Review of Intravascular Optical Coherence Tomography in Clinical Practice of Coronary Interventions

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Abstract

Optical coherence tomography (OCT) is an imaging modality that provides high resolution of intravascular tissue microstructure for coronary intervention. OCT is now widely applied to clinical scenarios of coronary artery disease, including the assessment of plaque and thrombi characteristics, lesion preparation strategy, stent optimization, and for decreasing complications post stent deployment. Accumulating data support the clinical role of OCT in assisting intervention decision-making. In this study, we comprehensively review the published data and provide a practical approach to OCT-guided percutaneous coronary intervention in coronary intervention practice.

Keywords: optical coherence tomography, coronary artery disease, intracoronary imaging

INTRODUCTION

Optical coherence tomography (OCT) is a method of obtaining tomographic images based on the coherence of near infrared light. Two Japanese researchers, Naohiro Tanno and James G. Fujimoto, developed OCT around 1990. In vitro observation of the retina and coronary artery was first performed in 1991.[1,2] OCT and intravascular ultrasound (IVUS) are two commonly used intravascular imaging modalities. Acknowledging that IVUS was developed earlier in the late 1980s, published data on OCT in coronary intervention is much less than that on IVUS. In the past, time-domain OCT (TD-OCT) required balloon occlusion and a complex procedure to obtain the image. Since the development of new generation OCT systems implementing frequency-domain OCT (FD-OCT) imaging methods, the previous limitations of time-domain OCT have been overcome.[3] FD-OCT has now been increasingly used in biomedical research and clinical practice for over two decades.

Although FD-OCT has markedly improved intracoronary image resolution as compared to IVUS, there are clear differences between OCT and IVUS. OCT has advantages in resolution, surface detail, automatic and fast-pullback system, while IVUS is better in penetration, media-to-media sizing and is a simultaneous real-time system.[4] For intervention cardiologists, the question of which image modality is better may

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be too simple; what matters is whether IVUS or OCT is more suitable and which one provides more significant assistance for decision-making in our cases. In this study, we review the definitive data of intravascular OCT in clinical applications, including image interpretation, diagnosis, lesion preparation, stent optimization, and the assessment of complications post stent deployment.

Image Interpretation of OCT

The coronary artery appears on OCT as a concentric three-layered structure, including (1) Internal elastic lamina: inner high-signal and 20-mm in thickness; (2) Medial layer: middle low-signal dark band; and (3) External elastic lamina: outer high-signal band (Figure 1A).[5] An atherosclerotic lesion on OCT appears as a segmental intimal thickening or loss of the normal arterial structure.

Atherosclerotic plaques can further be differentiated into three major kinds of plaques by OCT, including (1) Fibrous plaque: homogenous, brighter, lower attenuation signal (Figure 1B); (2) Calcified plaque: heterogeneous, darker, sharp edge, low attenuation signal (Figure 1C); and (3) Lipid-rich plaque: homogenous, darker, diffuse borders and high attenuation signal (Figure 1D).[6] Since the resolution of OCT (10–20 μm) is 10-times higher than that of IVUS (100–150

