Optical Coherence Tomography - Guided Percutaneous Coronary Interventions: From a Research Tool to Clinical Practice

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Introduction

Coronary angiography (CA) is considered the main method to assess severity of coronary artery disease (CAD) and guide percutaneous coronary interventions (PCI). However, the method supports only two-dimensional projections of the contrast-filled vessel lumen and is unable to examine the diseased vessel wall itself. Intravascular imaging (IVI) by means of ultrasound (IVUS) or optical coherence tomography (OCT) may provide the missing information on the vessel wall and improve the PCI guiding. Over the past decade, technical performance (e.g. higher resolution) and procedural aspects (e.g. faster pullback, automatic analysis) of the imaging have progressed remarkably. Moreover, a huge body of scientific evidence from observational studies, randomized trials, and meta-analyses has gathered to suggest that the use of IVI on top of the CA guidance not only enhances procedural results, but also improves long-term clinical outcomes [1]. Thus, the IVI guidance has definitely advanced from a primary research tool to a relatively frequently used adjunctive diagnostic modality in clinical practice [2].

In the current review, we sought to show potential opportunities of the OCT-guided PCI as compared to the CA-guided procedures and convey the recommendations of the European Society of Cardiology (ESC) on this subject [1,3].

History

OCT is a novel imaging modality that utilizes the near-infrared region of the electromagnetic spectrum to generate high-resolution cross-sectional images within the optical scattering media. Initially, it was applied for examination of the eye and the first tomograms of the human retina were documented in 1991 [4]. More recently, advances in the imaging technology have also made it possible to scan nontransparent tissues, thus enabling OCT to be used in a wide range of medical subspecialties. The first application of the intracoronary OCT was published by Jang., et al. in 2002 [5]. Bouma., et al. managed to carry out OCT before initial balloon dilatation and following stent deployment in 35 patients with obstructive CAD. They found the OCT guidance feasible and the acquired images superior to those provided by IVUS [6].

Physical principles of OCT imaging

OCT is an imaging modality analogous to IVUS, using light instead of sound. To generate images, a special OCT probe (2.7 French) is introduced in the coronary artery and an infrared laser activated to examine the vessel in a spiral-like manner. The laser beam penetrates the underlying vascular tissue 2 - 3 mm deep and is then reflected to the OCT device for further evaluation. Contemporary OCT systems create cross-sectional images by means of the Fourier domain interferometry; each specific image point is calculated from the delay the laser beam takes to cross the investigated tissue. Basically, two interactions between the beam of light and the tissue determine the appearance of the vessel wall components, namely backscattering (i.e. reflection) and absorption. Brighter images are obtained through...
increased reflection, while optical shadows are produced through light absorption. Images are acquired at a peak wavelength in the 1280 - 1350 nm band that enables a 10 - 15 µm axial resolution, 95 µm lateral resolution, and maximal scan distance of approximately 7 mm [7]. A single pullback is performed with a speed of 20 mm/s, takes less than 3 s, and surveys the length of 72 mm. Co-registration of OCT with CA conveniently adjusts the findings of both methods in real time. The result of the OCT pullback is a cylindrical dataset coaxial to the imaging catheter that is immediately available for further processing. An example of such processing is shown in figure 1.

**Figure 1:** An example of initial luminal measurements in a patient with obstructive coronary artery disease. Upper row - a cross sectional image of the vessel obstruction with a cut-plane indicator. Middle row - the system automatically creates a trace of the lumen contour on each frame. The lumen profile displays the lumen as an area graph. Lower row - a longitudinal mode display of the diseased vessel with the minimal lumen area at 18 mm and the guide catheter at 22 mm.

### OCT vs. IVUS

OCT and IVUS are two imaging modalities that are used in everyday clinical practice, as opposed to more research-oriented infrared spectroscopy. The methods are to some extent competitive, though they are mostly complementary. They can both describe numerous features of the vessel wall and lumen pathology, successful stent deployment, and mechanisms of the stent failure (i.e. stent restenosis and thrombosis) that cannot be captured by CA alone. However, benefits of the two methods depend largely on the interpretation and the operators’ reaction to these findings [1]. There are several advantages that support the OCT imaging: 1) OCT images are clearer and easier to interpret due to a ten-time higher resolution, 2) accurate vessel measures are directly computed, 3) more structural details can be recognized (e.g. edge dissection, struts malapposition), 4) tissue characterization is better (e.g. calcium, thrombi), and 5) OCT predictors of stent failure are well established. On the other hand, there are some important limitations of OCT as compared to IVUS: 1) pre-dilatation of the target lesion may be needed to advance the OCT probe, 2) flushing with additional radiographic contrast is required to remove the blood from the vessel lumen, 3) penetration of the infrared beam through the vascular tissue is shallower, not allowing for complete assessment of the plaque burden, 4) visualization of the ostial left main artery may be impossible, and 5) scientific evidence of the OCT guidance is less-well established [1].
Clinical applications of OCT imaging

