Basics of Invasive Imaging and Hemodynamic Tools for Coronary Artery Disease

Optical Coherence Tomography

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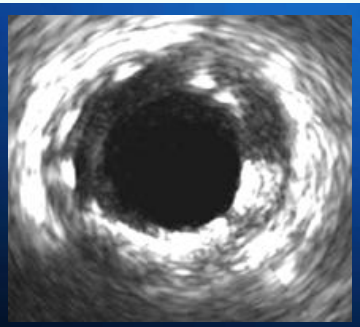
What's OCT?

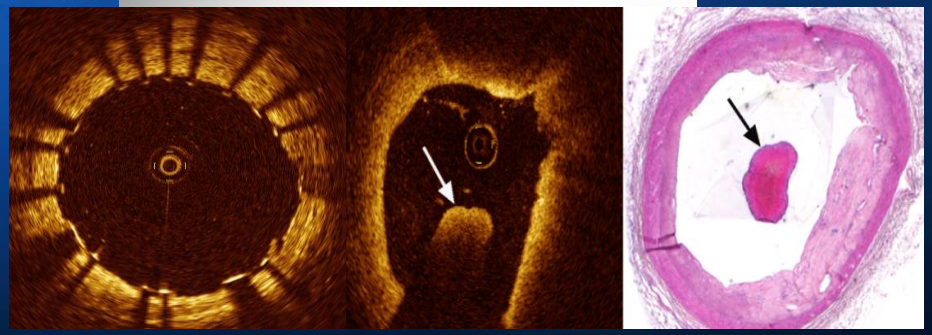
A high-resolution imaging technology that employs near-infrared light to probe micrometer-scale structures inside biological tissues

IVUS

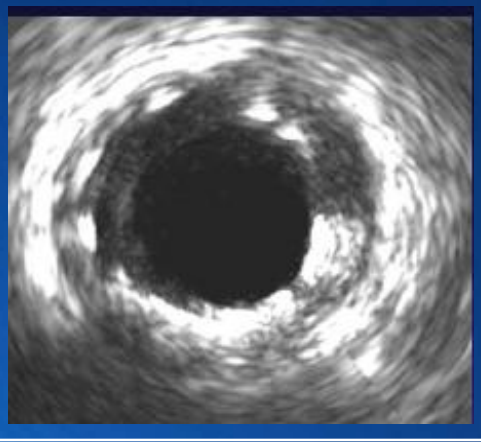


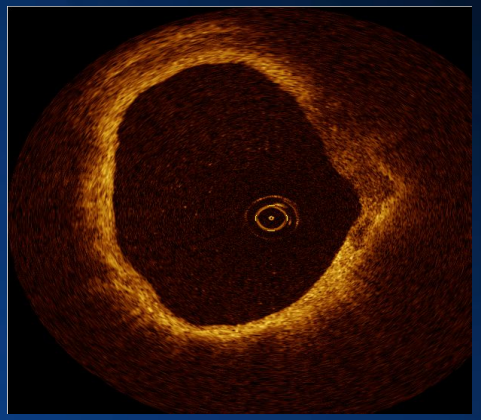
vs.

OCT



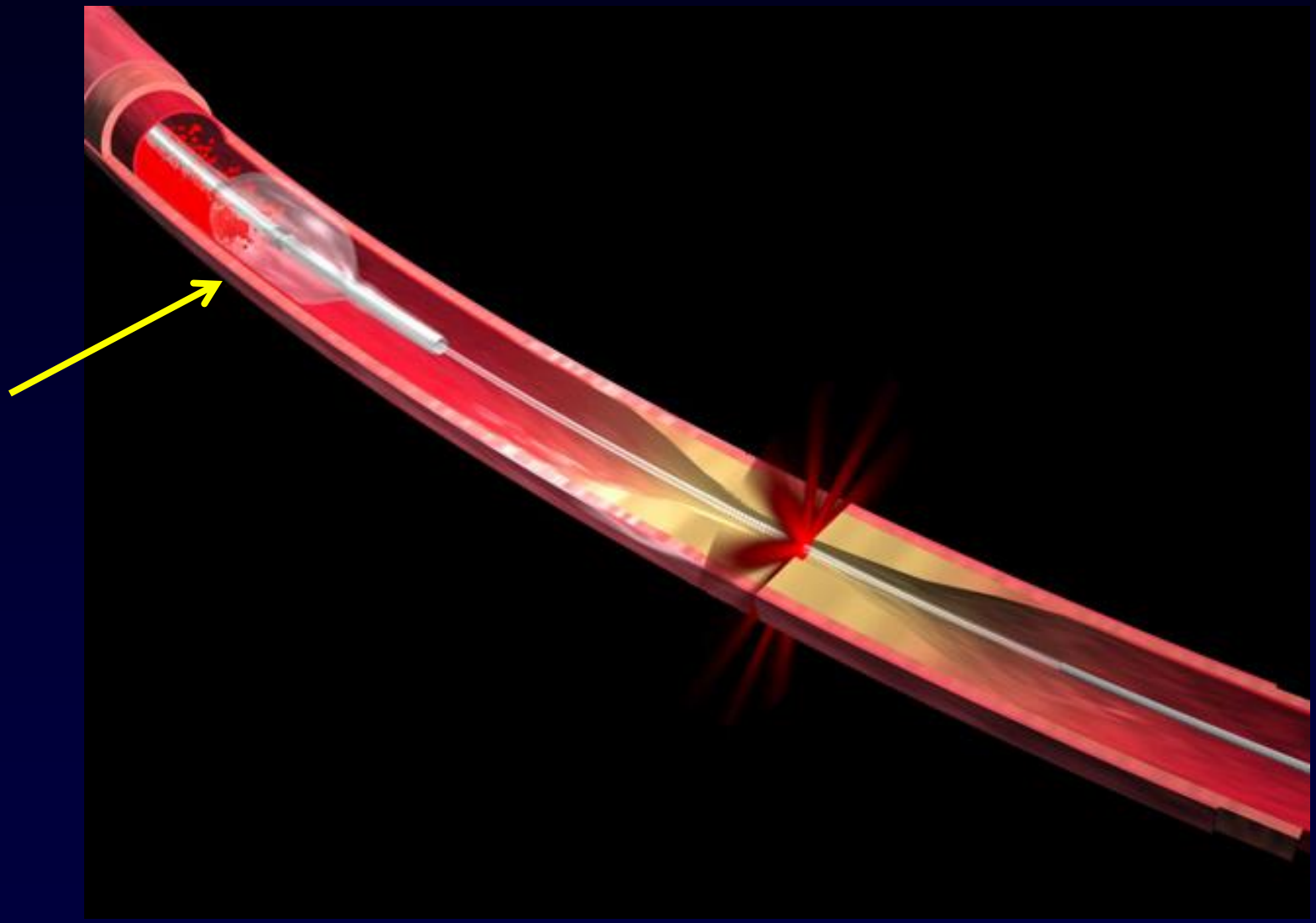
IVUS vs. OCT





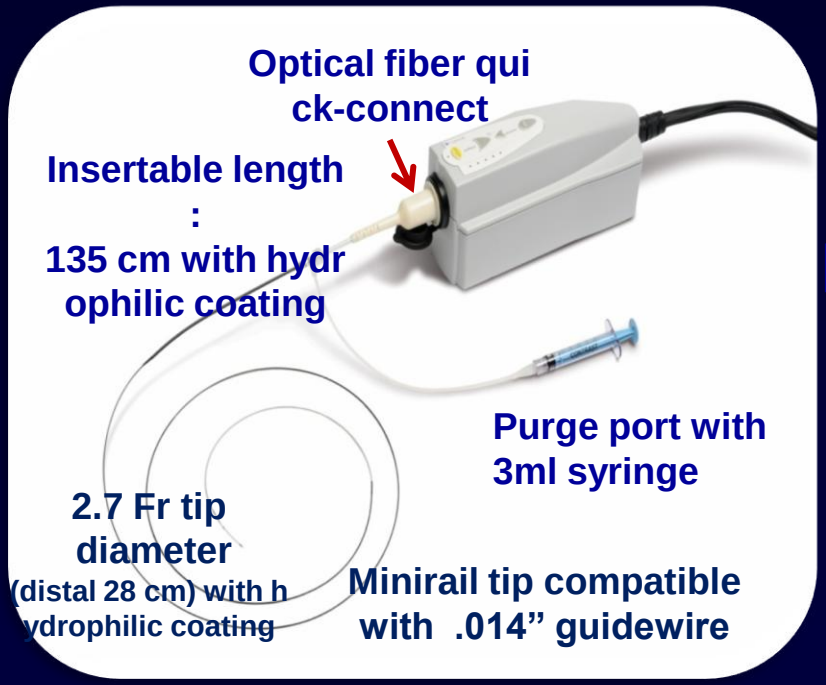
	IVUS	OCT
Resolution	Axial 100-150 μm Lateral 150-300 μm	15-20 μm 25-40 μm
Size of imaging core	0.8 mm	0.4 mm
Dynamic range	40-60 dB	90-110 dB
Frame rate	30 frame/s	15 frame/s

Pervious version; Time Domain OCT



New Version OCT, Frequency Domain OCT; *without balloon occlusion*

New OCT system consisting of console and Imaging Catheter (C7-XR Dragonfly™)



Today's talk

- Plaque characterization by an OCT
- Vulnerable plaque detected by an OCT
- Strut-level evaluation by an OCT
- Neointimal tissue characterization by an OCT

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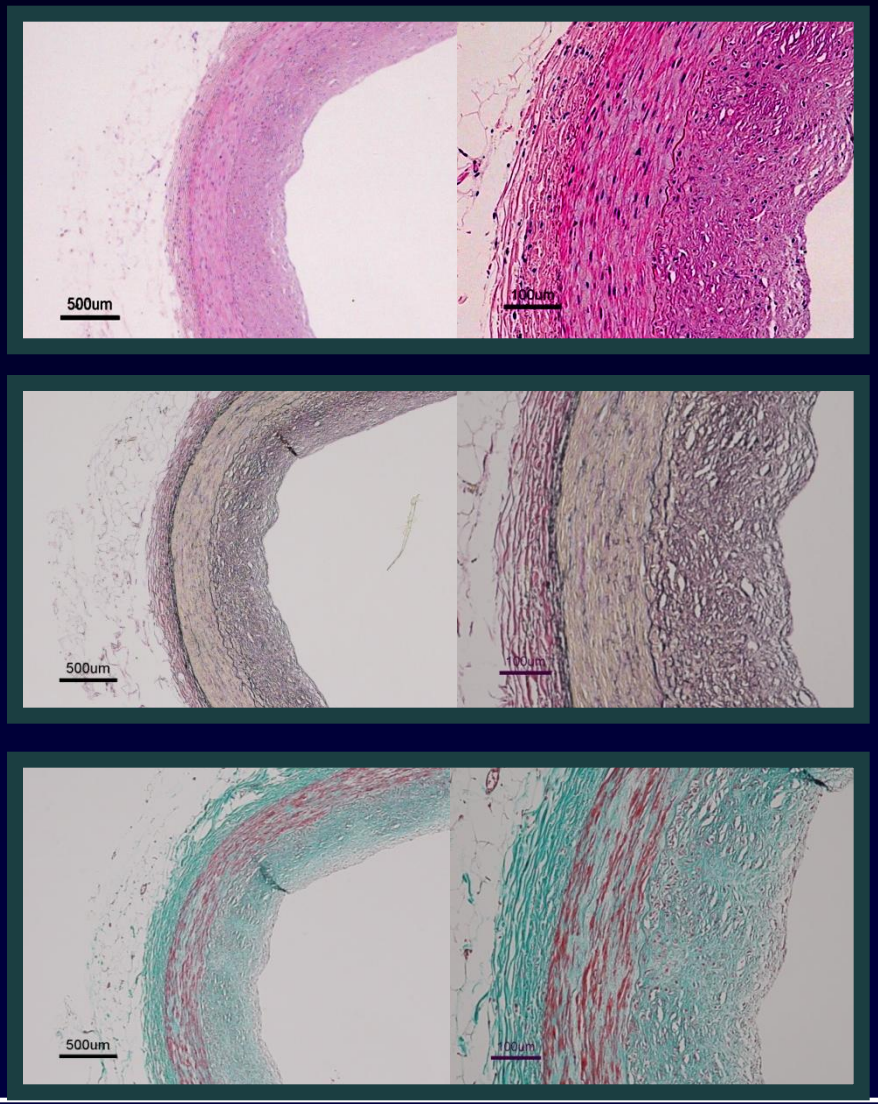
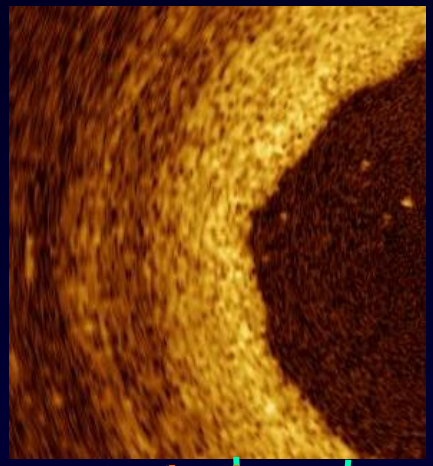
Coronary Artery : three layer

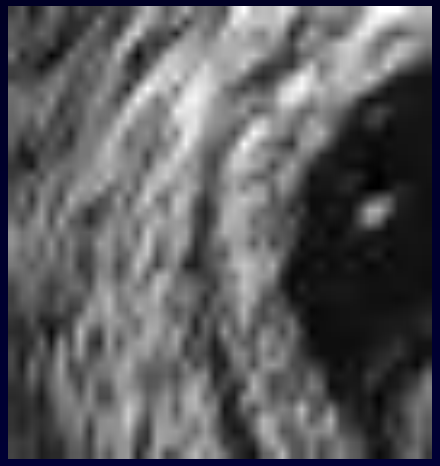




media

intima

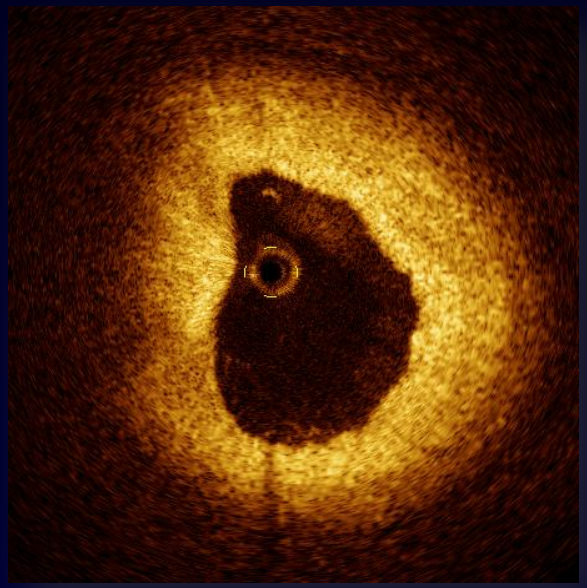
adventitia



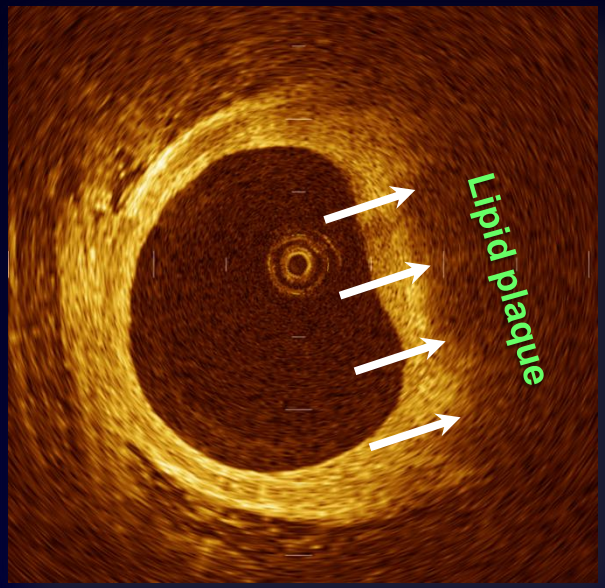
adventitia

Intima-media complex

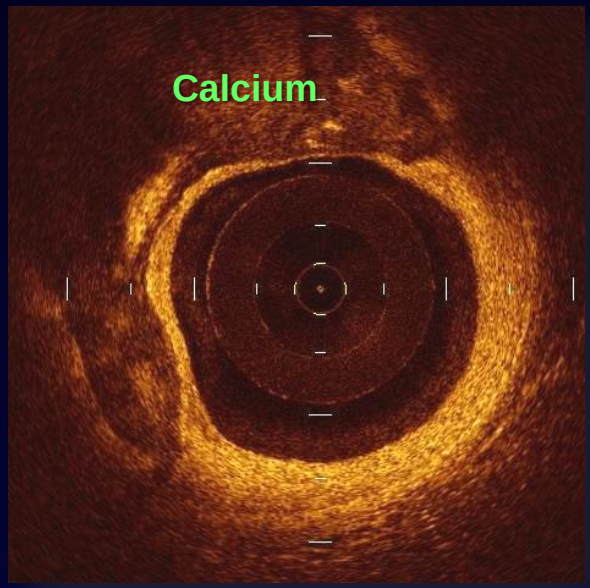
OCT image criteria for atherosclerotic plaque characterization



- **Fibrous plaques;** homogenous, signal-rich regions



- **Lipid-rich plaques;** signal-poor regions with diffuse borders

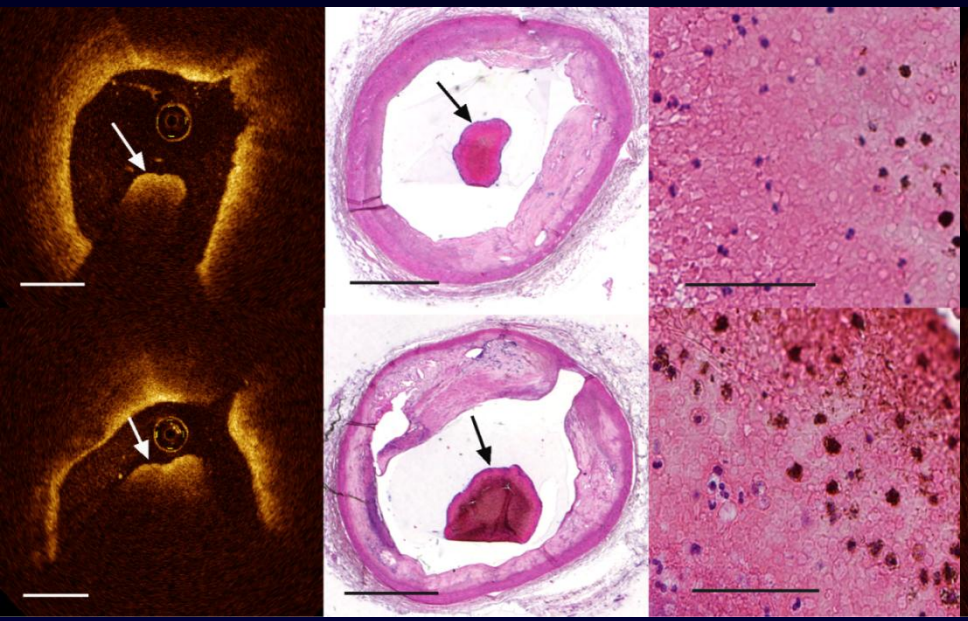


- **Fibrocalcific plaques;** well-delineated, signal-poor regions with sharp borders

