

Evaluation and Prediction of Late Stent Thrombosis by IVUS and OCT

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Potential conflicts of interest

I have the following potential conflicts of interest to report:

Consulting

Employment in industry

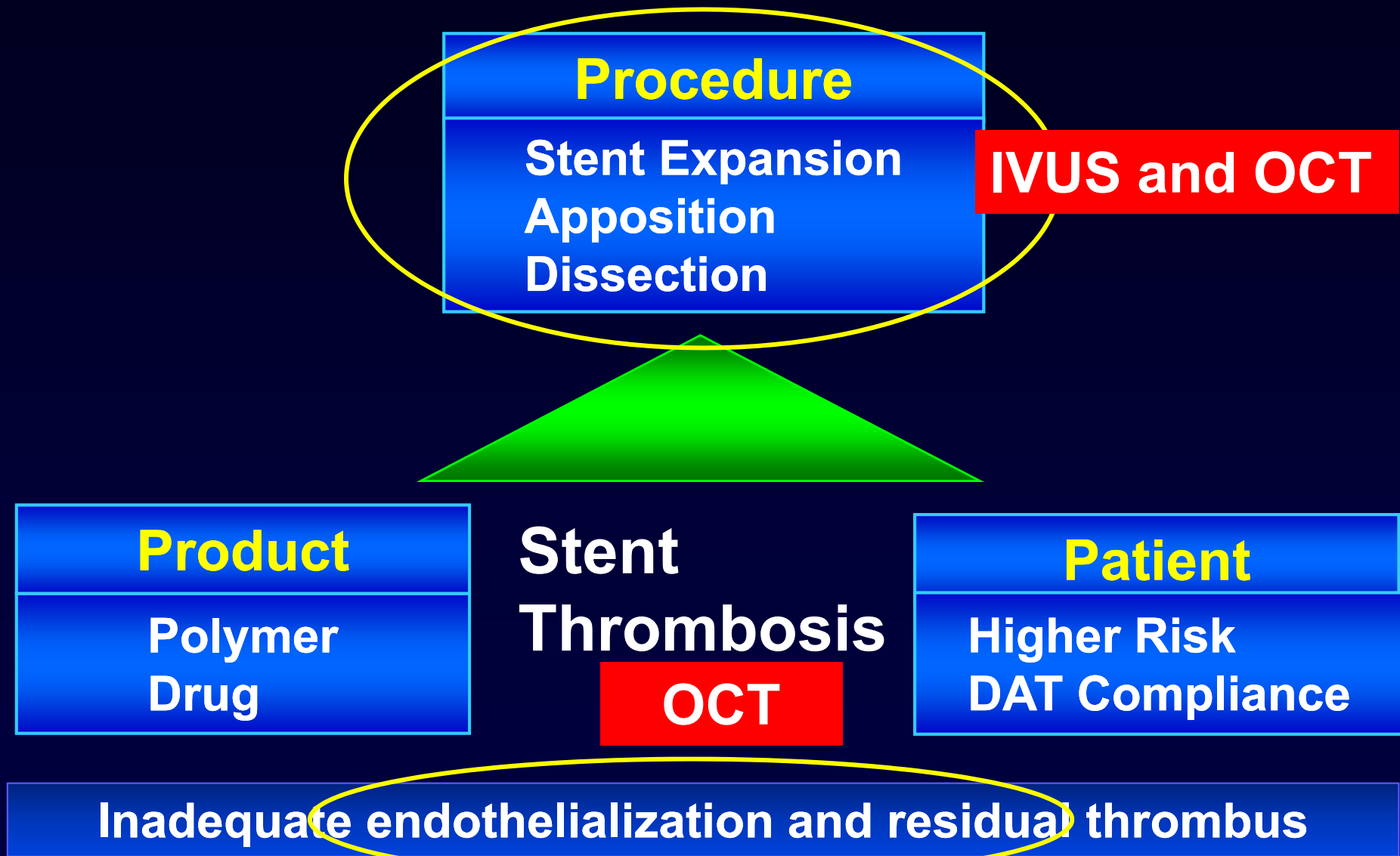
Stockholder of a healthcare company

Owner of a healthcare company

Other(s)

I do not have any potential conflict of interest

Stent Thrombosis



Late stent evaluation with OCT/IVUS

Uncovered stent struts

Stent malapposition

Intracoronary thrombus

Neoatherosclerosis

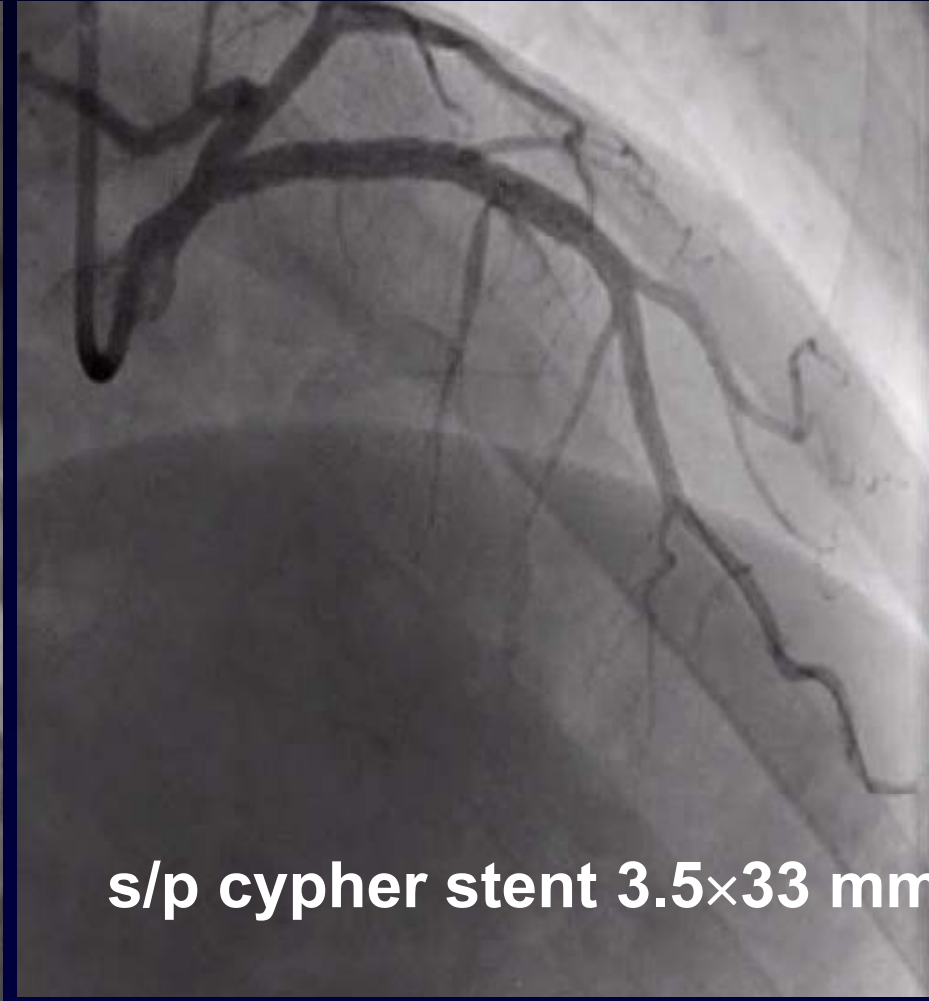


Possible factors related with
stent thrombosis

Late Stent Malapposition vs. Late Stent Thrombosis

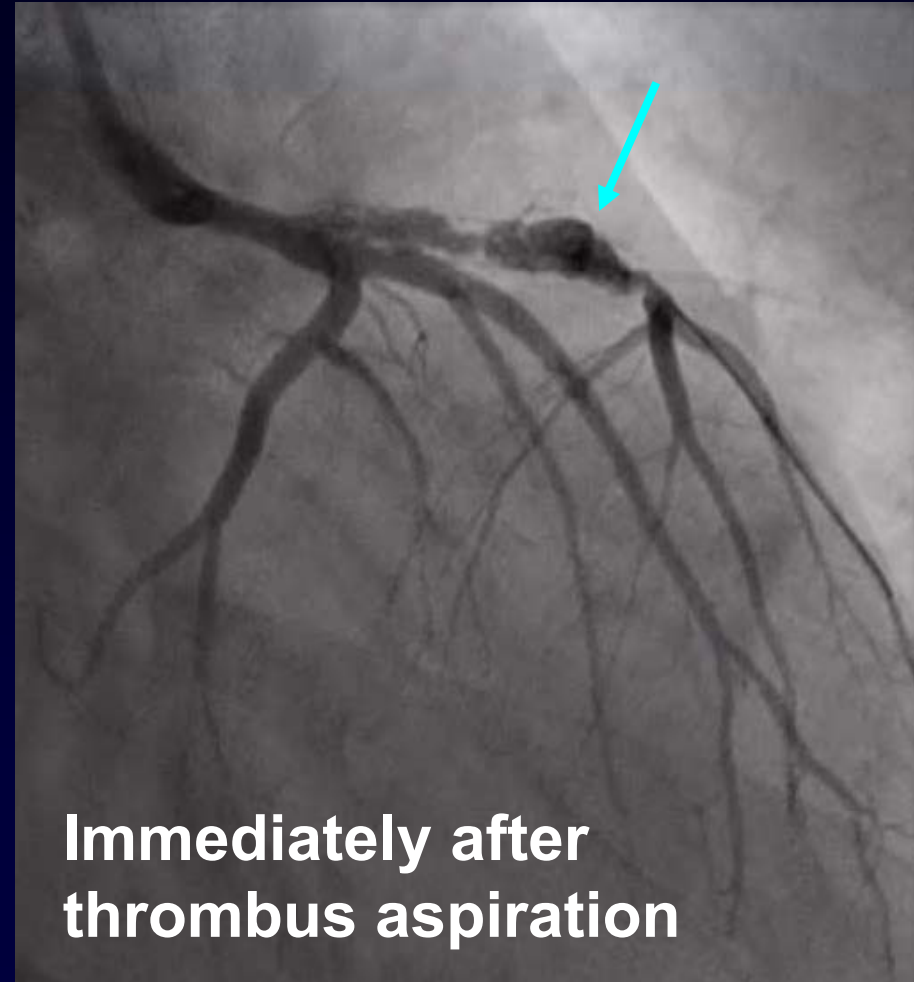
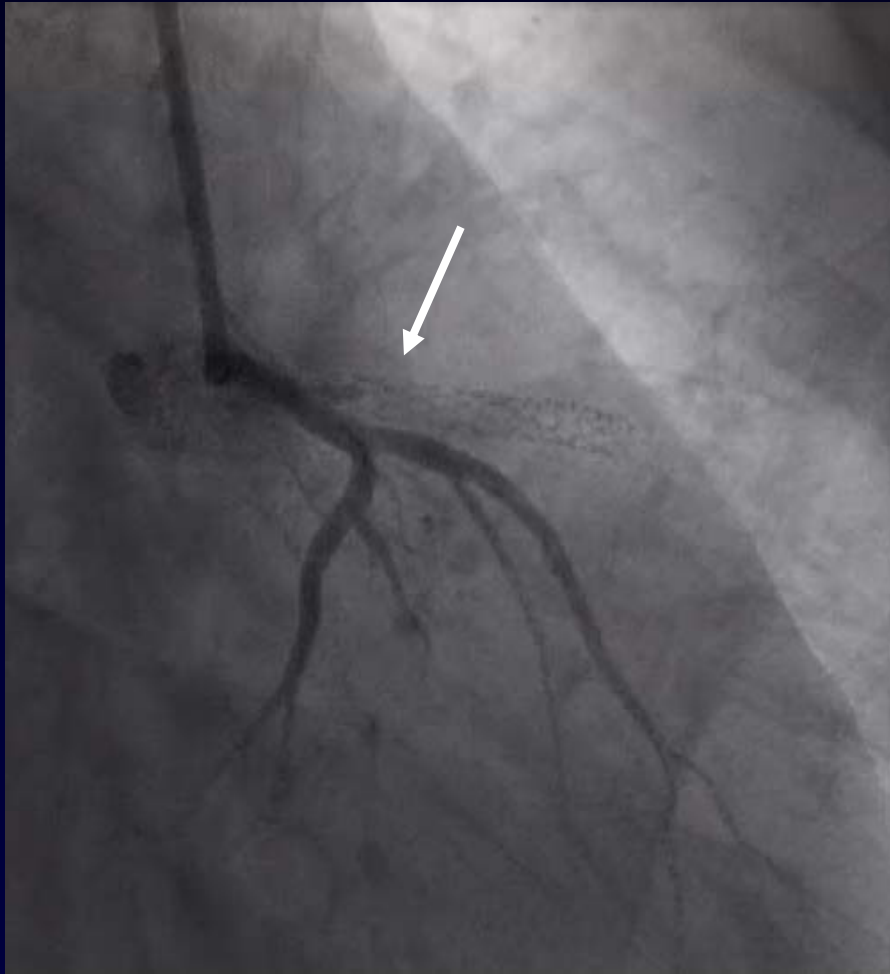
46 year-old male/stable angina, hypertension