The advent of IVI has opened a new pathway for the PCI guidance, enabling transition from the lumen-based approach to the appreciation of the vessel wall structure and its response to stenting [8]. OCT imaging in the PCI setting may appear in different scenarios: 1) lesion assessment (e.g. target lesion recognition), 2) pre-procedural assessment (e.g. strategic procedural planning), and 3) post-procedural assessment (e.g. appraising stent - vessel interaction). A typical flowchart for the OCT-guided PCI is shown in figure 2.


In normal vessels and the sites of thin plaques, the coronary artery wall appears as a three-layer structure consisting of intima, media, and adventitia. However, with advanced atherosclerosis the normal vessel structure breaks apart. Contemporary OCT systems distinguish between three plaque components, namely fibrous, calcific, and lipid tissues. Moreover, macrophage accumulations, microvessels, and
thrombi can be readily detected which is not always true with IVUS. Recent IVI studies have revealed features typically associated with culprit lesions in acute coronary syndromes: thin-cap fibroatheromas, plaque ruptures and erosions, thrombi, and calcified nodules [9]. Intraluminal haziness, thought to be a typical angiographic marker of thrombosis, may also result from different situations such as vessel dissections, calcifications, and vessel tortuosity. OCT can consistently differentiate between these entities and enables appropriate treatment.

OCT has been extensively used for strategic planning based on lesion morphology. The best example are heavy calcifications that may prevent adequate stent expansion. OCT can reliably distinguish between superficial or deep calcifications and between single and multiple deposits. Total calcium arch >180° and increased calcium thickness > 0.5 mm are related to a greater risk of stent under-expansion. Therefore, OCT can definitely indicate the need for targeted therapies such as rotation atherectomy or cutting balloon angioplasty [1,8].

Precise stent selection and positioning are very important steps in successful percutaneous treatment of the obstructive CAD. Selection of stent diameter and length critically depends on proximal and distal disease-free reference segments (Figure 1). However, necropsy studies have demonstrated that atherosclerosis usually involves arteries rather diffusely. As a result, “normal” reference segments could hardly be angiographically discernible, which makes stent measures based only on CA misleading [10]. Oversized stents are likely to impose unnecessary damage on the vessel wall, causing more hyperplasia, edge dissections, and even ruptures. Conversely, stent undersizing may result in incomplete stent apposition or under-expansion that increases the risk of stent failure [11]. In bifurcation lesions, carina shift provoked by oversized stents may compromise side branches [12]. Longitudinal geometric miss is defined as diseased or injured stenotic vessel segment not fully covered by stent. At long-term follow-up, increased rates of target vessel revascularization and myocardial infarction were found in patients with incomplete stenting [13]. On the other hand, longer stents have been declared as independent predictor of restenosis, at least in era of bare metal stents [14]. Finally, insufficient stent coverage of lipid pools was reported to have resulted in increased risk for post-procedural myocardial infarction [15]. Therefore, a meticulous analysis of the OCT pullback using the automated lumen detection feature can provide precise data concerning not only the minimal lumen area, but also proximal and distal reference sites. Aggressive stent optimization algorithms based on external elastic membranes of the reference segments, rather than lumen-based approach, might help in achieving larger stent dimensions and more complete lesion coverage, thus preventing short- and long-term ischemic events [16].

