Morning Roundtable Forum:
Meet the Experts over Breakfast

Invasive Imaging

Impact of OCT- vs IVUS-Guided PCI: OPINION and ILUMIEN

Takashi Akasaka MD, PhD, FESC
Department of Cardiovascular Medicine
Wakayama Medical University, Japan

Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

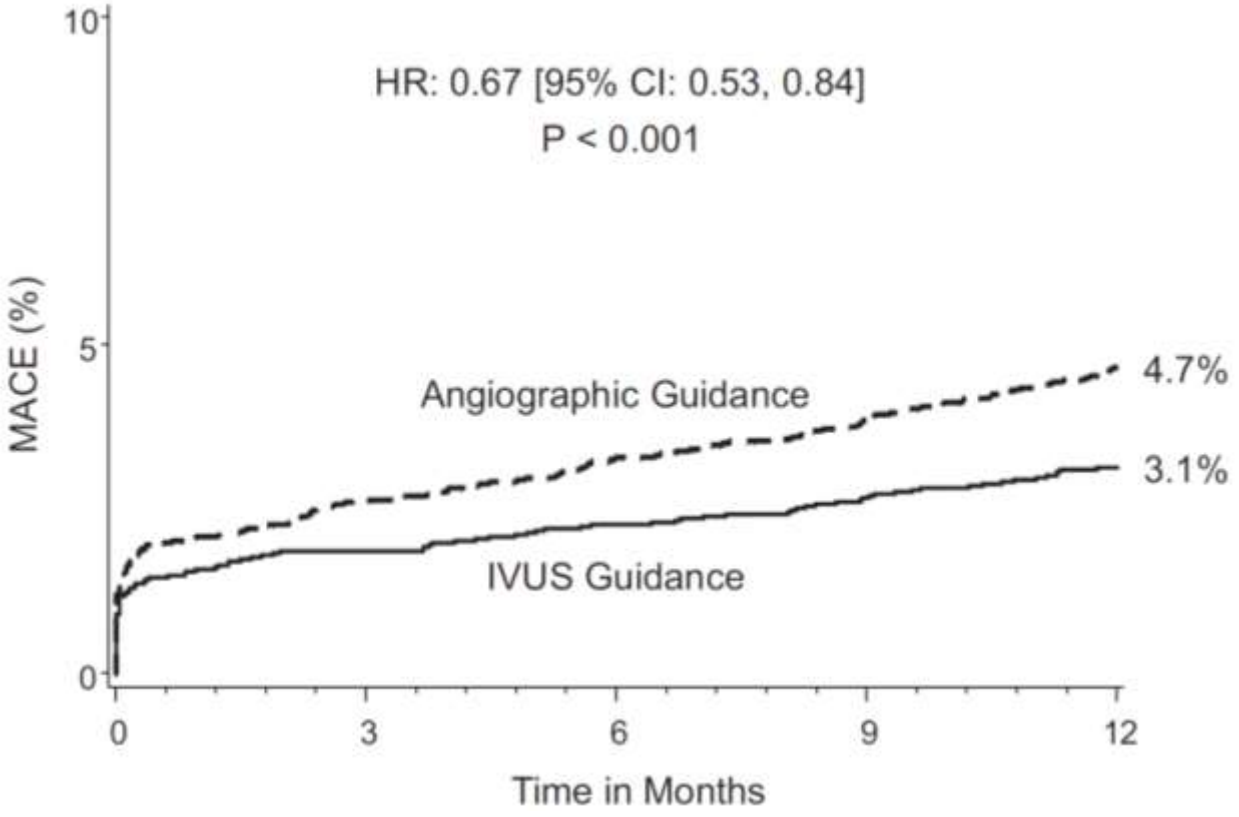
Affiliation/Financial Relationship

- **Grant/Research Support** : **Abbott Vascular Japan**
  Boston Scientific Japan
  Goodman Inc.
  St. Jude Medical Japan
  Terumo Inc.

- **Consulting Fees/Honoraria** : **Daiichi-Sankyo Pharmaceutical Inc.**
  Goodman Inc.
  St. Jude Medical Japan
  Terumo Inc.

IVUS- vs. angio-guided PCI with DES

Results from Assessment of Dual Antiplatelet Therapy With Drug-Eluting Stents (ADAPT-DES)

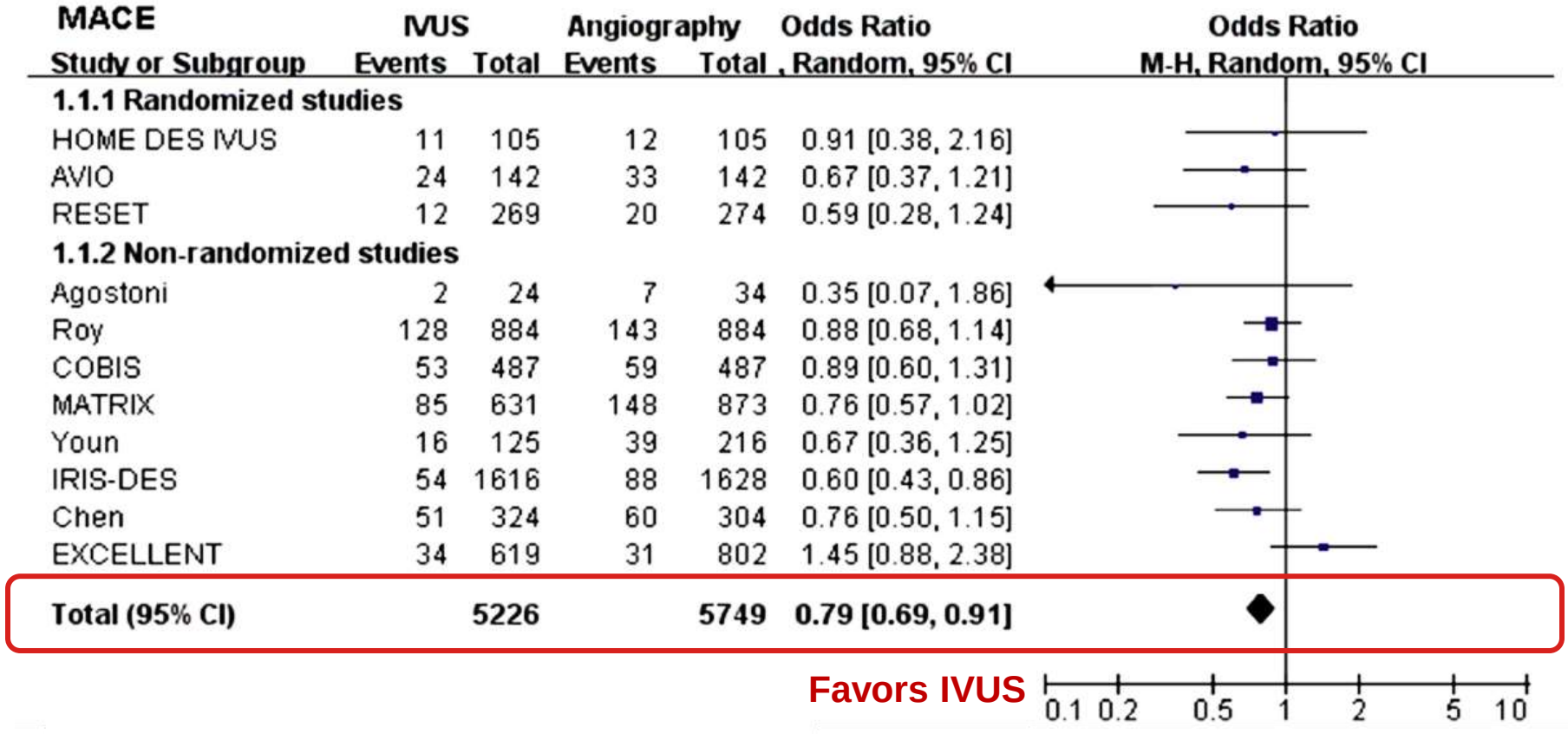


IVUS guidance was associated with a reduction in stent thrombosis, MI, and MACE within 1 year after DES implantation.

Witzenbichler, et al., Circulation. 2014;129:463-470

IVUS- vs. angio-guided PCI with DES

A meta-analysis of randomized trials and observational studies



MACE	IVUS		Angiography		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	, Random, 95% CI	M-H, Random, 95% CI
1.1.1 Randomized studies						
HOME DES IVUS	11	105	12	105	0.91 [0.38, 2.16]	
AVIO	24	142	33	142	0.67 [0.37, 1.21]	
RESET	12	269	20	274	0.59 [0.28, 1.24]	
1.1.2 Non-randomized studies						
Agostoni	2	24	7	34	0.35 [0.07, 1.86]	
Roy	128	884	143	884	0.88 [0.68, 1.14]	
COBIS	53	487	59	487	0.89 [0.60, 1.31]	
MATRIX	85	631	148	873	0.76 [0.57, 1.02]	
Youn	16	125	39	216	0.67 [0.36, 1.25]	
IRIS-DES	54	1616	88	1628	0.60 [0.43, 0.86]	
Chen	51	324	60	304	0.76 [0.50, 1.15]	
EXCELLENT	34	619	31	802	1.45 [0.88, 2.38]	
Total (95% CI)		**5226**		**5749**	**0.79 [0.69, 0.91]**	

IVUS-guided DES implantation is associated with significantly lower rates of adverse clinical events compared with angiography guidance.

