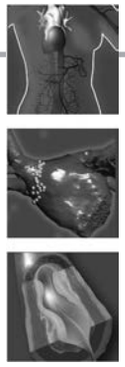

Evaluation of stent placement and outcomes with optical coherence tomography

Optical coherence tomography (OCT) is an imaging modality based on fiberoptic technology. OCT imaging systems use optical imaging catheters that emit near-infrared light to produce high resolution, real-time images. The frequencies and bandwidths of infrared light are far higher than medical ultrasound signals, resulting in greatly increased image resolution, which is approximately ten-times higher than that of intravascular ultrasound. Compared with conventional imaging modalities, OCT is superior for the evaluation of vulnerable plaque features, which may be associated with a higher risk of peri-interventional myocardial infarction, such as plaque rupture, thrombus, thin-capped fibroatheroma and macrophages within the fibrous caps. OCT can clearly visualize stent malapposition and tissue prolapse after stent deployment, as well as neointimal hyperplasia and persistent thrombus at follow-up. OCT provides new insight into the assessment and treatment of coronary artery disease with stent placement.

KEYWORDS: drug-eluting stent ■ frequency domain ■ guide for coronary intervention ■ optical coherence tomography ■ plaque characterization ■ time domain ■ vascular response

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Optical coherence tomography (OCT) is a new imaging technology that utilizes near-infrared light to obtain coronary cross-sectional images on a microscopic scale. The resolution of OCT is 15 µm, which is approximately ten-times higher than that of intravascular ultrasound (IVUS). The main obstacles to the adoption of OCT imaging in clinical practice are that OCT cannot image through red blood cells, as it requires clearing blood from the lumen and its penetration depth into the vessel wall is limited to approximately 2 mm. OCT technology is developing and the fundamental mode of image acquisition has been changing from the time domain to the frequency domain. Frequency-domain OCT (FD-OCT) systems have much higher frame rates and scanning speeds, enabling the acquisition of pullback images rapidly during a brief (2–3-s) infusion of contrast. Although OCT provides new insights into the assessment of coronary artery disease, this new modality requires experience to interpret the morphology of the target coronary arteries and a consensus about certain interpretations has not yet been achieved. The goal of this article is to provide a framework for the appropriate use and reporting of OCT imaging in the treatment of coronary artery disease with stent placement.

Coronary OCT usage in clinical settings

■ Time-domain versus frequency-domain OCT

The only commercial time-domain OCT (TD-OCT) system available today consists of an OCT imaging probe (ImageWire™, LightLab Imaging Inc., MA, USA), a proximal low-pressure occlusion balloon catheter (Helios™, LightLab Imaging, Inc.) and an OCT system console on a mobile cart that contains the optical imaging engine and computer for signal acquisition (M2/M3 CV OCT Imaging System, LightLab Imaging, Inc.). The imaging probe contains an optical fiber with a microlens assembly at its tip. To obtain a single cross-section OCT image, the optical fiber rotates within a stationary transparent protective sheath, scanning the OCT beam around the circumference of the vessel. An automatic pullback mechanism pulls the fiber back longitudinally with the vessel at 1–3 mm/s to obtain a series of cross-sectional images within a vessel segment.

In contrast to TD-OCT, which uses a broadband light source, the FD-OCT, uses a laser that emits near monochromatic light with an optical frequency that sweeps rapidly over a broad wavelength range. This rapid variation in the optical frequency makes it possible to obtain

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100 frames of data each second, while fewer than ten frames per second can be obtained at the same line density with a conventional TD-OCT system. Hence, FD-OCT increases the speed of data acquisition markedly and enables scanning of longer segments of the coronary arteries during a single flush. Takarada *et al.* reported that FD-OCT yielded a higher rate of clear images compared with TD-OCT without ischemic ECG changes in the clinical setting [1]. Better feasibility and performance with procedural safety of FD-OCT can overcome several limitations of conventional TD-OCT systems and facilitate practical application of OCT in the clinic, such as assessment of coronary lesion morphology, guidance for percutaneous coronary intervention (PCI) and long-term evaluation of the lesion treated.

The first commercial FD-OCT system, developed by LightLab Imaging, Inc., consists of an OCT imaging catheter (C7 Dragonfly™) and an OCT system console (C7 XRTM™). Other companies have announced plans to introduce FD-OCT systems in the coming years.

■ Intravascular ultrasound versus OCT

Since IVUS was first developed in the early 1990s, it has been widely used for the assessment of coronary artery morphology and the optimization of PCI [2]. IVUS provides useful information regarding vessel size, plaque area and morphology for stent implantation. However, the resolution of IVUS (100–150 µm), limits the ability of IVUS to detect detailed structures such as intimal tears, thrombus, stent malapposition and tissue prolapse during stent implantation. By contrast, the high resolution of OCT allows visualization of fine coronary structures. This new imaging modality may be useful not only for detecting different types of coronary plaque (lipid-rich, fibrous and calcified plaques) [2–4], but also for facilitating PCI procedures with visualization of intimal hyperplasia, intimal tears and intraluminal thrombi before PCI, and stent malapposition, strut distribution, stent edge dissection, tissue prolapse and mural thrombus after PCI [5–8]. However, in several applications, the shallower penetration of OCT may be a drawback (Table 1). Whole vessel structures, including the external elastic lamina, cannot be visualized consistently by OCT, especially through lesions with a high amount of lipid-rich plaque burden.