Initial angiography (2004-9-10)



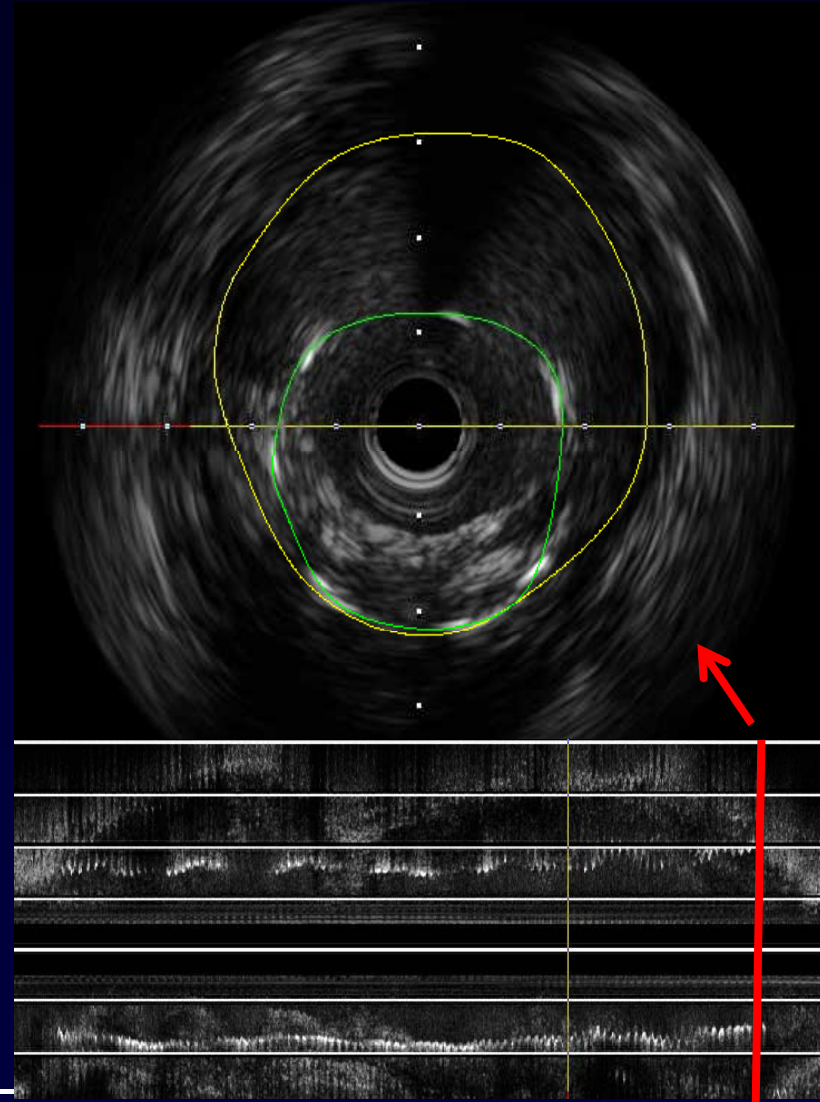
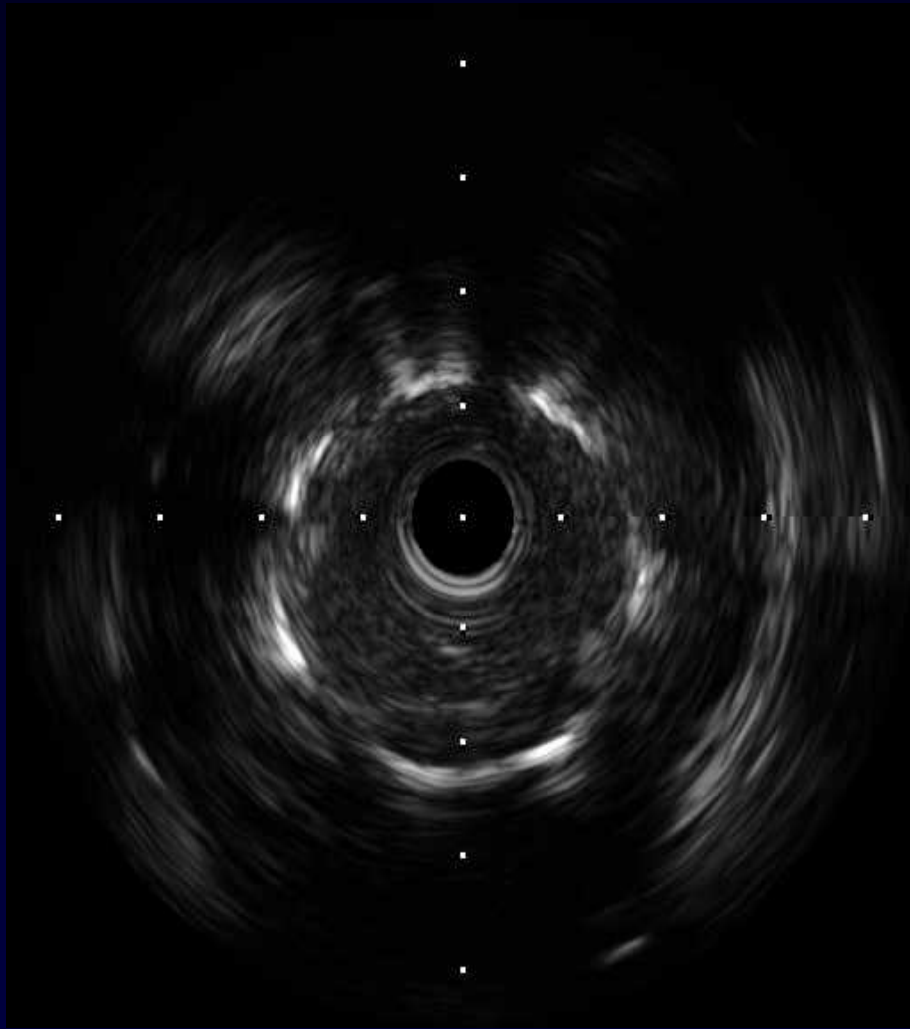
s/p cypher stent 3.5×33 mm

STEMI due to VLST: 6-year after stent implantation (2010-10-11)



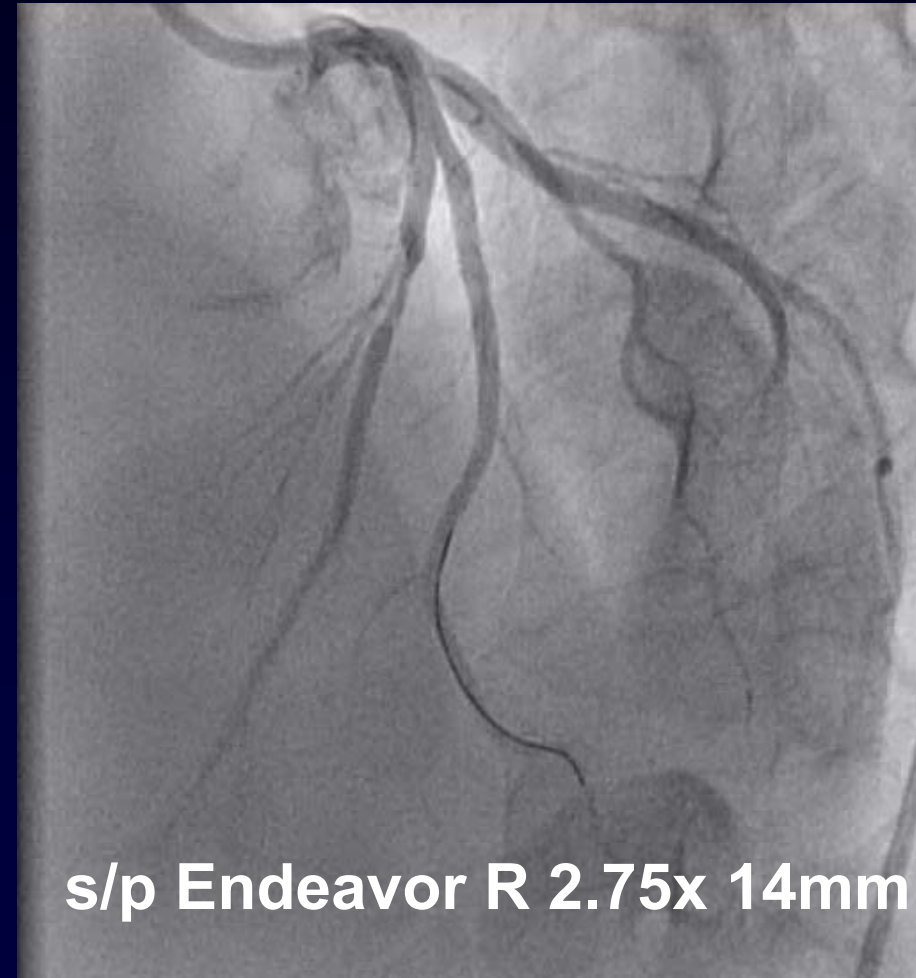
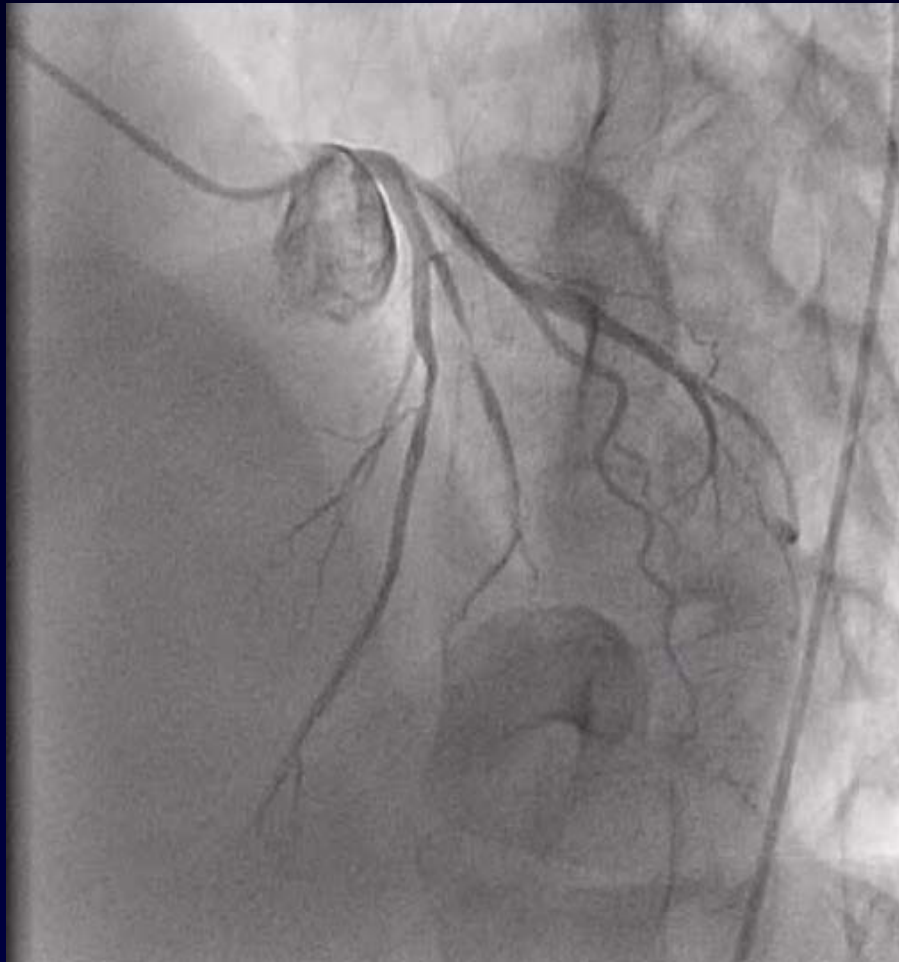
Very late ST due to malapposition (2010-10-11)

