Restenosis and Stent Thrombosis
A Lesson from IVUS

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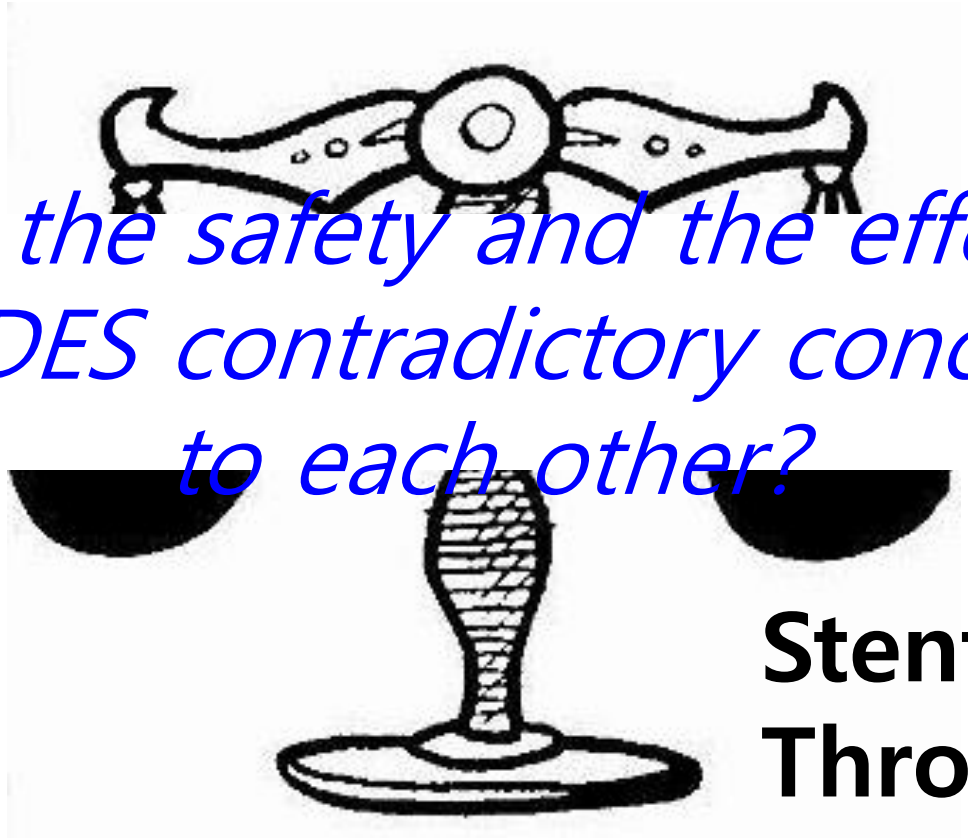
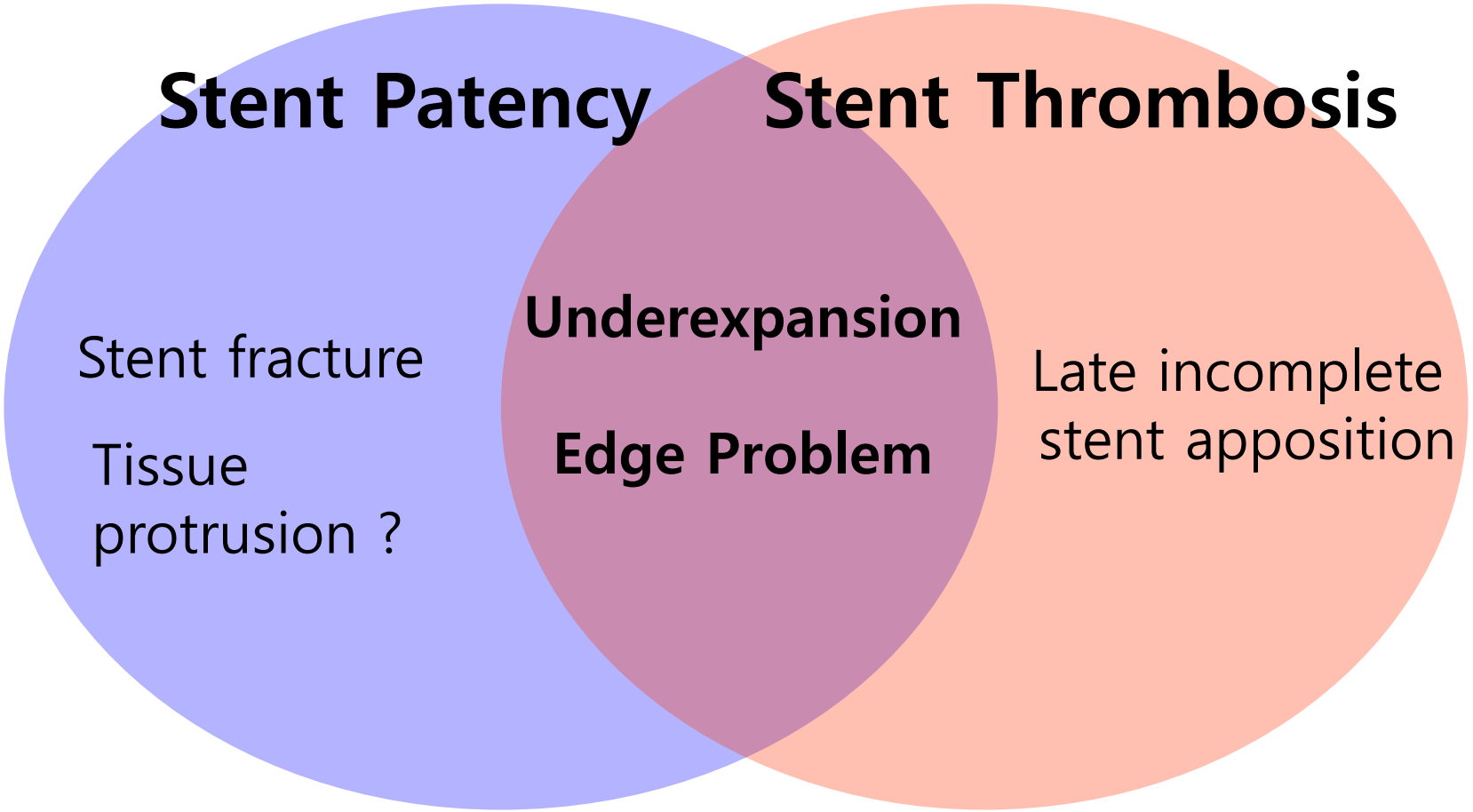
Safety vs Efficacy in Coronary Stent



Are the safety and the effcacy of DES contradictory concept to each other?