Table 1. Optic- and ultrasound-based imaging modalities.

Modalities	Frequency-domain optical coherence tomography	Intravascular ultrasound
Resolution (mm)	10–20	80–120
Frame rate (frames/s)	100	30
Pullback rate (mm/s)	20	0.5–1
Maximum scan diameter (mm)	10	15
Tissue penetration (mm)	1.0–2.5	10

Assessment of coronary lesions with OCT

■ Plaque characterization

Tissue characterization of atherosclerotic plaques with OCT was first carried out by comparing the OCT images to the matched histology using autopsy specimens [2]. Each of the three major plaque types is characterized by a specific set of features: fibrous plaques appear as homogeneous, signal-rich regions; lipid plaques as signal-poor regions with diffuse borders; and calcified plaques as signal-poor legions with sharp borders (Figure 1). Lipid pools are less sharply delineated than calcifications and show lower signal intensity. Lipids also exhibit more heterogeneous backscattering than fibrous plaques. OCT can also identify thin-cap fibroatheroma by measuring the thickness of the fibrous cap and the arc of lipid-rich plaque [3,9,10]. Thrombi are defined as protruding masses into the lumen that are discontinuous from the surface of the vessel wall, with a variable degree of OCT signal attenuation behind the mass (Figure 2) [4,9,10]. OCT images for red thrombi, which mainly consist of red blood cells, are characterized as high backscattering protrusions with strong signal attenuation. White thrombi, which consist mainly of platelets and white blood cells, are characterized by a signal-rich protruding mass [11]. Plaque ulceration or rupture can be visualized by OCT as a ruptured fibrous cap that connects the lumen with the lipid pool. Thrombi are frequently found in the culprit lesion of patients with acute coronary syndrome (ACS). A large amount of red thrombus may interrupt the visualization underneath plaque morphologies owing to signal attenuation. Tanaka *et al.* reported the frequency of no-reflow phenomena after PCI according to the lipid arc and related their findings with the frequency of thin-cap fibroatheroma in patients who present with non-ST-elevation ACS [10]. OCT may have the potential to detect high-risk coronary plaques for early intervention strategies in ACS patients [10]. Figure 3 shows an example of an OCT image of a lesion that exhibited no-reflow after stent placement. Mural red thrombi are possibly misdiagnosed as lipid-rich fibroatheroma, mainly owing to similar OCT signal attenuation patterns of the plaque components.

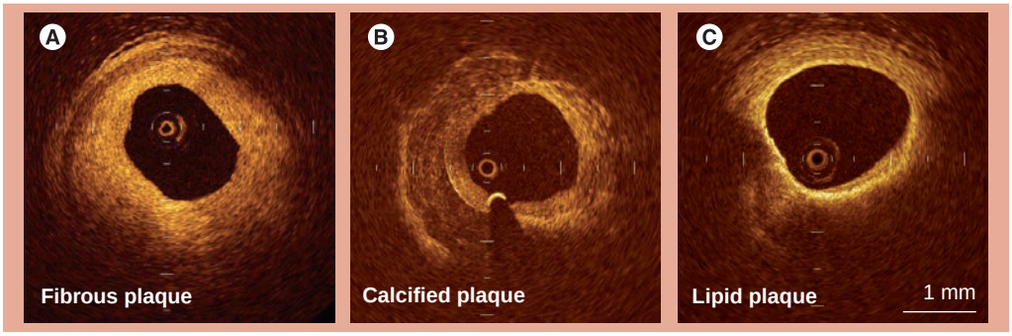

Figure 1. Optical coherence tomography example of typical plaque composition. (A) Fibrous plaque. Fibrous plaques consist of homogeneous, high backscattering areas. **(B)** Calcified plaque. Calcifications are identified by well-delineated, low backscattering, heterogeneous regions. **(C)** Lipid plaque. Lipid-rich plaques are diffusely bordered, highly attenuated, signal-poor regions.

Careful examinations assessing surface continuity and structure are needed to differentiate mural red thrombi and lipid-rich fibroatheroma.

■ Vessel sizing with OCT

Optical coherence tomography can provide cross-sectional images with clear delineation between the coronary lumen and vessel wall, although the shallow penetration of OCT may limit the visualization of whole-vessel structure when compared with IVUS. Yamaguchi *et al.* reported that the minimal lumen area and diameter measured on OCT images correlated well with those measured on IVUS images [12]. OCT can also provide accurate measurements of reference lumen diameters when applied to pre-PCI lesion evaluation (Figure 3). Kawamori *et al.* reported that lumen diameters at the proximal site of culprit lesions measured on TD-OCT images were almost identical to those measured with IVUS. However, the lumen diameter at the distal site of the culprit lesions on OCT images was smaller than that measured on IVUS images. This may be related to a decrease in intracoronary pressure during OCT imaging resulting from proximal vessel occlusion with a balloon [13]. Image acquisition without vessel occlusion by FD-OCT systems may be more convenient and effective for measurement of vessel size and estimation of the proper size of the coronary stent [1].