Yabushita H, et al. Circulation 2002;106:1640

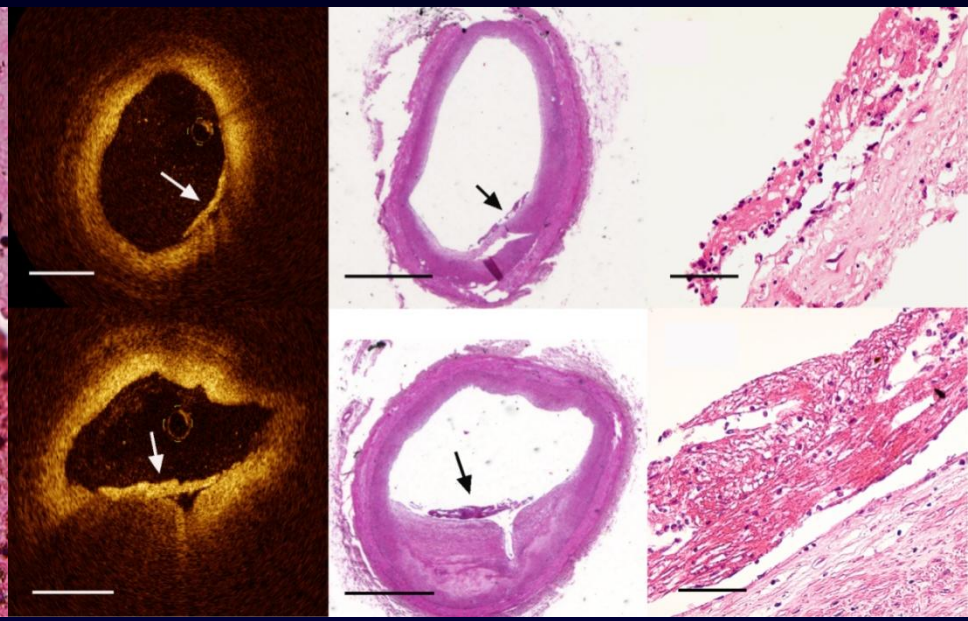
Intracoronary thrombi

Red Thrombus



; consisting mainly of red blood cells
→ identified as high-backscattering protrusions inside the lumen of the artery, with signal-free shadowing

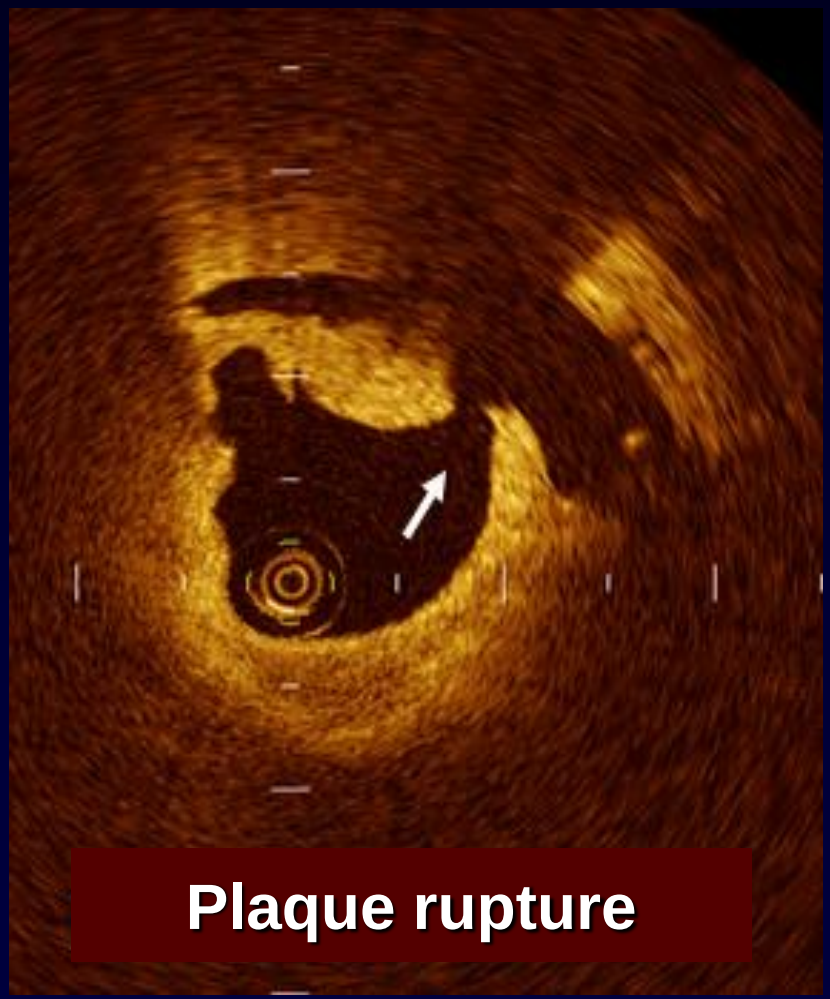
White Thrombus

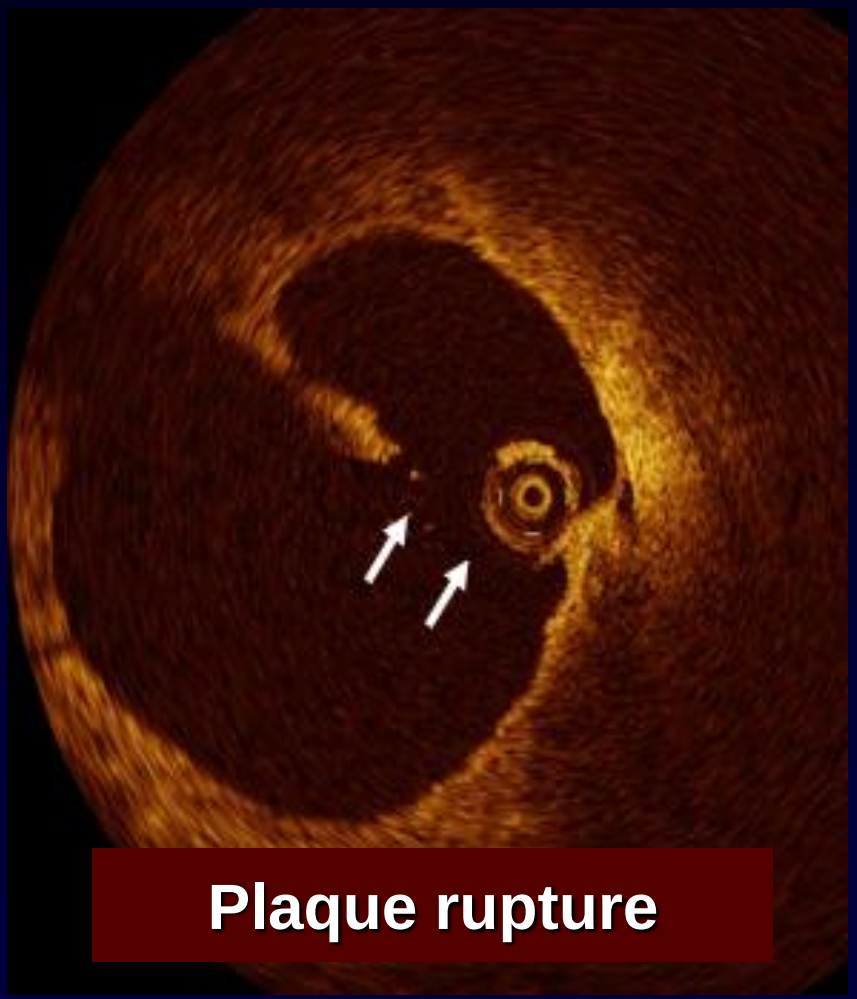


; consisting mainly of platelets and white blood cells
→ identified as signal-rich, low-backscattering projections protruding into the lumen

Akasaka, Am J Cardiol 2006

Ruptured Plaque, Dissection





Kim BK, Hong MK. Curr Cardiovasc Imaging Rep 2010; 3:197–206

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- **Vulnerable plaque detected by an OCT**
- Strut-level evaluation by an OCT
- Neointimal tissue characterization by an OCT

Vulnerable Plaques

thin cap fibroatheroma (TCFA)

Thin cap

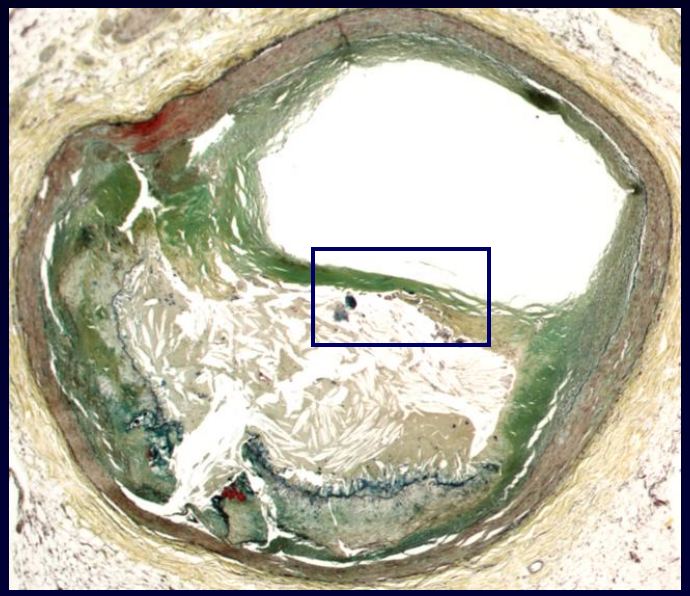
- Fibrous cape < 65 μm
- Collagen depletion (due to loss of smooth muscle)
- Inflammatory cells (macrophage, lymphocyte)

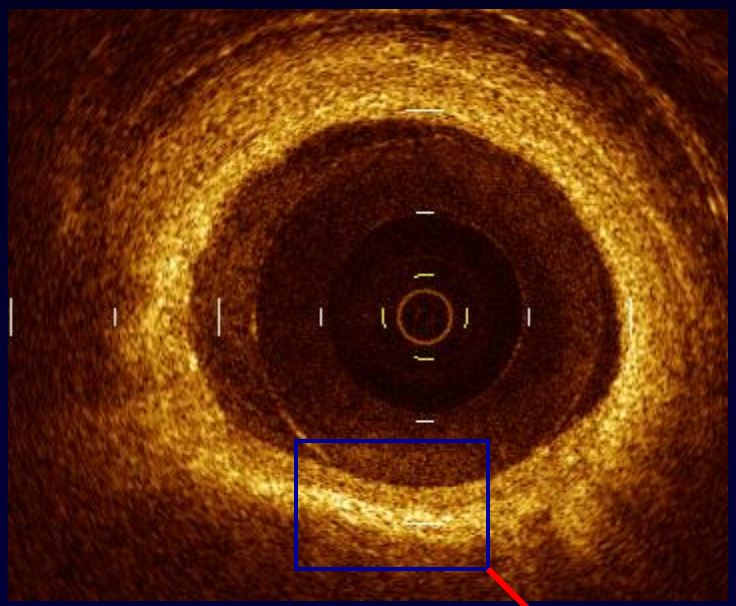
Lipid rich plaque

- Hemorrhagic, necrotic core (size > 1.0 mm^2 and/ or > 10% of the plaque area)
- Angiogenic blood vessels into intima from the adventitia

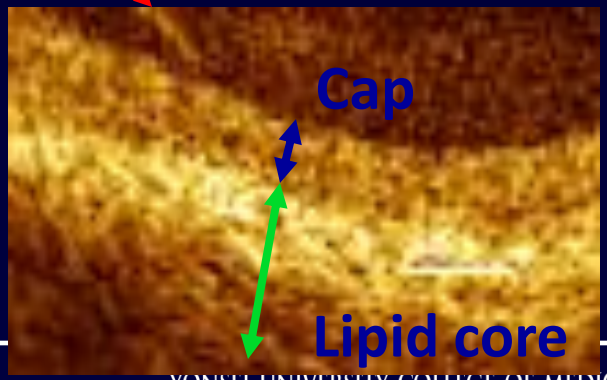
Thin Cap Fibroatheroma (TCFA)

1. Thin fiber cap; 2. large necrotic core; 3. macrophage infiltration

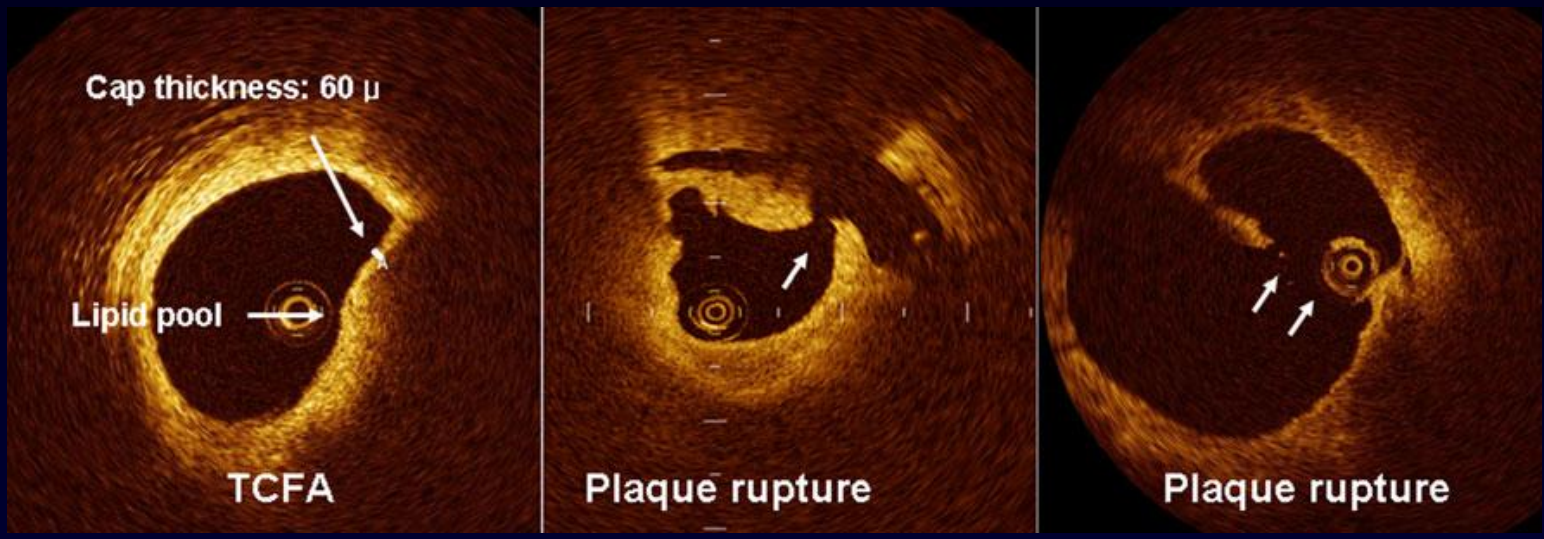




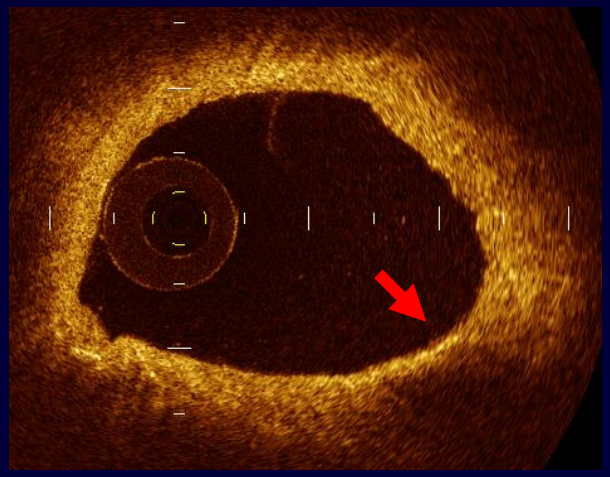
TCFA without macrophage infiltration:
Two-layer structure.
Boundary formed by the cap and the underlying core

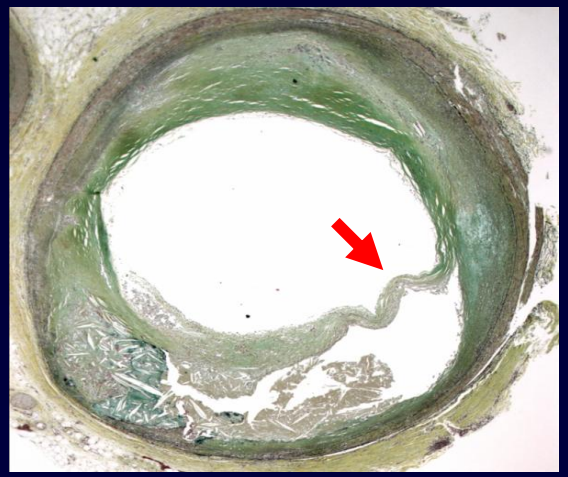


OCT images of TCFA and plaque rupture



Kim BK, Hong MK. Curr Cardiovasc Imaging Rep 2010; 3:197–206





Assessment of Culprit Lesion Morphology in AMI; Ability of OCT Compared with IVUS and Coronary Angioscopy

Fibrous cap disruption

- 30 patients with AMI, and analyzed the culprit lesions by OCT, Angioscopy, and IVUS.