Jang JS, et al., JACC interv 2014; 7:233–43

OCT- vs. angio-guided PCI with DES or BMS

The retrospective Centro per la Lotta contro l'Infarto-Optimisation of Percutaneous Coronary Intervention (CLI-OPCI) study

Events at 1-year follow-up	Angiographic guidance group (n=335)	Angiographic plus OCT guidance group (n=335)	*p*-value
Death	23 (6.9%)	11 (3.3%)	0.035
Cardiac death	15 (4.5%)	4 (1.2%)	0.010
Myocardial infarction	29 (8.7%)	18 (5.4%)	0.096
Target lesion repeat revascularisation	11 (3.3%)	11 (3.3%)	1.0
Definite stent thrombosis	2 (0.6%)	1 (0.3%)	1.0
Cardiac death or myocardial infarction	43 (13.0%)	22 (6.6%)	0.006
Cardiac death, myocardial infarction, or repeat revascularisation	50 (15.1%)	32 (9.6%)	0.034

The use of OCT can improve clinical outcomes of patients undergoing PCI.

Prati F, et al., EuroIntervention 2012;8:823-829

IVUS/OCT in ESC guideline 2014

Recommendations	Class	Level
IVUS in selected patients to optimize stent implantation.	IIa	B
OCT in selected patients to optimize stent implantation.	IIb	C

Eur Heart J. 2014;35:2541-2619

- The resolution of OCT is 10 times higher than that of IVUS.
- OCT is capable of providing accurate coronary measurements (OPUS-CLASS study).
- OCT is more accurate than IVUS in detecting subtle stent morphologies including malapposition, residual thrombus, plaque prolapse, and residual dissections (Kubo T, et al. JACC Img 2008;1:475-484).
- Further studies are needed to define the clinical value of OCT.

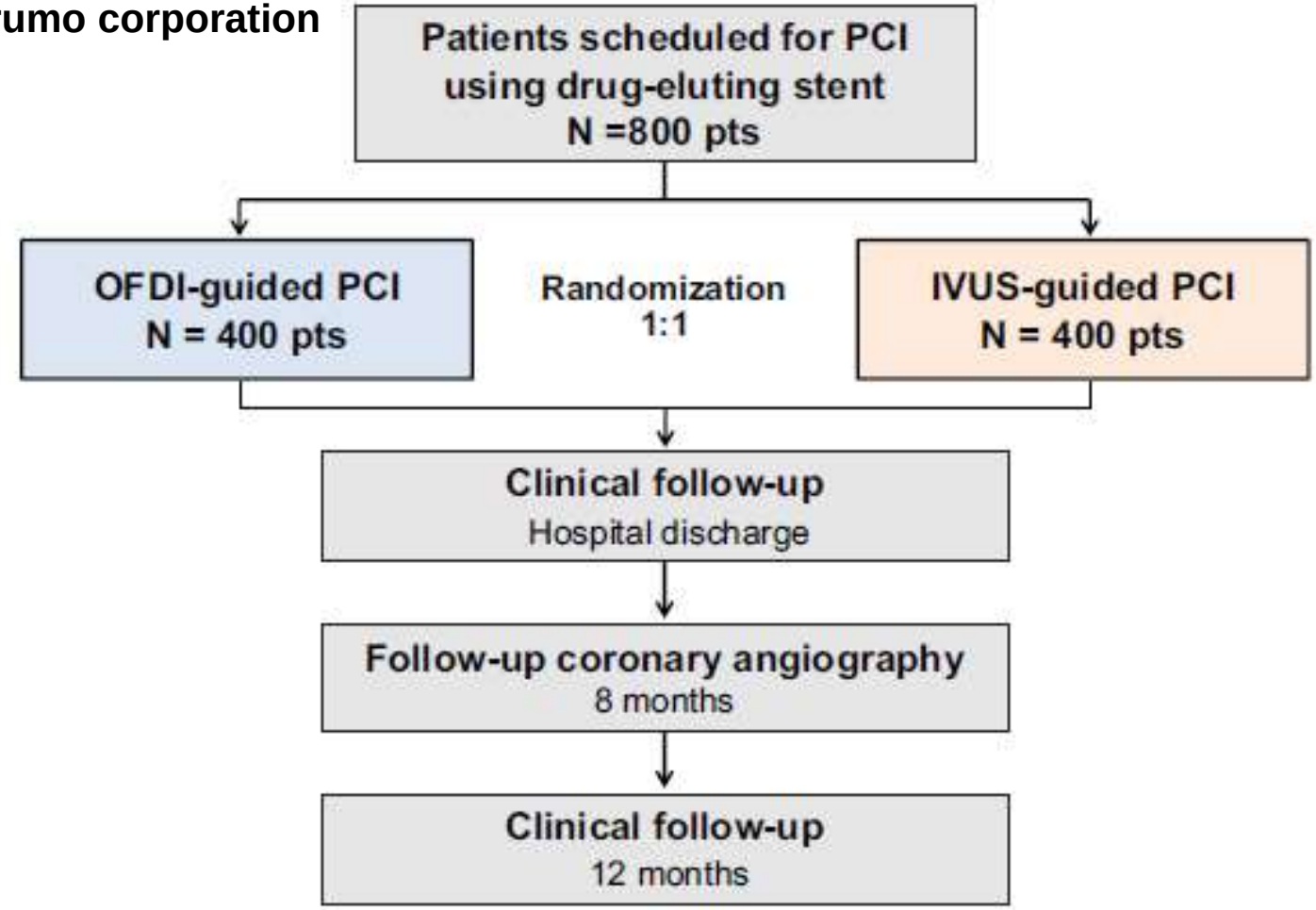
Objective

We designed the OPINION trial powered to evaluate the non-inferiority of OFDI-guided PCI compared with IVUS-guided PCI in terms of clinical outcomes.

The OPINION study design

Prospective, multi-center (n=42), randomized (1:1) non-inferiority trial comparing OFDI-guided PCI with IVUS-guided PCI

PI: Takashi Akasaka, MD,PhD, FESC
Sponsor: Terumo corporation



J Cardiol 2016 Jan 4. pii: S0914-5087(15)00373-1. doi: 10.1016/j.jjcc.2015.11.007.

Patient population

Inclusion criteria

Patients scheduled for PCI using DES to a de novo native coronary artery lesion

Exclusion criteria

STEMI or NSTEMI in previous 3 months
Cardiogenic shock
Congestive heart failure
Chronic kidney disease (eGFR < 30 ml/min/1.73 m^2 or serum creatinine >1.5mg/dl)
Hemodialysis or peritoneal dialysis
Three-vessel disease
Left main coronary artery disease
Aorto-Ostial lesion arising within 3mm of the origin of a coronary artery
Chronic total occlusion
Small vessel disease (reference vessel diameter < 2.5 mm)

J Cardiol 2016 Jan 4. pii: S0914-5087(15)00373-1. doi: 10.1016/j.jjcc.2015.11.007.

OFDI and IVUS criteria of optimal stent deployment

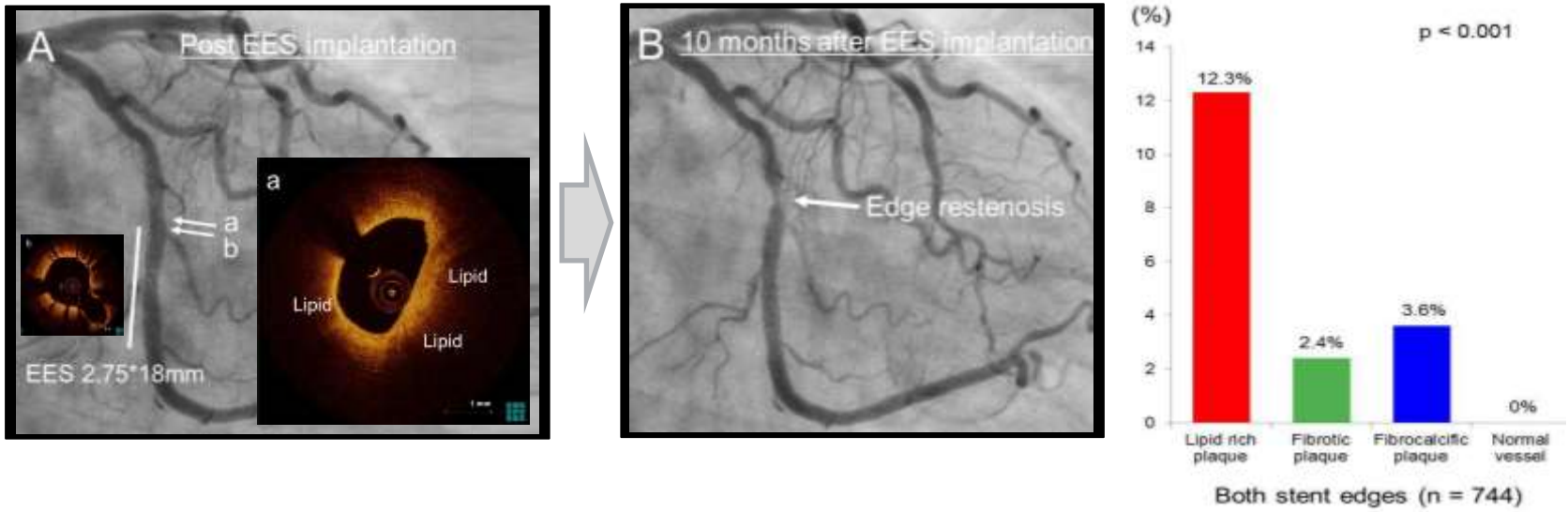
	OFDI-guided PCI	IVUS-guided PCI
Reference site	• Most normal looking • No lipidic plaque	• Largest lumen • Plaque burden < 50%
Determination of stent diameter	• By measuring lumen diameter at proximal and distal reference sites	• By measuring vessel diameter at proximal and distal reference sites
Determination of stent length	• By measuring distance from distal to proximal reference site	
Goal of stent deployment	• In-stent minimal lumen area ≥ 90% of the average reference lumen area • Complete apposition of the stent over its entire length against the vessel wall • Symmetric stent expansion defined by minimum lumen diameter / maximum lumen diameter ≥ 0.7 • No plaque protrusion, thrombus, or edge dissection with potential to provoke flow disturbances	

J Cardiol 2016 Jan 4. pii: S0914-5087(15)00373-1. doi: 10.1016/j.jjcc.2015.11.007.