Definition of percutaneous coronary intervention end points with OCT

Optical coherence tomography is useful for the evaluation of stent expansion and strut apposition to vessel wall immediately after stent deployment. Since OCT light cannot penetrate into the metal struts of the stent, the luminal surface shows a strong reflection with shadowing behind the struts (Figure 4A). Stent diameter and area postimplant can be measured accurately by OCT, with results nearly identical to those obtained by IVUS [14]. The stent area measured by OCT imaging could possibly be an alternative end point of PCI. Bouma *et al.* reported that dissection, prolapse and incomplete stent apposition were observed more frequently with OCT than with IVUS [5,13]. Figure 4 shows examples of OCT images immediately after stent deployment in a coronary lesion. Edge dissection after stent implantation is clearly visualized by OCT; a fraction of these could become occlusive over time and need additional stenting. Tissue prolapse also can be detected in most of the cases of post-stent implant by OCT [5,12]. Although minor tissue prolapse and thrombus formation may be spontaneously resolved within 1 month, it is still controversial which of these can be safely left without additional treatment and those that should be treated with additional balloon dilation. The lesion morphologies before and after coronary stenting and serial changes might be different between patients with stable angina pectoris and ACS. One study from Kubo *et al.*, suggested that although the inadequate lesion

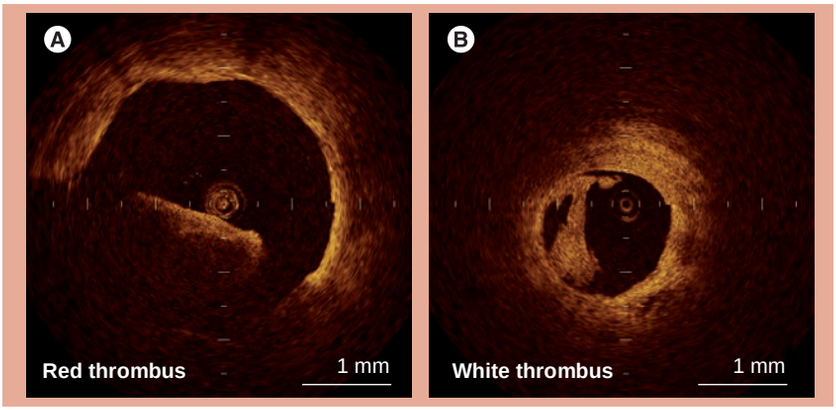

Figure 2. Optical coherence tomography examples of red and white thrombus. (A) Red thrombus shows signal attenuation due to the red blood cell component, while **(B)** white thrombus is platelet-rich and exhibits low signal attenuation.

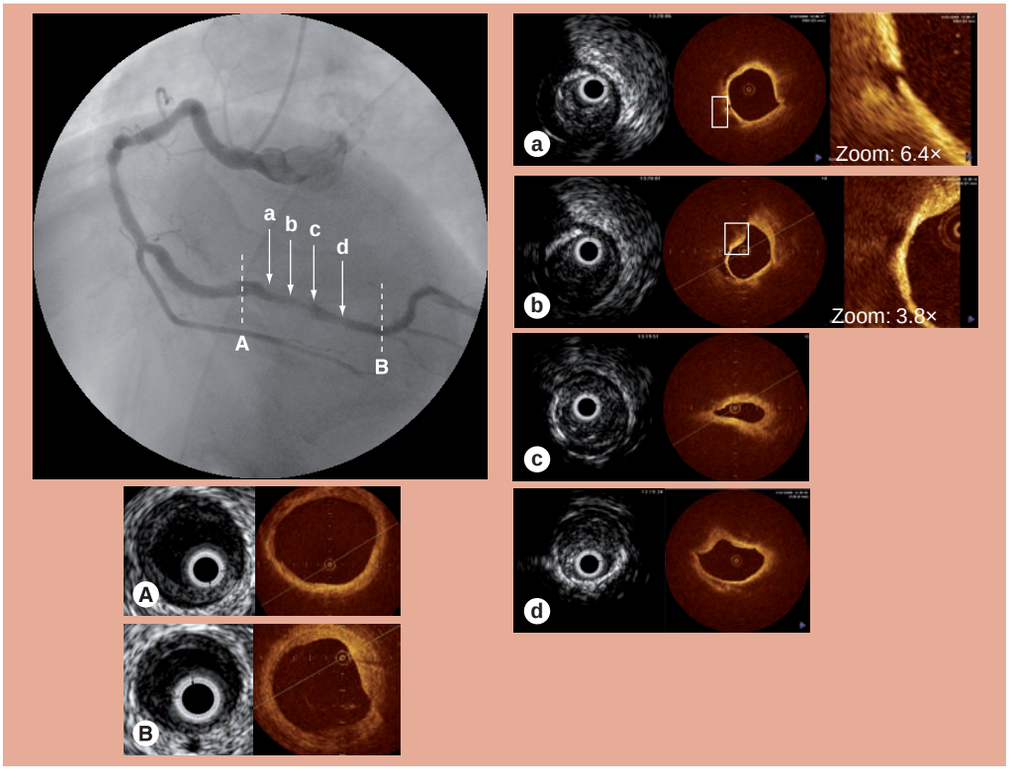

Figure 3. Case of no-reflow after stent implantation pre-percutaneous coronary intervention intravascular ultrasound showing plaque-rich long lesion. (A) Proximal reference site. **(B)** Distal reference site. **(a & b)** Thin-cap fibroatheroma with partial disruption of the fibrous cap and **(c)** continuity of lipid-rich plaque with **(d)** mural thrombi are manifested by optical coherence tomography. Proximal and distal reference segments are also assessed by optical coherence tomography and intravascular ultrasound.

morphologies after stenting such as inadequate stent apposition, tissue protrusion and plaque rupture were observed more frequently in unstable patients, these findings were not associated with adverse outcomes at 9 months in patients with antiplatelet therapy [15]. Although OCT definition of a PCI end point may be helpful, a larger study with greater follow-up time is warranted to analyze how incomplete stent apposition and tissue prolapse change over time in association with clinical outcome.