- IVUS after thrombus aspiration

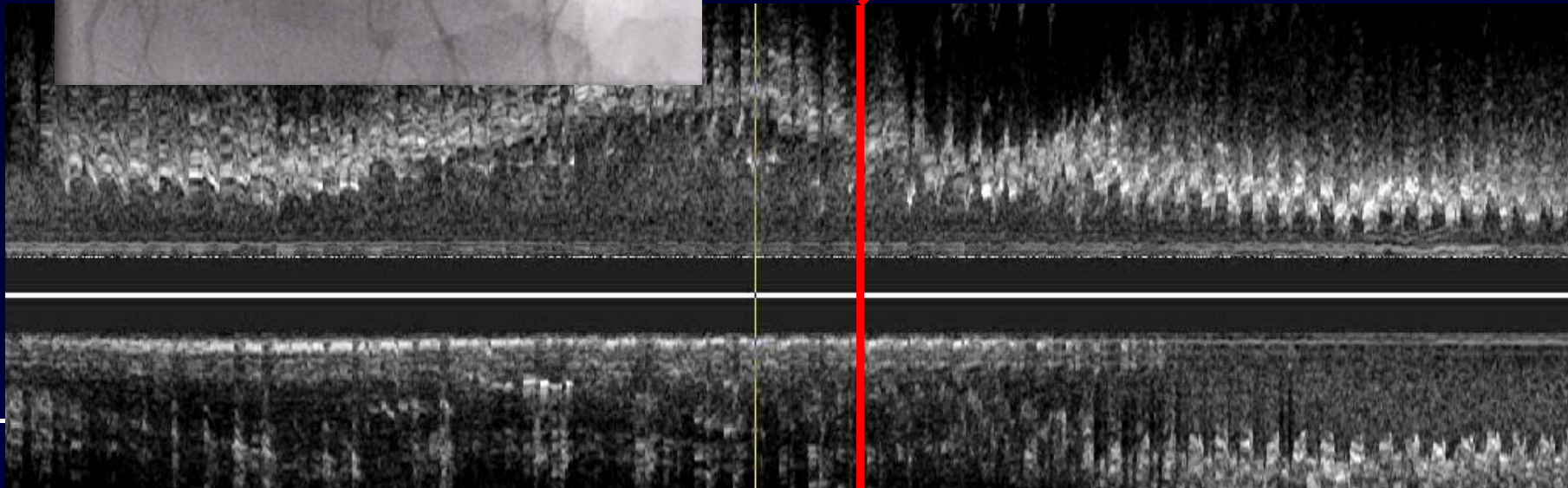
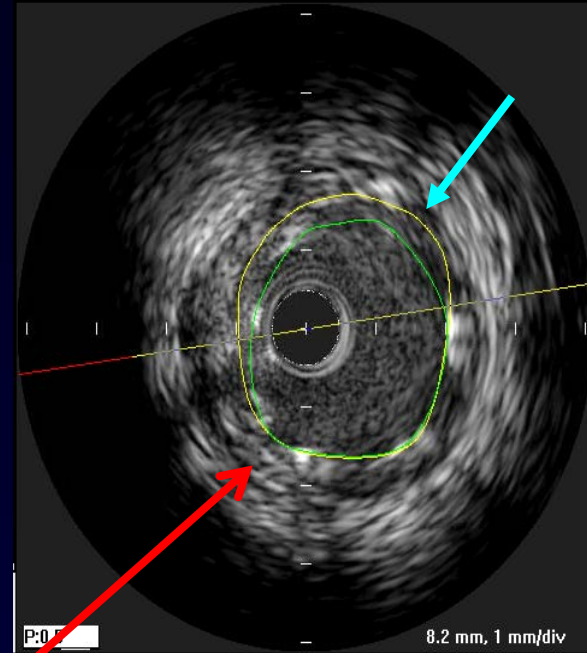
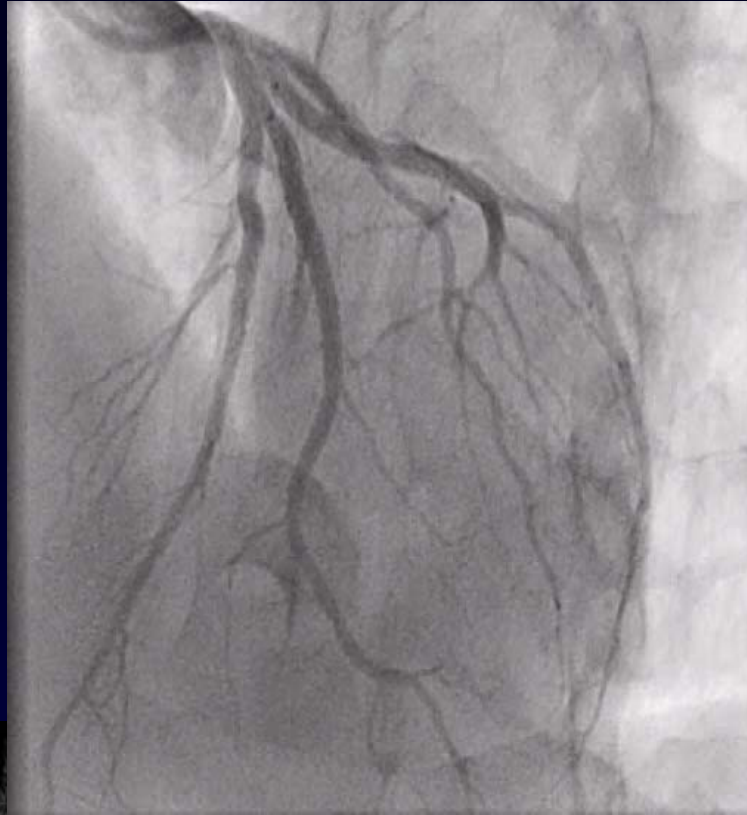


48 year-old male/unstable angina, resting chest pain, hypertension and smoking

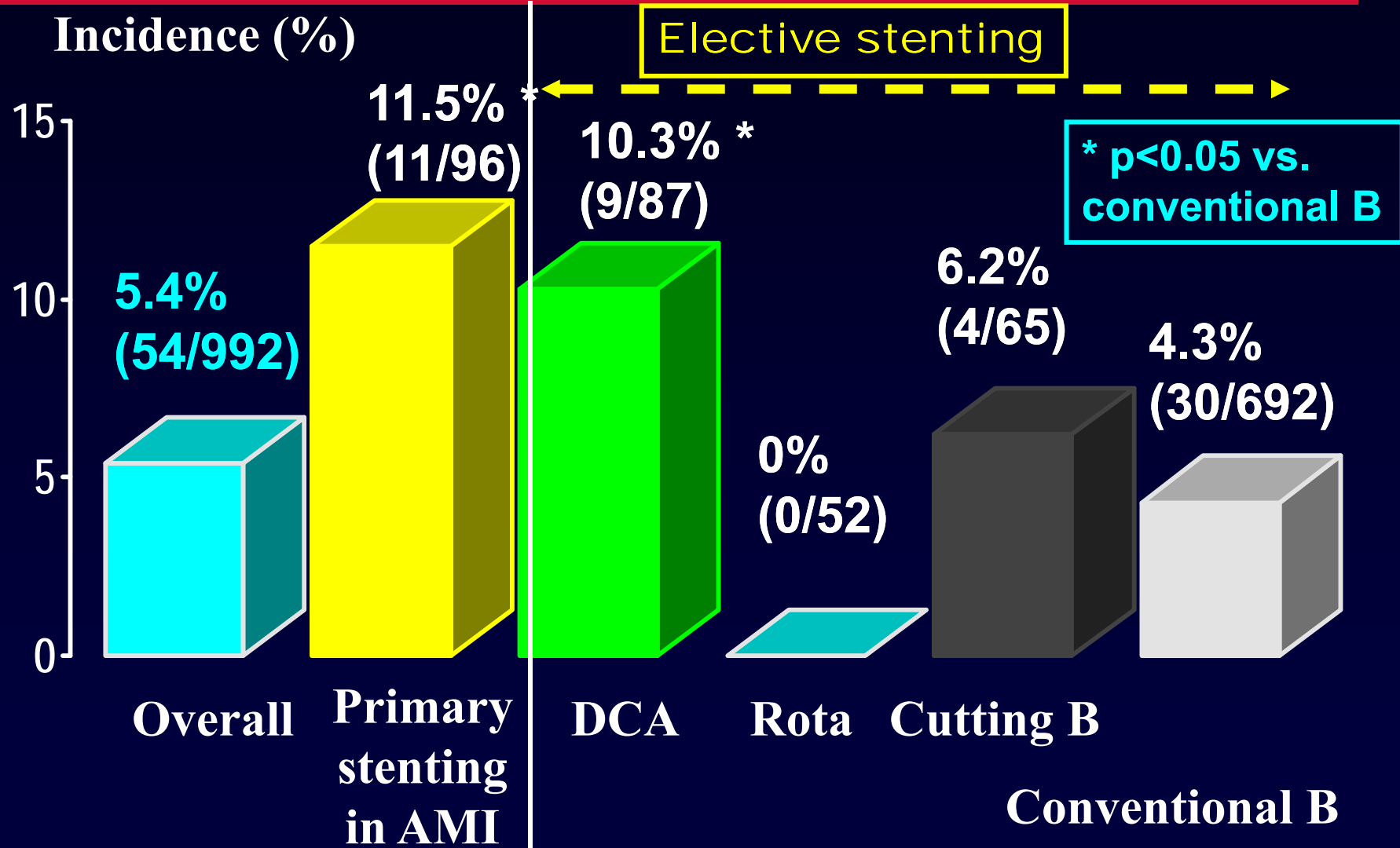
Initial angiography (2008-12-22)