Stent Thrombosis

IVUS Predictors of Restenosis and Stent Thrombosis



IVUS Predictors of DES Restenosis

- The most common predictors of BMS or even DES restenosis are stent underexpansion and inadequate lesion coverage or edge-related effects.
- Stent fractures related restenosis, also has been reported in several studies.
- However acute ISA or tissue protrusion through stent struts seems not to be related with restenosis.

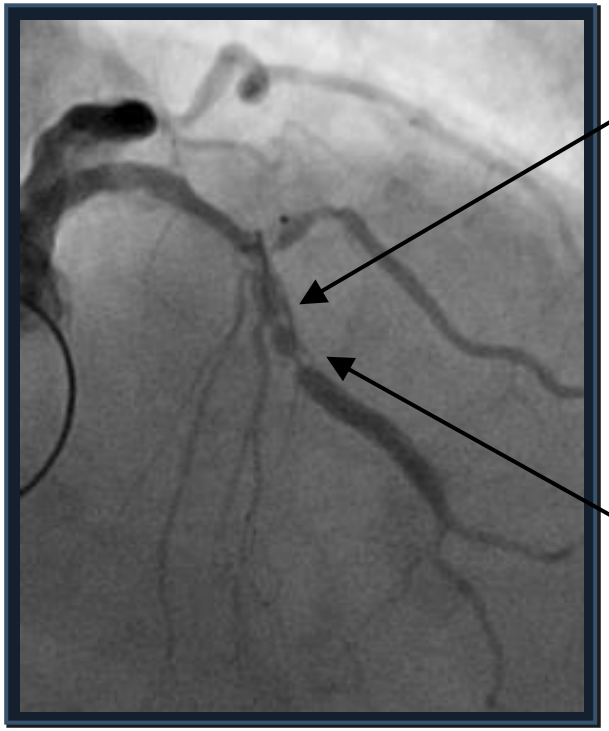
☝ Stent underexpansion

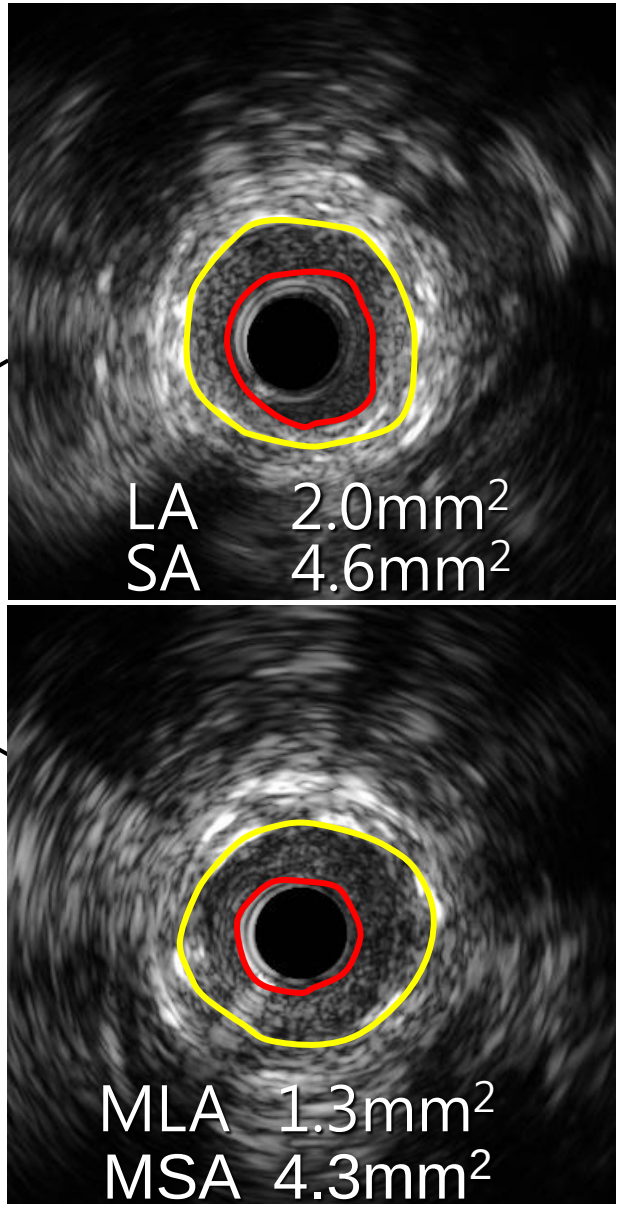
- Minimal stent area (MSA)
- Stent expansion

