Application of Optical Coherence Tomography in Percutaneous Coronary Intervention

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Optical coherence tomography (OCT) is a high resolution imaging technique that offers microscopic visualization of the coronary artery. The fast scanning speed and simple imaging procedure of new-generation frequency-domain OCT make this technology easy to use in the clinical setting. The OCT examination is useful for guidance and risk stratification of percutaneous coronary intervention (PCI). OCT-derived thin-cap fibroatheroma, which is characterized by large lipid-core and thin fibrous cap <65 μm, is a predictor of peri-PCI complications, such as angiographic no-reflow, microvascular obstruction, and post-PCI cardiac troponin I elevation. Stent malapposition, tissue protrusion, and stent edge dissection are assessed in more detail by OCT than with conventional intravascular imaging modalities. Neointimal coverage at strut level assessed by OCT could be a surrogate endpoint for quickly scrutinizing safety after drug-eluting stent implantation. The OCT findings of in-stent neoatherosclerosis, such as lipid-rich neointima, microvascular proliferation, and neointimal plaque rupture, are associated with very late stent failure, including thrombosis and restenosis. With its excellent ability to assess coronary atherosclerosis and to guide PCI, OCT provides new insights into interventional cardiology. (Circ J 2012; 76: 2076–2083)

Key Words: Drug-eluting stents; Optical coherence tomography; Percutaneous coronary intervention

OCT System and Technique

The OCT system consists of a light source, reference mirror, and photodetector. Compared with the initial time-domain (TD) OCT, newer generations of intravascular OCT systems, termed frequency-domain (FD) OCT, use a fixed mirror with a variable frequency light source, which makes image acquisition significantly faster. The pullback speed of the OCT catheter is up to 20 mm/s, and the scanning length reaches 50 mm. In addition, FD-OCT imaging can be achieved during contrast injection from a guiding catheter (<15 ml, 3–4 ml/s). The fast scanning speed of FD-OCT could be related to its clinical utility and patient safety. FD-OCT has a shorter procedure time and less ischemic symptoms during OCT image acquisition as compared to TD-OCT.

Quantitative Measurements

OCT provides robust and reproducible measurements of the vessel lumen. The high resolution of OCT images allows accurate recognition of the luminal boundary. When OCT was performed in a plexiglass phantom manufactured with a precision of 10 μm, the OCT measurement correlated extremely well with the real luminal dimension (relative standard deviation 1.8%, r=1.000, slope 1.02). In addition, the correlation between the measurements of OCT and IVUS was highly significant (R²=0.82, P<0.001). However, the luminal area measured by OCT seems to be smaller than that with IVUS, and the relative difference is approximately 11%–22%. The difference between the 2 methods could be related to the specific backscattering of either light or sound. The recognition of the luminal boundary might be inherently different because of the physical characteristics of the wave length used by these technologies. Moreover, the Z-offset, which is a manually adjustable calibration of OCT, is critical for accurate measurements. A 1% change in the magnitude of the ideal Z-offset can result in a 12–14% error in area measurements by OCT. The measurement bias in OCT may influence the assessment of lesion severity and device selection for PCI.
Pre-PCI Lesion Assessment

Plaque Characterization
OCT can discriminate 3 types of atherosclerotic plaque: fibrotic plaque, fibrocalcific plaque, and lipid plaque. Fibrous plaque is characterized by a homogeneous signal-rich region, fibrocalcific plaque by a signal-poor region with a sharp border, and lipid-rich plaque by a signal-poor region with a diffuse border. In the assessment of unstable plaque, OCT can detect plaque rupture, erosion, and intracoronary thrombus. Moreover, the high resolution of OCT has the potential to identify thin-cap fibroatheroma (TCFA), which is characterized by a large lipid-core and a thin fibrous cap (<65 μm).

Prediction of Peri-PCI Complications
OCT-derived TCFA is a predictor of peri-PCI complications. Tanaka et al investigated whether OCT could predict no-reflow after PCI in patients with acute myocardial infarction. OCT-derived TCFA was more often observed in the no-reflow group than in the reflow group (50% vs. 16%, P=0.005). The frequency of the no-reflow phenomenon increased according to the size of the lipid arc in the culprit plaque. Ozaki et al assessed whether OCT-derived TCFA was associated with microvascular obstruction after PCI in patients with acute coronary syndrome. OCT-derived TCFA was more frequently detected in patients with microvascular obstruction as estimated by magnetic resonance imaging (43% vs. 9%, P=0.012). The prevalence of microvascular obstruction increased as cap thickness decreased. Lee et al used OCT to study the relationship between pre-PCI plaque morphology and post-PCI cardiac troponin I elevation. OCT-derived TCFA was associated with post-PCI cardiac troponin I elevation and the presence of OCT-derived TCFA was an independent predictor of post-PCI myocardial infarction (odds ratio, 10.47; 95% confidence interval, 3.74–29.28; P<0.001). These results support OCT as a useful tool for risk stratification of PCI.

