Neointimal Tissue Evaluation after DES Implantation with OCT

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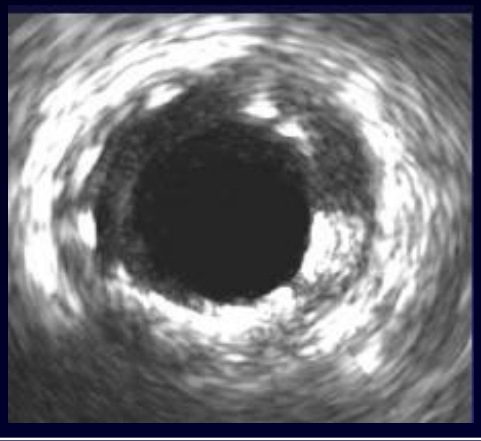
Potential conflicts of interest

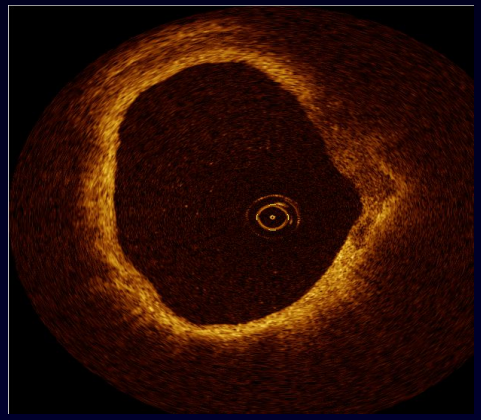
☐ I have the following potential conflicts of interest to report:

- Consulting
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other(s)

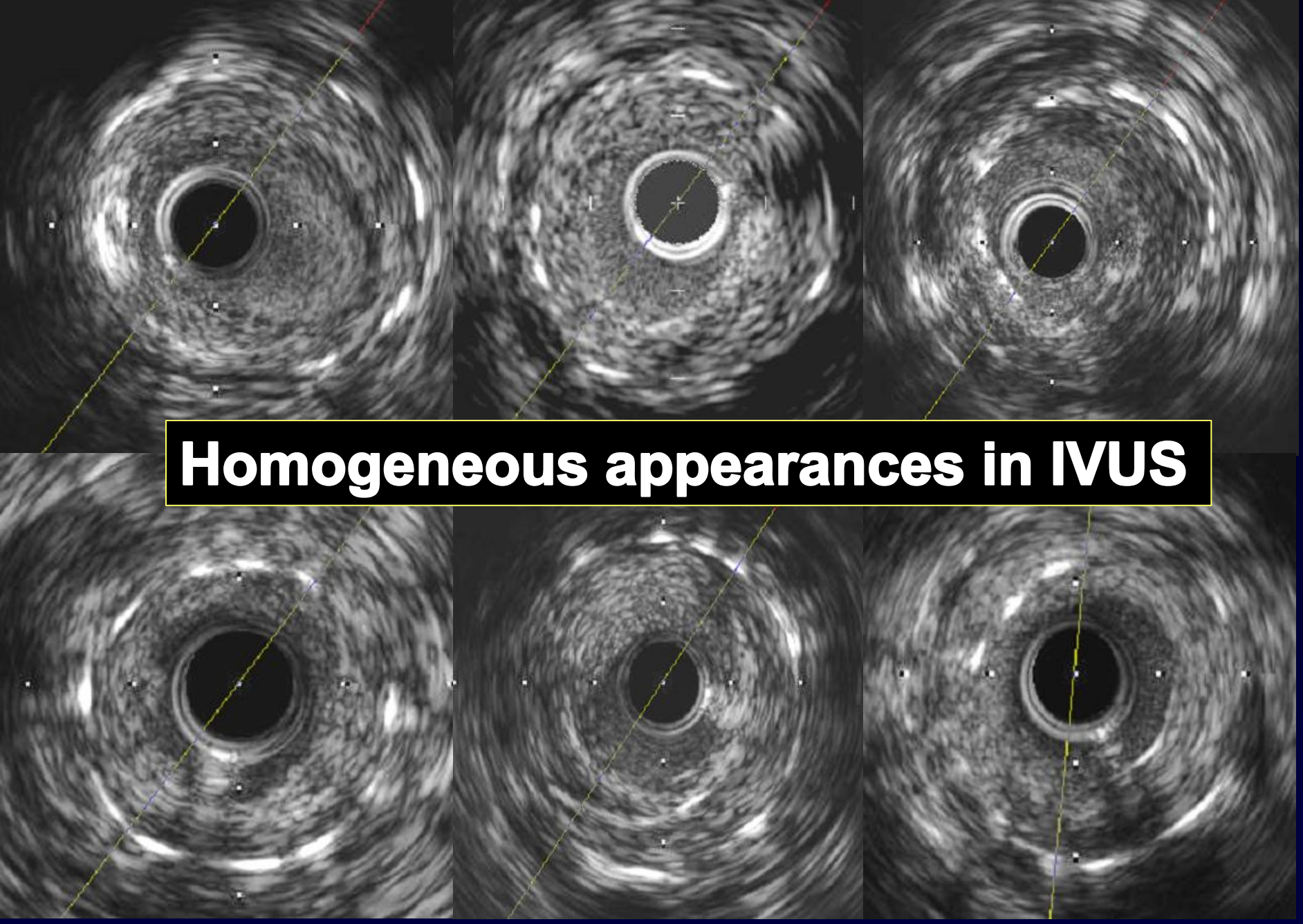
☒ I do not have any potential conflict of interest

IVUS vs. OCT



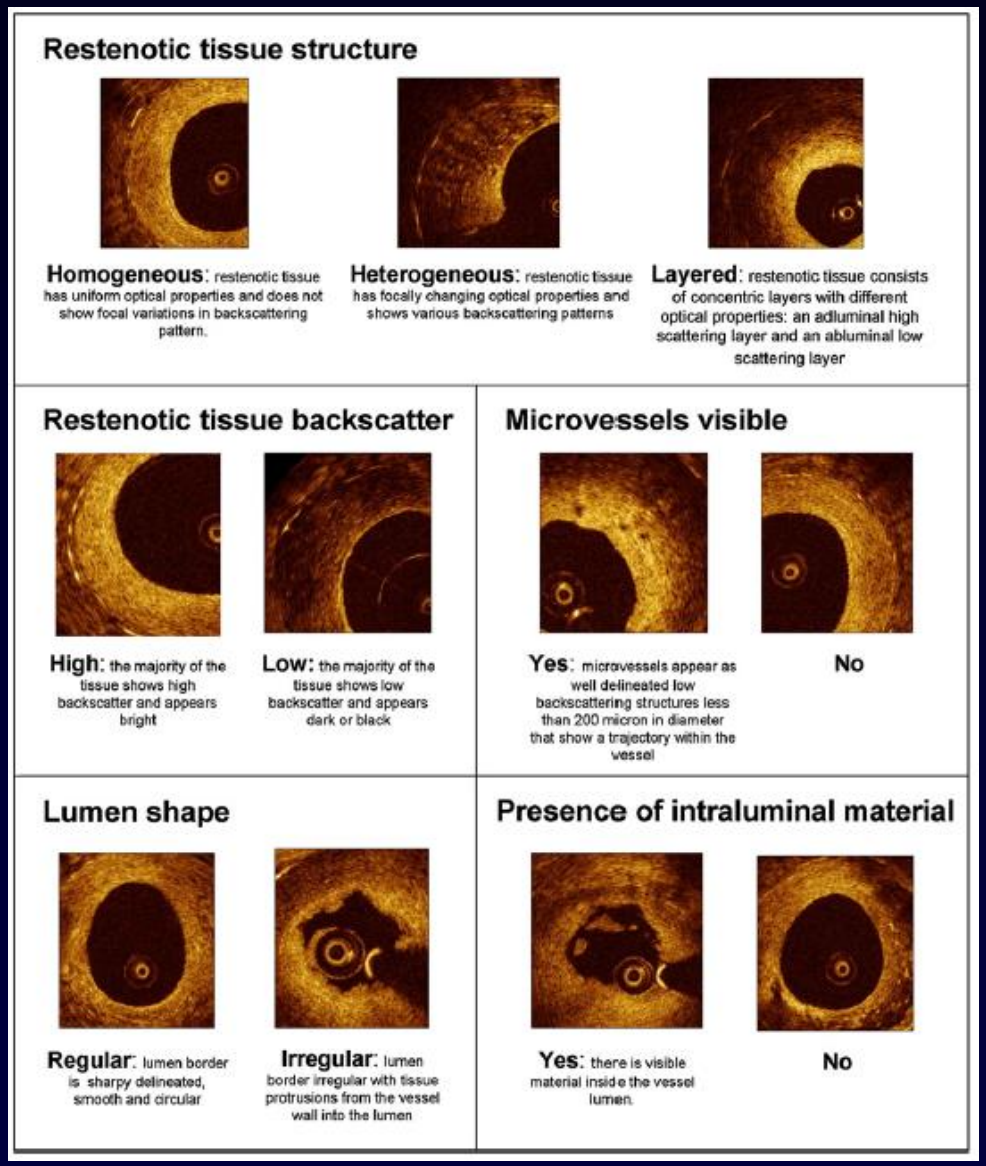


	IVUS	OCT
Resolution	Axial 100-150 μm Lateral 150-300 μm	15-20 μm 25-40 μm
Size of imaging core	0.8 mm	0.4 mm
Dynamic range	40-60 dB	90-110 dB
Frame rate	30 frame/s	15 frame/s



Homogeneous appearances in IVUS

OCT patterns of stent restenosis (24 patients, 25 vessels)



Restenotic tissue structure: layered in 52%, homogeneous in 28%, and heterogeneous in 20%.

The predominant backscatter was high in 72%.

