

Neoatherosclerosis

Something New or Nothing New?

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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 (Institutional)
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Company

- Boston Scientific Corporation
- Boston Scientific Corporation

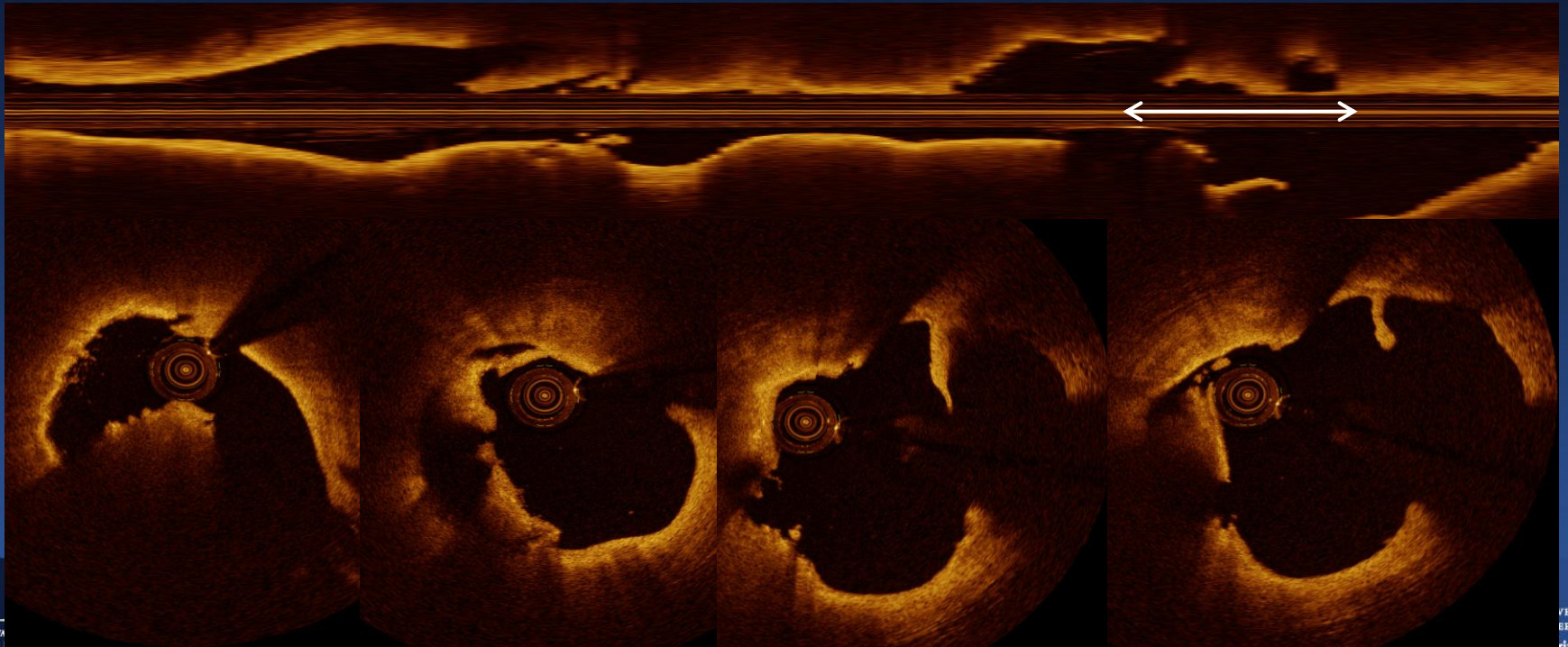
STEMI

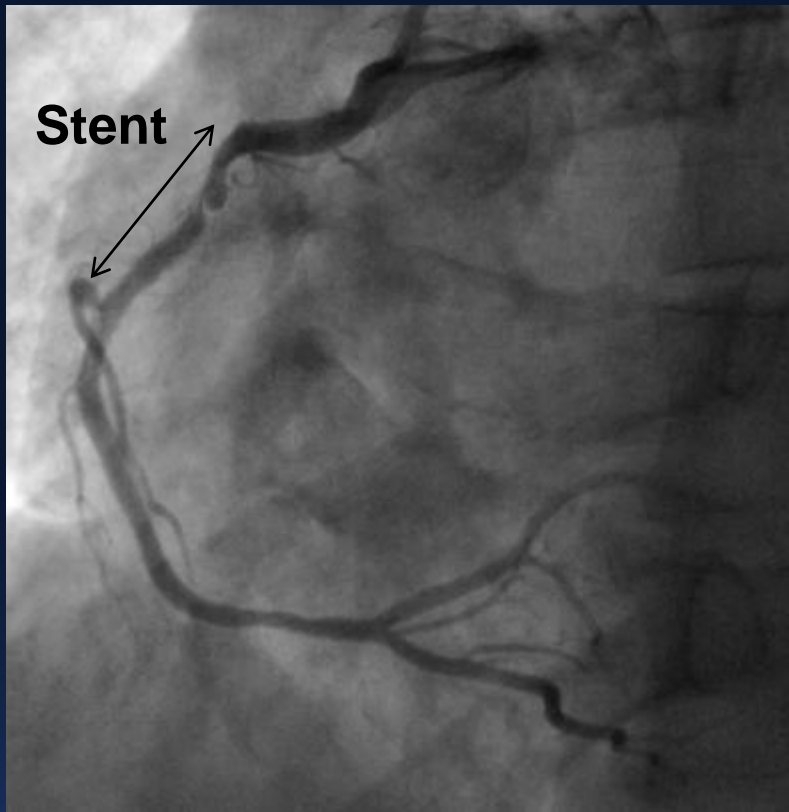
De novo lesion

Pre

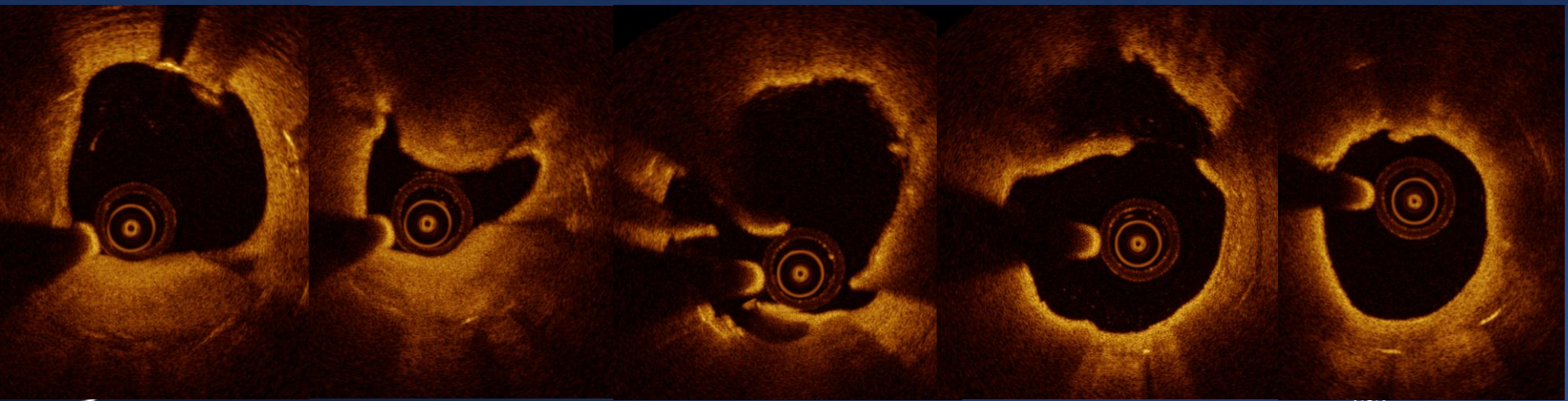
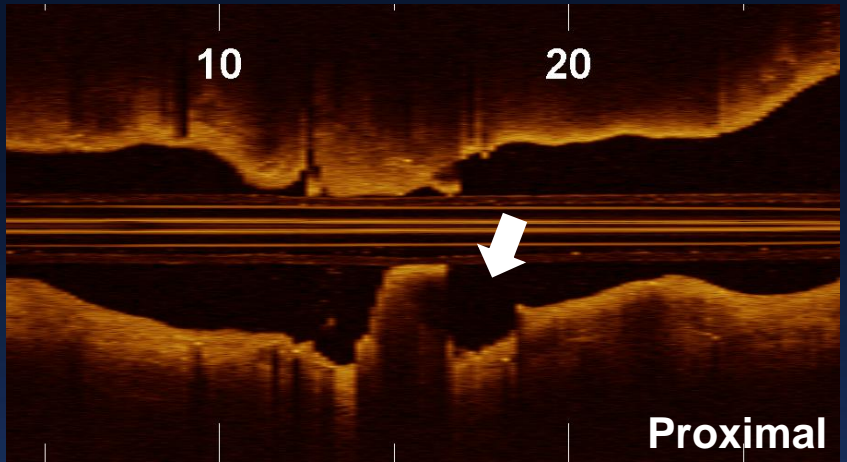