OCT follow-up of drug-eluting stents & bare-metal stents

■ Assessment of neointimal coverage with OCT

Drug-eluting stents (DES) dramatically decrease angiographic restenosis and target lesion revascularization compared with bare-metal stents (BMS) [16,17]. The long-term safety of first-generation DES is currently under debate with regard to their potential risk for late stent thrombosis (LST), a life-threatening complication, especially after discontinuation of dual antiplatelet therapy [18]. From pathological analyses using autopsy samples, Finn *et al.* reported that uncovered struts could be a marker of the lack of re-endothelialization, which correlates with stent thrombosis [19]. *In vivo* assessment of strut coverage emerged as an important surrogate for risk stratification of stent thrombosis. According to IVUS examinations, most DES appear uncovered by neointima at a chronic stage; however, the limited resolution of IVUS makes it difficult to evaluate the extent or thickness of neointimal coverage. Using OCT, strut coverage with neointima is clearly visible and both the conditions of the coverage of individual struts and the thickness of neointimal coverage can be evaluated [7]. Classification of strut coverage is illustrated in Figure 5.

Matsumoto *et al.* reported that at 6-month follow-up, 89% of the sirolimus-eluting stents (SES) lesions were covered by thin neointima, and that 64% of the stent struts were covered with neointima that had a thickness of less than 100 µm, which is undetectable by IVUS. Most of the SES lesions appeared to be covered by thin neointima, but the frequency of fully covered SES was only 16% at 6 months. Therefore, according to this study, most SES have partial uncovered struts at 6 months [7].

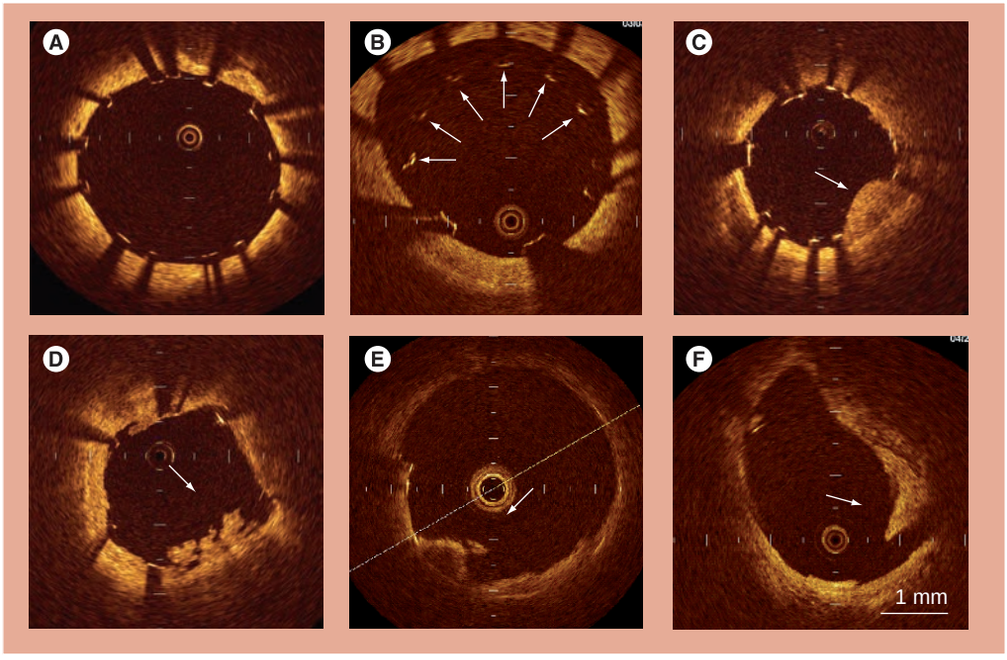

Figure 4. Examples of optical coherence tomography images post-stent deployment.
(A) Stent with full round-shape expansion and complete apposition to the vessel wall. **(B)** Struts malapposed to the vessel wall (arrow head). **(C)** Tissue prolapse between the stent struts (arrow head). **(D)** Thrombus formation after stent deployment (arrow head). **(E)** Struts penetrating into the original thrombi within the lesion (arrow head). **(F)** Dissection of the native coronary wall at the distal edge of the stent (arrow head).

Katoh *et al.* performed serial OCT follow-up of the same patients and reported a comparison of OCT findings at 6 months and at 12 months in identical SES. The neointimal thickness increased from 112 ± 123 µm to 120 ± 130 µm and frequency of uncovered struts decreased from 10.4 to 5.7% [8]. This indicates that SES undergoes long-term delayed neointimalization. An important unanswered question has emerged: when do most SES become fully covered by neointima? There is a possibility that partially uncovered struts remain long term, perhaps for more than 5 years in SES [20].