Microvessels were visible in 12%

Gonzalo N, et al. Am Heart J 2009;158:284-93

Comparison of neointimal tissue characteristics by OCT between the lesions with and without ISR

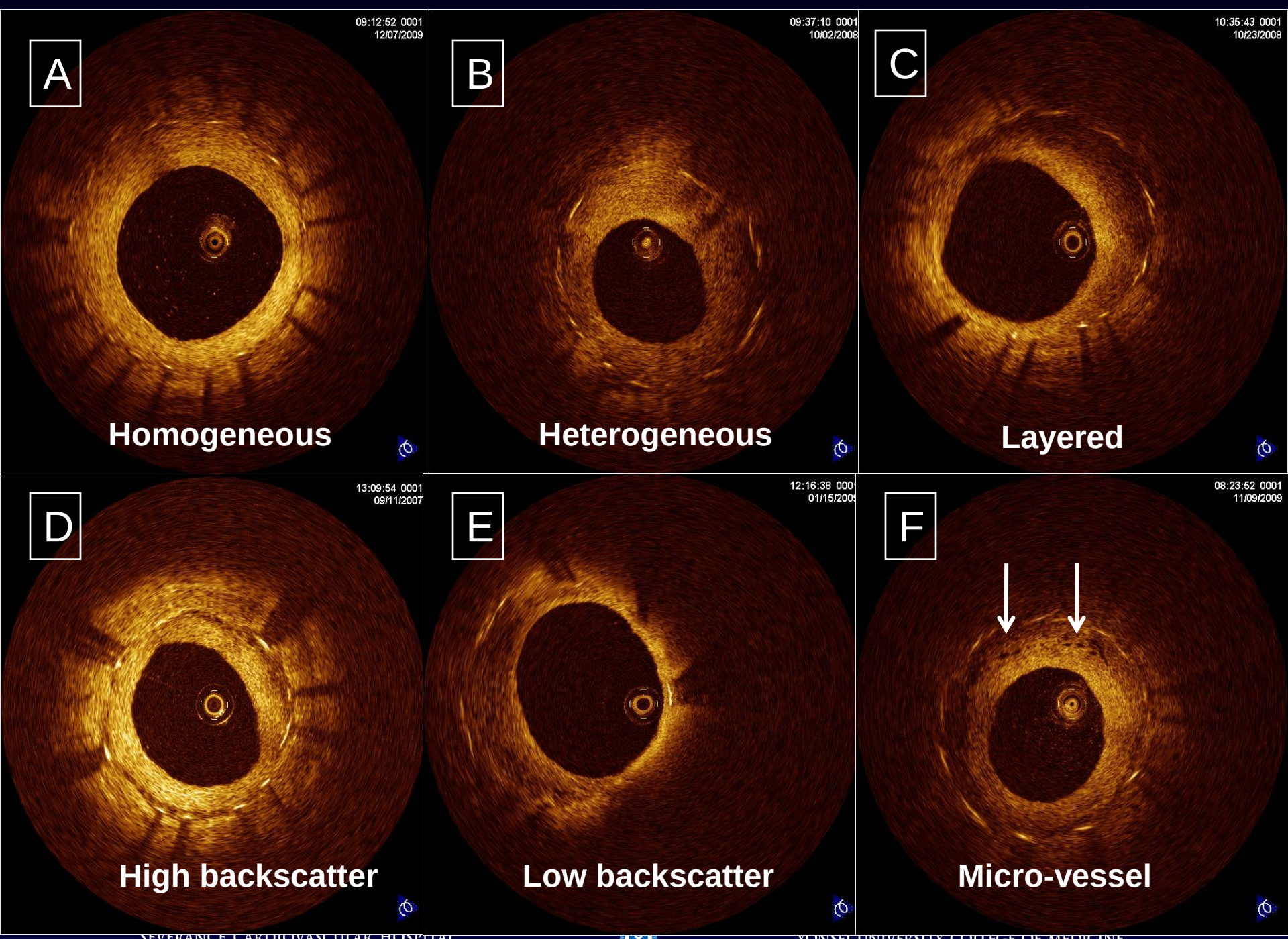
The lesions of ≥ 10% burden of neointimal tissue by OCT measurements were included in this study.

DES: SES (n= 52), PES (n= 57), ZES (n= 84), and EES (n= 32).

ISR was defined as ≥ 50% DS at the follow-up angiogram.

A follow-up OCT (mean follow-up duration: 12.0±10.5 months) was performed in 209 patients with 225 lesions (192 lesions without ISR and 33 lesions with ISR).

Lee SJ, MK Hong, et al. *Clin. Cardiol* 2011;34: 633-639


A
09:12:52 0001
12/07/2009
Homogeneous
B
09:37:10 0001
10/02/2008
Heterogeneous
C
10:35:43 0001
10/23/2008
Layered
D
13:09:54 0001
09/11/2007
High backscatter
E
12:16:38 0001
01/15/2009
Low backscatter
F
08:23:52 0001
11/09/2009
Micro-vessel

Comparison of Morphologic Characteristics of Neointimal Tissue by OCT between the Lesions with and without ISR

	No ISR (n=192)	ISR (n=33)	p-value
Tissue coverage structure			
Homogeneous	148 (77.1%)	7 (21.2%)	
Heterogeneous	32 (16.7%)	14 (42.4%)	<0.001
Layered	12 (6.2%)	12 (36.4%)	
Backscatter			
High	152 (79.2%)	13 (39.4%)	<0.001
Low	40 (20.8%)	20 (60.6%)	
Intraluminal material	9 (4.7%)	3 (9.1%)	0.4
Microvessels	11 (5.7%)	16 (48.5%)	<0.001

Lee SJ, MK Hong, et al. *Clin. Cardiol* 2011;34: 633-639

Qualitative assessment of neointimal tissue after DES implantation: Comparison between OCT and IVUS

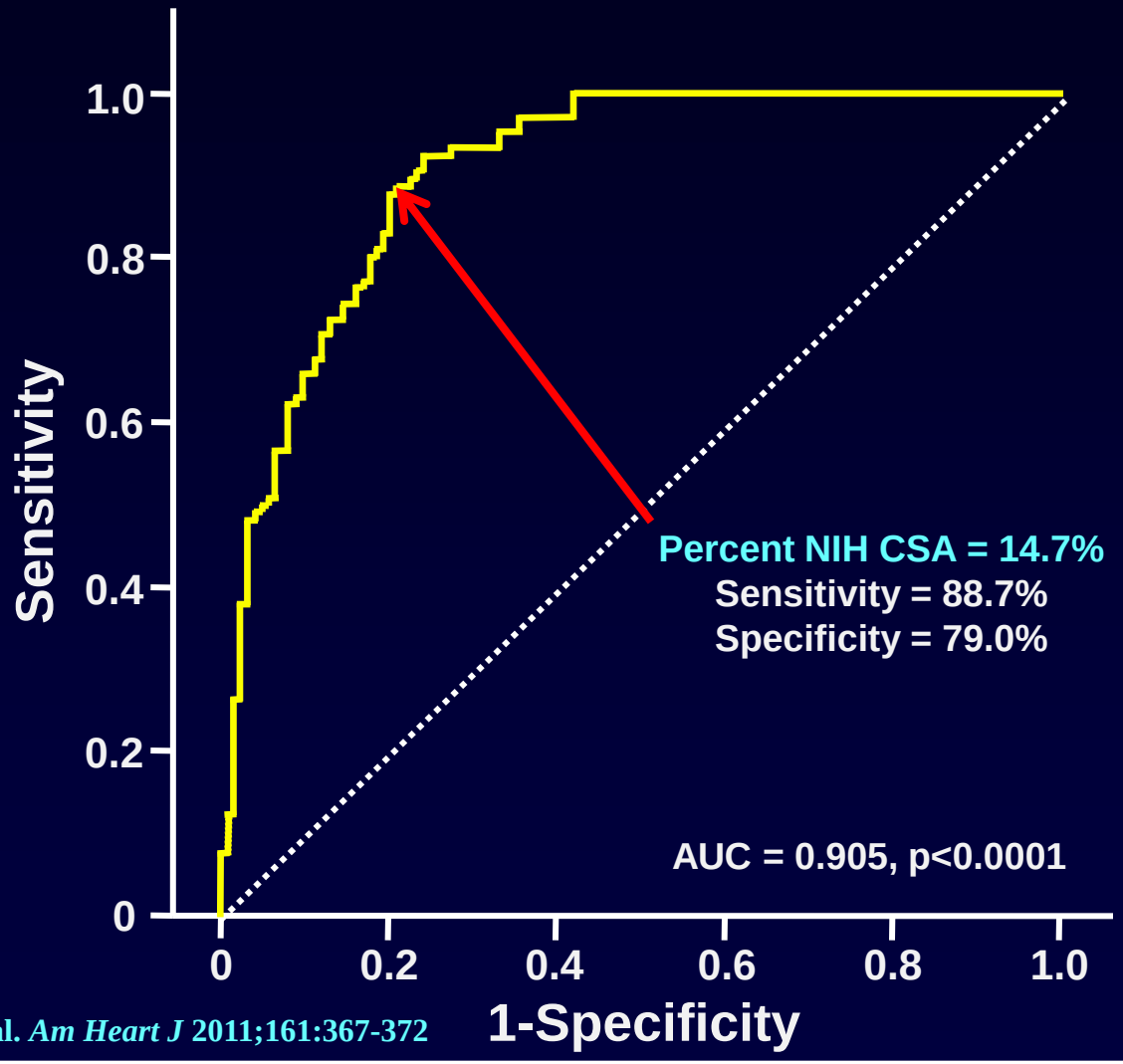
A total of 243 patients (250 lesions) underwent follow-up OCT and IVUS after DES implantation.

Mean time interval from DES implantation to follow-up OCT/IVUS was 12.0 ± 9.3 months.

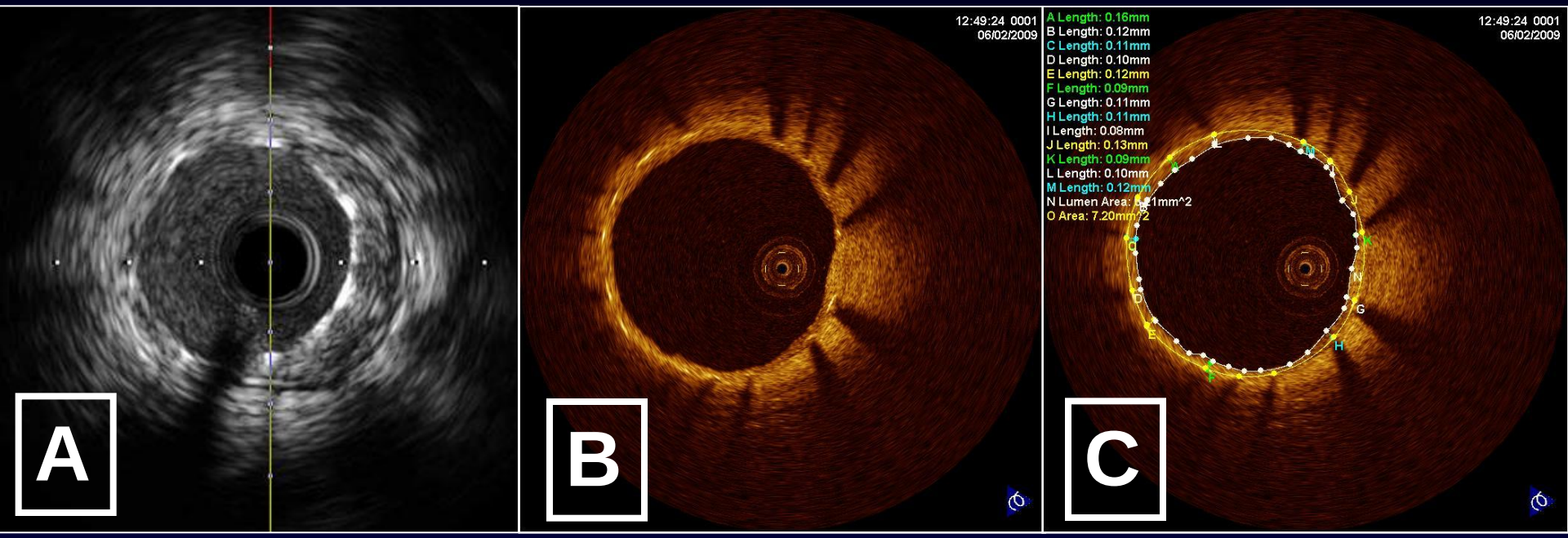
NIH was detected by both OCT and IVUS in 121 of 250 lesions, and categorized as homogenous (n=74, OCT; n=107, IVUS), heterogeneous (n=34, OCT; n=4, IVUS), or layered (n=13, OCT; n=10, IVUS).

