of these diameters to determine stent diameter or the proximal and distal lumen diameters were used if the EEM could not be visualized [9].

12.2.2 Lesion Segment

Lumen Measurements *Lumen CSA* is the area bounded by the luminal border. *Minimum lumen diameter* is the shortest diameter through the center of mass of the lumen. *Maximum lumen diameter* is the longest diameter through the center of mass of the lumen. *Lumen eccentricity* is calculated as (maximum lumen diameter minus minimum lumen diameter) divided by maximum lumen diameter.

OCT-measured lumen CSA is well correlated with IVUS-measured lumen CSA. In both phantom models and in vivo study comparing quantitative coronary analysis (QCA) for angiography vs IVUS vs OCT measurements, OCT was most precise to the real value, and IVUS measurement was 8% larger than OCT measurement [6]. The mean minimum lumen diameter (MLD) measured by QCA was 5% smaller than that measured by OCT, and the minimum lumen diameter measured by IVUS was 9% greater than that measured by FD-OCT [6].

Previously several studies regarding IVUS criteria for defining the functional significance evaluated with fractional flow reserve (FFR) demonstrated that MLD had a good correlation with the FFR values, but the utility of IVUS MLA as an alternative to FFR to guide intervention in intermediate lesions may be limited in accuracy and vessel dependent [10–13]. Anatomical measurements of coronary stenosis obtained by OCT show significant correlation with FFR. OCT-derived parameters were smaller than those reported in previous IVUS studies (Table 12.2) [14, 15]. Recent study assessing computational fractional flow reserve from OCT in patient with intermediate stenosis showed promising approach of it in assessment not only of anatomic information but also of the functional significance of intermediate stenosis [16].