Findings	OCT (n=30)	Angioscopy (n=30)	IVUS (n=30)	p-value
Fibrous cap disruption	**22 (73%)**	14 (47%)	12 (40%)	0.021
Fibrous cap erosion	**7 (23%)**	1 (3%)	0 (0%)	0.003
Thrombus	**30 (100%)**	30 (100%)	10 (33%)	<0.001

→ Only OCT could estimate the fibrous cap thickness

Kubo K, et al. JACC 2007; 50:933

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Traditional OCT image analysis

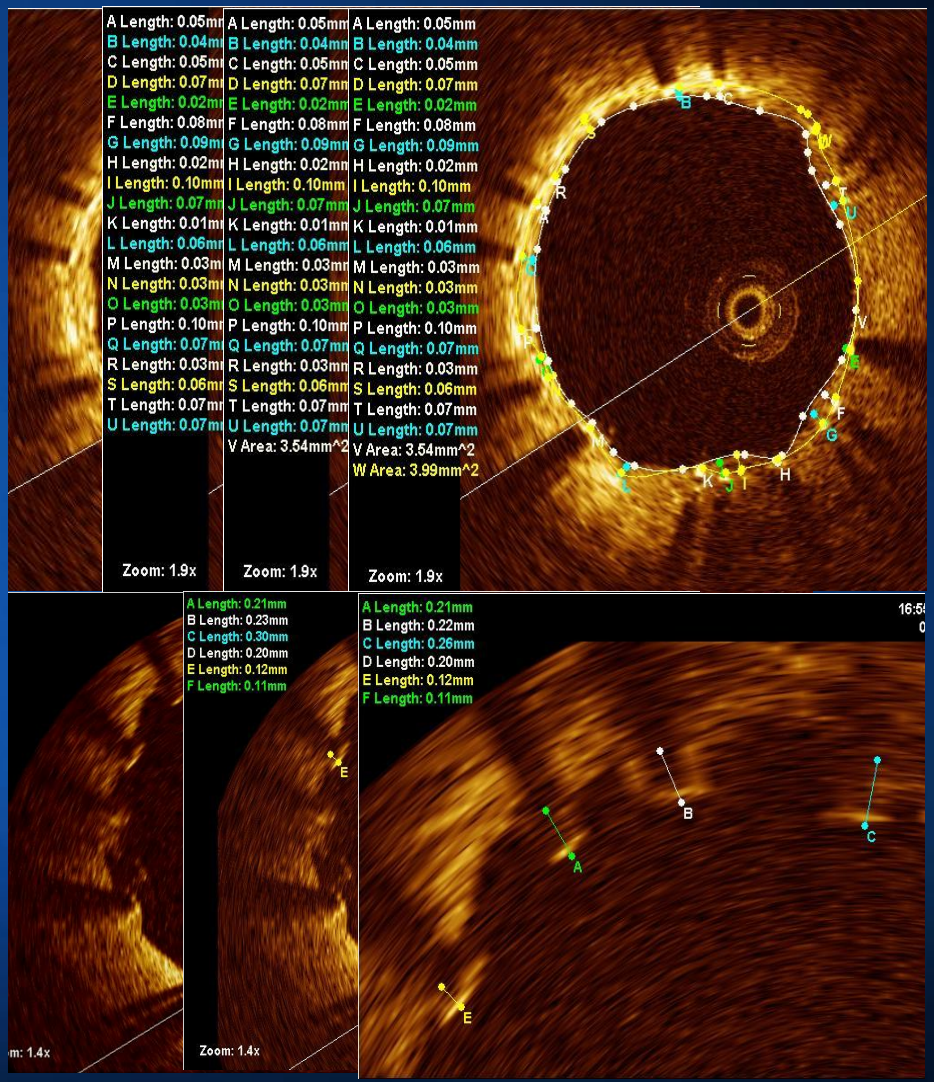
Analysis of cross-sectional OCT images at a 1-mm interval (every 15 frames).

1. Neointimal thickness

The distances between the endo-luminal surface of neointimal and the strut reflection

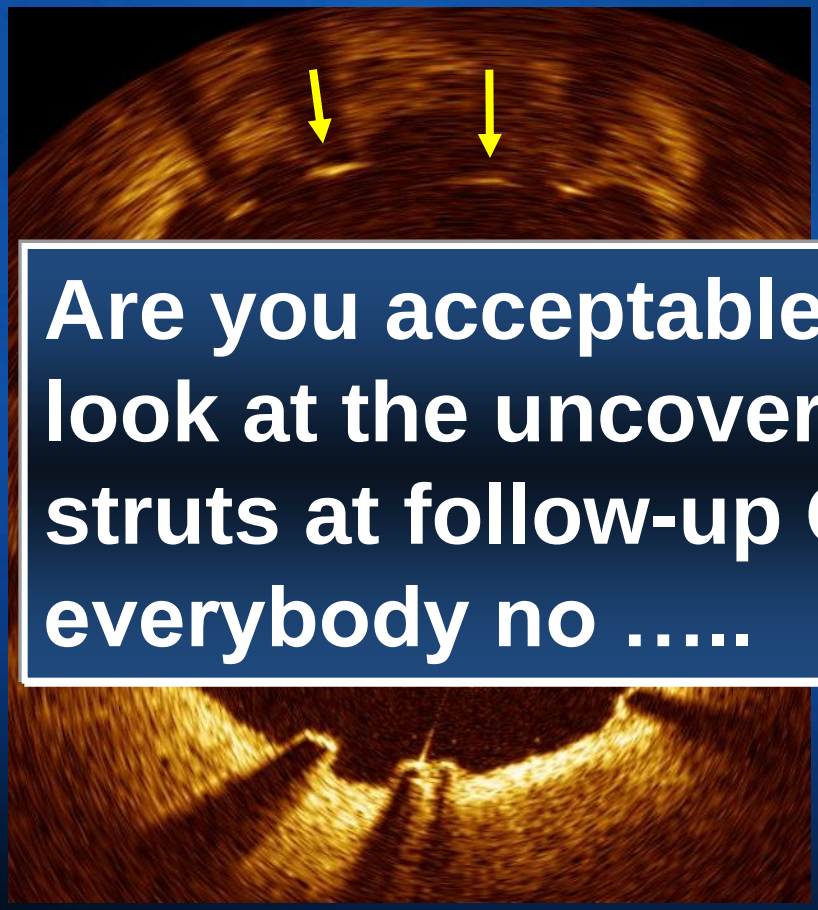
2. Stent apposition

The distances between the endo-luminal surface of the strut reflection and the vessel wall



9 months FU OCT - Cypher Stent

Malapposed and uncovered struts



Covered struts with neointima

Are you acceptable or OK when you look at the uncovered or malapposed struts at follow-up OCT ? Maybe everybody no …..

Pathological Correlates of Late Drug-Eluting Stent Thrombosis

Strut Coverage as a Marker of Endothelialization

The most powerful histological predictor of stent thrombosis was endothelial coverage.

The best morphometric predictor of LST was the ratio of uncovered to total stent struts.

The odds ratio for thrombus with a ratio of uncovered to total struts > 30% ⇒ 9.0 (95% CI , 3.5 to 22)

Finn AV, et al. Circulation 2007;115:2435-41

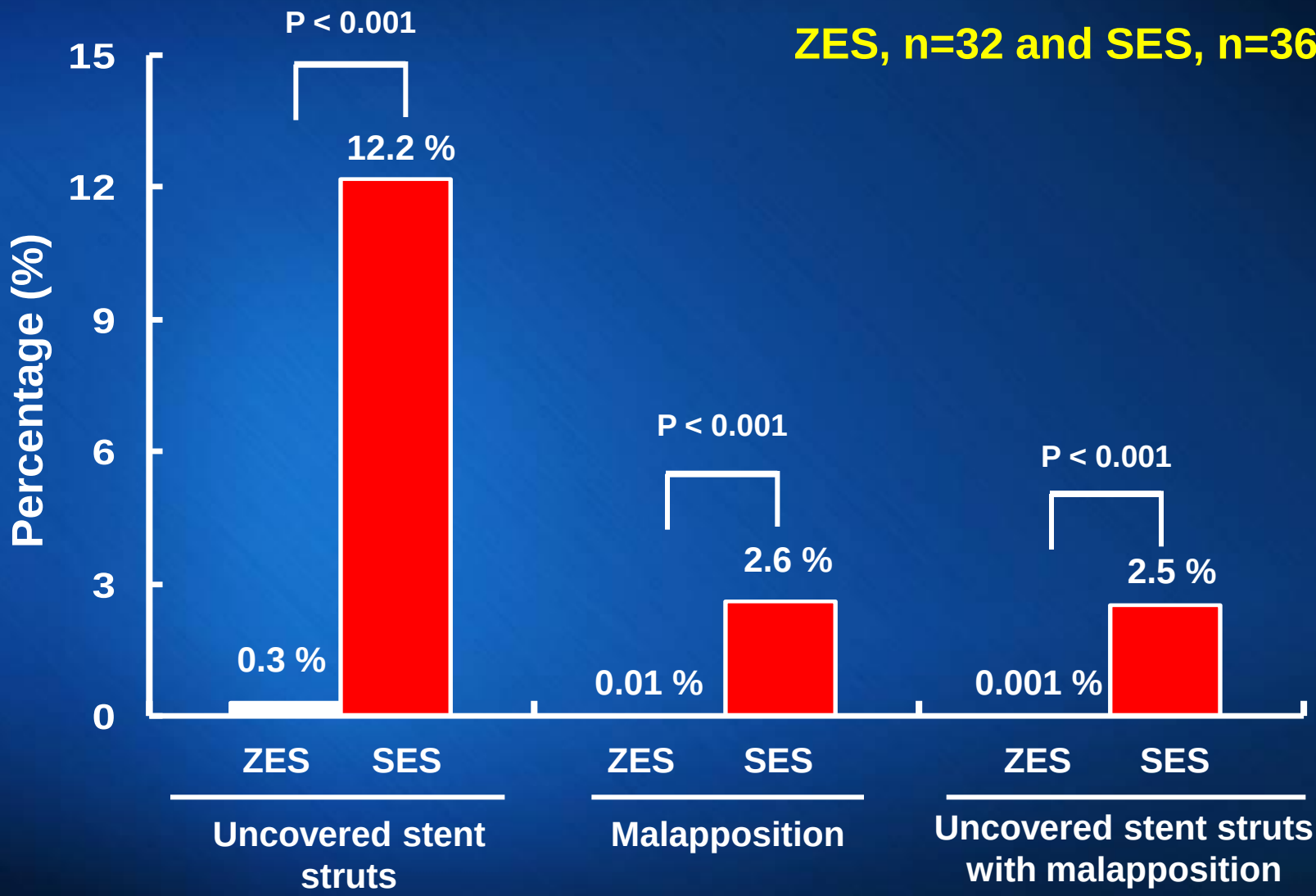
OCT definition

Uncovered strut = Neointimal hyperplasia (NIH) thickness of 0 μm

The percentage of uncovered struts = (number of uncovered struts/total number of struts in all cross-sections of the lesion) × 100

OCT Evaluation of ZES at 9 Month FU

ZES, n=32 and SES, n=36



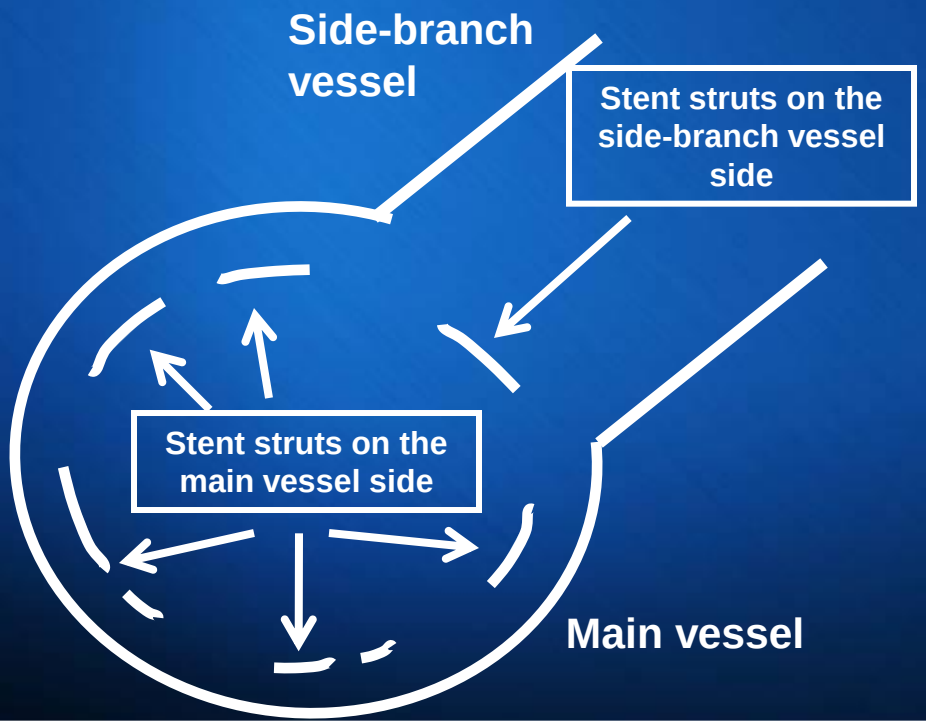
Kim JS, et al. Heart 2009;95:1907-12

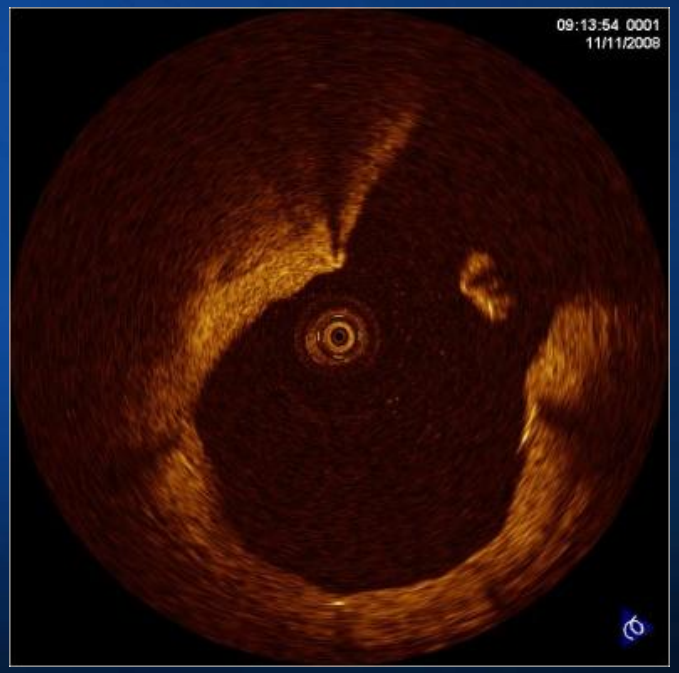
Stent struts on Side Branch ?

Neointimal Coverage on the DES Struts Crossing the Side-Branch Vessels: an OCT Study

Her AY, Hong MK et al, Am J Cardiol 2010;105:1565-69


0.067 mm
Main vessel
Stent
Side-branch vessel


Side-branch vessel
Stent struts on the side-branch vessel side
Stent struts on the main vessel side
Main vessel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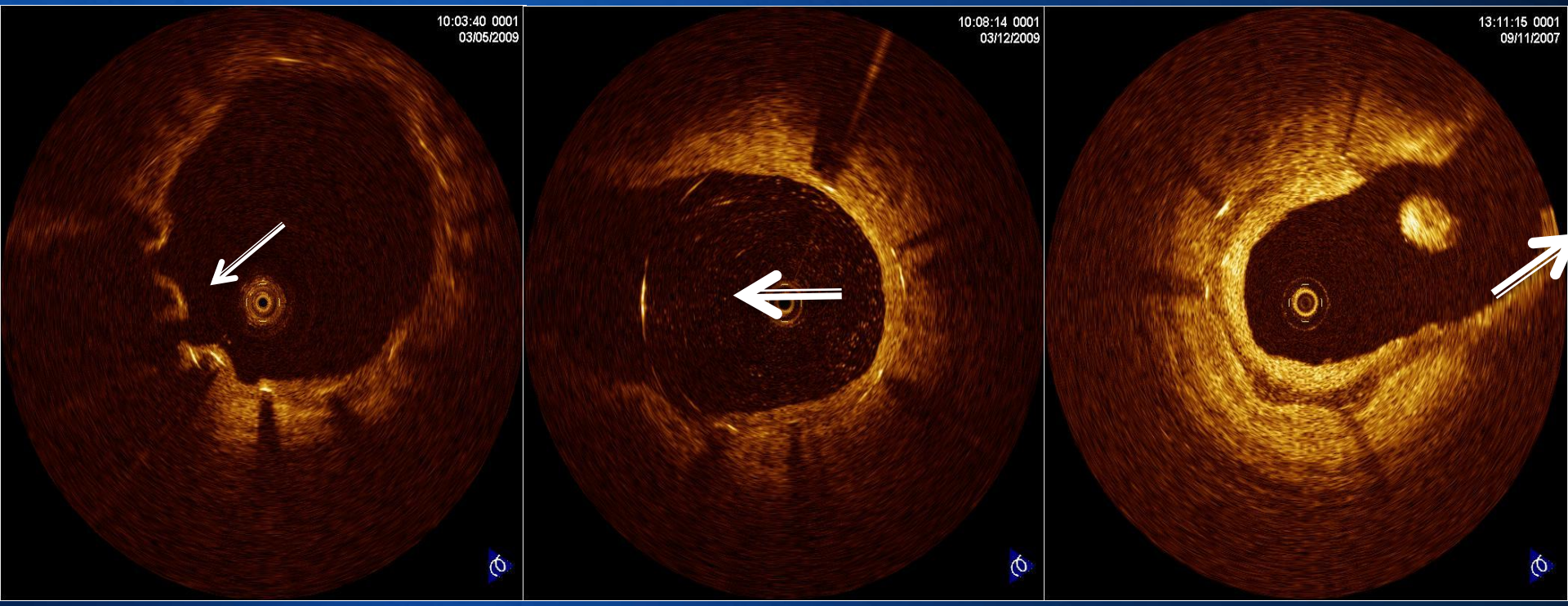
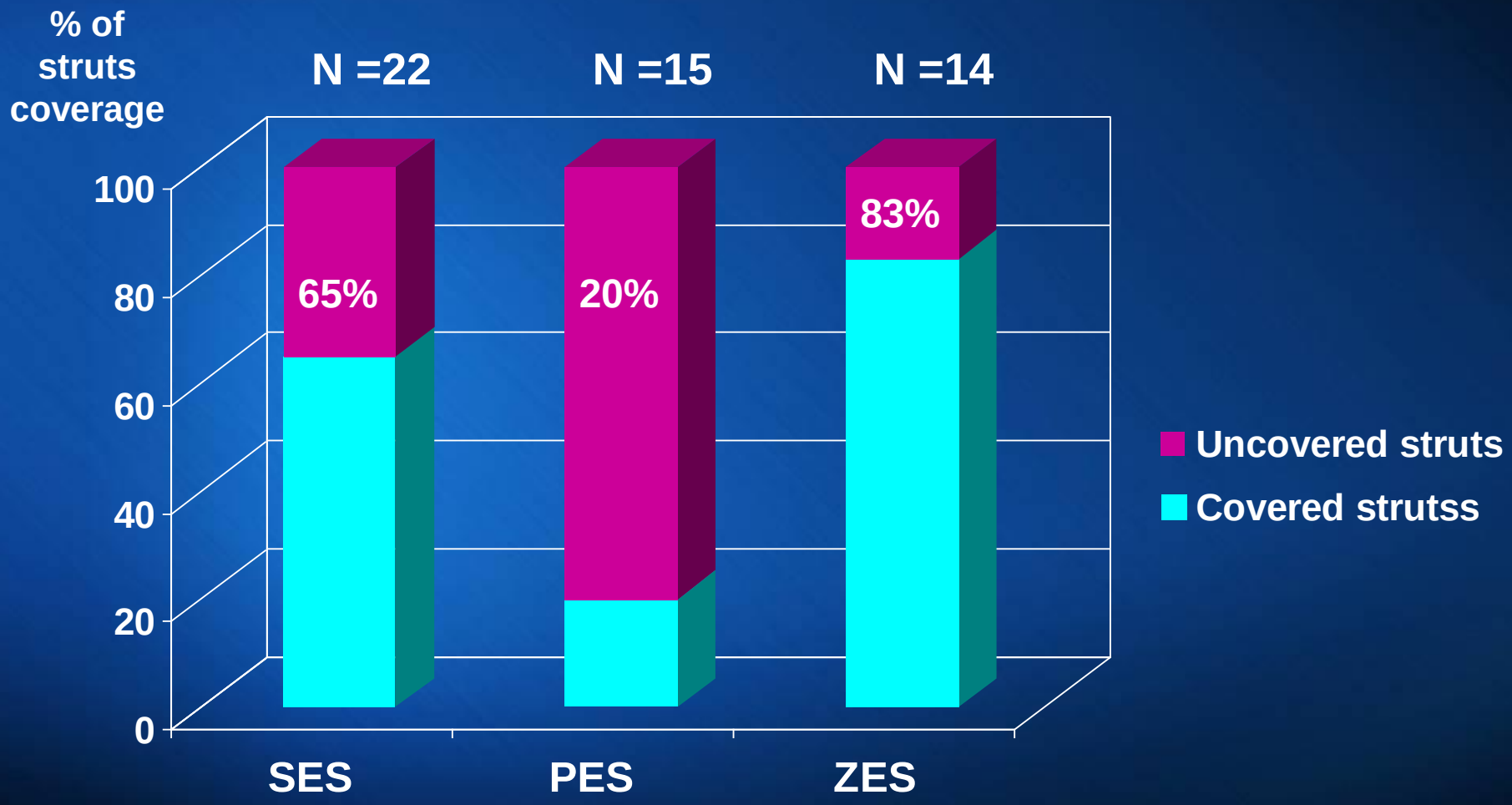
11/11/2008

