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iREVIEWS

STATE-OF-THE-ART PAPERS

IVUS-Guided Versus OCT-Guided Coronary Stent Implantation

A Critical Appraisal

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ABSTRACT

Procedural guidance with intravascular ultrasound (IVUS) imaging improves the clinical outcomes of patients undergoing percutaneous coronary intervention (PCI) by: 1) informing the necessity for lesion preparation; 2) directing appropriate stent sizing to maximize the final stent area and minimize geographic miss; 3) selecting the optimal stent length to cover residual disease adjacent to the lesion, thus minimizing geographic miss; 4) guiding optimal stent expansion; 5) identifying acute complications (edge dissection, stent malapposition, tissue protrusion); and 6) clarifying the mechanism of late stent failure (stent thrombosis, neointimal hyperplasia, stent underexpansion or fracture, or neoatherosclerosis). Optical coherence tomography (OCT) provides similar information to IVUS (with some important differences), also potentially improving acute and long-term patient outcomes compared to angiography-guided PCI. The purpose of this review is to describe the similarities and differences between IVUS and OCT technologies, and to highlight the evidence supporting their utility to improve PCI outcomes. (J Am Coll Cardiol Img 2017;10:1487–503)

In the past 3 decades, intravascular imaging—intravascular ultrasound (IVUS) and more recently optical coherence tomography (OCT)—has been increasingly used to guide percutaneous coronary intervention (PCI) procedures. Specifically, these imaging modalities help interventionalists optimize stent implantation in multiple ways: 1) informing the necessity for lesion preparation (1,2); 2) directing appropriate stent sizing to maximize the final stent area (3–5); 3) selecting the optimal stent length to cover residual disease adjacent to the lesion, thus minimizing geographic miss (GM) (6–8); 4) guiding optimal stent expansion (3,9–18); 5) identifying acute complications (e.g., edge dissection, stent malapposition, tissue protrusion) (16–26); and 6) clarifying the mechanism of late stent failure (e.g., stent thrombosis, neointimal hyperplasia, stent underexpansion, stent fracture, neoatherosclerosis) (27–29). The purpose of this review is to describe the similarities and differences of IVUS and OCT, and to highlight the evidence supporting the utility of each in patients undergoing PCI with stent implantation.

TECHNICAL DIFFERENCES BETWEEN OCT AND IVUS

There are several key differences between OCT and IVUS (**Figure 1**). OCT has ~10 times higher axial

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ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome(s)

BRS = bioresorbable vascular scaffolds

CI = confidence interval

DES = drug-eluting stent(s)

EEL = external elastic lamina

FFR = fractional flow reserve

GM = geographic miss

ISR = in-stent restenosis

IVUS = intravascular ultrasound

MACE = major adverse cardiac event(s)

MI = myocardial infarction

MSA = minimum stent area

OCT = optical coherence tomography

OR = odds ratio

PCI = percutaneous coronary intervention

PES = paclitaxel-eluting stent(s)

PSP = preparation, sizing, and post-dilatation

TLR = target lesion revascularization

TVF = target vessel failure

resolution than IVUS; requires blood clearance (IVUS does not); and has limited soft tissue penetration (1 to 2 mm) compared with IVUS (5 to 6 mm), especially in the presence of red thrombus, lipid, or necrotic core, which attenuate the OCT light signal (30–32) (**Table 1,** Online Table 1). IVUS uses ultrasound (~40-μm wavelength at 40 MHz), whereas OCT uses infrared light (1.3-μm wavelength), which confers significantly greater resolution but has lower tissue penetration. Because the wavelength of OCT is shorter than the 8-μm diameter of a red blood cell, backscattering from blood occurs with OCT such that the vessel wall cannot be seen without blood clearance. The combination of better resolution and clearance of blood during OCT imaging provides a much clearer interface between lumen and plaque surface, enabling accurate automatic lumen measurements, whereas with IVUS human interaction is required to accurately identify lumen contours. In addition, because of its superior resolution, the reproducibility of OCT measurements is better than IVUS (33). Conversely, one of the most useful features of IVUS that is lacking with OCT is full-thickness visibility of the vessel wall. Glagov et al. (34) introduced the concept of "vessel remodeling" in 1987, wherein the vessel enlarges as a compensatory mechanism during medial plaque accumulation to limit lumen compromise. By IVUS, it is possible to measure and use vessel size parameters for device sizing, theoretically enabling achievement of larger stent areas with low risk of vessel perforation. In contrast, OCT often cannot visualize the true vessel size at the lesion site, and many operators size stents to the reference lumen diameters, although this practice is evolving.

Most experts believe that OCT more accurately measures lumen dimensions than IVUS. An in vitro study by Kubo et al. (35) reported that the OCT area was similar to that of a phantom model (phantom = 7.45 mm^2; OCT = 7.45 ± 0.17 mm^2), whereas IVUS overestimated the area by 7.8% (8.03 ± 0.58 mm^2). In 100 lesions studied with both OCT and IVUS (in vivo), IVUS lumen area was larger than OCT (mean difference = 0.41 mm^2, 12.5%). However, these findings may not always hold in individual cases (35–37). For example, Bland-Altman plots in multiple IVUS-OCT comparative studies showed that in one-third of cases, OCT lumen area was larger than IVUS lumen area (35,37).

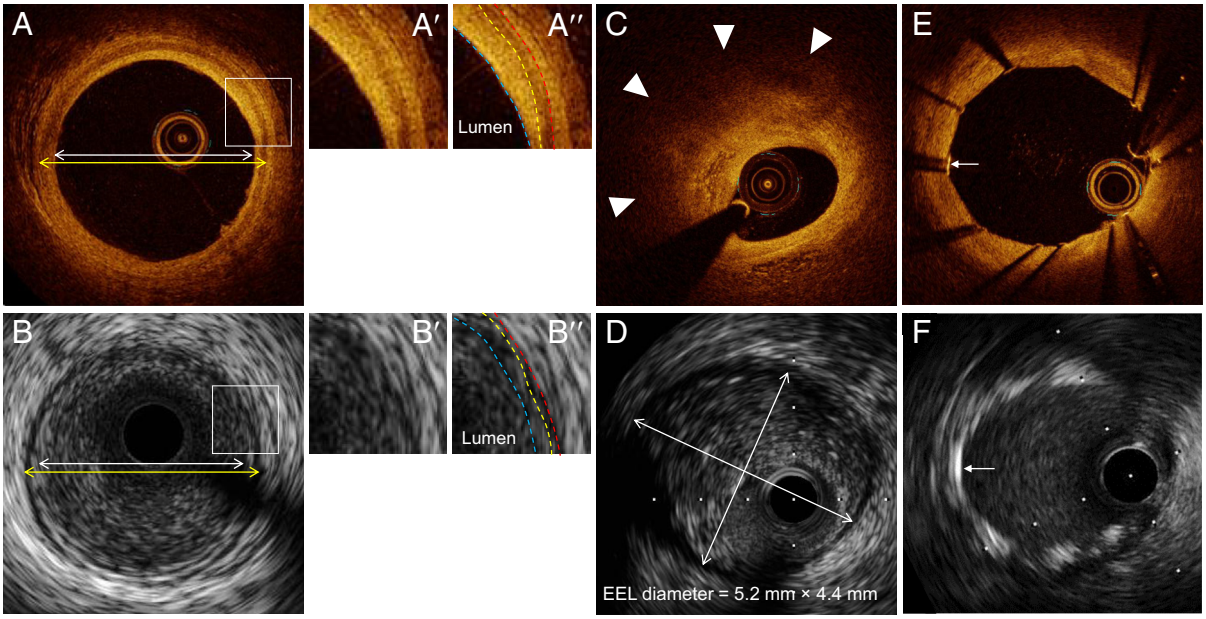
Compared to IVUS or angiography guidance, OCT guidance PCI requires 17 to 70 ml more contrast in order to clear the blood from the lumen (5,38–41). Because of the requirement for blood clearance, inability to visualize the aorto-ostial junction (including ostial lesions that have a high prevalence of restenosis) is a significant limitation of OCT. In a contemporary cohort including 1,142 frequency domain OCT (2.4-F to 2.7-F catheter) and 2,476 IVUS procedures (3.2-F to 3.5-F catheter), imaging-related complications were rare without any difference between OCT vs IVUS (0.6% vs. 0.5%), and most were self-limiting after removal of the imaging catheter (42).

