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Review

Current applications of optical coherence tomography for coronary intervention

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ABSTRACT

Optical coherence tomography (OCT) is the 'new kid on the block' in coronary imaging. This technology offers clinicians a high resolution (approximately 15 μm), that is ten times higher than the currently accepted gold standard of intravascular ultrasound and has emerged as the ideal imaging tool for the assessment of superficial components of coronary plaques and stent struts. Novel OCT systems can perform quick and safe scanning of coronary arteries with a non-occlusive technique. A brief summary containing the key physical principles of OCT technology with particular attention to the novel Fourier domain system is presented. This review will focus on clinical and research applications of OCT in interventional cardiology. The two main fields of OCT in vivo: coronary atherosclerosis assessment and the study of vessel wall response to stent implantation in terms of strut coverage and apposition will be delineated. Limitations and future perspectives of the technique are presented.

1. Introduction

A number of advances have seen percutaneous coronary intervention (PCI) becomes the mainstay invasive therapy for patients with coronary artery disease. Stents themselves have accounted for a significant reduction in adverse events compared to balloon angioplasty alone [1–4] with the spectrum of stent types continuing to change. Drug-eluting stents (DES) have dramatically reduced restenosis rates [5]. However, a new evil has appeared, namely stent thrombosis [6]. Fortunately, this complication remains rare, however considerable mortality results [7–11]. Clinicians and patients alike have therefore demanded increased scrutiny with DES, but to study these very rare complications would require trials with many thousands of patients and follow-up extending over numerous years. Such follow-up would often exceed the product life cycle of stents with refinements in design, platform and drug-elution continuing at a rapidly advancing pace. Hence, a surrogate marker of stent safety would be an attractive option and this is indeed where novel intracoronary imaging is positioning itself.

The 'new kid on the block' in coronary imaging is optical coherence tomography (OCT). This technology offers clinicians a high resolution (15 μm) and is ten times higher than the currently accepted gold standard of intravascular ultrasound (IVUS). OCT use is growing across many catheterization laboratories worldwide and has already been used extensively to examine strut coverage following stenting both in registry studies [12–14] and in large, randomized trials [15–17]. The attractive aspect of this device is that it is well positioned to detect and quantify tissue coverage over stent struts. Indeed, a lack of endothelialization has been linked to cases of stent thrombosis in post-mortem series [18–20] and is therefore seen to be a key predictor of long-term stent failure. This review will detail the principles of OCT imaging within the coronary artery and explore the key applications in coronary intervention that should propel this technology ahead of IVUS as the new gold standard for stent imaging.

2. Optical properties of light-based imaging

OCT is an imaging modality that emits a near infrared light that targets a sample of interest; the electric field amplitude of light reflected from the sample at a certain depth is measured using the principle of low coherence interferometry, with a short coherence length of the source of radiation [21,22]. The intensity of the interferometric signal is converted to a color-scale or gray-scale to produce cross section images of tissue sample. Two types of OCT systems exists: a) first generation OCT systems, known as Time domain (TD) OCT [21–23], and second generation systems, known as Fourier domain (FD) OCT [24–26] that differ mainly with regard to the method used to calculate the electric field amplitude. TD-OCT uses a broadband light source in the 1280–1350 nm band, performs multiple scanning of reference delay distance, and directly measures the electric field amplitude. By contrast, FD-OCT uses a monochromatic laser whose wavelength changes over time, while the reference delay distance remains constant, the electric field amplitude is computed through Fourier transformation and is detected at all depth points simultaneously. Multiple terms are

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currently in use for FD-OCT such as spectral radar and spectral-domain OCT for those systems using a spectrometer and swept-source OCT, frequency domain OCT, or optical frequency domain imaging (OFDI) for systems with a wavelength-swept laser, the latter type being the most commonly used in the setting of interventional cardiology [24–27].

OCT systems have a higher sensitivity than IVUS (Table 1), with 10–20 μm tissue axial resolution, 20–30 μm lateral resolution, although the emitted light has a lower depth penetration than IVUS. TD-OCT systems have a lower pullback, with a maximum of 3 mm/s, and a frame rate that varies from 15.6 to 20 frames/s, while FD-OCT systems have a higher pullback speed, up to 2 cm/s (Table 1). Therefore, FD-OCT systems can perform intracoronary imaging with a non-occlusive technique, thus avoiding ischemia-induced complications, and significantly reducing the time for image acquisition. These features have been responsible for the quick and growing widespread use of FD-OCT in modern catheterization laboratories worldwide. However, a common limitation to both TD and FD-OCT systems is the need for intracoronary contrast injection during image acquisition, to achieve adequate displacement of red blood cells that limit the penetration of the emitted light toward the target structures in the vessel wall, although the volume of contrast injected is enormously minimized with FD-OCT.

The greater sensitivity of OCT systems than IVUS, has made OCT the ideal imaging tool for the assessment of superficial components of coronary plaques and stent struts.

3. Plaque assessment

The feasibility of OCT to image atherosclerotic plaque morphology has been shown in early ex-vivo studies on explanted human aorta and coronary arteries [28–30], and in subsequent in vivo studies in animals [31,32]. A landmark post-mortem study has shown the ability of OCT to characterize human atherosclerotic plaques compared to histology [33]. In this study, 357 atherosclerotic segments from 90 cadavers were analyzed, OCT criteria for the various plaque components were established on 50 segments, allowing the identification of three types of histological plaques: 1) fibrous, 2) fibrocalcific, 3) lipid-rich. Fibrous plaques were defined as homogeneous, highly backscattering (i.e., signal-rich) plaque interiors free of OCT signal-poor regions. Fibrocalcific plaques presented signal-poor regions with sharply delineated upper and/or lower borders. Lipid-rich plaques showed diffusely bordered, signal-poor regions (so called lipid pools) with overlying signal-rich bands, corresponding to fibrous caps. A sensitivity and specificity of 96% and 97% for calcific lesion, 90% and 92% for lipid-rich plaques, 79% and 97% for fibrous plaque were obtained with OCT compared to histology. The inter and intra-observer agreements for plaque characterization by OCT were $k = 0.88$ and 0.91, respectively.