Another question is whether the uncovered struts are thrombogenic or not. Otake *et al.* reported that the frequency of mural thrombus detected by OCT in SES was 26% (14/53 lesions) at 6 months and subclinical thrombus was associated with a larger number of uncovered struts, uneven neointimal thickness, larger stent eccentricity and longer SES [21]. This suggests uncovered stent struts may be thrombogenic and mural thrombus in SES does not seem to be a rare phenomenon.

A contrary suggestion has been made by Murakami *et al.* that strut coverage with neointima on DES may not always prevent thrombus formation [22]. An important question remains about whether the tissue covering DES is antithrombogenic. According to pathologic studies, tissue covering DES may not always consist of endothelium containing smooth muscle cells, but may contain fibrin, proteoglycan or inflammatory cells [19]. According to our OCT studies, neointima covering DES often does not appear homogeneous in OCT images (Figure 6). The inhomogeneous regions in OCT images are likely to be related to atypical tissue growth in the neointima. As yet, there have been few comparison studies between OCT images of stent coverage and histopathology, due to the limited availability of autopsy samples. More extensive histological studies are needed to clarify these issues.

■ Assessment of stent restenosis with OCT

Restenosis caused by exaggerated neointimal proliferation was the main limitation for the long-term success of BMS. In the recent DES era, although its incidence has been dramatically reduced, restenosis still occurs and its pathophysiology is poorly understood. According to our observations, OCT images of stent restenosis are not homogeneous. Restenotic tissue growth evaluated by OCT can be categorized into three main patterns: homogenous, layered and heterogeneous (Figure 7). According to our data, the homogeneous pattern was observed in all BMS restenosis cases, in contrast to SES restenosis whereby 13% were

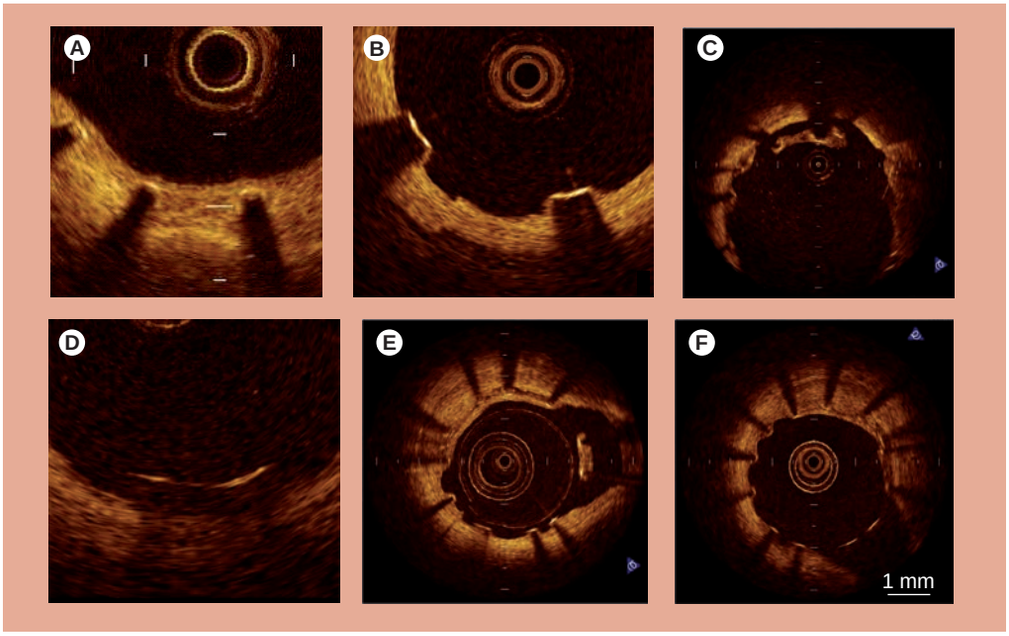

Figure 5. Optical coherence tomography classification of strut conditions at the chronic phase post-stent implant. (A) Well apposed with neointima, **(B)** well apposed without neointima, **(C)** malapposed with neointima, **(D)** malapposed without neointima, **(E)** side branch orifice with coverage and **(F)** side branch orifice without coverage.
Classification reproduced from [7].

classified as homogenous, 74% as layered and 13% as heterogeneous. In paclitaxel-eluting stent restenosis, 29% were classified as homogenous, 42% as layered and 29% as heterogeneous [23]. Gonzalo *et al.* reported a similar classification of restenotic tissue patterns assessed by OCT, including in different kinds of DES and BMS [24]. Neointimal tissue growth and its pathological tissue characteristics are expected to depend on the type of drug, coating and polymers on DES, as well as the original plaque composition of the stented lesion and the elapsed time after stent implantation.

