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Optical coherence tomography imaging during percutaneous coronary intervention impacts physician decision-making: ILUMIEN I study

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Aims ILUMIEN I is the largest prospective, non-randomized, observational study of percutaneous coronary intervention (PCI) procedural practice in patients undergoing intra-procedural pre- and post-PCI fractional flow reserve (FFR) and optical coherence tomography (OCT). We report on the impact of OCT on physician decision-making and the association with post-PCI FFR values and early clinical events.

Methods and results Optical coherence tomography and documentary FFR were performed pre- and post-PCI in 418 patients (with 467 stenoses) with stable or unstable angina or NSTEMI. Based on pre-PCI OCT, the procedure was altered in 55% of patients (57% of all stenoses) by selecting different stent lengths (shorter in 25%, longer in 43%). After clinically satisfactory stent implantation using angiographic guidance, post-PCI FFR and OCT were repeated. Optical coherence tomography abnormalities deemed unsatisfactory by the implanting physician were identified: 14.5% malapposition, 7.6% under-expansion, 2.7% edge dissection and prompted further stent optimization based on OCT in 25% of patients (27% of all stenoses) using additional in-stent post-dilatation (81%, 101/124) or placement of 20 new stents (12%). Optimization subgroups were identified *post hoc*: stent placement without reaction to OCT findings ($n = 137$), change in PCI planning by pre-PCI OCT ($n = 165$), post-PCI optimization based on post-PCI OCT ($n = 41$), change in PCI planning, and post-PCI optimization based on OCT ($n = 65$). Post-PCI FFR values were significantly different ($P = 0.003$) between optimization groups (lower in cases with pre- and post-PCI reaction to OCT) but no longer different after post-PCI stent optimization. MACE events at 30 days were low: death 0.25%, MI 7.7%, repeat PCI 1.7%, and stent thrombosis 0.25%.

Conclusion Physician decision-making was affected by OCT imaging prior to PCI in 57% and post-PCI in 27% of all cases.

ClinicalTrials.gov Identifier NCT01663896, Observational Study of Optical Coherence Tomography (OCT) in Patients Undergoing Fractional Flow Reserve (FFR) and Percutaneous Coronary Intervention (ILUMIEN I).

Keywords Optical coherence tomography • Percutaneous coronary intervention • Stent • Fractional flow reserve • Periprocedural myocardial infarction

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Introduction

Since its introduction in 1977, safety and efficacy outcomes after percutaneous coronary interventions (PCI) have improved significantly through advances in device technology, adjunctive peri-procedural pharmacology, and operator experience. Although the majority of PCIs are performed under angiographic guidance, use of fractional flow reserve (FFR) for confirmation of PCI appropriateness[1,2] and intracoronary imaging for optimization of procedural technique[3,4] may lead towards further improvement of PCI outcomes. Several components of procedural optimization cannot be accurately assessed by angiography, e.g. sizing of stent length and diameter, the presence of residual thrombus, wall coverage, and stent strut apposition. These features can be precisely evaluated with the use of intravascular Fourier domain optical coherence tomography (OCT). Optical coherence tomography acquires longitudinal sequences of cross-sectional images (100 frames/s) in a blood-free environment, resulting in sharp border definition between lumen and vessel wall. Together with high axial resolution (10–15 microns), volumetric segmentation of vessel and wall contours facilitates more rational selection of stent size and length, as well as ascertainment of full stent deployment and expansion.

ILUMIEN I is to date the largest prospective, non-randomized, observational study of PCI practice in patients undergoing pre- and post-PCI FFR and OCT. The objective was to define guidance parameters for stent optimization. This manuscript reports on the impact of OCT on physician decision-making, procedural findings, and early clinical events.

Methods

Study protocol

Inclusion and exclusion criteria

Patients providing written informed consent for inclusion in the study protocol presented with stable angina, unstable angina, or NSTEMI, and underwent elective or 'ad hoc' PCI of *de novo*, single or multivessel coronary artery stenosis. Up to two major vessels and three lesions could be treated, with no more than two lesions per major coronary artery. Subjects with acute STEMI, emergent PCI, cardiogenic shock, restenosis or stent thrombosis, target left main stenosis, aorto-ostial or diffuse disease, extreme angulation, or calcification were excluded, as well as planned use of bare metal stent (see detailed list of inclusion and exclusion criteria in Supplementary material online, *Appendix 1*). The study was conducted in 35 sites with balanced patient inclusion between continents: USA 36%, Europe 31%, Japan 23%, Asia 6%, Canada 41%, and Australia 3% (list of investigators and clinical sites in Supplementary material online, *Appendix 2*).

Study flowchart

Acquisition of pre- and post-PCI FFR and OCT was required for collection of paired functional and anatomical data, according to standardized technique and reporting. Further to indications for PCI based on clinical grounds, intervention was recommended in target vessels with abnormal FFR ($\leq$0.80). After angiography, investigators were requested to describe the planned PCI strategy based on available angiographic data. Pre-PCI OCT was intended to be documentary, but any changes from the initial plan were carefully recorded. Next, PCI and stent placement were performed using angiographic guidance, per individual investigator standard of care. When a 'best of care' angiographic result was obtained, post-PCI standardized documentary FFR was recorded and OCT data were acquired. When operators felt that the OCT result was clinically unsatisfactory, further optimization was performed followed by repeat imaging (*Figure 1*). Recommendations to intervene or not to intervene based on post-PCI angiographic and OCT findings were not prescriptive and limited to severe abnormalities: flow-limiting edge dissection, significant malapposition, thrombus/tissue protrusion with flow reduction, stent under-expansion $\geq$30% compared with reference distal lumen. All investigator treatment decisions were recorded on procedural worksheets at the time of intervention.