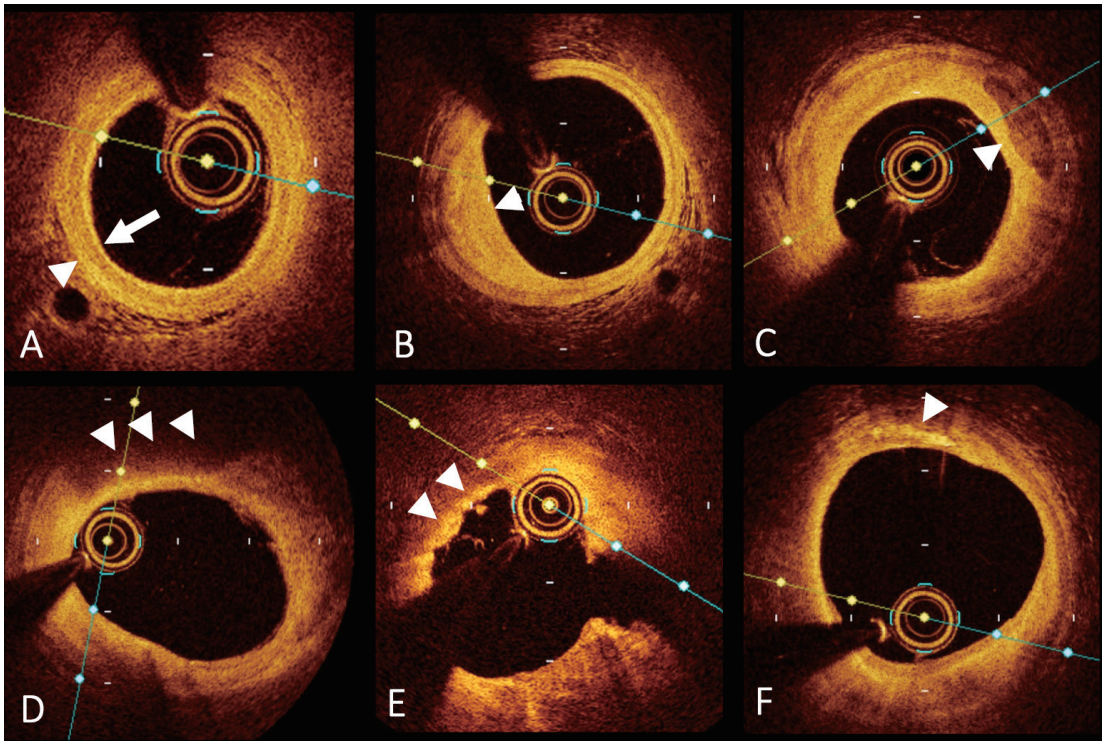

Figure 1. Normal coronary structure and different characteristics of plaques on OCT.
(A) 3-concentric layered structure of coronary artery. Internal elastic lamina *(white arrow)* is the inner layer with high-signal; External elastic lamina *(white arrow head)* is the outer layer with high signal; the middle low-signal dark band is the media layer. (B) Fibrous plaque *(white arrow head)* has homogenous, brighter, lower attenuation signal. (C) Calcified plaque *(white arrow head)* has heterogeneous, darker, sharp edge, low attenuation signal. (D) Lipid-rich plaque *(white arrow head)* has homogenous, darker, diffuse borders and high attenuation signal. (E) Macrophages *(white arrow head)* are punctate high-signal spots accumulated at the edge of necrotic core. (F) Cholesterol crystals *(white arrow head)* are very high-signal, high-scattering, linear structure associated with a lipid pool.

μm), macrophages and cholesterol crystals can be detected by OCT. Macrophages (Figure 1E) are punctate high-signal spots which sometimes accumulate at the border of the fibrous cap and necrotic core. Cholesterol crystals (Figure 1F) are very high-signal, high-scattering, linear structures associated with a lipid pool.[6]

Thin-cap fibroatheromas (TCFAs), defined as fibroatheroma with thin fibrous cap of < 65 μm, are the vulnerable plaque prone to rupture and highly implicated in acute coronary syndrome in autopsy studies.[7-9] OCT now makes it possible to measure the fibrous cap thickness exactly with an online image.[10] Patients with ACS have a higher proportion of OCT-TCFAs, which have thinner fibrous caps than those in non-ACS patients.[11,12] In patients with ACS, OCT-TCFAs are more commonly found in the proximal segments of the culprit vessel.[10,13] There is not yet enough evidence for an exact cutoff-value on OCT for the thickness of the fibrous cap or the lipid pool arc, to directly reflect clinical events. Further OCT studies are required to investigate the natural development of these vulnerable plaques in patients with ACS.