9-month follow up (2009-10-5)

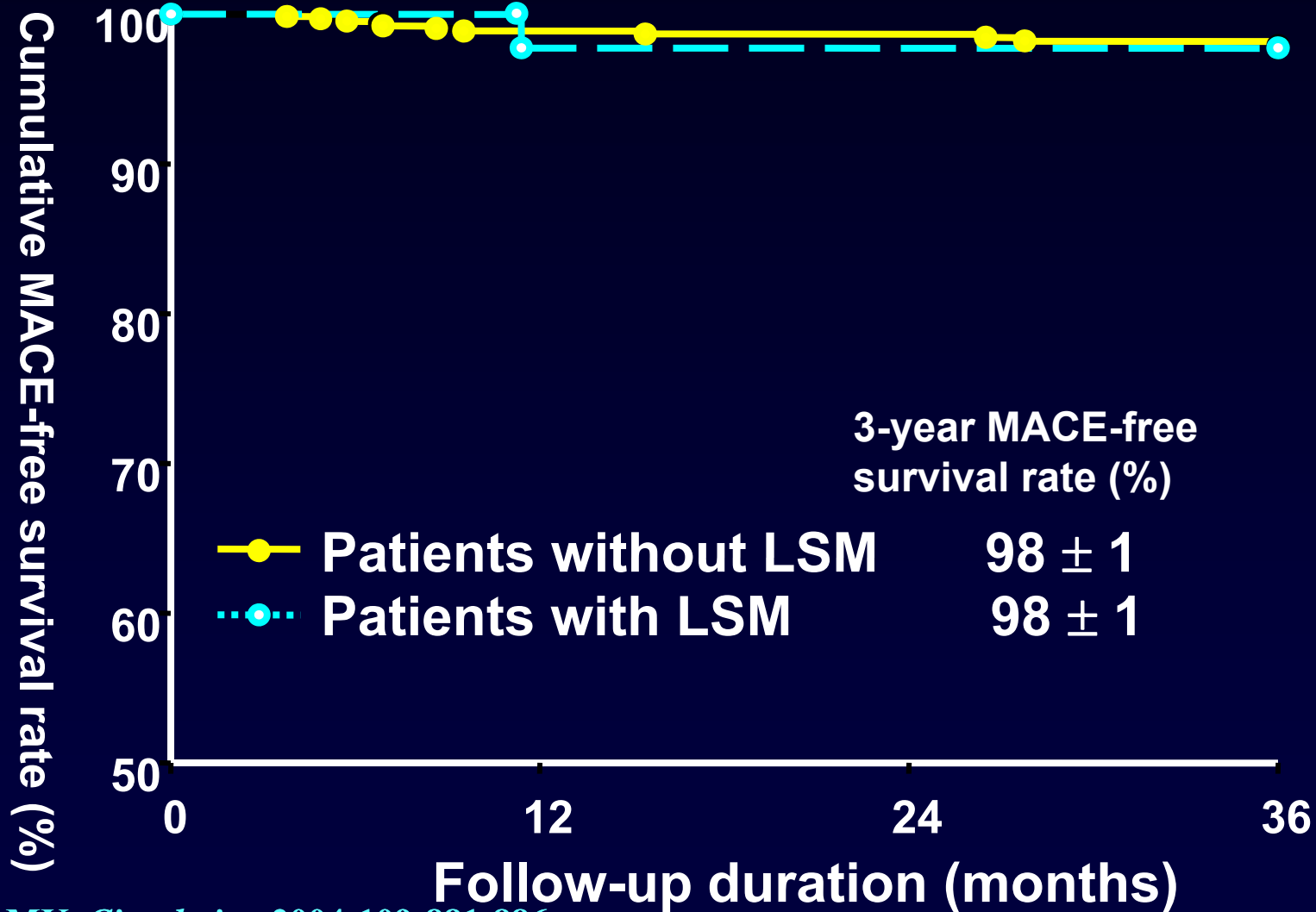


Incidence of LSM after BMS in 992 lesions



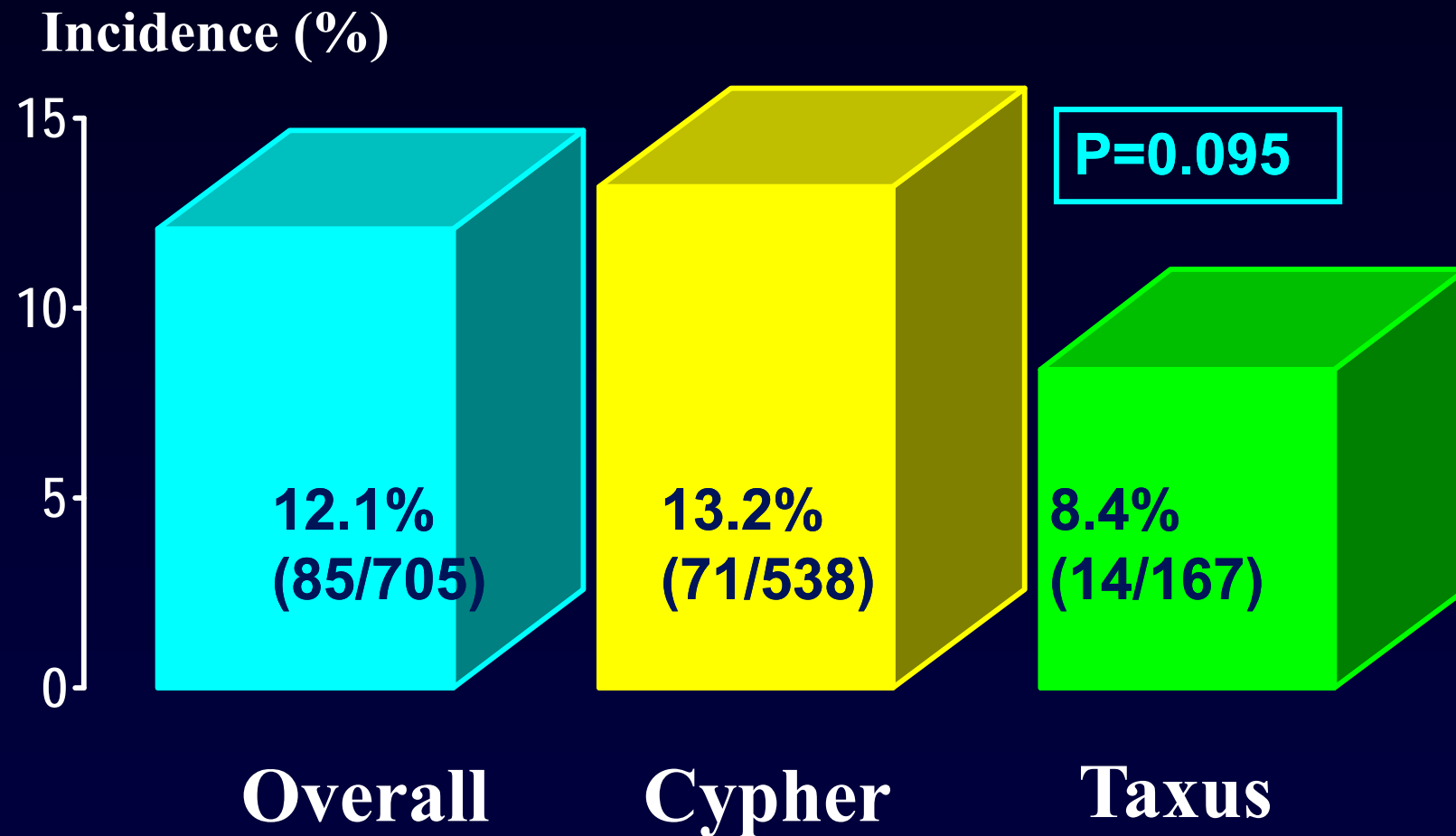
Hong MK, *Circulation* 2004;109:881-886

The cumulative (MACE) free survival curve



Hong MK, *Circulation* 2004;109:881-886

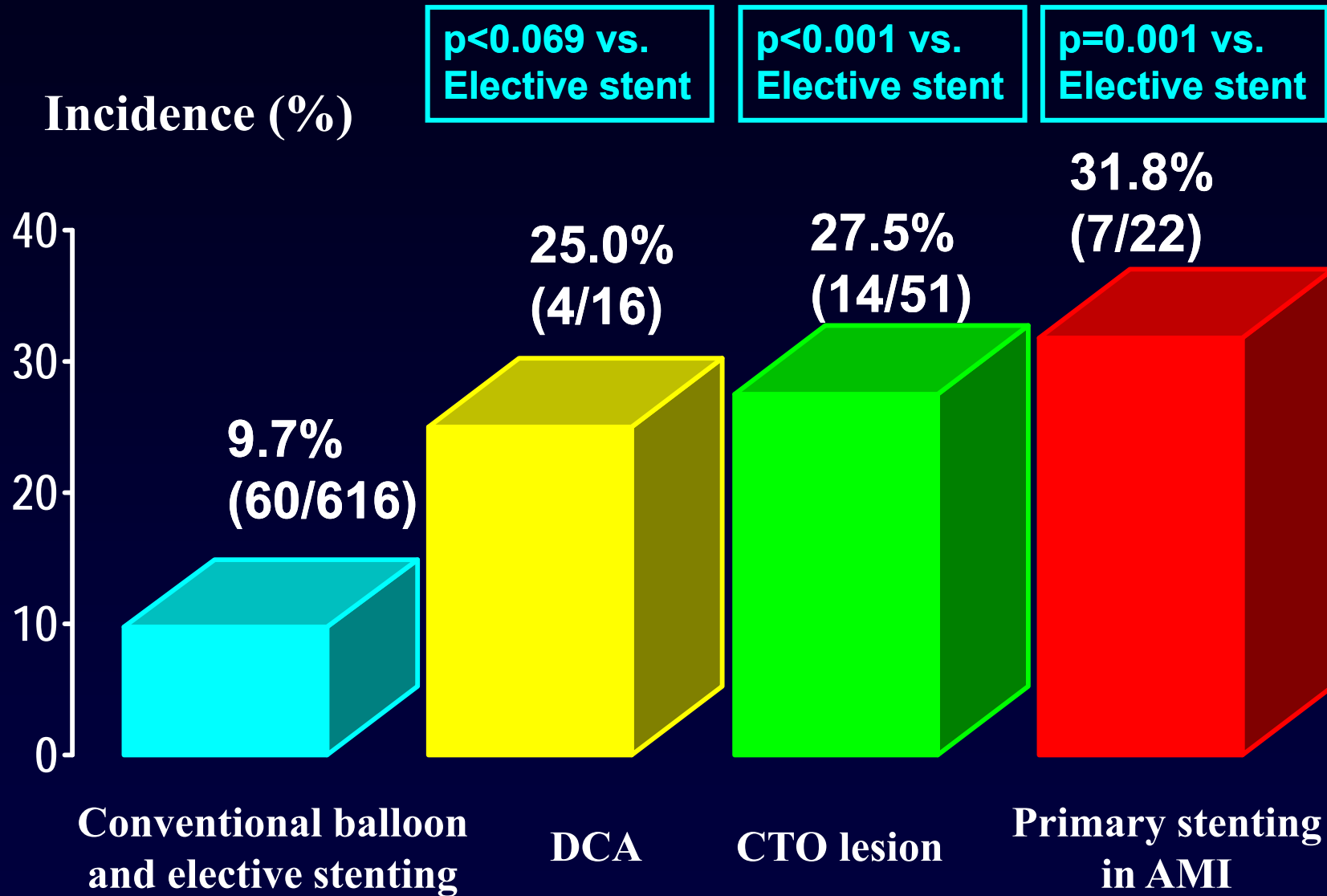
Incidence of LSM after DES in 705 lesions



Hong MK, *Circulation* 2006;113:414-419

Incidence of LSM after DES

LSM in DES



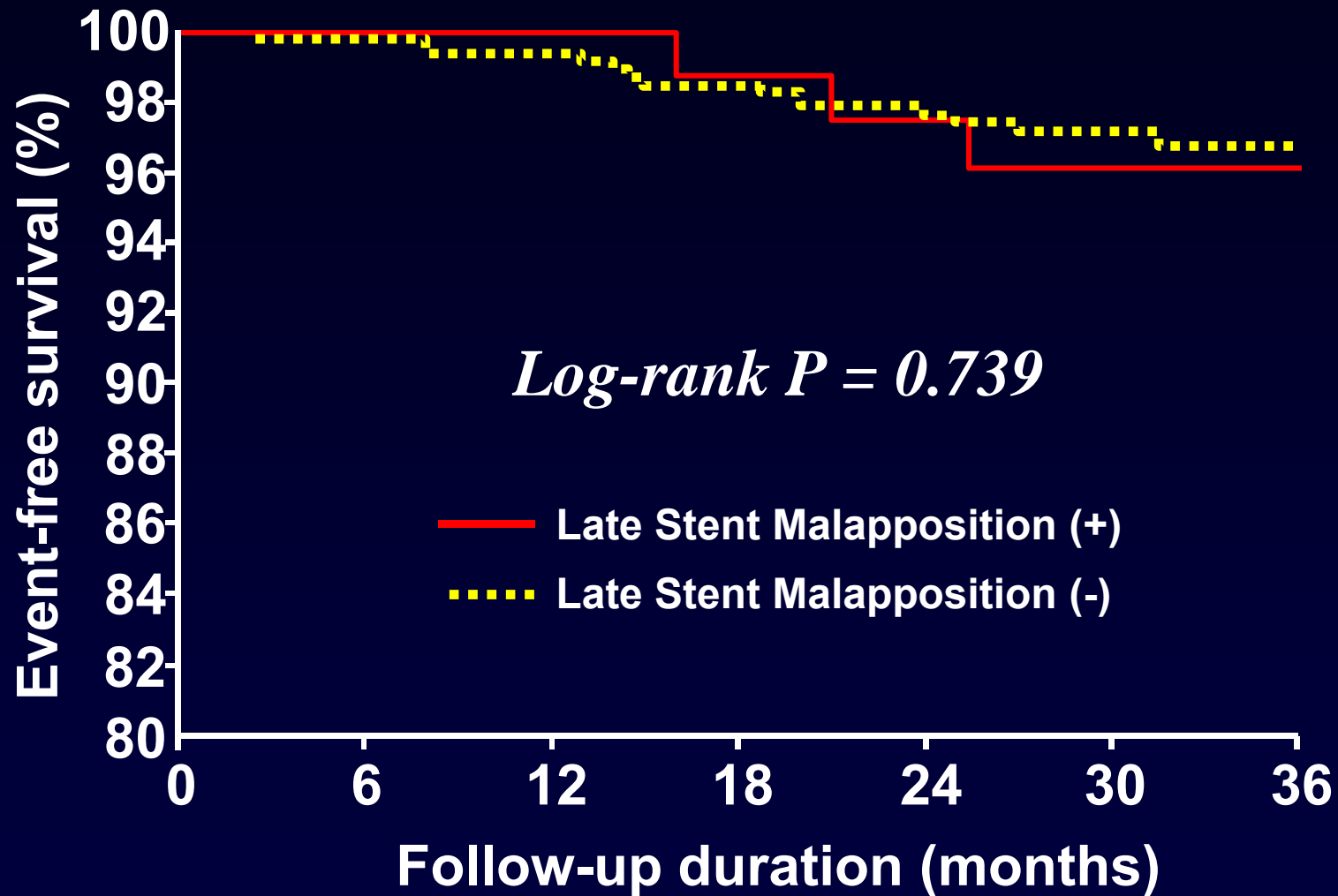
Hong MK, *Circulation* 2006;113:414-419

Long-term (> 1 yr) prognosis of LSM after DES

Favorable long-term prognosis of LSM

TAXUS II	No differences of clinical events between incomplete apposition (ISA) and non-ISA up to 12-month	<i>Tanabe K, et al. Circulation 2005</i>
SIRIUS	No negative clinical events at 12-month F/U	<i>Ako J, et al. JACC 2005</i>
TAXUS IV	No clinical events associated with ISA	<i>Weissman NJ, et al. JACC 2005</i>

The event free survival curve



Hong MK, et al. *J Am Coll Cardiol* 2007; 50; 1515-1516

Unfavorable long-term prognosis of LSM

Incomplete Stent Apposition and Very LST after DES

Patients. Thirteen patients with very LST were compared with 144 matched control patients who did not experience stent thrombosis for 2 years.

Results. More frequent incomplete stent apposition (77% vs. 12%; $P < 0.001$) and larger maximal incomplete stent apposition area (8.3 vs. 4.0 mm²; $P = 0.03$) were observed in patients with very LST compared with matched controls.

Conclusions. Incomplete stent apposition is highly prevalent in patients with very LST after DES implantation.

Cook S et al, *Circulation*. 2007;115:2426-2434.

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

Metaanalysis of LSM vs. late stent thrombosis