Microchannels in Chronic Total Occlusion
Chronic total occlusion consists of various degrees of fibroatheromatous plaque and thrombus. When the fibrous occlusion is densely organized and homogeneous, guidewire passage is less successful. On the other hand, endothelialized microchannels that traverse the occlusion increase the likelihood of passage with low-profile guidewires. OCT is capable of visualizing the microchannels in chronic total occlusion.

Post-PCI Lesion Assessment

Stent Malapposition
OCT cannot visualize whole stent strut. The stent surface is located at the center of the stent strut blooming. Stent malapposition is defined the measured distance from the stent surface to the lumen contour being greater than the total thickness of the stent strut and polymer. Acute stent malapposition is often seen in calcified lesions, because the calcified lesion is not expanded uniformly by PCI. The stent strut with a small malapposition, which is detected by OCT but not by IVUS,
Figure 2. Microchannels in chronic total occlusion. Angiography shows chronic total occlusion in mid-left circumflex artery (Left, arrow). The OCT images (Right) were obtained after dilatation with small balloon and microchannels appear as signal-poor voids that are sharply delineated. Numerous microchannels can be observed in the initially occluded segment. OCT, optical coherence tomography.

Figure 3. Relationship between intracoronary thrombus and tissue protrusion after stenting. PCI was performed for the treatment of a mid-right coronary artery lesion in a patient with non-ST-elevation myocardial infarction. At pre-intervention, the culprit lesion contains a large amount of thrombus and after stenting, angiography shows slow flow, and OCT disclosed a high-grade tissue protrusion between the stent struts. A thrombus-rich lesion has a higher risk for coronary slow flow and tissue protrusion after stenting. OCT, optical coherence tomography; PCI, percutaneous coronary intervention.
OCT in PCI could be covered by neointima during long-term follow-up. However, stent struts with a huge malapposition may be a risk for stent thrombosis.

**Tissue Protrusion**

Tissue protrusion includes plaque protrusion and thrombus protrusion. In OCT, plaque protrusion is characterized by a smooth surface and no signal attenuation, and thrombus protrusion by an irregular surface and significant signal attenuation. Tissue protrusion is frequently observed in the culprit lesion of acute coronary syndrome, because the unstable lesion contains soft lipid tissue and thrombi (Figure 3). At present, a significant
Figure 6. Very late stent failure because of neoatherosclerosis. Angiography (Left) shows in-stent restenosis at 8 years after bare metal stent (BMS) implantation in the mid-left anterior descending artery. OCT visualizes ① lipid-laden neointima, ② neointimal plaque rupture, ③ organized thrombus, and ④ macrophage infiltration within the neointima (arrows). In this case, thrombus formation following neointimal plaque rupture was associated with luminal narrowing in the stented segment. OCT, optical coherence tomography.

Figure 7. Three-dimensional OCT image of unstable plaque. Coronary catheter examination was performed in patients with unstable angina pectoris. Angiography showed irregular lumen contour and filling defect in the proximal right coronary artery. Two- and 3-dimensional OCT images demonstrated multiple plaque rupture in the culprit lesion. OCT, optical coherence tomography.
OCT in PCI

Relationship between tissue protrusion and stent restenosis has not been reported.  

Coronary Dissection
OCT can detect stent edge dissection better than IVUS.  
Coronary dissection is easier to observe at the distal stent edge because of the stent-vessel diameter mismatch. When there is no narrowing of the true lumen, an additional procedure may not be required for the treatment of coronary dissection.  
In addition, stent edge dissection could occur more frequently when the OCT-derived plaque type at the edge of the stent is fibrocalcific (44%) or lipid-rich (38%) than when the plaque is fibrous (10%) (P=0.009).  
OCT is a useful tool for predicting coronary dissection during PCI.

Follow-up Examinations

Neointimal Coverage of the Stent
Delayed healing and incomplete stent coverage by neointima is commonly observed in pathologic specimens of vessels treated with drug-eluting stents (DES). Although bare metal stents (BMS) develop neointimal coverage with an average thickness >500 μm, DES prevent the hyperplastic response, so the average late lumen loss for DES can be <100 μm. In an early OCT study, Matsumoto et al  
showed that OCT can clearly visualize thin neointima after DES implantation.  
At 6 months after sirolimus-eluting stent implantation, the median neointima thickness was 53 μm (25th, 75th percentiles: 28 μm, 148 μm, respectively) and 64% of the neointima observed by OCT was undetectable by IVUS.  
Chen et al  used OCT to demonstrate the delay in neointimal coverage after DES compared to BMS. The frequency of uncovered stent struts (17% vs. 0.3%, P<0.001) and malapposed stent struts (2% vs. 0%, P<0.001) was significantly higher in DES than in BMS at 8-month follow-up.  
Kubo et al disclosed the delayed healing process after DES in patients with unstable angina compared to stable angina. At 9-month follow-up, the frequency of malapposed stent struts (33% vs. 4%, P=0.012) and stent uncovered by neointima (72% vs. 37%, P=0.019) was significantly higher in the unstable angina group compared to stable angina. Takano et al  revealed more favorable vascular healing after second-generation DES compared to first-generation DES. The frequency of uncovered struts (2.3% vs. 5.2%, respectively; P<0.001) and malapposed struts (2.1% vs. 5.7%, P<0.001) was significantly lower in
everolimus-eluting stents compared to paclitaxel-eluting stents at 6-month follow-up. Furthermore, recent OCT studies suggest that stent overlapping, bifurcation stenting, stent design, and drug release kinetics have an impact on stent strut coverage. Autopsy studies have shown that the most powerful histological predictor of stent thrombosis is neointimal coverage. Neointimal coverage at the strut level assessed by OCT could be a surrogate endpoint for quickly scrutinizing the safety of DES.

