Chapter 7

Clinical and Research Applications of Optical Coherence Tomography Imaging in Coronary Artery Disease

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1. Introduction

Optical coherence tomography (OCT) is an optical analog of intravascular ultrasound (IVUS) that allows microscopic visualization of coronary plaque types and intracoronary tissue. The high-resolution images of OCT produce an intense interest in adopting this imaging technique for both clinical and research purposes.

In clinical aspects, OCT imaging for undergoing percutaneous coronary intervention (PCI) is feasible and provides superior resolution of arterial pathology than IVUS. During PCI, OCT can assess pre-procedural coronary plaque morphology and acute effects of coronary intervention (dissection, tissue prolapse, thrombi, and incomplete stent apposition (ISA)). Moreover, OCT provides more useful information to consider PCI strategy, such as distal protection, optimal stent landing zone.

In research aspects, OCT provides characterization of coronary plaque to assess factors associated with acute coronary syndrome (ACS) and vessel healing process after stent implantation. Recent studies have shown that OCT is useful for the assessment of coronary atherosclerotic plaques (plaque rupture, erosion, thin-cap fibroatheroma (TCFA), and intracoronary thrombi) in patients with ACS. In addition, OCT can detect the proliferation of vasa vasorum and the distribution of macrophages surrounding vulnerable plaques. OCT provides cardiologists with the tool they need to better understand the pathological condition of ACS.

According to vessel healing after stent implantation, OCT can provide stent strut coverage, ISA, and restenotic tissue characteristics at follow up. Previous OCT studies have shown that delayed neointimal coverage after drug-eluting stent (DES) implantation vs. bare metal

stent (BMS) implantation. Pathological studies have indicated that the proportion of delayed neointimal coverage represents the best morphometric predictor of late stent thrombosis. Recent OCT studies demonstrate that restenotic tissue characteristics is completely different between BMS and DES. Therefore, OCT can play an important role to assess the safety profile of novel DES systems.

Finally, we introduce usefulness of 3-dimensional reconstruction of the OCT images and 1-μm resolution OCT.

2. Differences between IVUS and OCT

OCT is an optical analog of IVUS, used to examine the coronary arteries. There is a pressing need for improved characterization of coronary pathology to better recognize the factors associated with coronary vessel disease and to guide the selection of better interventional strategies. The resolution and contrast of OCT is attractive for these applications and suitable catheters to access the coronary arteries in detail. There are several differences between IVUS and OCT, as shown in Table 1 [1]. The resolution of OCT (10-20 μm) is 10-fold higher than that of IVUS (100-150 μm), but the penetration depth is lower with OCT (1-2 mm) than with IVUS (4-8 mm) [2]. According to other important difference between IVUS and OCT, the removal of blood is not need for IVUS examination but OCT examination. To examine coronary arteries, blood must first be removed during an OCT examination because of the strong attenuation of light by blood [3].

OCT imaging uses an interferometry technique based on time-delay measurements of the light reflected or backscattered from the tissues [4]. We can use two processing modes used for intracoronary OCT imaging, the first generation time-domain OCT (TD-OCT) imaging systems and the more recently available second generation frequency-domain OCT (FD-OCT) imaging systems [5, 6].

The first-generation OCT (ImageWire and M2/3 OCT system; LightLab Imaging, Inc., Westford, Massachusetts) incorporated both an OCT imaging wire and an over-the-wire occlusion balloon. To deliver the image wire and remove blood from the target lesion, an over-the-wire occlusion balloon catheter was used. The OCT imaging procedure started with advancing a 0.014-inch coronary guide wire distal to the target lesion. The occlusion catheter is passed along the guide wire through the lesion. After the guide wire and OCT image wire were exchanged, the occlusion balloon is pulled back proximal to the lesion. Then, ringer's solution was continuously flushed at 0.5–0.6 ml/s through the occlusion catheter lumen using a power injector, and the balloon was inflated to 0.3–0.5 atm by an inflation device to block blood flow. When an OCT image well appeared, a motorized pullback was initiated from the imaging system console. The first-generation OCT was not user-friendly and had several disadvantages of complex procedure, such as balloon occlusion and relatively short length of image acquisition due to the limited frame rate. To improve these disadvantage, a new generation of OCT systems, termed FD-OCT imaging methods, has been developed.