Precursor lesion of stent edge restenosis

In 744 stent (EES) edge segments, OCT was used to evaluate morphological characteristics of the coronary plaques that developed stent edge restenosis.

Post-stenting | **10 months follow-up** | **Stent edge restenosis**



(A) Immediately after EES implantation, OCT images showed lipid rich plaque at the proximal stent edge (a, b).
(B) At 10-month follow-up, angiography demonstrated stent edge restenosis at the proximal edge of the stent.

Conclusion: Lipidic plaque in the stent edge segments at post- PCI was a predictor of late stent edge restenosis.

Ino Y, Kubo T, Akasaka T, et al. submitting

Endpoints

Primary endpoint

Target Vessel Failure: TVF* at 12 months after PCI

Composite of cardiac death, target vessel-related MI and clinically-driven TVR

Secondary endpoints

Following parameters at 12 months after PCI

- Cardiac death
- MI
- Stent thrombosis
- Binary restenosis
- Clinically-driven TLR
- Clinically-driven TVR
- MACE (Cardiac death, MI, and TLR)
- Stroke
- Contrast-induced nephropathy

J Cardiol 2016 Jan 4. pii: S0914-5087(15)00373-1. doi: 10.1016/j.jjcc.2015.11.007.

Baseline patient characteristics

	OFDI	IVUS	*p*-value
Age, yrs	68 ± 9	68± 9	0.431
Male	77%	79%	0.365
Hypertension	77%	74%	0.389
Dyslipidemia	76%	80%	0.279
Diabetes mellitus	41%	41%	0.917
Current smoker	16%	18%	0.396
Obesity (BMI > 25)	31%	28%	0.389
Stable AP	88%	87%	0.471
ACS	12%	13%	0.471

Interim data, as of 16 March, 2015

Angiographic findings

	OFDI	IVUS	*p*-value
LAD / LCX / RCA	54 / 20 / 26%	49 / 22 / 29%	0.422
Ostial	6%	7%	0.629
Bifurcation	38%	40%	0.595
Heavy calcification	8%	13%	0.011
Thrombus	1%	1%	0.721
Severe tortuosity	5%	4%	0.244
Reference vessel diameter	2.61 ± 0.54	2.58 ± 0.59	0.517
Minimal lumen diameter	0.93 ± 0.37	0.88 ± 0.38	0.103
% DS	64 ± 13	66 ± 13	0.104
Lesion length	17.9 ± 10.2	16.8 ± 10.2	0.226

Interim data, as of 16 March, 2015

OFDI / IVUS imaging

	OFDI	IVUS	*p*-value
No. of imaging procedure	3.1 ± 1.7	3.0 ± 1.1	0.326
Imaging at pre-stenting	98%	97%	0.324
Imaging at post-stenting	99.8%	99.5%	0.629
Total contrast volume, ml	164 ± 66	138 ± 56	< 0.001
Contrast volume for OFDI, ml	33 ± 30	-	-
Auto injection	72%	-	-
Manual injection	28%	-	-

Interim data, as of 16 March, 2015

Procedural characteristics

	OFDI	IVUS	*p*-value
Stent diameter, mm	2.93 ± 0.39	2.99 ± 0.40	0.032
Stent length, mm	22 ± 7	21 ± 7	0.248
No. of stents	1.2 ± 0.4	1.2 ± 0.4	0.500
Total stent length, mm	26 ± 13	25 ± 13	0.284
Post dilatation	78%	76%	0.593
Max. balloon diameter, mm	3.15 ± 0.79	3.28 ± 1.20	0.072
Max. inflation pressure, atm	16 ± 4	16 ± 4	0.840
PCI procedure success	99.5%	100%	0.499

QCA results immediately after PCI

	OFDI	IVUS	*p*-value
In-stent			
MLD, mm	2.56 ± 0.44	2.63 ± 0.46	0.058
DS, %	12 ± 6	11 ± 5	0.021
Acute gain, mm	1.63 ± 0.49	1.75 ± 0.50	0.003
In-segment			
MLD, mm	2.25 ± 0.52	2.28 ± 0.52	0.481
DS, %	21 ± 9	21 ± 9	0.912
Acute gain, mm	1.33 ± 0.54	1.40 ± 0.53	0.110

Interim data, as of 16 March, 2015

Peri-procedural complication

	OFDI	IVUS	*p*-value
No. of complication	37 (9.1%)	36 (9.3%)	0.956
Acute coronary occlusion	1 (0.2%)	0 (0.0%)	0.593
Air embolism	2 (0.5%)	2 (0.5%)	0.999
Slow / no flow	8 (2.0%)	9 (2.3%)	0.782
Distal embolization	2 (0.5%)	1 (0.3%)	0.999
Side branch occlusion	8 (2.0%)	7 (1.8%)	0.817
Coronary dissection	10 (2.5%)	7 (1.8%)	0.481
Thrombosis	1 (0.2%)	2 (0.5%)	0.622
Spasm	2 (0.5%)	5 (1.3%)	0.247
Arrhythmia	2 (0.5%)	1 (0.3%)	0.999
Others	1 (0.2%)	2 (0.5%)	0.622

Interim data, as of 16 March, 2015

OPINION baseline analysis Summary

- **OPINION is a trial powered to evaluate the non-inferiority of OFDI-guided PCI compared with IVUS-guided PCI in terms of late clinical outcome.**
- **In-segment MLD by QCA immediately after PCI was comparable between OFDI-guided PCI and IVUS-guided PCI, although the size of used stent was smaller in OFDI-guided PCI.**
- **Clinical follow-up is ongoing and 12 months clinical result will be shown in May 2016.**
- **OPINION will define the clinical value of OCT in PCI.**

Intracoronary imaging & physiology in ESC guideline 2014

Recommendations	Class[a]	Level[b]	Ref.[c]
FFR to identify haemodynamically relevant coronary lesion(s) in stable patients when evidence of ischaemia is not available.	I	A	50,51,713
FFR-guided PCI in patients with multivessel disease.	IIa	B	54
IVUS in selected patients to optimize stent implantation.	IIa	B	702,703,706
IVUS to assess severity and optimize treatment of unprotected left main lesions.	IIa	B	705
IVUS or OCT to assess mechanisms of stent failure.	IIa	C	
OCT in selected patients to optimize stent implantation.	IIb	C	

Eur Heart J. 2014;35:2541-2619

European Heart Journal
doi:10.1093/eurheartj/ehv367

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

William Wijns[1]*, Junya Shite[2], Michael R. Jones[3], Stephen V
Franco Fabbiocchi[6], Emanuele Barbato[1], Takashi Akasaka
and David Holmes[9]

[1]Cardiovascular Research Center, OLV Hospital, Moorselbaan 164, Aalst B 9300, Belgium; [2]Osaka Saiseikai Nakatsu Hosp
USA; [5]University of Hong Kong, Queen Mary Hospital, Hospital Authority, Pok Fu Lam, Hong Kong; [7]Scripps Clinic, La Jo
Italy; [7]Wakayama Medical University, Wakayama, Japan; [8]University Hospitals Case Medical Center, Harrington Heart an
Rochester, MN, USA

