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Update on Intracoronary Optical Coherence Tomography: a Review of Current Concepts

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Abstract
Purpose of review The advent of intracoronary optical coherence tomography (OCT) has been a significant leap forward in the ability to visualize coronary structures with unprecedented resolution. However, the clinical application of this imaging modality has lagged behind rapid technological advances. One of the main reasons for the lack of wider clinical uptake has been the paucity of appropriately designed prospective randomized studies to demonstrate the impact of OCT on outcome measures after percutaneous coronary intervention (PCI).
Recent findings Over the last couple of years, studies from large registries have shown the impact of OCT in decision-making in PCI, with several further reports providing valuable insights into the natural history of the atherosclerotic disease process and the modulating effects of therapies. Furthermore, guidance of PCI by OCT, including the appropriate use of newer generations of coronary stents, has been the focus of multiple studies.
Summary In this contemporary review, we provide a brief overview of the recently published data and highlight the multiple areas that need further clarification as OCT is further incorporated into routine clinical practice.

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Keywords Optimal coherence tomography · Intracoronary imaging · Percutaneous coronary intervention · Coronary artery disease

Abbreviations

ACS	Acute coronary syndrome
BMS	Bare metal stent
BRS	Bioresorbable vascular scaffold
CAD	Coronary artery disease
CAV	Cardiac allograft vasculopathy
DES	Drug-eluting stent
EEL	External elastic lamina
EES	Everolimus-eluting stent
FFR	Fractional flow reserve
IFC	Intact fibrous cap
IVUS	Intravascular ultrasonography
MACE	Major adverse cardiovascular events
MI	Myocardial infarction
MLA	Minimal luminal area
MLD	Minimal luminal diameter
MSA	Minimal stent area
NSTEMI	Non-ST segment myocardial infarction
OA	Orbital atherectomy
OCT	Optical coherence tomography
PCI	Percutaneous coronary intervention
RA	Rotational atherectomy
RFC	Ruptured fibrous cap
SS	SYNTAX score
ST	Stent thrombosis
STEMI	ST-segment elevation myocardial infarction
TCFA	Thin-cap fibroatheroma
VH-IVUS	Virtual histology intravascular ultrasonography
VLScT	Very late scaffold thrombosis

Introduction

One of the primary applications of OCT has been the evaluation of plaque composition, stability, progression, and functional significance. An important prerequisite for accurate quantification of plaque size and luminal dimensions by OCT is the reproducibility of serial measurements, which has recently been shown in two different studies [1, 2], with more consistency demonstrated in OCT measurements compared to intravascular ultrasonography (IVUS) [1]. Nevertheless, in a meta-analysis of five studies including more than 300 lesions assessed by OCT, minimal luminal diameter or area (MLD and MLA) only moderately correlated with fractional flow reserve (FFR), suggesting that quantitative assessment of coronary plaques by OCT cannot reliably predict their physiological significance [3].

In addition to quantitative analysis, OCT characterization of unstable plaques has been the focus of intensive research. For instance, in a recent study by Taruya et al., changes in the vasa vasorum and intraplaque neovascularization were highly prevalent in plaques with ruptured caps [4]. However, several issues with regards to detection of vulnerable plaques, in particular thin-cap fibroatheroma (TCFA) as defined by OCT, remain unresolved (refer to comprehensive review by Sinclair et al. [5] and an editorial comment by Narula et al. [6]). Critically, a validated consensus on the exact cutoff values for fibrous cap thickness and the extent of lipid arc on OCT to define TCFA is still lacking [5], which is further compounded by relatively low reproducibility in measurement of these parameters on OCT even among highly trained individuals in the core lab setting [7]. In a recent in vitro histopathological validation study of TCFA by Brown et al., a combined approach using OCT for measurement of cap thickness together with virtual histology IVUS (VH-IVUS) to overcome the known limitation of OCT in detecting a necrotic core [8] has been proposed as a strategy for more accurate identification of TCFA [9]—a conclusion similar to a different study comparing the performance of OCT and gray-scale IVUS in detecting TCFA [10]. An important implication of the study by Brown et al. is that the majority of TCFA identified by VH-IVUS in the landmark Study Predictors of Events in the Coronary Tree (PROSPECT) [11] may have been falsely positive and that OCT imaging would have halved the reported prevalence [9]. The definition of TCFA in PROSPECT (the presence of >10 % confluent necrotic core abutting the lumen in >30° of the lumen in 3 or more consecutive frames) did not take into account direct measurement of cap thickness due to lower resolution of IVUS. This highlights the need for an OCT-based study on the natural history of atherosclerosis and vulnerable plaques. "Plaque stabilization, " defined as an increase in cap thickness on OCT, has been shown by statin treatment [5, 12, 13] especially when very low levels of low-density lipoprotein are achieved [14]. Whether these effects actually mediate the lower clinical events conferred by statins is not currently known.