Kwon SW, Hong MK, et al. *Am Heart J* 2011;161:367-372

Percent neointimal hyperplasia (NIH) cross-sectional area (CSA) was calculated as (NIH CSA/stent CSA)×100 for receiver-operating characteristic analysis of NIH detection by IVUS



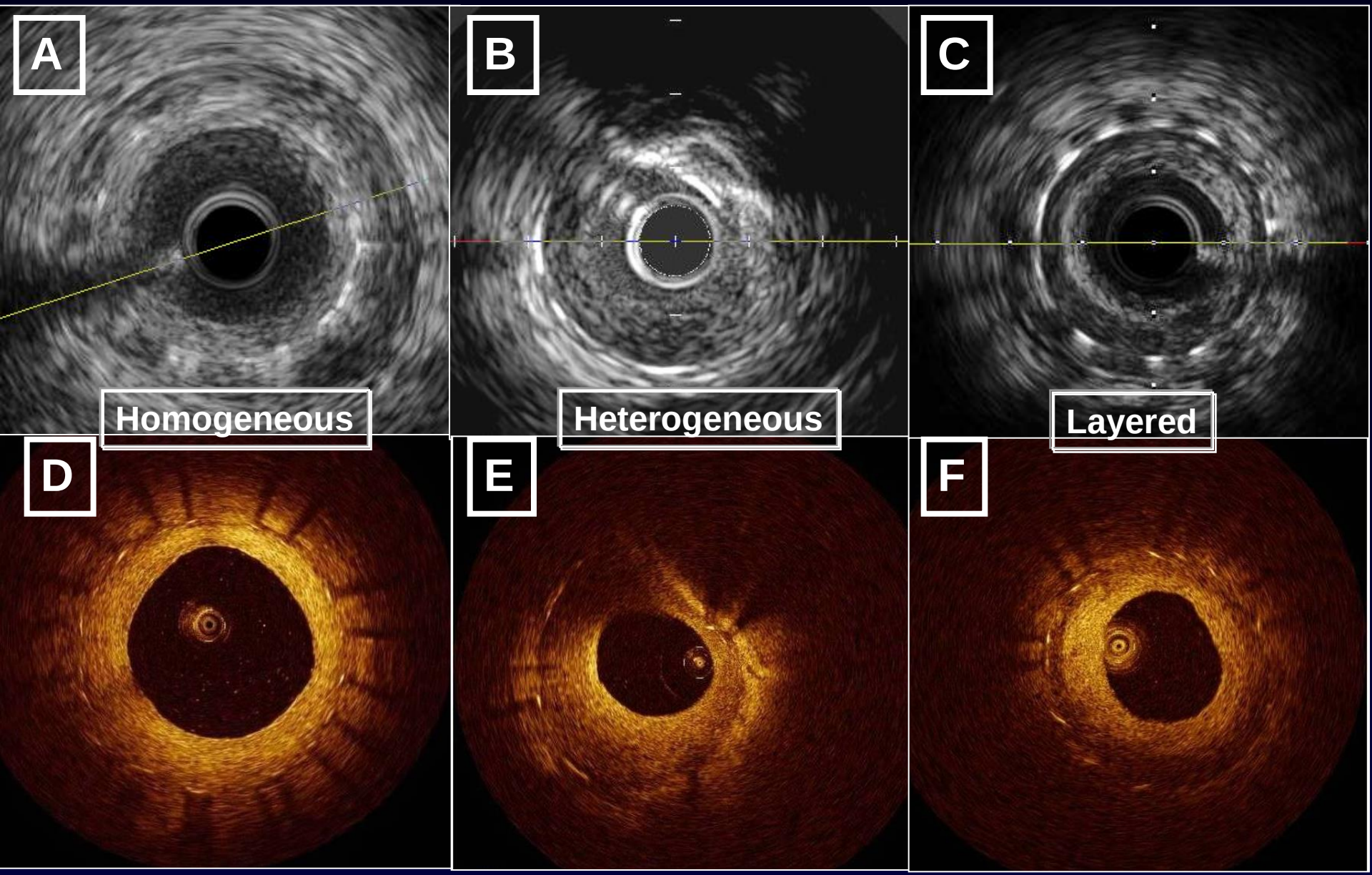
Kwon SW, Hong MK, et al. *Am Heart J* 2011;161:367-372



NIH undetectable by IVUS

NIH detected by OCT: percent NIH cross-sectional area = 13.8%, NIH thickness = 11.1 μm

Kwon SW, Hong MK, et al. *Am Heart J* 2011;161:367-372



Kwon SW, Hong MK, et al. *Am Heart J* 2011;161:367-372

Qualitative assessment of neointimal tissue after DES implantation: Comparison between OCT and IVUS

IVUS	OCT			
	Homogenous	Heterogeneous	Layered	Total
Homogenous	74	28	5	107
Heterogeneous	0	3	1	4
Layered	0	3	7	10
Total	74	34	13	121

Cramer's V nominal correlation: p-value <0.0001, r = 0.455

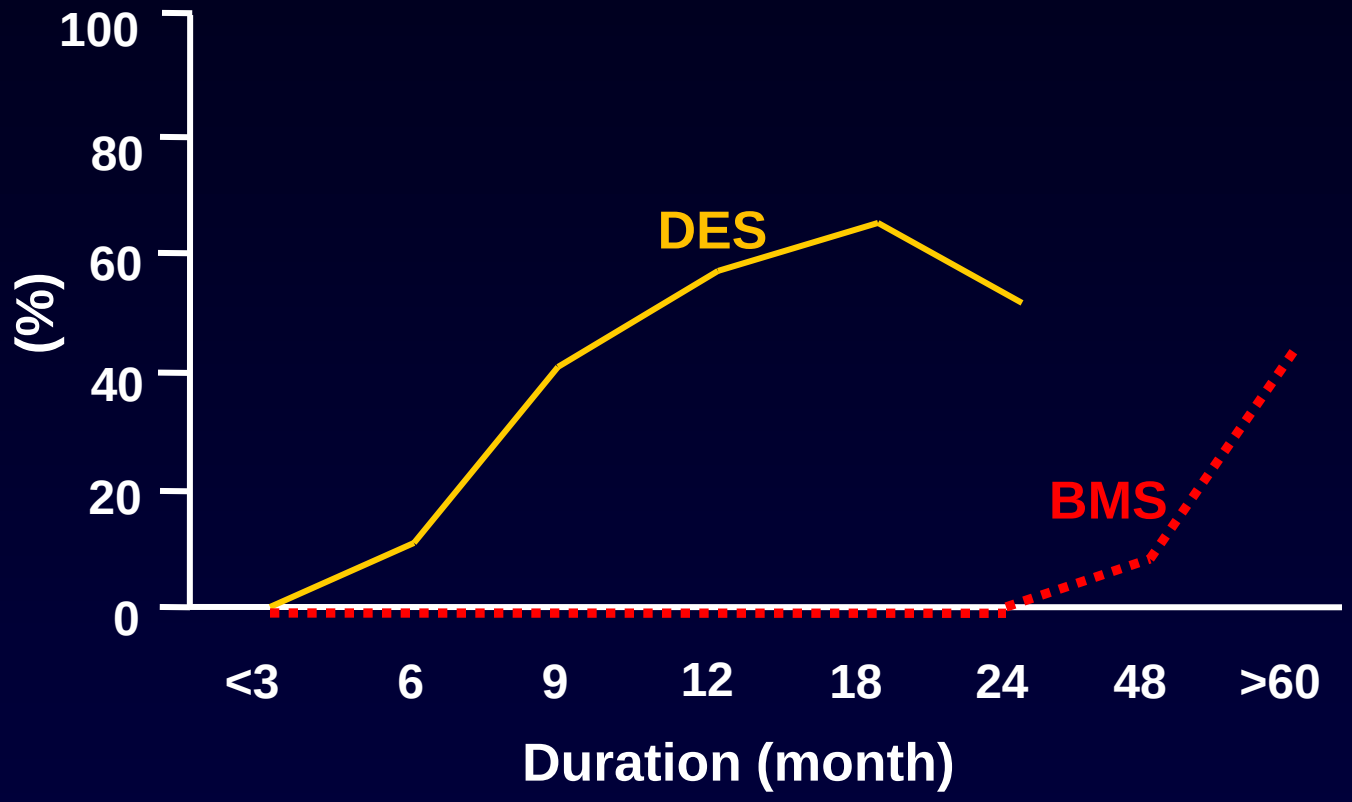
Of the 121 NIH lesions, non-homogenous NIH was detected in 14 (11.6%) by IVUS and 47 (38.8%) by OCT. OCT and IVUS assessments of NIH morphology showed a moderate correlation (p<0.001, r=0.455); however, assessments differed in 37 (30.6%) of 121 lesions.