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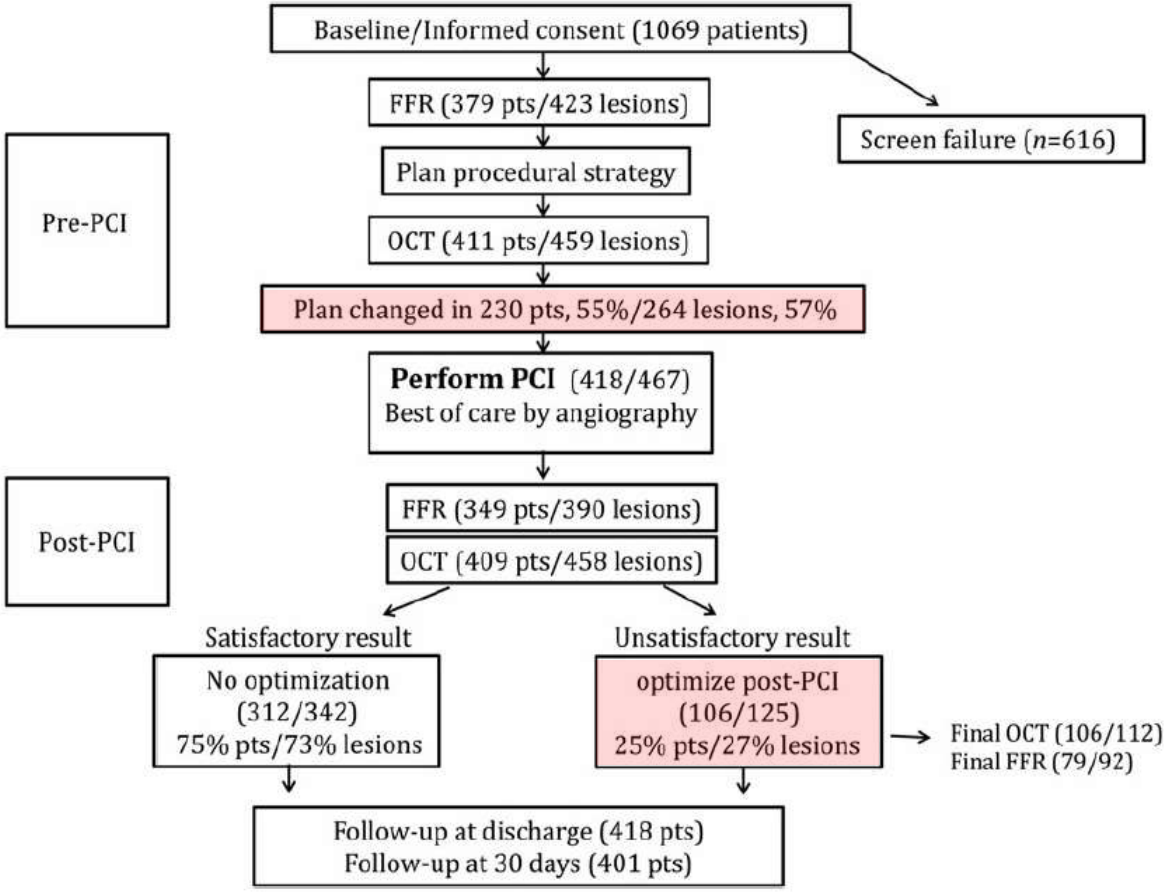
Change of PCI strategy could be observed in 55% (236) cases with 57% (264) lesions after OCT in cases with ischemia proved by FFR.

Stent optimization could be performed in 25% (349) cases with 27% (390) lesions after OCT in cases with sufficient improvement in FFR.



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)

Akiko Maehara, MD,*† Ori Ben-Yehuda, MD,*† Ziad Ali, MD,*† William Wijns, MD, PhD,‡ Hiram G. Bezerra, MD,§ Junya Shite, MD,‖ Philippe Généreux, MD,*†¶ Melissa Nichols, MS,† Paul Jenkins, PhD,† Bernhard Witzenbichler, MD,# Gary S. Mintz, MD,† Gregg W. Stone, MD*†

OBJECTIVES The present study sought t
a degree of stent expansion comparable t

BACKGROUND The most important pred
tion with IVUS guidance is the degree of s

METHODS We compared the relative degr
of the proximal and distal reference lumen
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.

ILUMIEN III Study

ILUMIEN III: OPTIMIZE PCI: Optical Coherence Tomography (OCT) Compared to Intravascular Ultrasound (IVUS) and Angiography to Guide Coronary Stent Implantation: a Multicenter Randomized Trial in PCI

- Primary Objective

  To demonstrate the safety and efficacy of an OCT guided strategy for stent implantation

- Trial Hypothesis

  OCT-guided stent placement with application of a novel algorithm is non-inferior to IVUS-guided stent placement and superior to Angiography, all as measured by post-PCI minimum stent area (MSA)

Primary Endpoints

Primary Efficacy Endpoint (powered)

- Post-PCI MSA assessed by OCT in each randomized arm, measured at the independent OCT core laboratory blinded to imaging modality assignment. Testing will be done in a hierarchal manner as follows:
  1. Non-inferiority of OCT guided stenting to IVUS guided stenting
  2. Superiority of OCT guided stenting to Angiography guided stenting
  3. Superiority of OCT guided stenting to IVUS guided stenting

Primary Safety Endpoint (non-powered)

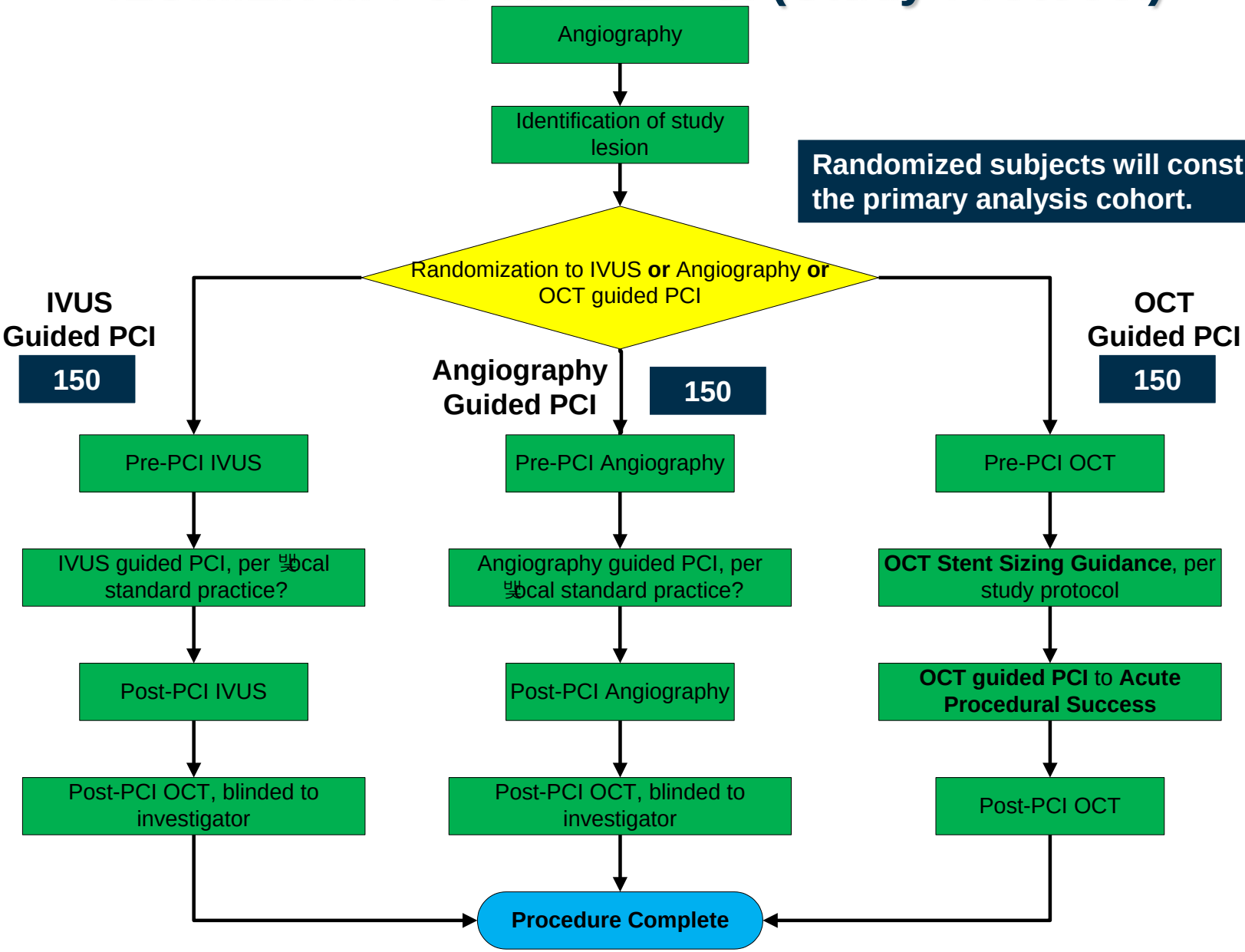
- Procedural MACE defined as procedural complications (angiographic dissection, perforation, thrombus, and acute closure) requiring active interventions (prolonged balloon inflations, additional stent implantation, or pericardiocentesis)