Post-Thrombectomy

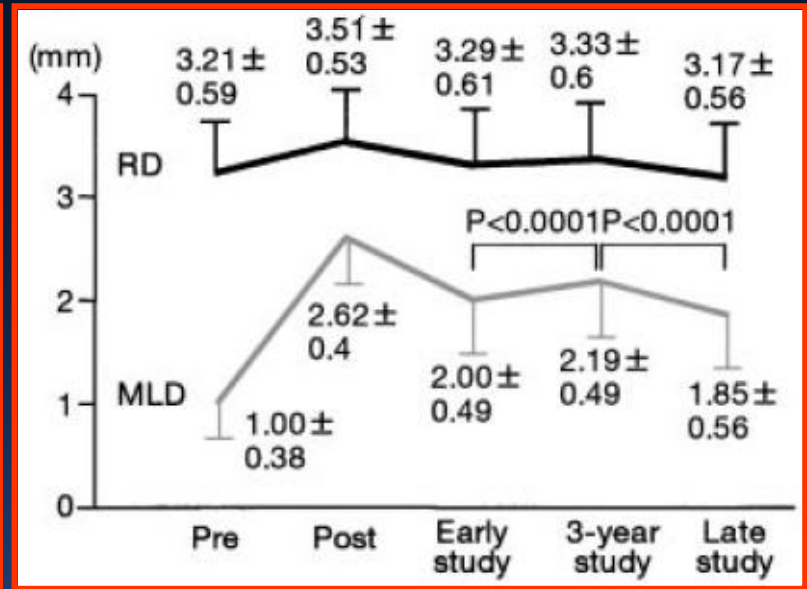
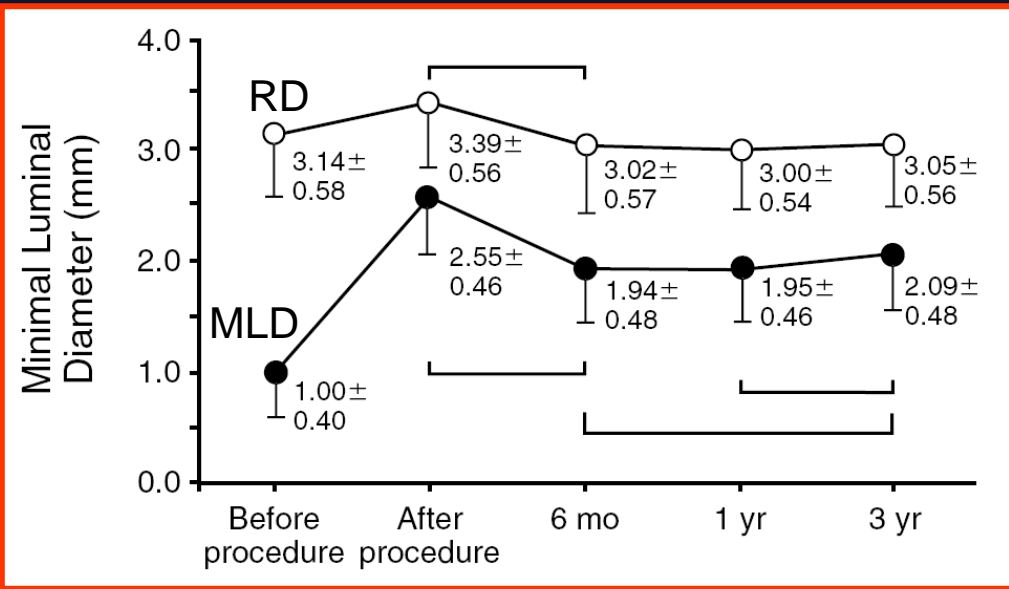




Unstable AP *Cypher in 2003*



Lumen loss at late stage

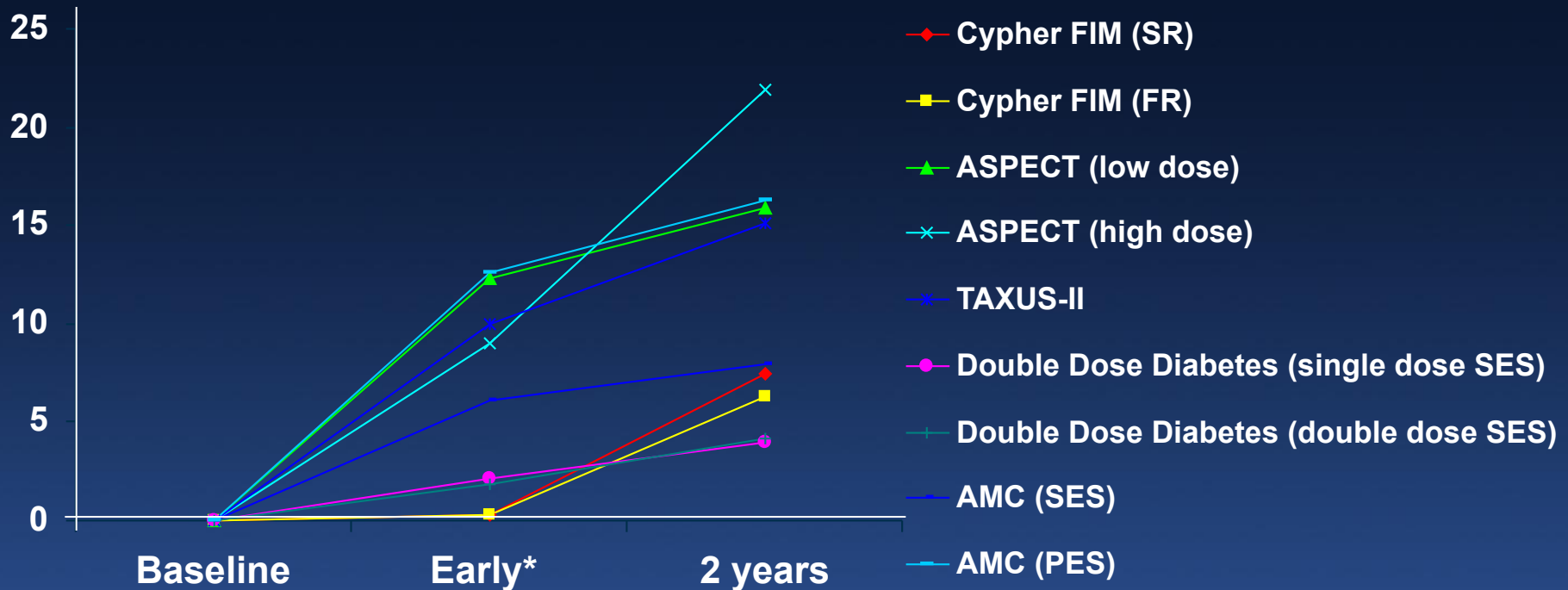


Kimura et al., N Engl J Med 1996;334:561-6

Kimura et al., Circulation 2002;105:2986-91

Late DES Catch-Up Among IVUS Substudy Patients

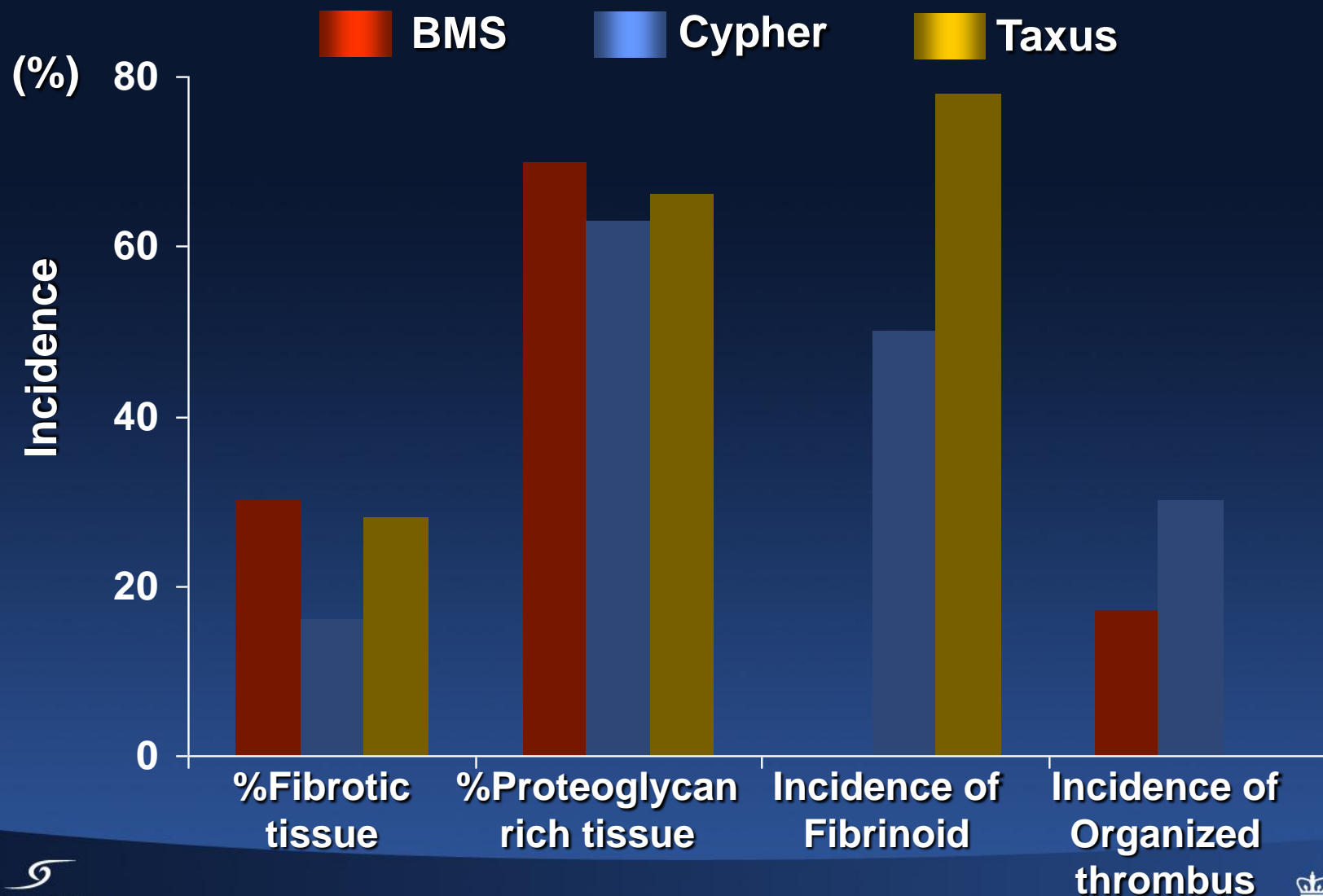
%IH volume



**defined as 4-9 months*

In-stent restenosis tissue shows “delayed healing”

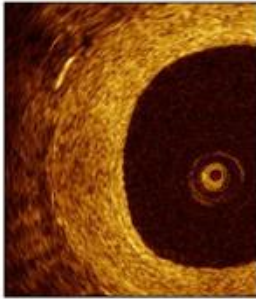
Tissue by DCA (10 Cypher, 9 Taxus, 6 BMS), 103-1472 days old



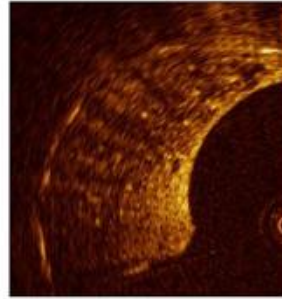
Pattern of restenotic tissue

Time from stent implantation to OCT=12 month (4-42)

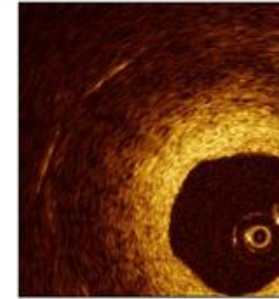
Restenotic tissue structure



Homogeneous: restenotic tissue has uniform optical properties and does not show focal variations in backscattering pattern.