Post-procedural imaging attempts to confirm the appropriateness of the stent deployment and exclude the important injuries of the vessel wall. Stent expansion describes the minimum cross-sectional area either as an absolute measure or compared with the predefined reference area. In principle, greater stent expansion has been related to better long-term stent patency, better clinical outcomes, and lower rates of stent failure [1]. In contrast to under-expansion, malapposition refers to lack of contact of stents’ struts with the vessel wall (Figure 3a-3e). Though there is no clear link between acute malapposition and subsequent stent failure, the findings of large stent thrombosis registries suggest that extensively malapposed struts should be corrected when anatomically feasible [1]. Tissue prolapse, typically defined as tissue extrusion from inside the stent area, may include either lesion protrusion or protrusion of athero-thrombotic material. It has been identified as a predictor of early stent thrombosis and has been related to adverse short-term prognosis, particularly in the context of acute coronary syndromes [17]. Finally, edge dissections are defined as disruptions of the arterial wall surface within the region five mm proximal and distal to the stent edges. They may be intimal, medial, or extending through the external elastic membrane. Most OCT-detected dissections are not visible by CA and may heal spontaneously. However, large, deep, and distal edge dissections should require additional stenting [18].
Figure 3: A. A 54-year-old male presented with Canadian Cardiovascular Society Class III angina. Angiography revealed a critical obstruction of the distal left main (LM) coronary artery.

B. After balloon pre-dilatation, a 3.5 x 26 mm drug-eluting stent was placed across the lesion and proximal optimization was performed with a NC balloon 4.0 x 9 mm with acceptable angiographic result.

C. A computer-imaged rendition of the implanted stent (lower row) showed a massive malapposition of the proximal stents’ struts (red color).

D. Three different displays of the same malapposition (red color): fly-through mode (9-11 o’clock) in the upper left row, cross-sectional view (12-6 o’clock) in the upper right row, and longitudinal view (at the 40-mm marker) in the lower row.

E. After post-dilatation with a NC balloon 4.5 x 9 mm at 24 At, the malapposition is hardly visible.
Optimal stent implantation

Pre- and post-procedural OCT imaging may be, ideally together, used to optimize stent implantation. The imaging frequently detects numerous adverse features that may be angiographically invisible. Therefore, it is crucial to understand the natural history and clinical impact of those abnormalities to define which features should be eventually corrected. The most relevant objectives to be achieved following stent implantation include optimal stent expansion, avoidance of landing zone insubstantial plaque burden or lipid rich tissue, avoidance of large malapposition regions, irregular tissue protrusion, and dissections.

The expert consensus group of the European Association of Percutaneous Cardiovascular Interventions (EAPCI) recommends key parameters that characterize an optimal PCI result and provides cut-offs to guide corrective measures and optimize the stenting result [1]. The following pre-defined stent optimization targets should be achieved at the end of the OCT-guided PCI (Figure 4): 1) relative stent expansion of > 80%, 2) mean stent area of > 4.5 mm² in non-left main lesions, 3) residual reference plaque burden < 4.5 mm², 4) stent malapposition < 400 µm with longitudinal extension < 1 mm, 5) edge dissection < 60° with longitudinal extension < 2 mm not involving deeper layers or distal stent edge, and tissue prolapse < 500 µm particularly in patients with acute coronary syndrome [1].

![Figure 4: Summary of pre-defined stent optimization targets. Source: Räber L., et al. EuroIntervention 39.35 (2018): 3281-330.](image)

The presence of suboptimal stent implantation, if not corrected, was confirmed a strong independent predictor of late major adverse coronary events, together with diabetes mellitus, chronic kidney disease, and ostial lesion location [6].

OCT-guided PCI: scientific evidence

There is abundant and convincing evidence that IVUS-guided PCI not only enhances the acute procedural results, but also improves clinical outcomes. With respect to clinical outcomes eight randomized controlled trials have compared IVUS-guided implantation of drug-eluting stents with CA-guided procedure [1]. Despite the relatively widespread use of OCT, clinical trials testing the ability of OCT to guide PCI and assess its impact on clinical outcomes have not been adequately performed so far. Currently, there are seven important observational studies [20-26], five randomized controlled trials [16,27-30] and two meta-analyses [31,32] of the OCT guidance performed in various clinical and procedural settings.
Observational studies

