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Comparison of Stent Expansion Guided by Optical Coherence Tomography Versus Intravascular Ultrasound

The ILUMIEN II Study (Observational Study of Optical Coherence Tomography [OCT] in Patients Undergoing Fractional Flow Reserve [FFR] and Percutaneous Coronary Intervention)

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ABSTRACT

OBJECTIVES The present study sought to determine whether optical coherence tomography (OCT) guidance results in a degree of stent expansion comparable to that with intravascular ultrasound (IVUS) guidance.

BACKGROUND The most important predictor of adverse outcomes (thrombosis and restenosis) after stent implantation with IVUS guidance is the degree of stent expansion achieved.

METHODS We compared the relative degree of stent expansion (defined as the minimal stent area divided by the mean of the proximal and distal reference lumen areas) after OCT-guided stenting in patients in the ILUMIEN (Observational Study of Optical Coherence Tomography [OCT] in Patients Undergoing Fractional Flow Reserve [FFR] and Percutaneous Coronary Intervention) (N = 354) and IVUS-guided stenting in patients in the ADAPT-DES (Assessment of Dual Antiplatelet Therapy With Drug-Eluting Stents) study (N = 586). Stent expansion was examined in all 940 patients in a covariate-adjusted analysis as well as in 286 propensity-matched pairs (total N = 572).

RESULTS In the matched-pair analysis, the degree of stent expansion was not significantly different between OCT and IVUS guidance (median [first, third quartiles] = 72.8% [63.3, 81.3] vs. 70.6% [62.3, 78.8], respectively, p = 0.29). Similarly, after adjustment for baseline differences in the entire population, the degree of stent expansion was also not different between the 2 imaging modalities (p = 0.84). Although a higher prevalence of post-PCI stent malapposition, tissue protrusion, and edge dissections was detected by OCT, the rates of major malapposition, tissue protrusion, and dissections were similar after OCT- and IVUS-guided stenting.

CONCLUSIONS In the present post-hoc analysis of 2 prospective studies, OCT and IVUS guidance resulted in a comparable degree of stent expansion. Randomized trials are warranted to compare the outcomes of OCT- and IVUS-guided coronary stent implantation. (J Am Coll Cardiol Intv 2015;8:1704–14) © 2015 by the American College of Cardiology Foundation.

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By intravascular ultrasound (IVUS) imaging, the strongest predictor of early stent thrombosis and restenosis is the absolute degree of stent expansion as assessed by the minimal stent area (MSA) after percutaneous coronary intervention (PCI) (1–6). By achieving greater stent expansion, IVUS guidance has been associated with improved event-free survival compared with angiographic guidance alone (7–9). Optical coherence tomography (OCT) has superior resolution compared with IVUS (10,11), but in many cases, the limited penetration depth of OCT prevents visualization of the vessel size (external elastic membrane [EEM]), a key parameter used during IVUS-guided stent sizing. Whether routine OCT guidance results in a degree of stent expansion comparable to that with IVUS guidance is unknown. We therefore compared the degree of stent expansion achieved after OCT and IVUS guidance in 2 large-scale, prospective studies, the ILUMIEN I (Observational Study of Optical Coherence Tomography [OCT] in Patients Undergoing Fractional Flow Reserve [FFR] and Percutaneous Coronary Intervention) study and the ADAPT-DES (Assessment of Dual Antiplatelet Therapy With Drug-Eluting Stents) study.

ABBREVIATIONS AND ACRONYMS

CSA = cross-sectional area
DS = diameter stenosis
EEM = external elastic membrane
IVUS = intravascular ultrasound
MLD = minimal lumen diameter
MSA = minimal stent area
OCT = optical coherence tomography
PCI = percutaneous coronary intervention
QCA = quantitative coronary angiography
RVD = reference vessel diameter
STEMI = ST-segment elevation myocardial infarction

METHODS

STUDY DESIGN AND ENDPOINTS. The present study (ILUMIEN II) was designed as a post-hoc analysis of the outcomes of OCT- versus IVUS-guided stent implantation from the prospectively performed, multicenter ILUMIEN I and ADAPT-DES studies. The study protocol and statistical analyses were specified before data analysis. The study flow is shown in **Figure 1**. Patients in whom bare metal or drug-eluting stents (but not bioresorbable scaffolds) were implanted in a native coronary artery in which post-PCI OCT or IVUS was performed and analyzed at an independent core laboratory were considered for inclusion. Patients with left main coronary artery, saphenous vein graft, in-stent restenosis, or chronic total occlusion stented lesions were excluded, as were ST-segment elevation myocardial infarction (STEMI) patients and patients in whom the reference segment could not be measured.

The primary endpoint was the final post-PCI stent expansion defined as the MSA divided by the mean of the proximal and distal reference lumen areas as assessed by OCT in the ILUMIEN I and by IVUS in the ADAPT-DES (1,12,13). This relative measure of stent expansion was used in preference to absolute MSA because IVUS measurements are typically larger than those by OCT (13–15). Major secondary endpoints included mean stent expansion defined as the mean stent volume divided by the mean reference lumen area and post-PCI in-stent and in-segment percentage of diameter stenosis (DS) measured by quantitative coronary angiography (QCA), both of which are independent of an intravascular imaging modality. Additional endpoints included in-stent and in-segment acute gain and minimal lumen diameter (MLD) by QCA and the prevalence of major stent malapposition, tissue protrusion, and edge dissections identified by IVUS or OCT, as defined in the following.