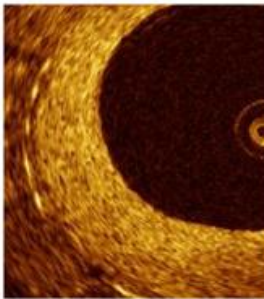


Heterogeneous: restenotic tissue has focally changing optical properties and shows various backscattering patterns

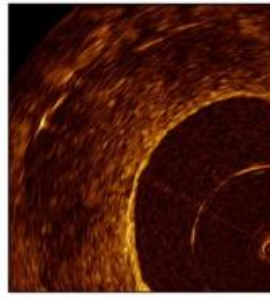


Layered: restenotic tissue consists of concentric layers with different optical properties: an adluminal high scattering layer and an abluminal low scattering layer

Restenotic tissue backscatter

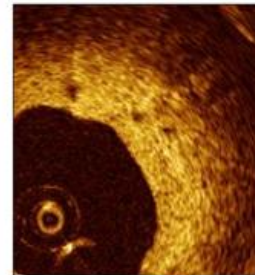


High: the majority of the tissue shows high backscatter and appears bright



Low: the majority of the tissue shows low backscatter and appears dark or black

Microvessels visible



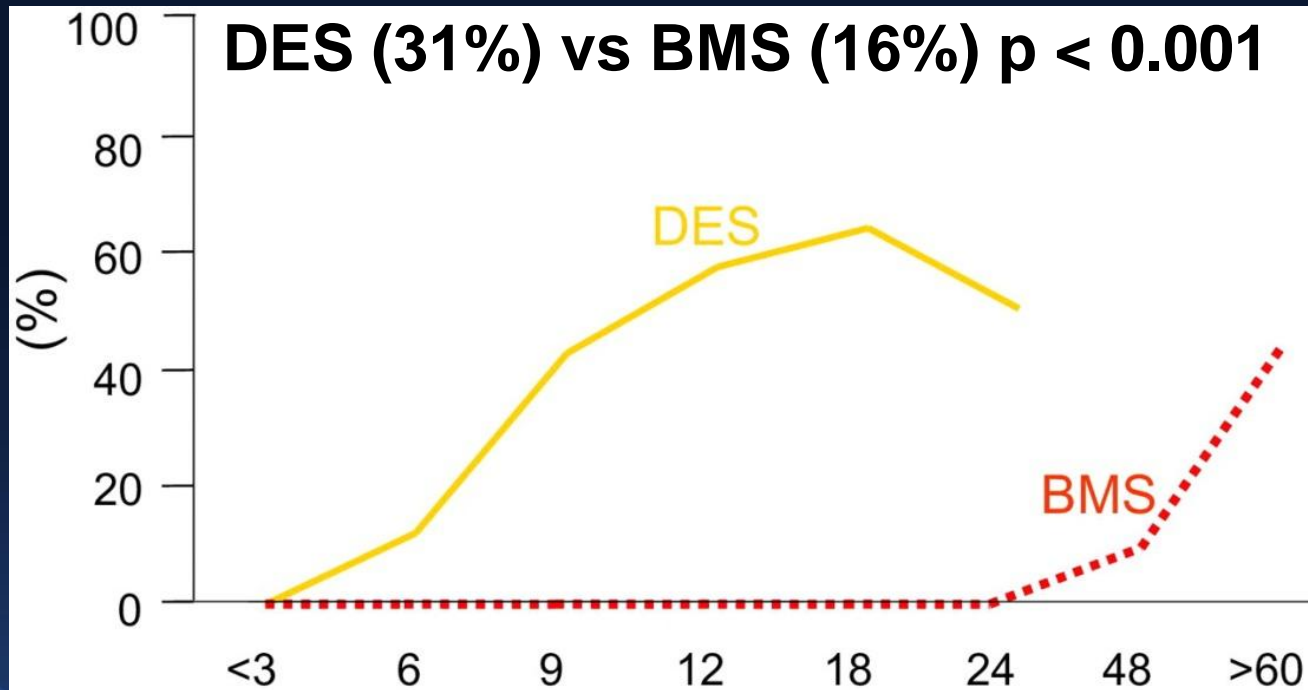
Yes: microvessels appear as well delineated low backscattering structures less than 200 micron in diameter that show a trajectory within the vessel



No

Pathology of In-stent Neointimal Hyperplasia

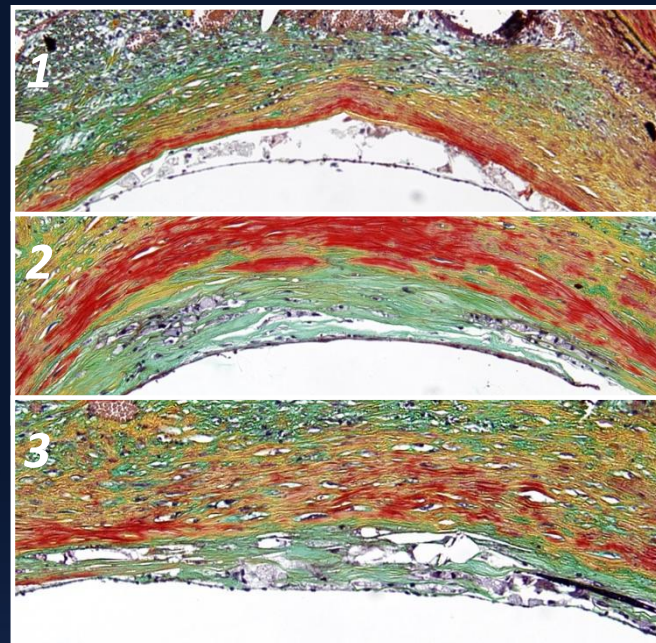
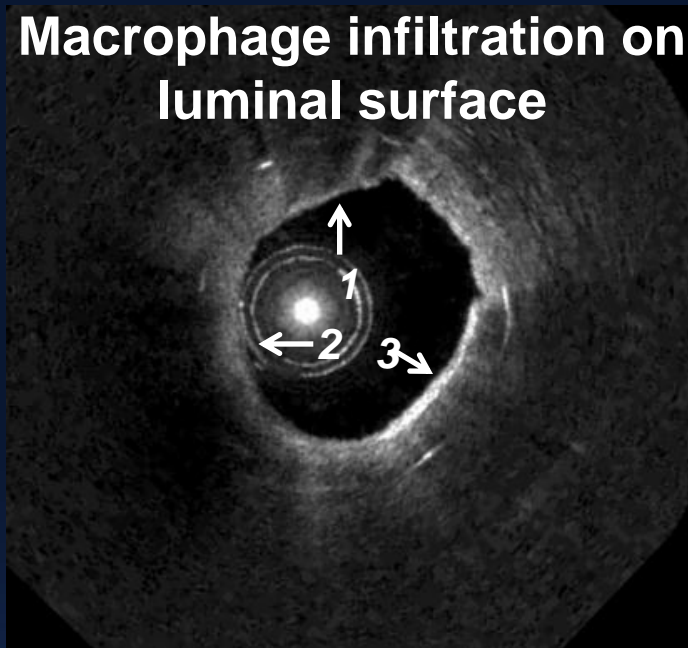
197 BMS, 103 SES, and 106 PES with implant duration >30 days



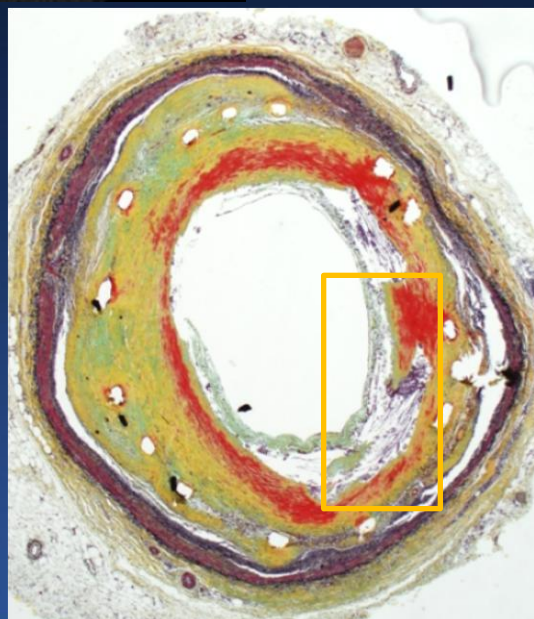
Variable	OR	95% CI	p value
Age/year	0.96	0.94-0.98	<0.001
Stent duration/month	1.03	1.02-1.04	<0.001
SES usage	6.53	3.39-12.59	<0.001
PES usage	3.20	1.58-6.47	0.001
Underlying unstable plaque	2.39	1.23-4.30	0.004