PRE-INTERVENTION EVALUATION OF PLAQUE TYPE RELATED TO ACUTE STENT OUTCOMES

LIPIDIC PLAQUE AND DISTAL EMBOLIZATION. Baseline IVUS or OCT may predict distal embolization and subsequent periprocedural myocardial infarction (MI) after PCI in native arteries and restenotic lesions (43–46). Morphological predictors of periprocedural MI in observational studies are attenuated plaque (indicating a large necrotic core) (47) or plaque rupture by IVUS, necrotic core by virtual histology IVUS, and thin-cap fibroatheroma or plaque rupture by OCT. Representative images of lipidic and calcified plaque by OCT and IVUS are shown in **Figure 2**. In a large IVUS study of 336 patients with acute coronary syndrome (ACS) and 351 patients with stable coronary artery disease, the prevalence of attenuated plaque was 43.8% and 27.9%, respectively, and its adjusted odds ratio (OR) to predict post-PCI Thrombolysis in Myocardial Infarction flow grade <3 was 5.9 (95% confidence interval [CI]: 2.4 to 14.5) and 6.6 (95% CI: 1.4 to 32.1), respectively (44). Furthermore, in 170 patients with ST-segment elevation MI, attenuated plaque ≥5 mm in length predicted post-PCI Thrombolysis In Myocardial Infarction flow grade <3 with OR of 20.1 (95% CI: 5.9 to 69.0) (45).

CALCIFICATION. The sensitivity of calcium detection by IVUS relative to pathology has been reported as 89% to 90%, with specificity of 97% to 100% (48,49). Mintz et al. (50) reported that IVUS detected calcium in 73% (841 of 1,155) of stable patients, whereas angiography detected calcium in only 40% (440 of 1,155). In general, angiographically detectable calcium corresponds to more calcium (larger angle and length) by IVUS compared to angiographically invisible calcium. OCT can penetrate calcium so that its thickness and area are often evaluable, whereas IVUS is unable to analyze calcium thickness or area

FIGURE 1 Differences in Lumen and Stent Measurements Between OCT and IVUS



Matched OCT and IVUS images from the same lesions are shown. Lumen area measured 8.40 mm^2 by OCT **(A)** and 8.83 mm^2 by IVUS **(B)**. Magnification of selected squares in **(A)** and **(B)** are shown in **(A′)** and **(A″)** (OCT) and in **(B′)** and **(B″)** (IVUS), and include the EEL **(red dotted line)**, internal elastic lamina **(yellow dotted line)**, and lumen surface **(blue dotted line)**. EEL diameter **(yellow double arrowhead)** measured 3.86 mm by OCT and 4.09 mm by IVUS. Lumen diameter **(white double arrowhead)** measured 3.28 mm by OCT and 3.54 mm by IVUS. At the lesion, although EEL diameter by IVUS **(D)** was visible (**white double head arrows**, 5.2 × 4.4 mm), OCT **(C)** failed to show the EEL border **(white arrowheads)** due to attenuation of plaque and limited penetration depth. Stent area measured 8.10 mm^2 by OCT **(E)** and 8.24 mm^2 by IVUS **(F)**. White arrow indicates stent strut. The difference of area measurement between OCT and IVUS was less in stented segments than in nonstented segments. EEL = external elastic lamina; IVUS = intravascular ultrasound; OCT = optical coherence tomography.

because ultrasound is almost entirely reflected from the calcium surface. Using OCT, Kobayashi et al. (2) reported that calcium area and angle were related to poor stent expansion. In other reports, thinner calcium (<0.5 mm in thickness) was associated with calcium fracture irrespective of calcium angle, and calcium fracture was, in turn, associated with greater stent expansion compared to the absence

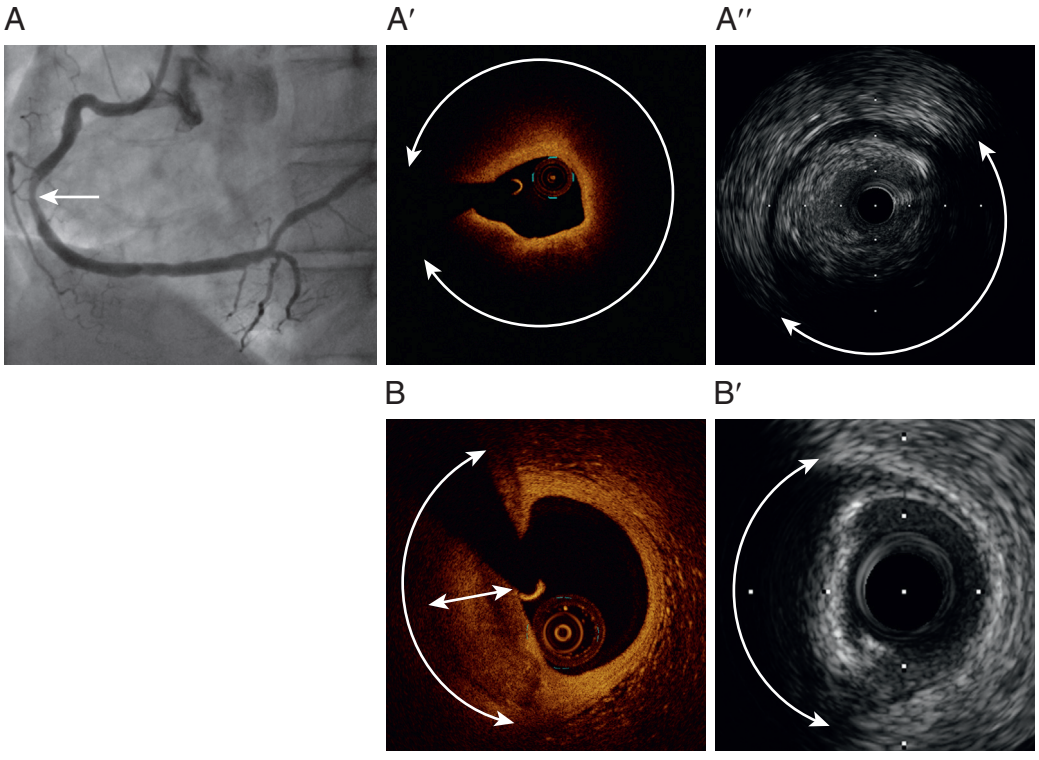
TABLE 1 Properties, Advantages, and Disadvantages of IVUS and OCT

	IVUS (40-45 MHz)*	IVUS (50-60 MHz)†	OCT Frequency Domain‡
Wave source	Ultrasound	Ultrasound	Near-infrared light
Axial resolution, μm§	38-46	20-40	15-20
Penetration depth in soft tissue, mm	>5	3-8	1-2
Distance between adjacent frames, mm	0.02-0.03	0.02-0.17	0.1-0.25
Maximum pullback length, mm	100-150	100-150	75-150
Blood issue	Moderate backscatter from blood	Strong backscatter from blood	Requires clearance of blood
Aorto-ostial lesion visualization	+	+	−
Cross-sectional calcium evaluation	Angle only	Angle only	Thickness, angle
Lipidic plaque evaluation	Attenuated plaque	Attenuated plaque	Lipidic plaque and cap thickness
Plaque burden at lesion site	+	+	−

*Includes Boston Scientific and Volcano. †Includes Infraredx, Boston Scientific, ACIST, and Terumo. ‡Includes St. Jude Medical and Terumo. §Except for ACIST, resolution data were based on engineering calculations and were not measured. Each manufacturer's data are shown in Online Table 1.

IVUS = intravascular ultrasound; OCT = optical coherence tomography.

FIGURE 2 Lipidic and Calcified Plaque by OCT and IVUS



(A′) and **(A″)** are OCT and IVUS images corresponding to the arrow in **(A)** in a patient with stable angina who suffered periprocedural myocardial infarction after stenting. There was a large lipid rich plaque defined by diffuse border with attenuation **(double-headed arrow)** by OCT **(A′)** and large attenuated plaque defined as echo attenuation without hyperechoic leading edge **(double-headed arrow)** by IVUS **(A″)**. **(B)** (OCT) and **(B′)** (IVUS) show calcified plaque. The thickness of calcium can be measured only by OCT (**double-headed arrow**, 1.05 mm), and the calcium angle measured 130° by both IVUS and OCT. Abbreviations as in Figure 1.