ILUMIEN I AND ADAPT-DES. ILUMIEN I was a prospective, multicenter study performed in 418 patients at 36 centers in the United States, Canada, European Union, Australia, and Asia designed to identify OCT stent parameters related to 1-year outcomes after PCI in de novo coronary artery lesions (16). Patients with stable angina, unstable angina, or non-STEMI having at least 1 lesion with angiographic DS >50% by visual estimation were enrolled. As many as 3 lesions in 2 vessels could be treated, but no more than 2 lesions per vessel. Fractional flow reserve and OCT were performed pre-PCI and post-PCI. If OCT assessment post-PCI was deemed unsatisfactory (flow-limiting edge dissection or tissue/thrombus protrusion, malapposition >0.2 mm, or stent expansion ≤70% compared with the distal reference lumen area and with an angiographic DS >20%), further optimization was recommended, and repeat OCT imaging performed. Only the final OCT image was assessed in the present study.

ADAPT-DES was previously described in detail (17). Briefly, ADAPT-DES was a prospective, multicenter registry of an "all-comers" population of 8,582 patients at 13 U.S. and German centers to determine the relationship between platelet reactivity and subsequent stent thrombosis through 2-year follow-up after successful drug-eluting stent implantation.

Boston Scientific, and Volcano Corporation. Dr. Shite has received consulting fees from St. Jude Medical. Dr. Witzenbacher is on the advisory board of Volcano Corporation. Dr. Stone is a former consultant for Boston Scientific and Infraredx. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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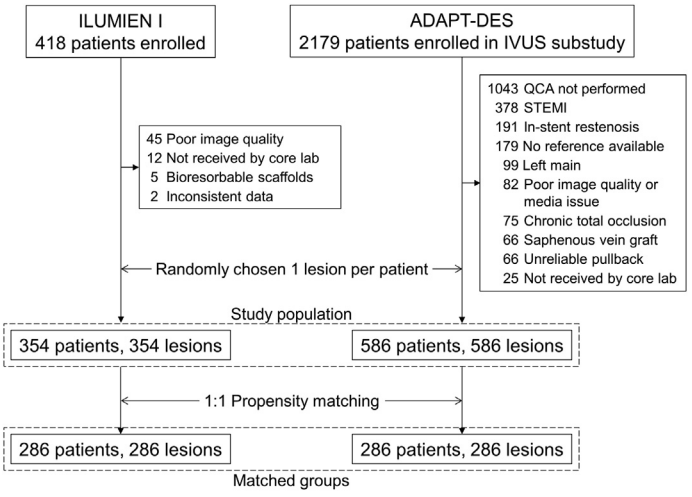
FIGURE 1 Enrollment, Exclusion, and Final Cohorts



In ILUMIEN I, 354 of 418 enrolled patients were included in the current study population. In ADAPT-DES, 586 of 2,179 patients enrolled in the IVUS substudy were included in the current study population. From these 940 patients, 286 propensity-matched groups were created. Note: QCA was not routinely performed in ADAPT-DES, but was completed in a subset of patients in the IVUS substudy (9). Reasons for exclusion were not mutually exclusive. IVUS = intravascular ultrasound; QCA = quantitative coronary angiography; STEMI = ST-segment elevation myocardial infarction.

Decisions whether and how to use IVUS were per operator discretion, although IVUS use was encouraged. The relationship between final IVUS parameters and clinical outcomes was determined in a prespecified substudy of 2,179 patients (9).

Both ILUMIEN I and ADAPT-DES were approved by the institutional review board at each participating center, and all participating patients signed written informed consent.

OCT AND IVUS IMAGING AND ANALYSIS. In the ILUMIEN I study, immediately after intracoronary nitroglycerin administration, an OCT catheter (C7 Dragonfly, Dragonfly, Duo or Dragonfly JP, St. Jude Medical, St. Paul, Minnesota) was introduced distal to the stented lesion, and contrast media was injected via the guiding catheter during pull back. A C7XR, ILUMIEN, or ILUMIEN OPTIS OCT imaging system (St. Jude Medical) was used for OCT image acquisition at 100 or 180 frames/s at a pull-back speed of 10 to 25 mm/s.

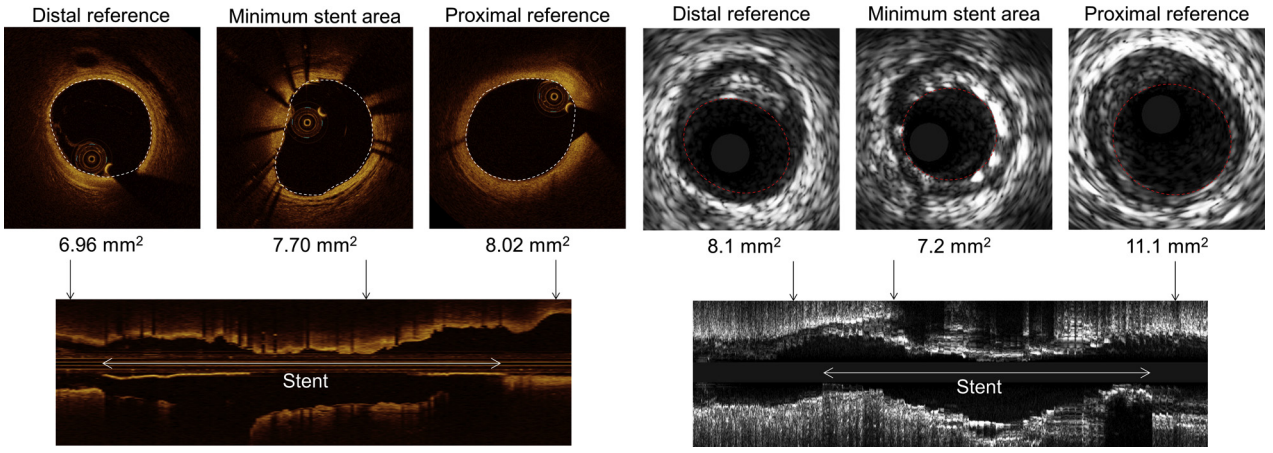
In the ADAPT-DES IVUS substudy, gray-scale IVUS was performed after administration of intracoronary nitroglycerin using a synthetic aperture array, 20 MHz, 3.2-F catheter (Eagle Eye, Volcano Corporation, Rancho Cordova, California) and an s5 console (Volcano Corporation). The IVUS catheter was advanced distal to the lesion and pulled backed at 0.5 mm/s to the aorto-ostial junction using the R-100 motorized catheter pull-back system (Volcano Corporation).