CLI-OPCI I study (670 patients) demonstrated that OCT-guided PCI was associated with a significantly lower one-year risk of cardiac death or myocardial infarction than CA-guided PCI (6.6% vs. 13.0%, P = 0.006), even at extensive multivariable analysis [20]. In CLI-OPCI II study (832 patients), suboptimal stent deployment according to specific quantitative OCT criteria was associated with an increased risk of major adverse cardiovascular events during six-month follow-up (hazard ratio 3.53, P < 0.001) [21]. In patients with acute coronary syndrome (507 patients), the presence of at least one of the OCT-defined suboptimal stent implantation parameters (hazard ratio 3.69, P = 0.002) and the residual intra-stent plaque/thrombus protrusion (hazard ratio 2.83, P = 0.008) were confirmed as independent predictors of device-oriented cardiovascular events at the median follow-up of 345 days [22]. In ILUMIEN I study (418 patients), physician decision-making was affected by OCT imaging prior to PCI in 57% and post-PCI in 27% of all cases [23]. In ILUMIEN II study (286 propensity matched pairs), the degree of stent expansion was not significantly different between OCT and IVUS guidance (P = 0.29). Although a higher prevalence of edge dissections was detected by OCT, the rates of major malapposition and tissue protrusion were similar after OCT- and IVUS-guided stenting [24]. The OCT-guided approach was reported in the number of stents used, number of patients treated with more than one stent, while there was no statistically significant difference in clinical endpoints [25]. In Pan-London PCI cohort (87,166 patients), OCT-guided PCI (1.3% patients) was associated with improved procedural outcomes, in-hospital events, and long-term survival at a median of 4.8 years (92.9% vs 84.3% in CA-guided PCI) [26].

Randomized controlled trials

In OCTACS study (100 patients with non-ST-segment-elevation myocardial infarction), the OCT-guided group had a significantly lower proportion of uncovered struts compared to CA-guided group at six-month follow-up (3.4% vs. 7.8%, P < 0.01) [27]. In ILUMIEN III study, 450 patients were randomly allocated to OCT (158 patients), to IVUS (146 patients), and to CA (146 patients). The final minimal stent area following OCT-guided PCI was not inferior to that of IVUS-guided PCI (P for non-inferiority =0.001) but also not superior to that of CA-guided PCI (P = 0.12). The rate of procedural adverse events was rather low in all groups [16]. In DOCTORS study, 240 patients with non-ST-segment-elevation myocardial infarction were randomly allocated to OCT-guided PCI and CA-guided PCI. OCT group was associated with higher post-procedural fractional flow reserve than CA group (0.94 ± 0.04 vs. 0.92 ± 0.05, P = 0.005). However, OCT did not increase procedural complications, type 4a myocardial infarction, or acute kidney injury [28]. In OPINION study, 829 patients were randomly allocated to OCT-guided PCI and IVUS-guided PCI. The 12-month clinical outcome in OCT patients was not inferior to that of IVUS patients (target vessel failure, 5.2% vs. 4.9%, P for non-inferiority = 0.042) [29]. Finally, Lee., et al. randomized 445 patients to OCT-guided PCI and 450 patients to CA-guided PCI. The median percentage of uncovered struts at 3 months was lower in the OCT-guided group than in the CA-guided group (7.5% vs. 9.9%, P = 0.009) [30].

Meta-analyses

Buccheri., et al. performed comprehensive hierarchical Bayesian network meta-analysis of 31 studies encompassing 17,882 patients. They showed that compared with CA guidance, the risk of all-cause death, myocardial infarction, target lesion revascularization, and stent thrombosis were significantly reduced by IVUS guidance as compared to CA guidance. No differences in terms of comparative clinical efficacy were found between IVUS and OCT for all the investigated outcomes [31]. Finally, Jiang., et al. found that OCT-guided DES implantation showed a tendency toward improved clinical outcomes compared to CA-guided implantation (odds ratio 0.72, P = 0.07) [32].

Future trials

The impact of OCT-guided vs. CA-guided PCI is currently being investigated in two randomized controlled trials. ILUMIEN-IV trial (OCT-guided PCI vs. CA-guided PCI in patients with high-risk clinical characteristics and/or with high-risk angiographic lesions. ClinicalTrials.gov Identifier: NCT03507777) will have been completed by July 2022 and OCTOBER trial (OCT-guided PCI vs. CA-guided RCA, Complex
bifurcation lesions, ClinicalTrials.gov Identifier: NCT03171311) by May 2029. The results of both trials will, hopefully, provide us with the long desired data when and how to use OCT imaging in the setting of everyday PCI.