OCT in Acute Coronary Syndromes

Several recent studies have shown the feasibility and safety of pre- and post-PCI intracoronary OCT in the setting of ACS [15], thus providing unique insights into the underlying substrate for myocardial infarction (MI). One such study, the Optical Coherence Tomography Assessment of Gender Diversity in Primary Angioplasty (OCTAVIA), enrolled 140 patients with ST-segment elevation MI (STEMI) (70 male and 70 female) and reported an intact fibrous cap (IFC) in approximately one third of patients, with a similar prevalence of IFCs in males and in females (thus not recapitulating the higher prevalence of IFCs noted in females in the autopsy studies). Moreover, there was no difference in the extent of covered stent struts in infarct-related lesions at 9 months regardless of the plaque substrate and no association between the culprit plaque morphology and specific clinical features or biological markers [16•, 17]. Compared to OCTAVIA, an OCT study of 112 patients with STEMI identified plaques with IFC at a relatively lower rate (one fourth) and found that primary PCI performed on this subset of culprit lesions was associated with less microvascular damage compared to the plaques with ruptured fibrous caps (RFCs) [18]. Lastly, the presence of RFCs in a population of patients presenting with ACS was an independent predictor of worse outcomes [19].

The overall similar outcomes for PCI with drug-eluting stents (DES) used in patients with IFCs and RFCs in OCTAVIA may implicate limited clinical utility of pre-PCI plaque characterization in ACS. However, healing processes may be dependent on the underlying pathology, which may suggest that these lesions can be treated differently [17]. Indeed, recent morphologic studies of ACS by OCT have shown the safety of a no-stenting approach and aggressive antiplatelet therapy in plaques with IFC [20, 21]. Appropriately designed prospective studies are needed to firmly establish whether this conservative strategy can be universally adapted in plaques with IFC in the context of ACS after establishment of blood flow by manual thrombectomy, particularly in stenoses with small plaque burden. In a substudy of the Thrombectomy versus PCI Alone (TOTAL) trial of 214 STEMI patients in whom OCT was performed, manual thrombectomy did not reduce pre-stent thrombus burden at the culprit lesion compared with PCI alone, and both strategies were associated with low thrombus burden at the lesion site after the initial intervention to restore flow [22]. Aspiration may extract cap fragments and/or necrotic core debris, with the post-aspiration OCT images revealing empty cores bounded by the fibrous strands of the residual cap and by the empty crater of the plaque core [17]. In serial OCT performed in the

months following resolution of acute thrombosis, the cavity of RFC plaques persists and is bordered by a smooth "neointima, " while IFC plaques show features suggesting partial incorporation of the deepest layers of thrombus in the plaque [20].

In addition to culprit lesions, important insights into the morphology of the non-culprit plaques have been provided in recent studies of patients with non-ST-segment elevation MI (NSTEMI) [23] and stable coronary artery disease (CAD) [24]. Parameters suggestive of higher vulnerability of non-culprit lesions on OCT—including thinner fibrous cap, lipid-rich plaques, and TCFA—were more frequently found in patients with greater extent of atherosclerosis as assessed by the SYNTAX score (SS) [23]. Furthermore, plaque rupture in the culprit lesion and along the culprit vessel was significantly higher in patients with higher SS [23]. Taken together, these results suggest that patients with high SS and ACS may have pancoronary plaque instability with heightened plaque vulnerability in culprit as well as non-culprit lesions. This finding is consistent with multiple studies showing the ability of the SS to predict the risk of adverse events [25], and a rationale for the residual SS post-PCI being a strong predictor of subsequent ischemic events [26].