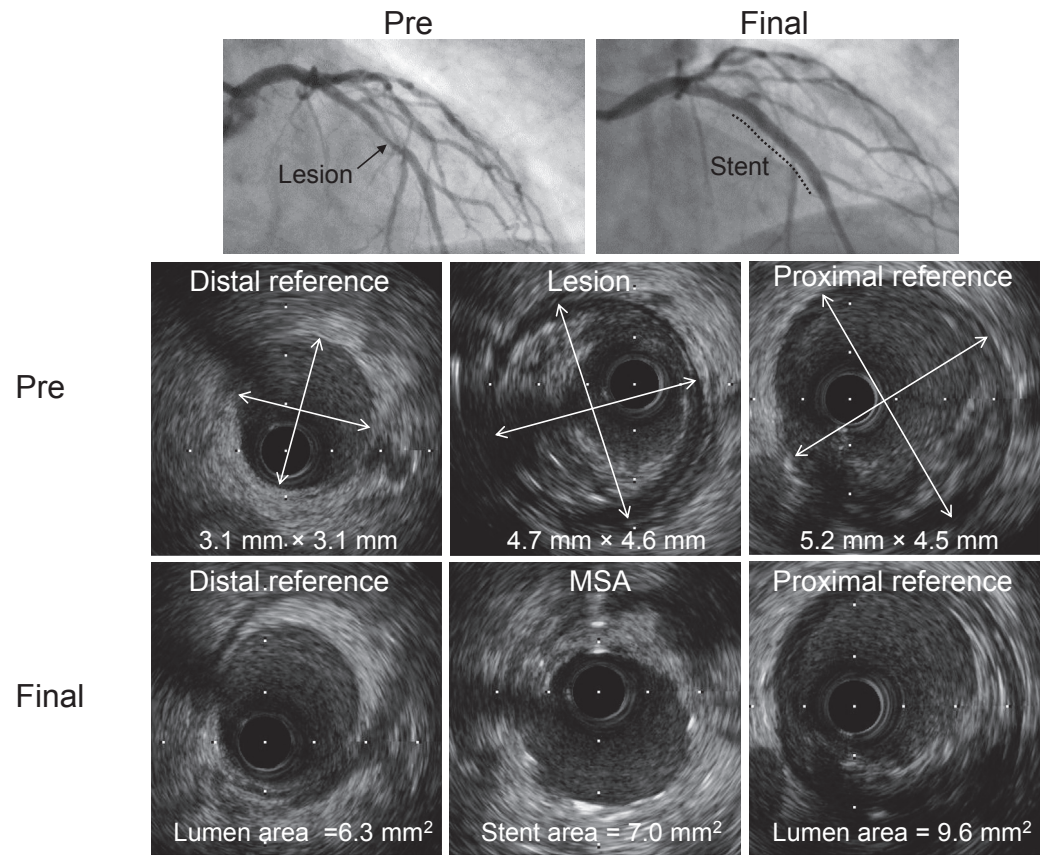
of calcium fracture (51,52). Thus, the presence of angiographically visible calcium or an IVUS or OCT calcium angle >180° that is >0.5 mm thick by OCT is associated with poor stent expansion and should prompt consideration for pre-stent adjunctive calcium modification with techniques such as rotational atherectomy, orbital atherectomy, or cutting or scoring balloons.

STENT SIZING BY IVUS

MUSIC (Multicenter Ultrasound Stenting in Coronaries Study), published in 1998, was the first major IVUS-guided stent optimization study (53). IVUS was used only after stent implantation, and key optimal stent implantation criteria were suggested: 1) minimum stent area (MSA) ≥90% of average reference lumen area or ≥100% of the smaller reference lumen area; or 2) if MSA >9 mm^2, then MSA ≥80% of average reference lumen area or ≥90% of smaller reference lumen. Lesions <15 mm in length treated with 3-mm-diameter bare metal Palmaz-Schatz stents were included; 81% met IVUS optimization criteria, and the study showed an overall low rate of target lesion revascularization (TLR) of 4.5% at 6 months.

In the drug-eluting stent (DES) era, IVUS-guided stent or post-stent balloon sizing recommendations have been based on either: 1) external elastic lamina (EEL) diameters of the proximal reference, distal reference, or lesion site, usually rounded down by (at least) 0.5 mm; or 2) reference lumen diameters. Both are typically larger than angiographic reference lumen diameter measures, especially in smaller vessels. A representative case of IVUS guided-stenting is shown in Figure 3. Chieffo et al. (3) proposed stent diameter selection criteria in the AVIO (Angiography

FIGURE 3 **Representative Case of IVUS-Guided Stenting**



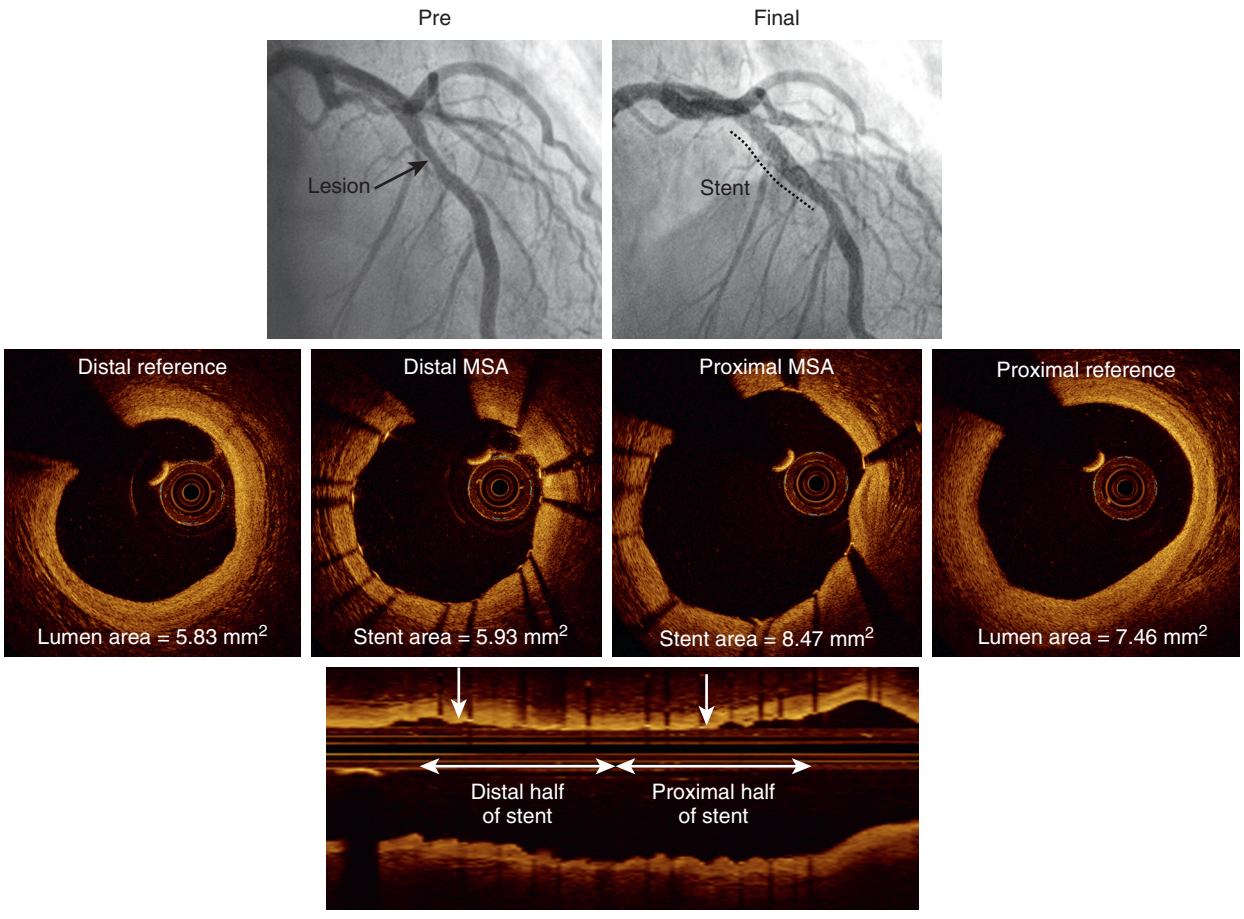
In the pre-PCI IVUS image, EEL diameters can be measured at the distal (3.1 × 3.1 mm) and proximal (5.2 × 4.5 mm) references and at the lesion (4.7 × 4.6 mm). The averages of all EEL diameters were rounded down to a 3.5-mm stent size because the distal reference looked normal and the EEL diameter was 3.1 mm. Post-stent images showed an MSA of 7.0 mm^2 and stent expansion (MSA/average of proximal and distal reference lumen area) of 88.2%. MSA = minimum stent area; PCI = percutaneous coronary intervention; other abbreviations as in Figure 1.

Versus IVUS Optimization) study. Optimal balloon size was determined by averaging the media to media diameters of distal and proximal stent segment, as well as at the site of narrowing within the stent. The optimal target stent area was based on the nominal optimally sized balloon area. For example, if using a 3-mm balloon (nominal balloon area = 7.1 mm^2), the target stent area was 6 mm^2, and if using a 3.5-mm balloon (nominal balloon area = 9.6 mm^2), the target stent area was 8 mm^2.