Table 2 Characteristics of the studies used for the assessment of the risk of (very) late stent thrombosis in patients with and without late stent malapposition

Study	Design	Clinical follow-up (months)	Type of stent	LSM	Patients number	Observed values for (very) late ST		Expected values for (very) late ST	Definition of ST
						Late ST (≤ 12 months)	Very late ST (> 12 months)		
Hoffmann et al. ³⁹	RCT	48	SES+BMS	Yes	57	0	1	0.18	Occurrence of acute symptoms in combination with angiographically documented TIMI flow 0 or 1 or the presence of flow-limiting thrombus (TIMI flow 1 or 2)
				No	268	0	0	0.82	
Tanabe et al. ³³	RCT	12	PES+BMS	Yes	46	0	NA	0.20	NA
				No	423	2	NA	1.80	
Hong et al. ⁴⁰	OS	36	SES+PES	Yes	82	NA	1	0.44	According to the Academic Research Consortium Criteria ⁴⁸
				No	475	NA	2	2.56	
Siqueira et al. ³⁸	OS	29 ^a	SES+PES	Yes	10	0	2	0.11	Angiographic documentation of partial or total stent occlusion with or without the presence of thrombus and sudden cardiac death or MI that is not clearly attributable to another coronary lesion
				NO	172	0	0	1.89	
Weissman et al. ³⁷	RCT	24	PES+BMS	Yes	33	0	0	0.06	NA
				NO	514	1	0	0.94	

BMS, bare metal stent; LSM, late stent malapposition; MI, myocardial infarction; NA, not available; OS, observational study; RCT, randomized controlled trial; ST, stent thrombosis; SES, sirolimus-eluting stent; PES, paclitaxel-eluting stent.
^aMean duration of clinical follow-up.

The risk of (very) late ST in patients with LSM was higher compared with those without LSM (OR = 6.51, CI 95% 1.34–34.91, P = 0.02)

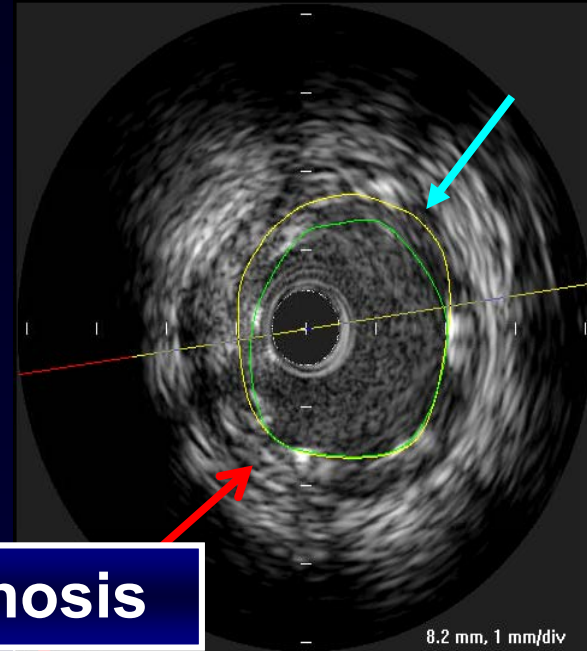
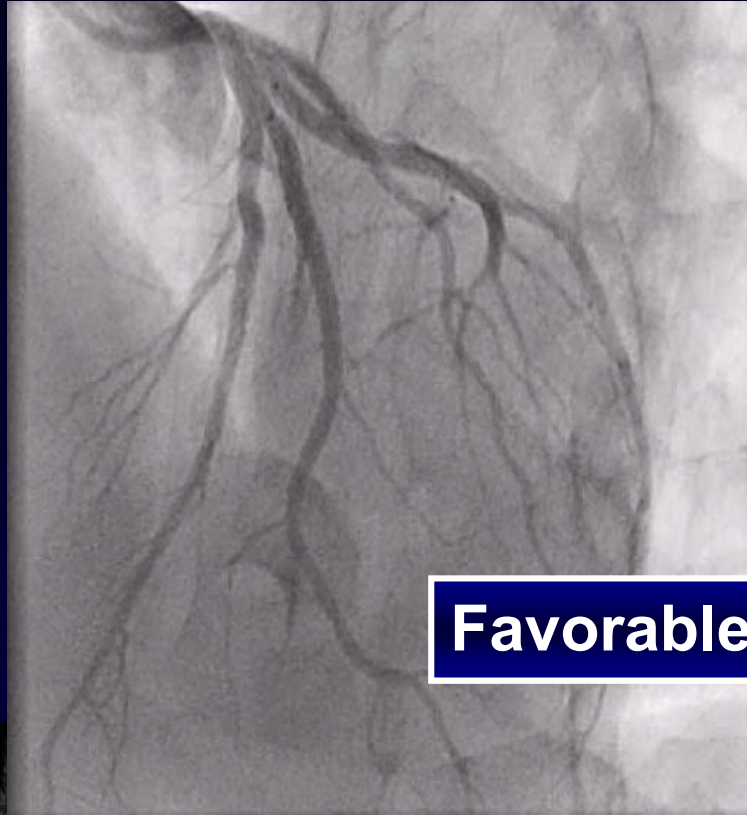
Hassan AKM, et al. *Eur Heart J* 2010;31;1172-1180

What are the differences among several studies?