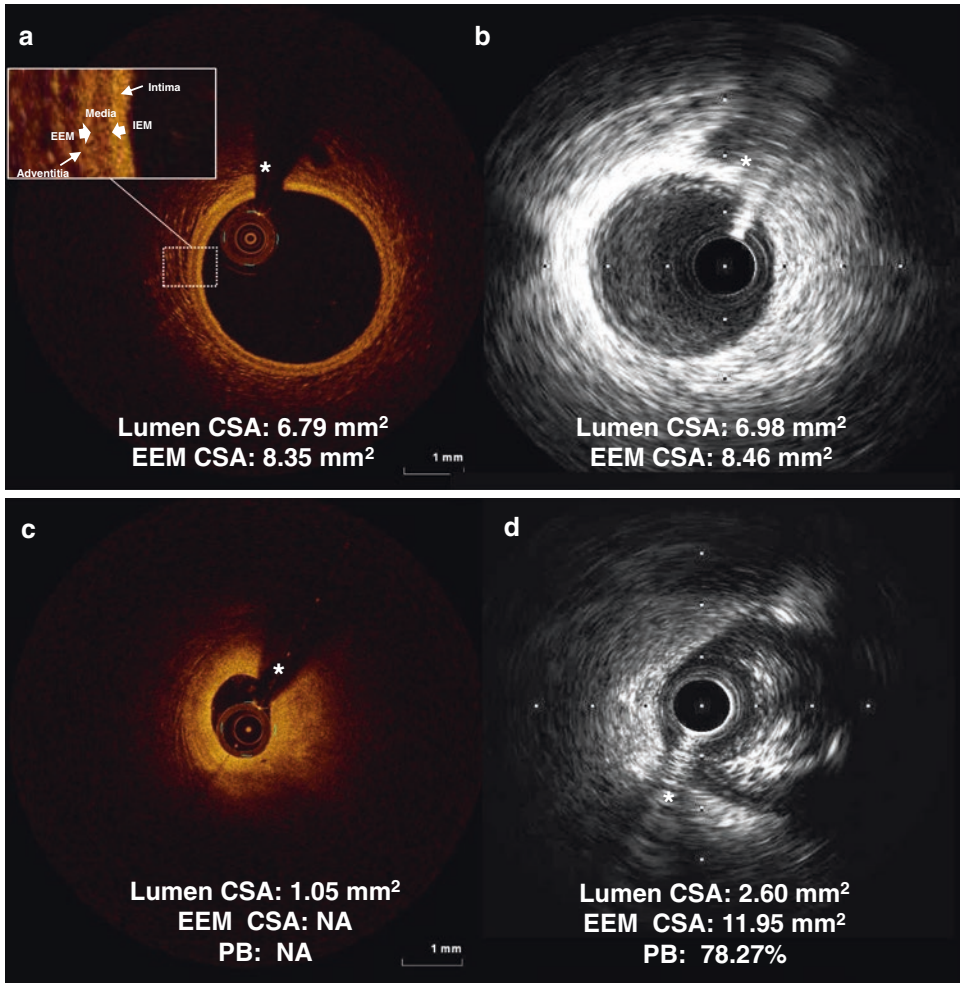

Fig. 12.1 Comparision of border detection between optical coherence tomography (OCT) and intravascular ultrasound (IVUS). Normal artery wall shows a 3-layered architecture, comprising a high backscattering, thin intima, a low backscattering media, a heterogeneous and/or high backscattering adventitia in both OCT (**a**) and IVUS (**b**). OCT could visualize internal elastic membrane (IEM) and external elastic membrane (EEM) (bold arrow heads) (inset, x3). The OCT-derived EEM or IEM measurement could not be made in cross-sectional image that contains diseased vessel (**c**) whereas IVUS demonstrate EEM border well (**d**). * represents wire artifact. *CSA* cross sectional area; *PB* plaque burden

Table 12.2 OCT-derived minimal lumen area predicting for physiologic significance assessed by fractional flow reserve

Study	Patients	FFR value	OCT	IVUS
Gonzalo et al. [14]	61 intermediate lesions in 56 patients	FFR < 0.8	1.95 mm² (AUC, 0.74; 95% CI, 0.61–0.84; sensitivity, 82%; specificity, 63%)	2.36 mm² (AUC, 0.63; 95% CI, 0.47–0.77, sensitivity, 67%; specificity 65%)
Shiono et al. [15]	62 intermediate lesions in 59 patients	FFR < 0.75	1.91 mm² (sensitivity, 94%; specificity, 77%)	NA

AUC area under curve; *CI* confidence interval; *FFR* fractional flow reserve; *IVUS* intravascular ultrasound; *OCT* optical coherence tomography

EEM Measurements *EEM CSA* is the area bounded by EEM border as a surrogated parameter for vessel area. A discrete interface at the border between the media and the adventitia is almost invariably present within OCT images and corresponds closely to the location of the EEM. Because of low penetration depth of OCT signal and rapid OCT signal attenuation within plaque, EEM circumference and area mostly cannot be measured reliably especially in lesion segment. If low signal involves a relatively small arc (<90°), planimetry of the circumference can be performed by extrapolation from the closest identifiable EEM borders, although measurement accuracy and reproducibility will be reduced.

Plaque (or Atheroma) Measurement *Plaque (or atheroma) CSA* is the EEM CSA minus the lumen CSA. *Maximum plaque (or atheroma) thickness* is the largest distance from the intimal leading edge to the EEM along any line passing through the center of mass of the lumen. *Minimum plaque (or atheroma) thickness* is the shortest distance from the intimal leading edge to the EEM along any line passing through the center of mass of the lumen. *Plaque (or atheroma) eccentricity* is calculated as (maximum plaque thickness minus minimum plaque thickness) divided by maximum plaque thickness. If EEM area could not be obtained, plaque measurement is not available.