Nakazawa et al. JACC
2011;57:1314-22

Macrophage infiltration on luminal surface

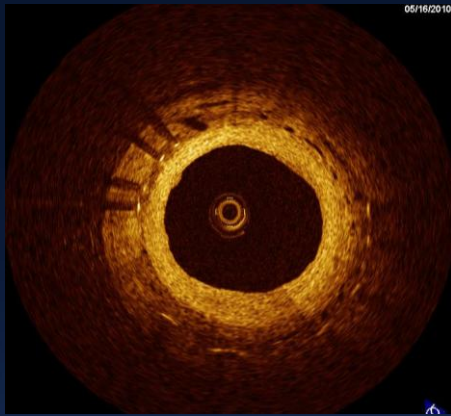


TCFA w/i neointima

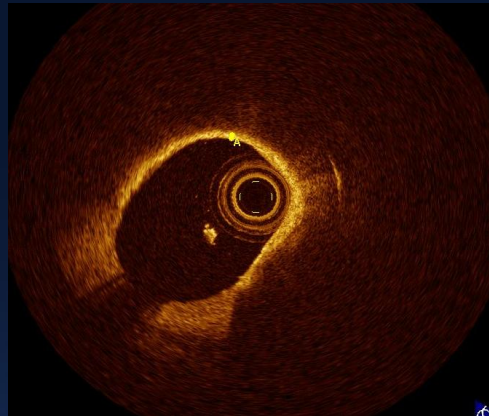


Late in-stent neoatherosclerosis in DES

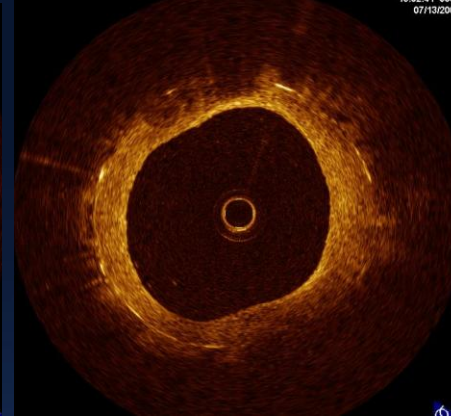
Microvessel



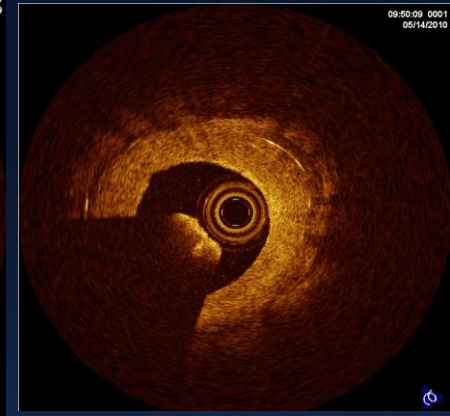
TCFA-like neointima



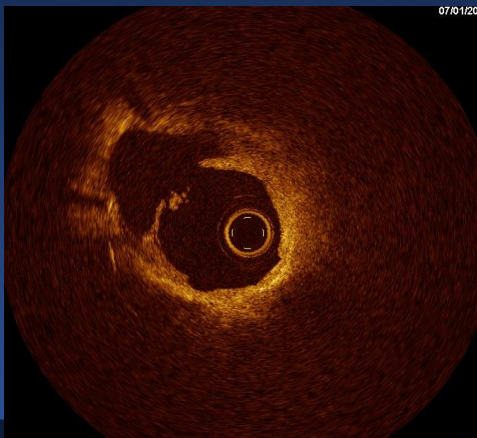
Calcium



Red thrombus



Neointimal rupture



Mixed thrombus



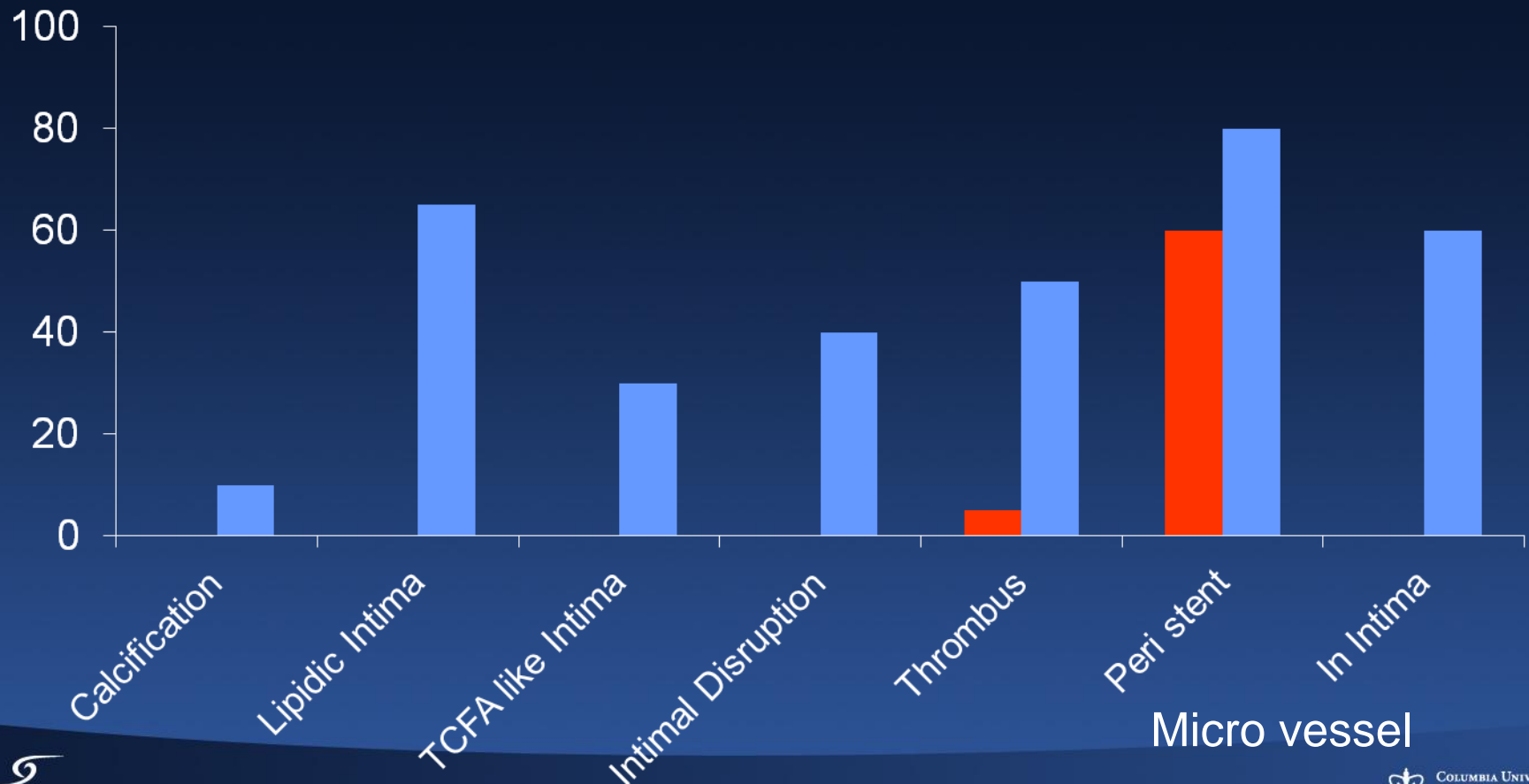
White thrombus



OCT In-stent Neoatherosclerosis in BMS

■ Early FU, n=20, 4.6±1.8 Month, no TLR, no ACS

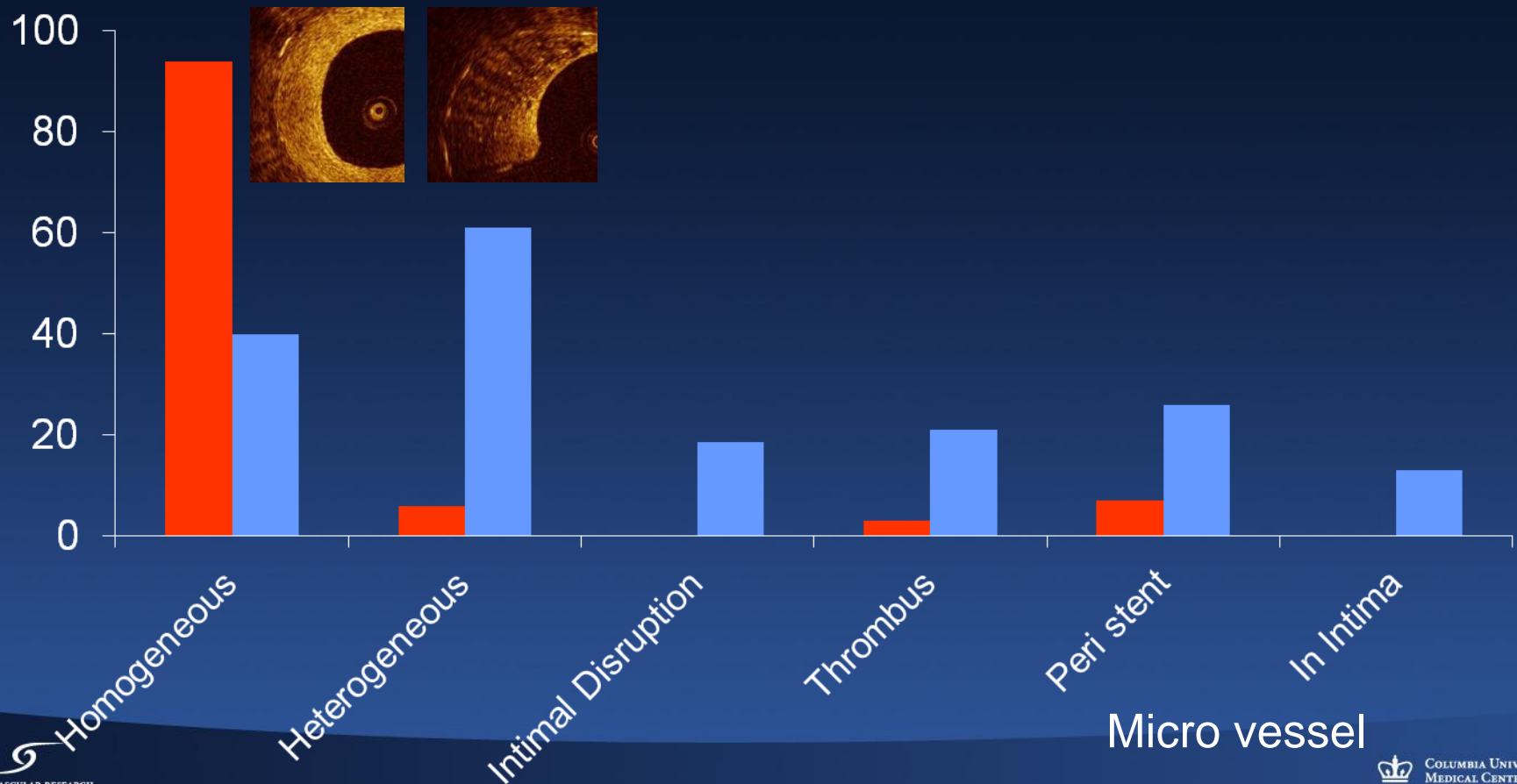
■ Late FU, n=21, 7.6±2.2 Year, 13 TLR, 4 ACS