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FD-OCT imaging methods, utilize a light source with variable wavelength that is tuned to continuously oscillate between 1250 and 1350 nm, a so-called wavelength swept laser, instead of the broadband light source used in TD-OCT. As a result, FD-OCT system can enable faster image acquisition and greater scan depths compared with TD-OCT system. Intravascular OCT examination has been frustrated by requiring blood removal. However, FD-OCT system can enable faster image acquisition and greater scan depths compared with TD-OCT system. As a result, only intermittent injection of transparent fluid through guiding catheter for a few seconds enables to obtain entire coronary images [6, 7]. FD-OCT system has been developed (Dragonfly imaging catheter and C7- XR OCT system; LightLab Imaging, Inc., St Jude Medical,St Paul, Minnesota, USA). Differences between TD- (M3) and FD-OCT (C7-XR) systems are shown in Table 1 [8]. This advance may provide dramatic improvements in understanding coronary atherosclerosis and response to intravascular interventions such as angioplasty and stenting.

3. Clinical applications of OCT imaging

In clinical aspects, OCT imaging for undergoing PCI is feasible and provides superior resolution of arterial pathology than intravascular ultrasound. During PCI, OCT can assess preprocedural coronary plaque morphology.

Regarding to plaque characterization, OCT can differentiate three types of coronary plaques, such as fibrous, calcified, and lipid-rich. Fibrous plaque is characterized by a homogenous high signal region with low attenuation, calcified plaque by a well-delineated, low-signal region with sharp borders, and lipid-rich plaques as a low-signal region with diffuse borders [9]. Importantly, a histology-controlled OCT study showed >90% sensitivity and specificity for detecting lipid-rich plaque in comparisons with pathological specimens. [9, 10]. Moreover, OCT can recognize vulnerable plaques, such as plaque rupture, erosion, intracoronary thrombus, TCFA.

Assessment of plaque characteristics before PCI is useful to choose optimal interventional strategy. Tanaka et al. showed that TCFA was often observed at target lesions of the patients with no reflow after PCI compared with good reflow (50% versus 16%, $P = 0.005$). The frequency of the no reflow phenomenon increased according to the lipid arc assessed by OCT [11]. When OCT detects lipid-rich plaque and TCFA especially in patients with ACS, we should consider to use distal protection devices to prevent no-reflow phenomenon.

Another aspect, plaque type at the stent edges has an impact on the occurrence of edge dissections. Gonzalo et al. showed that presence of edge dissection was significantly more frequent when the plaque type at the edge was fibrocalcific (43.8%) or lipid rich (37.5%) than when the plaque was fibrous (10%) [12]. This study demonstrated that complex plaque type at the stent edge might influence on the presence of edge dissections from OCT observation. The OCT guide stenting might be a useful assistance to achieve optimal landing zone.

After PCI, OCT can assess acute effects of coronary intervention (dissection, tissue prolapse, and ISA). Dissection, tissue prolapse, and ISA were observed more often with OCT than

with IVUS [13, 14]. Coronary dissection is frequently observed at the distal stent edge because of the oversized stent diameter or complex types of plaque at the stent edge by OCT. When there is no limited coronary flow by angiography and adequate area of the true lumen by OCT, no additional procedure might be necessary for the treatment of coronary dissection [15].

There are 2 types of tissue prolapse, plaque prolapse or thrombus prolapse. OCT can distinguish between plaque prolapse and thrombus prolapse. Plaque prolapse is characterized by smooth surface with no signal attenuation, and thrombus protrusion by irregular surface with significant signal attenuation. Minor tissue prolapse identified by IVUS was not found to be associated with angiographic in-stent restenosis [16]. However, the relationship tissue prolapse identified by OCT and angiographic in-stent restenosis has not been elucidated.

ISA by OCT was identified as clear separation between at least one stent strut and the vessel wall. To check the stent apposition to the vessel wall, the distance between surface of stent strut and adjacent inatima border should be measured because of differences of stent and polymer thickness [8]. Small ISA, which is detected by only OCT but not by IVUS, could disappear by neointimal growth during follow-up period [15].

4. Research applications of OCT imaging

In research aspects, OCT can provide characterization of coronary plaque to assess factors associated with ACS and vessel healing process after stent implantation.

The first OCT study to assess in vivo culprit lesion morphology in patients with ACS showed that higher frequency of TCFA in ACS compared with stable angina pectoris (72% in acute myocardial infarction (AMI), 50% in unstable angina pectoris, and 20% in stable angina pectoris; $P = 0.012$) [2]. Kubo et al. showed superiorities of TD-OCT for the detection of plaque rupture (73% vs. 40% vs. 43%, $P = 0.021$), erosion (23% vs. 0% vs. 3%, $P = 0.003$), and thrombus (100% vs. 33% vs. 100%, $P < 0.001$) compared with IVUS and coronary angioscopy in patients with AMI [17]. The frequency of vulnerable plaque (plaque rupture, erosion, and thrombus) by detected OCT was similar to that of the pathological reports. As described above, OCT is more useful to assess atherosclerotic plaque instability compared to other intracoronary imaging devices.