In acute coronary syndrome, OCT can also differentiate red or white thrombus as follows: (1) Red thrombi (Figure 2A) are identified by their low birefringence, and high attenuation protrusions

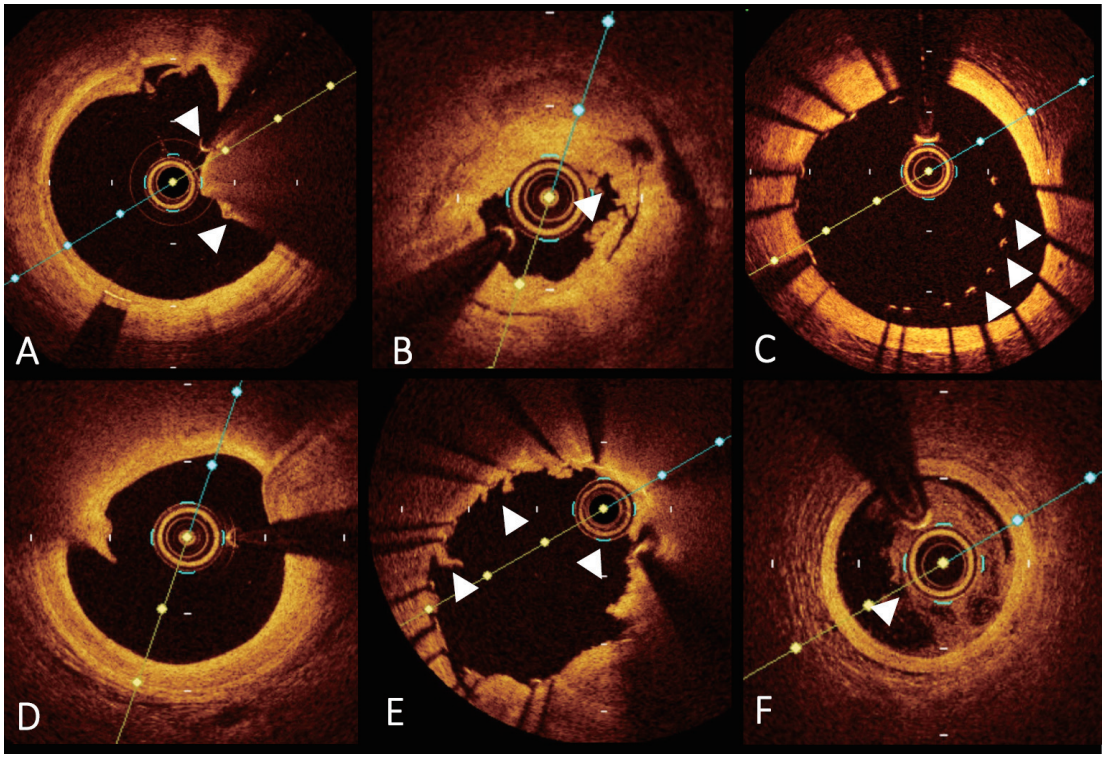

Figure 2. Assessment of intravascular thrombosis and complications post stent deployment assessment by OCT.
(A) Red thrombus *(white arrow head)* is acute and red blood cells rich, which has low birefringence, high attenuation signal on OCT. (B) White thrombus *(white arrow head)* is relative chronic and platelet rich, which has high birefringence, low attenuation signal on OCT. (C) Stent malapposition means stent struts *(white arrow head)* are not attached to the Internal elastic lamina of vessel wall. (D) OCT can detect edge dissection *(white arrow head)* in good sensitivity. (E) Tissue protrusion *(white arrow head)* can be easily detected by OCT. (F) Red blood cells *(white arrow head)* in the vessel inner lumen will interfere image interpretation of OCT.

inside the lumen of the artery. These are relatively acute and contain a high proportion of red blood cells. (2) White thrombi (Figure 2B) are of high birefringence and low attenuation. They are relatively chronic and platelet-rich. While there is no significant difference in peak intensity of OCT signal, the 1/2 attenuation width of the signal intensity curve is significantly different between red and white thrombi. The cut-off value of 250 μm can differentiate white from red thrombi with a sensitivity of 90% and specificity of 88%. Optical coherence tomography may allow us not only to estimate plaque morphology but also to distinguish red from white thrombi.[14]