Comparison of neointimal thickness on unapposed struts crossing the side-branch



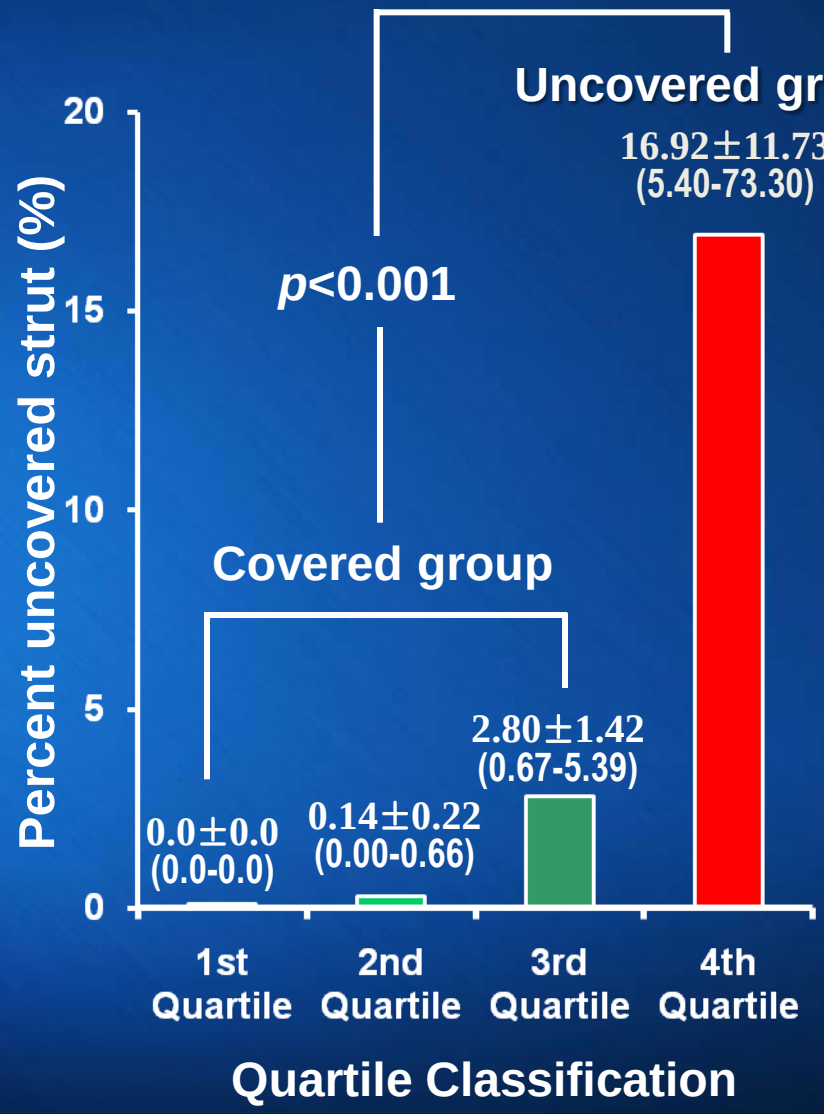
Cypher (SES) Taxus (PES) Endeavor (ZES)

Composition of struts coverage crossing the side branch



Her AY, Hong MK, et al. *Am J Cardiol* 2010;105:972-976

Major determinants of uncovered struts

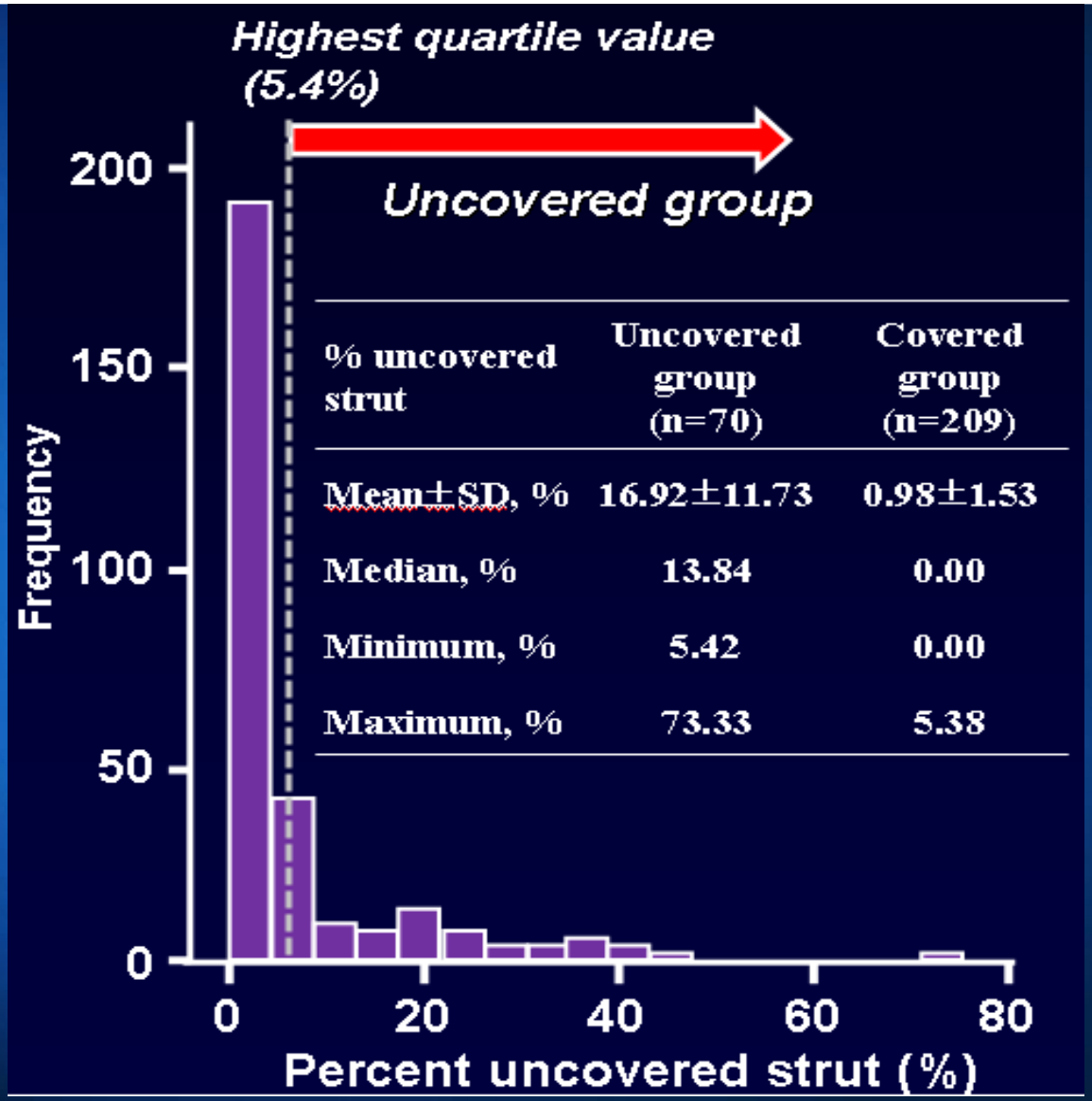


n=279 lesions,

70 uncovered and 209 covered groups

Kim BK, Hong MK, *Int J Cardiovasc Imaging (in press)*

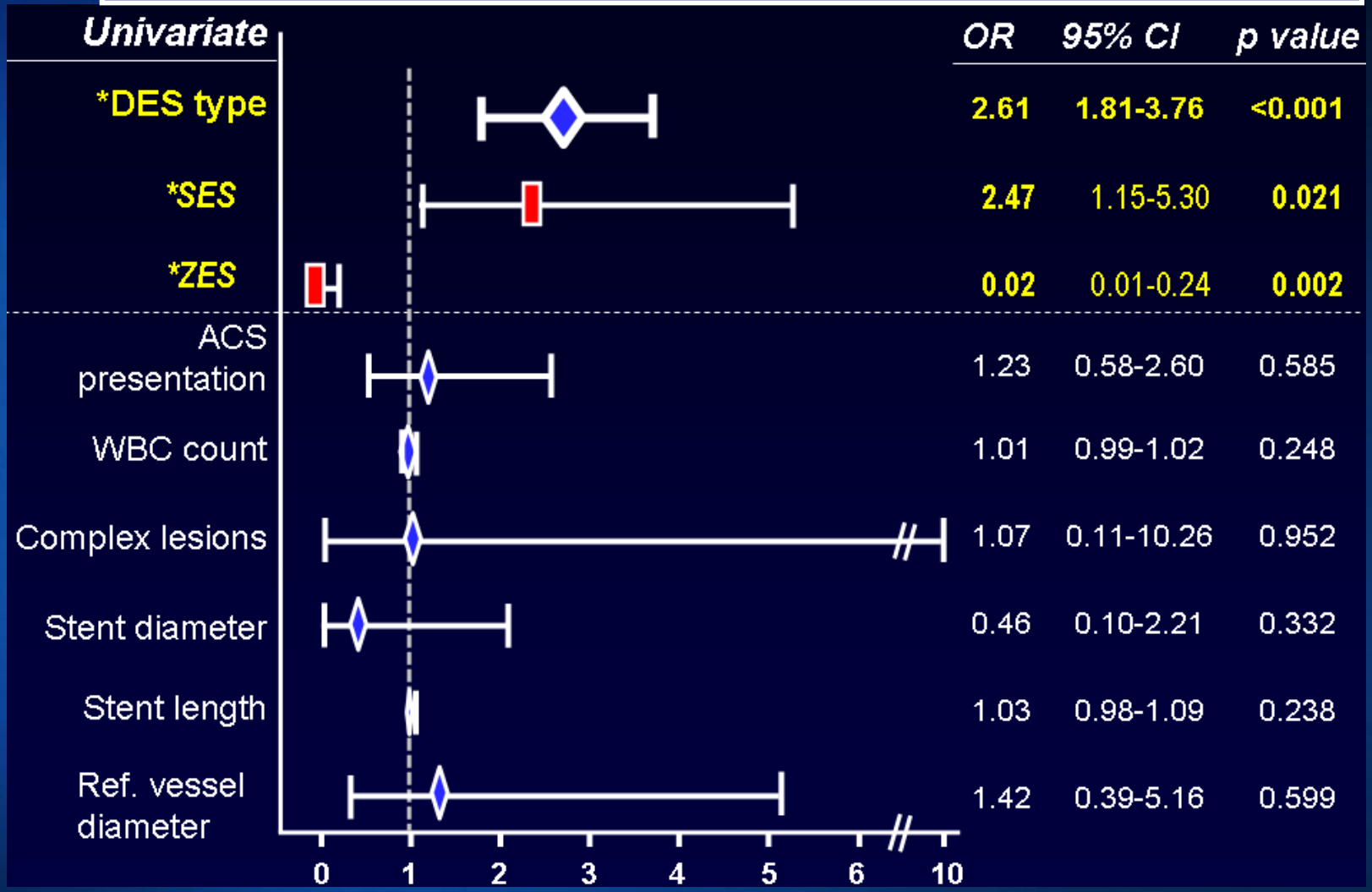
Major determinants of uncovered stent struts



% uncovered strut	Uncovered group (n=70)	Covered group (n=209)
Mean±SD, %	16.92±11.73	0.98±1.53
Median, %	13.84	0.00
Minimum, %	5.42	0.00
Maximum, %	73.33	5.38

Kim BK, Hong MK, *Int J Cardiovasc Imaging (in press)*

Major determinants of uncovered struts



Kim BK, Hong MK, *Int J Cardiovasc Imaging (in press)*

Serial Changes of Tiny Stent Malapposition Not Detected by Intravascular Ultrasound (Follow-up Optical Coherence Tomography Study)

Tiny post-SM: SM not detected by IVUS, but be visualized with OCT.

Study population

- 42 patients from the Yonsei OCT registry :
- Both post-stent & follow-up OCT examination after DES implantation

Initial tiny post-SM was found in 26 (62%) of 42 patients

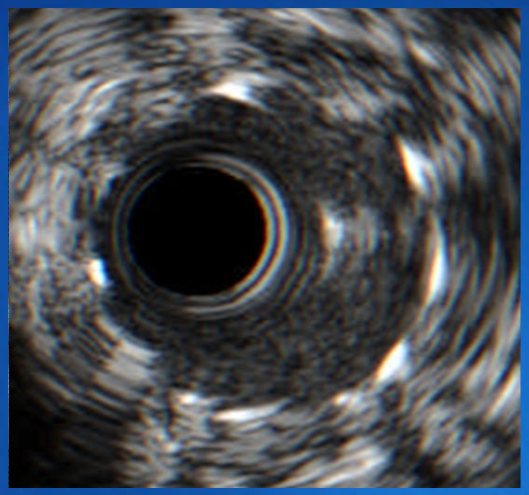
Kim WH, Hong MK et al, Clin Res Cardiol 2010;99:639-644

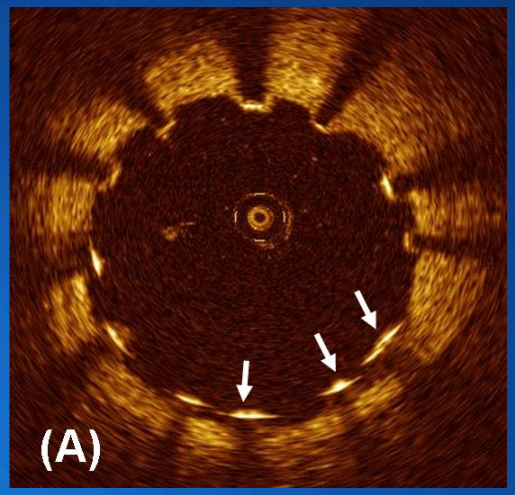
OCT measurements (n=26)

	Immediate post-stenting	Follow up	P Value
Number of analyzed stent struts	5615	5474	
Mean length of analyzed segment (mm)	22.8 ± 6.2	22.9 ± 5.1	0.22
Length of malapposition segment (mm)	2.3 ± 2.3	0.1 ± 0.3	<0.001
Num. of malapposed struts (n)	27 ± 26	2 ± 5	<0.001
% of malapposed struts (%)	12.2 ± 11.0	1.0 ± 2.2	<0.001
Mean stent area at the segment with malapposed struts (mm^2)	7.37 ± 1.71	7.39 ± 1.65	0.08
Mean extra-malapposition area (mm^2)	0.35 ± 0.16	0.04 ± 0.11	<0.001
Largest extra-malapposition area (mm^2)	0.54 ± 0.46	0.07 ± 0.18	<0.001
Mean NIH thickness at the segment with malapposed struts (mm)		0.15 ± 0.1	

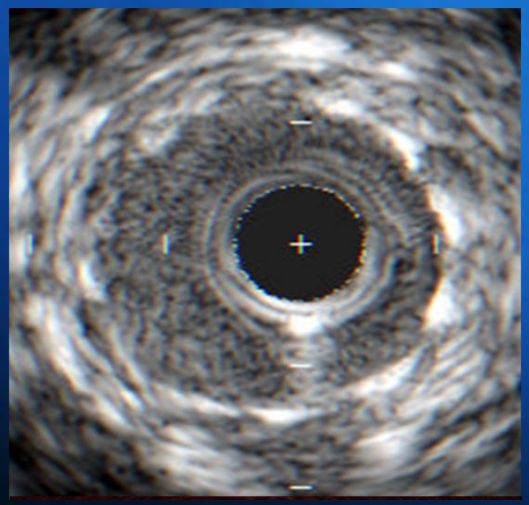
Kim WH, Hong MK et al, Clin Res Cardiol 2010;99:639-644

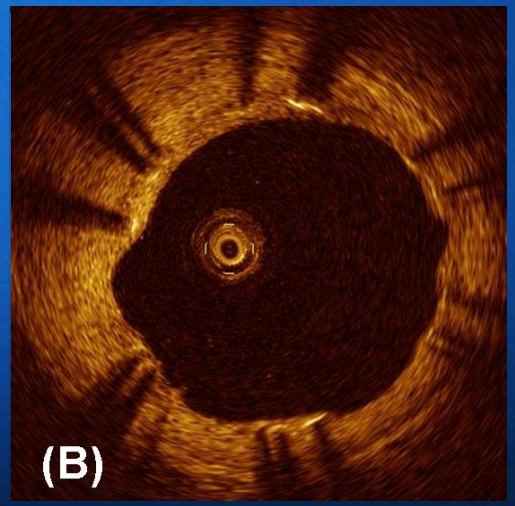
Corresponding images of IVUS & OCT





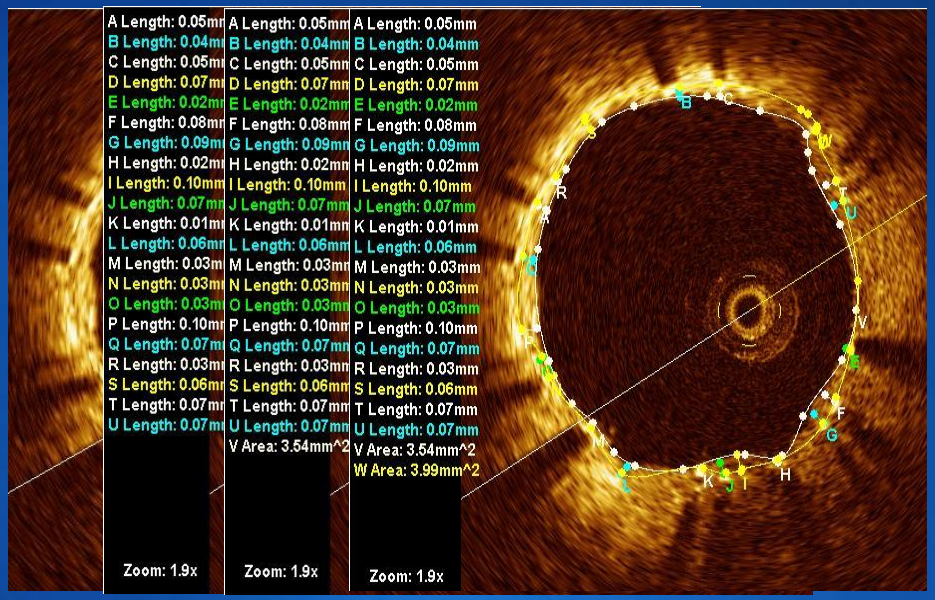
(A) Malapposed struts of an SES. 3 stent struts seem to float into the lumen with an extra-stent area (arrows). Small-sized post-SM is not be detected by IVUS, but be clearly visualized with OCT image follow-up OCT

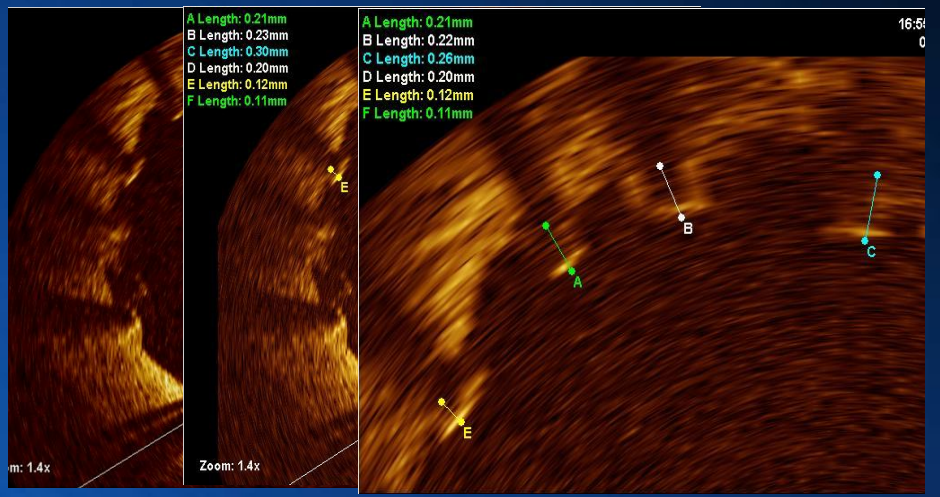




(B) Follow-up OCT images shows that all strut surfaces is covered by neointima

Is the traditional OCT analysis sufficient ?