Safety

The safety of OCT depends mainly on the mechanical characteristics of the catheter and the amount of contrast injected. However, miniaturization of the OCT probe, marked simplification of the acquisition procedures, and the inherent reduction in the required contrast volume has offset the procedural complication rate. According to the single-center registry data obtained from 1142 OCT procedures and 2476 IVUS procedures, imaging-related complications were rare (0.6% vs. 0.5%, \( P = 0.6 \)), and were self-limiting after retrieval of the imaging catheter or easily treatable in the catheterization laboratory [33]. No significant differences in post-procedural renal function were found comparing the OCT group vs. the CA group [20].

Costs

Several factors perceived to limit the use of OCT imaging were identified, including primarily high cost, reimbursement issues, and prolongation of the procedure. The use of OCT system to guide PCI leads to an additional cost to CA-guided PCI due to the cost of the device. As for IVUS technology, the increase of costs due to OCT technology is presently not covered by any increase of the diagnosis-related group reimbursement related to PCI. The OCT procedure extends the duration of the CA-guided PCI from a minimum of seven to a maximum 20 minutes and fluoroscopy time from a minimum of three to a maximum 4.4 minutes. The use of this technology does not require the employment of extra personnel with respect to habitual angiography procedures. Finally, IVUS-guided PCI was reported to be a cost-effective approach according to the dedicated economic analysis [2]. If the scientific evidence on presumed clinical impact was not limited in terms of quality and quantity of available studies, OCT-guided PCI would be considered cost-effective in a similar way. We expect that the completed ILUMIEN-IV trial will provide us with the missing data.

ESC recommendations

Clinical practice guidelines are supposed to summarize and evaluate all available evidence at the time of the writing process on a particular issue with the aim of assisting physicians in selecting the best management strategies for an individual patient with a given condition, taking into account the impact on outcome as well as the risk – benefit ratio of particular diagnostic or therapeutic means. Table 1 shows changes in the 2018 ESC/EACTS Guidelines on myocardial revascularization as compared with the 2014 version [3]. As a result, both IVI techniques, OCT and IVUS, are now suggested for selected patients to optimize stent implantation with the same class of recommendation and levels of evidence (Table 2). Furthermore, the Guidelines have recognized the role of IVI in providing unique insights into the underlying mechanisms of stent thrombosis and restenosis. Therefore, IVUS and/or OCT should be considered to detect stent-related mechanical problems leading to restenosis (Recommendation Class II a, Level of evidence C).

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<td>For PCI of bifurcation lesions, stent implantation in the main vessel only, followed by provisional balloon angioplasty with or without stenting of the side branch</td>
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<tr>
<td>Immediate coronary angiography and revascularization, if appropriate, in survivors of out-of-hospital cardiac arrest and an ECG consistent with STEMI</td>
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<tr>
<td>Assess all patients for the risk of contrast-induced nephropathy</td>
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Table 1: Changes in 2018 ESC/EACTS Guidelines class recommendations as compared to previous guidelines. Source: Neumann FJ., et al. Eur Heart Journal 40.3 (2019): 87-165.
An expert consensus document of the EAPCI summarizing the view of the expert panel on the clinical use of IVI to guide PCI in clinical practice was lately published in the *European Heart Journal* [1]. In a comprehensive paper, they tried to identify patients and lesions most likely to derive clinical benefit from the IVI-guided PCI. The relevance of the use of IVUS or OCT prior to PCI for optimizing stent sizing and planning the procedural strategy was discussed. Importantly, the consensus group recommended key parameters that characterized the optimal PCI result and provided cut-offs to guide corrective measures and optimize the stenting result (Figure 4). Finally, the panel highly recommended IVI and particularly OCT in the setting of stent failure. They stated that imaging facilitated identification of the mechanisms of stent failure (e.g. hyperplasia, under-expansion, stent fracture, and neo-atherosclerosis), guided appropriate treatment, minimized the risk of subsequent stent failure events, and raised awareness of any potential device related concerns.

**Conclusion**

IVI use has enabled us to better understand coronary pathology and consequences of stent implantation. Tremendous advances in the imaging technology have offered the OCT method as a histology-like modality, easy to use even in the PCI setting. OCT imaging may be applied in different scenarios and key parameters that characterize the optimal PCI result and provide cut-offs to guide corrective measures have been thoughtfully recommended. We believe that financial constraints will be overcome by new positive scientific data, specifically randomized controlled trials proving the clinical benefit of the OCT-guided PCI.

**Bibliography**


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