OCT AND IVUS ANALYSIS AND DEFINITIONS. Final post-stent placement OCT images were recorded digitally and analyzed offline using proprietary software (St. Jude Medical) at independent core laboratories (University Hospitals Imaging Core Laboratory, Cleveland, Ohio, and the Cardiovascular Research Foundation, New York, New York). Initial analyses performed at the University Hospitals' core laboratory were reassessed at the Cardiovascular Research Foundation core laboratory, and additional analyses were performed. Quantitative OCT measurements were done for all available slices including the lesion and 5-mm-long proximal and distal reference segments; stent measurements were done every 1 mm within the stent (10,11). Similarly, final post-stent, offline IVUS analyses were performed using computerized planimetry software (echoPlaque, INDEC Systems Inc., Santa Clara, California), at an independent IVUS core laboratory (Cardiovascular Research Foundation). Quantitative IVUS measurements were performed every 1 mm of the stented lesion including 5-mm-long proximal and distal reference segments (1–6).

For both IVUS and OCT, the slices with the minimal lumen cross-sectional area (CSA), the MSA within each lesion, and the smallest and largest lumen CSA within each reference segment were identified and assessed (**Figure 2**). Total and normalized volumes (volume divided by analysis length) were determined using Simpson's rule. The percentage of stent or lumen expansion was defined as MSA or minimal lumen CSA divided by the mean of the largest proximal and distal reference lumen CSAs. The percentage of mean stent or lumen expansion was defined as the mean stent or lumen CSA divided by the mean of the proximal and distal reference largest lumen CSAs. In lesions having only 1 reference (proximal or distal; e.g., a lesion abutting a bifurcation), the single reference lumen area was used.

The core laboratory also assessed the degree of intrastrut tissue protrusion (plaque and/or thrombus protrusion through stent struts into the lumen), stent malapposition (space behind stent struts not overlying a side branch), and edge dissection (intimal or medial dissection, intramural hematoma, or dissection outside of the media) (**Figure 3**) (5,10,11,15,18,19). Malapposition was considered major if the malapposition distance was >20% of the mean lumen diameter, equivalent to ~2.5 mm^2 or 35% malapposition CSA (malapposition CSA divided by the

FIGURE 2 Examples of Post-Stent Quantitative Measurements by OCT and IVUS

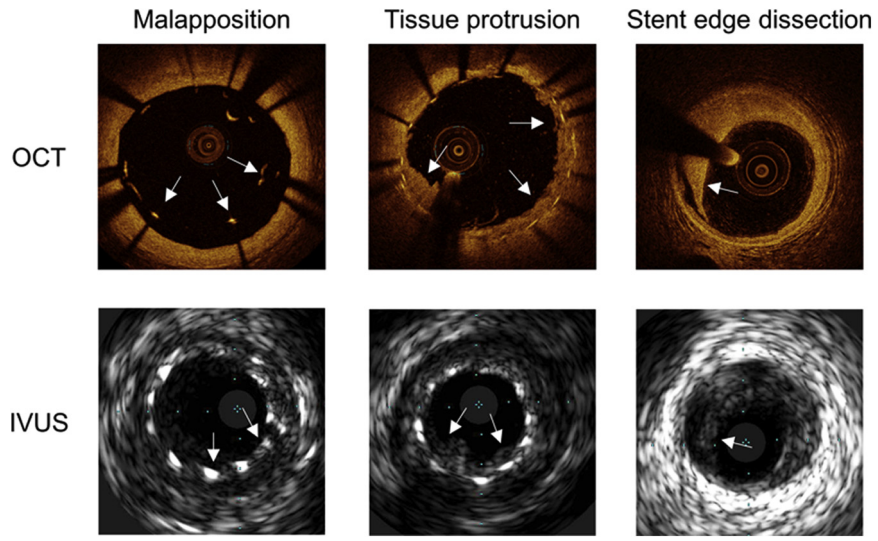


(Left) In the OCT example, the minimal stent area measured 7.70 mm^2, and the largest proximal and distal lumen areas measured 8.02 mm^2 and 6.96 mm^2, respectively, for a mean reference lumen area of 7.49 mm^2. Stent expansion was calculated to be 103%. **(Right)** In the IVUS example, the minimal stent area measured 7.2 mm^2, and the largest proximal and distal lumen areas measured 11.1 mm^2 and 8.1 mm^2, respectively, for a mean reference lumen area of 9.6 mm^2. Therefore, stent expansion was calculated to be 75%.

lumen CSA), assuming a 3-mm lumen diameter or a 7-mm^2 lumen CSA. Tissue protrusion was considered major if the percentage of tissue protrusion (tissue protrusion CSA divided by stent CSA) was >10%. Dissection was considered major when the measured length of the dissection was ≥3 mm (5,10,11,18,19).