  =MSA / mean reference lumen CSA
- Stent underexpansion

  <80% of MSA / mean reference lumen CSA

ISR at 6 months after stenting with BMS

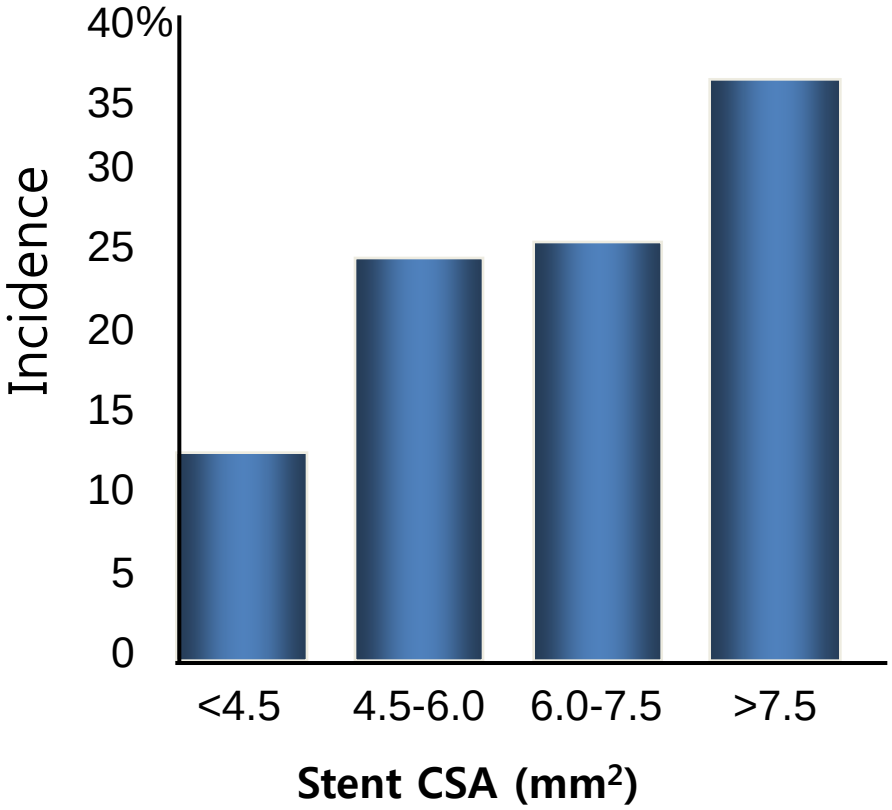




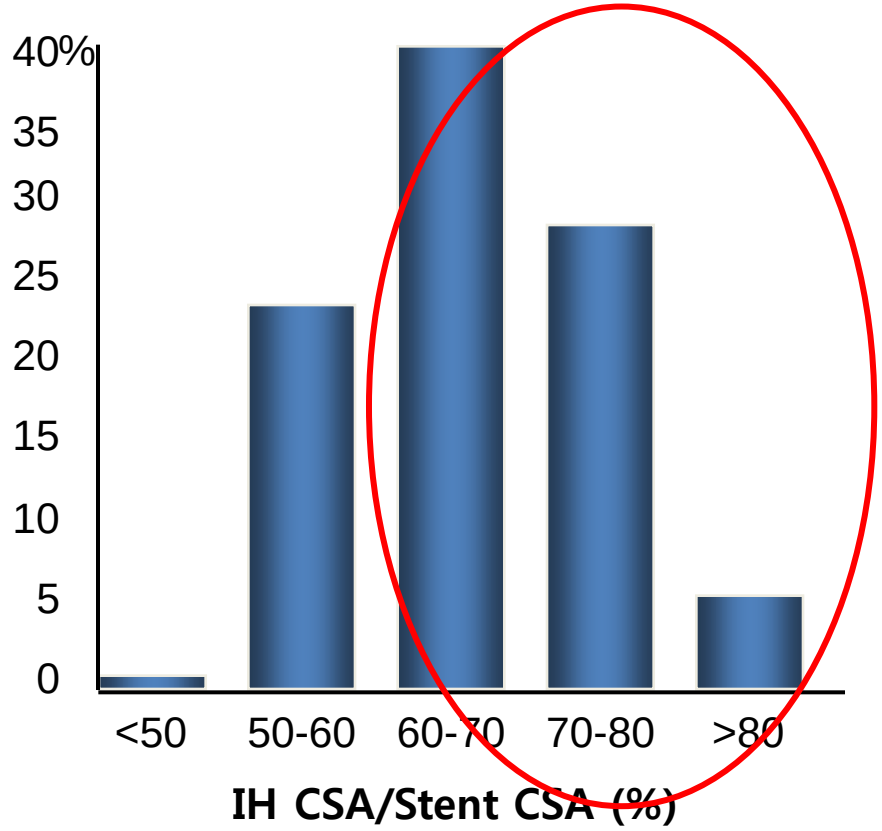
Mean reference lumen CSA = 12.6
Stent expansion = 4.3 / 12.6
"Underexpansion"