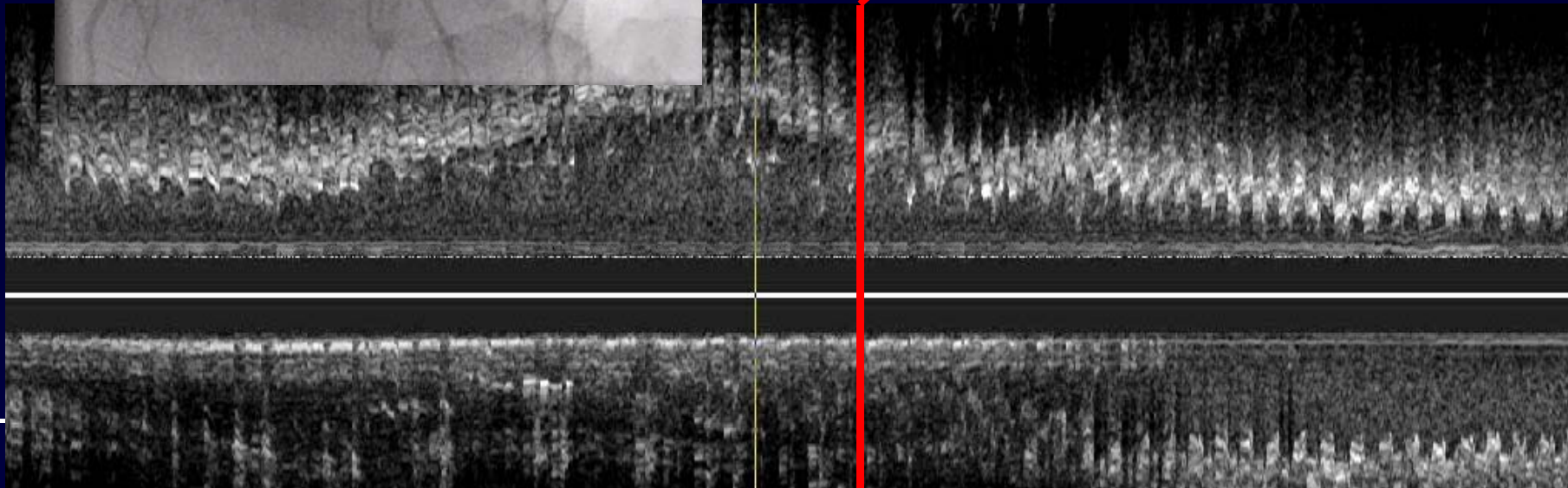
	LSM patients	Non-LSM patients	Index IVUS	LSM area, mm ²
Favorable				
Hong et al	80	452	yes	3.0 mm ²
TAXUS II	16	213	yes	SR (3.6mm ²), MR (2.1mm ²)
TAXUS IV	9	94	yes	NA
SIRIUS				
Unfavorable				
Cook et al				
Siqueira et al	10	112	yes	7.6 mm ² (volume:44.5mm ³ , length:7.4mm)
Alfonso et al	12	none	no	NA
Lee et al	23 LST		no	4.6 mm² ** (volume 17.8 mm ³)

*** LSM area might be under-estimated because IVUS was performed at the time of LST and some of thrombus was involved in the masking the part of LSM area.

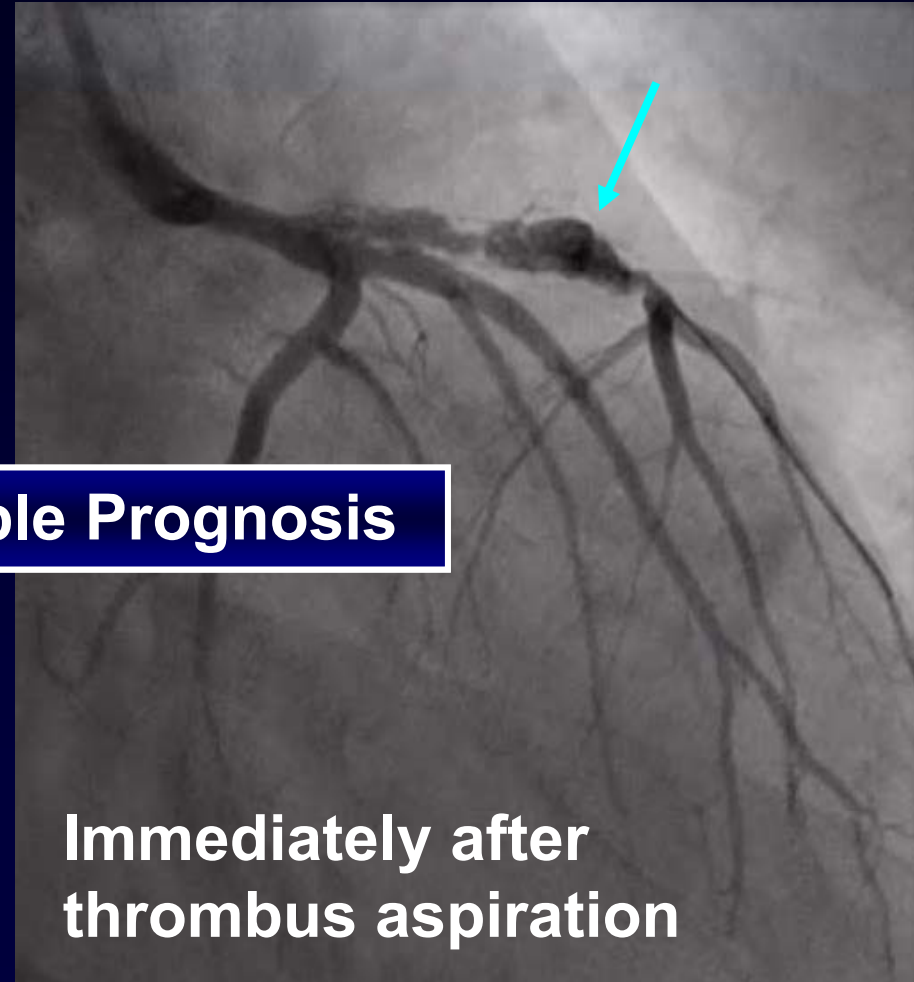
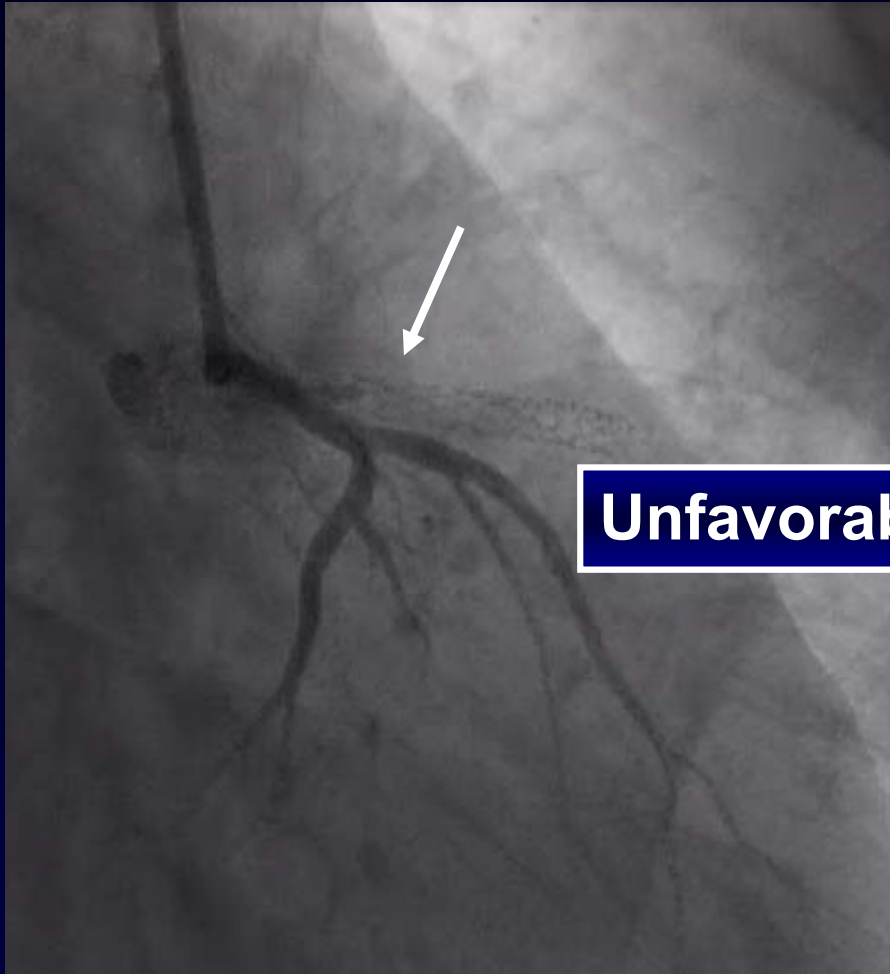
9-month follow up (2009-10-5)



Favorable Prognosis



STEMI due to VLST: 6-year after stent implantation (2010-10-11)