Plaque Burden *Plaque (or atheroma) burden* is assessed as plaque CSA divided by the EEM CSA. This parameter can only be defined when the EEM can be demonstrated. The plaque burden is distinct from the luminal area stenosis. The former represents the area within the EEM occupied by atheroma regardless of lumen compromise. The latter is a measure of luminal compromise relative to a reference lumen analogous to the angiographic diameter stenosis. If EEM area cannot be obtained, plaque burden cannot be assessed.

Lumen Area Stenosis *Lumen area stenosis* is assessed as reference lumen CSA minus minimum lumen CSA divided by reference lumen CSA.

Plaque Component and Other Measurements The presence of specific component within the plaque or over the plaque, such as calcium, lipid, or thrombus, could be assessed as quantitative measurements like angle, depth, thickness, or area. *Angle or arc* could be measured using the center of mass of the lumen as the angle point. *Depth* is the distance between the lumen and the leading edge of the plaque feature. *Thickness* is usually assessed as the thickest distance between the inner and outer surfaces of the plaque component (valid only if the deep boundary can be identified). *Area* of some component could be described as the CSA of the plaque component (valid only if the deep boundary can be identified).

Fibrous cap thickness can be measured by the thickness of a cap present over OCT-delineated lipid or necrotic core either at the single cross-section where the fibrous cap thickness is considered minimal or from multiple samples (three or more). Although studies have been performed to compare the OCT measurement of fibrous cap thickness with histologic measurements of cap thickness, it was generally considered that this area needs further validation, as the boundary between the cap and the necrotic core is not always straightforward to precisely determine.

Remodeling An index of remodeling can be assessed as lesion EEM CSA/reference EEM CSA, if the EEM CSA is identified in OCT image.

Because of its limited tissue penetration, OCT does not appear to be suited to study vessel remodeling.

12.3 Stent Measurements

OCT has been considered as an useful intracoronary imaging modality for the lesion assessment, stent sizing, and stent optimization during PCI (Figs. 12.2 and 12.3). The Clinical usefulness of OCT-guided PCI will be discussed in next chapter (Chap. 13).

OCT is capable of visualizing the vascular response between stent strut and vessel wall, and