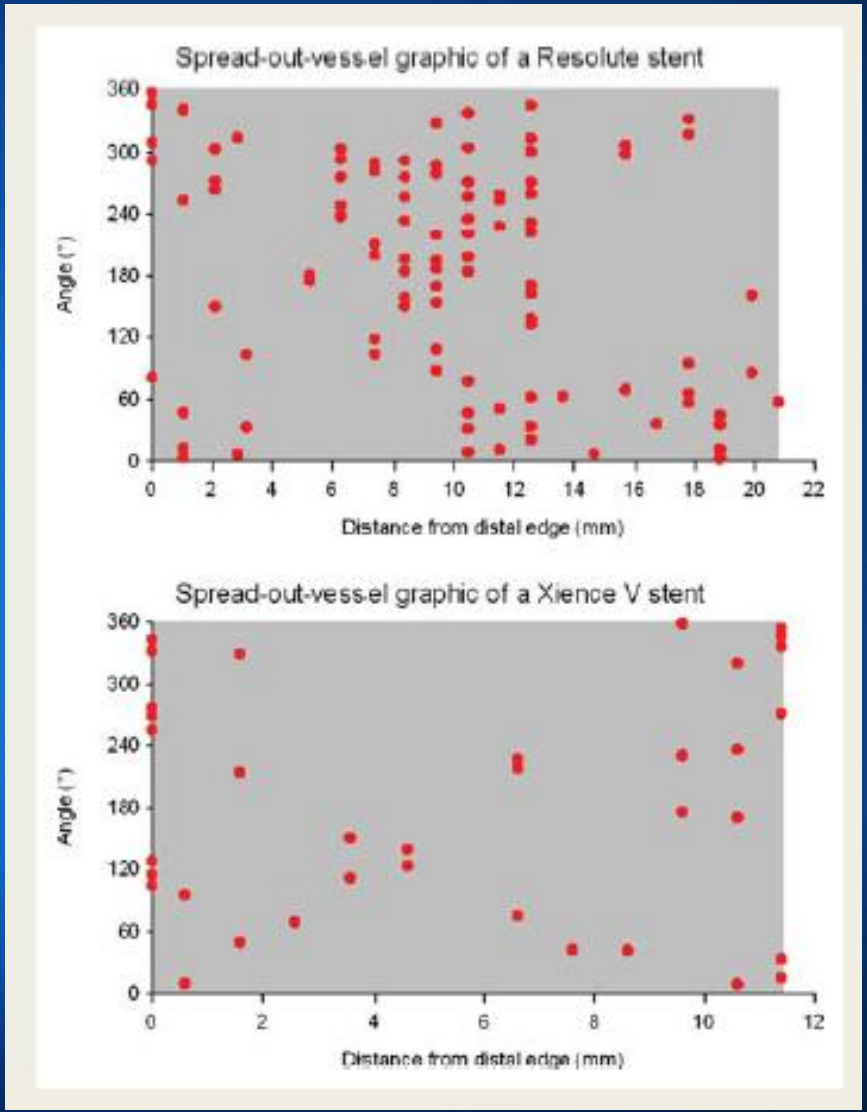


Neointimal thickness

Stent apposition

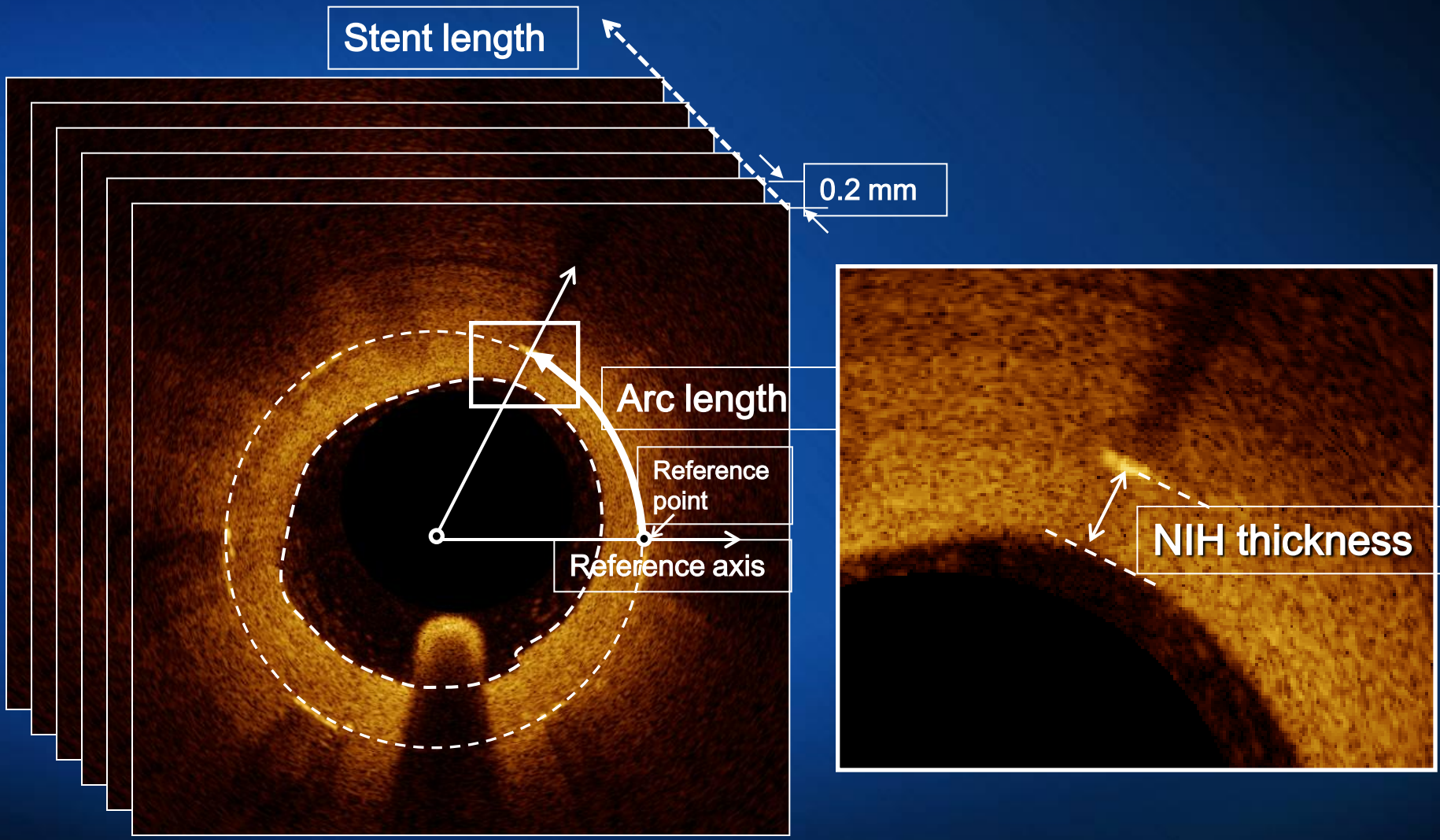
What are the spatial distributions of uncovered or malapposed struts ?

Spread-out-vessel graphic



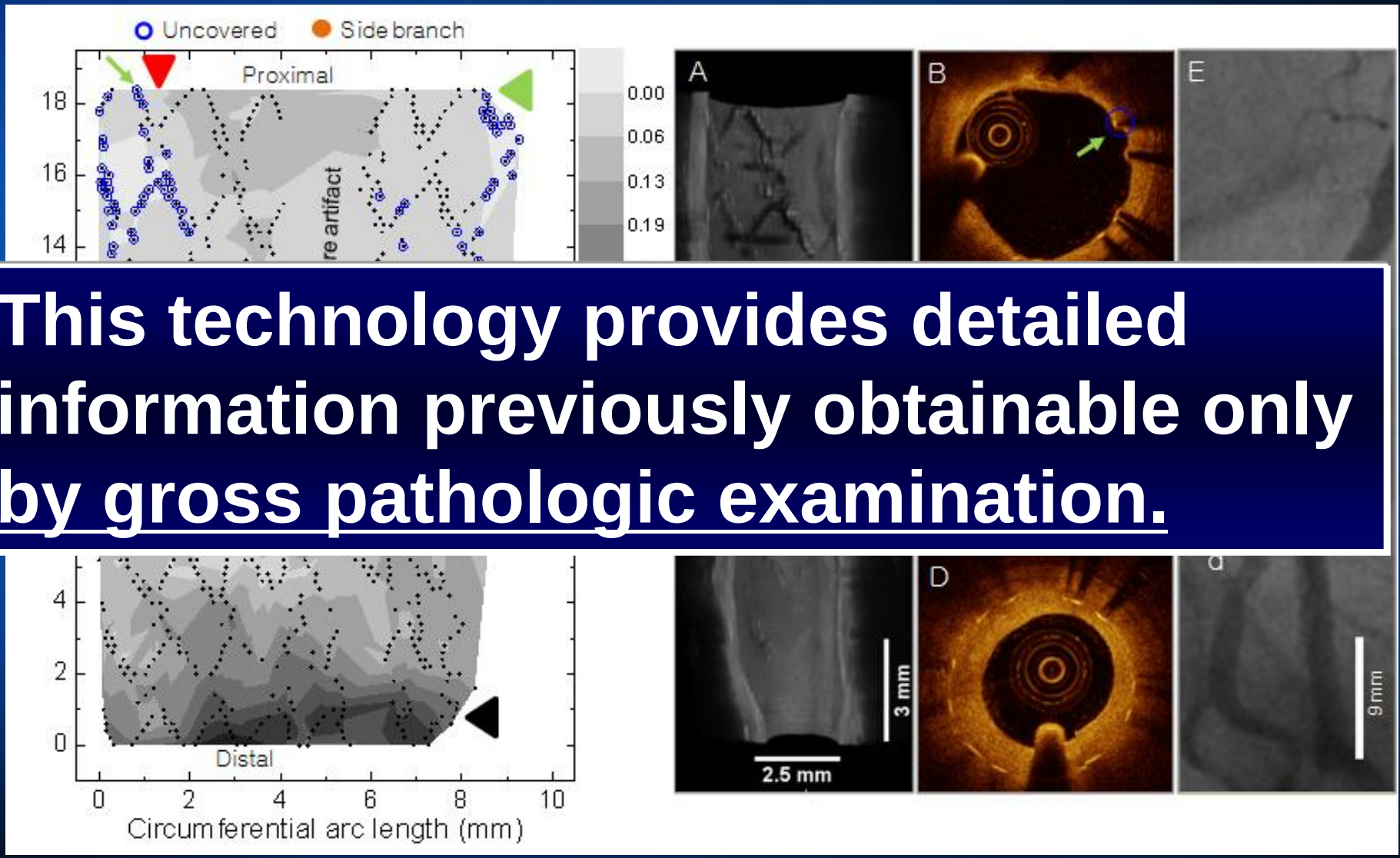
Gutie´rrez-Chico JL et al, *Eur Heart J* 2011; 32: 2454-2463

Creation of contour map



Data (x, y, z) = Data (arc length, stent length, NIH thickness)

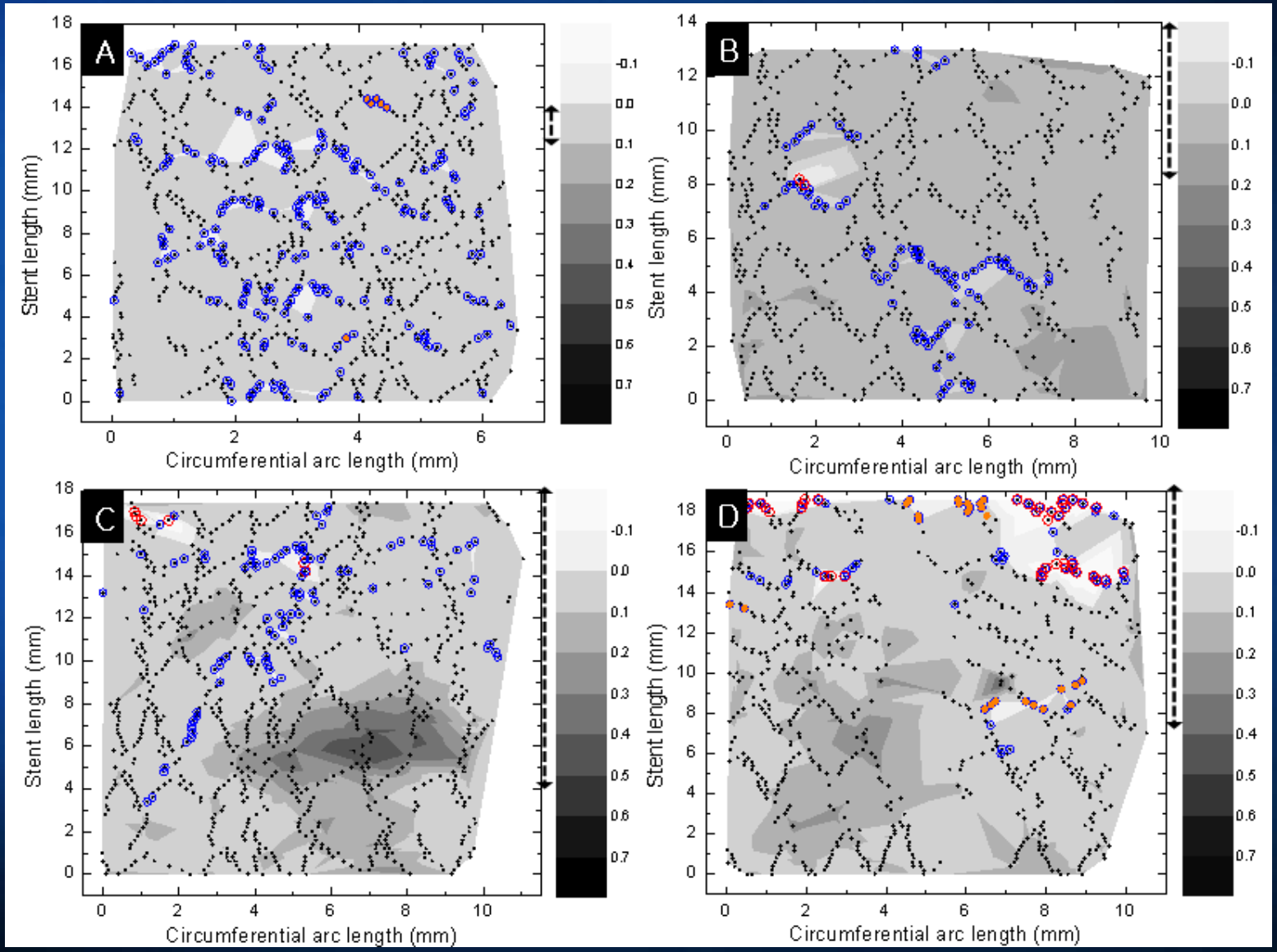
Creation of contour map



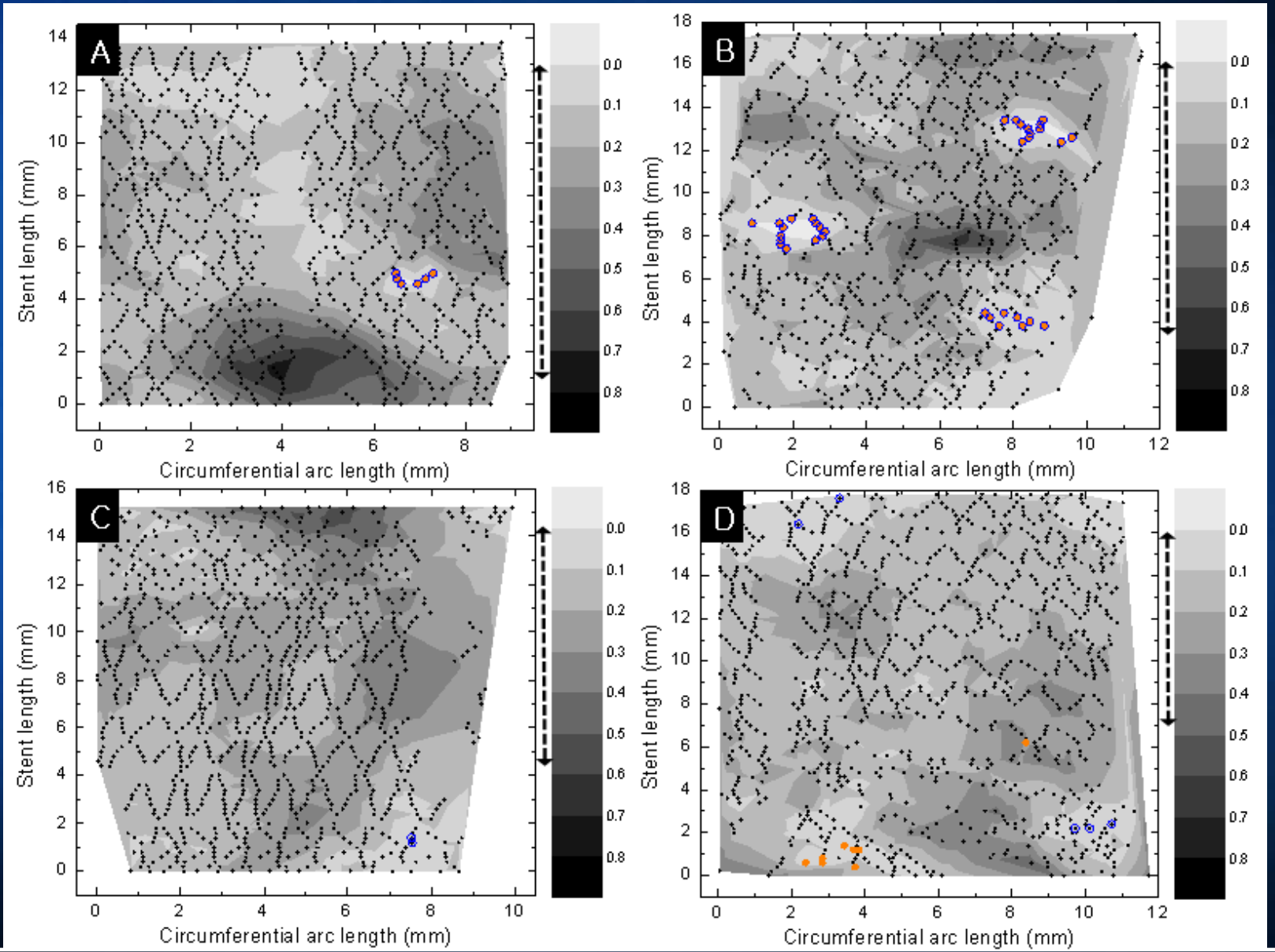
This technology provides detailed information previously obtainable only by gross pathologic examination.