QUANTITATIVE CORONARY ANGIOGRAPHY. Coronary angiograms from both ILUMIEN I and ADAPT-DES were analyzed at the angiographic core laboratory of the Cardiovascular Research Foundation using Medis Medical Imaging Systems software (QAngio XA 7.2, Leiden, the Netherlands). In-segment analysis

FIGURE 3 Examples of Post-stent Qualitative Findings by OCT and IVUS



OCT images **(top)** and IVUS images **(bottom)** from different cases. Malapposition appeared as floating stent struts with space between the struts and plaque surface. Tissue protrusion appeared as protruding tissue through the stent struts into the lumen. Medial stent edge dissection appeared as a flap of tissue separated from the media.

TABLE 1 Baseline Characteristics and Procedures in the Propensity-Matched Groups

	OCT (N = 286)	IVUS (N = 286)	p Value
Patient characteristics			
Age, yrs	66.0 (58.0, 72.0)	67.0 (59.0, 72.0)	0.97
Male	213 (74.5)	213 (74.5)	1.0
Diabetes mellitus	104/285 (36.5)	79/285 (27.7)	0.03
Current or former smoker	138/285 (48.4)	147/285 (51.6)	0.44
History of renal insufficiency	18/285 (6.3)	27/285 (9.5)	0.17
Previous myocardial infarction	70/283 (24.7)	63/283 (22.3)	0.49
Body mass index, kg/m^2	27.0 (24.2, 30.5)	26.9 (24.8, 29.4)	0.76
Clinical presentation			
Non-STEMI	29 (10.1)	65 (22.7)	<0.0001
Unstable angina	63 (22.0)	47 (16.4)	0.10
Stable coronary artery disease	194 (67.8)	174 (60.8)	0.09
Target vessel			
Left anterior descending	178 (62.2)	126 (44.1)	<0.0001
Left circumflex	53 (18.5)	81 (28.3)	0.005
Right coronary	55 (19.2)	79 (27.6)	0.02
Procedural information			
Drug-eluting stent implantation	282/285 (98.9)	284/285 (99.6)	0.63
Total stent length, mm	18.0 (15.5, 28.0)	23.0 (15.0, 32.0)	0.01
Maximal device diameter, mm*	3.0 (2.8, 3.5)	3.0 (3.0, 3.5)	<0.0001
Maximal device/artery diameter ratio	1.1 (1.0, 1.2)	1.2 (1.1, 1.3)	0.002

Values are median (first, third quartiles), n (%), or n/N (%). *Either balloon or stent.

IVUS = intravascular ultrasound; OCT = optical coherence tomography; STEMI = ST-segment elevation myocardial infarction.

included the stent plus 5-mm proximal and distal reference segments. Quantitative and qualitative analyses were done using standard methods (20). QCA was specified in all patients from the ILUMIEN I study and was performed in 1,136 patients from the ADAPT-DES IVUS substudy.

STATISTICAL ANALYSIS. If multiple lesions were treated, 1 lesion was randomly chosen for analysis. The effect of OCT versus IVUS on stent expansion and other parameters was examined in 2 ways: by analysis of propensity-matched pairs and in a covariate-adjusted analysis using all patients. Paired matched groups (IVUS vs. OCT) were created adjusting for 4 confounders that may affect the degree of stent expansion or its measurement: the extent of angiographic calcification (severe, moderate, mild/none); QCA lesion length; QCA reference vessel diameter (RVD); and whether both or only a single reference site (proximal and/or distal) were available for calculation of stent expansion. Regarding the latter, an OCT lesion with both references was matched with a corresponding IVUS lesion with both references, whereas an OCT lesion with only a proximal or distal reference was matched with a corresponding IVUS lesion with only a proximal or distal reference, respectively. The subject's propensity score was defined as the posterior probability of either OCT or IVUS guidance as estimated from a logistic regression model with the 4 variables as covariates. Matched pairs were created using greedy matching criteria with a caliper of 0.1. For the second analysis using the entire study population, the effect of OCT versus IVUS guidance on the primary and major secondary endpoints was evaluated by multivariable stepwise linear regression ($p < 0.2$ to enter, $p < 0.1$ to stay). Covariates included age, sex, diabetes, smoking, history of renal insufficiency, previous myocardial infarction, acute coronary syndrome presentation, body mass index, left anterior descending artery (LAD) location, QCA RVD, QCA MLD, QCA lesion length, the presence of angiographic moderate or severe calcification, tortuosity, bifurcation, thrombus, Thrombolysis In Myocardial Infarction flow, and availability of reference segments by IVUS or OCT. Imaging modality (OCT vs. IVUS) was forced into the model.

Categorical variables are presented as frequencies and were compared by the McNemar test or the exact McNemar test when <20 discordant pairs. Continuous variables are presented as medians and first and third quartiles and were compared by a paired Student *t* test (when normally distributed per the Shapiro-Wilk test) or Wilcoxon signed rank test (when not normally distributed). No formal hypotheses regarding superiority or noninferiority were pre-specified. All p values were 2 sided, and $p < 0.05$ was considered significant for all analyses. Statistical analyses were performed using SAS version 9.2 (SAS Institute, Cary, North Carolina).

RESULTS

Study enrollment is shown in **Figure 1**. A total of 354 of 418 patients enrolled in the ILUMIEN I study, and 586 of 2,179 patients enrolled in the formal IVUS substudy of ADAPT-DES were included in the present study. There were no significant differences in the baseline variables between the ILUMIEN I patients included and those not included (Online Table 1). There were several baseline differences between the ADAPT-DES patients included and those not included (Online Table 2). Of the 940 total study patients, 286 propensity-matched pairs were derived (572 total patients). Of note, 88.8% of pairs had both proximal and distal reference segments measured by OCT and IVUS, 10.5% had only a distal reference, and 0.7% had only a proximal reference.