OCT has also been used to evaluate the morphological characteristics of the culprit segments in patients with spasm-induced ACS. In a study by Shin et al., most spasm sites had atherosclerotic plaques, with two thirds having lumen irregularity without a thrombus and more than one fourth containing plaque erosion [27]. These findings are consistent with previous IVUS studies showing atherosclerotic plaques and negative remodeling at the spasm sites in patients with vasospastic angina [28–30], thus challenging the notion that coronary spasm occurs in normal coronary arteries and highlights the need for additional novel imaging modalities in patients presenting with ACS and non-obstructive CAD [31]. In another OCT-based study, intimal tear, erosion, and intraluminal thrombi were more frequent in patients with spasm-induced ACS than in those with chronic stable vasospastic angina [32]. Although spontaneous vasoconstriction relieved by intracoronary nitroglycerin was noticed in spasm-induced ACS, vascular injury per se can induce vasoconstriction unrelated to inherent smooth muscle hyperreactivity; therefore, a cause-and-effect relationship cannot be established [31]. Findings of intimal erosion and thrombus on OCT in this patient population suggest potential beneficial effects of antiplatelet therapy.

Role of OCT in PCI

Accumulating evidence supports a role for intracoronary OCT in guiding multiple steps of PCI, assessment of new intracoronary devices for PCI, surveillance of the treated vessels, and identification of the mechanisms for stent failure. The high resolution of OCT provides sharp border definition between the lumen and the vessel wall, allowing for automated measurements of vessel dimensions. This feature facilitates a more rational approach for selection of stent size and length. Moreover, it aids in identification of the underexpanded stent segments and, guided by angiography co-registration on newer commercial OCT systems, allows for targeted correction of the underexpanded segments (illustrated in Fig. 1).

Observational Study of OCT in Patients Undergoing FFR and PCI I (ILUMIEN I), one of the key recent OCT-based studies in PCI, is a large prospective, non-randomized, observational study that includes pre- and post-PCI FFR and OCT in its design with the objective of defining parameters for stent optimization and the impact of OCT on physician decision-making. The initial procedural findings and 30-day outcomes in ILUMIEN I have been published [33••], with 1-year outcomes recently reported. The key findings included feasibility and safety of successfully performing OCT both pre- and post-PCI in the vast majority of patients/coronary lesions, significant influence of OCT findings either pre-PCI and/or post-PCI on physician decision-making (particularly in patients with more complex disease), and more in-stent post-dilatations and stent implantations used to correct unsatisfactory post-PCI results (e.g., stent underexpansion and malapposition) that were not apparent on angiography. Importantly, changes in pre- and post-PCI strategy based on OCT findings were associated with low rates of MI [33••], with 12.1 % MI in patients with no optimization compared to zero in patients with pre- and post-PCI optimization. These findings raise the interesting hypothesis that safety of PCI could be improved by OCT. Some of the putative mechanisms for a reduction in peri-PCI MI include OCT guidance of "lesion preparation" based on the type of the atherosclerotic plaque (e.g., avoidance of high-pressure balloon dilatation in lesions with large lipid burden and necrotic core to avoid distal embolization), as well as identification and correction of severe stent underexpansion and malapposition, known to induce turbulence and platelet aggregation, especially with high residual platelet reactivity, thus leading to distal embolization [33••]. Consistent with these hypotheses, fibrous cap thickness on OCT is a strong predictor of peri-PCI MI [34].

Another recent report on the role of OCT in PCI was a post hoc propensity-matched retrospective analysis of the outcomes of OCT-guided stent implantation in ILUMIEN I compared to IVUS-guided PCI in Assessment of Dual Antiplatelet Therapy With Drug-Eluting Stents (ADAPT-DES) studies—i.e., ILUMIEN II study. Based on this analysis, the use of OCT in ILUMIEN I resulted in a similar stent expansion compared to the grayscale IVUS in ADAPT-DES [35•]. A major limitation of this study was its non-randomized retrospective design comparing two separate registries with different operators at different centers [35•]. The clinical impact of OCT findings during PCI has also been reported in a recent retrospective