Analysis of angiography, fractional flow reserve, and optical coherence tomography

Devices used in the present study are described in Supplementary material online, *Appendix 3*. Co-registered images from coronary angiography, FFR, and OCT were analysed by the core laboratory for pre-specified variables including lesion morphology and extent of disease, vessel injury (dissection, thrombus, tissue prolapse) and stent apposition, volume, area, diameter, expansion, positioning, length, and geographical miss[4–6] To report on physician decision-making, on-site classified occurrence of malapposition, under-expansion, thrombus/tissue protrusion, and edge dissection are based on the recommended definitions below.

- Edge dissection $>$180° in more than five frames on OCT.
- Significant malapposition defined as $>$200 micron in axial diameter and present in at least five consecutive frames on OCT.
- The presence of thrombus and/or tissue protrusion on OCT causing flow reduction (i.e. TIMI $<$ 3 and/or obstruction visible by angiography).
- Under-expansion $\geq$30% by OCT compared with reference distal lumen area and when quantitative coronary angiogram (QCA) shows $>$20% in-stent residual diameter stenosis.

Event definition and adjudication

MACE events by ARC definitions[7,8] included both device-oriented composite endpoint [cardiac death, myocardial infarction (MI) not clearly attributable to a non-target vessel, and target lesion revascularization] and patient-oriented composite endpoint (all-cause mortality, any MI, and any repeat revascularization). Stent thrombosis was classified as definite, probable or possible, and as early or late.[7] Cardiac enzymes were collected within 48 h prior to PCI and between 6 and 48 h post-procedure or in case of chest pain or ECG changes. Classification and criteria for biomarker diagnosis of periprocedural MI required troponin or CK-MB $>$3 times URL, with baseline value $<$URL. Myocardial infarction was reported according to two definitions: per protocol (ARC definition) as well as type 4a from the Universal MI definition consensus document.[9] In the absence of clinical symptoms, the elevation of cardiac enzymes was required to be at least 3 times the UNL and 5 times the baseline value to conservatively classify patients with elevated baseline values. All relevant data were collected at screening, baseline, pre-PCI, during and post-PCI, at hospital discharge, at 1-, 6-, and 12-month follow-up.

The Clinical Event Committee (CEC) adjudicated on an ongoing basis the adverse events reported during the study. The CEC consisted of interventional cardiologists who were blinded to individual subject and site identities (see Supplementary material online, *Appendix 4*). They classified reported adverse events according to adverse event type/code, severity, relatedness, and unanticipated category. Listings were reviewed on a quarterly basis to check whether events met adjudication criteria. Furthermore, all MACE events (MI, death, revascularization, and stent thrombosis) were adjudicated.