STENT SIZING BY OCT

Stent sizing based on EEL measures will usually result in larger-diameter stents being selected than sizing based on reference measures. The ILUMIEN (Observational Study of Optical Coherence Tomography in Patients Undergoing Fractional Flow Reserve and Percutaneous Coronary Intervention) III study thus pre-specified a novel OCT-guided stent optimization algorithm to overcome the fact that OCT often cannot visualize the EEL at the lesion site (5). Rather, stent sizing was based on the proximal and distal reference segment EEL measurements. If the EEL circumference was visible for ≥180°, the EEL diameter was used to estimate the true vessel size. Then the stent diameter was chosen by the smaller EEL diameter of the proximal or distal reference and rounded down to the nearest 0.25-mm stent diameter (e.g., if the proximal EEL diameter is 3.83 mm and the distal EEL

FIGURE 4 Representative Case of OCT-Guided Stenting From the ILUMIEN III Trial



In the pre-OCT study (images not shown), the mean EEL diameters at the proximal and distal references measured 3.48 mm and 3.14 mm, respectively. Based on the smaller EEL diameter (3.14 mm), a 3-mm diameter stent was chosen. Post-dilation was performed using a noncompliant 3.5-mm balloon with high pressure. In the post-stent OCT (Final), the proximal half and the distal half MSA were compared with the adjacent reference lumen area. Stent expansion in the proximal half (114% [8.47 of 7.46]) and distal half (102% [5.93 of 5.83]) were excellent, and the procedure was completed. Abbreviations as in **Figures 1 and 3**.

diameter is 3.62 mm, then the smaller EEL diameter is 3.62 mm, and a 3.5-mm diameter stent would be chosen). If the operator could not see EEL circumference ≥180°, stent size was based on 100% of lumen diameter. Stent implantation criteria took into account the potential for coronary artery tapering. The stent segment was divided into proximal and distal halves, and on the post-PCI OCT the MSA of each half was compared to the respective reference lumen area; ≥95% was considered optimal and ≥90% was considered acceptable stent expansion. A representative case of OCT-guided stenting is shown in **Figure 4**. This protocol allowed OCT-guided stenting to achieve similar MSA results as IVUS-guided stenting.

POST-INTERVENTION PREDICTORS OF CLINICAL OUTCOMES

UNDEREXPANSION AND THE MSA. The most consistent and strongest parameter to predict both restenosis and stent thrombosis is the post-PCI MSA (9–18), and MSA has been used as a surrogate of clinical outcomes in previous studies (5) (**Table 2**). The cutoffs of IVUS MSA to optimize sensitivity and specificity of angiographic binary restenosis are similar with different types of DES: sirolimus-eluting stents 5.5 mm^2, paclitaxel-eluting stents (PES) 5.7 mm^2, everolimus-eluting stents 5.4 mm^2, and zotarolimus-eluting stents 5.3 mm^2 (10–12). Of note, however, these cutoffs do not define optimal stenting, and a

TABLE 2 IVUS- or OCT-Detected Morphological Parameters Associated With Clinical Outcomes

First Author/Study (Ref. #)	Image	N	Minimum Stent Area	Malapposition	Tissue Protrusion	Edge Disease	Edge Dissection	Endpoint
Fujii et al. (14)	IVUS	60	Yes	No	No	Yes	No	Subacute definite/probable stent thrombosis
TAXUS trials (6,11,23)	IVUS	1580	Yes	No	Not reported	Yes	Not reported	Binary in-stent restenosis or edge restenosis
Kang et al. (7), Song et al. (12)	IVUS	912	Yes	Not reported	Not reported	Yes	No	Binary in-stent restenosis or edge restenosis
HORIZONS-AMI (13,16,22)	IVUS	389	Yes	No	No	Yes, for stent thrombosis	Yes, for stent thrombosis	Stent thrombosis or binary in-stent restenosis
ADAPT-DES (24–26)	IVUS	2,062	No	No	Yes*	No	Yes	Target lesion revascularization
Ino et al. (8)	OCT	319	Not relevant	No	Not relevant	Yes	No	Binary edge restenosis
MGH OCT registry (17)	OCT	786	Yes	No	Yes, if irregular†	No	No	Target vessel failure
CLI-OPCI II (18)	OCT	832	Yes, if <4.5 mm^2	No	No	Yes, if <4.5 mm^2	Yes, if distal edge	Target vessel failure

*Associated with less target lesion revascularization. †Associated with worse target vessel failure.

ADAPT-DES = Assessment of Dual Antiplatelet Therapy with Drug-Eluting Stents; CLI-OPCI = Centro per la Lotta contro l'Infarto-Optimisation of Percutaneous Coronary Intervention; HORIZONS-AMI = Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction; MGH = Massachusetts General Hospital; other abbreviations as in Table 1.

larger MSA is still associated with less coronary artery restenosis until a plateau is reached at an MSA of ~8 mm^2. Although stent underexpansion is common in both early stent thrombosis and in-stent restenosis (ISR), underexpansion is more severe and diffuse in patients with stent thrombosis compared to ISR (15).

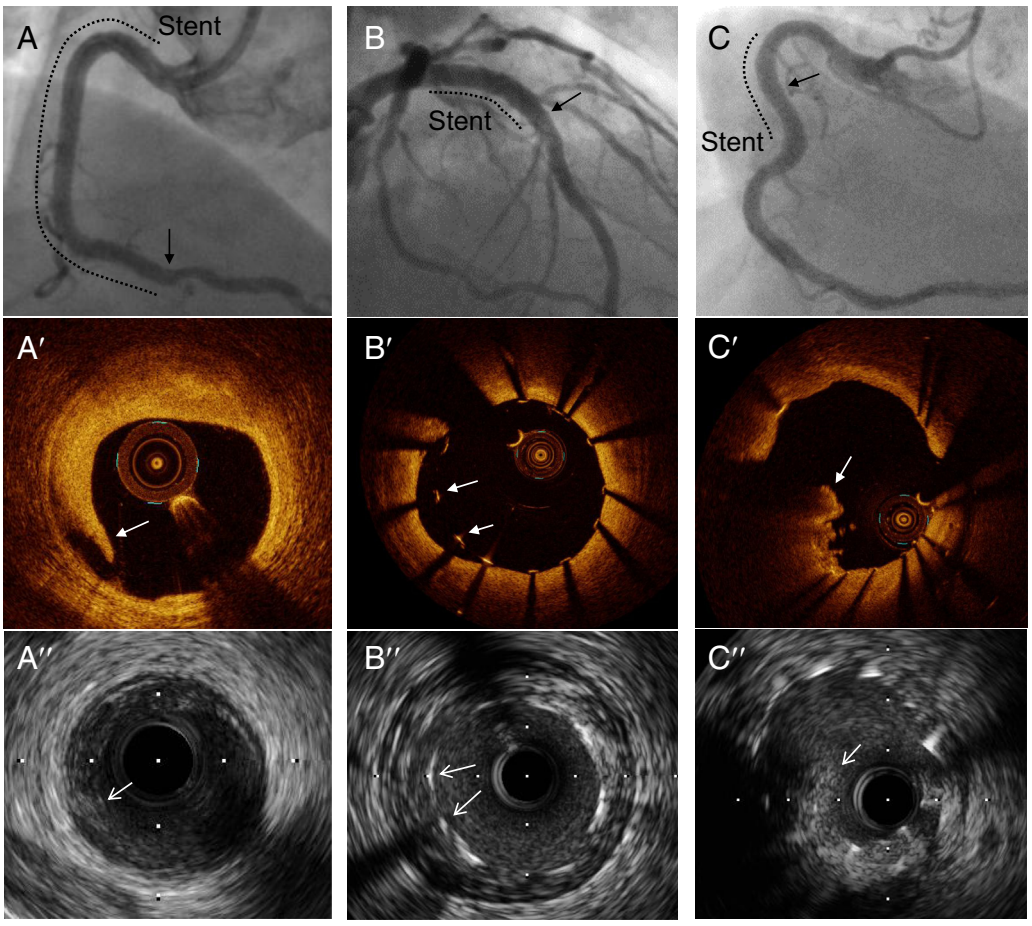
In a large OCT registry, Soeda et al. (17) reported a 4.5% (33 of 727) rate of 1-year device-oriented clinical endpoints (cardiac death, target vessel MI, TLR, or stent thrombosis), and OCT-MSA was found to be an independent predictor of device-oriented clinical endpoints and TLR, with an MSA cutoff value of 5.0 mm^2 for DES and 5.6 mm^2 for bare metal stents. Similarly, Prati et al. (18) showed MSA <4.5 mm^2 was associated with major adverse cardiac events (MACE) (adjusted hazard ratio [HR]: 1.64) in 832 patients. In ILUMIEN III, in which patients were randomized to OCT-guided, IVUS-guided, or angiography-guided stenting, OCT MSA <5.0 mm^2 was found in about one-third of patients (28.6% in the OCT arm and 31.1% in the IVUS arm), emphasizing that a small stent area and/or underexpansion is not infrequent even in contemporary practice (5).