Acquired Stent Apposition
The role of acquired stent malapposition in the pathogenesis of late stent thrombosis remains controversial. A previous IVUS study demonstrated that stent malapposition was highly prevalent in patients with very late stent thrombosis after DES implantation. Subsequently, an angiographic registry showed that late acquired peri-stent contrast staining after DES implantation, which might represent an abnormal vessel wall response such as stent malapposition and positive vessel remodeling, was associated with subsequent target-lesion revascularization and very late stent thrombosis (Figure 4). Recently, Guagliumi et al performed an exploratory study with OCT and IVUS imaging to investigate the underlying mechanisms of late stent thrombosis after DESs implantation. In their case-control study, malapposed struts as assessed by OCT (odds ratio [95% confidence interval]: 4.60 [1.85–7.19] vs. 1.81 [0.00–2.99], P<0.001) and positive remodeling as imaged by IVUS (mean vessel cross-sectional area 19.4±5.8 mm² vs. 15.1±4.6 mm², P=0.003) were associated with late stent thrombosis. These OCT data offer important insights into the mechanisms underlying late stent thrombosis after DES.

Restenotic Tissue Characteristics
Restenosis still exists in the DES era, and its pathophysiology is poorly understood. OCT is a useful technique for evaluating not only the extent and distribution of the neointima but also the morphological appearance of restenotic tissue (Figure 5). With respect to tissue characterization, Gonzalo et al proposed a classification of the OCT appearance of restenotic tissue as homogeneous, heterogeneous, or layered type. The homogeneous appearance is commonly observed in BMS restenosis, which is primarily composed of smooth muscle cells. On the other hand, a heterogeneous or layered appearance is often observed in DES restenosis, which includes mature/immature smooth muscle cells and persistent fibrin or extracellular matrix, such as proteoglycans. Although further validation of the OCT findings in comparison with histology is required, OCT could be an excellent opportunity to understand the pathogenesis of stent restenosis in vivo.

Neatherosclerosis
In-stent restenosis is not necessarily a stable process. Atherosclerosis could develop over time in the neointimal tissue within the stent. Recent OCT studies have reported that neointima within the stent often transforms into lipid-laden tissue over an extended period of time and that expansion of neovascularization from peri-stent to intra-intima contributes to atherosclerotic progression of neointima. In-stent neatherosclerosis could occur earlier after DES implantation than after BMS implantation. Takano et al showed that lipid-laden neointima was more frequently detected late (>5 years) compared to early (<6 months) after BMS implantation (P<0.001). Kang et al also demonstrated that DES >20 months in comparison with DES <20 months after implantation had a higher incidence of TCFA-containing neointima (P=0.012). BMS, neoatherosclerosis might be an important mechanism of very late stent failure, including thrombosis and restenosis (Figure 6).

Limitations of OCT
An inherent limitation of OCT is the need for a blood-free imaging zone, which means it may be not applicable for assessment of left main coronary artery disease, ostial coronary disease, severe stenotic lesion and totally occluded lesions. In addition, OCT has a relatively shallow axial penetration depth of 2 mm. The OCT signal does not reach the back wall of thick atherosclerotic lesions. OCT is not appropriate for estimating vessel size and arteri remodeling.

Future Directions
Recently, 3-dimensional (3D) OCT technology has made rapid progress. The higher frame rates and rapid spiral pullback of FD-OCT enable imaging of the 3D microstructure of long coronary segments in vivo. The application of this emerging technology to coronary artery disease allows assessment of unstable plaques (Figure 7), stented segments, and coronary bifurcations lesions (Figure 8) with a level of detail not previously reported. Furthermore, the combination of tissue characterization and 3D OCT reconstruction is a further, promising area of research in this technology. Although 3D visualization provides a powerful technique of representing the OCT data, it is currently time-consuming. Ease of use of this new technology will bring it closer to becoming a practical imaging technique in cardiac catheterization laboratories.

Conclusions
OCT is a promising technology in the evaluation of coronary microstructure and stent architecture. The OCT examination might help us to understand the vascular response to coronary intervention and might eventually improve clinical outcomes. With its excellent ability to assess coronary atherosclerosis and to guide PCI, OCT will provide new insights into interventional cardiology.

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