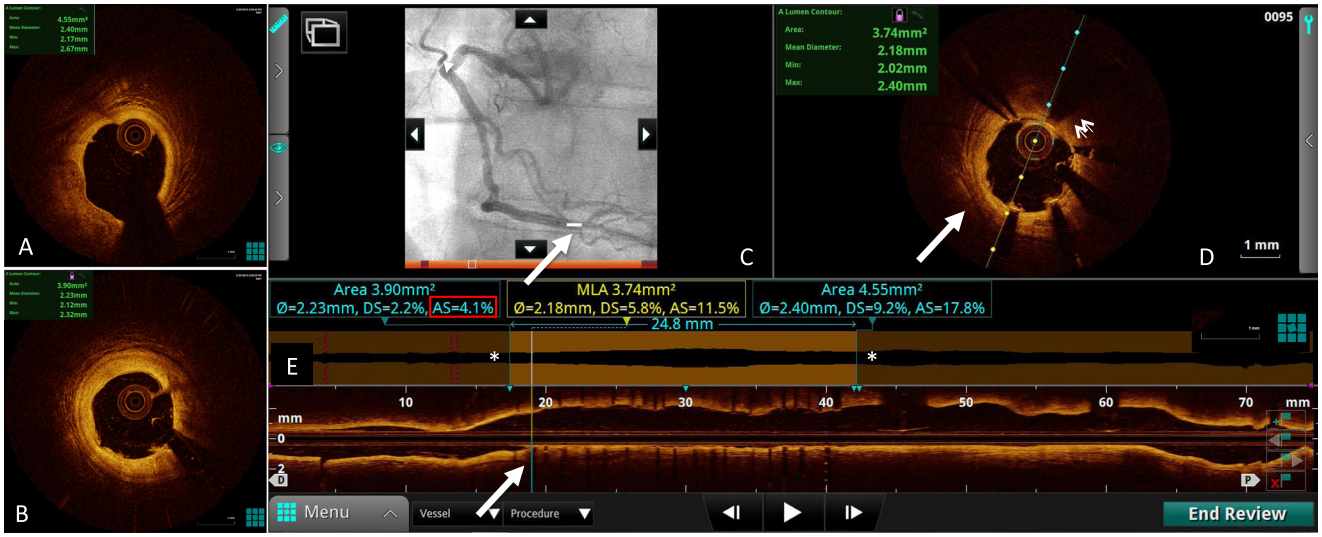

Fig. 1 Automated measurements on OCT used to guide PCI. After the PCI, the first frames outside the stent edges without visible stent struts are defined as proximal (**a**) and distal (**b**) reference segments. The *blue lines* (*asterisk*) mark these frames on the automated measurement panel (**e**), with their corresponding diameter and area measurements displayed in the *blue boxes*. The segment with the lowest cross-sectional area within the stent can be identified on OCT automation (**d**) (*yellow line*, measurements displayed in the *yellow box*) and marked on co-registration with angiography (**c**, *large white arrows*). Minimal stent area of 3.74 mm^2 on this segment compared to the distal reference area of 3.90 mm^2 indicates a 4.1 % degree of stent underexpansion (displayed in the distal reference segment measurements and outlined in *red*), which was corrected with post-dilatation

analysis of the multicenter Centro per la Lotta contro l'Infarto-Optimisation of Percutaneous Coronary Intervention (CLI-OPCI) registry [36••]. A total of 984 stented lesions were assessed by post-PCI OCT at a core laboratory. Suboptimal stent implantation was identified in 31 % of lesions, which was predictive of increased incidence of major adverse cardiovascular events (MACE) (all-cause mortality, MI including periprocedural MI, and target lesion revascularization). In particular, in-stent minimal luminal area (MLA) <4.5 mm^2, dissection >200 μm at the distal stent edge, and reference lumen area <4.5 mm^2 at either distal or proximal stent edges were independent predictors of MACE. In contrast, in-stent MLA/mean reference lumen area <70 %, stent malapposition >200 μm, intrastent plaque/thrombus protrusion >200 μm, and dissection >200 μm at the proximal stent edge were not associated with worse outcomes. In propensity-adjusted Cox hazard analysis, the presence of at least one significant criterion on OCT for suboptimal stent deployment was an independent predictor of MACE (HR 3.53; 95 % confidence interval 2.2 to 5.8) [36••]. These observations in CLI-OPCI II study replicate some of the characteristics associated with MACE reported in IVUS-guided PCI [37]. As discussed in an editorial comment on this report, the uncontrolled, retrospective study of a large and varied patient population in CLI-OPCI II, particularly with the many findings suggestive of suboptimal PCI identified by the core laboratory that were either not recognized by the proceduralists or left uncorrected, necessitate caution in the interpretation of the results [38]. Lastly, in a multicenter registry of PCI performed in 900 coronary lesions, abnormal findings frequently detected on post-PCI OCT included smooth tissue protrusion (93 %), disrupted fibrous tissue protrusion (61 %), irregular protrusion (54 %), incomplete stent apposition (39 %), and stent edge dissection (29 %) [39••]. Small minimal stent area (MSA), defined as MSA < 5.0 mm^2 in a DES or <5.6 mm^2 in a bare metal stent (BMS), was observed in 40 % of lesions. One-year device-oriented clinical end points occurred in 4.5 %, with irregular protrusion and small MSA being the independent predictors of 1-year device-oriented clinical end points, which were primarily driven by target lesion revascularization [39••].