GM AND PREDICTORS OF STENT EDGE RESTENOSIS. Mintz et al. (54) reported that only 7% (60 of 884) of angiographically normal-appearing coronary artery segments were normal by IVUS. The plaque burden corresponding to the angiographically normal coronary artery segments was 51 ± 13%. Costa et al. (55) defined longitudinal GM as an angiographic-injured or diseased segment not covered by a stent, and axial GM as balloon/artery size ratio <0.9 or >1.3. GM occurred in 66.5% of patients; 47.6% had longitudinal GM, 35.2% had axial GM, and 16.5% had both. We evaluated the impact of coregistration between angiography and OCT on OCT-defined longitudinal GM (residual disease or significant stent edge dissection) (56). Stent length was based on normal-to-normal landing zones by pre-PCI OCT, and stents were implanted with versus without coregistration. The overall rate of longitudinal GM was 31.3% (62 of 198) without any difference between procedures done with versus without coregistration (26.7% vs. 32.3%). Thus, even using OCT-guidance coupled with coregistration between angiography and OCT, GM is not infrequent.

GM has been associated with restenosis and stent thrombosis (6-8,14,16) (**Figure 5**). In the ADAPT-DES (Assessment of Dual Antiplatelet Therapy with Drug-Eluting Stents) study, greater stent expansion at the stent edge and the presence of a greater stent edge plaque burden or amount of calcium or attenuated plaque were associated with edge dissections (25). In turn, an untreated edge dissection was associated with TLR, especially if the lumen area within the dissection was <5.0 mm^2, the dissection length was >3 mm, and the dissection flap radial extent was $>60°$. In the combined post-procedural IVUS data from the TAXUS IV, TAXUS V, and TAXUS VI trials (n = 531), only edge plaque burden was a predictor of edge restenosis with a similar cutoff value of plaque burden in bare metal stents (47.1%) and PES (47.7%) (6). Kang et al. (7) reported similar findings with cutoff values ranging from 54.2% to 57.3% edge plaque burden among different types of second-generation DES.

Using OCT, Prati et al. (18) reported that residual distal edge dissection >200 μm in width and residual reference stenosis with minimum lumen area <4.5 mm^2 were associated with MACE.

FIGURE 5 Stent Edge Dissection, Stent Malapposition, and Tissue Protrusion Through Stent Struts by OCT and IVUS



Matched OCT and IVUS images are shown. The site corresponding to an OCT or IVUS cross section is indicated as a black arrow in the angiogram **(A, B, C)**, with the black dotted line showing the stent segment. OCT **(A′)** and IVUS **(A″)** show a medial dissection flap **(arrow)**. OCT **(B′)** and IVUS **(B″)** show stent malapposition **(arrows)**. Stent area measured 8.03 mm^2 by OCT and 8.15 mm^2 by IVUS. OCT **(C′)** and IVUS **(C″)** show tissue protrusion with attenuation indicating lipidic plaque **(arrows)** through the stent strut. Abbreviations as in Figure 1.

Ino et al. (8) reported that OCT-defined stent edge large lipidic plaque (≥185°) as well as lumen area ≤4.1 mm^2 were associated with edge restenosis. In ILUMIEN III, OCT-detected major stent edge dissections (dissection flap ≥60° or ≥3 mm in length) were less common in the OCT-guided arm versus the IVUS-guided arm, and, when present, they were observed less frequently with IVUS than with OCT (5).

TISSUE PROTRUSION WITHIN THE STENT. By IVUS, tissue protrusion through stent struts has been found in 17% to 31% of patients with stable coronary artery disease and 46% to 69% of patients with ACS (16,26). In ADAPT-DES, tissue protrusion was not related to worse outcomes. This was in part due to greater stent expansion in lesions with tissue protrusion (26). However, by OCT, irregular tissue protrusion (presumably lipidic plaque or thrombus) has been associated with target vessel failure (TVF) (17). In an IVUS substudy of HORIZONS-AMI (Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction), which included 401 ST-segment elevation MI patients with post-stent IVUS after primary PCI, tissue protrusion was found in 74% of patients (16). When the tissue protrusion was large resulting in a small residual lumen area, it was associated with early stent thrombosis.

ACUTE MALAPPOSITION. When the same lesions were evaluated by both IVUS and OCT, acute malapposition was detected by OCT more than twice as frequently as with IVUS: 14% versus

TABLE 3 Summary of Reports Showing an Effect of IVUS on Outcomes

	Steinvil (62)	Elgendy (61)	IVUS-XPL (60)	de la Torre Hernandez (64)	ADAPT-DES (4)
Uniqueness of study	Largest meta-analysis	Meta-analysis of randomized controlled trials	Largest randomized controlled trial, stent length ≥28 mm	Largest propensity matched pooled analysis of unprotected left main lesions	Largest all-comers registry
Percent IVUS guidance (N)	46.9 (31,283)	50 (3,192)	50 (1,400)	50 (1,010)	39 (8,582)
No. of studies included	25	7	1	4	1
Follow-up time, yrs	1 (in 56%)	1 (in 73%)	1	3	2
	Unadjusted OR or HR				
	OR (95% CI)	OR (95% CI)	HR (95% CI)	Prevalence	HR (95% CI)
Major adverse cardiac event	0.76 (0.70–0.82)	0.60 (0.46–0.77)	0.48 (0.28–0.83)	11.7%/16%*	0.65 (0.54–0.78)
Death	0.62 (0.54–0.72)	0.46 (0.21–1.00)	3/5*	3.3%/6.0%*	0.70 (0.51–0.96)
Myocardial infarction	0.67 (0.56–0.80)	0.52 (0.26–1.02)	0/1*	4.5%/6.5%*	0.62 (0.49–0.77)
Stent thrombosis	0.58 (0.47–0.73)	0.49 (0.24–0.99)	2/2*	0.6%/2.2%*	0.47 (0.28–0.80)
Target lesion revascularization	0.77 (0.67–0.89)	0.60 (0.43–0.84)	0.51 (0.28–0.91)	7.7%/6.0%*	0.79 (0.85–0.95)
Target vessel revascularization	0.85 (0.76–0.95)	Not reported	Not reported	Not reported	0.84 (0.73–0.97)

*IVUS guidance/angiography guidance.

CI = confidence interval; HR = hazard ratio; IVUS-XPL = Impact of Intravascular Ultrasound Guidance on Outcomes of Xience Prime Stents in Long Lesions; OR = odds ratio; other abbreviations as in Tables 1 and 2.

39% in OPUS-CLASS (Optical coherence tomography compared to intravascular ultrasound in coronary lesion assessment study) (35) and 19.3% versus 38.5% in ILUMIEN III (5). Similarly, in large IVUS and OCT cross-sectional studies, the prevalence of acute malapposition was 8% to 15% by IVUS (22–24) and 39% to 62% by OCT (17–21), with approximately one-half of the cases resolved at 9-month follow-up (19–21). In the absence of stent underexpansion, neither OCT- nor IVUS-detected acute malapposition has been associated with adverse early or long-term outcomes regardless of the amount of malapposition (length, thickness) (16–24).

IVUS-GUIDED PCI TO IMPROVE OUTCOMES

Eleven meta-analyses (the largest involving 31,283 patients) of various combinations of randomized clinical trials with or without registry studies have reported a reduced overall MACE rate with IVUS guidance compared to angiographic guidance (**Table 3**) (57–63). Hong et al. (60) randomized 1,400 patients to angiography versus IVUS guidance in long coronary lesions (all implanted stents were ≥28 mm in length) treated with a single type of stent (XIENCE, Abbott Vascular, Santa Clara, California) with minimal crossover and found that MACE was significantly lower in the IVUS-guidance cohort than the angiography-guidance cohort (2.9% vs. 5.8%; p = 0.007), mainly driven by a lower rate of TLR. Furthermore, lesions that met the optimal IVUS criteria (minimum stent area ≥ distal reference lumen area) showed a significantly lower MACE rate than those that did not meet the optimal implantation criteria (1.5% vs. 4.6%; p = 0.02). In the most recent meta-analysis of randomized trials of IVUS guidance versus angiography guidance in the DES era (8 trials; 3,276 randomized patients), at mean follow-up of 1.4 ± 0.5 years, IVUS guidance was associated with a 36% reduction in MACE and a 40% reduction in target vessel revascularization, with nonsignificant differences in stent thrombosis and death (63). In the meta-analysis by Zhang et al. (59), the benefit of IVUS guidance in reducing MACE was more pronounced in patients with complex lesions (defined as left main, bifurcation, chronic total occlusions, or long lesions) or ACS (OR: 0.69; 95% CI: 0.60 to 0.79) compared to patients with any lesion or any clinical presentation (OR: 0.81; 95% CI: 0.74 to 0.90). de la Torre Hernandez et al. (64) reported the effect of IVUS guidance during stenting of unprotected left main lesions in propensity matched cohorts from 4 registries. The effect of IVUS was more pronounced in the distal left main location (adjusted HR: 0.54; 95% CI: 0.34 to 0.90) compared to the overall cohort (adjusted HR: 0.70; 95% CI: 0.52 to 0.99), a reduction driven by fewer deaths (but not MI or TLR), consistent with the earlier report by Park et al. (65). Similar benefits of IVUS guidance during left main stenting were recently reported from a large propensity adjusted experience from Sweden (66).