SES

Contour map of SES at follow-up OCT

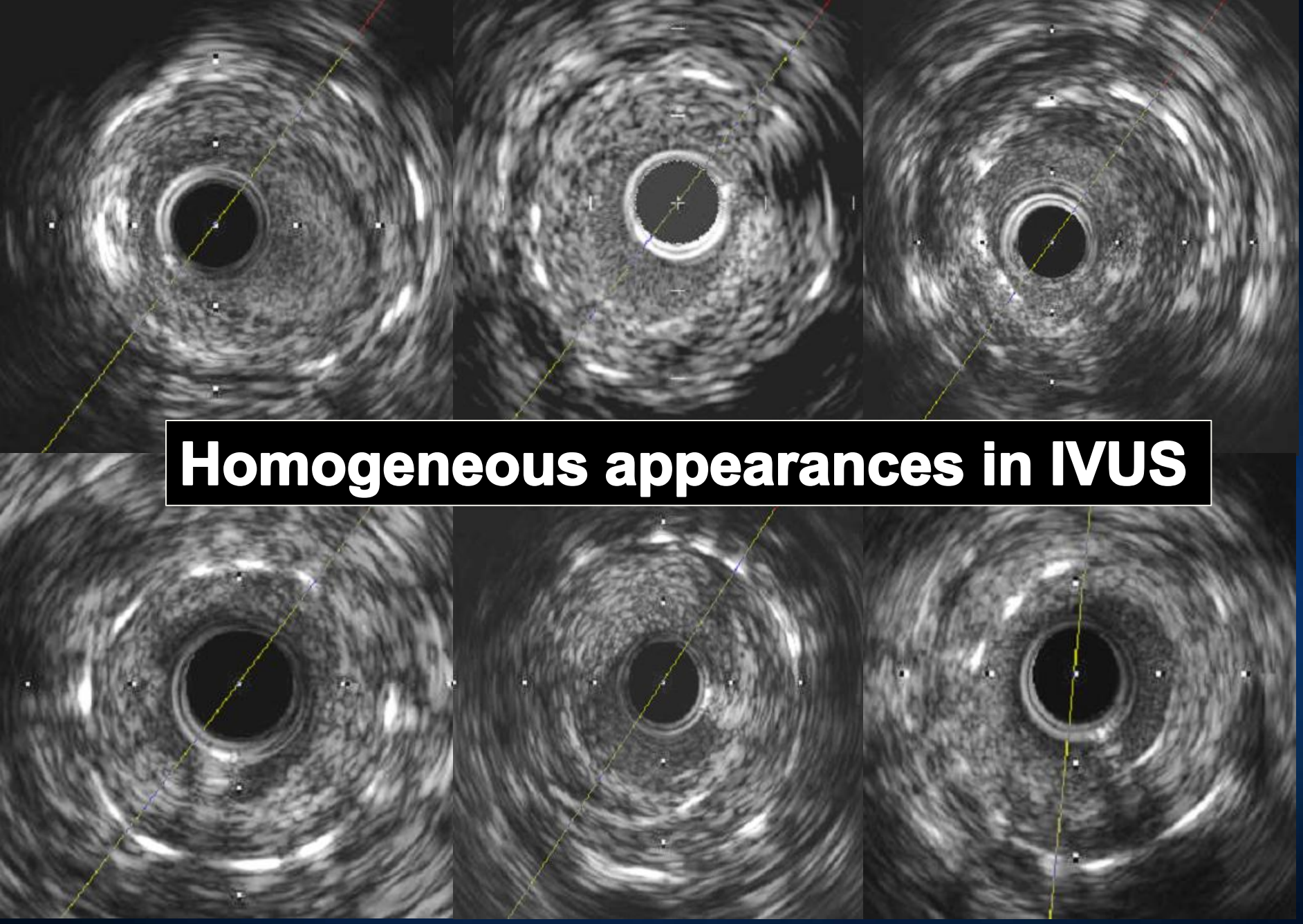


Contour map of ZES at follow-up OCT

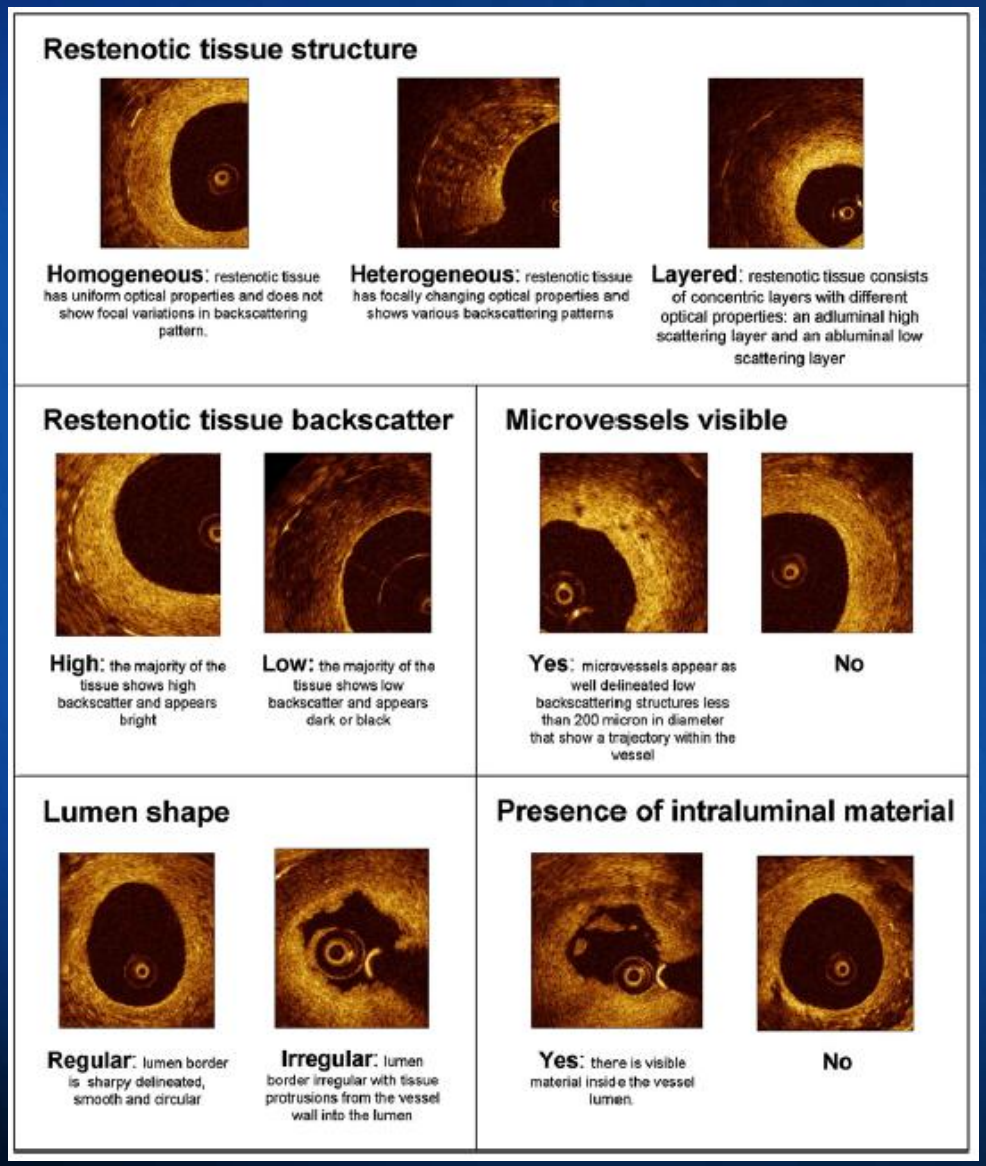


Today's talk

- Plaque characterization by an OCT
- Vulnerable plaque detected by an OCT
- Strut-level evaluation by an OCT
- **Neointimal tissue characterization by an OCT**


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

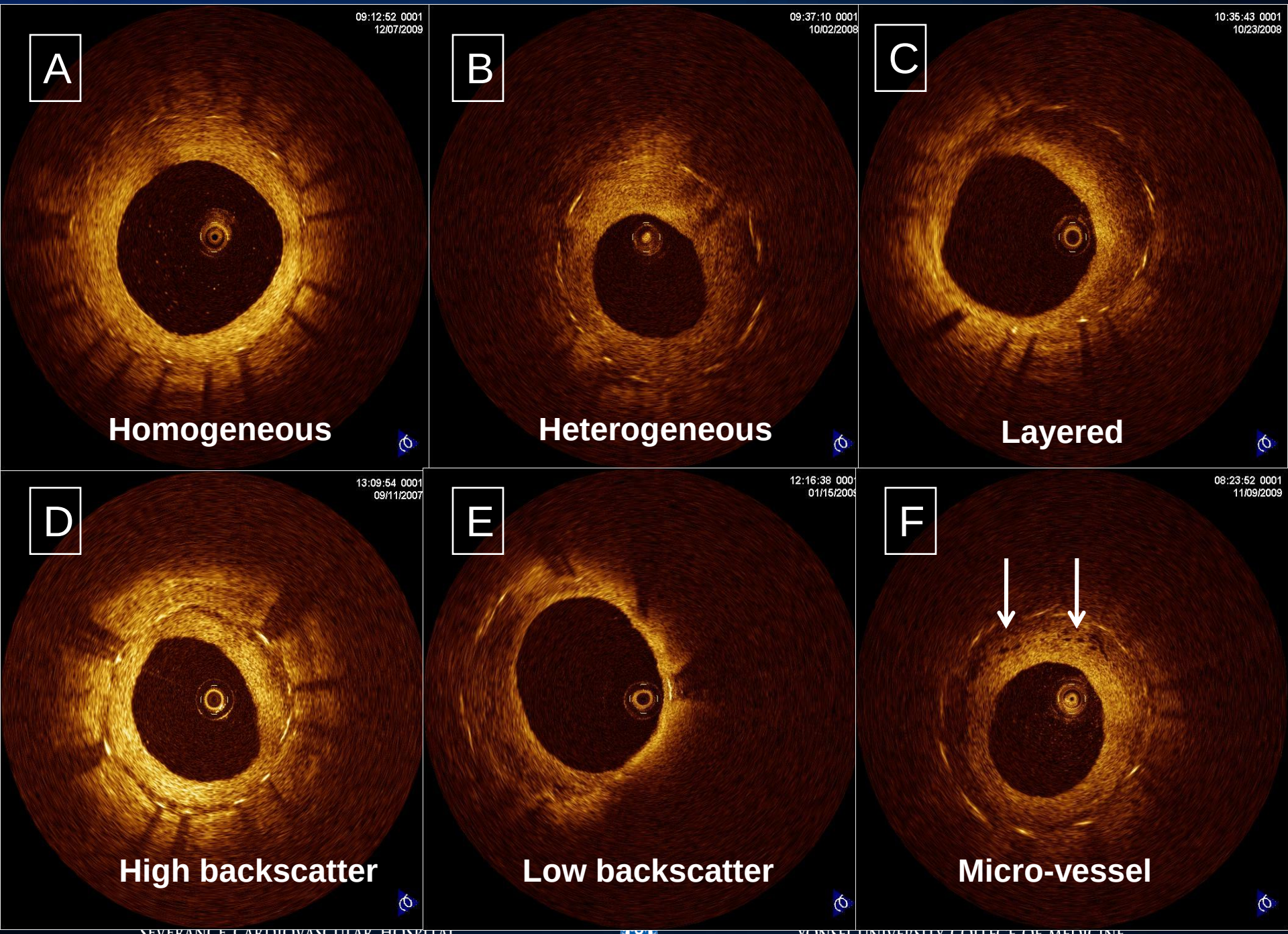
The lesions of ≥ 10% burden of neointimal tissue by OCT measurements were included in this study.

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

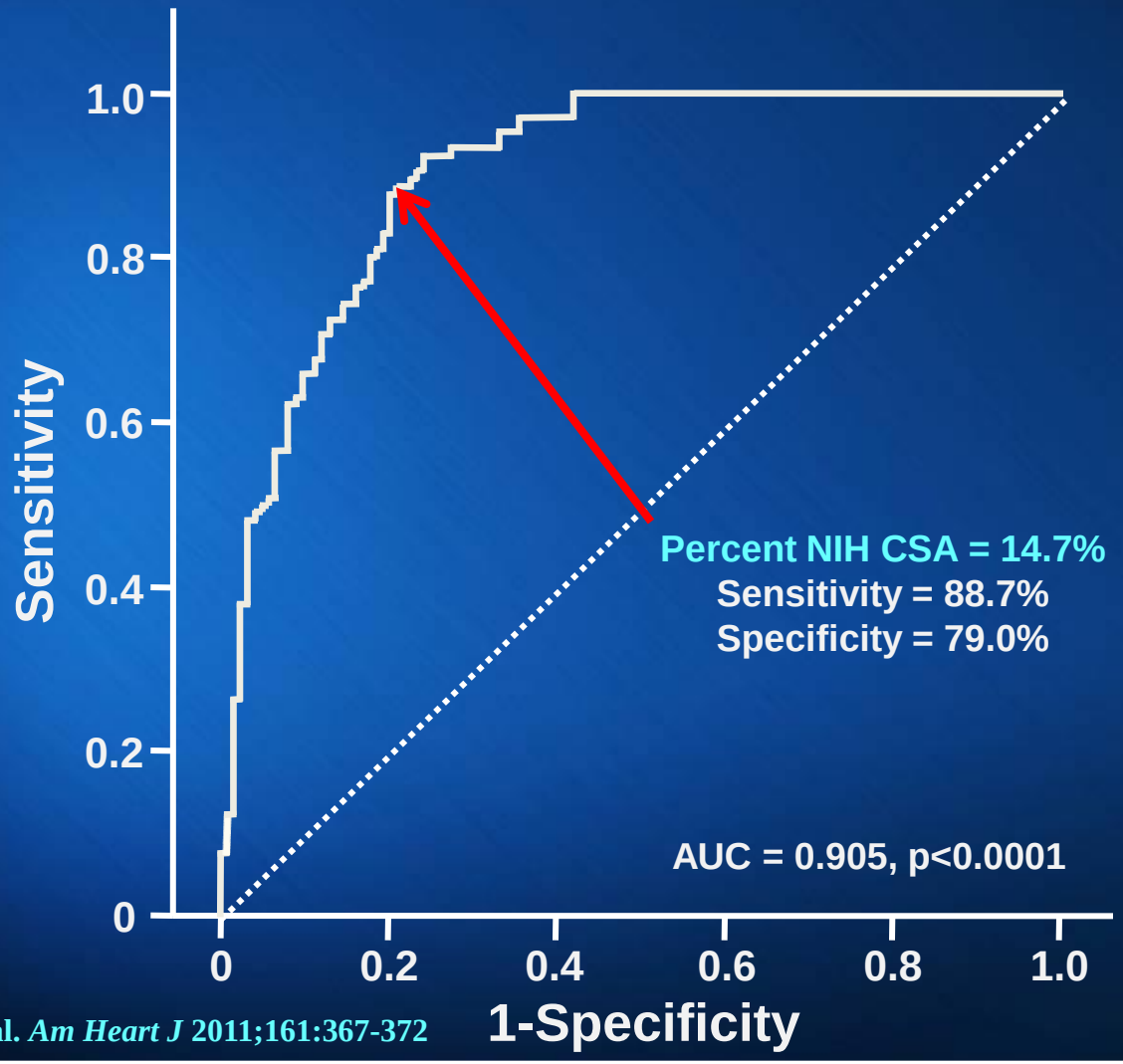
A total of 243 patients (250 lesions) underwent follow-up OCT and IVUS after DES implantation.

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

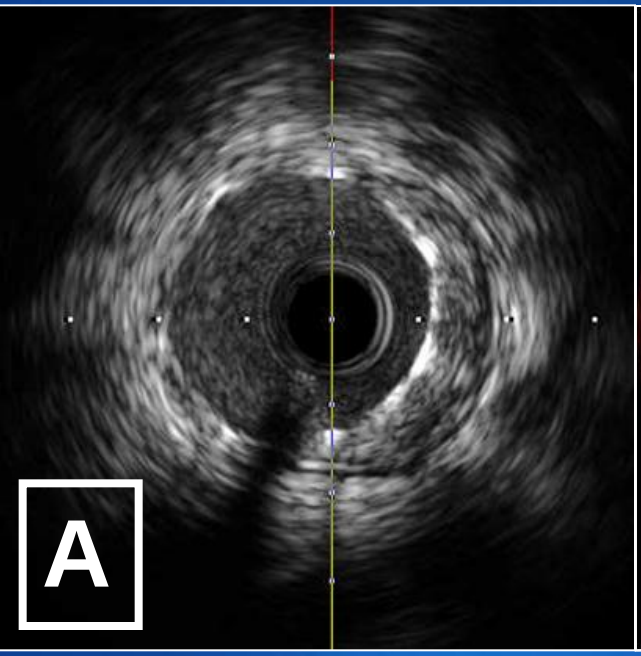
NIH was detected by both OCT and IVUS in 121 of 250 lesions, and categorized as homogenous (n=74, OCT; n=107, IVUS), heterogeneous (n=34, OCT; n=4, IVUS), or layered (n=13, OCT; n=10, IVUS).