The major limitation of ILUMIEN I and II studies was the lack of pre-specified criteria for stent sizing and optimization that will be addressed in the ILUMIEN III study, which is a prospective, multicenter, randomized trial with 1:1:1 randomization for PCI with either OCT, IVUS, or angiography guidance. In addition, a blinded post-PCI OCT run will be performed in the angiography and IVUS groups to allow for comparison of OCT-derived MSA across all groups as the primary end point of the study. One important novel aspect of the ILUMIEN III study is the introduction of an algorithm for OCT-guided selection of stent size and optimization of PCI, which overcomes the limitation of measurements with OCT versus IVUS due to the inherent different properties of light and sound [40]. By selecting the proximal and distal reference segments in areas where >180° of the external elastic lamia (EEL) can be visualized, this algorithm uses EEL-EEL measurements for stent sizing on OCT, thus overcoming the limitation of the widely used luminal measurements on OCT that can potentially result in underestimation of the true reference diameters and smaller MSA achieved with OCT-

versus IVUS-guidance [41•]. This might be the case in the ongoing Optical Frequency Domain Imaging vs Intravascular Ultrasound In Percutaneous Coronary Intervention (OPINION) study, a randomized clinical trial comparing the impact of OCT (lumen-guided) versus IVUS (EEL-guided) PCI, with the primary end point of target vessel failure (composite end point comprised of cardiac death, target vessel-related MI, and clinically driven target vessel revascularization). These two randomized clinical trials will be critical initial steps in filling the current void in robust and reliable data on the potential impact of OCT-guided PCI on clinical outcomes.

Several small observational studies have reported the utility of OCT in all steps of PCI including lesion preparation, stent deployment (in particular DES with bioresorbable polymer and bioresorbable vascular scaffold (BRS)), prediction of acute complications such as peri-PCI MI, and post-stenting surveillance. OCT can provide clear delineation of the depth and extent of calcification in the coronary artery wall; thus, it can potentially guide lesion preparation in fibrocalcific plaques, which includes visualization of the modifying effects of athero-ablation devices such as rotational atherectomy (RA) and orbital atherectomy (OA). Plaque modification by both OA and RA has been shown to result in a similar incidence of dissections detected on OCT [42]. However, OA causes deeper tissue modifications, which might partly explain better stent apposition after OA as compared to RA [42].

Due to the critical importance of meticulous lesion preparation for treatment using BRS and the unique ability of OCT to image scaffolds as clearly delineated "hollow" structures, several reports on OCT-guided optimization of BRS implantation have been published. Although post-dilation of BRS at high pressure has been reported to result in adequate expansion with low rates of scaffold malapposition and edge dissection [43], reports of longitudinal scaffold elongation detected on OCT have raised the possibility of issues such as scaffold protrusion through ostia, excessive overlapping, geographical miss, and side-branch compromise [44]. Case reports of side-branch occlusion by BRS as evaluated by OCT suggest that in addition to previously known causes, the thickness of scaffold struts plays a significant role in side-branch compromise even if the diameter of the side-branch exceeds 1.0 mm [45] (an example is shown in Fig. 2). On a positive note, restoration of native vessel lumen and physiology by BRS at long term may rationalize its utility in the setting of STEMI where thrombus-rich lesions containing a large necrotic core are associated with delayed arterial healing and impaired DES-related outcomes. This hypothesis has been tested in ABSORB-STEMI TROFI II, a multicenter, single-blind, non-inferiority, randomized controlled trial with 1:1 randomization to treatment with the Absorb BRS or an everolimus-eluting stent (EES) [46]. Stenting of culprit lesions with Absorb in the setting of STEMI resulted in nearly complete "arterial healing" as assessed on OCT (defined as the presence of uncovered and/or malapposed stent struts and intraluminal filling defects), which was comparable with that of the metallic EES at 6 months [46].