Secondary Endpoints

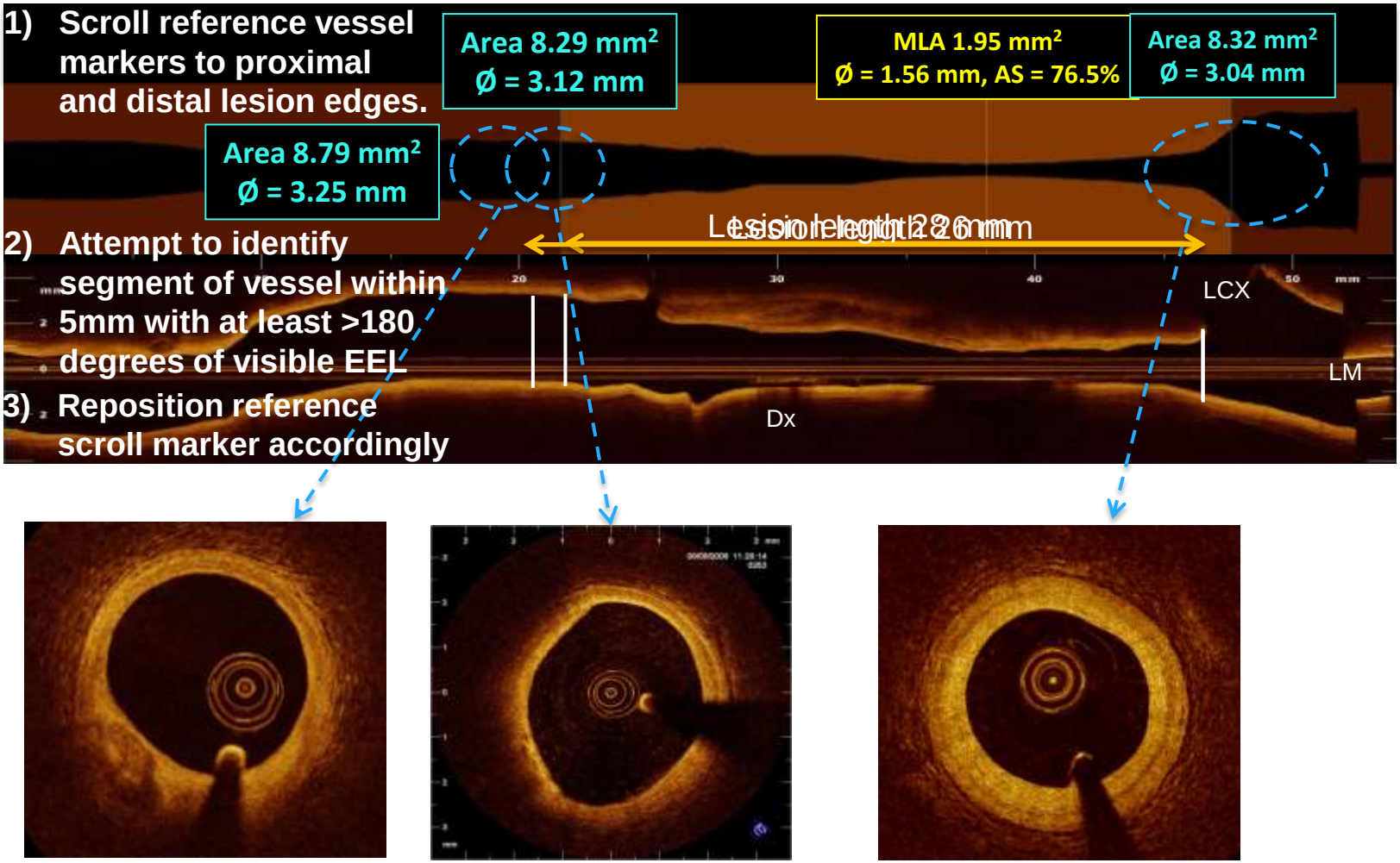
- **12 secondary endpoints relating to procedural findings**
  - acute procedural success,
  - post PCI stent expansion,
  - intra-stent plaque protrusion and thrombus,
  - untreated reference segment disease,
  - edge dissection,
  - stent malapposition,
  - boarder detection [OCT arm only],
  - altered clinical decision-making,
  - intra-stent lumen area,
  - effective lumen area,
  - OCT vs. IVUS differences

Note: Secondary endpoints will be assessed in OCT, IVUS, and Angiography groups by the OCT run at the end of the procedure (unless otherwise indicated in Investigational Plan)

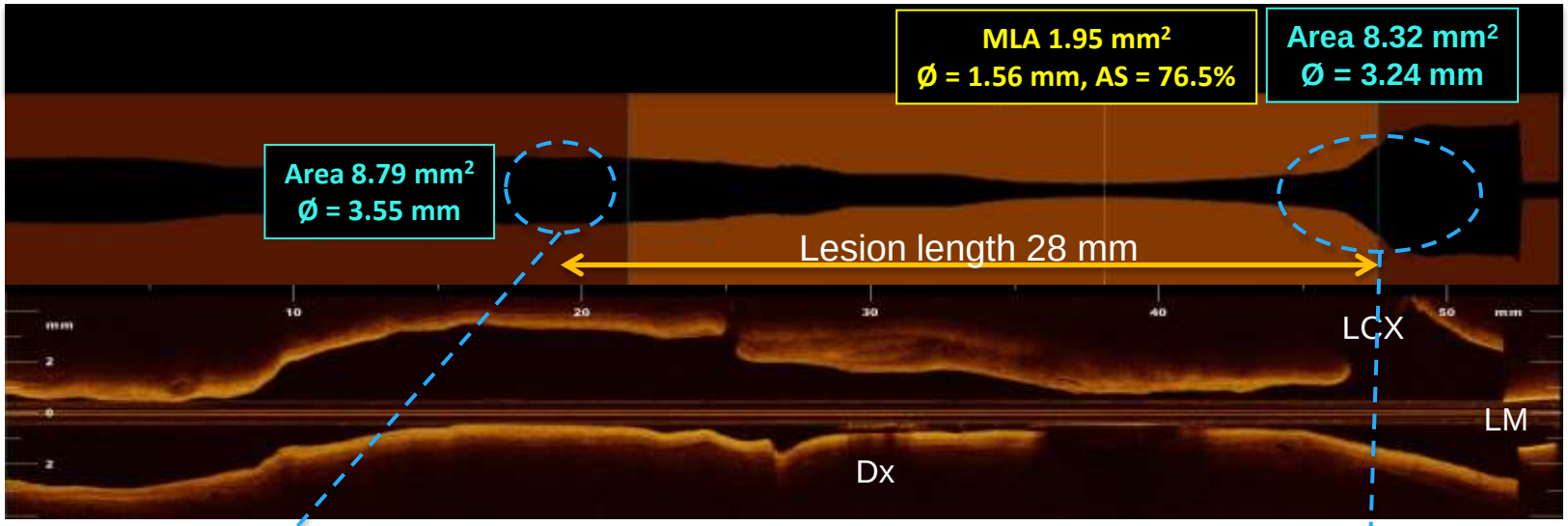
ILUMIEN III : OPTIMIZE PCI (Study Protocol)

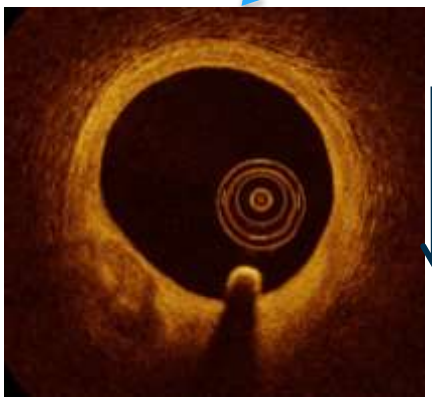


How to identify reference segments; stent length



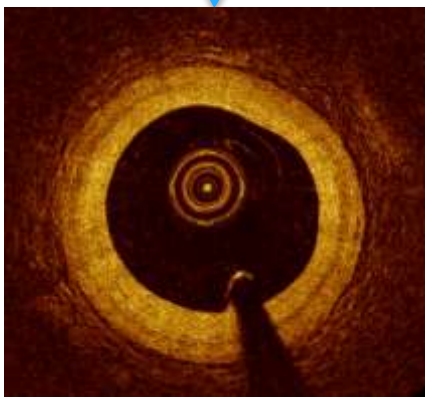
How to identify the EEL; stent diameter



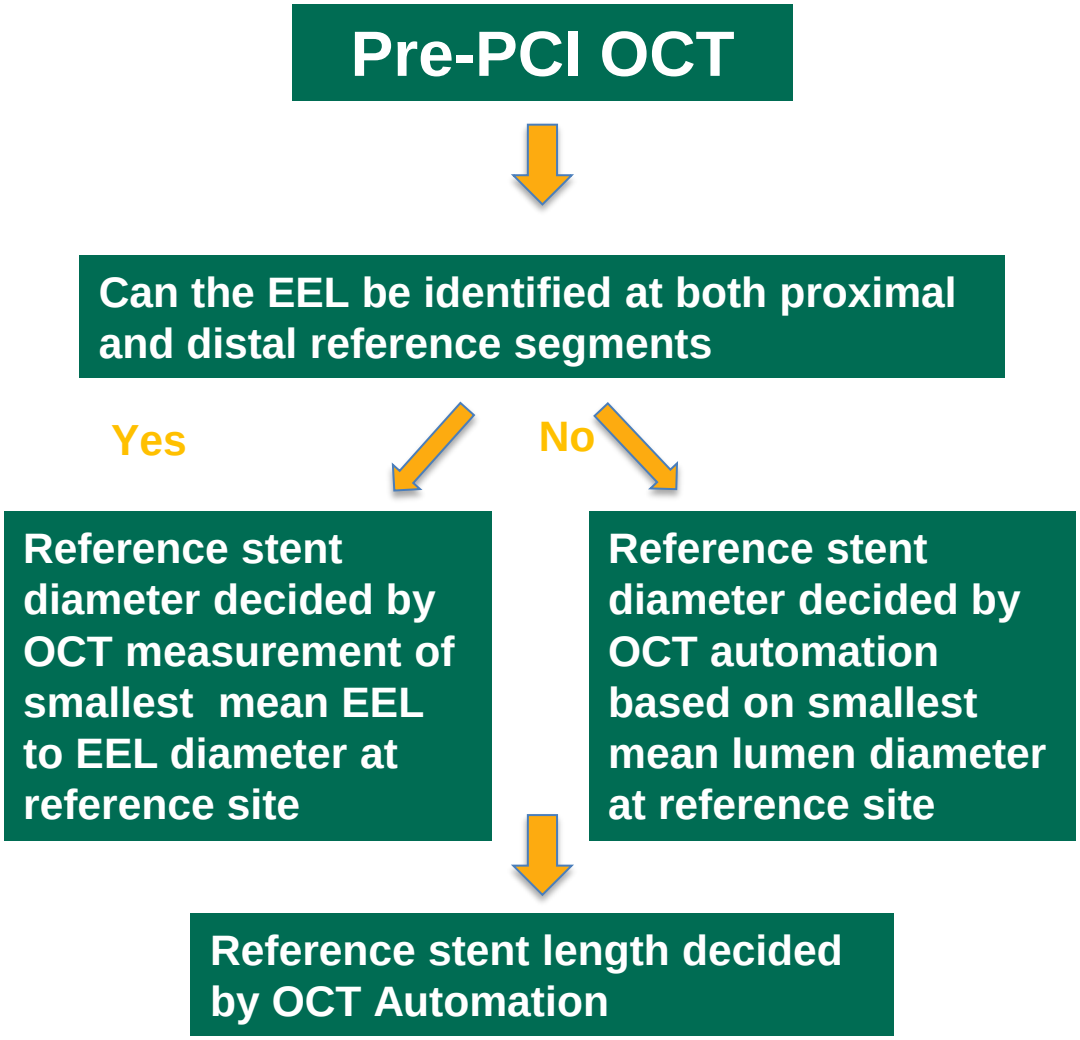


Increasingly aggressive

- Largest reference lumen (prox or dist)
- Mid-wall
- Media-to-media (typically discounted)