Kwon SW, Hong MK, et al. *Am Heart J* 2011;161:367-372

Plaque rupture

	De novo lesions	ISR lesions
Lesions	Vulnerable plaques	Lipid-laden intima
Clinical presentation	ACS	Stent thrombosis

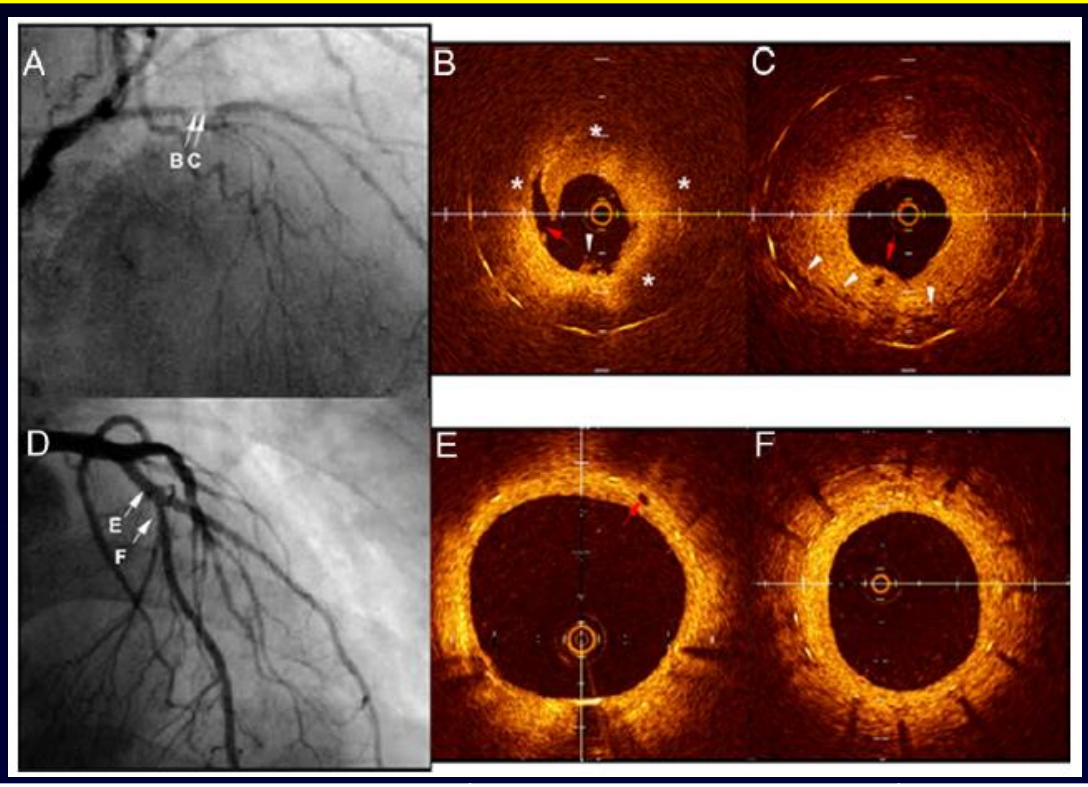
Atherosclerotic changes in DES vs. BMS in relation to duration of implant at autopsy



The atherosclerotic change in SESs is seen in 40% of cases by 9 months; in BMS, the atherosclerotic change does not begin to appear until 2 years and remains a rare finding until 4 years

Nakazawa G, et al. JACC: Cardiovascular imaging 2009;2:625-8

Appearance of lipid-laden intima and neovascularization after BMS implantation



	Early phase (< 6 months, n=20)	Late phase (> 5 years, n=21)
Lipid-laden intima	0	67%
Intraintima neovascularization	0	62%

Takano M, et al. J Am Coll Cardiol 2010;55:26-32

IVUS findings of very late stent thrombosis (DES=23; BMS=7)

Stent malapposition was observed in 73.9% of DES patients, but in no BMS patients (p= 0.001).

Disease progression with neointimal rupture within the stent was observed in 10 DES patients (43.5%) and 7 BMS patients (100%; p= 0.010).

Conclusion: Stent malapposition plays a key role in DES-related VLST whereas neoatherosclerosis with plaque rupture plays a key role in BMS-related VLST.

Lee CW, et al. *J Am Coll Cardiol* 2010;55:1936-42

OCT findings of very late stent thrombosis

Very Late Stent Thrombosis (VLST) Group

- 18 patients from 4 PCI centers.
  presented with VLST after implantation of DES and OCT examination was performed
- April 2008~July 2010

Neointimal Hyperplasia (NIH) Group

- 57 patients from Yonsei OCT Registry
  showed luminal narrowing >40% within the DES on coronary angiography and underwent OCT exam.
- September 2007~May 2010

Ko YG, Hong MK, et al. *Int J Cardiovasc Imaging (in press)*

Procedure/OCT data

Variables	VLST with neointimal rupture (n=4)	VLST without neointimal rupture (n=14)	p
QCA at the index procedure			
Stent length (mm)	28.0±5.0	27.6±5.0	0.945
Reference diameter (mm)	3.0±0.3	3.1±0.7	>0.999
Pre-intervention MLD (mm)	0.6±0.5	0.9±0.4	0.346
Post-intervention MLD (mm)	2.8±0.6	2.9±0.4	0.814
OCT findings			
Uncovered struts	0 (0.0)	9 (64.3)	0.082
Malapposed struts	0 (0.0)	7 (50.0)	0.092
Lipid-laden neointima	4 (100.0)	4 (28.6)	0.023

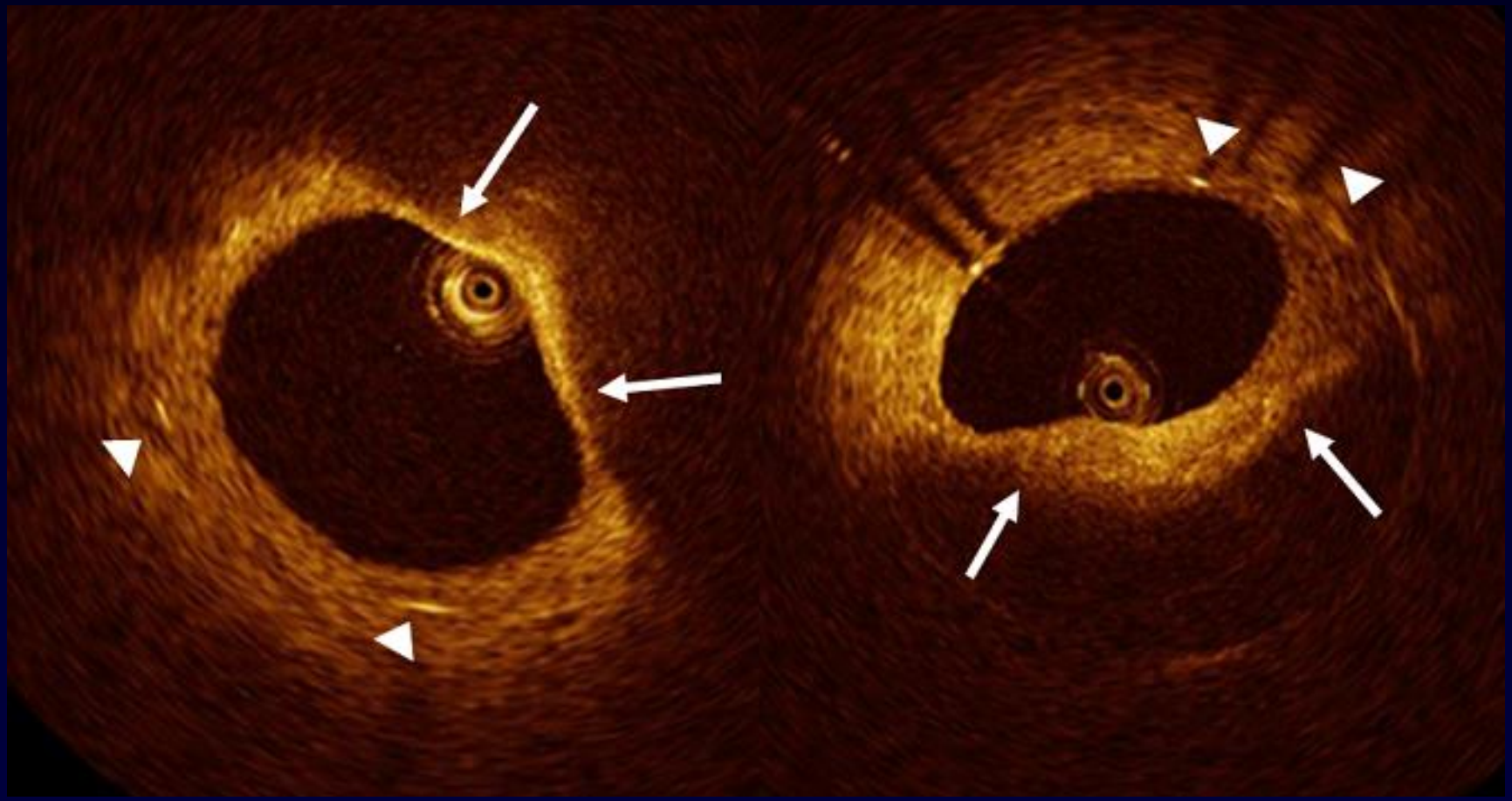
Ko YG, Hong MK, et al. *Int J Cardiovasc Imaging (in press)*

Clinical Characteristics

Variables	NIH with lipid-laden neointima (n=8)	NIH without lipid-laden neointima (n=49)	p
Diabetes mellitus	2 (25.0%)	18 (36.7%)	0.699
Hypertension	3 (37.5%)	28 (57.1%)	0.448
Hypercholesterolemia	6 (75.0%)	25 (51.0%)	0.207
Clinical diagnosis at the index procedure			0.810
Stable angina	2 (25.0%)	18 (36.7%)	
Unstable angina	3 (37.5%)	15 (30.6%)	
Acute myocardial infarction	3 (37.5%)	16 (32.6%)	
Time to OCT study, months	45.5±17.7	11.7±7.2	<0.001
Time to OCT study, years			
≤1 yr	0 (0.0%)	38 (77.6%)	
1 ~ 2 yrs	1 (12.5%)	8 (16.3%)	
2 ~ 3 yrs	2 (25.0%)	2 (4.1%)	
>3 yrs	5 (41.7%)	1 (2.0%)	