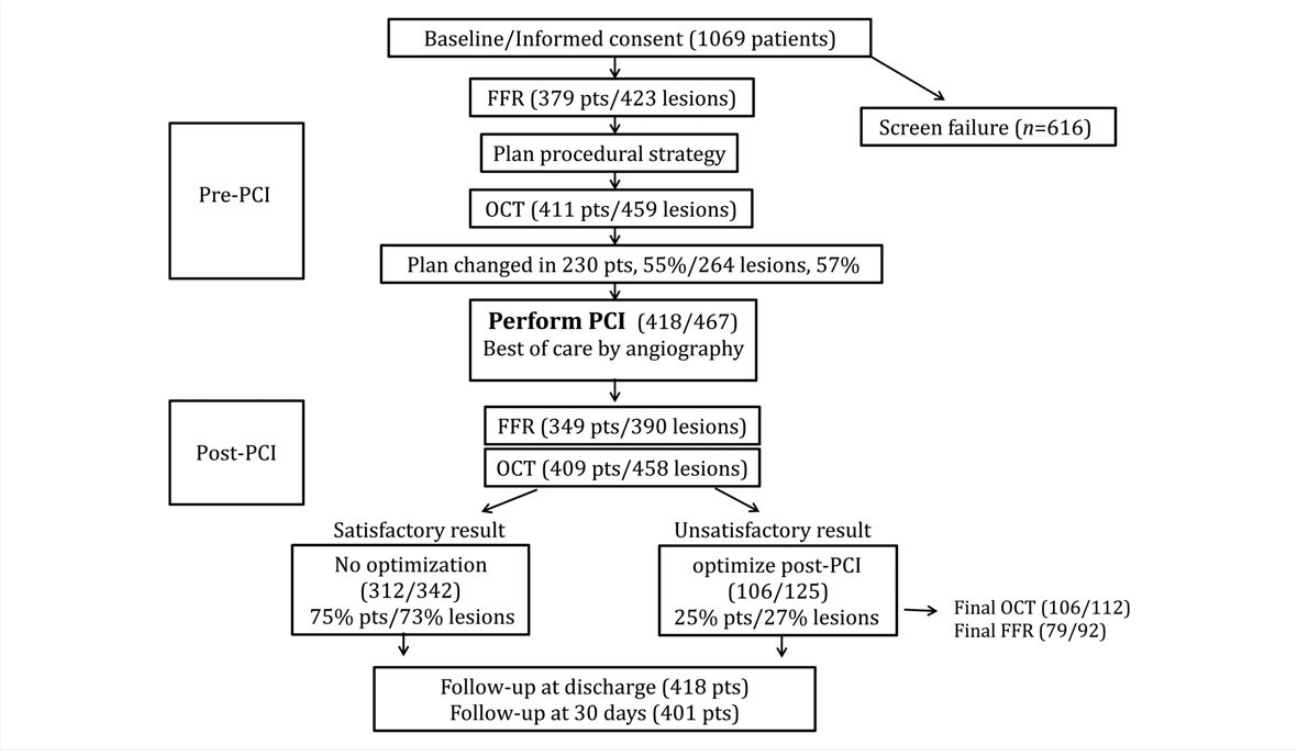

Figure 1 Consort diagram: study flowchart, procedural steps, and patient disposal. FFR, fractional flow reserve; OCT, optical coherence tomography; PCI, percutaneous coronary intervention.

Study objectives, statistical analysis, and reporting

No formal sample size calculation was applied since this was an observational study. The study objective was to define guidance parameters for stent optimization. This manuscript reports on the impact of OCT on physician decision-making and the association with post-PCI FFR values and early clinical events. Data analysis was performed on a per subject basis, unless specified otherwise (lesion or stent-related variables are shown on a per stenosis basis). Demographic variables, procedure characteristics, adverse event rates, and additional characteristics were analysed. Continuous and categorical variables were assessed using an ANOVA *F*-test and Fishers Exact MCMC *P*-values, respectively.

Informed consent process

Prior to enrollment, patients were fully informed of the details of the study protocol that was approved by local Medical Ethics Committee and relevant authorities. Written informed consent was obtained from all participating patients.

Results

Demographics and baseline characteristics

Of 1069 patients screened, 418 patients (467 stenoses) qualified for inclusion (Consort diagram on *Figure 1*). Mean age was 64.6 ± 10.2, 24.5% female, with typical risk factors (family history 34%, BMI 29 ± 15, diabetes 37%, treated arterial hypertension 72%, peripheral vascular disease 10%, present or past smoking 47%, prior or current hyperlipidaemia 76%).

Clinical presentation was stable angina (63%), unstable angina (22%), NSTEMI (11%), or silent ischaemia (4%). Previous MI was present in 24% and prior PCI in 20%. Target vessel was left anterior descending coronary artery in 59%, right coronary artery in 22%, and circumflex in 19%, with mostly PCI of a single lesion (90%) or two lesions in the same vessel (10%). Stenosis severity at baseline was 73 ± 15% diameter stenosis by angiography and 0.72 ± 0.14 by FFR.

Detailed use of medication at baseline and at 30 days is available in Supplementary material online, *Appendix 5*. At 30 days, aspirin was used in 96% of patients, clopidogrel in 82%, and other antiplatelet agents in 20%. Anticoagulation (mostly for atrial fibrillation) was prescribed in 8% of patients.

Impact of optical coherence tomography on physician decision-making

Following pre-PCI angiography, FFR, and OCT, PCI was performed in 418 patients/467 lesions. In this study population, pre-PCI FFR was obtained in 379 patients/423 lesions, and pre-PCI OCT was obtained in 411 patients/459 lesions (*Figure 2*). Pre-PCI FFR was not performed in 9.4% and pre-PCI OCT was not performed in 1.7% of the treated lesions. Following pre-PCI OCT, treatment planning was modified in 55% of patients (57% of all stenosis), in 7–80% of cases per site.

Stent implantation was performed based on angiography by best practice. Additional unplanned stent implantation and post-

dilatations were performed in 40 cases until the PCI result was seen as satisfactory by angiographic standards, as determined by the investigator. Post-PCI FFR was documented in 83% of patients (84% of all lesions) and post-PCI OCT in 98% of all patients/stenoses (*Figure 2*). Edge dissection, malapposition, and under-expansion were commonly observed on post-PCI OCT (*Table 1*). Post-PCI result was deemed as unsatisfactory by OCT imaging which led to further optimization in 106 patients (25%) or 125 stenoses (27% of all lesions), in 8–55% of cases per site.

Post hoc subgroup analysis per optimization strategy (*Table 2*) accounts for changes in treatment planning and performance based on OCT findings: pre-PCI only, post-PCI only, pre-PCI and post-PCI, or no change based on OCT (neither pre- or post-PCI). Few baseline variables were significantly different between optimization subgroups (*Table 2*). Pre- and post-PCI treatment changes based on OCT occurred less often when the lesions were single, in which post-PCI % diameter stenosis was low (13.6 ± 16.0) and post-PCI FFR was high (0.89 ± 0.07).

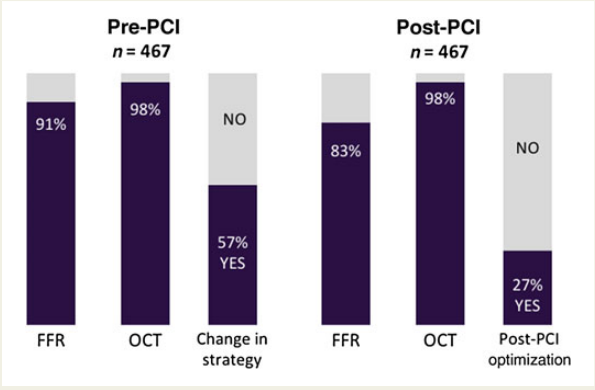

Figure 2 Impact of optical coherence tomography (OCT) on percutaneous coronary intervention (PCI) planning and procedural technique. Per-patient rates of fractional flow reserve (FFR) and optical coherence tomography pre- and post-percutaneous coronary intervention.