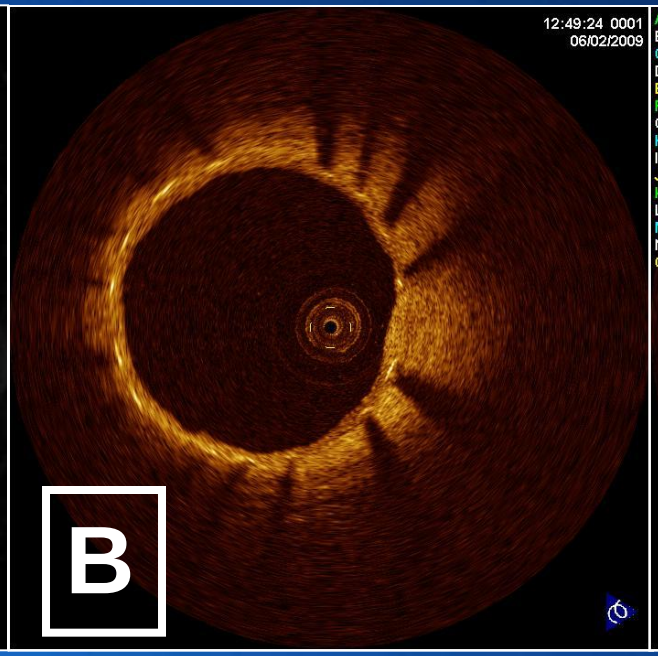
Kwon SW, Hong MK, et al. *Am Heart J* 2011;161:367-372

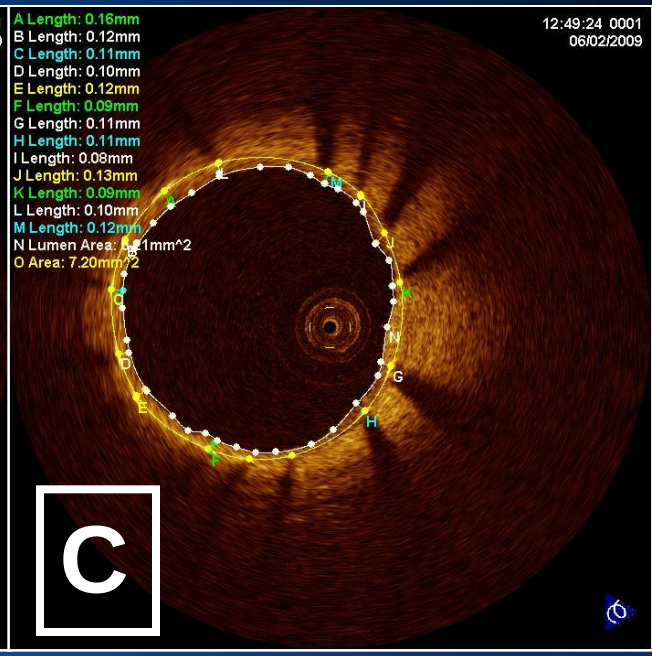
Percent neointimal hyperplasia (NIH) cross-sectional area (CSA) was calculated as (NIH CSA/stent CSA)×100 for receiver-operating characteristic analysis of NIH detection by IVUS



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



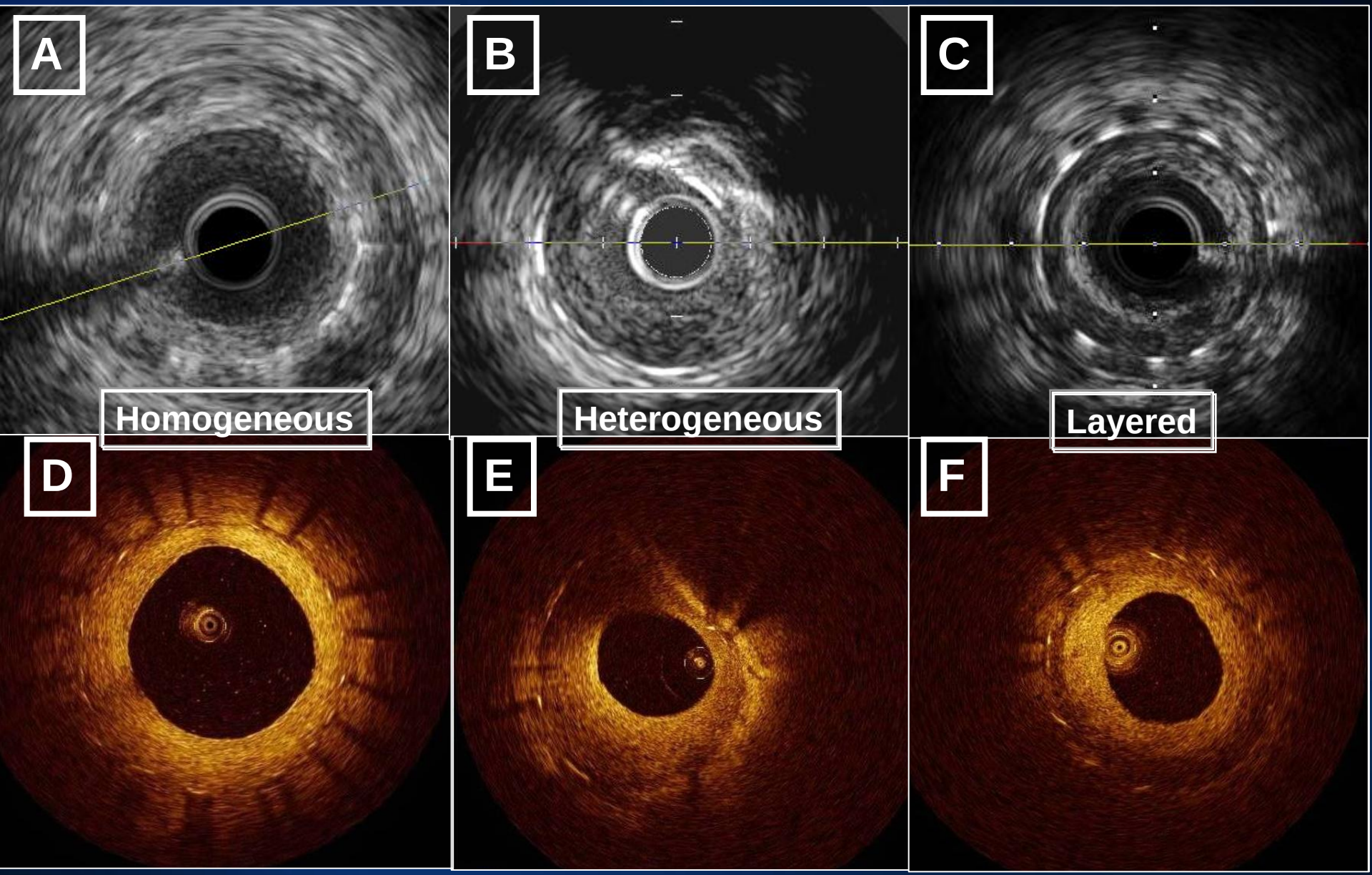




NIH undetectable by IVUS

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

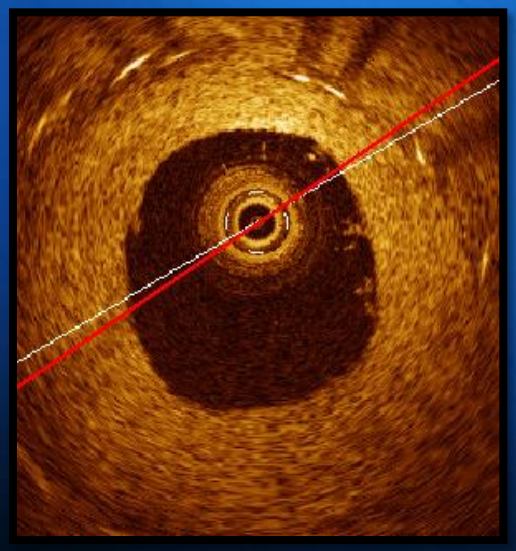
Of the 121 NIH lesions, non-homogenous NIH was detected in 14 (11.6%) by IVUS and 47 (38.8%) by OCT. OCT and IVUS assessments of NIH morphology showed a moderate correlation (p<0.001, r=0.455); however, assessments differed in 37 (30.6%) of 121 lesions.

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

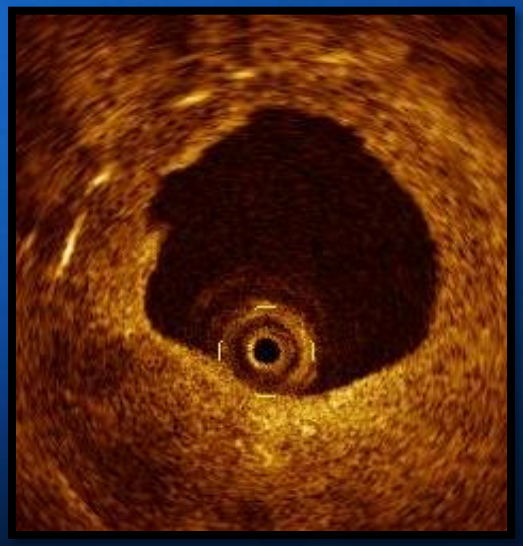
Clinical implications of OCT patterns of in-stent restenosis following implantation of DES

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

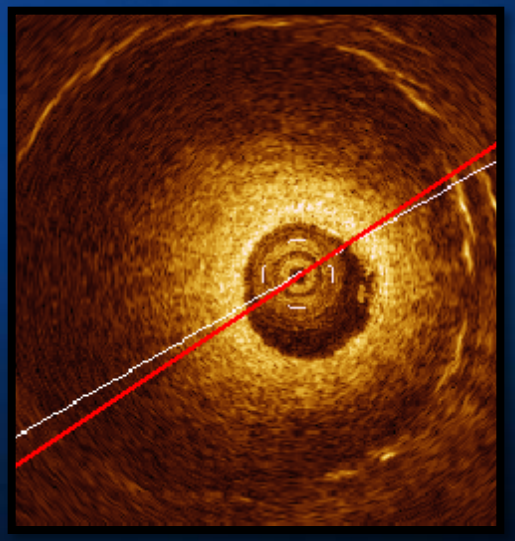
1. **Homogeneous;** uniform optical properties and not showing focal variations in backscattering pattern
2. **Heterogeneous;** focally changing optical properties and showing various backscattering patterns
3. **Layered;** concentric layers with different optical properties.



Homogeneous



Heterogeneous



Layered

Study at a glance

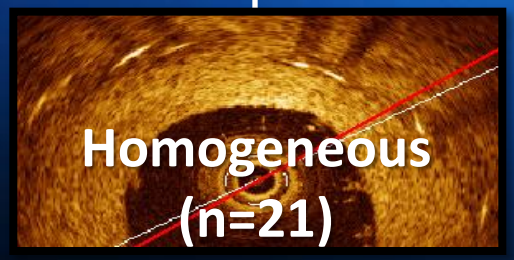
A total of 574 lesions in 510 patients were followed by an OCT in OCT registry

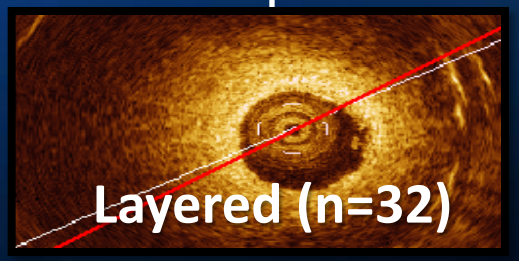
SES (n=170)	PES (n=99)	EES (n=109)	ZES (n=114)	ZES-R (n=82)

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%)	

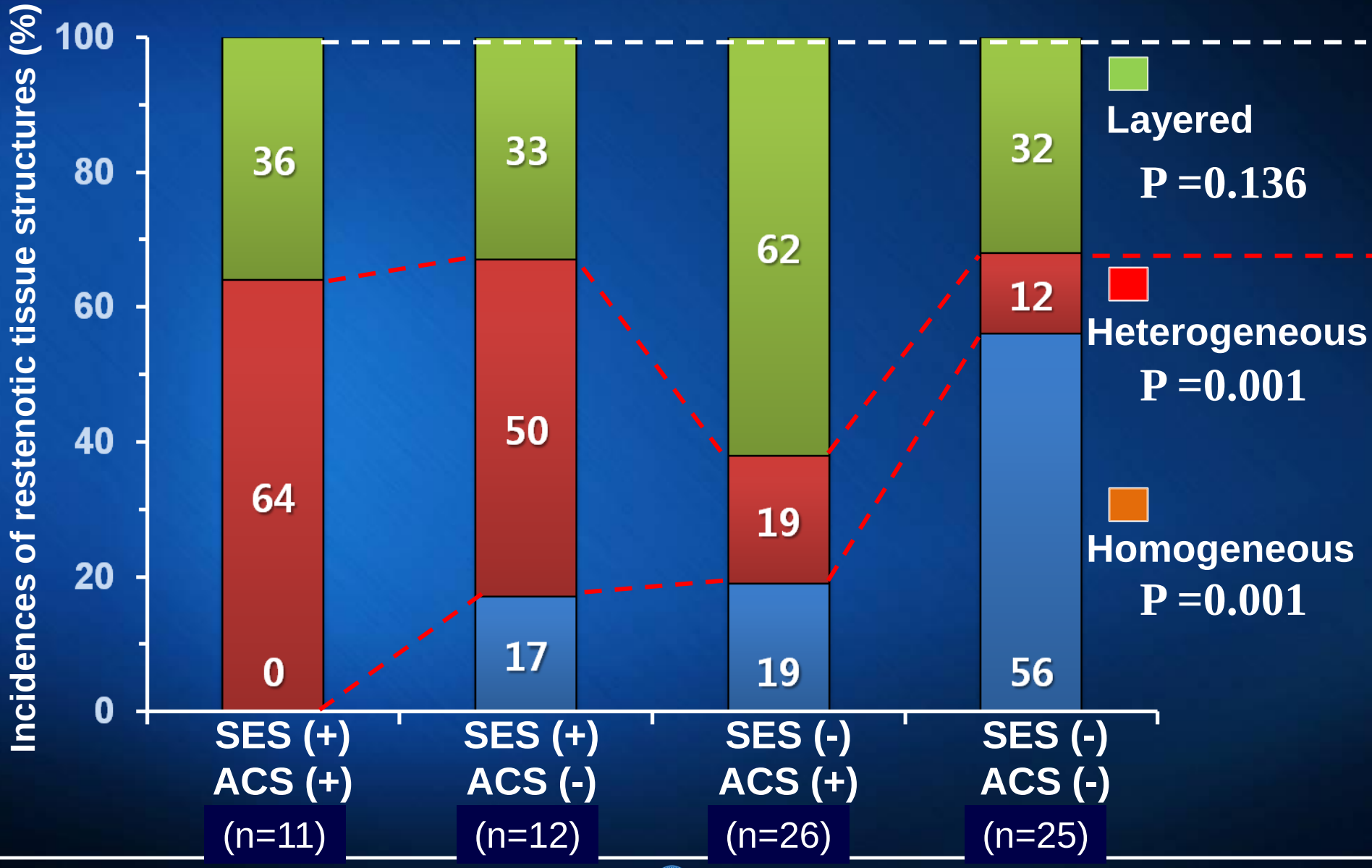
*p<0.01 compared to homogenous structure.

§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

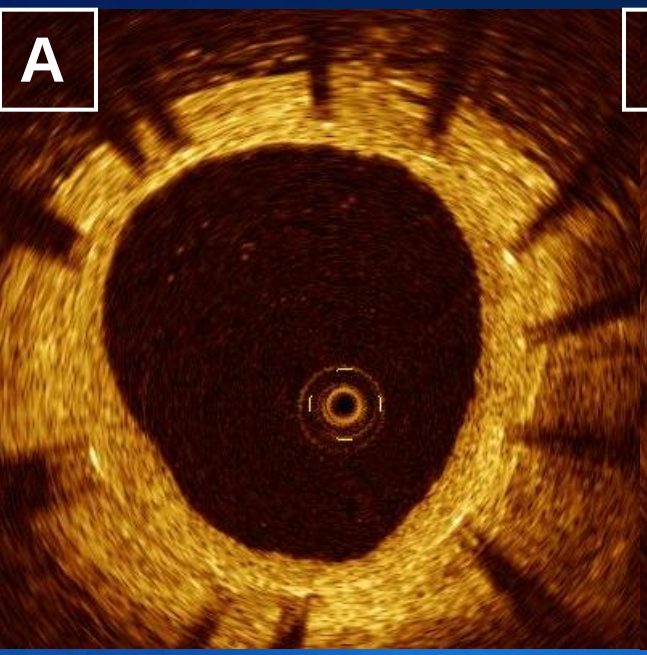


Serial OCT

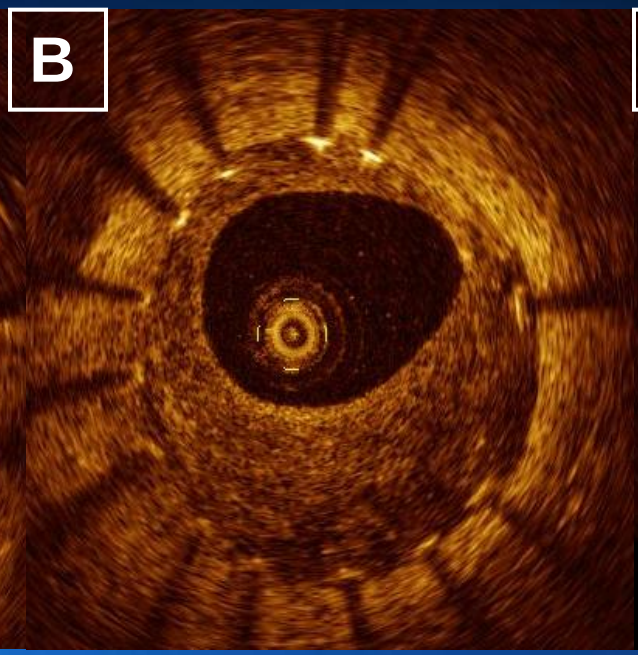
Study population

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.