Unfavorable Prognosis

**Immediately after
thrombus aspiration**

Pathological Correlates of Late Drug-Eluting Stent Thrombosis

Strut Coverage as a Marker of Endothelialization

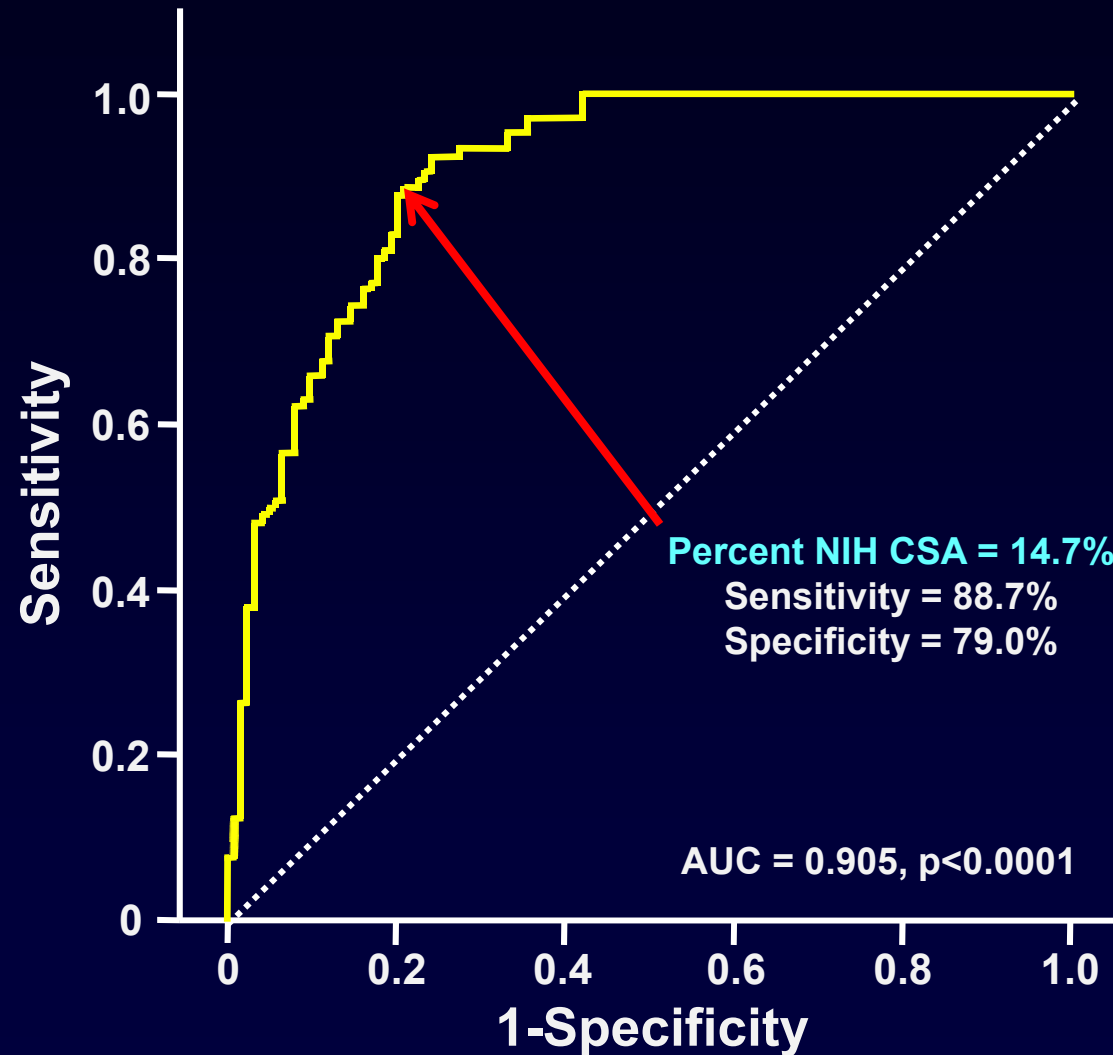
The most powerful histological predictor of stent thrombosis was endothelial coverage.

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

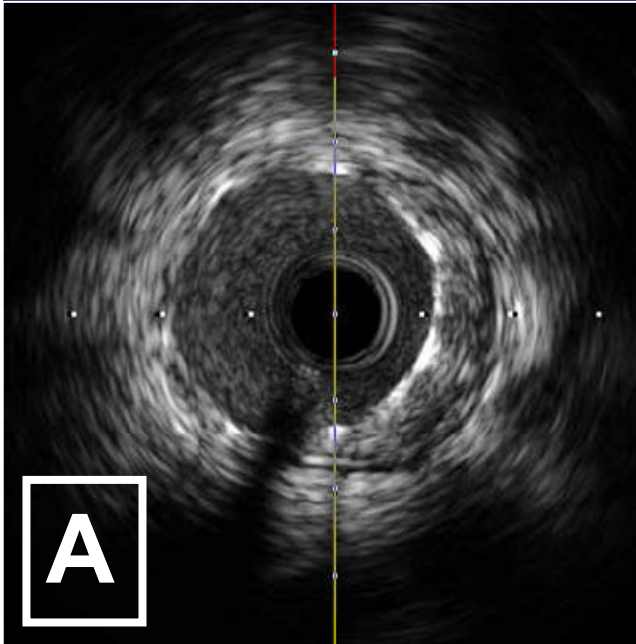
The odds ratio for thrombus with a ratio of uncovered to total struts $> 30\%$ $\Rightarrow 9.0$ (95% CI, 3.5 to 22)

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

Percent neointimal hyperplasia (NIH) cross-sectional area (CSA) was calculated as $(\text{NIH CSA}/\text{stent CSA}) \times 100$ for receiver-operating characteristic analysis of NIH detection by IVUS in 243 patients with 250 lesions who underwent both follow-up OCT and IVUS

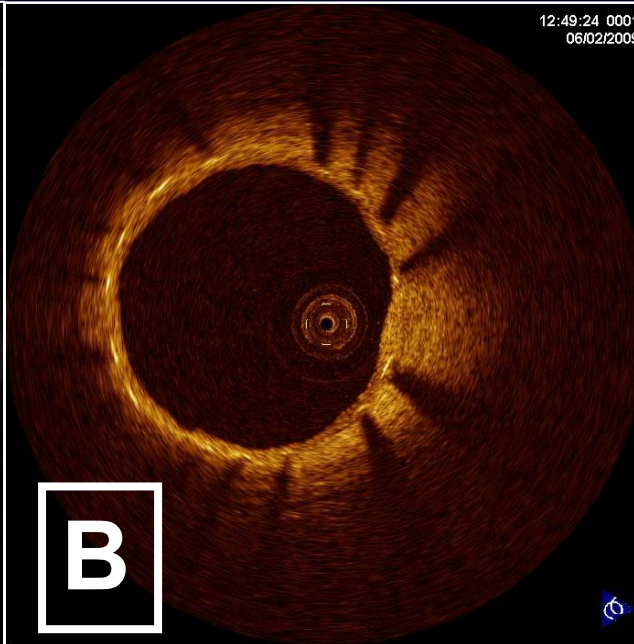


Kwon SW, Hong MK et al. *Am Heart J* 2011;161: 367-372



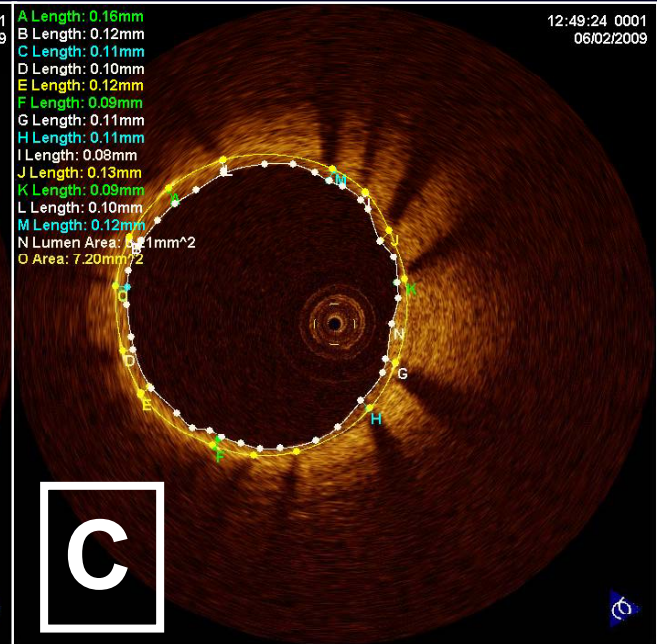
A

**NIH undetectable
by IVUS**



B

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



C

12:49:24 0001
06/02/2009

A Length: 0.16mm
B Length: 0.12mm
C Length: 0.11mm
D Length: 0.10mm
E Length: 0.12mm
F Length: 0.09mm
G Length: 0.11mm
H Length: 0.11mm
I Length: 0.08mm
J Length: 0.13mm
K Length: 0.09mm
L Length: 0.10mm
M Length: 0.12mm
N Lumen Area: 6.1mm²
O Area: 7.20mm²

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06/02/2009

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

Malapposed vs. Uncovered Struts.

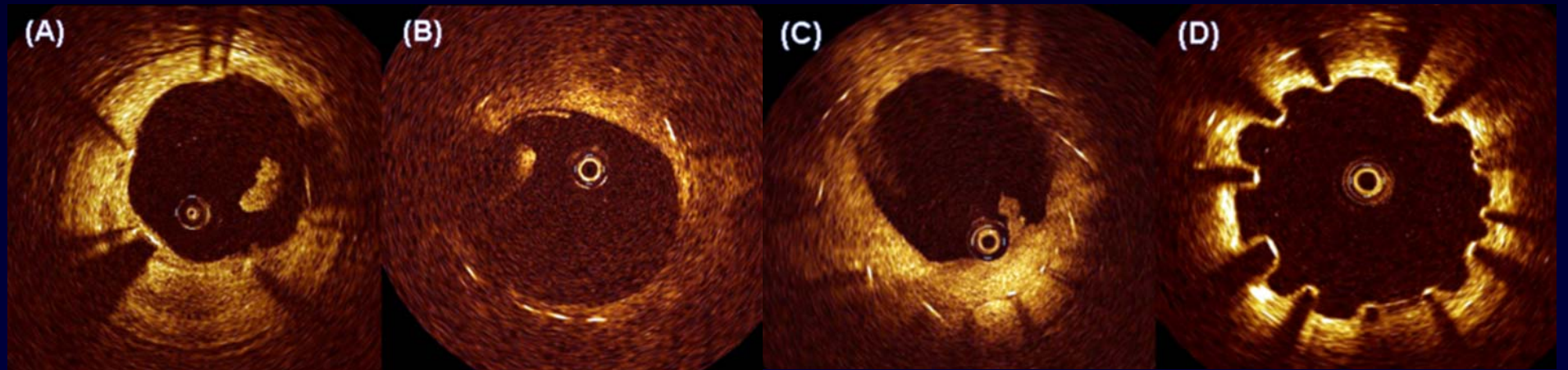
Variables	Non-malapposition (n=232)	Malapposition (n=74)	p value
No. of cross section, n	5448	1731	-
No. of total struts analyzed, n	47382	15356	-
% malapposed struts, %	0	3.2 ± 4.9	-
% uncovered struts from all cross sections, %	3.7 ± 6.4	11.6 ± 13.3	<0.001
% uncovered struts in the cross sections without malapposition, %	3.7 ± 6.4	10.1 ± 12.0	<0.001
Thrombi, n (%)	20 (9%)	18 (24%)	<0.001
Types of DES used			<0.001
SES, n (%)	59 (25%)	37 (50%)	
PES, n (%)	44 (19%)	10 (14%)	
ZES-Sprint, n (%)	54 (23%)	4 (5%)	
ZES-Resolute, n (%)	38 (16%)	15 (20%)	
EES, n (%)	37 (16%)	8 (11%)	

Malapposed vs. Uncovered Struts.