Analysis of 1089 Consecutive Patients with **BMS-ISR**

30% Under-expansion



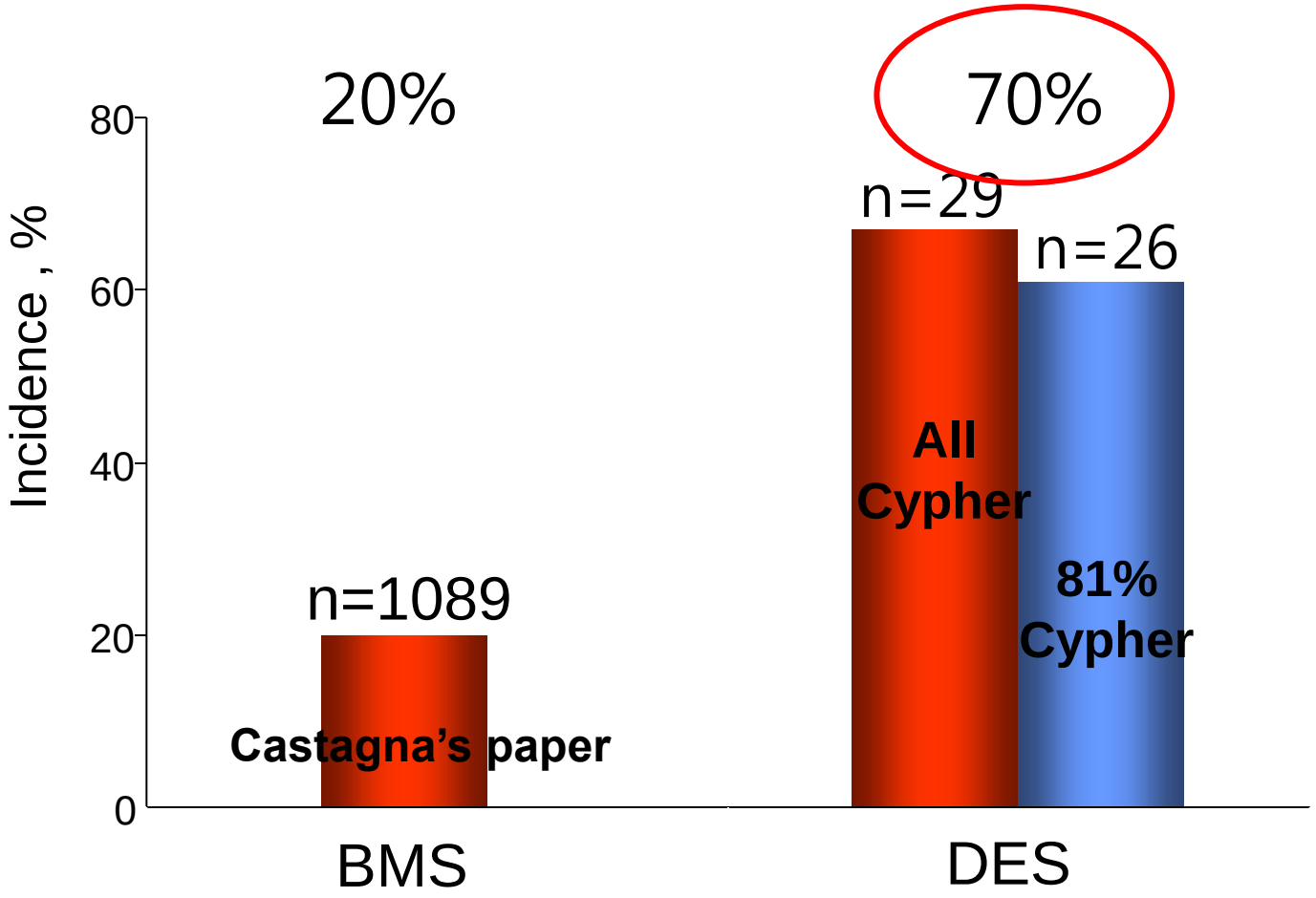
70% Intimal Hyperplasia



Castagna et al, AHJ 2001

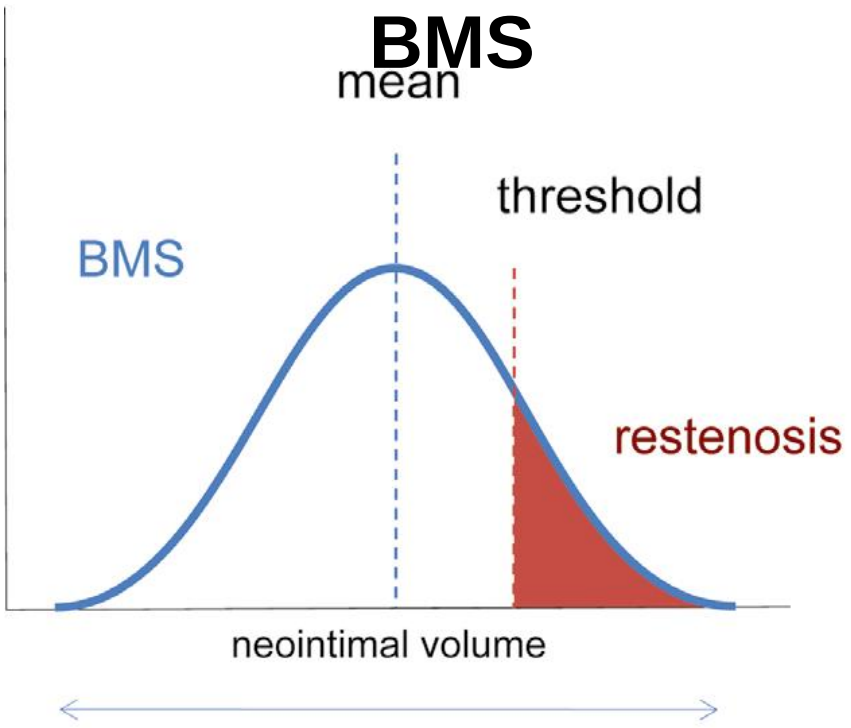
Incidence of MSA ≤5mm^2 in ISR

BMS vs. DES



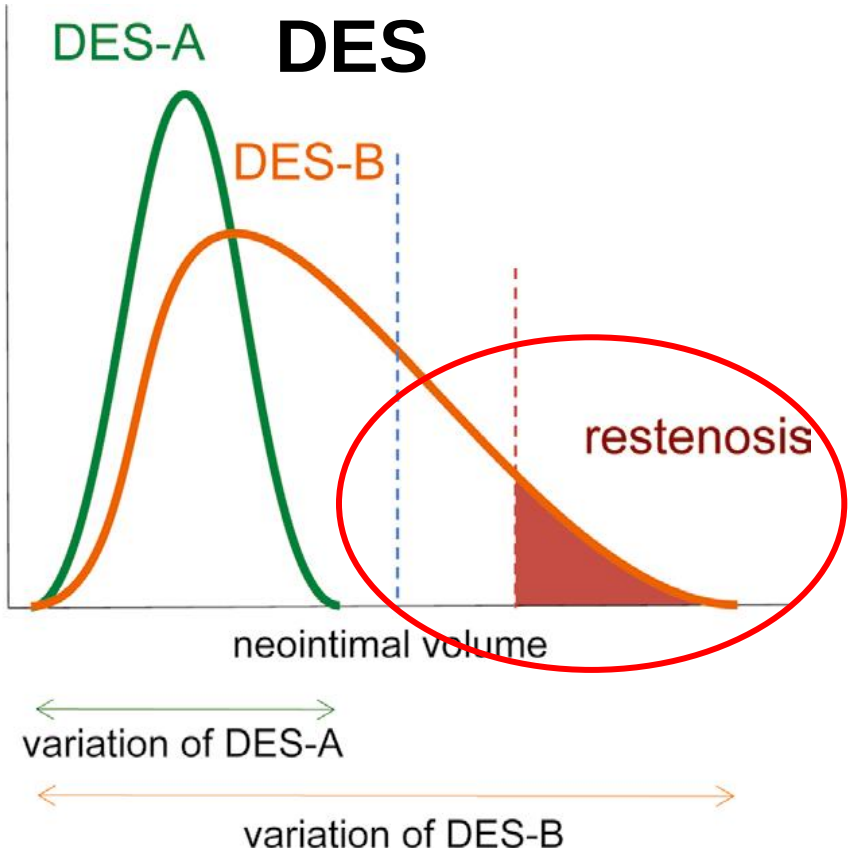
Takebayashi et al, AJC 2005
Kim et al AJC 2006

Frequency Distribution of IH



patient variation in biologic response

% IH volume is normally distributed around a mean value of 30-35% of stent volume.