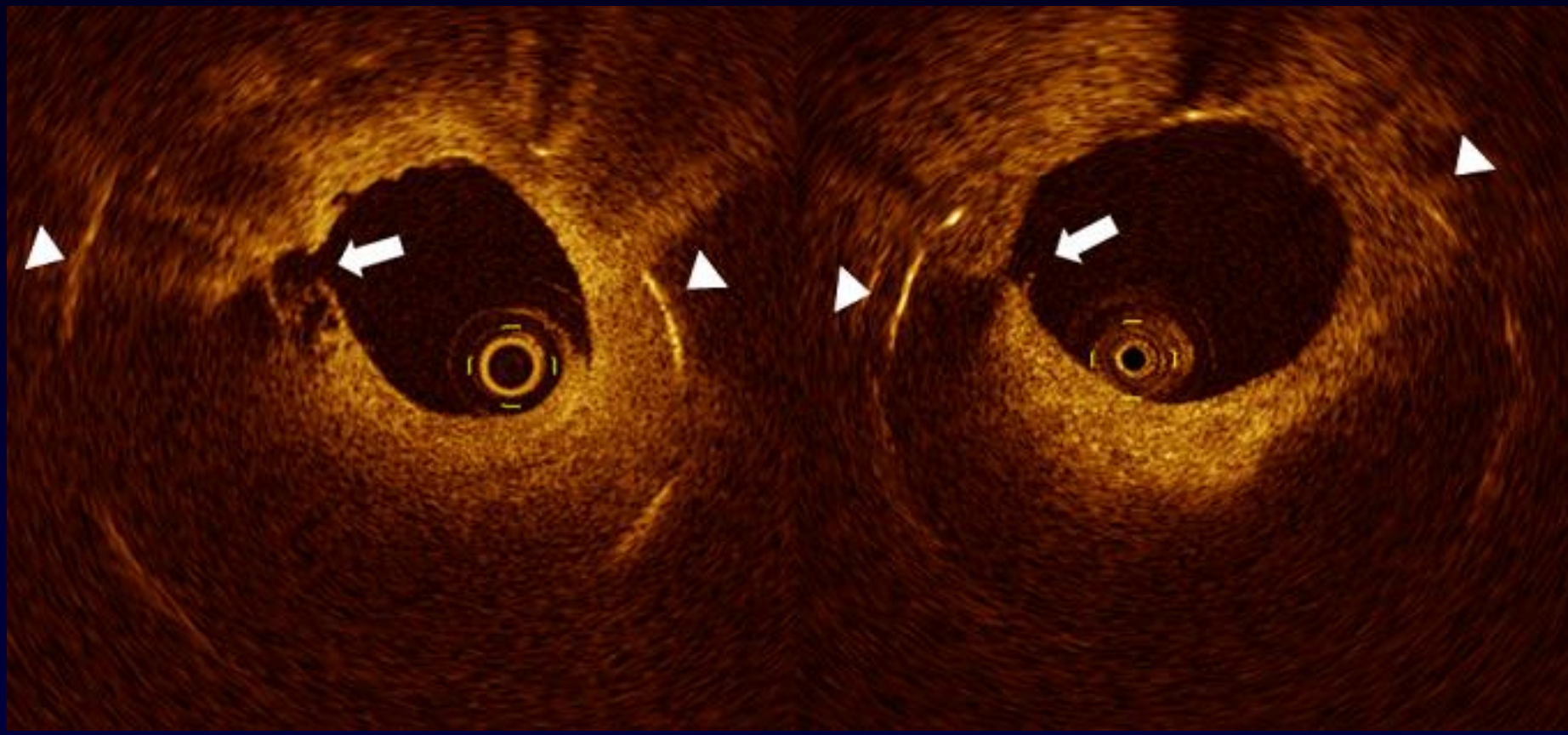
Ko YG, Hong MK, et al. *Int J Cardiovasc Imaging (in press)*

Lipid-laden neointima



Ko YG, Hong MK, et al. *Int J Cardiovasc Imaging (in press)*

Neointimal rupture



Ko YG, Hong MK, et al. *Int J Cardiovasc Imaging (in press)*

Summary: OCT in VLST

Rupture of lipid-laden neointima did exist inside DES in some patients with VLST after DES implantation.

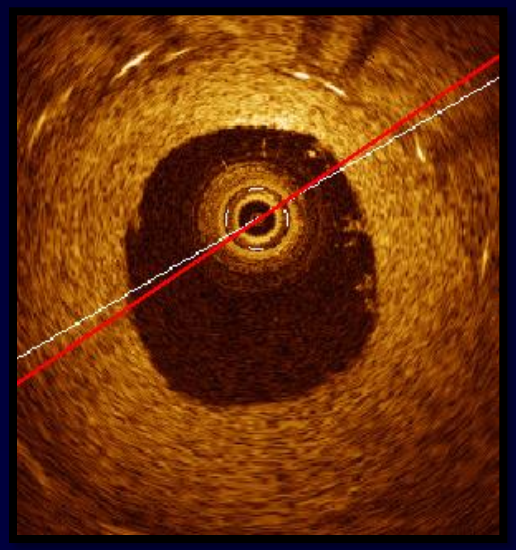
Lipid-laden neointima inside DES was identified in 8 (44.4%) of 18 patients with VLST as well as in 8 (42.1%) of 19 patients with moderate to severe NIH who underwent follow-up OCT procedure beyond 1-year after DES implantation.

In addition, uncovered and malapposed struts were identified in 9 (50.0%) and 7 (38.9%) of 18 patients with VLST, respectively.

Clinical implications of OCT patterns of in-stent restenosis following implantation of DES

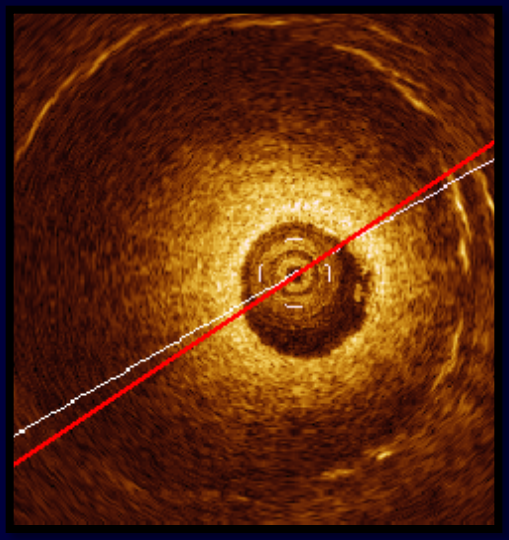
Determined according to the optical properties and backscattering patterns in the segment with maximal lumen narrowing;

1. **Homogeneous;** uniform optical properties and not showing focal variations in backscattering pattern
2. **Heterogeneous;** focally changing optical properties and showing various backscattering patterns
3. **Layered;** concentric layers with different optical properties.



Homogeneous

Heterogeneous



Layered

Study at a glance

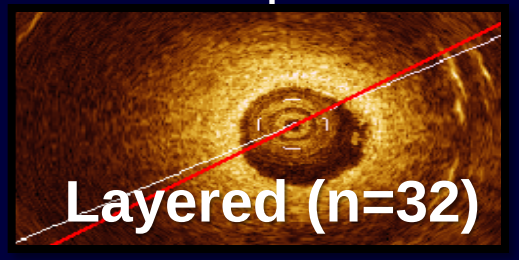
A total of 574 lesions in 510 patients were followed by an OCT in OCT registry

SES (n=170)	PES (n=99)	EES (n=109)	ZES (n=114)	ZES-R (n=82)

A total of 74 lesions with DES restenosis were identified in 69 patients.

SES (n=23)	PES (n=29)	EES (n=7)	ZES (n=10)	ZES-R (n=5)

OCT assessment and classifying restenosis into 3 tissue structures



Follow-up OCT measurements - I

Variables	Restenotic tissue structure			p
	Homogenous (n=21)	Heterogeneous (n=21)	Layered (n=32)	
Time to follow-up OCT (days)	652 ± 495	1036 ± 693	767 ± 684	0.139
Quantitative OCT assessment				
Entire segments				
Mean stent CSA (mm^2)	7.0 ± 1.9	6.2 ± 1.7	7.1 ± 1.7	0.165
Mean lumen CSA (mm^2)	4.5 ± 1.2	4.2 ± 1.8	4.4 ± 1.5	0.790
Mean NIH CSA (mm^2)	2.5 ± 1.2	2.0 ± 0.9	2.7 ± 1.5	0.173
Mean % NIH CSA (%)	34 ± 11	32 ± 15	37 ± 17	0.522
Segments with minimal lumen CSA				
Stent CSA (mm^2)	6.4 ± 2.2	5.8 ± 2.1	6.9 ± 2.1	0.168
Lumen CSA (mm^2)	2.1 ± 1.0	1.8 ± 1.1	1.9 ± 1.3	0.625
NIH CSA (mm^2)	4.4 ± 2.2	4.1 ± 1.9	5.0 ± 1.9	0.204
% NIH CSA (%)	65 ± 18	69 ± 19	73 ± 12	0.208

Follow-up OCT measurements - II

Variables	Restenotic tissue structure			p
	Homogenous (n=21)	Heterogeneous (n=21)	Layered (n=32)	
Qualitative OCT assessment				
Backscatter				<0.001
High	18 (86%)	3 (14%)*	3 (9%)*	
Low	3 (14%)	18 (86%) *	29 (91%) *	
Presence of thrombi	6 (29%)	11 (52%)**, §	5 (16%)	0.016
Micro-vessels	5 (24%)	2 (10%)	10 (31%)	0.183

*p<0.01 and **p<0.05 compared to homogenous structure.
§p<0.05 compared to layered structure.