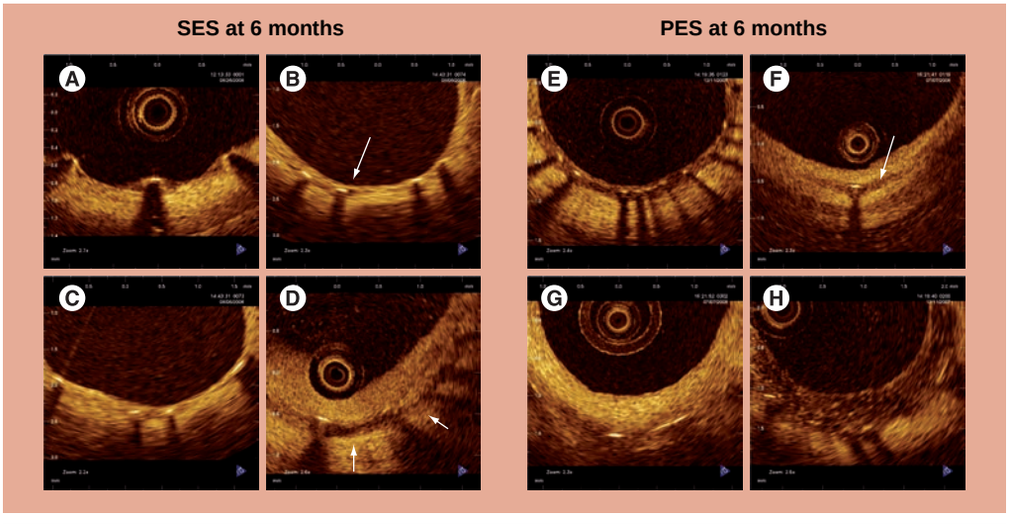

Figure 6. Different morphological types of neointima at 6 months after sirolimus-eluting stent and paclitaxel-eluting stent implantation. Although all stent struts are considered to be covered, optical coherence tomography signal intensity and texture patterns are various.
(A) Protruding struts with tissue attachment, **(B)** neointimal with peristrut low-signal area (arrow head), **(C)** homogeneous high-signal neointima, **(D)** layered neointima of homogeneous high- and low-signal area (arrow heads), **(E)** heterogeneous low-signal neointima, **(F)** neointimal with peristrut low-signal area (arrow head), **(G)** homogeneous high-signal neointima and **(H)** heterogeneous low-signal neointima, including multiple speckled spots.
PES: Paclitaxel-eluting stent; SES: Sirolimus-eluting stent.

Future progress in OCT tissue characterization will enable us to address pathological neointimal features in this unknown entity.

■ OCT observations of very late stent thrombosis after DES implant

As previously mentioned, subclinical thrombus formation is not rare in the current generation of DESs. However, in the study by Otake *et al.*, none of the cases suffered major adverse cardiac events in follow-up (up to 485 days) [21]. The mechanisms leading to very LST are complex and incompletely understood. Delayed arterial healing and incomplete re-endothelialization have emerged as the prevailing mechanism of thrombosis in autopsy studies [19]. Cook *et al.* demonstrated that very late DES thrombosis is associated with histopathological signs of inflammation and IVUS evidence of vessel remodeling, which correlates with the extent of stent malapposition [25]. Sawada *et al.* reported OCT observations of very LST 29 months after SES implant. IVUS presented positive arterial remodeling at SES-implanted sites and OCT revealed multiple interstrut ulcer-like appearances and late strut malappositions (Figure 8) [26]. These might be OCT signs of a critical situation for very LST, which can be detected by OCT follow-up examination for current-generation DES. Hopefully, newer generations of DES will attempt to address these concerns by aiming to improve vascular healing while maintaining potent neointimal suppression.

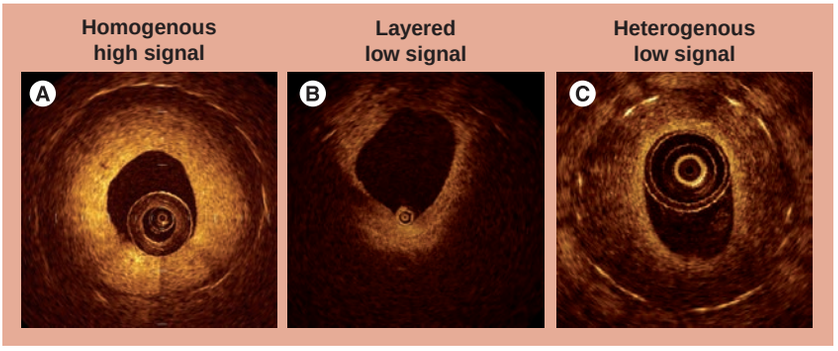

Figure 7. Representative optical coherence tomography patterns of restenotic tissue structure. (A) Homogeneous optical properties without significant focal variations of signal intensity. **(B)** Layered optical properties with inner high intensity and abluminal attenuated low signal intensity. **(C)** Heterogeneous changing optical properties with high speckled spots inside of neointima.

Conclusion

Optical coherence tomography provides new insights into the assessment of coronary artery disease. The high resolution of OCT enables detailed evaluation of coronary atherosclerosis; fibrous plaques, lipid-rich plaques with thin fibrous caps, dense calcified lesions and angiographically hazy stenosis containing thrombus can be accurately