OCT GUIDANCE of PCI

Lesion Preparation

Lesion preparation is the most important step to avoid stent under-expansion and to decrease peri-procedure complications. As interventional cardiologists treat more and more complex lesions today, intravascular image assistance is more commonly used in complex procedures. Different types of plaques detected by OCT may lead to different strategies for lesion preparation.[15] As mentioned before, a large lipid burden and TCFA are more vulnerable, and have a stronger relationship with peri-procedural myocardial infarction (MI).[16,17] Therefore, undersized balloon inflation or direct stenting can reduce the infarction rate in these lipid-rich plaques. This inference was proven in the ILUMIEN I study. Rates of clinically significant peri-procedural MI were found to be different when procedural changes were made based on pre- and post-PCI OCT (P = 0.029). The overall rate of in-hospital MI was 6.9% by Academic Research Consortium and 6.4% by Universal MI definitions.[18]

Calcium has always been the worst enemy of the interventionist. Calcium impedes stent crossability, expansion, embedment, and coverage.[19,20] Among these, stent expansion is the single most important parameter related to clinical outcomes.[21] Aggressive non-compliant balloon pre-dilatation, a cutting / scoring balloon, or atherectomy device should be considered in calcified or undilatable plaques. OCT and IVUS both have high sensitivity for detecting the calcification arc. OCT can more precisely determine the calcium thickness and depth than IVUS.[22,23] Non-compliant balloon inflation can be first considered in wide arc, low thickness, or deep calcium plaque on OCT (with cutoff values of < 227-degree calcium arc and <0.67 mm in thickness, respectively) to induce calcium fracture.[23] Instead, rotational atherectomy should be chosen directly in superficial circumferential calcification (> 227-degree calcium arc). If the stenotic lesion is still undilatable after non-compliant balloon or if the calcium thickness is too high, cutting or scoring balloons can make the incisions at the edges between calcified and non-calcified components to improve vessel compliance under controlled dissection.[23] Prospective studies are needed to determine whether OCT-guided lesion preparation for calcified plaque would improve clinical outcomes or not.[18]

Stent Optimization

Stent optimization is determined by vessel size measurement, stent selection, landing zones and post-dilatation. FD-OCT can measure the vessel size automatically by the clear border between the lumen and vessel wall. While vessel linear dimensions are overestimated by IVUS by about 10% in the phantom model, FD-OCT measurement is closer to the actual size.[24]

Unlike IVUS, there is still no well-established method for stent sizing with OCT. The low-depth penetration of light through lipid-rich plaque results in an inability of OCT to visualize the external elastic lamina (EEL) at the lesion site in some cases. Most previous OCT studies have thus used luminal dimensions for selection of stent size, not the external elastic lamina.[18,25] In the ILUMIEN II study, the post hoc retrospective analysis between the ILUMIEN I and ADAPT-DES study, optical coherence tomographic

guidance resulted in similar stent expansion but a smaller final minimal stent area (MSA) compared with IVUS guidance.[26] In the OPINION trial, OCT also led to smaller stent diameter (2.92 ± 0.39 mm^2 vs. 2.99 ± 0.39 mm^2; $p < 0.005$) and post-procedural MSA (5.17 mm^2 [IQR: 4.06 to 6.29] vs. 5.63 mm^2 [IQR: 4.76 to 7.52]; $p = 0.088$) than did IVUS.[25] The ILUMIEN III study conducted a novel EEL-based OCT-guided sizing strategy to overcome the shortage: it measured the proximal and distal reference mean EEL diameters and used the smaller of these diameters rounded down to the nearest 0.25 mm to determine stent diameter. If necessary, high pressure or larger non-compliant balloon inflations can be used to achieve at least acceptable stent expansion (a MSA of at least 90% in both the proximal and distal halves of the stent relative to the closest reference segment). Under this strategy, Post-PCI MSA achieved after OCT-guided PCI was non-inferior to that achieved with IVUS-guided PCI. Both OCT and IVUS resulted in better post-PCI MSA compared to angiography guidance. OCT guidance led to less major stent malapposition than both IVUS guidance and angiography guidance.[27] Thus, whether OCT guidance of stent implantation can achieve similar luminal dimensions as IVUS guidance or not remains unclear. This may depend on the different strategy of inner lumen-based or EEL-based OCT-guided stent sizing. Further large studies are needed to investigate whether OCT guidance results in better clinical outcomes than does IVUS guidance or angiography guidance.