Clinical presentations at the onset of restenosis and their treatment modalities for restenosis

Variables	Restenotic tissue structure			p
	Homogenous (n=21)	Heterogeneous (n=21)	Layered (n=32)	
No. of patients	20	18	31	-
Clinical presentations of restenosis				**0.012**
Stable angina	19 (95%)	10 (56%) *, §	25 (81%)	
Acute coronary syndrome	1 (5%)	8 (44%) *, §	6 (19%)	
Treatment for in-stent restenosis				**0.014**
Medical treatments	6 (28%)	1 (5%)	12 (38%)	
Repeat revascularization	15 (72%)	20 (95%)	20 (62%)	

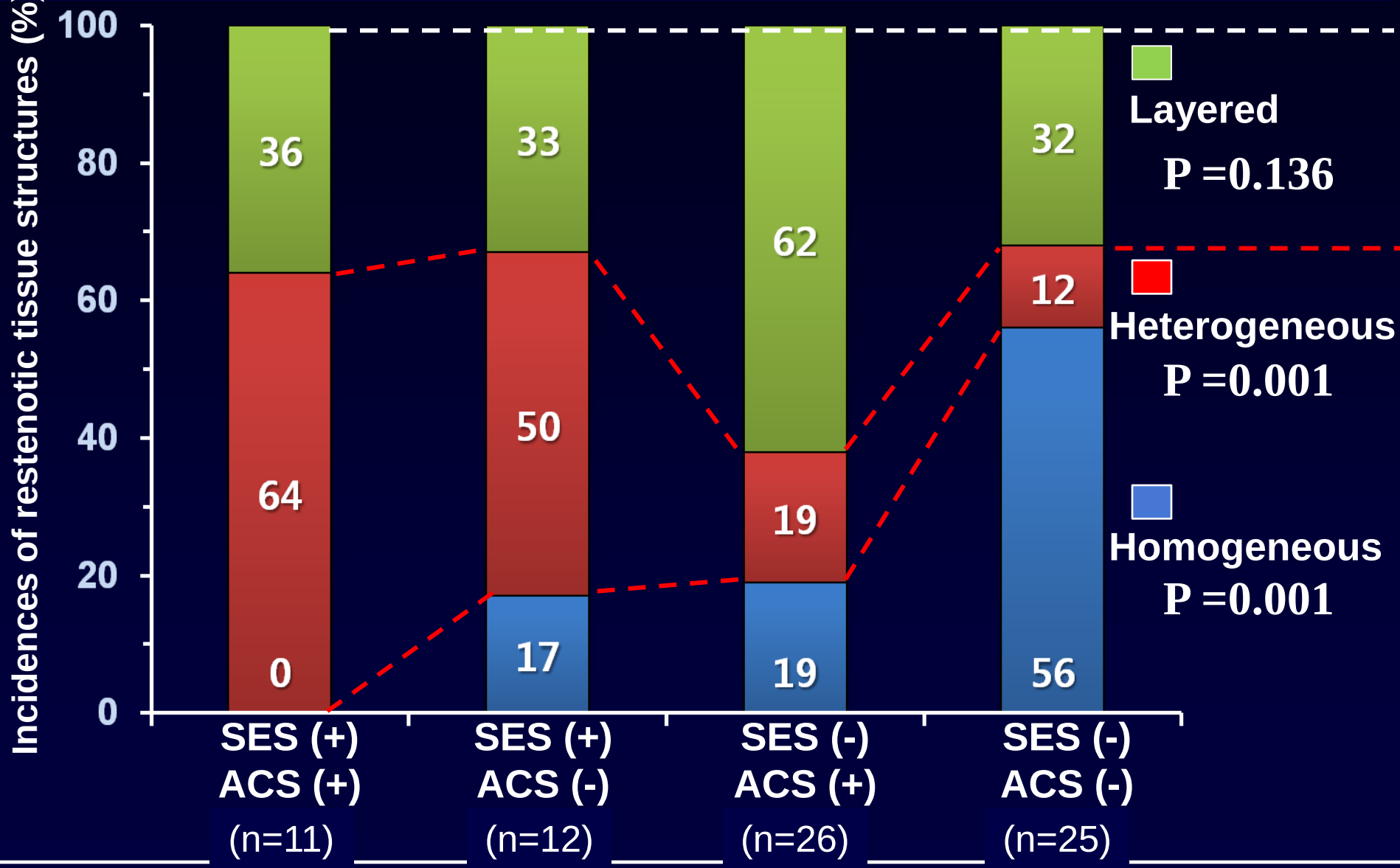
*p<0.01 compared to homogenous structure.

§p<0.05 compared to layered structure.

Predictors of heterogeneous tissue structure

	Univariate analysis			Multivariate analysis		
	OR	95% CI	p	OR	95% CI	p
Clinical variables						
Age	1.03	0.97 – 1.09	0.476	1.01	0.92 – 1.11	0.802
Diabetes mellitus	2.98	1.07 – 10.03	0.042	2.98	0.60 – 22.08	0.107
Acute coronary syndrome	4.88	1.25 – 18.32	0.032	**8.01**	**1.10 - 53.80**	**0.042**
Time to follow-up OCT	1.00	1.00 – 1.01	0.044	1.01	1.00 – 1.01	0.077
Angiographic or procedural variables						
Reference vessel size	0.35	0.08 – 1.50	0.256	0.56	0.02 – 16.60	0.734
Post-procedural MLD	0.27	0.05 – 1.41	0.223	0.68	0.02 – 21.88	0.845
Stent diameter	1.17	0.02 – 1.25	0.090	0.33	0.01 – 10.74	0.530
Stent length	1.04	0.96 – 1.15	0.543	1.07	0.89 – 1.18	0.798
Use of sirolimus-eluting stents	8.33	2.75 – 30.47	0.001	**7.71**	**1.35 – 43.41**	**0.024**

Comparison of restenotic tissue types among 4 groups according to the use of SES or initial ACS presentation



Summary

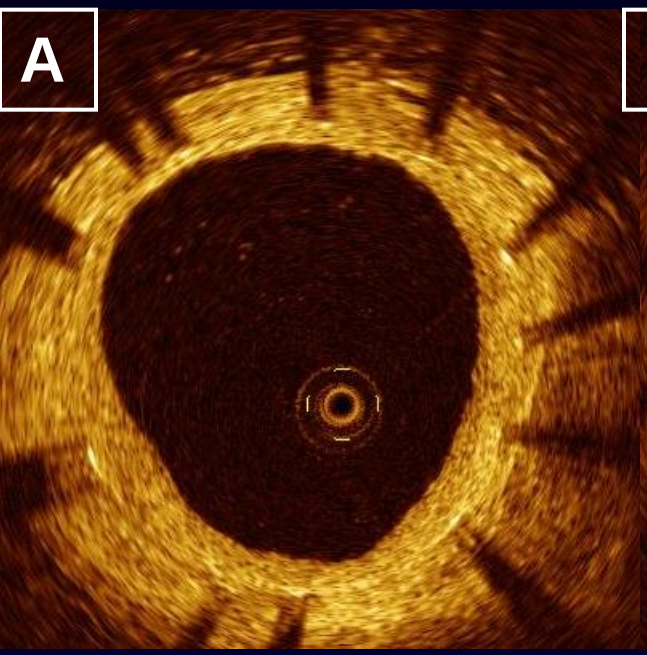
- ✓ **This OCT study showed that OCT-based tissue appearances may be associated with their specific clinical and procedure-related characteristics.**
- ✓ **Serial OCT study with a larger population will be needed in the future for the definite conclusions regarding the association between various parameters and OCT-based tissue characteristics.**

Serial OCT

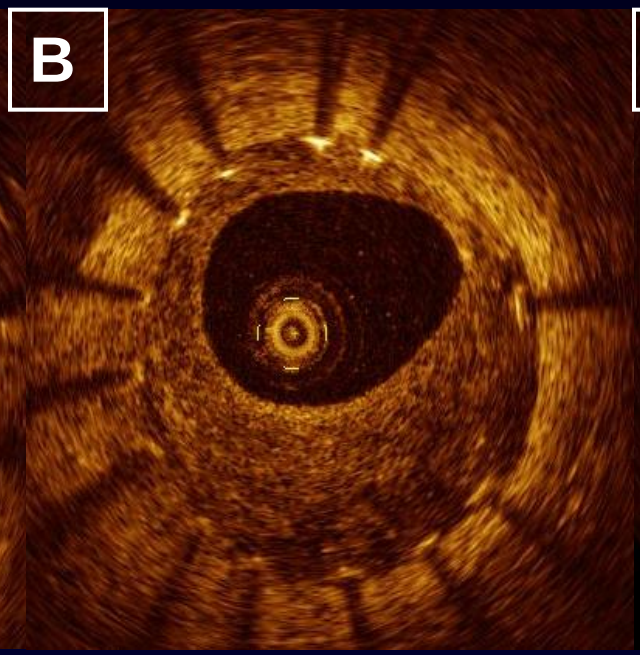
Study population

From the OCT registry database of our institute, we identified 250 patients who underwent follow-up OCT examination at 9 months (±3 months) after DES implantation.

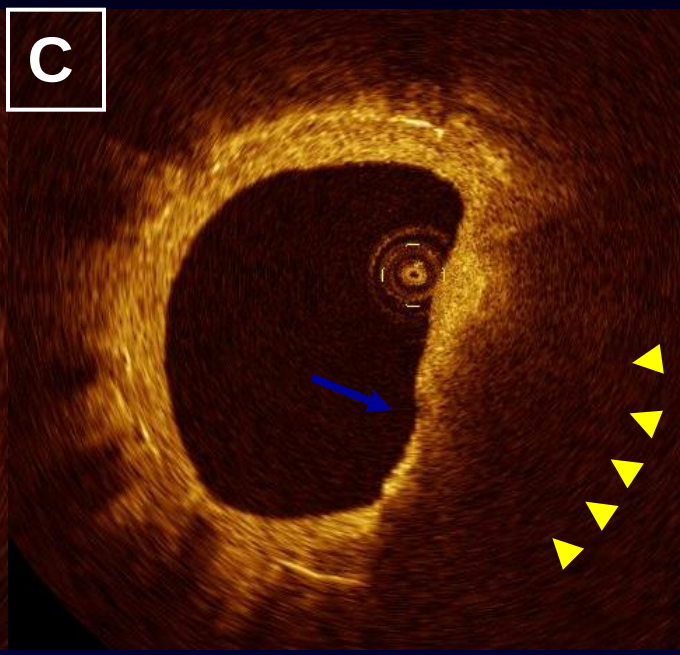
Among these patients, a second serial follow-up OCT examination at 2 years (±3 months) after stent implantation was performed in 72 patients with 76 stented lesions: 23 SESs, 20 PESs, 25 ZESs and EESs.