Alberti et al. (67) assessed the cost-effectiveness of IVUS guidance on DES implantation from the Italian health care payer perspective using data from the meta-analysis by Ahn et al. (58). If the IVUS benefit was assumed to be limited to the first year, the

incremental cost-effectiveness ratio per quality-adjusted life-year gained was €9,624, which is lower than the €25,000 per quality-adjusted life-year gained used in Italy as its willingness-to-pay threshold. Cost-effectiveness was even greater in patients with renal insufficiency, diabetes, and ACS. In the meta-analysis by Elgendy et al. (61), which included 7 randomized trials, subgroup analysis showed similar effects on MACE at 1 year (OR: 0.56; 95% CI: 0.40 to 0.77) and 2 years (OR: 0.67; 95% CI: 0.46 to 0.97). In the largest all-comers registry (ADAPT-DES) (4), the effect of IVUS use was maintained at 2 years, and the number needed to treat with IVUS guidance to prevent 1 MACE event was reduced from 67 at 1 year to 47 patients at 2 years.

OCT-GUIDED PCI TO IMPROVE OUTCOMES

Prati et al. (38) retrospectively compared 335 OCT-guided PCI cases to 335 angiography-guided PCI cases that were randomly chosen during the same time period without propensity matching. OCT guidance was associated with a lower risk of cardiac death or MI (OR: 0.49; 95% CI: 0.25 to 0.9; $p = 0.04$) after adjustment for clinical and procedural factors. However, the rate of cardiac death at 1 year in the angiography-guided group was unexpectedly high (4.5%), thus putting in question whether these were chance findings.

Randomized trials are more appropriate to compare outcomes of different therapeutic approaches. DOCTORS (Does Optical Coherence Tomography Optimize Results of Stenting) was a multicenter, randomized trial comparing OCT-guided with angiography-guided PCI in 240 patients with non–ST-segment elevation ACS using the post-PCI fractional flow reserve (FFR) value as the primary endpoint (39). In the OCT group, stent size was chosen based on the reference vessel size, and if stent expansion (MSA/reference lumen area) was ≤80%, post-dilation was performed. Post-PCI FFR and the prevalence of post-PCI FFR >0.9 were significantly higher in the OCT-guided group compared with the angiography-guided group (0.94 ± 0.04 vs. 0.92 ± 0.05; $p = 0.005$; and 82.5% vs. 64.2%; $p = 0.0001$), and the final angiographic diameter stenosis was lower (7.0 ± 4.3% vs. 8.7 ± 6.3%; $p = 0.01$, respectively). The use of OCT led the operator to optimize the procedural strategy in 50% of cases compared to 22.5% in the angiography-guided group. After stent optimization, stent expansion increased from 78.9 ± 12.4% to 84.1 ± 7.3% in the OCT arm. The cutoff value of MSA to predict FFR >0.9 was 5.44 mm^2 (sensitivity = 91.3%; specificity = 60.2%). The prevalence of MACE at 6 months was low in both groups (1.6% [n = 2] in the angiography-guided arm and 2.5% [n = 3] in the OCT-guided arm).

OCT-GUIDED VERSUS IVUS-GUIDED PCI

Habara et al. (40) randomized 70 de novo coronary lesions to OCT-guided versus IVUS-guided stenting (**Table 4**). MSA evaluated by IVUS was significantly larger by IVUS guidance (7.1 ± 2.1 mm^2) compared to OCT guidance (6.1 ± 2.2 mm^2), in part due to better EEL visualization by IVUS compared with OCT, leading to larger stent and balloon sizes. Overall, 40% of OCT-guided stenting was based on angiographic sizing due to limited EEL visualization by OCT.

The OPINION (Optical Frequency Domain Imaging vs. Intravascular Ultrasound in Percutaneous Coronary Intervention) trial was a prospective, multicenter, randomized trial performed in Japan on 829 patients to evaluate whether OCT-guided PCI was noninferior to IVUS-guided PCI using TVF at 1 year as the primary endpoint (41). Stent diameter was chosen based on reference lumen diameter by OCT and reference vessel diameter (EEL) by IVUS. TVF was noninferior by OCT compared to IVUS (5.2% vs. 4.9%; $p_{noninferiority} = 0.04$). Although the difference was minimal, the chosen stent size was significantly smaller in the OCT arm compared with the IVUS arm (2.92 ± 0.39 mm vs. 2.99 ± 0.39 mm; $p = 0.005$).

ILUMIEN III was a prospective, randomized, multicenter trial designed to evaluate a novel OCT-based stent sizing strategy using reference segment EELs for sizing and to compare the efficacy and safety of OCT guidance to IVUS guidance and angiographic guidance (5). The primary efficacy endpoint was final post-PCI MSA measured by OCT (blinded in the IVUS-guided and angiography-guided arms), and the primary safety endpoint was procedural MACE. Among 450 randomized patients, the final median MSA was 5.79 (first, third quartiles: 4.54 to 7.34) mm^2 after OCT guidance, 5.89 (4.67 to 7.80) mm^2 after IVUS guidance, and 5.49 (4.39 to 6.59) mm^2 after angiography guidance. OCT guidance was noninferior ($p = 0.001$) but not superior to IVUS guidance ($p = 0.42$). OCT guidance was not superior to angiography guidance for MSA ($p = 0.12$) but did lead to greater stent expansion ($p = 0.02$). OCT guidance also led to fewer cases of major dissection and major malapposition than IVUS guidance and angiography guidance. Overall procedural MACE was 3.8% (6/158) without differences between groups. In the OCT guidance arm, EEL visibility ≥180° was apparent in 69% of proximal and 77% of distal reference segments by the operator; and stent size was based on EEL diameters

TABLE 4 OCT- Versus IVUS- Versus Angiography-Guided Studies

First Author/Study (Ref. #)	N	Study Design	Endpoints and Findings
Habara, et al. (40)	70 (OCT vs. IVUS)	Randomized; superiority of IVUS vs. OCT	• Smaller final minimum stent area by OCT than IVUS (6.1 ± 2.2 mm^2 vs. 7.1 ± 2.1 mm^2) • Less EEL visibility (63% vs. 100%) and more residual disease at reference by OCT than IVUS • Residual malapposition and procedure time/contrast volume were similar
CLI-OPCI (38)	670 (OCT vs. angio)	Retrospective; not matched	• OCT led to additional procedures in 35% of OCT-guided cases • At 1 yr, major adverse cardiac events (cardiac death, myocardial infarction, or revascularization) were less prevalent in OCT than angiography guidance (9.6% vs. 15.1%; $p = 0.03$), although a high rate of cardiac death (4.5%) in the angiography arm was observed
OPINION (41)	829 (OCT vs. IVUS)	Randomized; noninferiority of OCT	• Target vessel failure by OCT at 1 yr was noninferiority compared to IVUS guidance (5.2% vs. 4.9%; $p_{noninferiority} = 0.04$) • Stent diameter was chosen based on reference lumen diameter by OCT and vessel diameter by IVUS; stent diameter was larger in the IVUS group, although the difference was minimal
ILUMIEN III (5)	450 (OCT vs. IVUS vs. angiography)	Randomized; noninferiority of OCT vs. IVUS, superiority of OCT vs. angiography	• Primary endpoint: OCT-evaluated minimum stent areas were 5.79 mm^2 (OCT), 5.89 mm^2 (IVUS), and 5.49 mm^2 (angiography) shown as median. OCT was noninferior vs. IVUS ($p_{noninferiority} = 0.01$) and not superior vs. angiography ($p = 0.12$) • OCT-evaluated untreated major dissection (14% vs. 26%; $p = 0.009$) and major malapposition (11% vs. 21%) were less frequent in the OCT arm compared to the IVUS arm • EEL visibility (core lab) ≥180° at either reference was 95% by OCT and 100% by IVUS; stent diameter was chosen based on EEL diameter in about 70% of cases in both the OCT and IVUS arms
DOCTORS (39)	240 (OCT vs. angiography)	Randomized; superiority of OCT	• Primary endpoint: Post-procedural FFR was greater in OCT guidance (0.94 ± 0.04) than angiography guidance (0.92 ± 0.05), with higher rates of post-procedural FFR >0.9 (82.5% vs. 64.2%), both $p < 0.01$ • OCT led to additional procedures in 50% of OCT-guided cases

DOCTORS = Does Optical Coherence Tomography Optimize Results of Stenting; EEL = external elastic lamina; FFR = fractional flow reserve; ILUMIEN = Observational Study of Optical Coherence Tomography (OCT) in Patients Undergoing Fractional Flow Reserve (FFR) and Percutaneous Coronary Intervention; OPINION = Optical Frequency Domain Imaging vs. Intravascular Ultrasound in Percutaneous Coronary Intervention; other abbreviations as in Tables 1 and 2.