Otherwise, there were no significant differences in clinical background, demographic variables, or PCI indications between subgroups. There was no difference in use of medication at baseline and at 30 days between optimization subgroups (see Supplementary material online, *Table S1*, *Appendix 5*).

Change in percutaneous coronary intervention procedure and resource utilization

Change in planned treatment strategy based on pre-PCI OCT led to changes in selection of stent length (shorter in 25%, longer in 43%, and was unchanged in 32%). Selection of stent diameter decreased in 31%, increased in 8%, and was unchanged in 61%. The number of stents was unchanged in 87%, and the number of implanted stents per patient did not change (1.12 ± 0.34 planned vs. 1.21 ± 0.45 implanted, $P = 0.49$).

Post-PCI OCT findings prompting further procedural optimization were malapposition, under-expansion (both $P < 0.001$), and edge dissection ($P = 0.0034$) (see Supplementary material online, *Table S2, Appendix 6*). These OCT findings led mostly to additional in-stent post-dilatation (81%, 101/124), new stent placement (13%), or both (3%). Further to implantation of 20 additional stents (in 4% of all stenoses treated), the number of stents per patient was significantly higher after optimization based on post-PCI OCT (*Table 3*).

Fluoroscopy time and procedure duration increased when operators decided to react to OCT findings. Total amount of contrast used was not different and no case of contrast-induced nephropathy or other serious adverse events related to OCT imaging were observed.

Procedural outcomes, in-hospital and 30-day follow-up

Pre-PCI FFR values were similar between optimization subgroups (*Table 3*). Functional effect of PCI on FFR measurements was different between optimization subgroups ($P = 0.003$): 0.89 ± 0.07, 0.89 ± 0.07, 0.89 ± 0.08, and 0.86 ± 0.09, lower in cases with pre-

Table 1 Rates and types of abnormal findings by post-PCI OCT imaging

OCT variables	All abnormalities by core Laboratory, *n/N*	Rate (%)	Abnormalities deemed unsatisfactory by operator, *n/N*	Rate (%)
Edge dissection	107/388	27.6	11/408	2.7
Malapposition	126/392	32.1	59/408	14.5
Under-expansion	159/385	41.3	31/408	7.6
Edge dissection and malapposition	34/388	8.8	2/408	0.5
Edge dissection and under-expansion	35/385	9.1	2/408	0.5
Malapposition and tissue protrusion	44/392	11.2	2/408	0.5
Edge dissection, malapposition, and under-expansion	14/385	3.6	0/408	0
Thrombus or tissue protrusion[a]	100/392	25.5	4/408	1.0

FFR, fractional flow reserve; OCT, optical coherence tomography; PCI, percutaneous coronary intervention.
[a]Tissue protrusion was qualitatively analysed, and it was defined as intimal tissue protruding and disturbing lumen contour.

Table 2 Demographics and PCI indications (per optimization subgroup)