OCT In-stent Neointerthrosclerosis in BMS

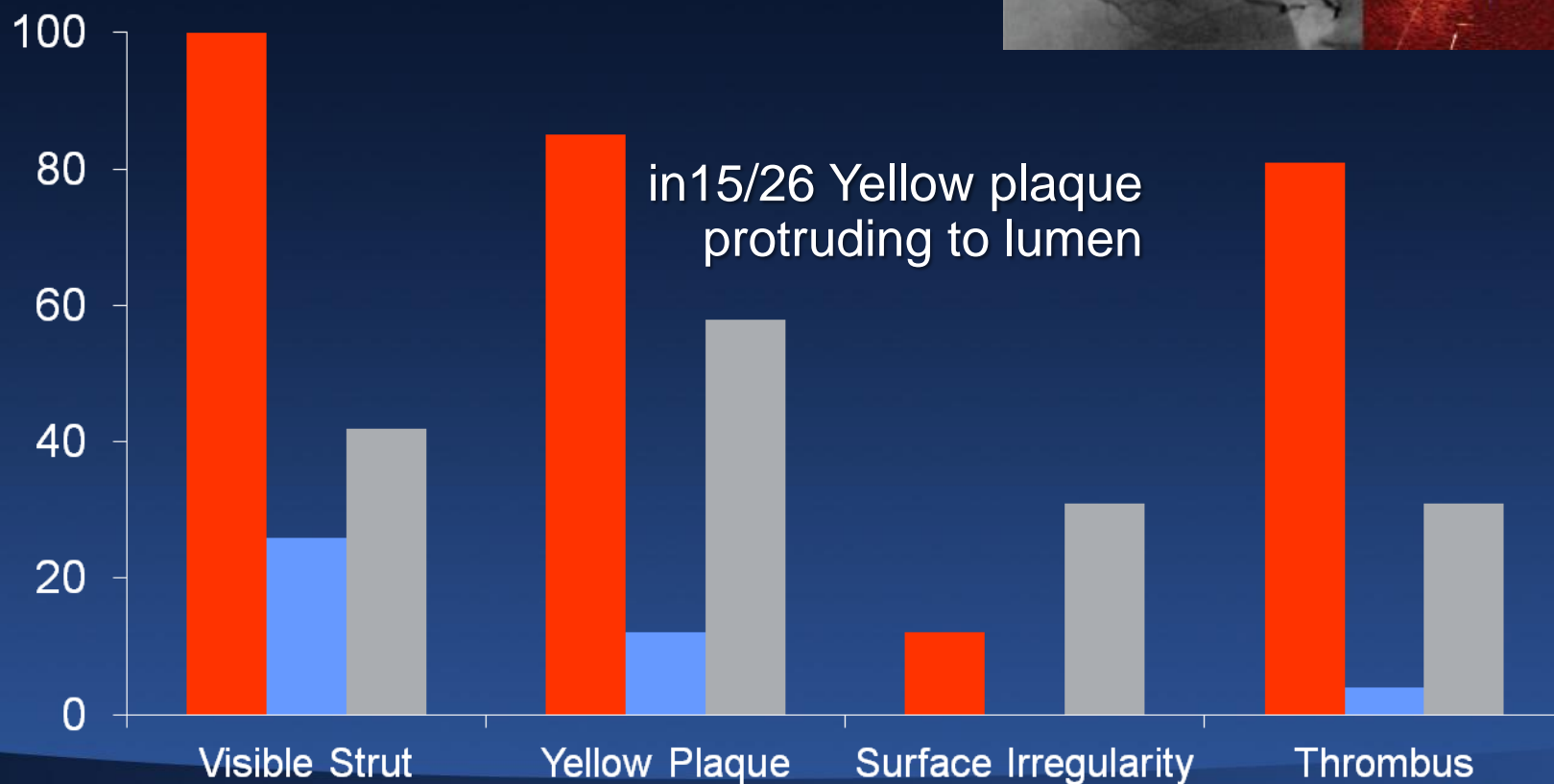
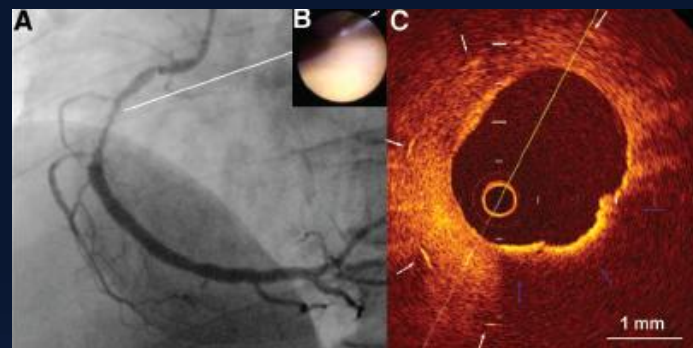
■ Early FU, n=39, 8.7±4.1 Month, TLR 59%, ACS 13%

■ Late FU, n=43, 9.5±2.5 Year, TLR 72%, ACS 21%



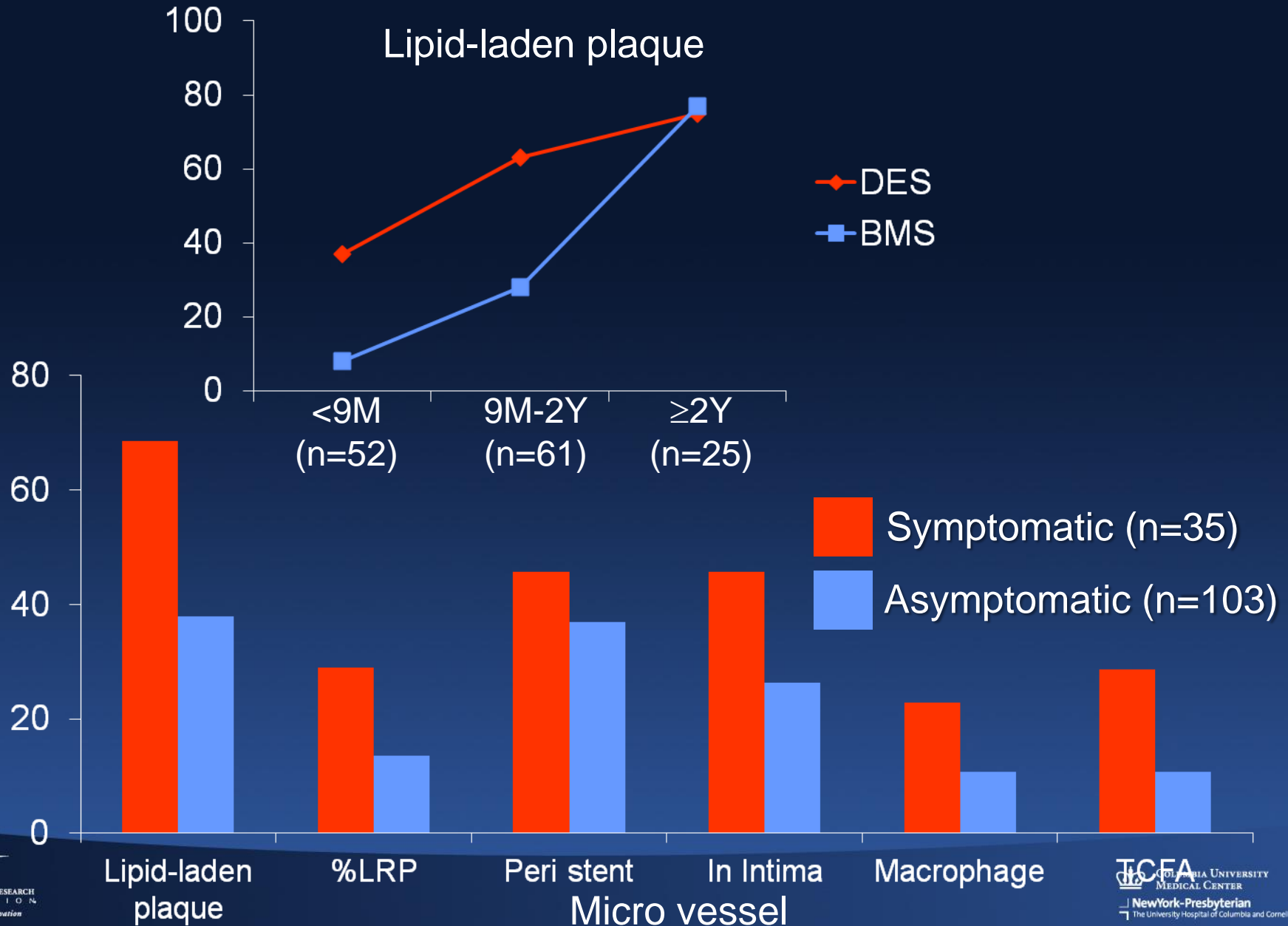
Serial Angioscopy Neoatherosclerosis in BMS (n=26)

- Baseline, 73% ACS
- Early FU, 7.1±2.7 Month, no TLR
- Late FU, 7.9±2.9 Year, no TLR



OCT In-stent Neointimal Hyperplasia in DES

Yonetsu et al. Am J Cardiol 2012; 110: 933-939

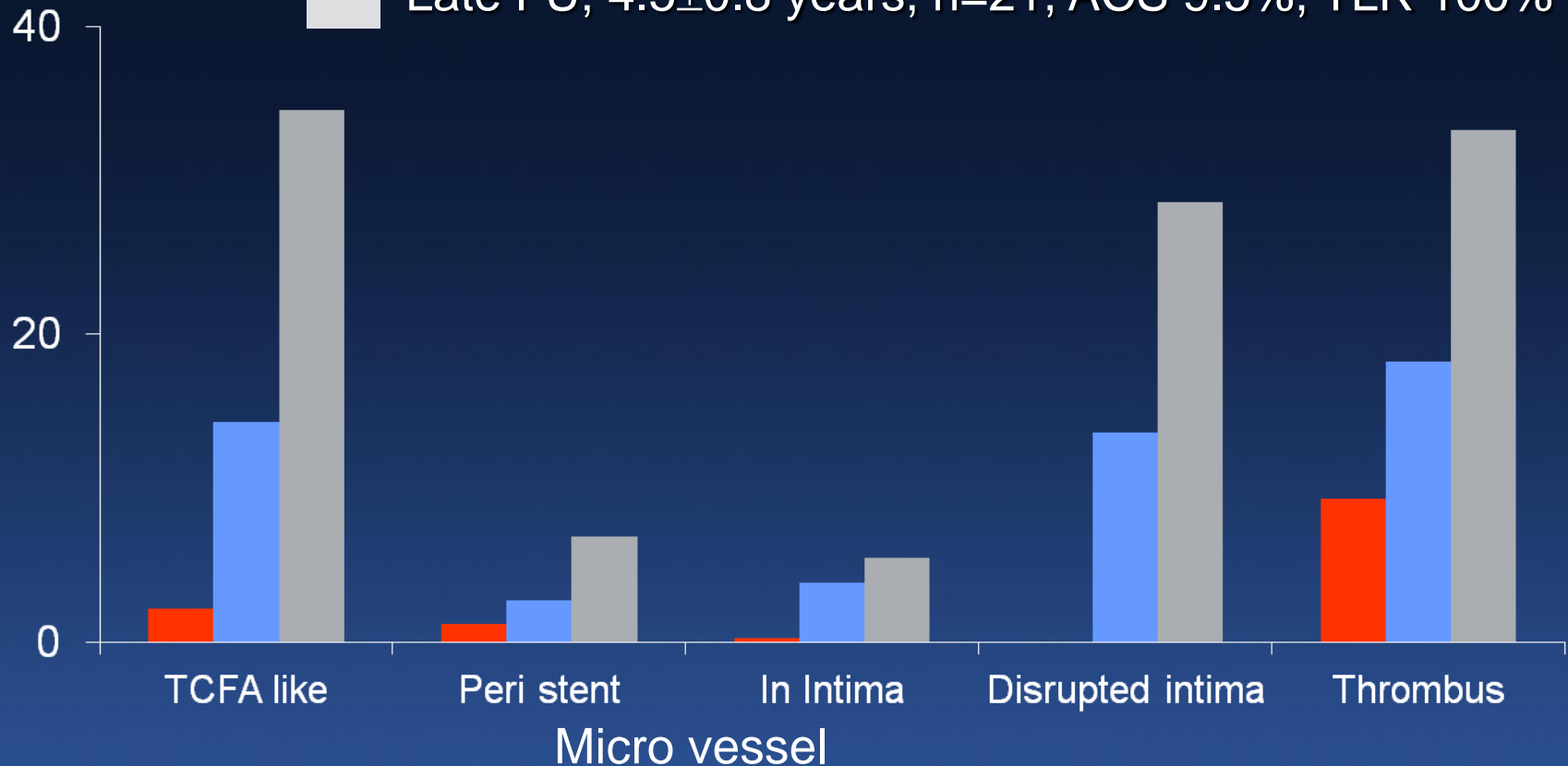


Independent Predictors for Neoatherosclerosis

	Odds Ratio	95% CI	p-value
Stent age>2 y	10.5	3.7-29.4	<0.001
DES			
SES	3.9	1.4-10.4	0.007
PES	24.1	6.0-97.2	<0.001
EES	6.5	1.7-25.3	0.007
Smoking	7.0	2.5-20.4	<0.001
CKD	3.7	1.1-12.4	0.035
ACE-I/ARB use	0.39	0.17-0.91	0.028