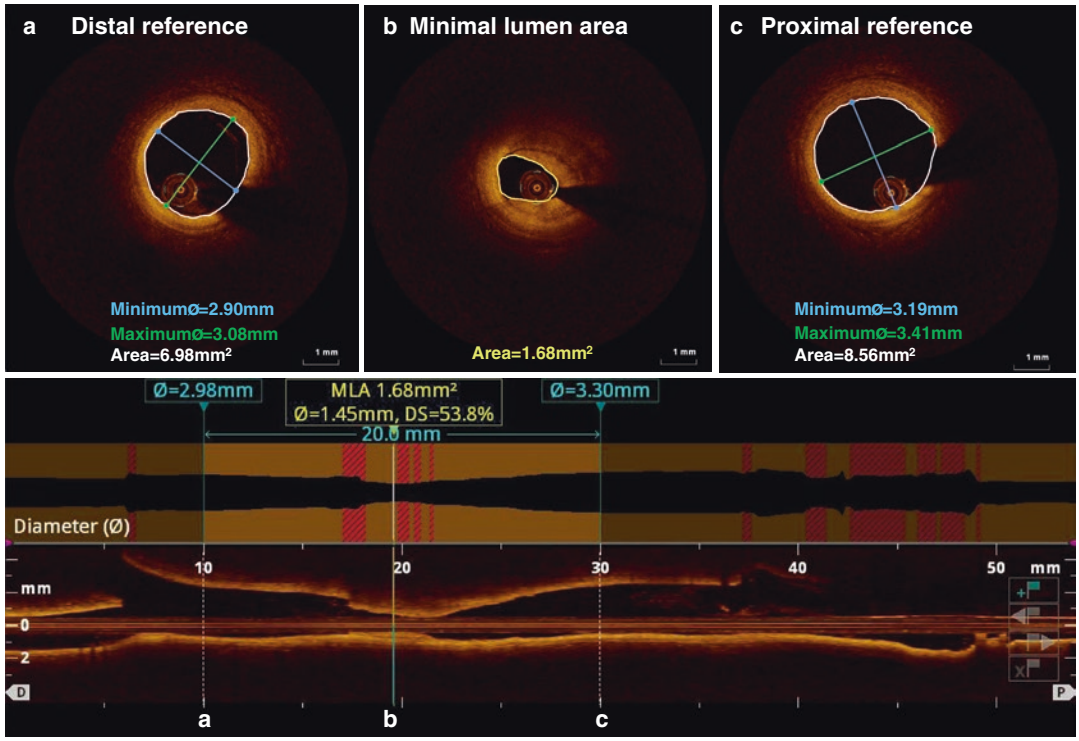

Fig. 12.2 Pre-percutaneous coronary intervention optical coherence tomography measurements. Both proximal and distal reference was obtained at normal looking segments from longitudinal and cross-sectional images. Mean reference lumen diameter (ø) was assessed from the each cross-sectional images (**a** and **c**) and the lesion length was the distance between proximal and distal reference segments. Minimum lumen area (*MLA*) was measured by detection of lumen border at the most narrowest site (**b**)

identifying tissues surrounding stent struts. Most metallic stent struts have strong reflection to optic signal creating a bright hyperintense signal at the surface of strut (blooming appearance) with a shadow that obscures deeper structure within the vessel. The polymeric struts of bioabsorbable vascular scaffolds are transparent to the optic signal, allowing visualization of the vascular wall structure behind the struts without shadowing (Fig. 12.4).

Strut assessment is limited by the axial resolution of the OCT system, and OCT could not allow the visualization of a single layer of endothelial cells. Furthermore the biological and clinical significance of some OCT-derived stent measurements within stent segment has not been fully understood. Recently a retrospective data evaluating OCT measurements to predict very late stent thrombosis demonstrated that malapposition, neoatherosclerosis, uncovered struts, and stent underexpansion, without differences between patients treated with early- and new-generation drug-eluting stents, were leading OCT findings associated with very late stent thrombosis in descending order [17].

12.3.1 Stented Segment

Stent Area Measurements *Stent CSA* is the area bounded by the stent border. *Minimum stent diameters* are the shortest diameter through the center point of the stent. *Maximum stent diameters* are the shortest and the longest diameter through the center point of the stent. *Stent eccentricity (symmetry)* is calculated as (maximum stent diameter minus minimum stent diameter) divided by maximum stent diameter.