For early assessments of stents post-PCI, OCT has a unique ability in identifying minor degrees of neointimal proliferation, malapposition, and the presence of strut coverage, which has been used as a surrogate marker of safety and efficacy of new stents. Recent examples using strut coverage as an end point include the use of a new DES for treatment of NSTEMI [47], a DES with biodegradable polymer [48], and a comparison of such stent type versus DES with a durable polymer [49], and assessment of BRS [50]. A recent strut-level meta-analysis showed distinct temporal kinetics of strut coverage according to stent type, raising the possibility that these observations may underlie differences in rates of stent thrombosis (ST) observed with different stents [51]. Although strut coverage has been assumed to inherently represent re-endothelialization, evidence from non-human experimental studies suggest the resolution of OCT may not be adequate to detect endothelial coverage of stents [52, 53]. Indeed, fibrin-targeted near-infrared fluoroscopy imaging revealed that the majority of struts deemed covered by OCT, especially in DES, are actually covered by fibrin; therefore, covered struts may in fact be more prone to thrombosis [54]. Moreover, higher strut coverage was observed in smokers, albeit with a different, heterogeneous pattern after DES deployment [55], and no relationship has been established between strut coverage and endothelium-dependent vasomotor relaxation in response to acetylcholine and vascular endothelial growth factor levels in patients treated with BMS or various types of DES [56]. These observations have major implications in the utility of OCT alone in assessing re-endothelialization and point to a need for additional molecular imaging to reliably examine the components of neointima.

Accumulating evidence suggests that chronic inflammation and impaired endothelial function induce late de novo neoatherosclerosis (NA) inside BMS and DES, which may be an important mechanism for stent restenosis and late ST (for a comprehensive overview, refer to the study by Otsuka et al. [57]). OCT-based studies have significantly contributed to detection and morphological assessment of NA and have highlighted the role of traditional risk factors for atherosclerosis in native coronary artery—such as hypertension, high low-density lipoprotein levels, and chronic kidney disease—as well as time since PCI as independent predictors of NA [58]. This concept was confirmed in an OCT study of patients included in Sirolimus-Eluting Versus Paclitaxel-Eluting Stents for Coronary Revascularization (SIRTAX) 5 years after PCI with a DES. In-stent NA was observed in 16 % of lesions with the majority of plaques being fibroatheromas (11.4 %) followed by fibrocalcific plaques (5.7 %) [59]. Furthermore, in-stent NA has higher prevalence among patients with angiographic