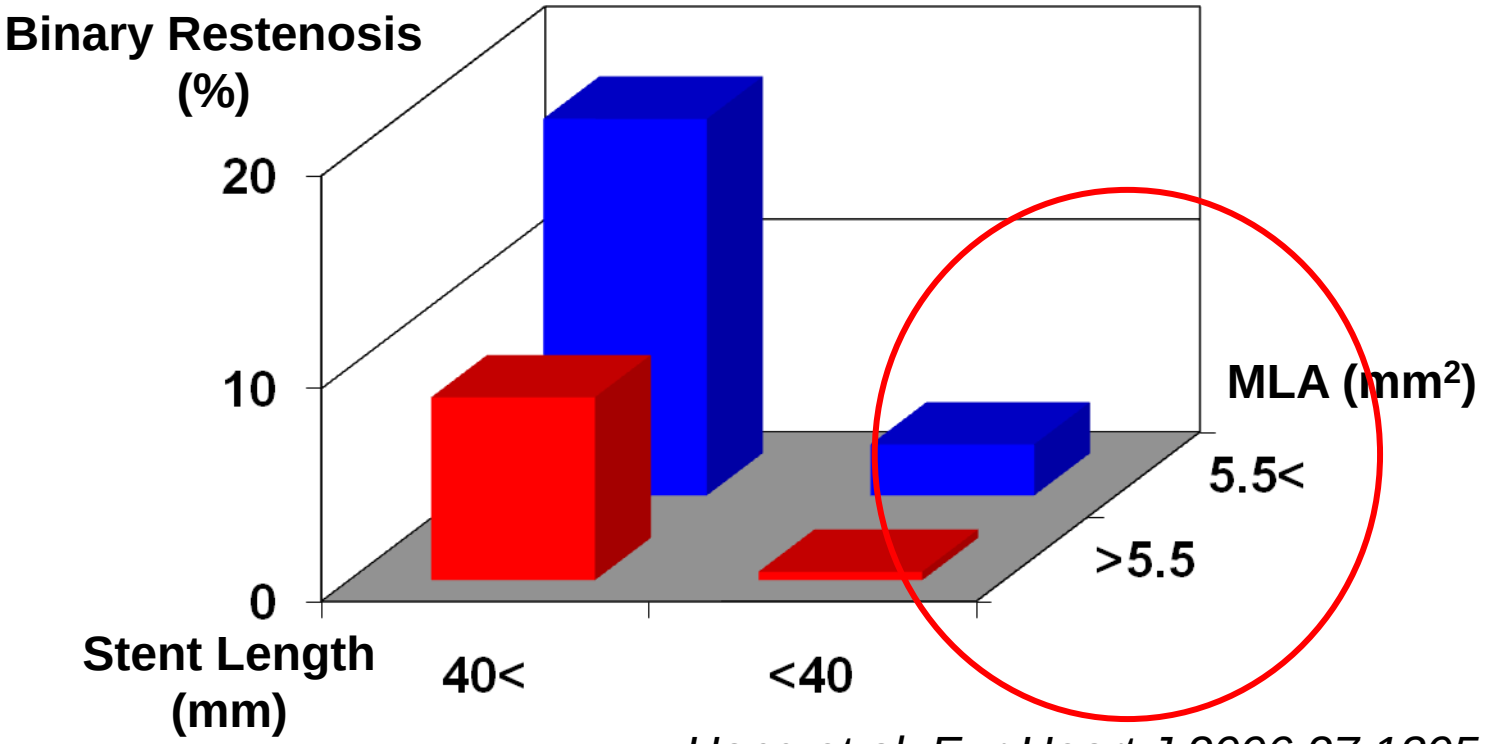


Mean value of % IH volume is not well correlated with the restenosis rate.

Honda. Cir J 2009;73:1371-80

Predictors for SES-ISR by IVUS

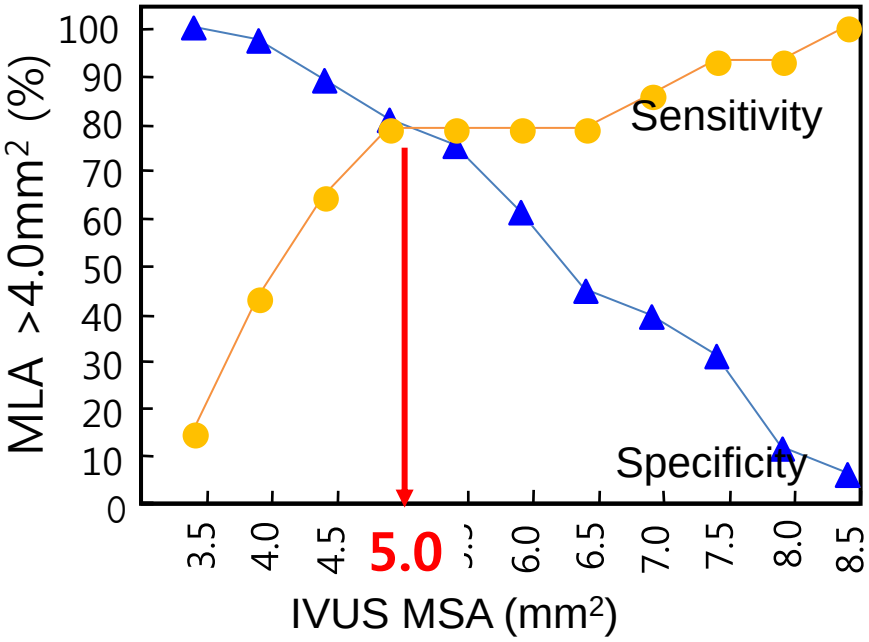
Final stent area/Stent length



Hong et al. Eur Heart J 2006;27:1305-10

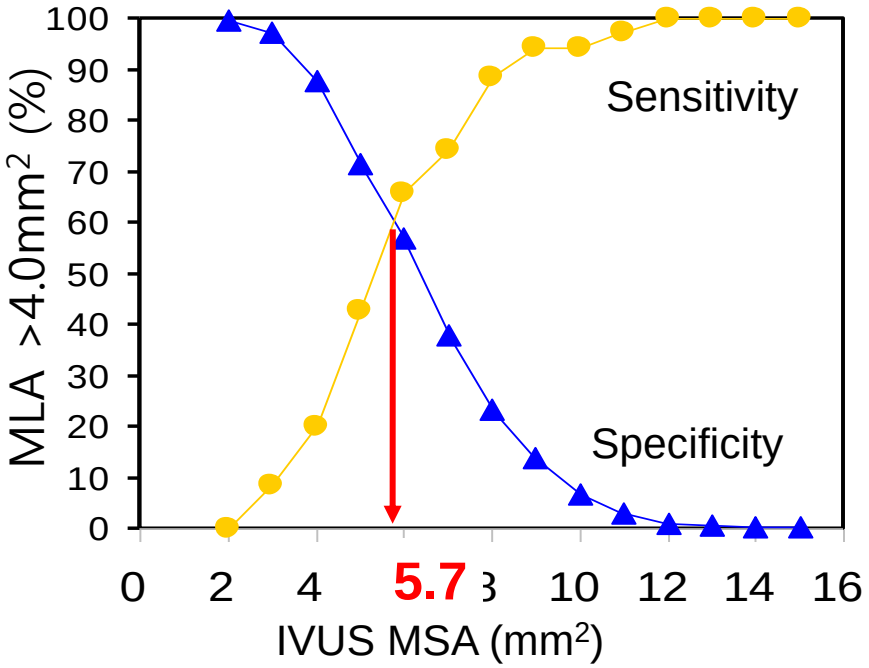
Final MSA that Best Predicted Restenosis