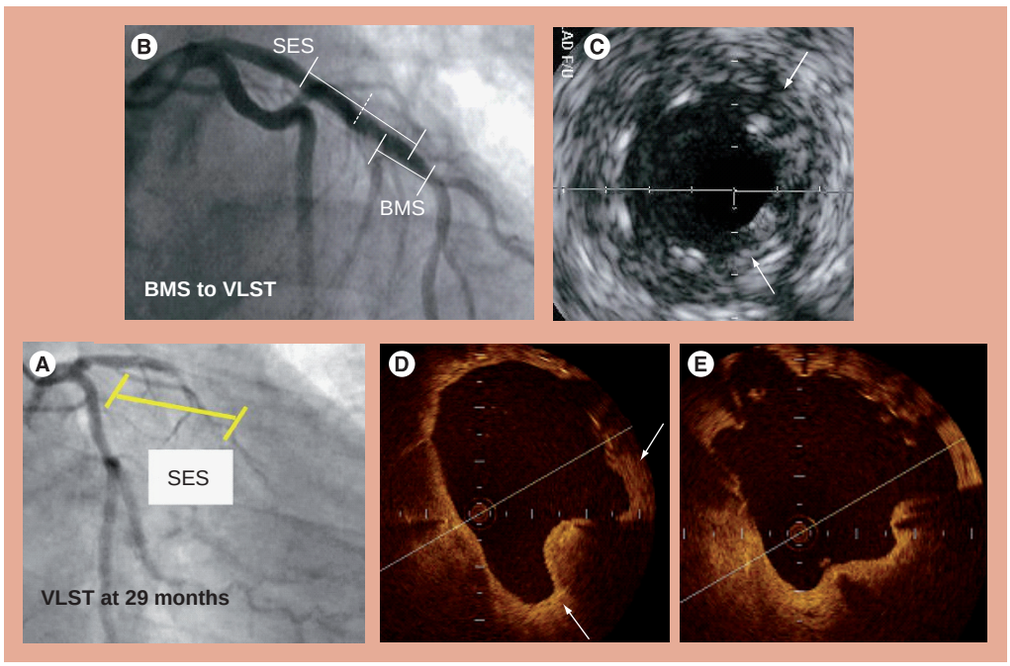

Figure 8. A case of very late stent thrombosis 29 months after sirolimus-eluting stent implantation (64-year-old male). (A) Proximal left anterior descending artery was occluded at the site of SES. **(B)** BMS was implanted to open the left anterior descending artery. **(C)** Intravascular ultrasound showed positive remodeling of the stented segment. **(D & E)** Optical coherence tomography clearly visualized a peristrut ulcer-like appearance and malapposed struts (arrow heads). BMS: Bare-metal stent; SES: Sirolimus-eluting stent; VLST: Very late stent thrombosis.

identified. Furthermore, vascular response to coronary intervention such as stent expansion, tissue prolapse within the stent and thrombus formation can be clearly visualized. OCT can also measure the thickness of neointima and strut conditions at follow-up examination, which may help to stratify the risk of thrombotic events associated with DES.

Future perspective

Penetration depth of OCT is limited to approximately 2 mm, either by TD-OCT or FD-OCT. Thus, although the current OCT system can visualize thin fibrous caps of fibroatheroma and thin neointimal coverage on DES, it is unable to quantify whole vascular structures and total plaque volume, which can be surrogates in response to specific treatments aimed at regression or cessation of progression. Development of new devices equipped with both IVUS and OCT functions should be helpful for patient evaluation and large clinical trials.

At present, standard OCT interpretation is limited to the evaluation of grayscale images generated by near-infrared light reflections at tissue interfaces and the identification of individual plaque components by OCT requires experience. The application of postprocessing color-mapping software based on OCT light backscatter and attenuation should improve the characterization of both atherosclerotic coronary plaques and neointimal tissue on DES by providing more objective assessment [27].

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Executive summary

- Optical coherence tomography (OCT) is an imaging modality based on fiberoptic technology that provides high resolution (~ten-times higher than that of intravascular ultrasound) and real-time intracoronary images. OCT enables us to characterize plaque types, such as fibrous, calcified and lipid plaques. OCT can also identify thin-cap fibroatheroma by measuring the thickness of the fibrous cap and the arc of lipid-rich plaques.
- OCT is superior to intravascular ultrasound in detecting detailed structures, such as intimal tears, dissections, thrombus, stent apposition and incomplete apposition and tissue prolapse during stent implantation, which may facilitate percutaneous coronary intervention procedures.
- OCT is useful for the evaluation of vascular healing after drug-eluting stent implantation in assessing neointimal coverage, incomplete stent apposition and thrombus formation.
- Frequency-domain OCT will overcome several limitations of time-domain OCT. In the near future, frequency-domain OCT is expected to be adopted extensively in clinical use.

Bibliography

Papers of special note have been highlighted as:
- of interest
- **Optical coherence tomography (OCT) assessment of neointimal coverage post-drug-eluting stent (DES).**

1 Takarada S, Imanishi T, Liu Y *et al.*: Advantage of next-generation frequency-domain optical coherence tomography compared with conventional time-domain system in the assessment of coronary lesion. *Catheter. Cardiovasc. Interv.* 75, 202–206 (2010).

2 Mintz GS, Nissen SE, Anderson WD *et al.*: American College of Cardiology Clinical Expert Consensus Document on Standards for Acquisition, Measurement and Reporting of Intravascular Ultrasound Studies (IVUS). A report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. *J. Am. Coll. Cardiol.* 37, 1478–1492 (2001).

3 Jang IK, Bouma BE, Kang DH *et al.*: Visualization of coronary atherosclerotic plaques in patients using optical coherence tomography: comparison with intravascular ultrasound. *J. Am. Coll. Cardiol.* 39, 604–609 (2002).

4 Tearney GJ, Yabushita H, Houser SL *et al.*: Quantification of macrophage content in atherosclerotic plaques by optical coherence tomography. *Circulation* 107, 113–119 (2003).