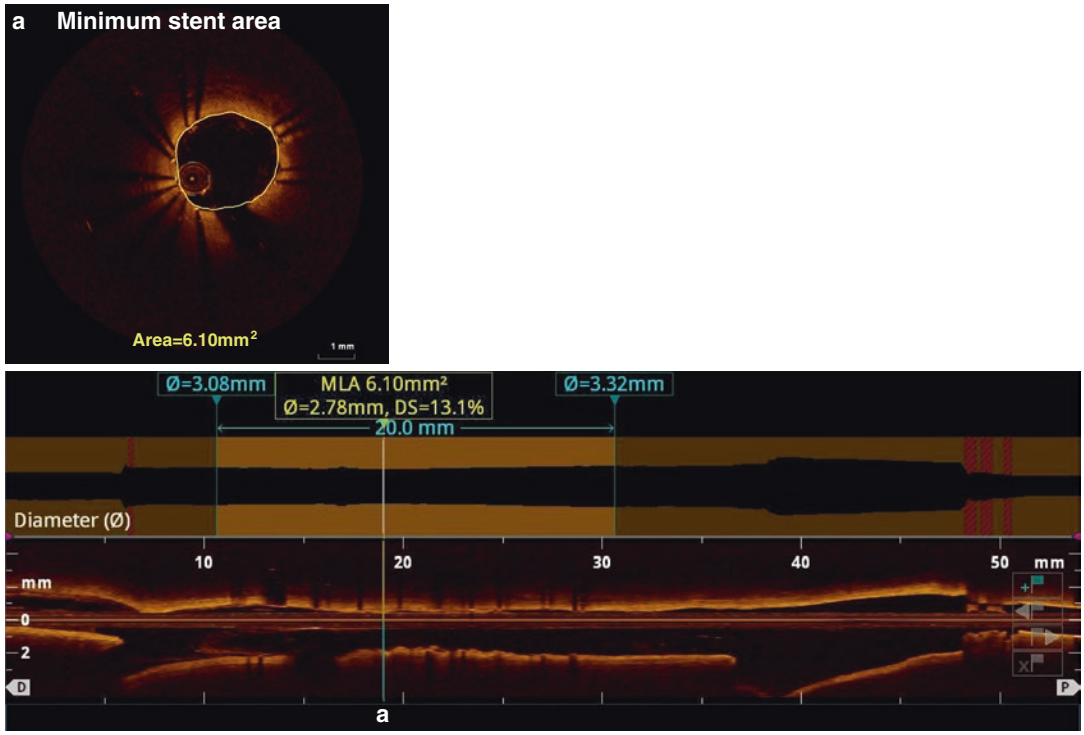

Fig. 12.3 Post-percutaneous coronary intervention optical coherence tomography measurements. The minimum stent area was obtained by detection of stent border at the most narrowest cross-sectional area (a). *MLA* minimum lumen area

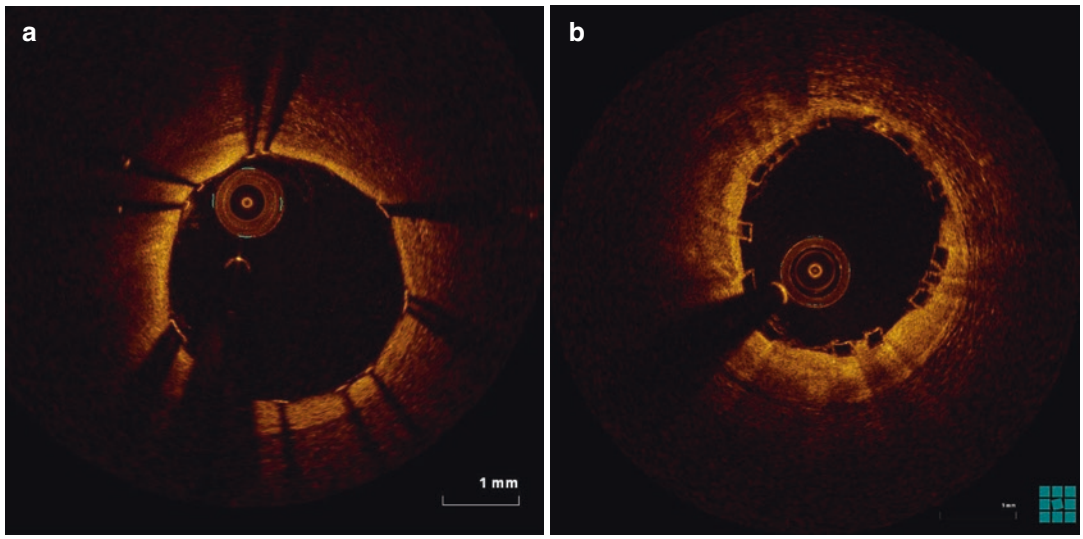

Fig. 12.4 Comparison of stent struts detection between metal stent and bioabsorbable vascular scaffolds (BVS) assessed by optical coherence tomography. Metallic drug eluting stent struts have strong reflection to optic signal creating a bright hyper-intense signal at the surface of strut (blooming appearance) with a shadow that obscures deeper structure within the vessel (**a**). BVS are transparent to the optic signal, allowing visualization of the vascular wall structure behind the struts without shadowing (**b**)

Stent expansion is calculated as the minimum stent CSA compared with the predefined reference area which can be the average reference lumen area or EEL area if possible. An underexpanded stent has an in-stent minimal lumen area less than 90% of the average reference lumen area. In the CLI-THRO study, which compared OCT parameters between in patient with subacute stent thrombosis and in those without, stent thrombus group had smaller OCT stent CSA (5.6 ± 2.6 vs 6.8 ± 1.7 mm^2, $p = 0.03$) and higher incidence of stent underexpansion (42.8% vs 16.7%, $p = 0.05$) when compared with control group [18].