MATCHED-PAIR ANALYSIS. The baseline clinical and angiographic characteristics of the propensity-matched patients undergoing OCT versus IVUS guidance were

well balanced for the variables expected to affect stent expansion and measurement: angiographic moderate/severe calcification, QCA RVD and lesion length, and reference segment availability (Tables 1 and 2). Regarding other variables, the OCT cohort had a slightly higher prevalence of diabetes and LAD lesion location, whereas non-STEMI, vessel tortuosity, and lesion thrombus were slightly more frequent in the IVUS cohort.

The primary endpoint of stent expansion was not significantly different between the OCT and IVUS cohorts (median [first, third quartiles]: 72.8% [63.3, 81.3] vs. 70.6% [62.3, 78.8], respectively, p = 0.29) (Table 3, Figure 4). The major secondary endpoint of mean stent expansion was also not significantly different (89.6% [79.7, 98.1] vs. 86.2% [76.6, 94.1] respectively, p = 0.17). However, as expected, absolute IVUS area measurements were systematically larger than OCT area measurements.

As shown in Table 4, and also as expected, any stent malapposition, tissue protrusion, and stent edge dissection were detected in a substantially greater proportion of OCT cases compared with IVUS. However, the prevalence of *major* malapposition, *major* tissue protrusion, *major* edge dissection, and intramural hematoma were infrequent and not significantly different between groups.

The major QCA secondary endpoints of post-PCI in-stent and in-segment DS were not significantly different with OCT versus IVUS guidance, although the MLD at the stent edges (in-segment) was slightly smaller in the OCT group (Table 2). Severe complications such as no reflow, abrupt closure, and perforation were uncommon in both groups.

ENTIRE STUDY POPULATION ANALYSIS. As shown in Online Tables 3 and 4, there were substantial differences in baseline clinical and angiographic characteristics between the unmatched groups. By multivariable analysis (Table 5), OCT versus IVUS guidance was not a significant predictor of stent expansion (p = 0.84), mean stent expansion (p = 0.30), or in-stent QCA DS (p = 0.19). OCT guidance was significantly associated with a greater in-segment DS, although the difference was small (13.3% [8.9, 20.2] vs. 11.2% [7.6, 17.2], adjusted p = 0.009).

TABLE 2 Quantitative Coronary Angiography Findings in the Propensity-Matched Groups

	OCT (N = 286)	IVUS (N = 286)	p Value
Pre-PCI measurements			
Reference vessel diameter, mm	2.7 (2.3, 3.0)	2.7 (2.4, 3.0)	0.17
Minimum lumen diameter, mm	0.9 (0.7, 1.2)	0.9 (0.6, 1.2)	0.12
Diameter stenosis, %	64.3 (57.0, 72.1)	64.0 (56.9, 75.5)	0.03
Lesion length, mm	14.9 (10.9, 21.3)	14.1 (9.8, 23.5)	0.54
Bifurcation lesion	97 (33.9)	93 (32.5)	0.71
Calcification (moderate or severe)	60 (21.0)	56 (19.6)	0.63
Angulation (moderate or severe)	21 (7.3)	23 (8.0)	0.75
Tortuosity (moderate or severe)	22/283 (7.8)	42/283 (14.8)	0.009
Thrombus present	8 (2.8)	20 (7.0)	0.02
TIMI flow grade 3	257 (89.9)	255 (89.2)	0.78
Worst morphology during PCI			
Dissection type B or C*	7 (2.4)	8 (2.8)	1.0
Slow flow or no reflow	3 (1.0)	9 (3.1)	0.14
Abrupt closure	2 (0.7)	1 (0.3)	1.0
Perforation	0 (0.0)	3 (1.0)	–
Final PCI measurements			
Reference vessel diameter, mm	2.6 (2.3, 2.9)	2.7 (2.4, 3.0)	0.12
MLD, mm			
In-stent	2.5 (2.3, 2.9)	2.6 (2.3, 2.8)	0.78
In-segment	2.2 (2.0, 2.6)	2.3 (2.1, 2.6)	0.01
In-stent mean lumen diameter, mm	2.9 (2.6, 3.2)	2.9 (2.7, 3.2)	0.76
Diameter stenosis, %			
In-stent	6.3 (2.8, 9.6)	6.4 (2.9, 11.9)	0.07
In-segment	13.0 (8.6, 19.8)	12.3 (8.2, 17.3)	0.07
Acute gain, mm			
In-stent	1.6 (1.3, 1.9)	1.6 (1.4, 1.9)	0.60
In-segment	1.3 (1.0, 1.6)	1.4 (1.1, 1.7)	0.005
Proximal stent edge MLD, mm	2.8 (2.5, 3.2)	2.8 (2.5, 3.2)	0.046
Distal stent edge MLD, mm	2.3 (2.0, 2.6)	2.4 (2.1, 2.8)	<0.0001
Dissection type B*	0 (0.0)	1 (0.4)	–
Perforation	0 (0.0)	2 (0.7)	–
TIMI flow grade 3	268/278 (96.4)	274/278 (98.6)	0.18

Values are median (first, third quartiles) or n (%). *No other dissection type was observed.

MLD = minimal lumen diameter; PCI = percutaneous coronary intervention; TIMI = Thrombolysis In Myocardial Infarction; other abbreviations as in Table 1.

DISCUSSION

In the present study, the largest to date to compare the acute procedural outcomes of OCT- and IVUS-guided coronary stenting, the relative degree of stent expansion was not significantly different with the 2 imaging techniques. Similarly, OCT and IVUS guidance were associated with comparable rates of major stent malapposition, tissue protrusion, and stent edge dissection.