5 Bouma BE, Tearney GJ, Yabushita H *et al.*: Evaluation of intracoronary stenting by intravascular optical coherence tomography. *Heart* 89, 317–321 (2003).

6 Sawada T, Shite J, Shinke T *et al.*: Persistent malapposition after implantation of sirolimus-eluting stent into intramural coronary hematoma. *Circ. J.* 70, 1515–1519 (2006).

7 Matsumoto D, Shite J, Shinke T *et al.*: Neointima coverage of sirolimus-eluting stents at 6-month follow-up: Evaluated by optical coherence tomography. *Eur. Heart J.* 28, 961–967 (2007).

8 Katoh H, Shite J, Shinke T *et al.*: Delayed neointimalization on sirolimus-eluting stents: 6-month and 12-month follow up by optical coherence tomography. *Circ. J.* 73, 1033–1037 (2009).

9 Jang IK, Tearney GJ, MacNeill B *et al.*: *In vivo* characterization of coronary atherosclerotic plaque by use of optical coherence tomography. *Circulation* 111, 1551–1555 (2005).

10 Tanaka A, Imanishi T, Kitabata H *et al.*: Lipid-rich plaque and myocardial perfusion after successful stenting in patients with non-ST-segment elevation acute coronary syndrome: an optical coherence tomography study. *Eur. Heart J.* 30, 1348–1355 (2009).

11 Kume T, Akasaka T, Kawamoto T *et al.*: Assessment of coronary arterial thrombus by optical coherence tomography. *Am. J. Cardiol.* 97, 1713–1717 (2006).

12 Yamaguchi T, Terashima M, Akasaka T *et al.*: Safety and feasibility of an intravascular optical coherence tomography image wire system in the clinical setting. *Am. J. Cardiol.* 101, 562–567 (2008).

13 Kawamori H, Shite J, Shinke T *et al.*: Findings and usefulness of optical coherence tomography guided percutaneous coronary intervention. *Cardiovasc. Interven. Therap.* 1, A1–A99 (2009) (Abstract).

14 Sawada T, Shite J, Negi N *et al.*: Factors that influence measurements and accurate evaluation of stent apposition by optical coherence tomography. *Circ. J.* 73, 1841–1847 (2009).

15 Kubo T, Imanishi T, Kitabata H *et al.*: Comparison of various response after sirolimus-eluting stent implantation between unstable angina and stable angina pectoris: a serial optical coherence tomography study. *JACC Cardiovasc. Imag.* 1, 475–484 (2008).

16 Moses WJ, Leon MB, Popma JJ *et al.*: Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. *N. Engl. J. Med.* 349, 1315–1323 (2003).

17 Simonton CA, Brodie B, Cheek B *et al.*: Comparative clinical outcomes of paclitaxel- and sirolimus-eluting stents: results from a large prospective multicenter registry – STENT Group. *J. Am. Coll. Cardiol.* 50, 1214–1222 (2007).

18 Stone GW, Moses JW, Ellis SG *et al.*: Safety and efficacy of sirolimus- and paclitaxel-eluting coronary stents. *N. Engl. J. Med.* 356, 998–1008 (2007).

19 Finn AV, Nakazawa G, Joner M *et al.*: Vascular response to drug eluting stents: importance of delayed healing. *Arterioscler. Thromb. Vasc. Biol.* 27, 1500–1510 (2007).

20 Ishigami K, Uemura S, Morikawa Y *et al.*: Long term follow-up of neointimal coverage of sirolimus-eluting stents: evaluation with optical coherence tomography. *Circ. J.* 73, 2300–2307 (2009).

21 Otake H, Shite J, Ako J *et al.*: Local determinants of thrombus formation following sirolimus-eluting stent implantation assessed by optical coherence tomography. *JACC Cardiovasc. Interv.* 2, 459–466 (2009).

- **OCT assessment of thrombus formation post-DES.**

22 Murakami D, Takano M, Yamamoto M *et al.*: Advanced neointimal growth is not associated with a low risk of in-stent thrombus – optical coherence tomographic findings after first-generation drug-eluting stent implantation. *Circ. J.* 73, 1627–1634 (2009).

23 Shinke T, Shite J, Kato H *et al.*: Optical coherence tomography (OCT) analysis of target vessel failure after drug eluting and bare metal coronary stent. *Am. J. Cardiol.* 104, C1–C64 (2009) (Abstract).

24 Gonzalo N, Serruys PW, Okamura T *et al.*: Optical coherence tomography patterns of stent restenosis. *Am. Heart J.* 158, 284–293 (2009).

25 Cook S, Ladich E, Nakazawa G *et al.*: Correlation of intravascular ultrasound findings with histopathological analysis of thrombus aspirates in patients with very late drug-eluting stent thrombosis. *Circulation* 120, 364–365 (2009).

26 Sawada T, Shite J, Shinke T *et al.*: Very late thrombosis of sirolimus-eluting stent due to late malapposition: serial observations with optical coherence tomography. *J. Cardiol.* 52, 290–295 (2008).

27 Xu C, Schmitt JM, Carlier SG, Virmani R: Characterization of atherosclerosis plaques by measuring both backscattering and attenuation coefficients in optical coherence tomography. *J. Biomed. Opt.* 13, 034003 (2008).

- **Quantitative assessment of optical properties of plaque tissue.**