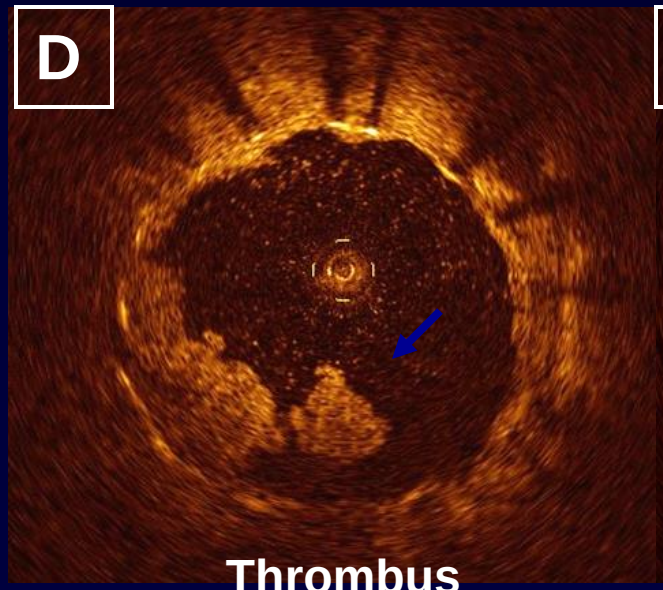
Homogeneous



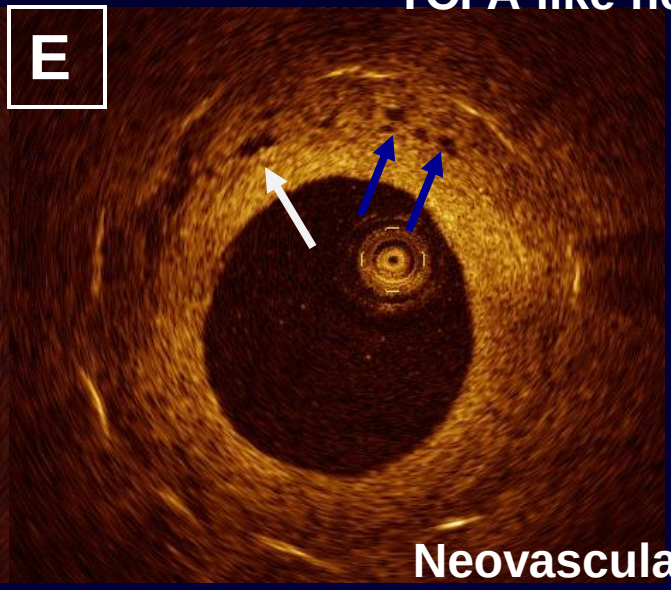
Heterogeneous



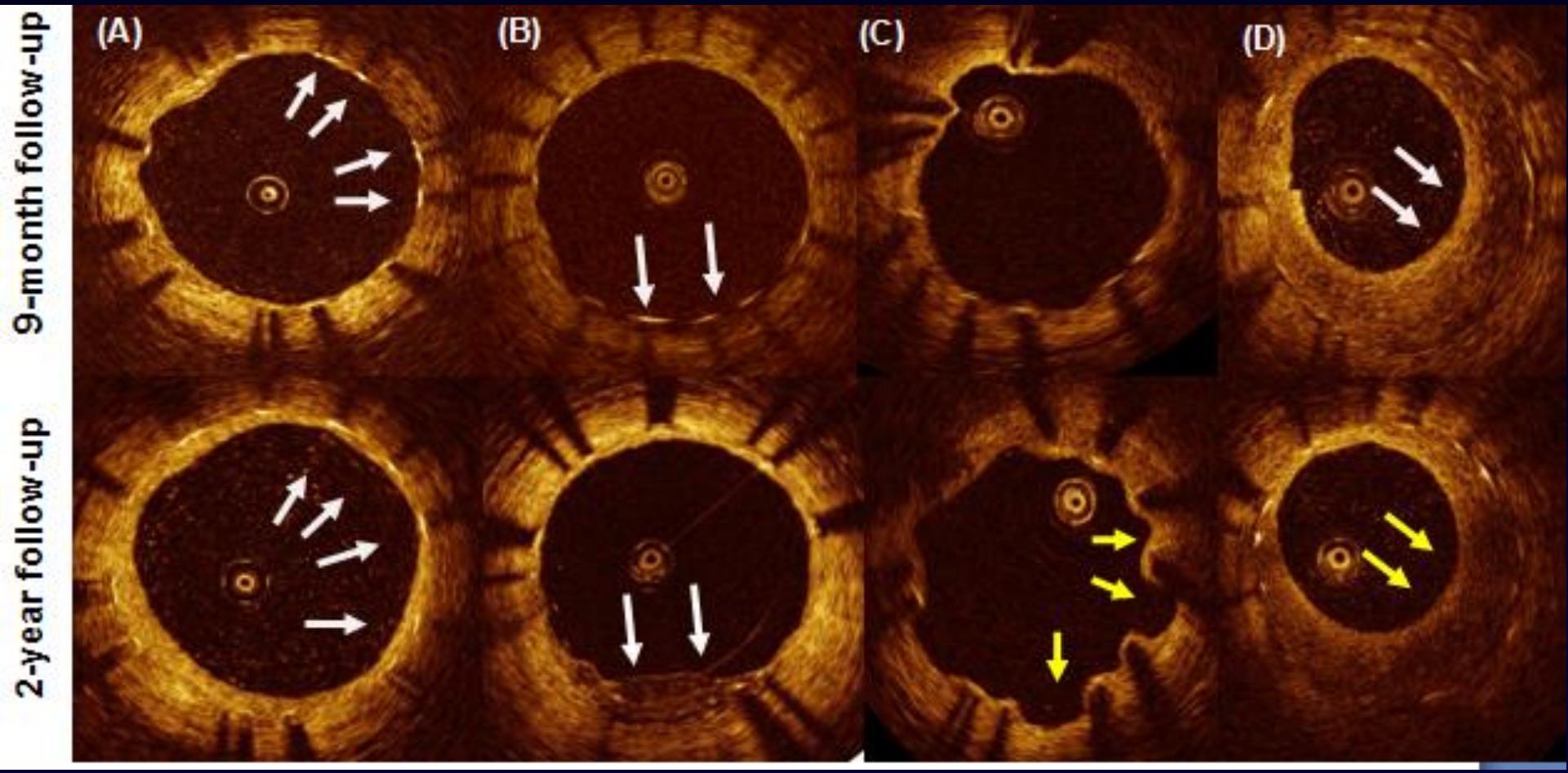
Lipid-laden neoinitma and
TCFA-like neointima



Thrombus



Neovascularization


9-month follow-up
2-year follow-up
(A)
(B)
(C)
(D)

Neointimal rupture

9-month

2-year

Quantitative OCT analysis

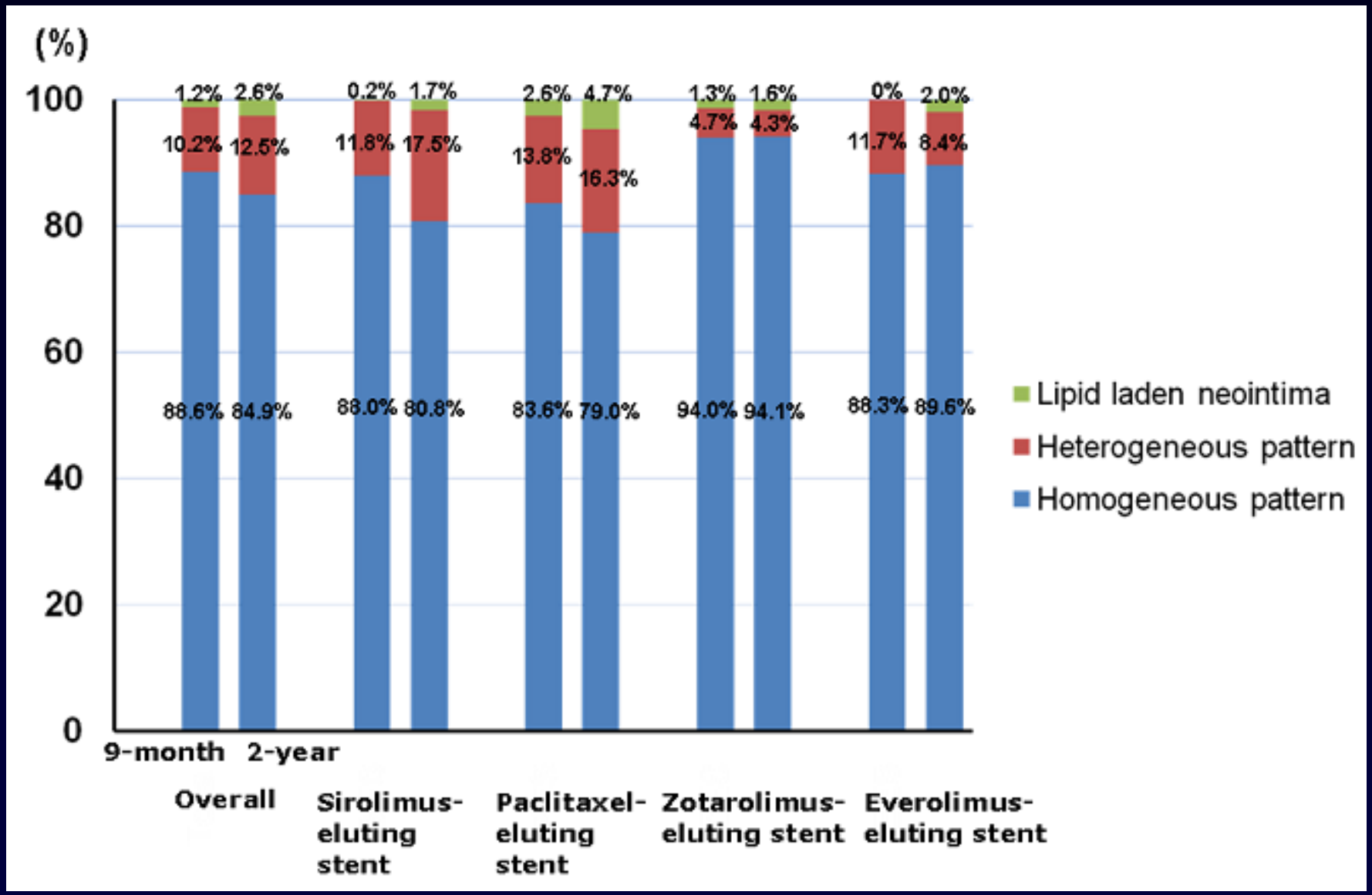
Cross-section (CS) level analysis	9-month	2-year	p
Total cross sections	1947	1947	
Mean stent CSA (mm^2)	7.0 ± 1.6	7.0 ± 1.6	0.92
Mean lumen CSA (mm^2)	5.7 ± 1.4	5.4 ± 1.6	0.01
Mean NIH area (mm^2)	1.3 ± 0.9	1.7 ± 1.1	0.001
Percent NIH CSA (%)	18.7 ± 11.3	23.4 ± 14.5	<0.001
CSs with any uncovered strut	418 (21.5%)	244 (12.5%)	<0.001
CSs with uncovered strut ratio > 0.3	153 (7.9%)	91 (4.7%)	<0.001
CSs with any malapposed strut	50 (2.6%)	70 (3.6%)	0.36