OCT VERSUS IVUS: QUANTITATIVE COMPARISONS. By intravascular imaging, the most important determinant of early stent thrombosis and restenosis after stent implantation is the MSA achieved (1–6). Whether OCT guidance achieves an MSA comparable to that with IVUS guidance is unknown. In the present study, we compared OCT-measured stent dimensions after OCT guidance from the ILUMIEN I study with IVUS-measured stent dimensions after IVUS guidance from the ADAPT-DES study. As IVUS measurements are known to be consistently larger than OCT measurements (13–15), directly comparing the MSA achieved in these 2 studies would not

TABLE 3 Quantitative Intravascular Imaging in the Propensity-Matched Groups

	OCT (N = 286)	IVUS (N = 286)	p Value
Stent measurements			
Expansion, %	72.8 (63.3, 81.3)	70.6 (62.3, 78.8)	0.29
<90	259 (90.6)	266 (93.0)	0.26
<60	50 (17.5)	54 (18.9)	0.66
<50%	22 (7.7)	14 (4.9)	0.18
Lumen expansion, %	71.1 (62.1, 80.4)	70.0 (61.9, 78.7)	0.40
Mean stent expansion, %	89.6 (79.7, 98.1)	86.2 (76.6, 94.1)	0.17
Mean lumen expansion, %	91.8 (80.9, 99.9)	86.0 (76.9, 93.9)	0.001
Minimal stent CSA, mm^2	5.0 (3.9, 6.4)	5.5 (4.4, 7.0)	<0.0001
Minimal lumen CSA, mm^2	5.0 (4.0, 6.3)	5.5 (4.4, 6.9)	<0.0001
Mean stent CSA, mm^3/mm	6.4 (5.1, 7.8)	6.7 (5.5, 8.3)	<0.0001
Mean lumen CSA, mm^3/mm	6.5 (5.3, 7.9)	6.7 (5.5, 8.3)	0.002
Reference measurements, mm^2			
Proximal reference largest lumen CSA	8.3 (6.2, 10.7)	8.8 (7.1, 11.2)	0.02
Proximal reference minimum lumen CSA	5.6 (4.3, 7.5)	7.4 (5.8, 9.5)	<0.0001
Distal reference largest lumen CSA	6.1 (4.7, 7.7)	6.9 (5.3, 9.0)	<0.0001
Distal reference minimal lumen CSA	3.9 (2.9, 5.4)	5.8 (4.4, 7.5)	<0.0001

Values are median (first, third quartiles) or n (%).
CSA = cross-sectional area; other abbreviations as in Table 1.

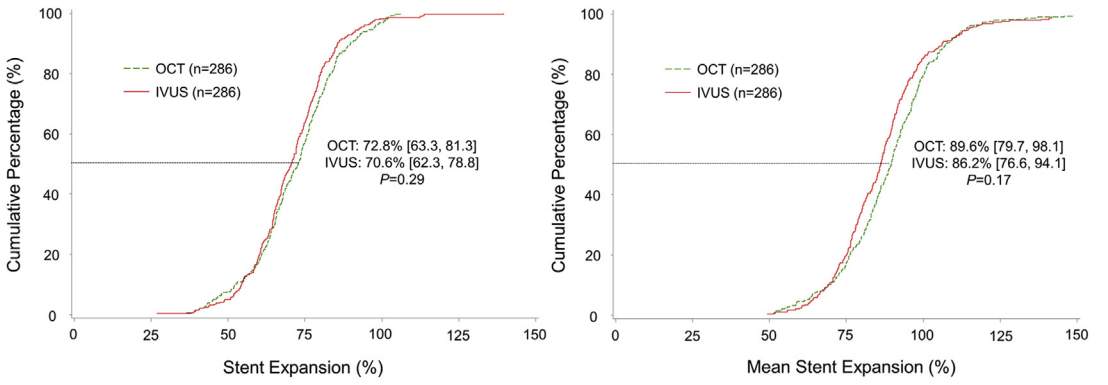
provide a valid comparison. Therefore, we used the percentage of stent area expansion (MSA relative to the reference lumen area) to compare the cross-study results, which should be technique independent. With this approach, we found the degree of stent expansion with OCT and IVUS guidance to be comparable in the propensity-matched pair analysis, as well as after multivariable analysis in the entire study population of 940 patients.

A second measurement technique that we used to assess acute stent outcomes was QCA, analyzed at the same core laboratory. Although less sensitive than intravascular imaging to detect small changes in stent dimensions, QCA (like relative stent expansion) is not dependent on the choice of intravascular imaging modality. In this analysis, in-stent QCA measures of acute gain and post-PCI MLD and DS were similar after stenting with both intravascular imaging techniques. However, the QCA MLD at the distal stent edge was significantly smaller in the OCT group compared with the IVUS group, and OCT was an independent predictor of a greater in-segment DS compared with IVUS. Of note, although the lesions were well matched for QCA reference diameter, the OCT group had more LAD lesions than the IVUS group, potentially leading to a smaller distal edge MLD due to greater vessel tapering in LAD vessels (21). Moreover, the observed QCA differences were small and of uncertain clinical significance.