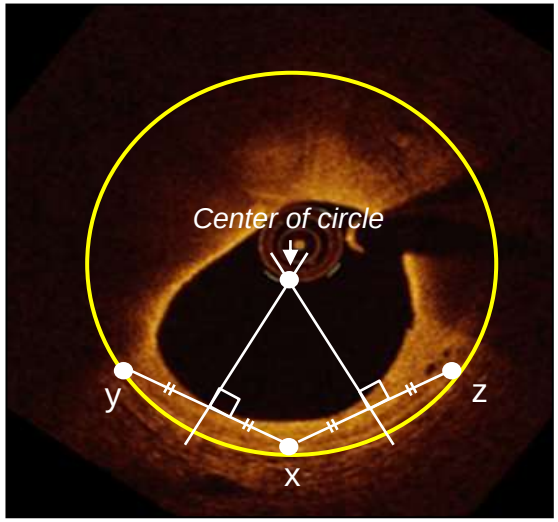


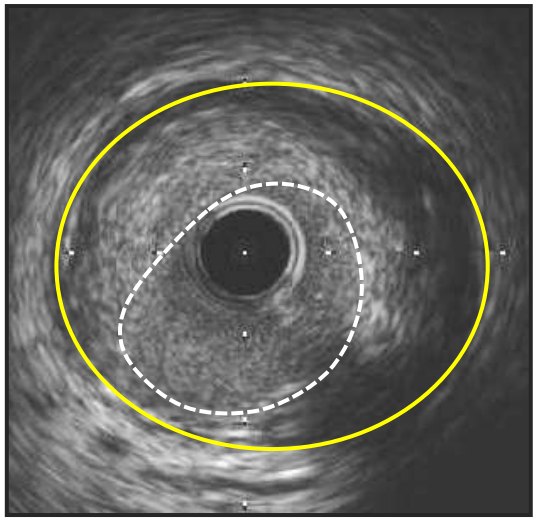
ILUMIEN III: Stent sizing

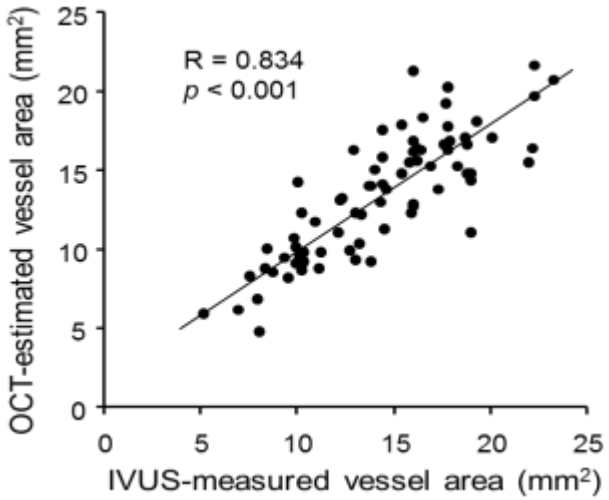


Vessel circumference approximation in OCT

Feasibility of approximating algorithm of vessel circumference in OCT were evaluated in 80 coronary artery segments.