Safe landing zone is difficult to decide or easy to miss on long diffuse plaque by angiography alone. High resolution intravascular image by OCT can prevent stent landing in eccentric calcium or lipid-rich plaques, which is useful to prevent edge dissections or longitudinal geographic miss. The fast pullback OCT acquisition system makes precise stent length measurements because it is less susceptible to heart movements. Integration of real time angiographic co-registration (ACR) with OCT is feasible now. This OCT-ACR integrated system may reduce human errors in corresponding OCT findings to the angiogram. In the Doctor fusion study, the OCT-ACR system reduced the number of implanted stents through improved sizing and positioning.[28] Future studies are needed to compare or combine the OCT guided anatomic lesion length with the FFR guided "physiological" lesion length to optimize the stent selection. Real time OCT-ACR integrated system can also quickly identify under-expanded stent struts automatically. This function can avoid unnecessary post-dilatation and over-dilatation of stent struts, thus decreasing peri-procedural complications.[29]

Post Stent Deployment

Intravascular images are widely used after stent deployment for early detection and prevention of clinical events. Stent malapposition, stent edge dissection and tissue protrusion can be visualized in detail by OCT. The relationship of these findings to subsequent adverse events and how they should be managed remains uncertain.[30] The ongoing ILUMIEN IV study will help determine whether correction of post-deployment findings will translate to fewer stent-related adverse events.

Stent malapposition (Figure 2C), which is most frequently observed at stent edges, may be related to stent/vessel size or contour mismatch.[31] Some cases of stent malapposition can be resolved by time with re-endothelialization. While multiple factors will affect endothelium healing after stenting (i.e., stent design, strut thickness, types of polymer, underlying plaque morphology), there is no consensus on the maximum distance between stent struts and vessel lumen that can be associated with endothelialization or adverse events.[32,33]

Intravascular OCT has a very high sensitivity for stent edge dissections (Figure 2D) and operators should not over-react to it. Most of the "minor" edge dissections without flow limitation can be healed without clinical events.[34] In the CLI-OPCI II study, "major" stent edge dissections detected by OCT > 200 μm were independent predictors of MACE (composite of all-cause

death, MI, and target lesion revascularization, Hazard ratio 2.54, p = 0.004).[35] Operators should be prepared to treat this degree of edge dissection or if complicated with intramural hematoma to avoid vessel collapse.

Tissue protrusion (Figure 2E) detected by IVUS is reported to be associated with poor short-term outcomes, including no-reflow phenomenon, peri-procedural MI, and stent thrombosis.[36] High resolution OCT can identify tissue protrusions with unprecedented precision.[37] Tissue protrusion can be categorized into 3 groups, including (1) smooth protrusion: minimal vessel injury, (2) disrupted fibrous tissue protrusion: mild vessel injury, and (3) irregular protrusion: moderate to severe vessel injury with a high likelihood of medial disruption and lipid core penetration. Only irregular protrusion was an independent predictor of device-oriented clinical events and target lesion revascularization in a large cohort study.[38]

NOW and FUTURE

Special Considerations

Bioresorbable Vascular Scaffold

Bioresorbable vascular scaffold (BVS) is a newly emerging stent technique in recent decades. However, improper implantation of current-generation BVSs is associated with a higher risk of scaffold thrombosis. These improper implantations include malapposition, underexpansion, and incorrect sizing.[39] For the best possible results with BVS, PSP technique is highly recommended: Predilatation adequately, Sizing scaffold correctly, and Post-dilation to avoid underexpansion.[40] Hence, the use of an intravascular imaging tool, and especially OCT, should be mandatory in BVS implantation. As mentioned, the automatic measurement and high-resolution OCT image can provide significant assistance for lesion preparation and stent optimization. Additionally, only OCT can grant clear visualization of the vascular scaffold structure to evaluate scaffold fracture, endothelium healing, scaffold bioresorbing process, edge dissection, and malapposition in post-implantation assessment.[41]