There are many different approaches to stent sizing, and a single standardized strategy has not been established. Stents can be sized angiographically, usually ~1:1 to the RVD (either by visual assessment or online QCA), by IVUS sized to the proximal and/or distal reference lumen dimensions or to the midwall or to the true vessel dimension (EEM) at the lesion site, and by OCT, most often sized to the reference lumen dimensions as the limited penetration of OCT often precludes EEM measurement (13). Conversely, some operators size stents angiographically and then use IVUS or OCT just to confirm adequate expansion and absence of other major deficiencies (with varying criteria for what constitutes a suboptimal result requiring reintervention). There are also differences between QCA, IVUS, and OCT in how the reference segments are identified (which may affect stent length selection as well as sizing). IVUS studies have shown that residual plaque burden is an important predictor of stent edge restenosis, and as such, intermediate disease segments should be covered (22). Although OCT may be unable to assess reference segment plaque burden, the axial resolution of OCT is sufficiently greater than IVUS (~20 μm vs. 150-200 μm, respectively) (11–13). The extent to which these varying factors affect stent length determination, lesion coverage, and stent expansion with IVUS versus OCT guidance is uncertain, especially because these decisions must be made in real time by interventional operators in the cath lab (not in a core laboratory).

In this regard, before the present report, only 1 small study compared OCT- and IVUS-guided intervention. Habara et al. (13) randomized 70 de novo coronary lesions at a single center to OCT- or IVUS-guided stenting. Good visibility of the vessel wall was defined as visualization of ≥270° of the EEM circumference. Approximately 90% of patients underwent post-dilation after image evaluation revealed an unsatisfactory result (defined as MSA <90% of the distal reference lumen area). Post-dilation balloon size was chosen based on the vessel diameter at the MSA site if there was good visibility of the EEM (11% vs. 94% on OCT vs. IVUS, respectively, $p < 0.001$); otherwise, post-dilation balloon size was based on angiography. However, because the vessel wall was not visible in 89% of the OCT-guided cases, the result was optimized by angiography. Likely as a result, MSA and stent expansion (measured by IVUS in both groups) were smaller after OCT compared with IVUS guidance ($6.1 \pm 2.2\ mm^2$ vs. $7.1 \pm 2.1\ mm^2$, $p = 0.04$, and $64.7 \pm 13.7\%$ vs. $80.3 \pm 13.4\%$; $p = 0.002$, respectively). In contrast, the present large-scale, multicenter study suggests that similar degrees of stent expansion may be achieved with OCT and IVUS guidance.

FIGURE 4 Cumulative Frequency Distribution of Relative Stent Expansion and Mean Stent Expansion



Cumulative frequency distribution of relative stent expansion **(left)** and mean stent expansion **(right)** after OCT guidance **(dashed green line)** and IVUS guidance **(solid red line)**. No significant differences with OCT and IVUS guidance were found for stent expansion or mean stent expansion.

OCT VERSUS IVUS: QUALITATIVE COMPARISONS. Due to its higher resolution, stent malapposition, tissue prolapse, and edge dissections are detected more commonly by OCT than IVUS (14,15,23) For example, Kubo et al. (15) reported greater rates of stent malapposition (39% vs. 14%; $p < 0.001$), tissue protrusion (95% vs. 18%; $p < 0.001$), intrastent thrombus (13% vs. 0%; $p = 0.01$), and stent edge dissections (13% vs. 0%; $p = 0.001$) with OCT compared with IVUS imaging. However, many of these abnormalities are small and of uncertain clinical relevance. Several studies have demonstrated that acute stent malapposition is not a risk factor for stent thrombosis or restenosis unless accompanied by a small MSA (18,19,24). Similarly, in an IVUS study of 389 patients undergoing primary PCI for STEMI, tissue protrusion was unrelated to stent thrombosis as long as the residual lumen area was sufficient (5). In a study of 249 post-stent lesions evaluated by OCT, edge dissections were found in 37.8% of lesions, 84% of which were not visible on angiography (23). Additional stents were implanted in 22.6% of these lesions at operators' discretion, and 1-year outcomes were similar in lesions with and without untreated edge dissection. Conversely, in other studies, large edge dissections detected by IVUS have been related to both early stent thrombosis and restenosis (5). In our study, OCT detected many more cases of acute stent malapposition, tissue prolapse, and edge dissection than IVUS, likely due to its superior resolution. However, the rates of major malapposition, tissue prolapse, and edge dissection, which, as defined, would be expected to be detected with

TABLE 4 Qualitative Intravascular Imaging in the Propensity-Matched Groups

	OCT (N = 286)	IVUS (N = 286)	p Value
Presence of stent strut malapposition			
Any malapposition	76 (26.6)	39 (13.6)	0.0002
Distance >0.2 mm	65 (22.7)	38 (13.3)	0.004
Distance/mean lumen diameter >10%	38 (13.3)	22 (7.7)	0.04
Distance/mean lumen diameter >20%	4 (1.4)	2 (0.7)	0.69
Distance/mean lumen diameter >10% and expansion <60%	8 (2.8)	10 (3.5)	0.81
Presence of tissue protrusion			
Any tissue protrusion	182 (63.6)	78 (27.3)	<0.0001
Tissue protrusion cross sectional area >10%	33 (11.5)	23 (8.0)	0.17
Tissue protrusion >10% and expansion <60%	10 (3.5)	6 (2.1)	0.45
Presence of stent edge dissection			
Any dissection	66 (23.1)	15 (5.2)	<0.0001
Intimal dissection	27 (9.4)	3 (1.0)	<0.0001
Medial dissection	40 (14.0)	7 (2.4)	<0.0001
Intramural hematoma	2 (0.7)	5 (1.7)	0.45
Dissection with arc ≥60°	14 (4.9)	5 (1.7)	0.04
Dissection with length ≥3 mm	7 (2.4)	3 (1.0)	0.29
Proximal stent edge location	3 (1.0)	0 (0.0)	—
Distal stent edge location	4 (1.4)	3 (1.0)	1.0

Values are n (%).
Abbreviations as in Table 1.