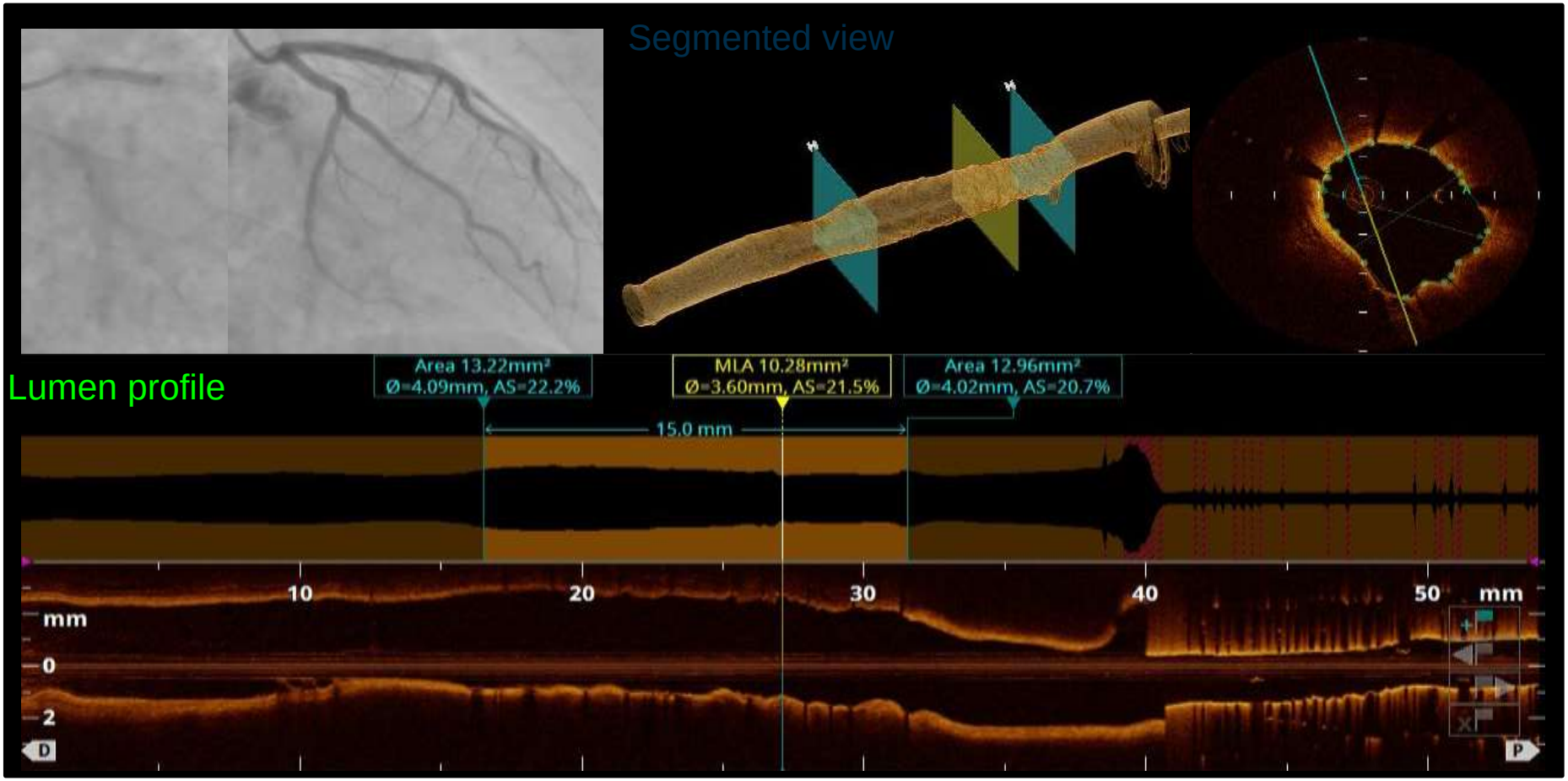




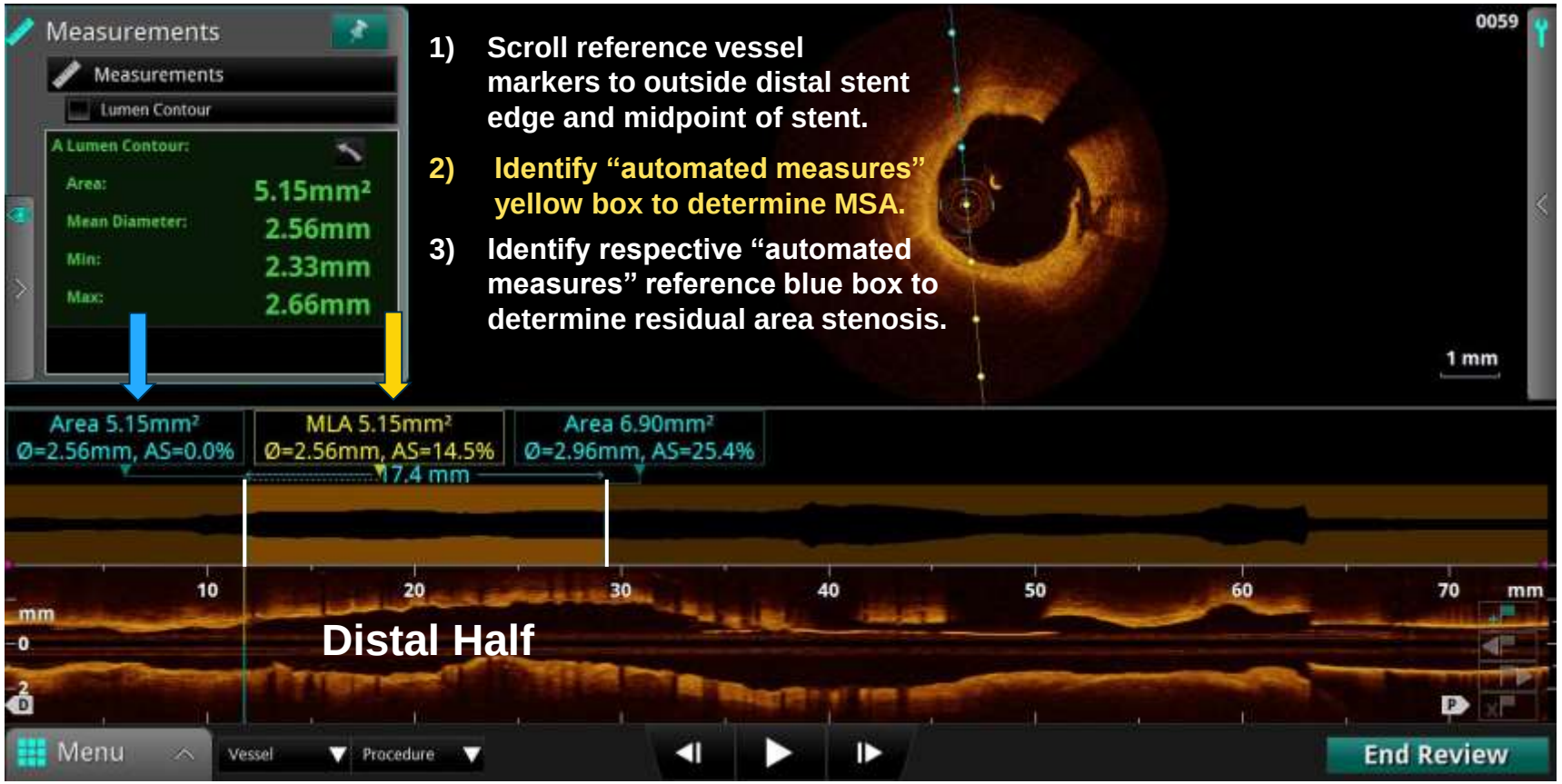
Three points (x, y, z) are placed on the visible circular arc. The central point (x) is connected with the other two points (y and z) by straight lines. Through the mid-point of each straight line, perpendicular line is drawn. Intersection of the two perpendicular lines is assumed to be the center of the circle. This makes circular approximation.

Conclusion: By approximating algorithm of vessel circumference, OCT can estimate vessel area even in coronary arteries with lipidic plaque.

Post-PCI assessment, #6 90%, (MultiLink 4.0×15mm)



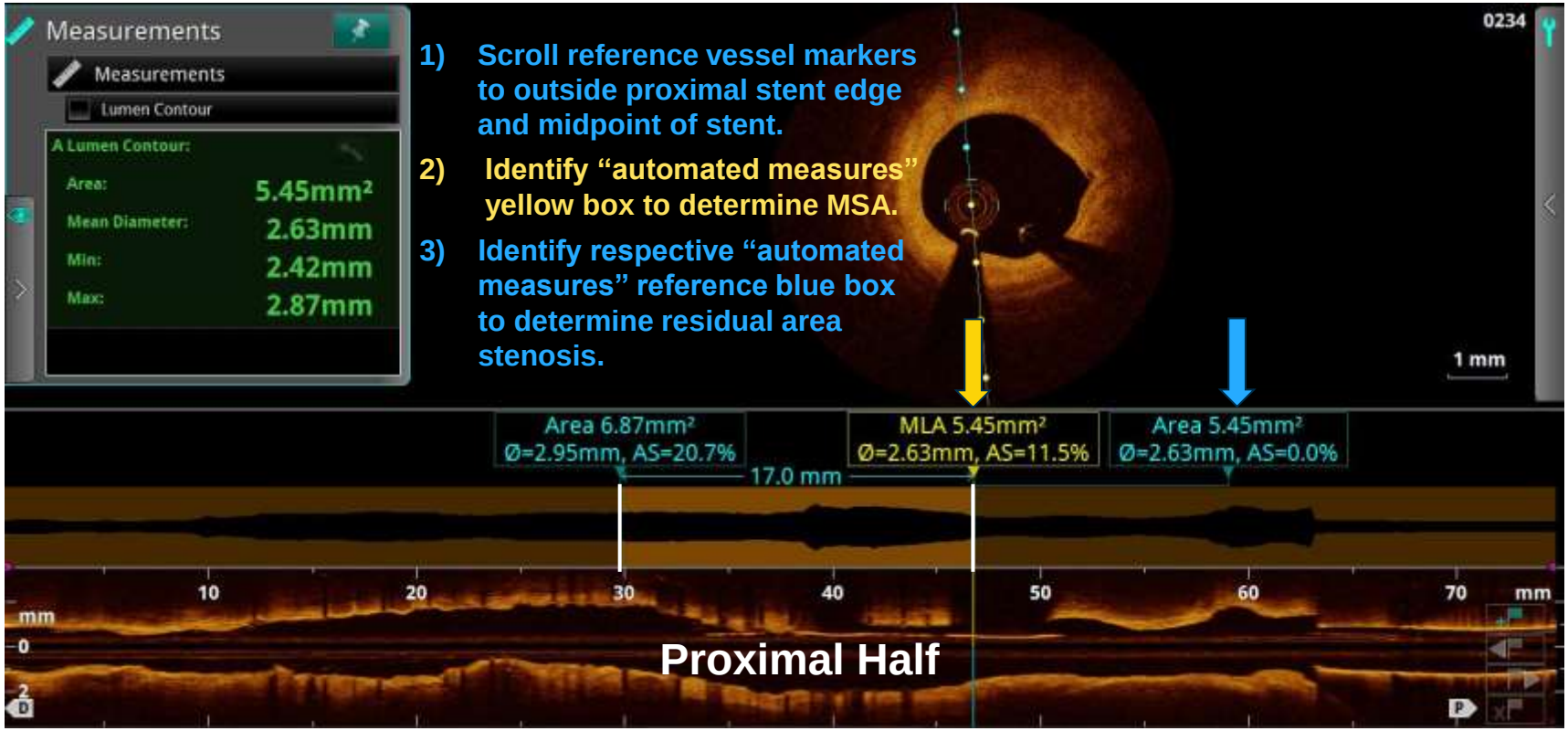
DETERMINE EXPANSION/MSA - DISTAL



1) Scroll reference vessel markers to outside distal stent edge and midpoint of stent.
2) Identify "automated measures" yellow box to determine MSA.
3) Identify respective "automated measures" reference blue box to determine residual area stenosis.

95% of distal reference lumen area
90% of distal reference lumen area
Distal MSA meets ideal criteria

DETERMINE EXPANSION/MSA - PROXIMAL



95% of proximal reference lumen area
90% of proximal reference lumen area
Proximal MSA meets ideal criteria

ILUMIEN III finishing enrollment Summary

- **ILUMIEN III is a trial powered to evaluate the non-inferiority of OCT-guided PCI compared with IVUS-guided PCI in terms of procedural outcome.**
- **Vessel & stent sizing by were based on vessel size (media to media) in OCT and IVUS.**
- **There is no clinical follow-up and data analysis is ongoing and final result will be demonstrated soon.**
- **ILUMIEN will define the similar value of OCT guidance as compared with IVUS in PCI.**

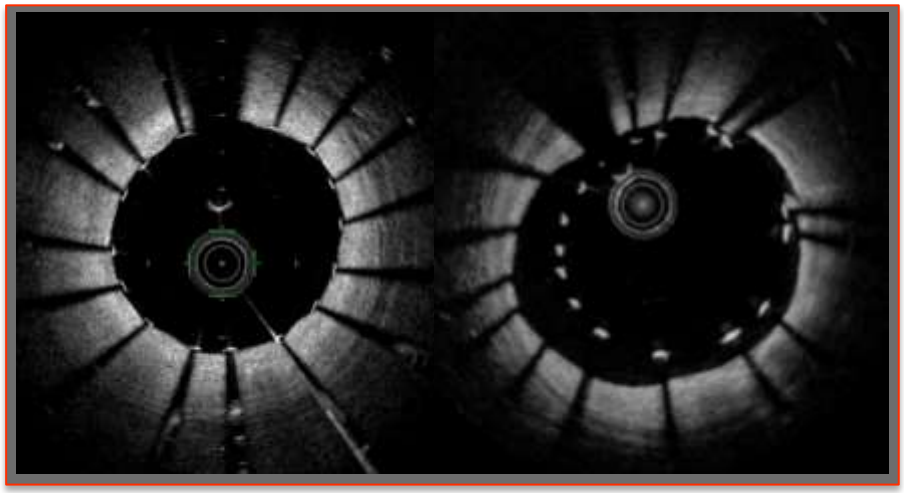
Impact of OCT- vs IVUS-Guided PCI
OPINION and ILUMIEN
Conclusions