Table 1
Physical characteristics of OCT vs IVUS.

	TD-OCT[a]	FD-OCT[b]	IVUS[c]
Energy source	Near-infrared light	Near-infrared light	Ultrasound (20–45 MHz)
Wave-length	1.3 μm	1.3 μm	35–80 μm
Resolution	15 μm (axial) 40 μm (lateral)	15 μm (axial)	100–200 μm (axial) 200–300 μm (lateral)
Frame rate	15–20 frames/s	100 frames/s	30 frames/s
Pull-back rate	1–3 mm/s	2 cm/s	0.5–1 mm/s
Max. scan diameter	7 mm	10 mm	15 mm
Tissue penetration	1.5–2 mm	2 mm	10 mm

Modified from Eur Heart J. 2010 Feb;31(4):401–15.
[a] Based on specification of the LightLab M2/M2-X OCT systems.
[b] Based on specification of the C7XR OCT System.
[c] Based on specification of Volcano, Boston Scientific IVUS systems.

Jang et al. [34] performed the first in vivo study of intracoronary OCT in 10 patients, comparing OCT with IVUS for the assessment of coronary pathology. In addition to identifying the same atherosclerotic components detected by IVUS, such as fibrous plaque, and calcifications, OCT allowed the identification of intimal hyperplasia, the internal and external elastic lamina, and echolucent regions difficult to assess by IVUS. Further, OCT was able to identify the position of calcium within the vessel wall due to the lack of saturation and shadowing artifacts of calcium deposits, therefore enabling the visualization of adjacent tissues. OCT allowed the detection of the fibrous cap as strong contrast between lipid-rich cores and fibrous regions and the quantitative measurement of thin fibrous cap (<65 μm), due to its high spatial resolution. This launched OCT as an imaging tool for the detection of the thin-cap fibroatheroma (TCFA) that is considered the prototype of vulnerable plaque and precursor of plaque rupture. Other studies confirmed the ability of OCT to assess in vivo coronary plaque morphology, enrolling patients with acute coronary syndromes [35]. Furthermore, the OCT signal variance derived parameter, known as normalized standard deviation (NSD), showed a good correlation with CD68-positive cells assessed by immunohistochemical analysis in postmortem specimens ($r = 0.84$), allowing the quantification of macrophage infiltration within superficial portion of atherosclerotic plaque [36]. This parameter has been successfully used for the measurement of macrophage densities also in vivo [37]. In another study of 108 coronary arterial segments of 40 consecutive human cadavers Kume et al. [38] showed that OCT can correctly discern between red and white thrombi, on the basis of the attenuation width of signal intensity, with the 1/2 attenuation width of the signal intensity curve being significantly higher in red than in white thrombi (324 ± 50 vs 183 ± 42, $p < 0.0001$), and no significant differences in peak intensity of OCT signal. Red thrombi appeared as high-backscattering protrusions inside the lumen of the artery, with signal-free shadowing, and white thrombi as low-backscattering projections. Kubo et al. [39] assessed culprit lesion morphology in 30 patients with acute ST elevation myocardial infarction (STEMI) by OCT, IVUS and coronary angioscopy. OCT detected fibrous cap disruption with a higher prevalence (73%) compared to coronary angioscopy (47%, $p = 0.035$) and IVUS (40%, $p = 0.009$). The prevalence of plaque erosion differed among techniques (23%, 3%, and 0% in OCT, coronary angioscopy, and IVUS, respectively; $p = 0.003$), with OCT reporting a prevalence similar to that of previous post-mortem studies. The presence of intracoronary thrombus was observed in all cases by OCT and coronary angioscopy, but it was identified only in 33% by IVUS ($p < 0.001$). In addition, only OCT could estimate the fibrous cap thickness. Intraobserver variability yielded acceptable concordance although interobserver variability showed slightly lower concordance. Other studies have used OCT as imaging tool to study in vivo the mechanisms of acute coronary syndromes, therefore limiting the effect of selection bias, typical of post-mortem studies. In one study, the authors assessed the morphology of the culprit lesion, classifying the ruptured plaque as with rupture as at the shoulder or in the central portion of the fibrous cap by OCT. They investigated the relation between the morphology of plaque rupture with the type of patient activity at the onset of symptoms (i.e. exertion or rest) [40]. This study found that patients with exertion triggered acute coronary syndrome usually present with shoulder type plaque rupture, while those with rest acute coronary syndrome onset show a ruptured plaque in the central portion of the fibrous cap. Another study investigated the relation between culprit lesion morphology, such as plaque rupture or plaque erosion with luminal thrombi and systemic levels of inflammatory biomarkers, such as myeloperoxidase and C-reactive protein, in 25 consecutive patients with acute coronary syndrome [41]. This study showed that patients with plaque erosion present with significantly higher levels of myeloperoxidase than those with plaque rupture, while the levels of C-reactive protein did not significantly differ between the two groups. Other studies have shown that OCT can monitor the change in plaque fibrous cap thickness over time in response to drug administration [42].