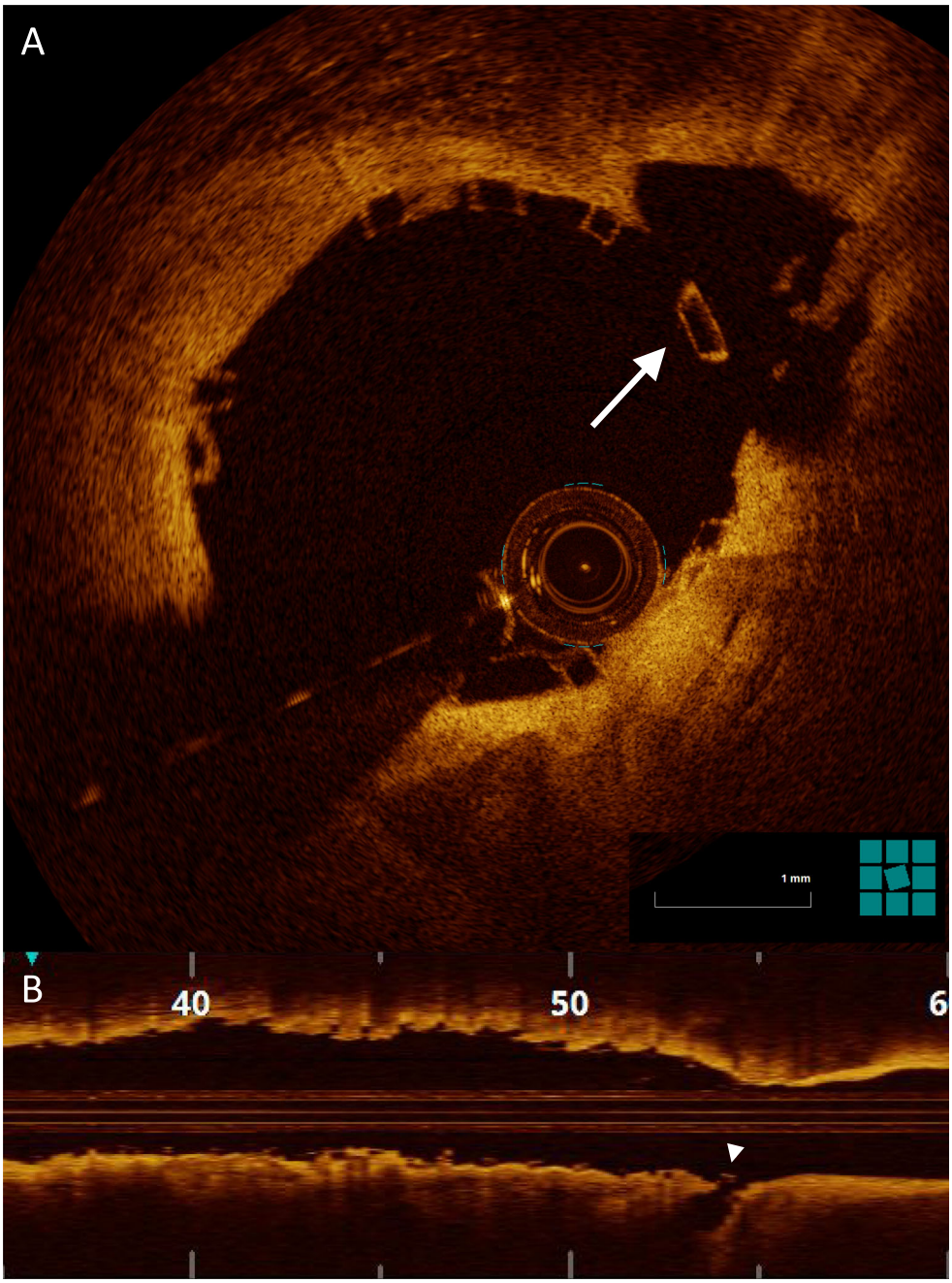

Fig. 2 OCT of an everolimus-eluting bioresorbable vascular scaffold. A scaffold strut overlying the ostium of a large first diagonal branch is shown in the cross-sectional (**a**) and longitudinal (**b**) views on OCT. The high strut diameter may represent a significant obstruction to the flow into the side branch

and clinical evidence of native atherosclerosis progression as assessed by quantitative angiography, suggesting similar underlying pathophysiological mechanisms [59]. NA is more common, occurs earlier, and develops more diffusely along the stented vessel in DES than in BMS [60]. Based on findings on OCT combined with near-infrared spectroscopy, NA can be classified as type I (thin-cap), type II (thick-cap NA), and type III (peri-strut NA), with greater lipid pool and type I NA detected in DES [60]. The axial length of NA and presence of thin-cap NA [61], in particular with DES [60], is associated with higher rates of peri-PCI MI compared to PCI performed on NA in BMS [60] and is one of the underlying causes of late and very late ST (for a comprehensive overview of intravascular imaging in ST, refer to the review by Ong and Jang [62]).

In a recent analysis from Morphological Parameters Explaining Stent Thrombosis assessed by OCT (PESTO) registry, an underlying cause for ST was found in 97 % of 120 patients with definite ST [63•]. This high rate might be explained by the frequent use of a two-step approach, i.e., initial treatment of the culprit lesion followed by deferred intracoronary imaging after optimal medical therapy. This approach may also explain the differences in the underlying causes of ST found in this study compared to previous reports [64]—while malapposition (48 %) and underexpansion

(26 %) were putatively considered the main reasons for acute and subacute ST, late and very late ST were mainly related to malapposition (31 %) and neoatherosclerosis (28 %) [63•]. Malapposition was the leading cause of late and very late ST in another retrospective study [65] with frequencies of causes for very late ST in a prospective registry including 85 patients with very late ST being strut malapposition (35 %), neoatherosclerosis (28 %), uncovered struts (12 %), and stent underexpansion (7 %) [66]. Malapposition might be due to acute inadequate stent apposition, which in 30 % of cases does not resolve over time (late-persistent malapposition) or may subsequently develop due to vascular remodeling around DES (late-acquired malapposition) [63•]. Although the types of malapposition were not specified in these reports, the longitudinal extent [66] and distance from the vessel wall were substantial [63•]. Lastly, very late scaffold thrombosis (VLScT) with Absorb BRS assessed by OCT has recently been reported in four cases [67]. As discussed in the editorial comment by Stone and Granada, potential causes for VLScT in these cases include uncovered struts with adherent thrombus, apparent detection of poly L-lactide material as suggested by "preserved boxes" appearance on OCT, intraluminal scaffold dismantling, and small luminal scaffold area [68].