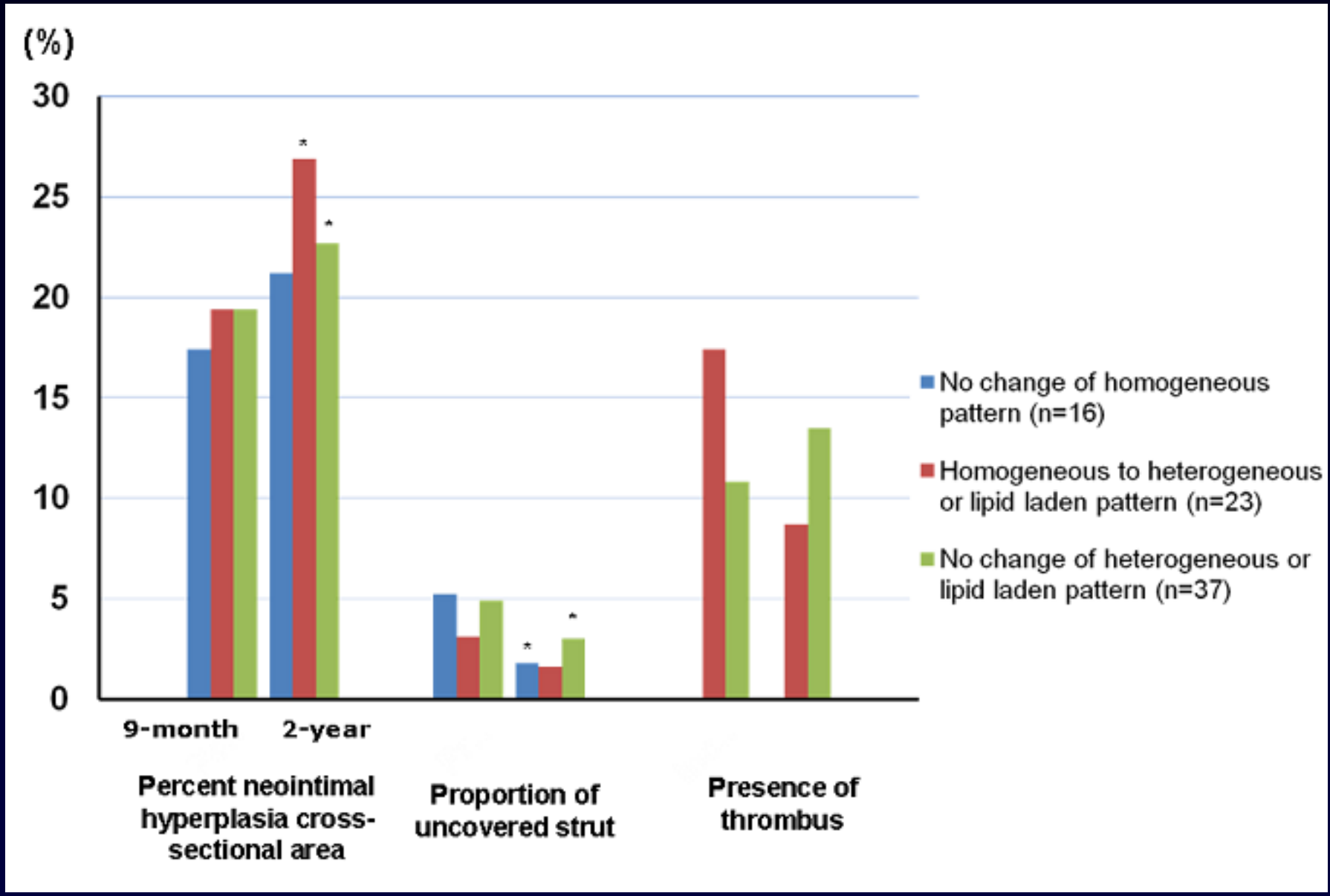
Quantitative OCT analysis

Strut level analysis	9-month	2-year	p
Total strut number	19430	19475	
Mean NIH thickness (μm)	164 ± 95	214 ± 132	<0.001
Percentage of uncovered struts	787 (4.1%)	468 (2.4%)	<0.001
Percentage of malapposed strut	127 (0.7%)	183 (0.9%)	0.24
Percentage of uncovered and malapposed struts	76 (0.4%)	82 (0.4%)	0.89

Qualitative OCT analysis

Qualitative analysis	9-month	2-year	p
Intracoronary thrombus	8 (10.5%)	7 (9.2%)	0.79
Lipid-laden neointima	11 (14.5%)	21 (27.6%)	0.047
TCFA-like neointima	3 (3.9%)	10 (13.2%)	0.04
Heterogeneous pattern	49 (64.5%)	47 (61.8%)	0.73
Neovascularization	34 (44.7%)	56 (73.7%)	<0.001


(%)
100
80
60
40
20
0
1.2%
2.6%
0.2%
1.7%
2.6%
4.7%
1.3%
1.6%
0%
2.0%
10.2%
12.5%
11.8%
17.5%
13.8%
16.3%
4.7%
4.3%
11.7%
8.4%
88.6%
84.9%
88.0%
80.8%
83.6%
79.0%
94.0%
94.1%
88.3%
89.6%
9-month
2-year
Overall
Sirolimus-eluting stent
Paclitaxel-eluting stent
Zotarolimus-eluting stent
Everolimus-eluting stent
Lipid laden neointima
Heterogeneous pattern
Homogeneous pattern

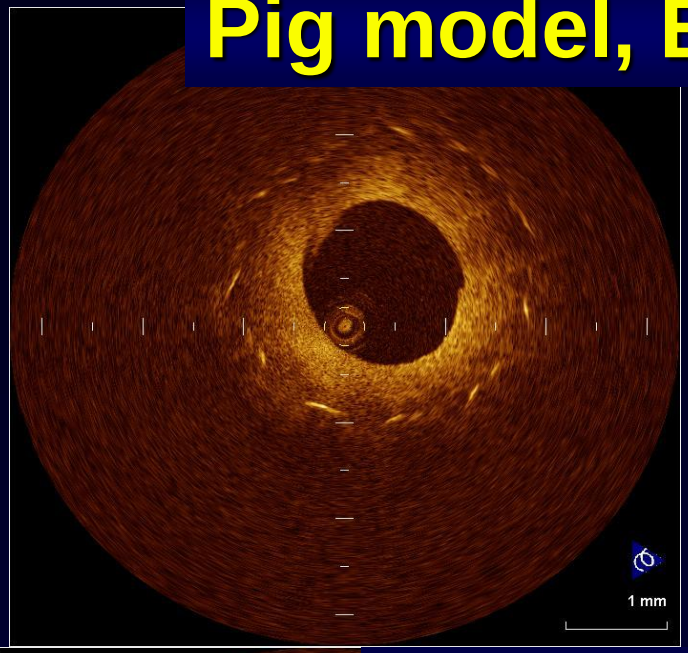

(%)
30
25
20
15
10
5
0
*
*
*
*
9-month
2-year
Percent neointimal hyperplasia cross-sectional area
Proportion of uncovered strut
Presence of thrombus
No change of homogeneous pattern (n=16)
Homogeneous to heterogeneous or lipid laden pattern (n=23)
No change of heterogeneous or lipid laden pattern (n=37)

Summary

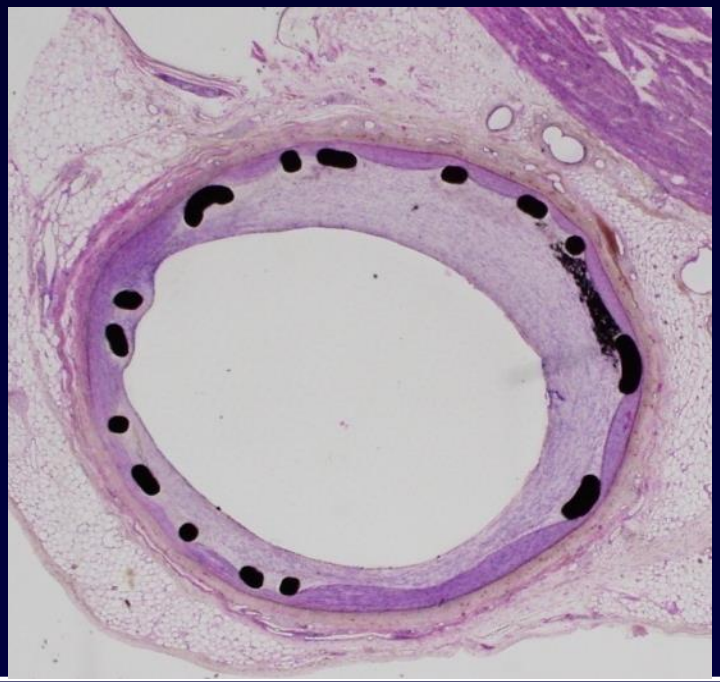
This OCT study suggested that neointimal coverage improved from 9 months to 2 years without significant changes in the incidence of malapposed struts and intracoronary thrombus.

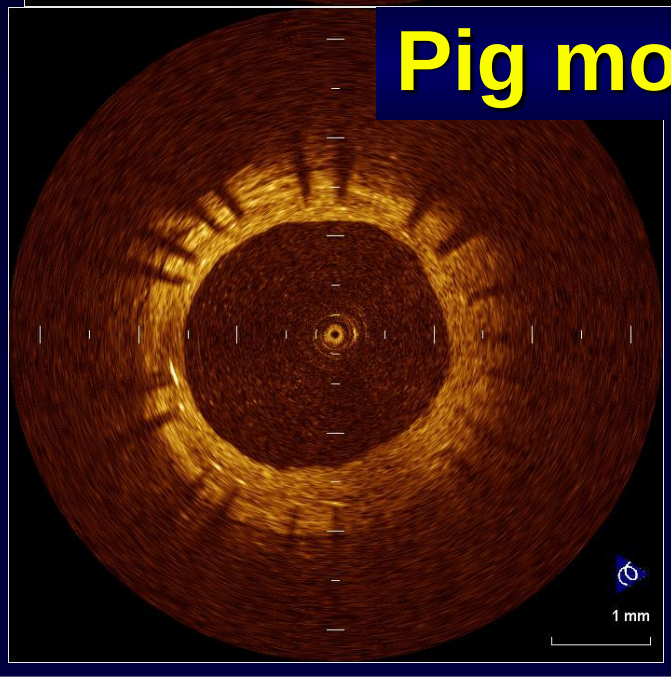
Additionally, in-stent neoatherosclerosis including transformation to lipid-laden neointima might progress during extended follow-up periods after DES implantation.

Pig model, Endeavor



Pig model, BMS





Conclusions

OCT examination could be a useful tools to evaluate neointimal tissue characteristics after DES implantation, which might be associated with the future occurrence of stent thrombosis and in-stent restenosis.


Dreams will
come true