TABLE 5 Multivariable Analysis in the Entire Study Population (N = 940)

	Endpoints			
	Stent Expansion, %	Mean Stent Expansion, %	Diameter Stenosis In-Stent, %	Diameter Stenosis In-Segment, %
Measurement by OCT (N = 354)	72.6 (63.5, 81.4)	89.6 (79.2, 98.5)	6.4 (2.7, 9.9)	13.3 (8.9, 20.2)
Measurement by IVUS (n = 586)	70.5 (62.1, 79.5)	86.8 (77.1, 96.8)	6.4 (3.0, 10.7)	11.2 (7.6, 17.2)
	Adjusted p Values			
OCT vs. IVUS guidance	0.84	0.30	0.19	0.009
Age	0.04	*	*	*
Previous myocardial infarction	*	*	0.04	*
Lesion length	<0.0001	0.0009	<0.0001	*
Reference vessel diameter	*	0.07	*	0.04
Bifurcation lesion	0.0006	*	*	0.07
Tortuosity (moderate or severe)	0.01	*	*	*
Calcification (moderate or severe)	*	0.0007	*	*
Left anterior descending location	*	*	0.02	*
Reference availability	<0.0001	<0.0001	*	*

Values are median (first, third quartiles) unless otherwise indicated. *p > 0.1 and thus not selected in the final model. OCT vs. IVUS was forced into the multivariable model.

Abbreviations as in Table 1.

similar facility with both imaging techniques, were comparable in the 2 groups and were infrequent.

STUDY LIMITATIONS. The present study is a nonrandomized, retrospective comparison from 2 separate registries with different operators at different centers. However, both ILUMIEN I and ADAPT-DES were carefully controlled, prospective, multicenter studies, and all IVUS, OCT and QCA images were assessed at the same core laboratory, ensuring standardized assessment techniques. Nonetheless, differences in baseline clinical features and angiographic measures between the study groups were evident. There were substantial imbalances in the regional distribution of enrollment in the current study: all of the patients in the ADAPT-DES cohort were enrolled from German sites (N = 586), whereas the ILUMIEN I cohort included 124 patients (35.0%) from multiple North American sites, 118 patients (33.3%) from multiple European sites, and 112 patients (31.6%) from multiple Asian sites. The impact of different regional practice patterns on technique and therefore image-guided stenting should be explored in a large-scale, multicenter, international randomized trial. Moreover, QCA was only performed in 48% of the 2,179 patents in the ADAPT-DES IVUS substudy, introducing potential selection bias. There are also fundamental differences in the manner in which IVUS and OCT images are acquired and measured. For example, the resolution with the 20-MHz IVUS catheter is ~10% of that with OCT, there are differences in pull-back speeds between IVUS and OCT (and the IVUS pull back is less accurate), and OCT measurements do not take into consideration the cardiac cycle. For the entire cohort (OCT, N = 354; IVUS, N = 586), the prevalence of pre-intervention imaging was 57.7% for IVUS and 93.7% for OCT ($p < 0.0001$). Pre-intervention imaging may affect device sizing and thus stent expansion. We therefore cannot rule out the influence of unmeasured confounders, although the major determinants of stent expansion were controlled for either in the matching process or by multivariable analysis.

Second, neither study specified the method of stent sizing or criteria for optimal stent implantation; thus, the generalizability of these findings is uncertain. Third, whether relative stent expansion is as good a predictor of long-term outcomes as is the absolute MSA is not entirely clear (1–6,25). Stent expansion measurements may also be less precise in long, tapering lesions. However, total stent length in the current study was relatively short (~20 mm) and therefore less likely to affect the final results. Fourth, in ~10% of cases, both reference segments could not be measured and were excluded. Fifth, multiple lesions were present in 7.3% of ILUMIEN I patients and in 15.8% of ADAPT-DES patients. The protocol pre-specified that in patients with multiple lesions, only 1 lesion per patient would be randomly chosen and analyzed before matching. Given the relatively low frequency of multiple lesions, it is unlikely that the results would have been materially changed had all lesions had been analyzed. Sixth, procedural data, such as inflation pressure, was not available in ILUMIEN-I, precluding a complete comparison of procedural factors. Finally, long-term outcome data are not yet available from ILUMIEN I, and the present study was not designed to determine clinical differences between OCT- and IVUS-guided stent implantation. Prati et al. (12) retrospectively compared 335 OCT-guided PCI cases with 335 propensity-matched angiography-guided PCI cases. OCT guidance was associated with a lower risk of cardiac death or MI (odds ratio: 0.49 [0.25, 0.96], $p = 0.04$) after adjustment for clinical and procedural factors. However, the rate of death at 1 year in the angiography-guided group was unexpectedly high (6.9%), raising the possibility of play of chance.

CONCLUSIONS

The present study suggests that OCT guidance may achieve a comparable degree of stent expansion as that with IVUS guidance, with a similarly low frequency of major stent malapposition, tissue prolapse, and edge dissections. Randomized studies are thus warranted to determine whether similar clinical outcomes are obtained after stenting guided by these 2 intravascular imaging modalities.

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PERSPECTIVE

WHAT IS KNOWN? By achieving greater stent expansion, IVUS guidance has been associated with improved event-free survival compared with angiographic guidance alone.

WHAT IS NEW? In this study, OCT guidance showed a similar degree of stent expansion compared with IVUS guidance.

WHAT IS NEXT? Further studies are warranted to determine whether OCT and IVUS guidance can be translated into improved long-term outcomes compared with angiographic guidance alone.

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

APPENDIX For supplemental tables, please see the online version of this article.