12.3.2 Stent Strut Measurements

OCT has been considered as the most useful intracoronary imaging modality to assess immediate- and long- term vascular response after stent implantation. Stent strut measurements can be obtained at a cross-section level or can be evaluated at the strut level analysis. (Fig. 12.5). The assessment of stent struts requires strict interval ranging from every 0.5 mm to 1 mm to obtain high rate of reproducibility. Stent strut maps can be computed with the *x* axis representing the length of the stent (millimeters) and the *y* axis representing the circumference (0–360°).

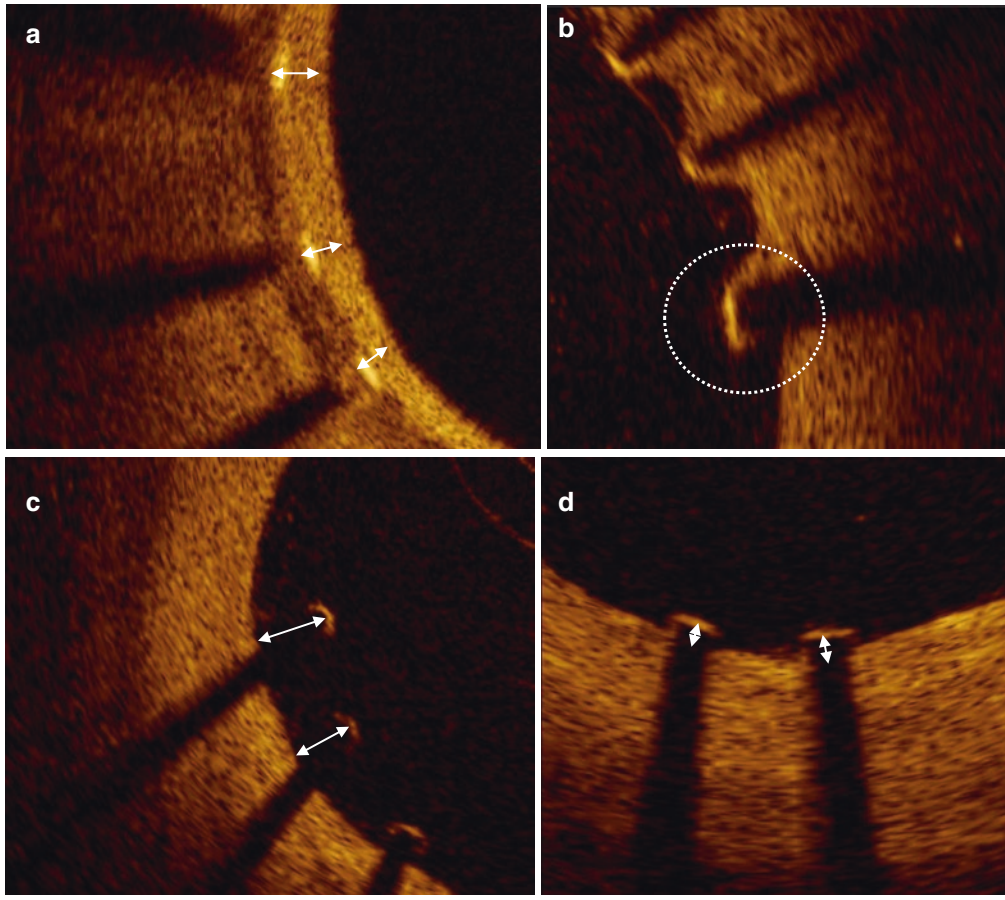

Fig. 12.5 Example of stent strut coverage and apposition assessment. (**a**) shows three covered struts and (**b**) represents an uncovered strut. In (**c**) and (**d**) examples of malapposed and apposed struts are, respectively, presented

A contour plot optical coherence tomography analysis for evaluating stent strut may provide more useful information to understanding the serial changes in strut coverage [19].