Variables	Statistic Mean ± SD (*N*) (Min, Max) or *n*/*N* (%)				*P*-value*
	PCI optimization without change based on OCT (*n* = 137)	PCI optimization based on Pre-PCI OCT only (*n* = 165)	PCI optimization based on post-PCI OCT only (*n* = 41)	PCI optimization based on pre-PCI *and* post-PCI OCT (*n* = 65)	
Age (years)	64 ± 9.9 (137) (36, 86)	65.4 ± 10.2 (165) (37, 88)	65.8 ± 10.7 (41) (43, 87)	63 ± 10.4 (65) (39, 88)	0.2825
Gender					
Female	27/137 (19.7%)	45/165 (27.3%)	14/41 (34.1%)	14/65 (21.5%)	0.1900
Male	110/137 (80.3%)	120/165 (72.7%)	27/41 (65.9%)	51/65 (78.5%)	
BMI (kg/m^2)	28.6 ± 6.2 (135) (17.3, 52.4)	28.5 ± 5.6 (164) (18.6, 64.7)	33.5 ± 35.2 (41) (17.6, 246.9)	30 ± 20.9 (65) (18, 191)	0.2302
CVA	10/137 (7.3%)	12/164 (7.3%)	3/41 (7.3%)	4/65 (6.2%)	1.0000
TIA	3/137 (2.2%)	0/165 (0%)	0/41 (0%)	1/65 (1.5%)	0.1820
Family history of CAD	41/137 (29.9%)	60/164 (36.6%)	17/41 (41.5%)	20/64 (31.3%)	0.4385
Renal insufficiency/failure	6/137 (4.4%)	9/164 (5.5%)	4/41 (9.8%)	3/65 (4.6%)	0.5751
Diabetes mellitus	56/137 (40.9%)	52/164 (31.7%)	12/41 (29.3%)	32/65 (49.2%)	0.0462
Peripheral vascular occlusive disease	12/137 (8.8%)	20/164 (12.2%)	5/41 (12.2%)	5/65 (7.7%)	0.6521
Tobacco use—smoking	56/137 (40.9%)	87/164 (53%)	17/41 (41.5%)	33/65 (50.8%)	0.1590
Hyperlipidaemia	101/137 (73.7%)	130/164 (79.3%)	33/41 (80.5%)	46/65 (70.8%)	0.4299
Taking hypertension medications at baseline	97/137 (70.8%)	123/165 (74.5%)	31/41 (75.6%)	45/65 (69.2%)	0.7845
Previous PCI in target vessel	26/134 (19.4%)	41/163 (25.2%)	7/39 (17.9%)	9/65 (13.8%)	0.2607
Previous MI	29/134 (21.6%)	37/163 (22.7%)	9/39 (23.1%)	23/65 (35.4%)	0.1884
Pre-procedure indication					
NSTEMI	19/137 (13.9%)	17/165 (10.3%)	2/41 (4.9%)	6/65 (9.2%)	0.7273
Other	4/137 (2.9%)	10/165 (6.1%)	2/41 (4.9%)	2/65 (3.1%)	
Stable angina	85/137 (62%)	97/165 (58.8%)	29/41 (70.7%)	44/65 (67.7%)	
Unstable angina	29/137 (21.2%)	41/165 (24.8%)	8/41 (19.5%)	13/65 (20%)	
Vessel identification					
Multi vessel	2/138 (1.4%)	2/168 (1.2%)	2/42 (4.8%)	2/69 (2.9%)	0.0031
Single vessel, multi lesion	7/138 (5.1%)	17/168 (10.1%)	2/42 (4.8%)	15/69 (21.7%)	
Single vessel, single lesion	129/138 (93.5%)	149/168 (88.7%)	38/42 (90.5%)	52/69 (75.4%)	
Target vessel (per FFR)					
Circumflex	30/140 (21.4%)	34/170 (20%)	7/44 (15.9%)	10/70 (14.3%)	0.1624
LAD	76/140 (54.3%)	108/170 (63.5%)	22/44 (50%)	45/70 (64.3%)	
Right	34/140 (24.3%)	28/170 (16.5%)	15/44 (34.1%)	15/70 (21.4%)	
Diameter stenosis (%)					
By angiography	73.9 ± 14.7 (134) (32, 99)	72.6 ± 15.1 (145) (0.8, 99)	75.1 ± 12.1 (33) (44, 99)	70.2 ± 13.4 (51) (50, 99)	0.3683

*Continuous and categorical *P*-values were calculated using an ANOVA *F*-test and Fishers Exact MCMC statistics, respectively.
FFR, fractional flow reserve; OCT, optical coherence tomography; PCI, percutaneous coronary intervention.

Table 3 Stenosis and procedural characteristics (per optimization subgroup)

		PCI optimization without change based on OCT	PCI optimization based on Pre-PCI OCT only	PCI optimization based on post-PCI OCT only	PCI optimization based on pre-PCI *and* post-PCI OCT	*P*-value*
Stenoses	*n*	146	185	46	79	
Planned number of stents prior to OCT	Mean ± SD	1.1 ± 0.37	1.14 ± 0.41	1.17 ± 0.44	1.22 ± 0.41	0.293
Actual number of stents per patient	Mean ± SD	1.17 ± 0.41	1.22 ± 0.47	1.32 ± 0.57	1.49 ± 0.75	0.0004
Pre-PCI % stenosis[a]	Mean ± SD	64.2 ± 16.1	64.5 ± 17	69.1 ± 20	59.5 ± 17.5	0.159
Post-PCI % stenosis[a]	Mean ± SD	13.6 ± 16	14.4 ± 12.7	22.3 ± 14.7	22.3 ± 19.7	0.007
Pre-PCI FFR	Mean ± SD	0.72 ± 0.14	0.73 ± 0.14	0.72 ± 0.14	0.72 ± 0.13	0.931
Post-PCI FFR	Mean ± SD	0.89 ± 0.07	0.89 ± 0.07	0.89 ± 0.08	0.86 ± 0.09	0.0035
Final FFR	Mean ± SD	—	—	0.9 ± 0.1	0.9 ± 0.1	0.2417
Pre-PCI MLA[b]	Mean ± SD	1.9 ± 1.2	1.7 ± 0.8	1.6 ± 0.9	1.8 ± 0.8	0.113
Post-PCI MLA[b]	Mean ± SD	6.1 ± 2.5	5.2 ± 2.1	5.3 ± 1.8	5.0 ± 2.0	0.004
Fluoroscopy duration	min	21 ± 14.7	25.7 ± 35.2	23.9 ± 13.1	31.9 ± 25.7	0.0536
Procedure duration	min	87.6 ± 37	89.7 ± 34.9	93.6 ± 26.1	106.4 ± 39.5	0.0043
Contrast agent used	mL	275.5 ± 127.6	260.7 ± 122	251.8 ± 132	256.3 ± 124.5	0.6012

*Continuous and categorical *P*-values were calculated using an ANOVA *F*-test and Fishers Exact MCMC statistics, respectively.
FFR, fractional flow reserve; OCT, optical coherence tomography; PCI, percutaneous coronary intervention.
[a]percent diameter stenosis by OCT (%).
[b]MLA, minimal luminal area by OCT (mm^2).