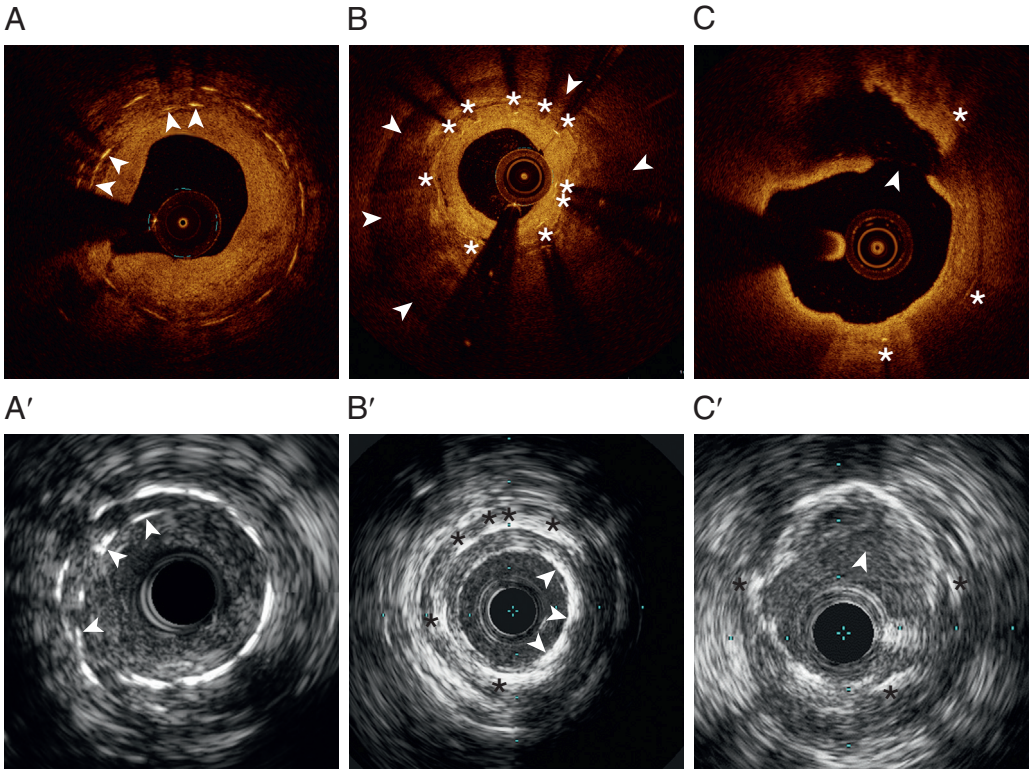
for almost all of these cases. By core lab, EEL visibility ≥180° was noted in 81% of proximal and 95% of distal reference segments.

Thus, considering the results of OPINION and ILUMIEN III, an OCT-guided PCI strategy appears to be noninferior compared to IVUS for both acute and long-term outcomes.

IMAGING GUIDANCE FOR BIORESORBABLE VASCULAR SCAFFOLD IMPLANTATION

Bioresorbable vascular scaffolds (BRS) are composed of fully absorbable polymers or metals designed to provide the drug delivery and mechanical support functions of metallic DES within the first year, and then resorb over the next 2 to 3 years, restoring vasomotion and vascular adaptive responses. The struts of first-generation BRS are substantially thicker and wider than those of contemporary metallic DES, and the bioabsorption process may result in novel failure modes. Optimal vessel preparation, sizing, and post-dilatation (PSP) have been emphasized to optimize clinical outcomes after BRS implantation. In the pooled data of ABSORB Cohort B, ABSORB II, and ABSORB EXTEND (n = 1,232), a high density of scaffold in the lumen (large scaffold size compared to proximal or distal maximum diameter [Dmax] in the lesion) was associated with periprocedural MI (68). In a large all-comers population (n = 1,305), Puricel et al. (69) reported that a greater footprint (maximum percentage of the vascular circumference occupied by struts) and smaller final BRS dimensions were associated with scaffold thrombosis. Using a PSP implantation

FIGURE 6 Stent Fracture and Neoatherosclerosis



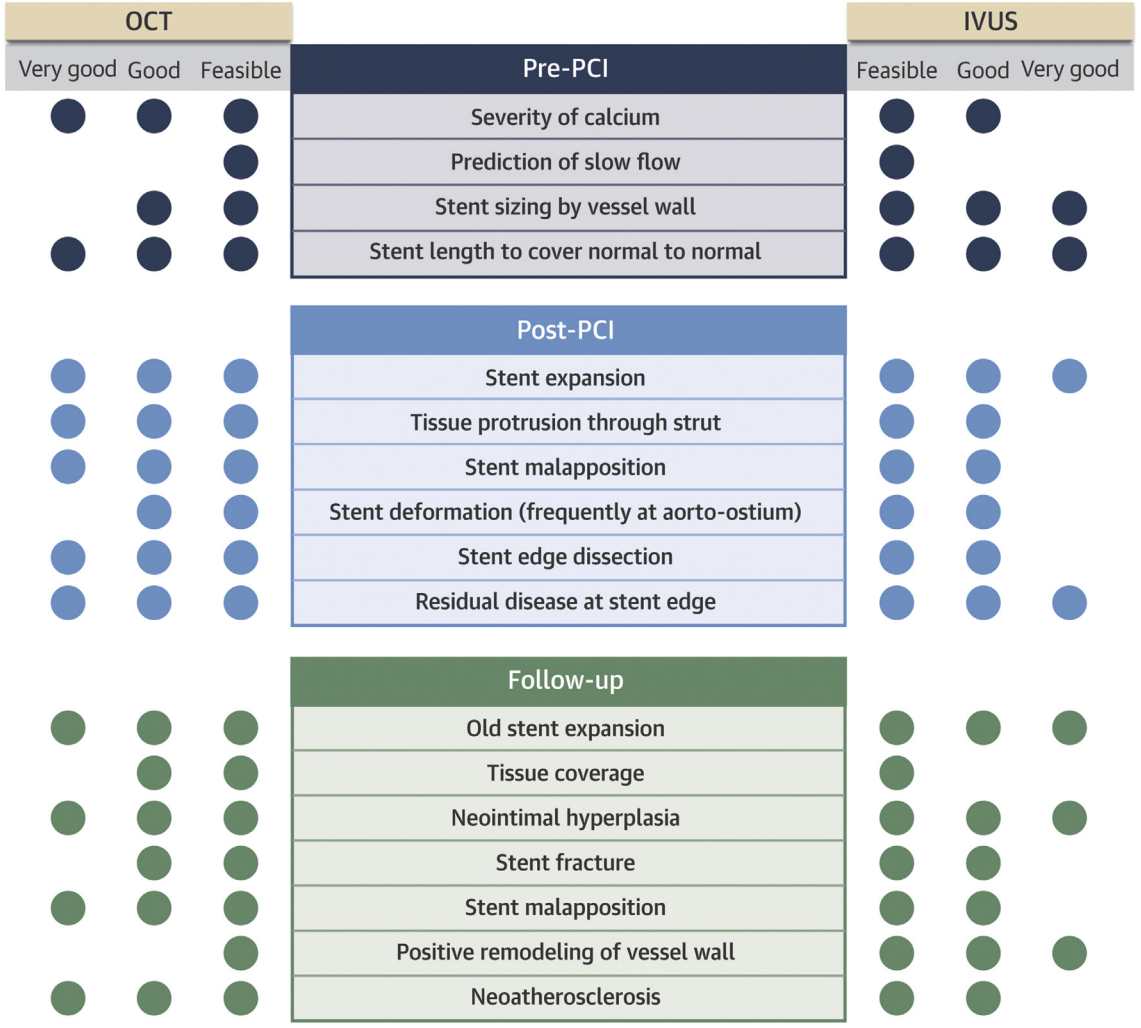
OCT **(A, B, C)** and IVUS **(A′, B′, C′)** images from different cases. In **(A)** and **(A′),** the overlapped stent struts **(arrowheads)** were consistent with stent fracture. In OCT **(B),** calcification (**arrowheads**; poor signal with clear leading edge) behind the stent **(white asterisks)** was observed, and minimum stent area measured 2.75 mm^2 with limited neointimal tissue inside the stent. The major cause of this restenosis was stent underexpansion due to circumferential calcium behind the stent. In IVUS **(B′),** the stent **(black asterisks)** was well expanded (8.0 mm^2) along with neointimal calcification (**white arrowheads**; hyperechoic leading edge with acoustic shadow). The differentiation between the old stent struts and neointimal calcification was unclear. Neointimal rupture in the lipidic plaque within the stent struts **(white asterisks)** was observed in OCT **(C)** but was unclear by IVUS **(C′) (white arrowhead)** within the stent struts **(black asterisks)**. Abbreviations as in Figure 1.