Variables	Non-malapposition (n=232)	Malapposition I % malapposed struts <1.3% (n=37)	Malapposition II % malapposed struts ≥1.3% (n=37)	p value
% malapposed struts, %	0%	0.7 ± 0.3%	5.6 ± 6.1%	<0.001
% uncovered struts from all cross sections, %	3.7 ± 6.4	5.5 ± 5.6	17.6 ± 15.9	<0.001
% uncovered struts in the cross sections without malapposition, %	3.7 ± 6.4	5.2 ± 5.7	15.0 ± 14.4	<0.001
Thrombi, n (%)	20 (9%)	8 (22%)	10 (27%)	<0.001
Time to OCT (days)	312 ± 92	303 ± 68	315 ± 81	0.785
FU after OCT (days)	480 ± 315	484 ± 282	475 ± 210	0.921
Duration of DAT after OCT (days)	252 ± 214	299 ± 227	313 ± 258	0.129
MACE after OCT	0	0	1 STEMI	

Intracoronary thrombus

Intracoronary Thrombus Formation After DES Implantation; OCT Study



Representative images of intracoronary thrombus in each stent (SES in A, PES in B and ZES in C), and malapposed struts without neointima in D

Kim JS, Hong MK et al. Am Heart J 2010;159:278-83

Intracoronary Thrombus Formation After DES Implantation; OCT Study

- Intracoronary thrombus was detected in **35/244 stents (14%)**
 - **27/95 SES (28%)**
 - **7/62 PES (11%)**
 - **1/87 ZES (1 %) (p<0.001)**

Kim JS, Hong MK et al. Am Heart J 2010;159:278-83

Determining Factors of IC Thrombus

	Univariate analysis			Multivariate analysis		
	OR	95% CI	p value	OR	95% CI	p value
OCT parameters						
MLA follow-up	1.00	0.81-1.24	0.97			
Mean neointima thickness	0.92	0.87-0.97	0.001	1.00	0.94-1.06	0.97
Presence of malapposed struts	5.18	2.44-10.97	<0.001	2.19	0.83-5.78	0.11
≥ 8 struts without neointima in stent	9.19	4.04-20.90	<0.001	3.29	1.07-10.17	0.04

Is LSM a strong predictor for the occurrence of LST ?

- LSM is the one of the unique features in DES era.

Is all LSM a strong predictor for the occurrence of LST regardless of LSM size? Maybe not.

struts. Occurrence of LST may depend on the severity of LSM.

- The prospective & longer follow-up with larger population will be required.

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

Clinical Characteristics

Variables	VLST with neointimal rupture (n=4)	VLST without neointimal rupture (n=14)	p
Clinical presentation at the onset of VLST			>0.999
ST elevation MI	3 (75.0)	9 (64.3)	
Non-ST elevation MI	1 (25.0)	5 (35.7)	
Antiplatelet therapy at the onset of VLST			0.213
Aspirin only	1 (25.0)	10 (71.4)	
Aspirin plus clopidogrel	1 (25.0)	2 (14.3)	
None	2 (50.0)	2 (14.3)	
Time to onset of VLST, months	41.5±20.7	40.9±17.5	1.000
Time to onset of VLST, years			
≤1 yr	0	0	
1 ~ 2 yrs	1	2	
2 ~ 3 yrs	1	4	
>3 yrs	2	8	

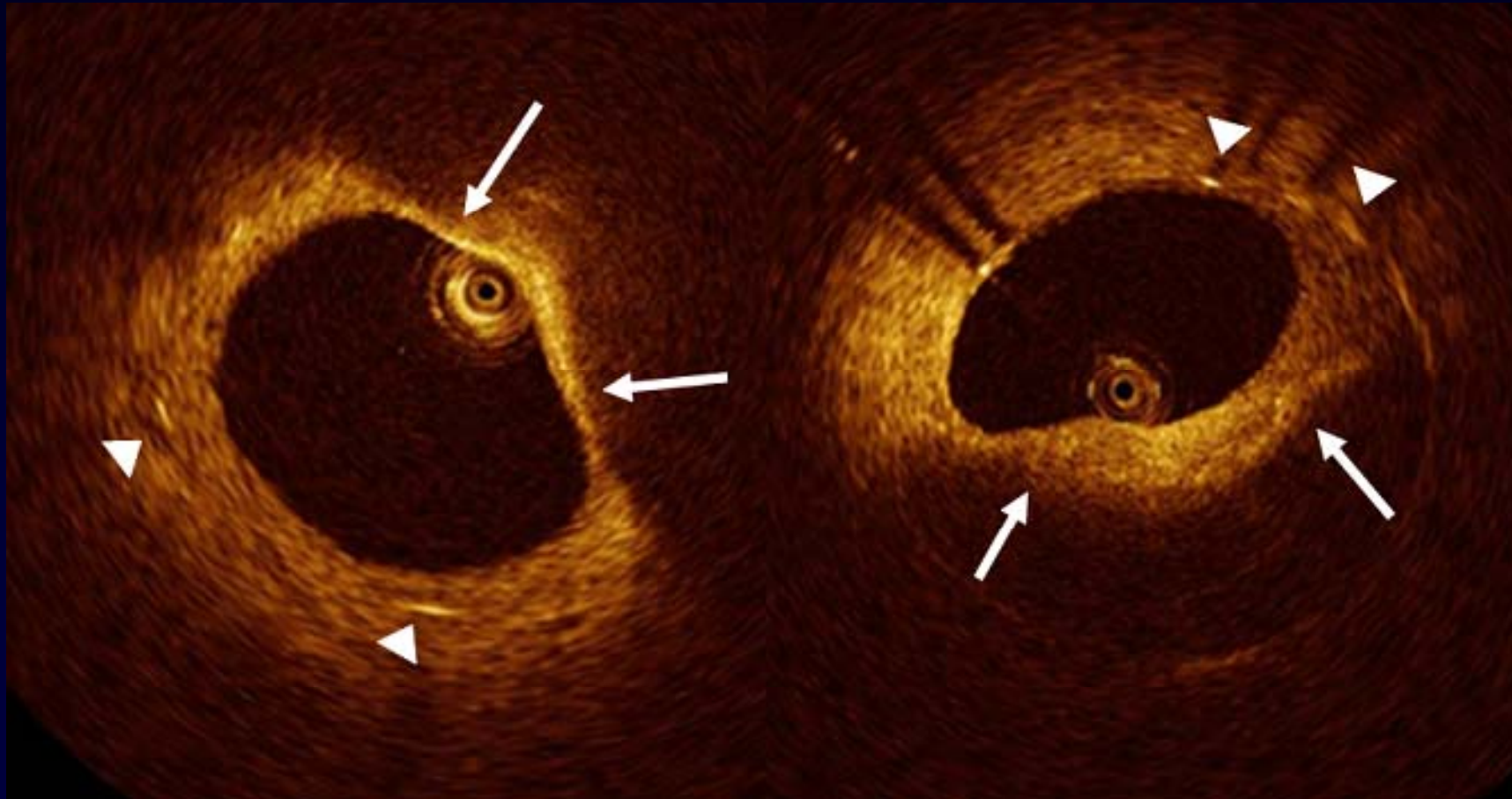
Procedure/OCT data

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

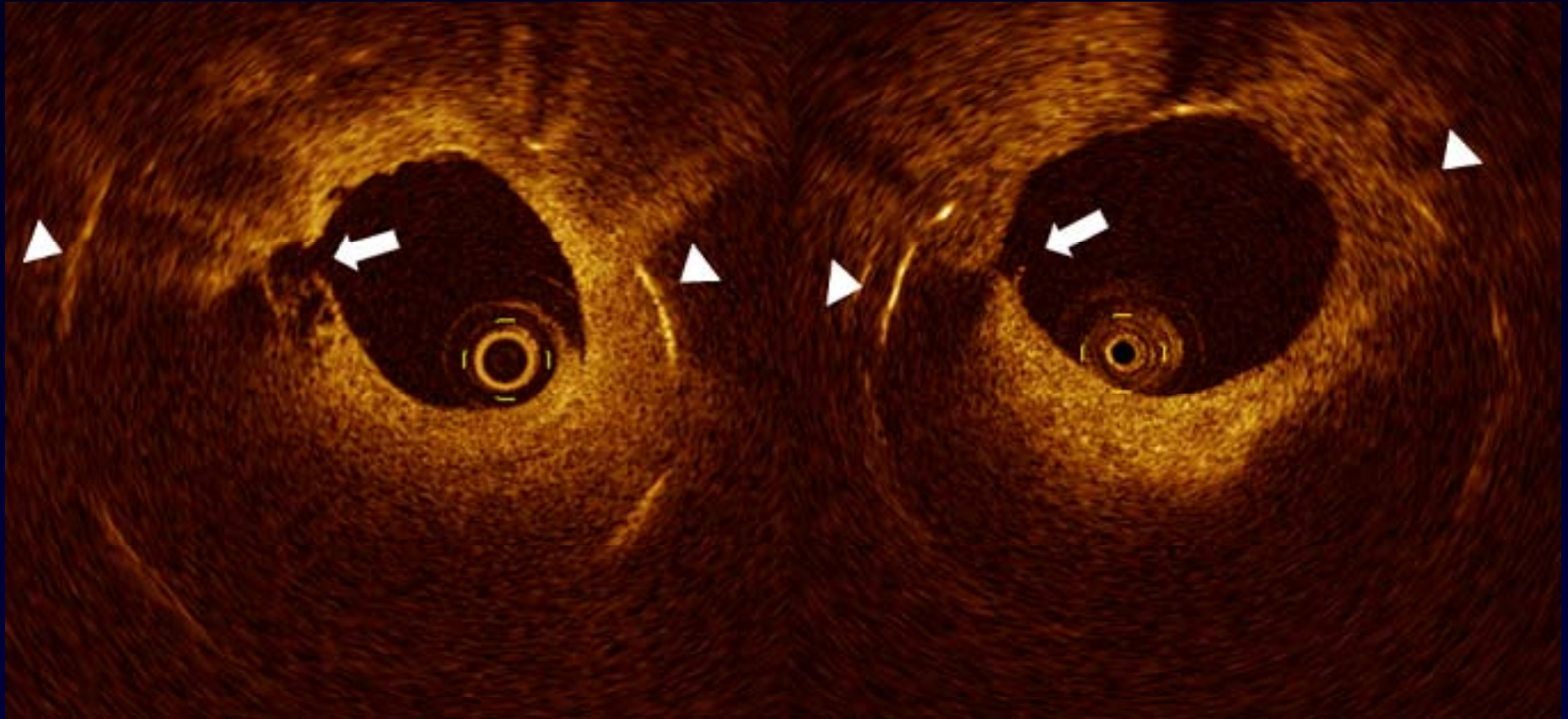
Clinical Characteristics

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%)	

Lipid-laden neointima



Neointimal rupture



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.

Conclusion: Evaluation with OCT/IVUS

Uncovered stent struts

Stent malapposition

Intracoronary thrombus

Neoatherosclerosis



Possible factors related with
late stent thrombosis

Dreams will come true