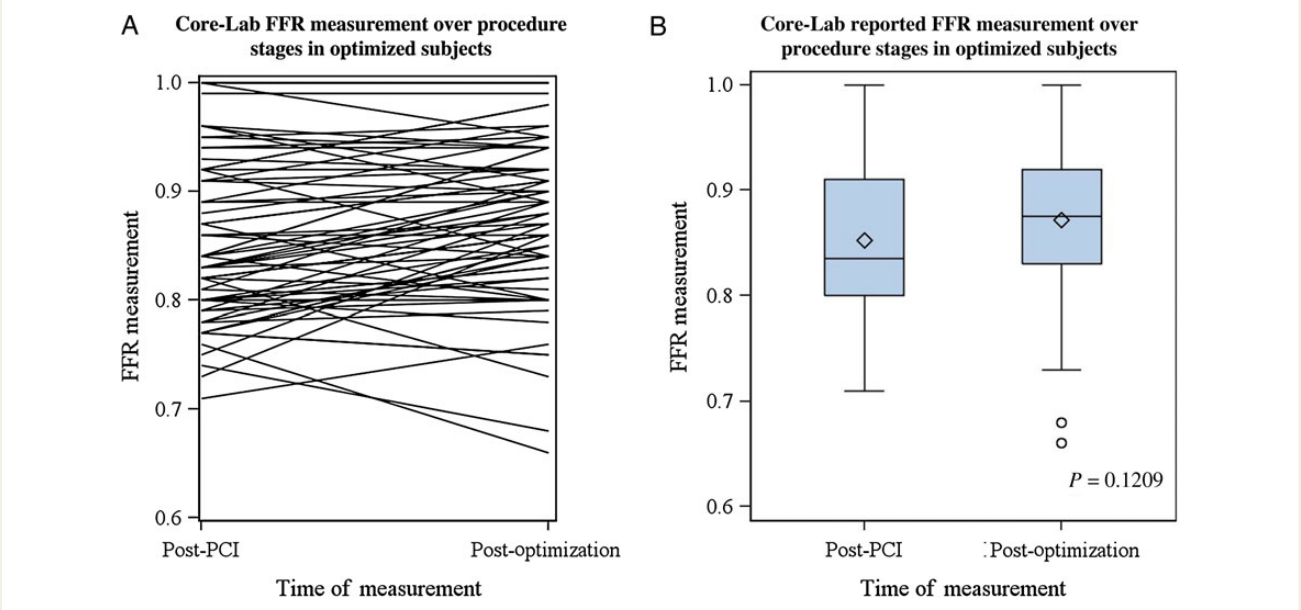

Figure 3 Changes in distal fractional flow reserve (FFR) from post-percutaneous coronary intervention (PCI) to final measurement after optical coherence tomography (OCT)-driven percutaneous coronary intervention optimization. Individual (left, panel A) and group (right, panel B) changes are shown in the subset of optimized subjects with paired measurements ($n = 70$, $P = 0.1209$).

PCI and further post-PCI optimization. Final FFR values were not statistically different between the four optimization subgroups. In the subset of cases with paired final FFR and OCT measurements following optimization, FFR values improved from 0.86 ± 0.07 to 0.90 ± 0.10 (*Figure 3*) following correction of OCT findings that were deemed unsatisfactory by the operator. Unsatisfactory

Table 4 Adverse events in hospital and at 30 days (per optimization subgroup)

	PCI optimization without change based on OCT	PCI optimization based on pre-PCI OCT only	PCI optimization based on post-PCI OCT only	PCI optimization based on pre-PCI and post-PCI OCT	*P*-value
	[*n* events], % patients (*n*)	[*n* events], % patients (*n*)	[*n* events], % patients (*n*)	[*n* events], % patients (*n*)	
Device-oriented MACE					
In hospital	[12], 8.8% (137)	[11], 6.7% (165)	[5], 12.2% (41)	[1], 1.5% (65)	0.118
30 days	[12], 8.8% (137)	[15], 8% (163)	[5], 12.5% (40)	[1], 1.5% (65)	0.127
Cardiac death (%)					
In hospital	0	0	0	0	
30 days	0	0	0	0	
MI—ARC definition					
In hospital	[12], 8.8%	[11], 6.7%	[5], 12.2%	0%	0.023
30 days	[12], 8.8%	[13], 8%	[5], 12.5%	0%	0.024
MI—Third Universal definition					
In hospital	[11], 8%	[11], 6.7%	[4], 9.8%	0%	0.051
30 days	[11], 8%	[13], 8%	[4], 10%	0%	0.047
Target lesion revascularization					
In hospital	0%	0%	0%	[1], 1.5%	0.26
30 days	0%	[2], 1.2%	0%	[1], 1.5%	0.485
Patient-oriented MACE					
In hospital	[13], 9.5% (137)	[11], 6.7% (165)	[5], 12.2% (41)	[1], 1.5% (65)	0.091
30 days	[16], 10.9% (137)	[19], 9.8% (163)	[5], 12.5% (40)	[1], 1.5% (65)	0.077
All-cause mortality					
In hospital	[1], 0.7%	0%	0%	0%	0.596
30 days	[1], 0.7%	0%	0%	0%	0.596
MI—ARC definition					
In hospital	[12], 8.8%	[11], 6.7%	[5], 12.2%	0%	0.023
30 days	[14], 10.2%	[14], 8.6%	[5], 12.5%	0%	0.017
MI—Third Universal definition					
In hospital	[11], 8%	[11], 6.7%	[4], 9.8%	0%	0.051
30 days	[13], 9.5%	[14], 8.6%	[4], 10%	0%	0.029
Any revascularization					
In hospital	0%	0%	0%	[1], 1.5%	0.26
30 days	[1], 0.7%	[5], 3.1%	0%	[1], 1.5%	0.448
Stent thrombosis					
Definite					
In hospital	0%	0%	0%	0%	
30 days	0%	[1], 0.6%	0%	0%	1
Probable (%)					
In hospital	0	0	0	0	
30 days	0	0	0	0	
Possible (%)					
In hospital	0	0	0	0	
30 days	0	0	0	0	
Early					
In hospital	0%	0%	0%	0%	
30 days	0%	[1], 0.6%	0%	0%	1