OCT In-stent Neoatherosclerosis in DES

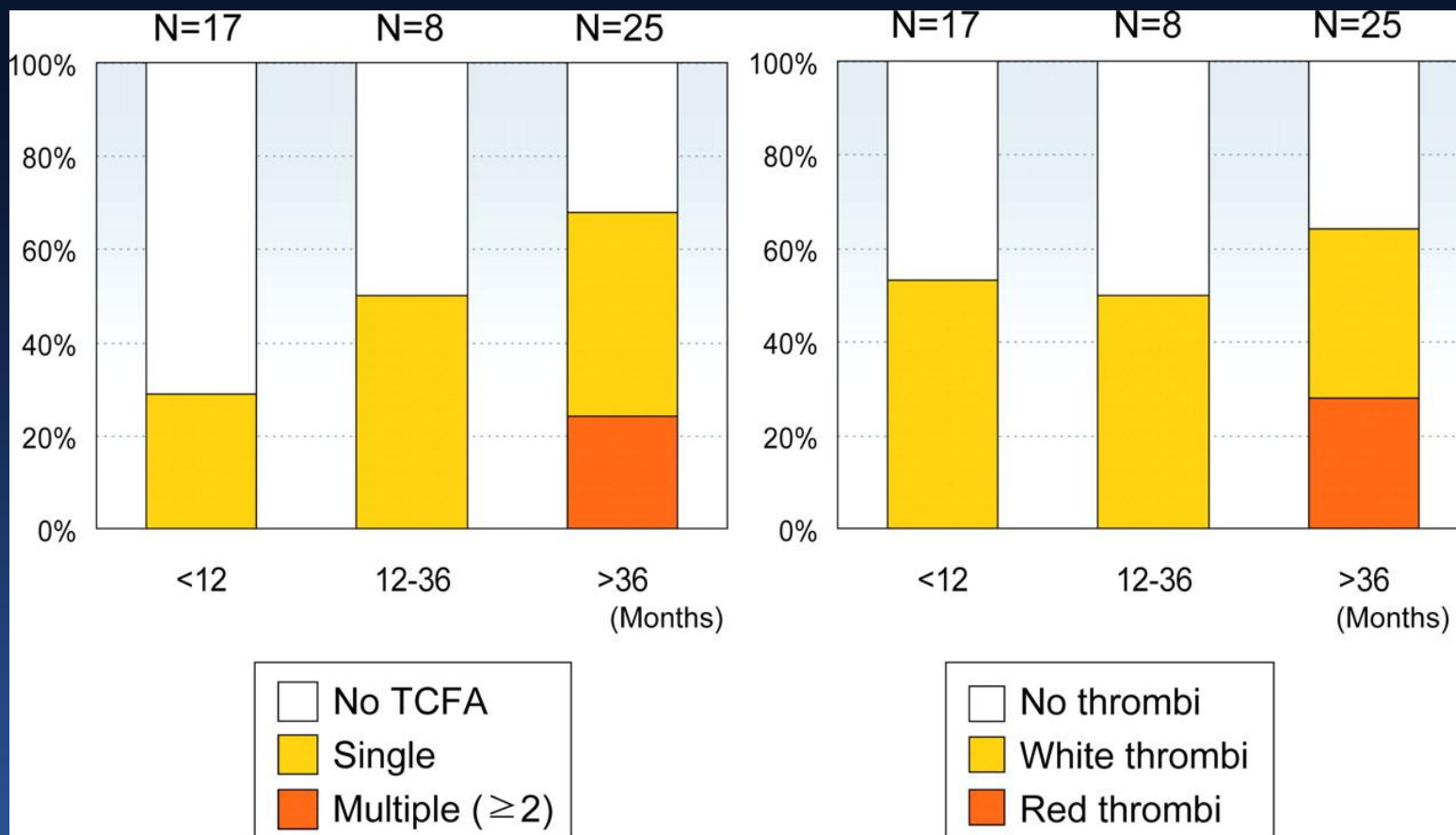
- Early FU, 0.7 ± 0.2 years, n=43, ACS 2.3%, TLR 95%
- Mid FU, 1.9 ± 0.6 years, n=22, ACS 22.7%, TLR 96%
- Late FU, 4.5 ± 0.8 years, n=21, ACS 9.5%, TLR 100%



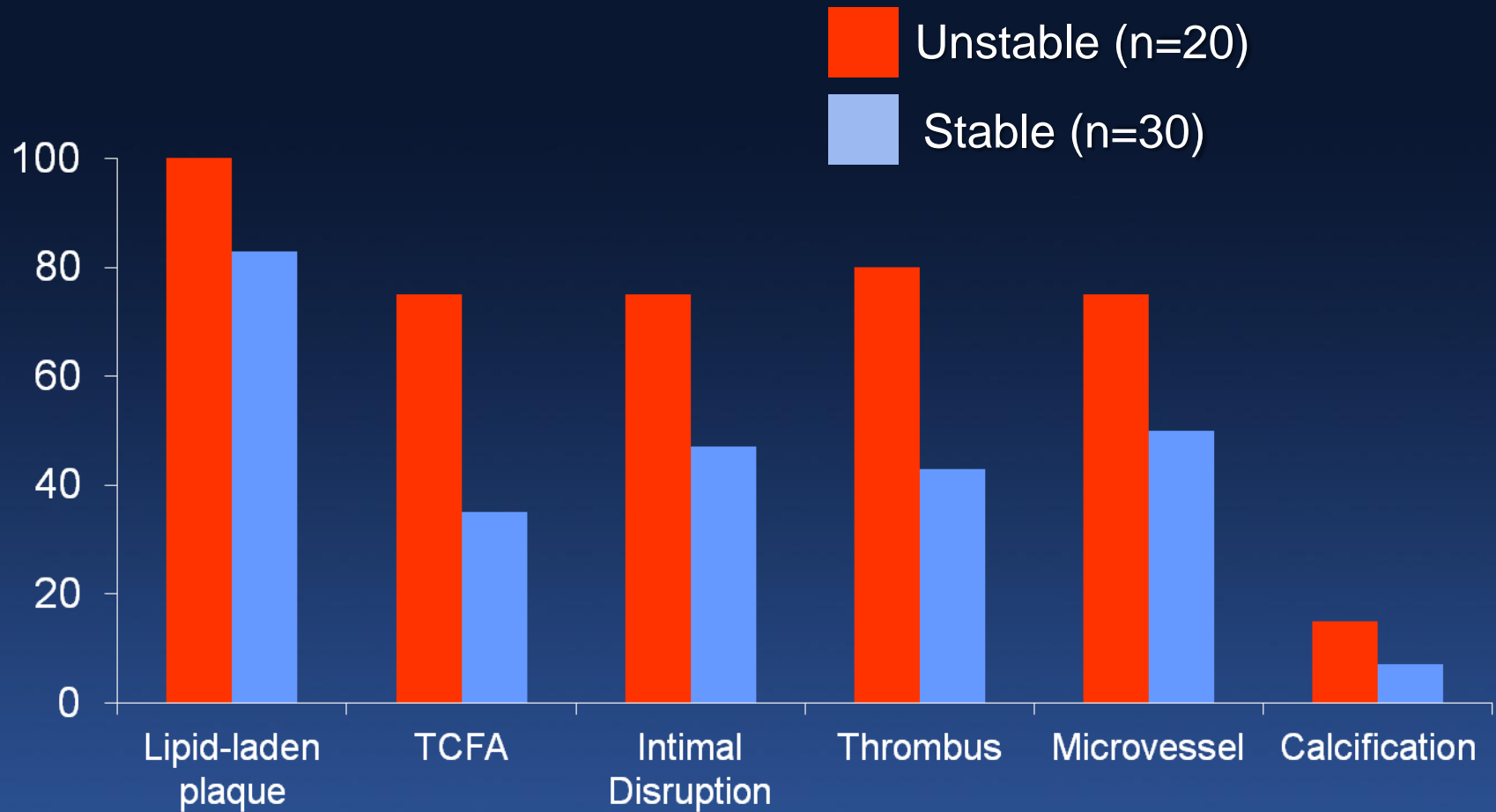
Late in-stent neoatherosclerosis in DES

(n=50, median follow-up of 32 months)

20 months post-implantation was the best cut-off to predict TCFA-like neointima.