Stent Apposition Incomplete stent apposition or malapposition occurs if there is a separation of a stent strut from the vessel wall. Malapposition is defined as a measured distance greater than the strut thickness for stent materials (metal or metal plus polymer). *Malapposition distance* could be measured as the distance between the luminal surface of the covering tissue and the luminal surface of the strut. The area between the endoluminal midpoint of the struts and the vessel wall was measured as *malapposition area*.

Acute, late-persistent, and late-acquired stent malapposition assessed by OCT has relatively high incidences, but their clinical importance and the mechanism have been shown different. The clinical outcome of acute malapposition is favorable, but late malapposition has been considered as a predictor of stent thrombosis [20].

Strut Coverage and Neointima Measurements *Strut coverage thickness* is the distance between the luminal surface of the covering tissue and the luminal surface of the strut. *Percentage of uncovered stent struts* is calculated as the number of struts without distinct overlying tissue, in which the luminal reflection of the strut surface is directly interfacing with the lumen, divided by total number of analyzable struts.

Variable thickness of stent struts which consisted of metal and polymer should be considered to determine whether struts are "covered" or "uncovered." OCT cannot visualize a single layer of endothelium over the strut, or it does not demonstrate accurate nature of tissue. In a case-controlled study, the presence of uncovered stent struts assessed by OCT was associated with late stent thrombosis after DES implantation [21]. Won et al. showed that the best cutoff value of percentage of uncovered struts for predicting major safety events (a composite occurrence of cardiovascular death, myocardial infarction, and stent thrombosis) was 5.9% using the maximal χ [2] method (area under the receiver-operating characteristic curve, 0.779; 95% confidence interval, 0.648–0.910; $p = 0.019$, a sensitivity of 83.3% and a specificity of 70.3%) [22].

Neointima area is defined as stent CSA minus lumen CSA. *Percent neointima area* is defined as (neointima area divided by stent CSA) X 100. The qualitative assessment of the neointima pattern is assessed at the site of the largest cross-sectional area of neointima within stent. OCT has been considered as the best tool to evaluate tissue characterization of neointima, and it also could discriminate neoatherosclerosis from intimal hyperplasia by OCT qualitative measurements.

The rates of stent strut coverage or the characteristics of neointima assessed by OCT surveillance differed according to stent type. The clinical implications of these differences require further study but may imply on the differences in rates of stent thrombosis observed in clinical trials with different stent types [23–26].

12.4 Length and Volume Measurements

OCT image acquisition is performed using motorized transducer pullback commonly at 100 frames/s with an automatic pullback speed of 20 mm/s. Longitudinal view is obtained automatically, and length measurements can be assessed from longitudinal view or calculated as the number of seconds by the pullback speed. This approach can be used to determine the length of a lesion, stenosis, stent, or any other longitudinal features (calcium, lipid, thrombus, etc.). OCT offered more accuracy than IVUS in longitudinal geometric measurement of coronary artery [27].

Lesion length is determined as the distance from distal to proximal reference site using the OCT automated lumen detection feature. Stent length is determined as the distance from distal to proximal edge of stent using the OCT automated lumen detection feature. Length measurements

of any longitudinal features can be performed using motorized transducer pullback (number of seconds x pullback speed).

Volume measurements are calculated by Simpson's rule and area measurements from every single frame usually at 0.5–1 mm.

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