technique reduced 1-year scaffold thrombosis from 3.3% to 1.0%. ABSORB III 2-year data also showed that when PSP was performed, the rate of target vessel revascularization (ABSORB = 8.7%) or scaffold thrombosis (ABSORB = 1.1%) is comparable to those treated by Xience (8.2% and 0.8%, respectively) (70). Although not yet subjected to randomized evaluation, many experts believe that intravascular imaging guidance may be particularly useful to optimize procedural results with BRS. Tanaka et al. (71) reported outcomes from a complex cohort of 264 patients undergoing BRS implantation (53.2 ± 32.5 mm of total scaffold length per patient), with intravascular imaging guidance in 85% of patients. Scaffold sizing and optimization were performed based on the AVIO algorithm (3), and PSP was performed in almost all cases. Even after PSP, IVUS or OCT findings necessitated additional treatment in 24.5% of lesions (84% underexpansion, 11% malapposition, and 5% either edge dissections or incomplete lesion coverage). At 2 years, scaffold thrombosis and TVF were reported as 1.2% (3 of 264) and 11.6% (22 of 264), respectively; there were no cases of scaffold thrombosis beyond 1 year. Further studies are required to determine the utility of intravascular imaging guidance of BRS procedures.

OCT VERSUS IVUS FINDINGS AND PCI GUIDANCE IN CASES OF STENT FAILURE

Intravascular imaging is most useful in patients with stent failure (restenosis or thrombosis) to determine the mechanism and choose the appropriate treatment (Figure 6). In 298 ISR lesions evaluated by IVUS, stent underexpansion (MSA <5 mm^2) was more frequent in DES (32%) than in bare metal stents (22%) (27). In 171

CENTRAL ILLUSTRATION **IVUS and OCT: Similarities and Differences**



Maehara, A. et al. J Am Coll Cardiol Img. 2017;10(12):1487–503.

The ability of morphological evaluation is shown as • • • (very good), • • (good), or • (feasible). In pre-intervention evaluation, OCT is better for evaluating the thickness of calcium, and IVUS can detect only the presence of calcium. Although IVUS can visualize the entire vessel wall, OCT cannot visualize the vessel wall when the wall thickness is beyond the penetration depth. In post-intervention, both OCT and IVUS are good for evaluating stent expansion. A stent complication such as edge dissection is better visualized by OCT than IVUS. During follow-up, stent underexpansion can be visualized by OCT. IVUS is sometimes difficult when neointimal calcification is present. Neoatherosclerosis is better visualized by OCT than IVUS. IVUS = intravascular ultrasound; OCT = optical coherence tomography; PCI = percutaneous coronary intervention.

patients with second-generation DES restenosis evaluated by OCT, the dominant cause was stent underexpansion (MSA <4 mm^2 and neointimal hyperplasia <50% of stent area) in 40% of ISR cases occurring within 1 year versus 28% beyond 1 year, presumably because symptomatic lumen compromise is quicker in the setting of a smaller MSA (28). In addition, neointimal calcification was found in 20% of ISR cases occurring >1 year after implantation. Because identification of neointimal calcification within an old stent is difficult by angiography and may be challenging by IVUS because of radiopacity of the old stent, calcification behind stents, and neointimal calcification, OCT to recognize neointimal calcium may be useful to determine the optimal treatment strategy.

In the PESTO (Morphological Parameters Explaining Stent Thrombosis assessed by OCT) registry (29),

which included 60% DES (one-half were first-generation DES) and 40% bare metal stents, the morphology underlying early (within 1 month) definite stent thrombosis (n = 23) included stent malapposition in 48% of cases, severe stent underexpansion (MSA <70% of average of proximal and distal reference lumen area or <80% of smaller reference lumen area) in 26%, and residual edge dissection or disease in 8%, consistent with IVUS data (16). The underlying morphology of late or very late stent thrombosis (n = 97) included stent malapposition in 32%, ruptured neoatherosclerosis in 28%, evagination in 10%, isolated uncovered struts in 10%, stent edge-related disease progression in 8%, severe stent underexpansion in 7%, and thrombus with neointima (presumably erosion of neointima) in 5%, although a cause-and-effect direct mechanism (vs. an incidental coexisting finding), especially for malapposition (including persistent acute malapposition and late acquired malapposition), was not entirely clear. In large IVUS and OCT cross-sectional studies, the prevalence of acute malapposition was 8% to 15% by IVUS (22–24) and 39% to 62% by OCT (17–21). As a separate phenomenon compared to acute malapposition, late-acquired stent malapposition is the result of either positive vessel remodeling and/or thrombus resolution behind the stent struts. One meta-analysis that included persistent and late acquired malappositions in 2,080 patients from 5 randomized trials of first-generation DES (sirolimus-eluting stent, PES) suggested that there was an increase of very late stent thrombosis in cases with late stent malapposition (OR: 6.5; 95% CI: 1.3 to 34.9; p = 0.02) versus those without late stent malapposition, but this meta-analysis did not differentiate between persistent and late acquired malapposition (72). In cases in which angiography suggests late acquired stent malapposition (persistent staining, aneurysmal change), IVUS is recommended because evaluation of the entire vessel wall is possible only by IVUS. Conversely, OCT is superior to IVUS for the identification of neoatherosclerosis (a common cause of very late stent restenosis or very late stent thrombosis). One of the potential mechanisms of stent thrombosis is uncovered stent struts (29). Compared to IVUS, OCT can evaluate completeness of tissue coverage of stent struts, typically defined as visible smooth tissue on the top of the stent strut (73).

In this registry, the percentage of operator-defined "unidentified mechanism of stent thrombosis" decreased from 48% by angiography alone to 13% by OCT, and the use of new stents (31%) was one-half compared to a large angiography-guided stent thrombosis cohort (63.5%) (74) with acceptable subsequent outcomes (9.5% of MACE at 6 months).

Finally, in a multicenter report of scaffold thromboses after BRS implantation evaluated with OCT or IVUS at the time of the event, Sotomi et al. (75) reported that of 17 thrombosis cases occurring within 30 days, the most common underlying findings were malapposition (n = 4), GM (n = 3), and underdeployment (n = 2). Among 26 cases of scaffold thrombosis after 30 days, the most common underlying findings were malapposition (n = 9), late strut discontinuities (n = 8), peristrut low-intensity areas (n = 5), uncovered struts (n = 4), and underdeployment (n = 4). Acute scaffold malapposition may be more problematic after BRS than acute stent-vessel wall malapposition after metallic DES implantation. First, acute thrombogenicity may be related to scaffold thickness. Second, lack of scaffold-vessel wall apposition may limit incorporation into the vessel such that late intraluminal dismantling may occur at the time of scaffold absorption.

SUMMARY AND CONCLUSIONS

Clinical studies and meta-analyses have demonstrated that both OCT and IVUS may improve PCI outcomes in the DES and BRS eras. Based on current studies, the benefits of intravascular imaging guidance may be greatest in high-risk patients and complex lesions, and in those with stent failure. IVUS and OCT do differ, each possessing important advantages and limitations, and whether OCT is superior to IVUS (or vice versa) in optimizing PCI outcomes is unknown (**Central Illustration**). All interventionalists should become familiar with at least 1 of these 2 modalities based on individual preference and availability. Based on the present data, increased OCT or IVUS usage by operators who normally rely on angiography-guided PCI is warranted. Further evidence regarding the long-term benefits of OCT-guided DES implantation is anticipated from the large-scale ILUMIEN IV trial, which is set to begin in late 2017. In addition, advanced technologies that combine OCT with IVUS in a single catheter or OCT with spectroscopic tissue characterization (also in a single catheter and similar to the currently available IVUS near-infrared spectroscopy) are under development (76,77).

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KEY WORDS intravascular ultrasound, optical coherence tomography, percutaneous coronary intervention, stent(s)

APPENDIX For a supplemental table, please see the online version of this paper.