Late in-stent neoatherosclerosis in DES



Various Neointimal VH Composition at the Maximal %IH Sites

6-mo Taxus

%NC 8%
%DC 2%

9-mo Taxus

%NC 28%
%DC 8%

22-mo Taxus

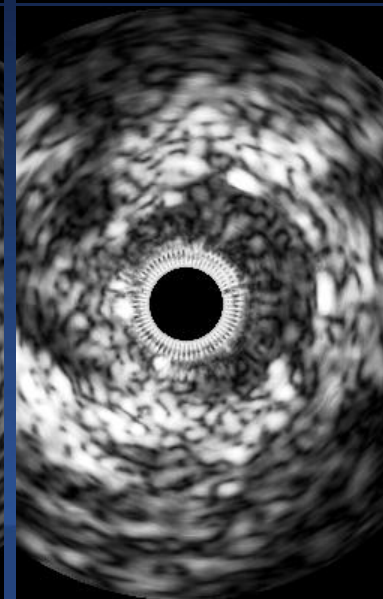
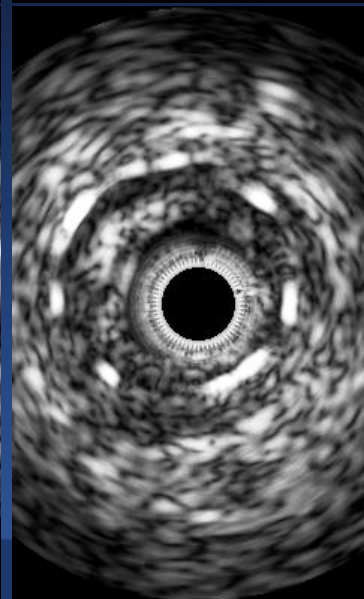
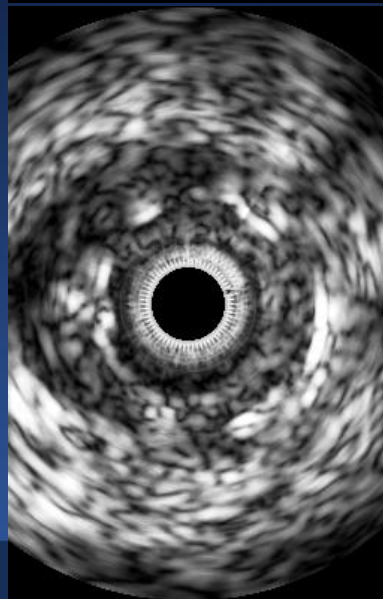
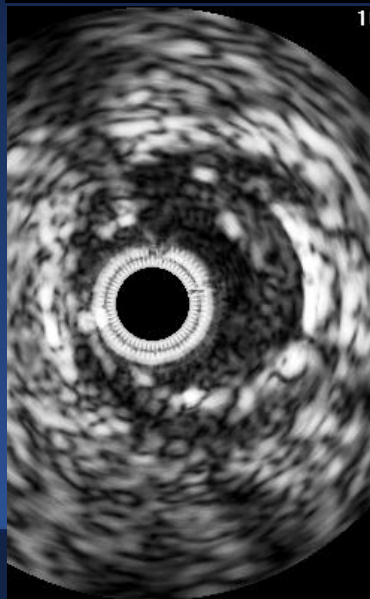
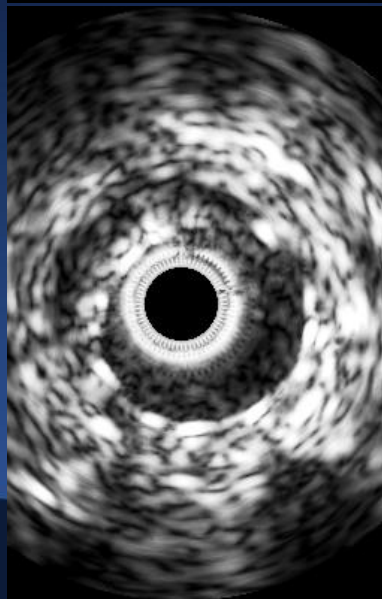
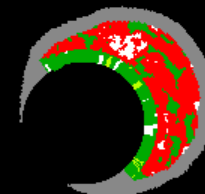
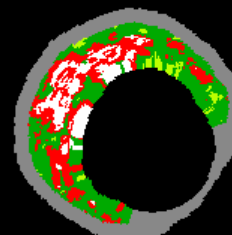
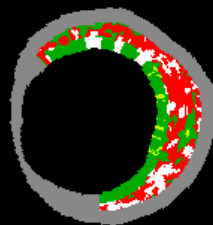
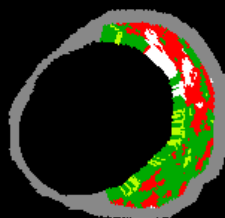
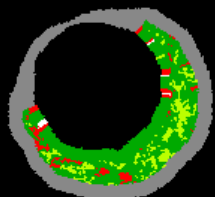
%NC 39%
%DC 20%

48-mo BMS

%NC 40%
%DC 25%

57-mo BMS

%NC 57%
%DC 15%



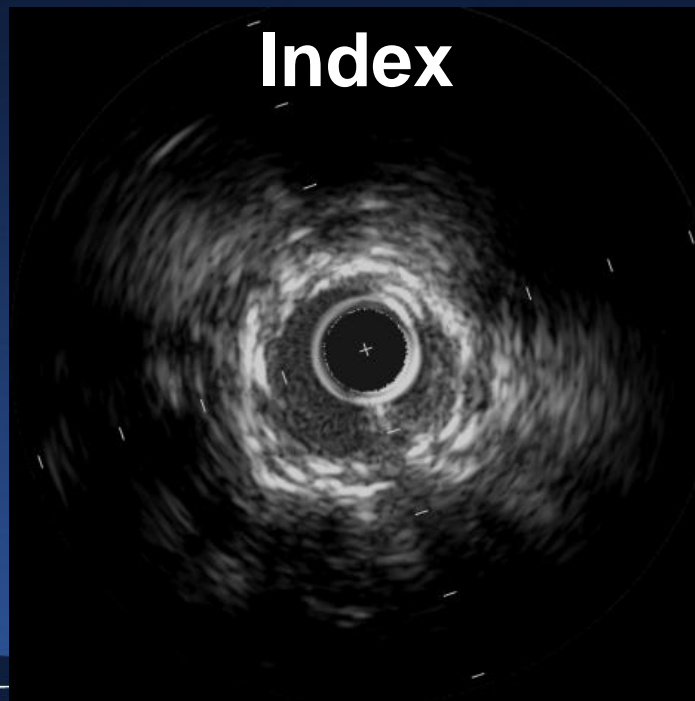
VH Composition of Neointima at Various Follow-Up Times in 117 ISR Lesions Combining 47 BMS and 70 DES



*p<0.01 and #p<0.05, vs. lesions at follow-up time <6 months

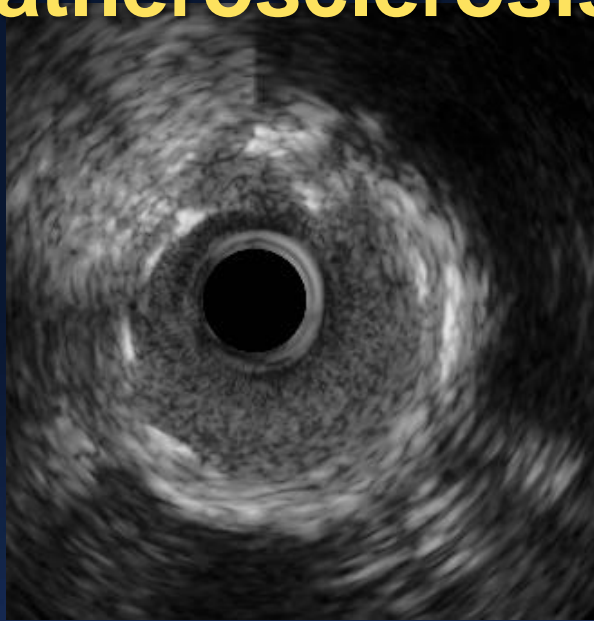
Late in-stent neoatherosclerosis in DES

- 54 Lesions in 46 patients with 2.8years (1.6-4.8) follow-up
- Calcification in NIH in 22% (12/54)
- Calcification increase behind stent (55→78 degree, $p<0.001$), proximal (34→65 degree, $p<0.0001$) and distal reference (20→25 degree, $p=0.002$).
- Only 2 lesions showed stent recoil ($>15\%$ of decrease of stent area).

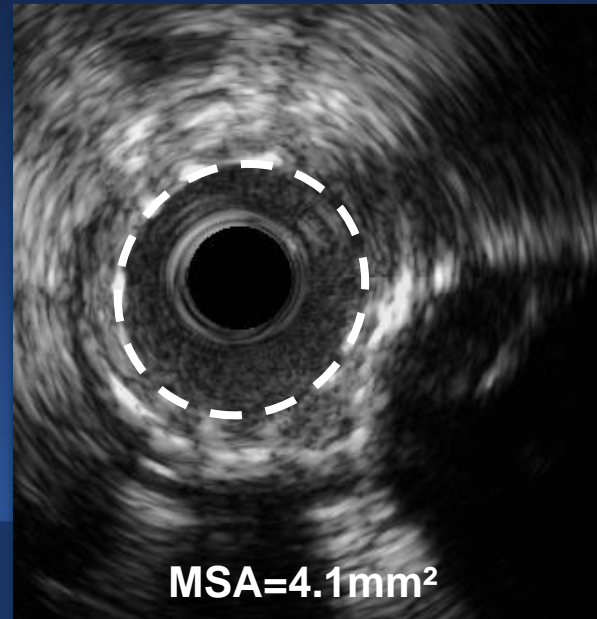
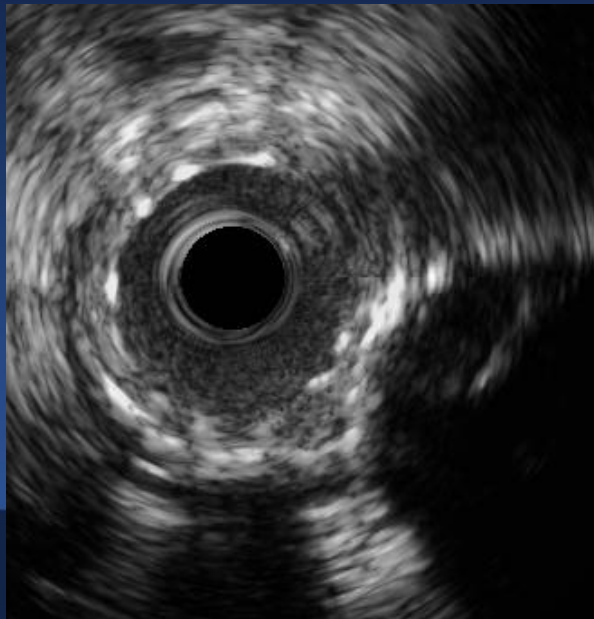