OCT has been proposed as a high resolution imaging modality that can identify vasa vasorum as microchannels with tiny black holes (50-100 μm). The proliferation of vasa vasorum has been identified recently as a common feature of vulnerable plaque [18]. Kitabata et al. demonstrated increase of microvessels counts in TCFA [19]. An observational study of OCT revealed that the presence of microvessels in the plaques was also associated with positive remodeling and elevated high-sensitive C-reactive protein levels [19]. The OCT evaluation of microvessels counts might be helpful for assessing plaque vulnerability.

Moreover, the other unique aspect of OCT is the detection of macrophages. Degradation of the fibrous cap matrix by macrophages is associated with atherosclerotic plaque instability

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[20]. Macrophages detected by OCT were observed as a 'bright spot', with a high signal variance from the surrounding tissue. Tearney et al. [21] and MacNeill et al. [16] descried OCT is capable to evaluate cap macrophage content accurately. High degree of positive correlation was observed between OCT and histological measurements of macrophage density in fibrous cap ($r < 0.84$, $P < 0.0001$). OCT provided to detect a cap macrophage density > 10% with 100% sensitivity and specificity [19].

According to vessel healing after stent implantation, OCT can provide stent strut coverage, ISA, and restenotic tissue characteristics at follow up. Previous OCT studies have shown that delayed neointimal coverage after DES implantation vs. BMS implantation [22]. Pathological studies have indicated that the proportion of delayed neointimal coverage represents the best morphometric predictor of late stent thrombosis [23, 24]. Recent OCT studies demonstrate that restenotic tissue characteristics is completely different between BMS and DES [21, 25]. Therefore, OCT can play an important role to assess the safety profile of novel DES systems.

5. Future directions of OCT imaging

Recently, a second-generation OCT technology, termed FD-OCT, has been developed that solves the TD-OCT limitations by imaging at much higher frame rates with slightly deeper penetration depth and greater scan area. In combination with a short, non-occlusive flush and rapid spiral pullback, the higher frame rates generated by FD-OCT enable imaging of the 3-dimensional reconstruction of longer segments of coronary arteries. The 3-dimensional OCT can express all of the coronary microanatomy and pathology previously visualized by OCT, including lipid pools, calcium, macrophages, thin fibrous caps, cholesterol crystals, thrombus, stent, and stents with neointimal hyperplasia [26]. The 3-dimensional OCT may be useful as a research tool for assessing human coronary pathophysiology and as a clinical tool for guiding the management of coronary artery disease.

Progress in understanding, diagnosis, and treatment of coronary artery disease has been hindered because of inability to observe cells and extracellular components associated with human coronary atherosclerosis *in situ*. A μOCT system with a very broad bandwidth light source and common-path spectral-domain OCT technology provides 1-μm axial resolution ranging in tissue [27]. The μOCT is possible to visualize many key cellular and subcellular features relevant to atherogenesis, plaque rupture, thrombosis, and neointimal healing after stenting *in situ*. The μOCT technology has the potential to make a significant impact in cardiovascular pathology.

6. Conclusion

The high resolution of OCT provides histology-grade definition of the microstructures of coronary atherosclerosis in vivo. Introduction of this attractive imaging method contributes

significant progression in both clinical and research aspects. Clinically, OCT can provide more useful information to consider PCI strategy for getting the optimal interventional results. On the other hand, OCT is a useful imaging device for understanding, diagnosis, and treatment of coronary artery disease. In the future direction of OCT systems, 3-dimensional OCT and μOCT may be upcoming in the field of coronary artery disease. These novel OCT technologies will play an important role for investigation of coronary artery disease.

	IVUS	TD-OCT (M3)	FD-OCT (C7)
Axial resolution, μm	100-150	15-20	12-15
Lateral resolution, μm	150-300	39	19
Frame rate, fps	30	20	100
Pullback speed, mm/s	0.5-2.0	0.5-2.0	10-25
Scan diameter, mm	8-10	6.8	10
Penetration depth, mm	4-8	1-2	1-2
Balloon occlusion	Unnecessary	Necessary	Unnecessary

IVUS, intravascular ultrasound; OCT, optical coherence tomography; TD, time-domain; FD, frequency-domain; fps, frames per second.

Modified from Terashima M et al, korean j intern med 2012;27:1-12.

Table 1. Differences among IVUS, TD-OCT, and FD-OCT

	IVUS	OCT
Dissection	○	◎
Tissue prolapse	△	◎
ISA	○	◎
Stent expansion	◎	○
Lesion coverage	○	○

IVUS, intravascular ultrasound; OCT, optical coherence tomography; ISA, incomplete stent apposition.

Table 2. Acute effects of coronary intervention between IVUS and OCT

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