OCT, optical coherence tomography; PCI, percutaneous coronary intervention.

malapposition decreased from 48 to 9% ($P < 0.001$), stent under-expansion from 27 to 0% ($P < 0.001$), and edge dissection from 8 to 0% ($P = 0.014$).

Low rates of device-oriented and patient-oriented MACE were noted (*Table 4*) both in hospital and at 30 days. Rates of clinically significant periprocedural MI were found to be different when procedural changes were made based on pre- and post-PCI OCT ($P = 0.029$). The overall rate of in-hospital MI was 6.9% by ARC and 6.4% by Universal MI definitions. Other event rates were very low, including stent thrombosis (*Table 4*).

Discussion

ILUMIEN I study aims at defining and evaluating OCT parameters for optimization of PCI procedures and clinical outcomes. The initial procedural findings and 30-day outcomes are important to report based on the high impact of OCT imaging on physician decision-making, as listed below:

- Optical coherence tomography could be applied both pre-PCI and post-PCI with success rates of 98% of patients (91% of all lesions).
- Physician decision-making was influenced by OCT findings either pre-PCI and/or post-PCI in 66% of patients (68% of lesions).
- Physician decision-making was influenced both pre- and post-PCI more often in patients with more complex disease.
- As reported by Prati *et al.*[10] abnormal findings by OCT imaging were common after 'optimal' PCI by angiographic standards. Physician decision to react on post-PCI OCT abnormalities identified a subset of coronary lesions with more frequent malapposition, edge dissection, and stent under-expansion.
- Additional in-stent post-dilatations and stent implantations were used to correct unsatisfactory post-PCI results, namely stent under-expansion and malapposition by OCT that were not apparent on angiography.
- MACE events, including stent thrombosis, were very low in all optimization subgroups. Changes in pre- and post-PCI procedure based on OCT imaging were associated with low rates of periprocedural MI.
- Identical final FFR values were obtained through different optimization sequences.

Clinical relevance

Residual risk and opportunities for further outcome improvement of PCI remain, especially in complex patient and lesion subsets currently treated in real-life practice. In patients with multivessel revascularization, MI rates remain high with PCI compared with bypass surgery at all early and later time points.[11] In the FAME 2 trial, potential benefit of revascularization over best of medical care was jeopardized by higher event rates in the PCI group than in the medical therapy group (2.2% vs. 0.9%; hazard ratio, 2.49), mostly periprocedural MIs occurring within the first 7 days after PCI.[12] In patients undergoing elective PCI, any periprocedural event will jeopardize the potential long-term benefit of revascularization.[13] In-hospital findings of ILUMIEN I do raise the intriguing hypothesis that safety of PCI could be further improved by reducing the rates of periprocedural MI. Severe stent under-expansion and malapposition are known to induce turbulences and pressure loss.[14] Platelet aggregation and distal emboli may occur, especially with high residual platelet reactivity.[15,16] This hypothesis should inform the design of prospective, randomized trials aiming at establishing the clinical superiority of OCT-guided PCI vs. sole angiographic guidance. In addition to anticipated reductions in mortality, death, stent thrombosis, or repeat revascularization in the longer term, prospective guidance trials should be powered to assess a difference in periprocedural MI rates, as an important metric of PCI optimization for improved safety.

Role of optical coherence tomography and fractional flow reserve for percutaneous coronary intervention optimization

Interestingly, pre-PCI OCT imaging had a high impact on the decision-making process, especially pre-PCI when OCT was intended to be documentary in the absence of prescriptive 'guidance' recommendations. Indeed the planned strategy was modified in more than half of the cases. Optical coherence tomography imaging post-PCI seemed to offer additional opportunities for optimization of procedural PCI technique. Residual edge dissections have been associated with both DES thrombosis and restenosis.[5,10] Stent under-expansion and small minimal luminal area are strong predictors of late stent failure.[17] Other 'abnormalities' may not be of clinical relevance.[18] Analysis of 1-year outcomes in ILUMIEN I, including additional events, will likely contribute to further defining which OCT parameters and degree of abnormality require optimization, along with other studies.[10]

Using documentary FFR as an intermediate yardstick for PCI optimization was attempted in the present study. Final post-PCI FFR is known as a strong predictor of outcome.[19] This parameter is a better indication for reduction of ischaemic flow than angiography and quantitative coronary angiography.[20] A detailed analysis of the crosstalk between stent/vessel anatomy by OCT and functional outcome by post-PCI FFR may help qualifying the significance of "abnormal" OCT findings, for potential inclusion in future procedural optimization strategies.[21,22]