Cypher



Sonoda et al. J Am Coll Cardiol 2004;43:1959-63

Taxus



Doi et al. JACC Cardiovasc Interv. 2009;2:1269-75

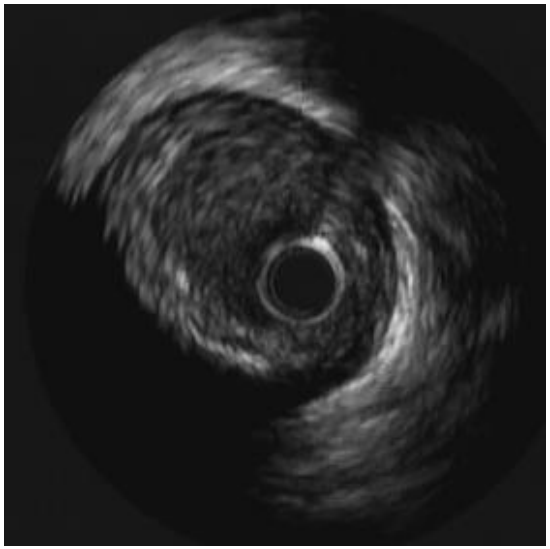
Final MSA of 5.0-5.5mm^2 for Stent Patency in DES

- It is not enough in big arteries.
- It is difficult to achieve in
  - Small arteries
  - Heavily calcified lesions
  - Multiple layered stents
  - Negative remodeling / ostial lesions

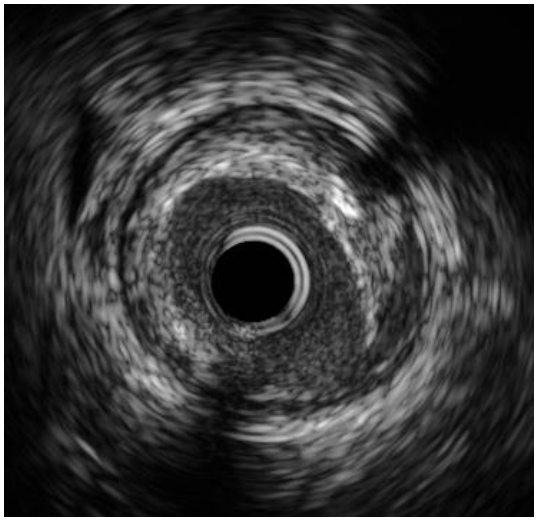
Edge Problems

- Geographic miss
- Residual diseases (secondary lesions)
  - lumen CSA <4.0mm^2 with ≥70% plaque burden
- Edge dissection
  - more than medial dissection with lumen CSA <4mm^2