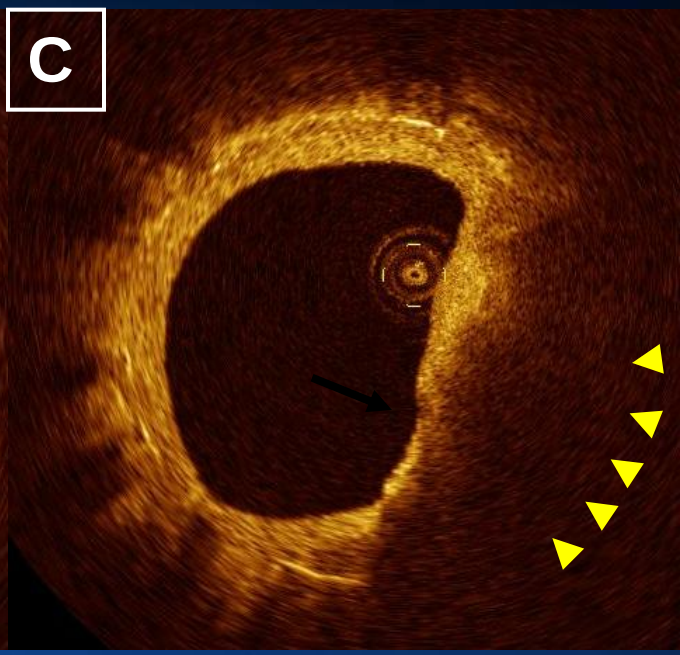
Among these patients, a second serial follow-up OCT examination at 2 years (±3 months) after stent implantation was performed in 72 patients with 76 stented lesions: 23 SESs, 20 PESs, 25 ZESs and EESs.



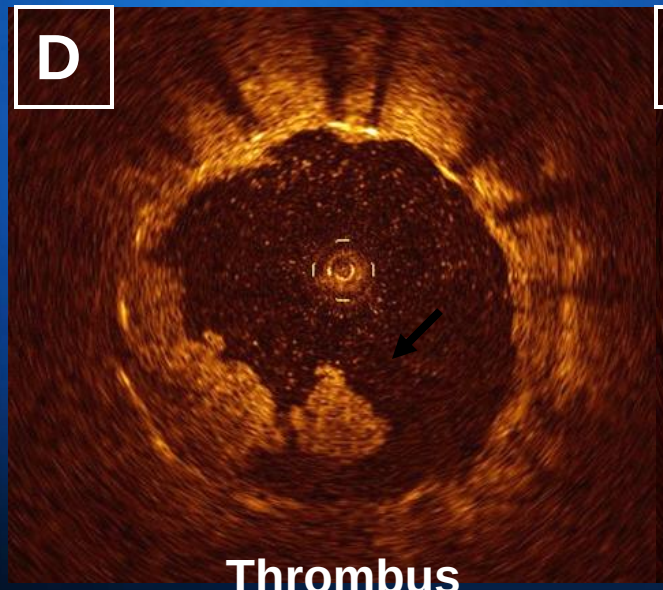
Homogeneous



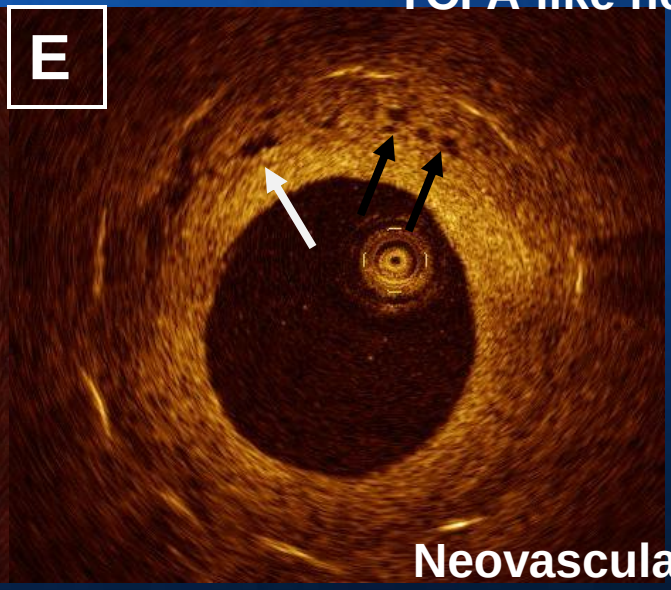
Heterogeneous



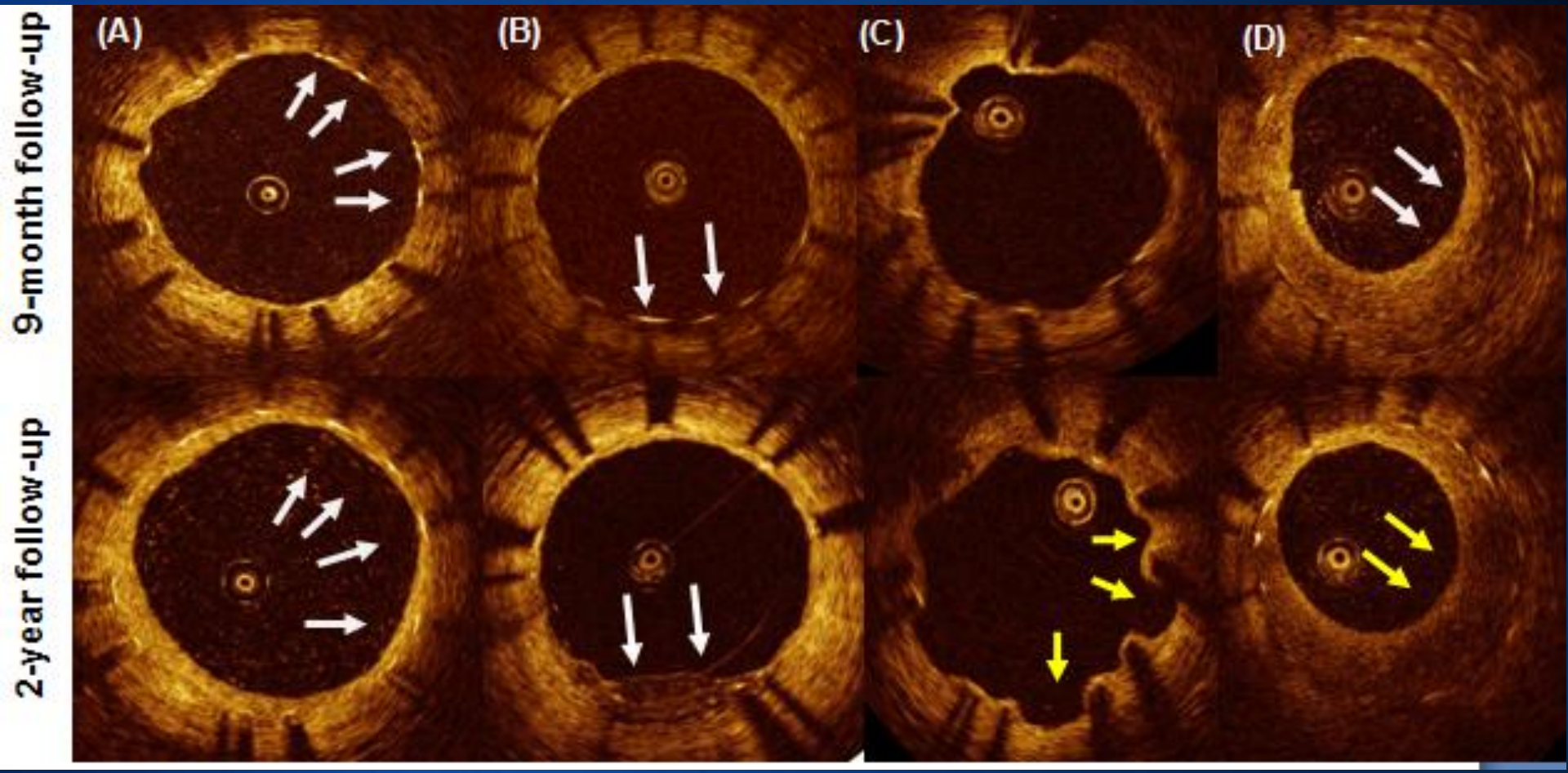
Lipid-laden neoinitma and
TCFA-like neointima



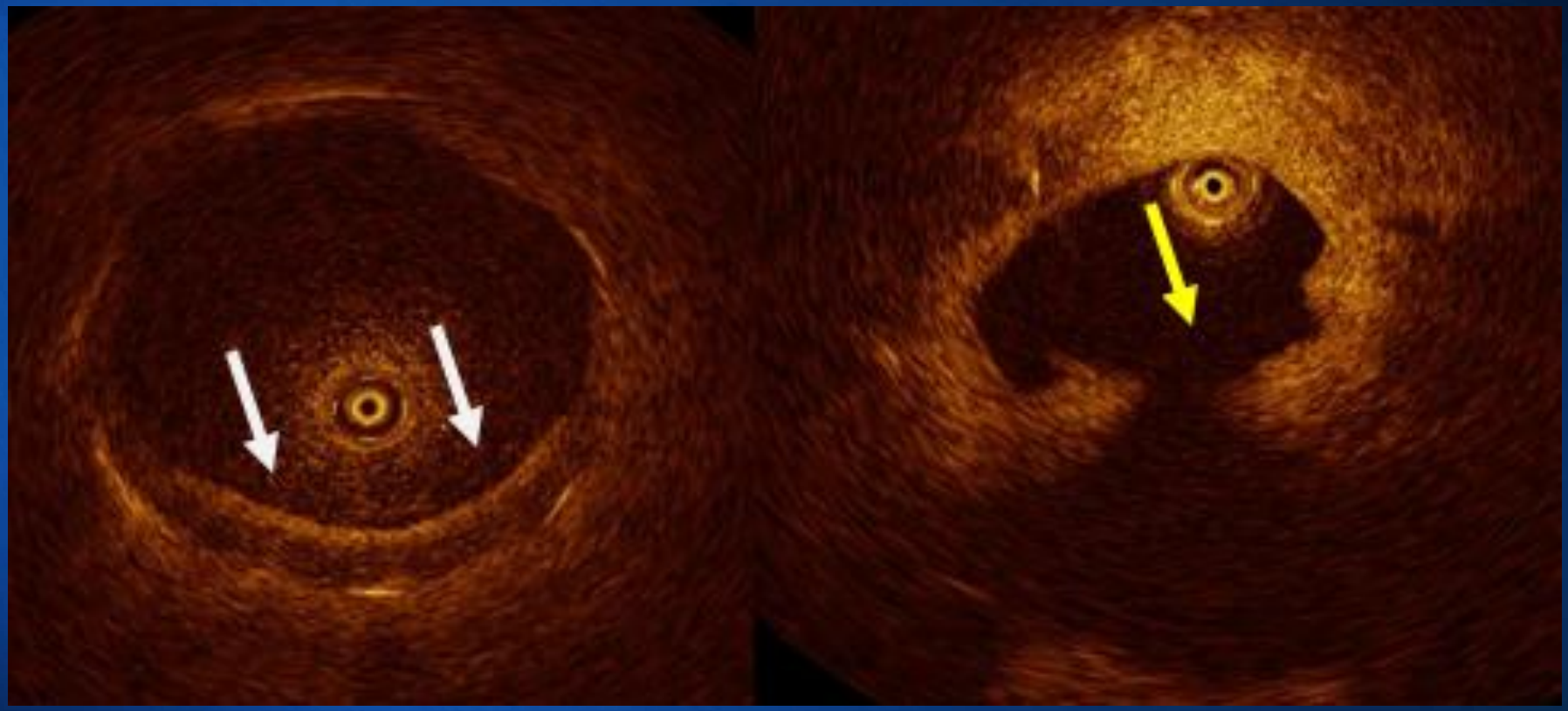
Thrombus



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

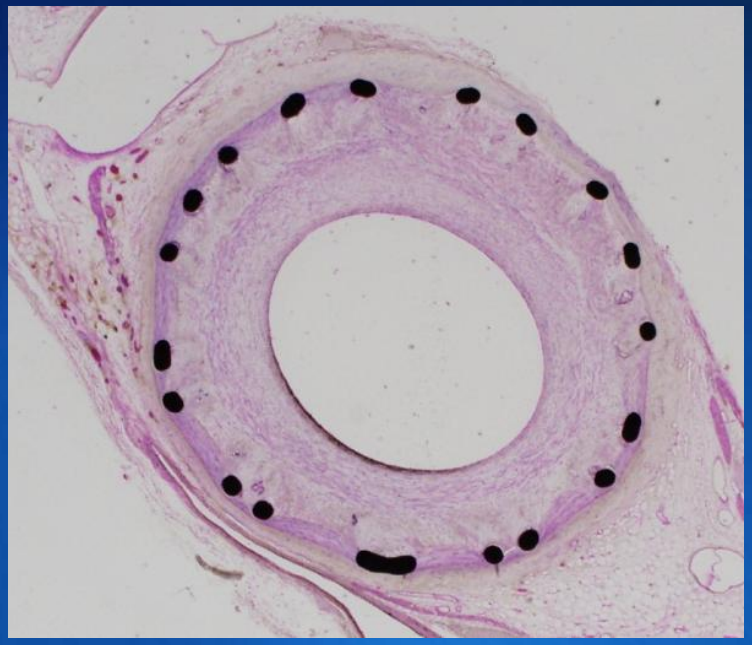
Quantitative OCT analysis

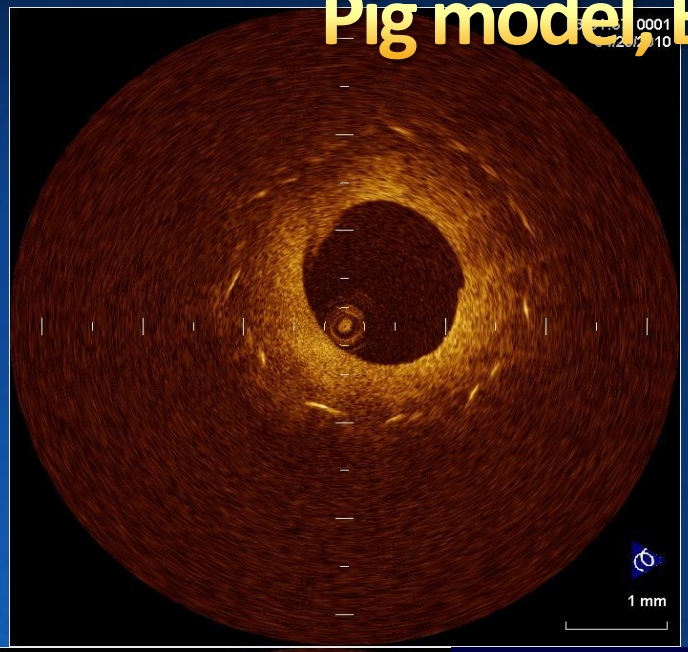
Strut level analysis	9-month	2-year	p
Total strut number	19430	19475	
Mean NIH thickness (μm)	164 ± 95	214 ± 132	<0.001
Percentage of uncovered struts	787 (4.1%)	468 (2.4%)	<0.001
Percentage of malapposed strut	127 (0.7%)	183 (0.9%)	0.24
Percentage of uncovered and malapposed struts	76 (0.4%)	82 (0.4%)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

Qualitative OCT analysis

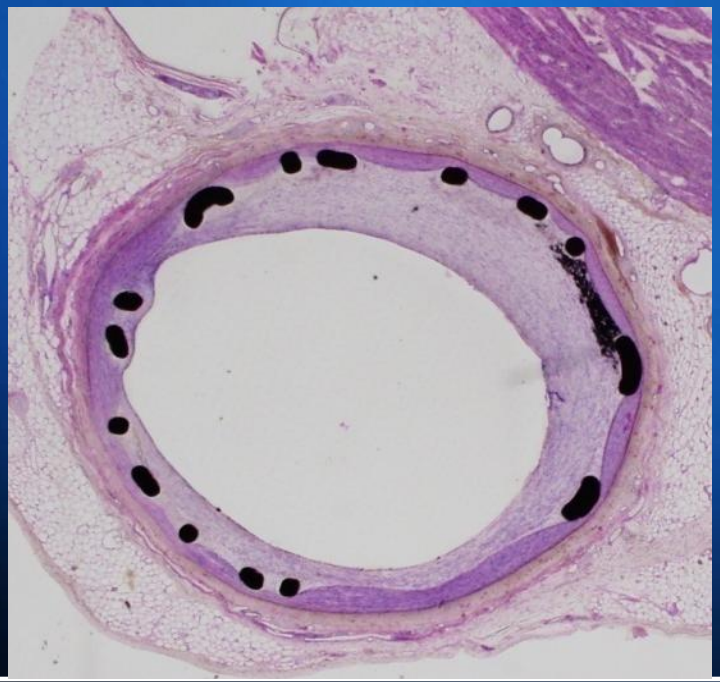
Qualitative analysis	9-month	2-year	p
Intracoronary thrombus	8 (10.5%)	7 (9.2%)	0.79
Lipid-laden neointima	11 (14.5%)	21 (27.6%)	0.047
TCFA-like neointima	3 (3.9%)	10 (13.2%)	0.04
Heterogeneous pattern	49 (64.5%)	47 (61.8%)	0.73
Neovascularization	34 (44.7%)	56 (73.7%)	<0.001

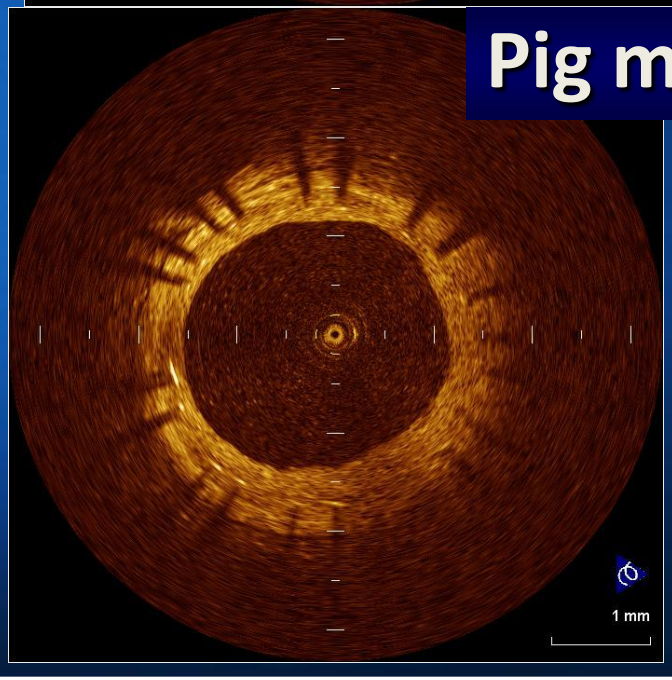
Pig model, Endeavor





Pig model, BMS





Conclusion

- OCT provides various new information in many different fields as mentioned below;
  - ✓ Plaque Characterization
  - ✓ Vulnerable Plaque Detection
  - ✓ Strut-level evaluation
    ; Uncovered or Malapposed struts
  - ✓ Neointimal tissue characterization
    ; Evaluation of DES failure

- However, its related clinical relevance needs to be clarified through further clinical follow-up studies.