Study limitations

Study population was restricted to elective procedures in patients with either stable or unstable condition. PCI complexity was fair, not excessive; single vessel PCI was dominant; no planned bare metal stents or bioresorbable scaffolds were used. Patients with acute STEMI, left main PCI, severe chronic kidney disease, and a number of other high-risk features were not included. Physicians were provided general recommendations when to and when not to intervene but were not required to follow them in the context of an observational study. In addition, these short-term results, although important, may vary after the 12-month results are tallied in terms of clinical events. Since no prescriptive recommendations were provided in the protocol, a wide variation in physician behavior was expected and observed. This design will allow to evaluate the clinical consequences of a wide range of residual OCT 'abnormalities'. Given the high rate of procedure planning change after pre-PCI OCT, clear recommendations as to stent length and size selection, based on pre-PCI OCT imaging, will be applied in ILUMIEN III, a

prospective, randomized trial comparing PCI optimization strategies using angiography, OCT, or intravascular ultrasound (ClinicalTrials.gov NCT 2471586). There is clear indication that operators reacted to post-PCI OCT findings primarily in the presence of less satisfactory PCI results. Not surprisingly, these were seen more often with advanced or more complex disease. In addition to the cost of the OCT catheter itself, post-PCI optimization resulted in increased resource utilization. Extra cost will be weighed against clinical benefit from the analysis of 1-year outcomes.

The operator's decision to make use of pre- and/or post-PCI OCT findings was associated with varied periprocedural MI rates, an hypothesis-generating finding that remains to be tested prospectively. Overall, periprocedural MI rate was 7.7%, higher than in stent trials. Absolute MI rates tend to be higher even with the use of identical definitions, when more sensitive assays are used.[8] Today's clinical practice is based on better assays, with increased ability to detect myocardial damage. Given the study population and definitions applied in the present study, the observed figures are realistic and pertain to clinically relevant MI's.

Conclusion

Short-term results of ILUMIEN I, a prospective, non-randomized, observational study of PCI procedural practice in patients undergoing pre- and post-PCI FFR and OCT show that both physician decision-making and procedural strategy were influenced by OCT findings either pre-PCI and/or post-PCI in the majority of patients.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

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CARDIOVASCULAR FLASHLIGHT

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Lost guidewire protrudes through the heart and chest

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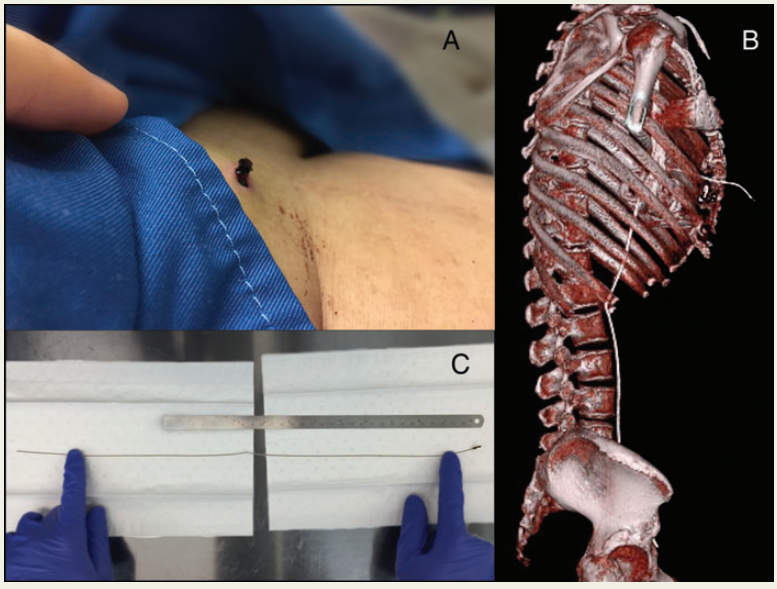
A 65-year-old woman was referred to our institution with an 'iron wire' that protruded through her chest (*Panel A*). She had no dyspnoea, pain, or fever. Her medical history included a mitral- and tricuspid valve repair 15 years ago and she was on permanent dialysis. Computed tomography scan (*Panel B*) showed a guidewire of ~40 cm protruding the right atrium and subsequently the anterior chest wall. On retrospective review of chest X-rays, the guidewire was visible for the first time 6 months before, when she was admitted in the referring hospital for dialysis. During that admission a central venous catheter was placed in the right femoral vein. Presumably the guidewire was lost during placement of the central venous catheter. In a 6-month period, the guidewire migrated to the right atrium, protruded through the chest and moved on every heartbeat (Supplementary material online, *Video S1*). Because of the adhesions of her previous cardiac surgery, the risk of developing pericardial tamponade after extraction was expected to be low. However, for safety reasons, extraction of the guidewire was scheduled with a fully equipped cardiac surgery team and the heart–lung machine on standby. The guidewire was mobilized at skin level and gently extracted under trans-oesophageal echocardiography surveillance (*Panel C*) (Supplementary material online, *Video S2*). There was no pericardial effusion after extraction, which was also absent during follow-up transthoracic echocardiography. On post-operative Day 1, the patient was discharged after an uneventful admission. We advise to treat similar complications under optimal safety conditions.



Panel A. 'Iron' wire protrudes through chest.
Panel B. Three-dimensional reconstruction of the computed tomography scan.
Panel C. The extracted retained guidewire.

Supplementary material is available at *European Heart Journal* online.