Residual Stenosis

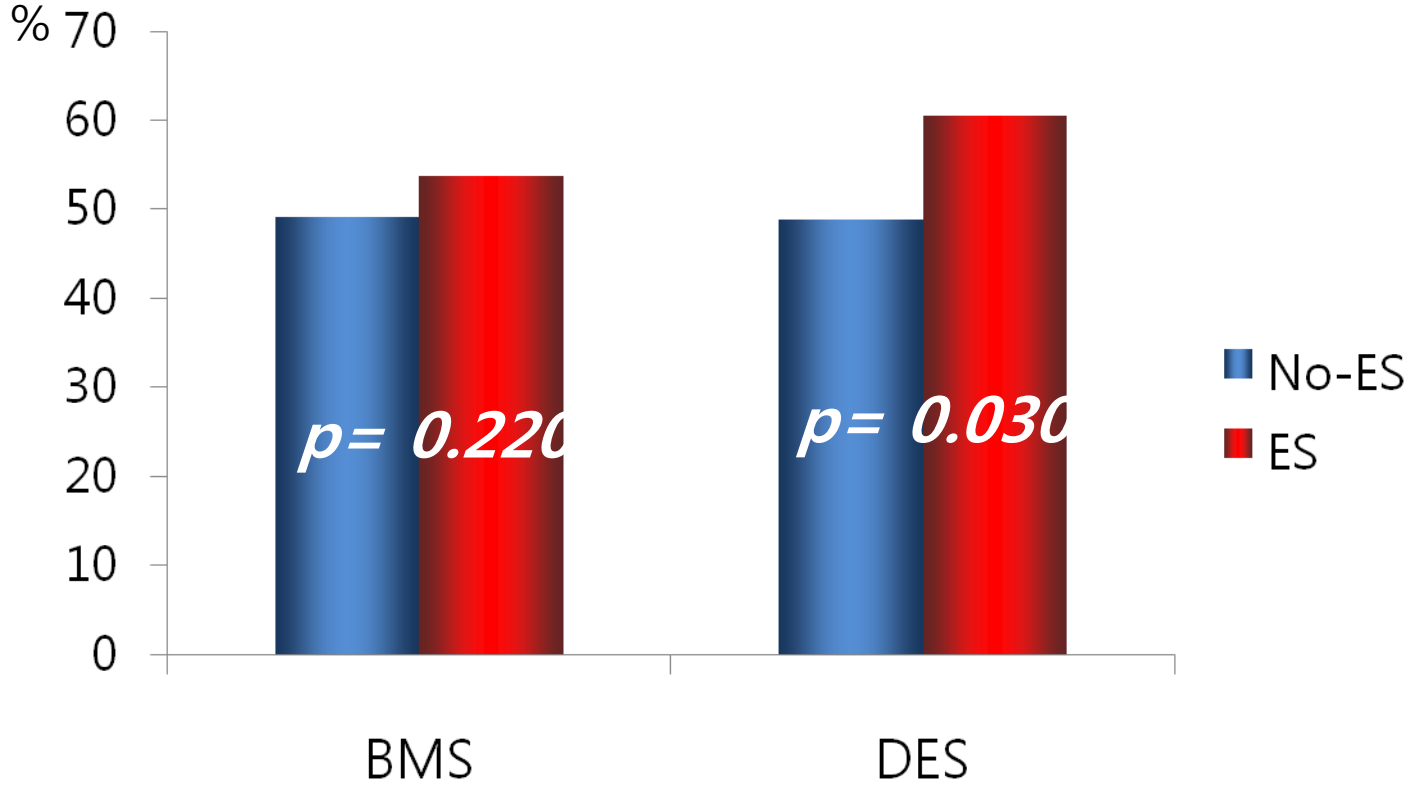


Edge Dissection



Reference Plaque Burden%
as a predictor for stent edge restenosis

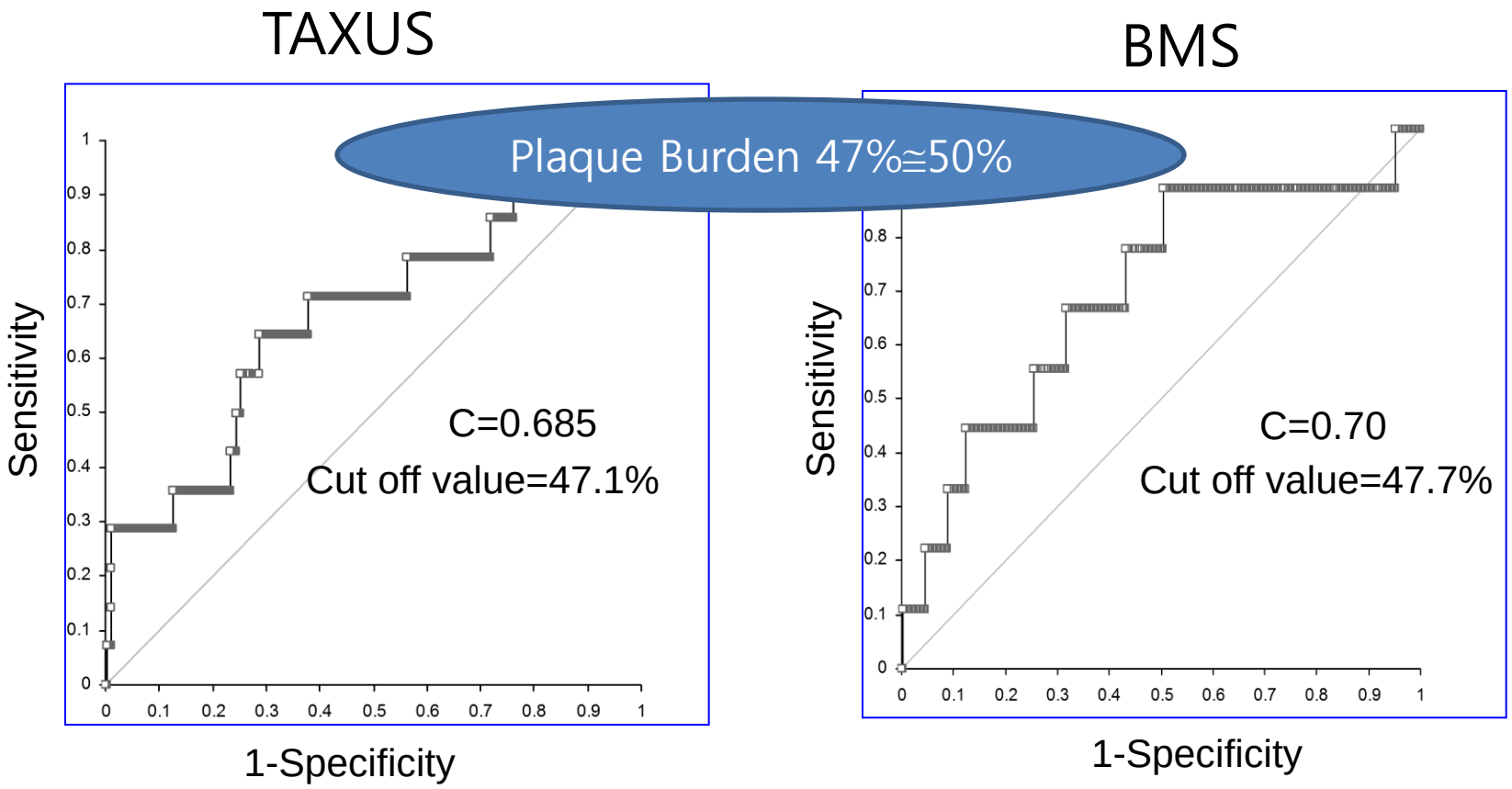
Edge restenosis; Cypher 3.7%, BMS 8.8%



Sakurai et al. Am J Cardiol 2005;96:1251-3

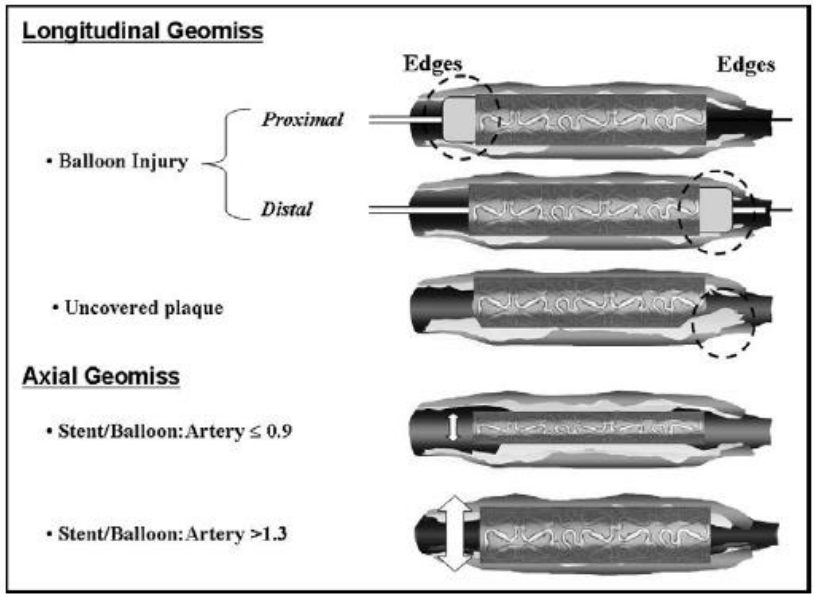
Reference plaque burden% as a predictor for stent edge restenosis from TAXUS IV, V, VI (n=810)

Edge restenosis; TAXUS 5.6%, BMS 4.9%

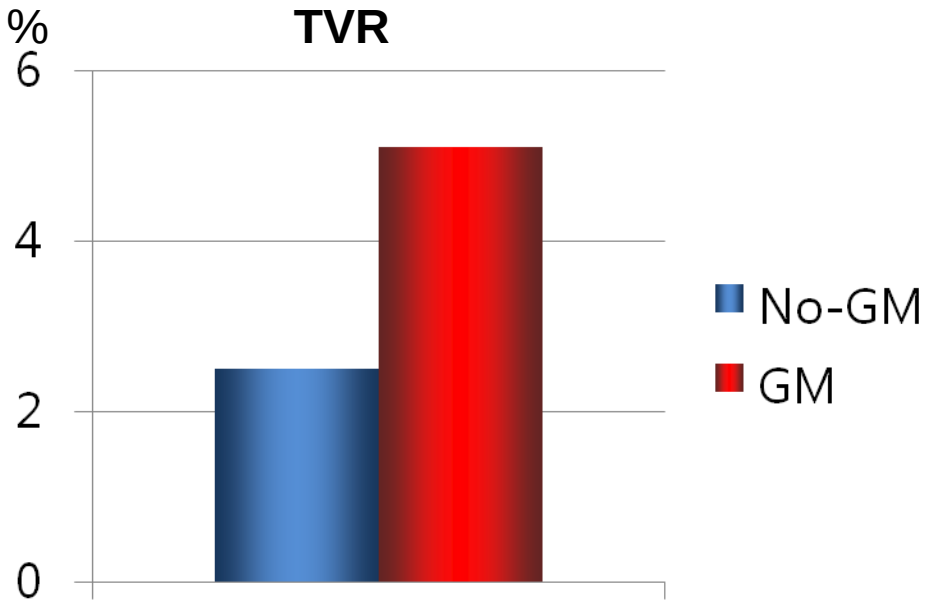


Liu et al, Am J Cardiol 2009;103:501-6

Geographic Miss as a predictor for stent edge restenosis
1, 557 patients treated with SESs in 41 US hospitals