- **OPINION & ILUMIEN are trials powered to evaluate the non-inferiority of OCT-guided PCI compared with IVUS-guided PCI, although there are several differences in stent sizing, the endpoints, etc.**
- **These trials may demonstrate non-inferiority of OCT-guided PCI compared with IVUS-guided PCI in terms of not only procedural outcome just after PCI but also late clinical outcome.**
- **Final results will be presented soon.**
- **Guideline for OCT in PCI would be reevaluated in the near future by the evidence including these trials.**

Imaging modalities and Stent

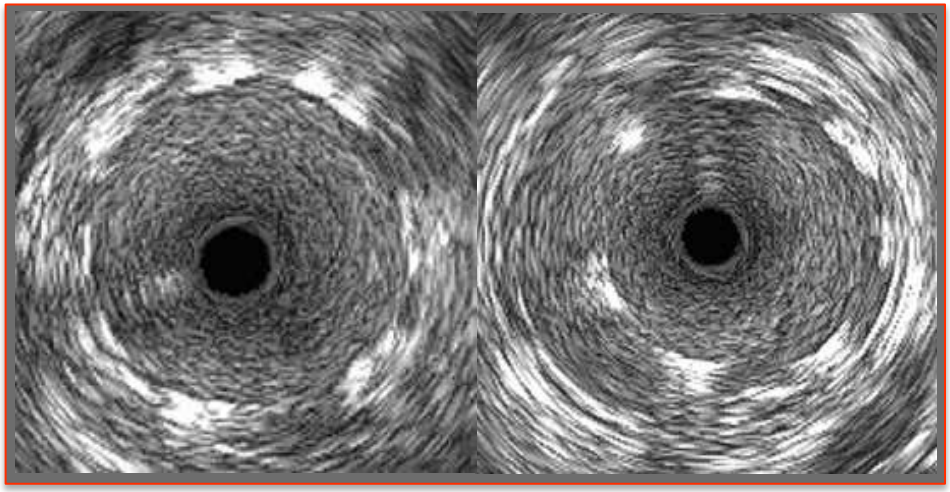
OFDI

LUNAWAVE and FastView



IVUS

VISIWAVE and ViewIT (40MHz)



DES

NOBORI, biolimus-eluting stent

Sample size calculation

- With the assumption of 9% TVF rate at 12 months after IVUS-guided PCI with BES, a total of 774 patients would yield 80% power to detect non-inferiority with a non-inferiority margin of 7% at a one-sided significance level of 0.05.
- A total of 800 patients are to be enrolled considering possible dropout during follow-up.

Impact of OCT- vs IVUS-guided PCI （Summary）

- Pre- & post-PCI lesion morphology can be assessed easily & precisely by OCT because of higher resolution with high frame rate, auto-pullback & auto-measurement systems, etc.

- Improvement of clinical outcomes can be expected in PCI by the guidance of OCT, although there are not enough data to support the reduction of the adverse clinical events by OCT-guided PCI.

- Randomized prospective studies should be planned to demonstrate the improvement of clinical outcome by OCT-guided PCI in the near future.

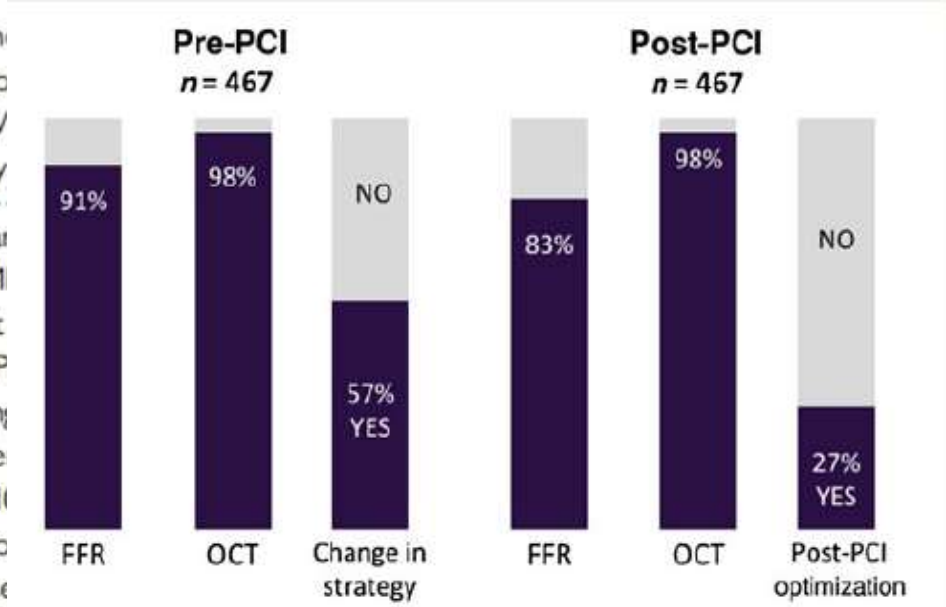
ILUMIEN I Study

Aims

ILUMIEN I is the largest prospective, non-ran
(PCI) procedural practice in patients undergo
and optical coherence tomography (OCT). W
association with post-PCI FFR values and early

Methods and results

Optical coherence tomography and documentar
oses) with stable or unstable angina or NSTEM
(57% of all stenoses) by selecting different stent
implantation using angiographic guidance, post-P
malities deemed unsatisfactory by the implantin
2.7% edge dissection and prompted further ste
using additional in-stent post-dilatation (81%, 1
were identified *post hoc*: stent placement witho
PCI OCT ($n = 165$), post-PCI optimization base
timization 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.

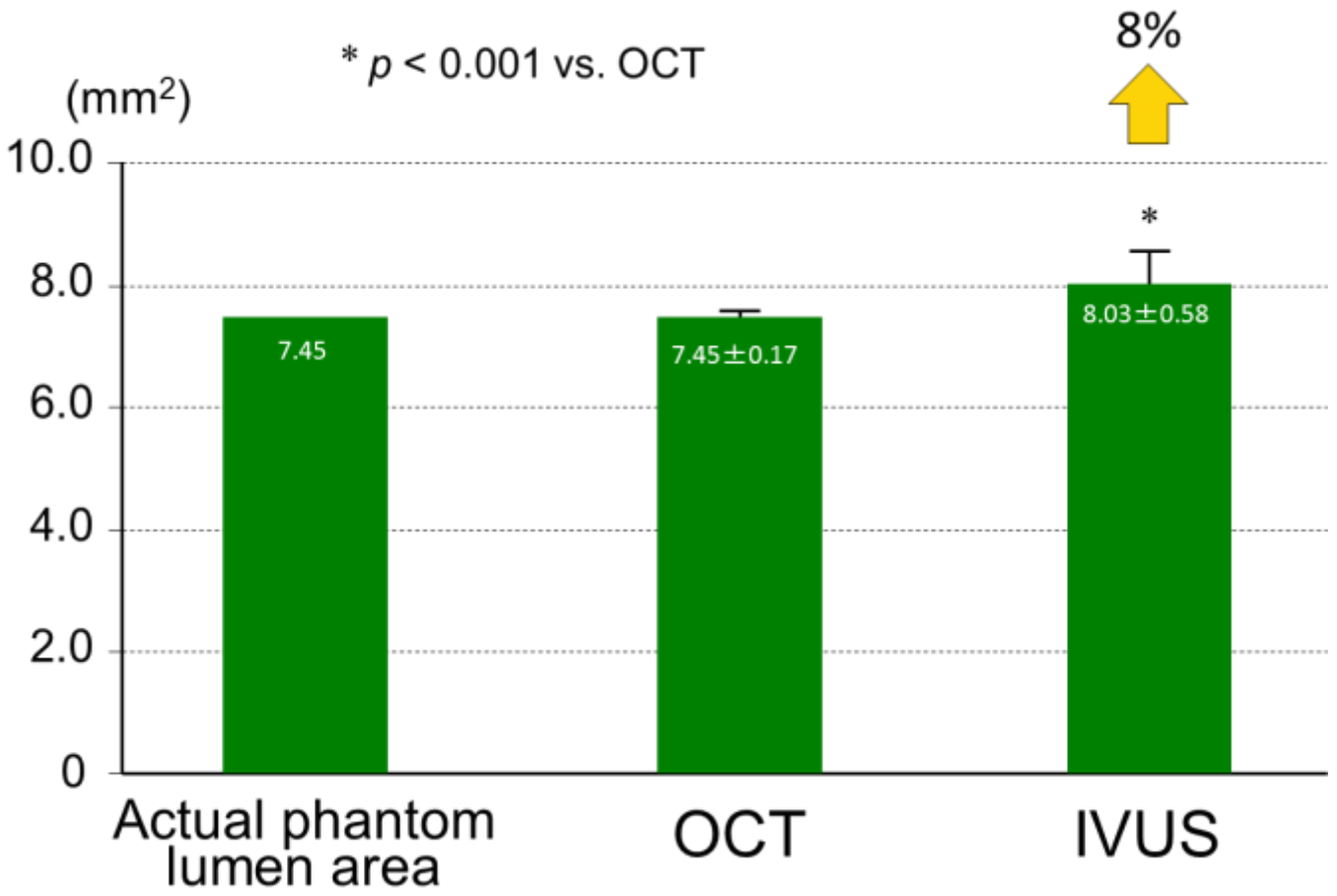
ClinicalTrials.gov Identifier

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

Accuracy for measurement (MLA)
(**OPUS-CLASS Study**)



Kubo T, et al., JACC Cardiovasc Img. 2013;6:1095-1104