Late Stent Recoil due to Progression of atherosclerosis behind Stent

Index

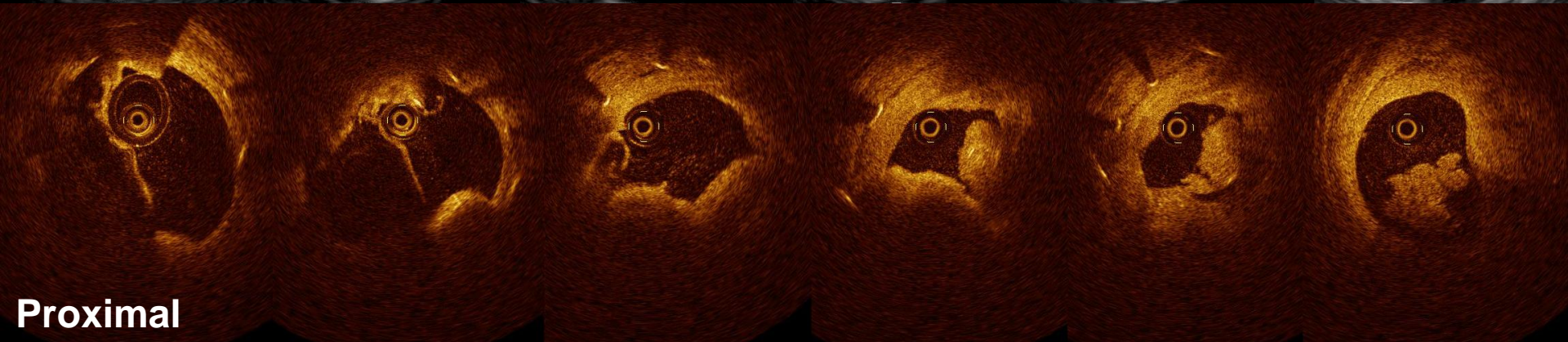
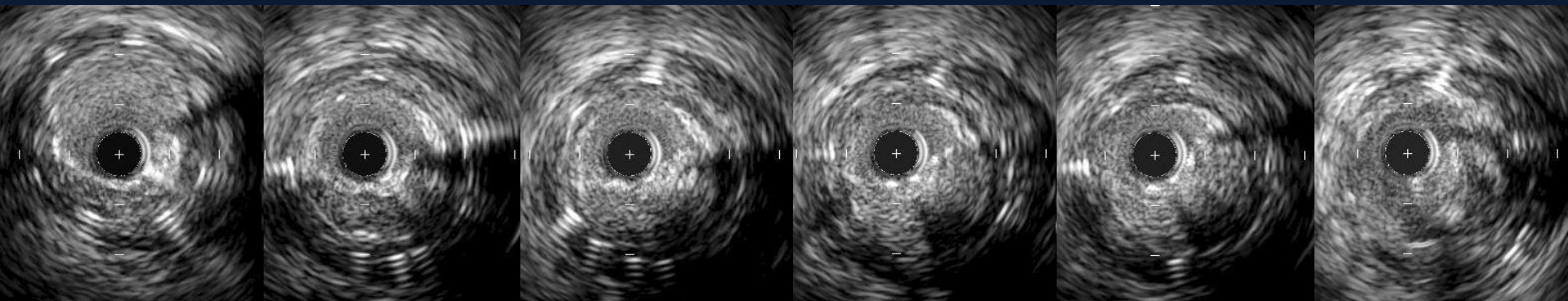


Follow-up



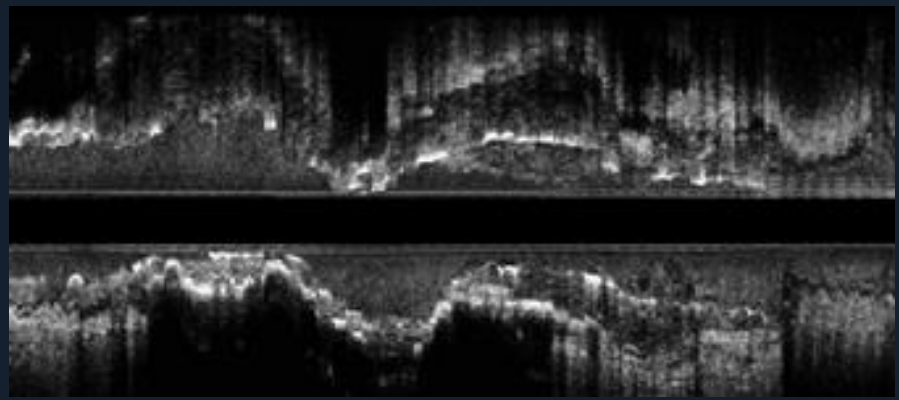
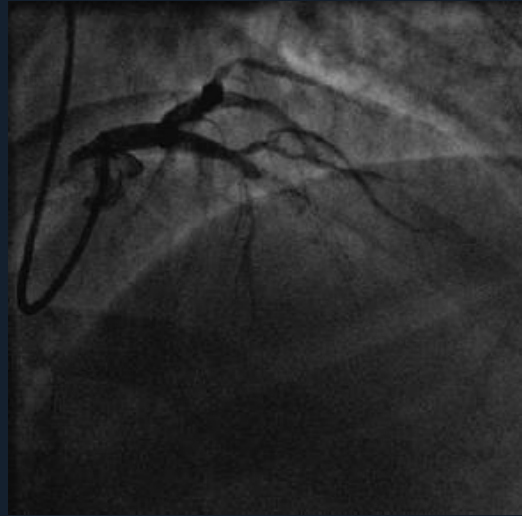
IVUS analysis of 23 very late DES thrombosis cases at Asan Medical Center

- Late Stent Malapposition: 17 DES patients (73.9%)
- Neointimal rupture in 10 (43.5%) and reference segment plaque rupture in another 5 (21.7%)



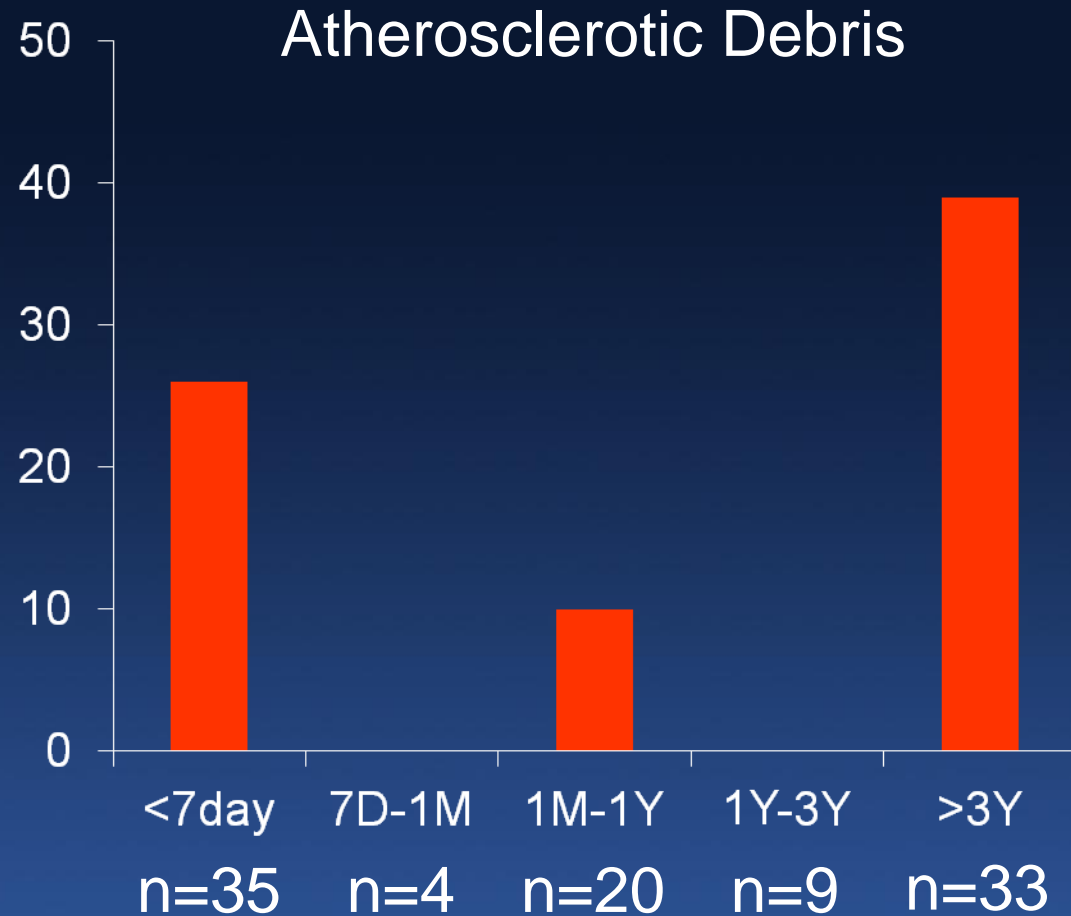
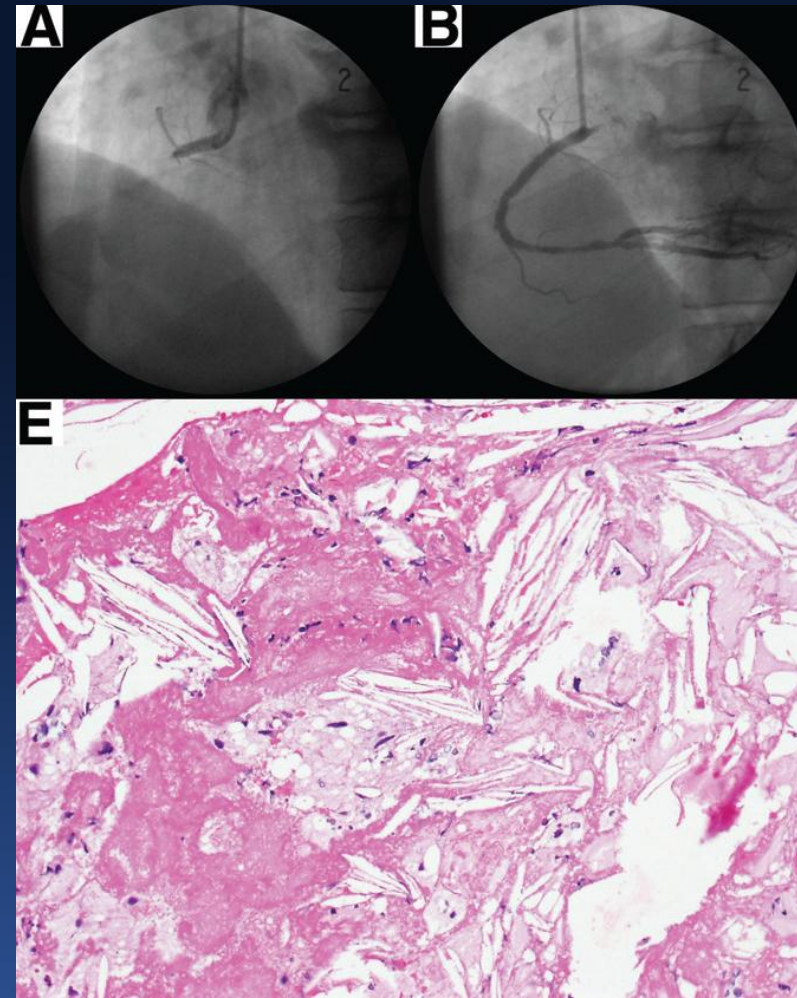
Proximal

18 Late Stent Thrombosis Cases



	LST (n=18)	Control (n=36)	p-value
IVUS remodeling index	1.24	0.99	<0.001
IVUS malapposition	78%	42%	0.01
IVUS malappo area (mm ²)	4.1 ±2.3	1.2±1.5	0.001
OCT max uncoverage length	3.3	0.9	<0.001
OCT uncovered strut	12.3%	4.1%	0.001

Bare Metal Stent Thrombosis (102 definite ST)



Summary

- 1.** Neointimal hyperplasia is similar to the *de novo* atherosclerosis, but develops earlier (BMS=5 years, DES=2 years) based on vessel injury and chronic reaction to the stent.
- 2.** The predictor to induce neointimal hyperplasia may be similar to those for atherosclerosis in addition to stent type.
- 3.** Neointimal hyperplasia can cause very late stent thrombosis.
- 4.** OCT is the best imaging modality to evaluate neointimal hyperplasia.