Imaging of Inflammation in the Vasculature on OCT

Due to its high resolution, OCT can provide unique insights into inflammatory processes in the coronary artery. A substantial body of work has described the ability of OCT to visualize macrophages, key inflammatory cells involved in all phases of atherosclerosis, as distinct, signal-rich, or confluent punctate regions in the vessel wall [69]. A recent histopathological correlation study reported that while 57 % of "bright spots" identified on OCT anywhere on the arterial wall were associated with macrophages, 31 % of bright spots detected in TCFA were definitely caused by macrophages. Of note, not all bright spots were due to macrophage accumulation; other causes included cholesterol crystals, elastin/collagen, and microcalcifications [70, 71].

Imaging of inflammation in the vessel wall is of particular interest in chronic allograft vasculopathy (CAV), an accelerated form of CAD with major implications in heart transplant recipients. OCT is superior to coronary angiography and IVUS, as the subtle changes of the coronary intima in early CAV are not identified by coronary angiography and exceed the resolution of IVUS (refer to the review by Guddeti et al. [72]). Patients with high-grade rejection are more likely than those with mild/no rejection to have thicker intima, higher prevalence of macrophages, and a higher prevalence of intimal microchannels, all identified on OCT [73]. OCT-identified microchannels rapidly increase within the first year and are correlated with intimal volume [74], and vasa vasorum volume correlates with plaque volume in CAV [75], thus suggesting that neovascularization may play an important role in the progression of CAV. The presence of vulnerable plaque features such as TCFA and macrophage infiltration increases with time from transplantation, and complex lesions such as intimal laceration and plaque rupture are also more prevalent [76].

Recent Advances in OCT Technology

One of the notable technological advancements at preclinical level is the recent development of "Heartbeat" OCT. Combining a fast Fourier domain mode-locked laser, fast pullback, and a micromotor actuated catheter; this system acquires images at 4000 frames/s (25 times the current commercial systems) at 100 mm/s pullback speed, which can image an entire coronary artery in less than one cardiac cycle [77]. This system can therefore provide faithfully rendered, motion artifact-free, fully sampled vessel wall architecture and overcome the artifacts due to heart movement and non-uniform rotational distortion in commercial OCT systems [77]. Importantly, the extremely rapid pullback should result in a significant reduction in the volume of contrast flush media needed, which is one of the major drawbacks of the current OCT technology. Although this OCT system has been tested in porcine models, more preclinical data on the safety and performance are required before this promising iteration in OCT imaging can be tested in humans. Lastly, micro-OCT (μOCT), developed a few years ago, utilizes spectral-domain OCT with several key improvements resulting in tenfold higher resolution compared to conventional OCT [78]. Cellular and subcellular features can be visualized on μOCT, including individual macrophages and morphology of extracellular cholesterol crystals [78] and, more recently, the interaction of macrophages and crystalline cholesterol [79]; suggesting that μOCT might be useful to assess the response to therapeutics that affect crystal-inflammasome interaction.

Conclusions

With the wealth of information that can be gained with high-resolution imaging by intravascular OCT and accumulating evidence in a multitude of settings in the diagnosis, treatment, and surveillance of athero-thrombotic/inflammatory CAD, OCT appears ready for prime time. Randomized clinical trials recently started to answer key questions on clinical impact of OCT, in particular in the context of PCI, will determine whether OCT would eventually be integrated into routine clinical care.

Compliance with Ethical Standards

Conflict of Interest KKG and GWS declare that they have no conflicts of interest. AM reports grant support from Boston Scientific, consulting honoraria from Boston Scientific and ACIST, and speaker's bureau membership for St. Jude Medical, outside the submitted work. GSM reports grants from Boston Scientific, InfraRedx, and St. Jude and consulting honoraria from Volcano, Boston Scientific, ACIST, Abbott, St. Jude, and InfraRedx, outside the submitted work. RAS reports grants and personal fees from St. Jude Medical, outside the submitted work. ZAA reports grants and personal fees from St. Jude Medical, outside the submitted work.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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