Bifurcation Lesion

Bifurcation lesions are one of the major complex coronary interventions, related to higher rates of in-stent restenosis and stent thrombosis.[42] While provisional single-stenting is now the most recommended strategy, two-stent strategy is still required for some complex bifurcation lesions.[43] Understanding the bifurcation anatomy, including carina angle, vessel size discrepancy and plaque location, is a significant step in determining the intervention strategy. Online 3-dimensional reconstruction of the intravascular image by OCT is very helpful for the intervention cardiologist to understand the bifurcation structure.[44,45] Automatic stent strut detection systems are also effective in evaluating the points of wire re-crossing through the main stent struts, the size and shape of side branch openings, and the stent design integrity.[46] These are the key factors to optimize the kissing balloon technique in bifurcation stenting, which lead to favorable outcomes.

Limitations of OCT

OCT facilitates the precise visualization of vessel anatomy and plaque morphology. Its ability to determine plaque vulnerability (i.e., thin-cap fibrotic atheroma, high-attenuation plaque, and macrophage accumulation) is helpful in deciding a PCI strategy in high-risk patients.[47] However, OCT has some limitations including low tissue penetration, blood clearance and uncertain physiological significance.

The low tissue penetration (1 to 2 mm) of current OCT systems is a major limitation. Assessment of plaque volume or visualization of plaques in the deep layers of the vessel wall may not always be feasible by OCT, especially when there is a large plaque burden. As mentioned, lipid-rich plaque and red thrombus can cause signal attenuation which can obscure the EEL of the vessel wall.[48]

Since OCT image acquisition requires

contrast to achieve blood clearance, poor blood clearance by the contrast will result in a poor OCT image (Figure 2F), which is difficult to interpret. Although it may be feasible to use non-contrast flush media to clear blood, renal function deterioration should be monitored in patients with advanced chronic kidney disease. Because of the blood clearance issue and low tissue penetration, OCT is not recommended in aorto-ostial lesions, large left main body and distal small vessels.[49]

In the ILUMEIN I study, pre-procedural OCT evaluation of the MLA with a cut-off value of 1.6 to 1.9 mm^2 is modest, correlated with FFR and impacts physicians' PCI decision-making strategy.[18] Although OCT-derived MLA has high positive physiological predictive value (80 to 92%) with FFR, the decision whether to perform PCI based on OCT-derived MLA alone is not recommended due to lower negative predictive value for physiological significance (66 to 89%).[50,51] These limitations should be taken into account to avoid misleading interpretation and unnecessary procedure.

Future Directions

OCT is a relatively new imaging modality, with fewer data on its use in PCI compared with IVUS.[24,49,52] Large-registry data in percutaneous coronary intervention (PCI) have raised questions regarding the clinical significance of the detailed findings on high-resolution imaging by OCT, highlighting the paucity of data from prospective clinical trials.[30] In the future, OCT will also be able to accumulate a tremendous amount of evidence and have more quantitative metrics like IVUS. We believe that intravascular OCT should position itself as a peri-procedural tool to take full advantage of its superior plaque characterization, ACS applications, stent planning, and volumetric lumen segmentation for stent optimization. Real time angiographic co-registration with OCT has made precise "anatomical" evaluation more feasible for stent optimization. In the future, OCT may be combined with simultaneous "physiological" assessment to optimize the treatment strategy. Whether optical coherence tomography guidance for PCI results in improved clinical outcomes compared with angiographic guidance alone will be addressed in the large-scale multicenter randomized ILUMIEN IV trial.

CONCLUSION

OCT provides a detailed coronary intravascular image of anatomical findings and potential pathological changes. It has unrealized potential for applications in the diagnosis and treatment of coronary artery disease. Systematic efforts to educate the interventional cardiology community about the appropriate use of OCT and the demonstration of improved clinical outcomes from randomized trials are required to further integrate this novel modality into clinical practice.

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