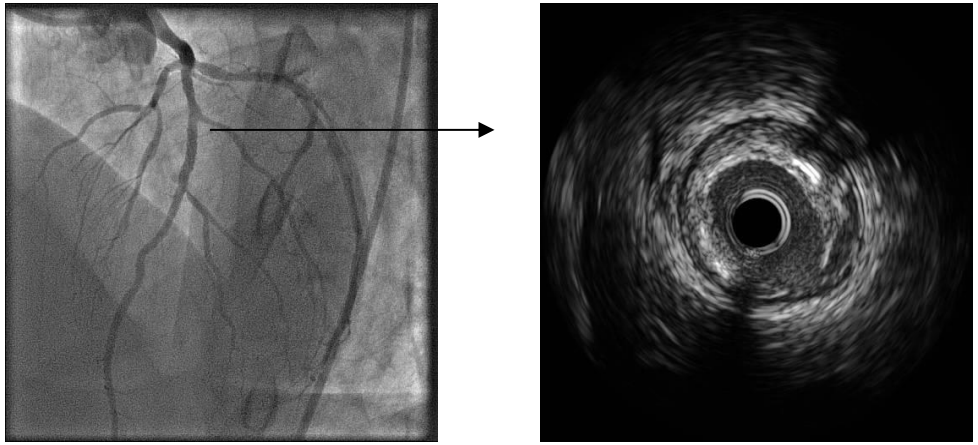
GM in 943 patients (66.5%):
LGM 48%
Axial GM 35%
Both 7%

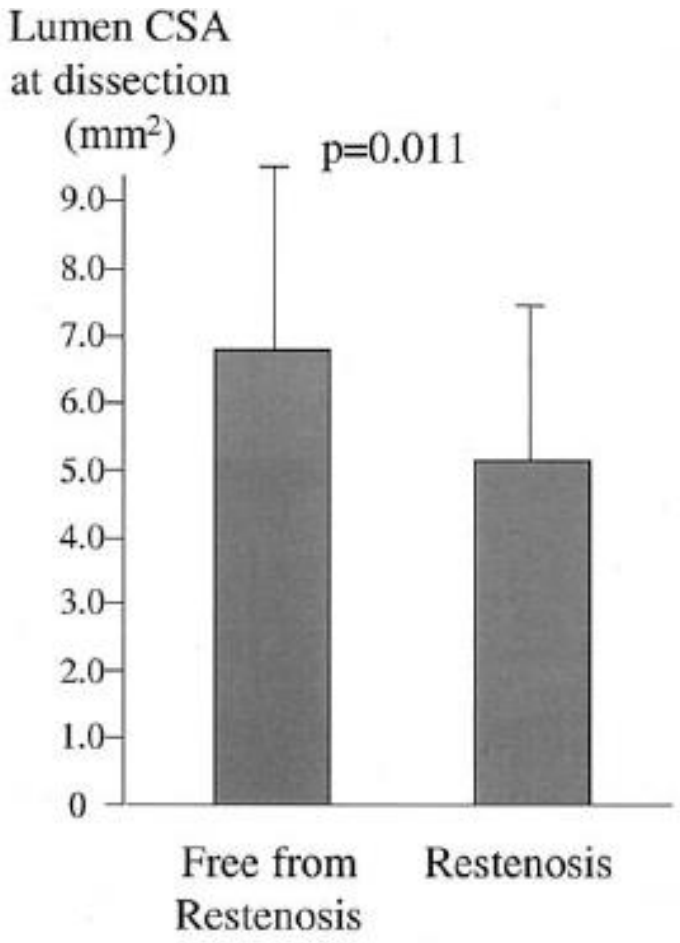


The association of GM was independent predictor of TVR (HR 2.0, 95% CI 1.0-4.02, p=0.05).

Costa et al, Am J Cardiol, 2008;101:1704-11

Edge dissection





- **The lumen CSA at the dissection site negatively correlates with the incidence of angiographic restenosis.**
- **The mean lumen CSA was 5.2±2.3 mm2 in lesions with restenosis (n=27) at follow-up angiography and 6.8±3.4 mm2 in the remaining lesions without restenosis (n=71).**

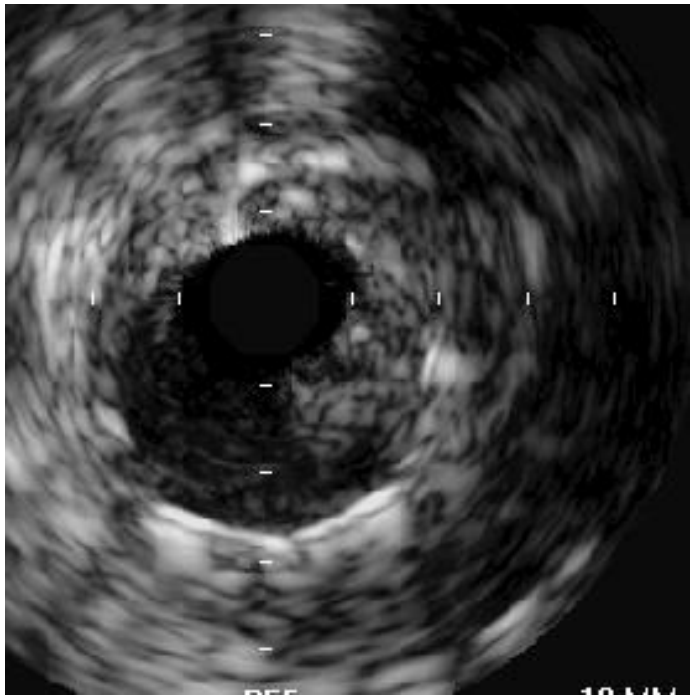
Nishida et al. Am J Cardiol 2002;89:1257–1262

Stent Fracture

- Cypher > TAXUS
- Incidence 1-2.6%
- Predictors: overlapped stent, longer stent, vessel angulations & hinge movement, aneurysm
- TLR 50-70%
- Avoid overlapping near the hinge movement
- Angiogram missed 25% of stent fractures which could be detected by IVUS.

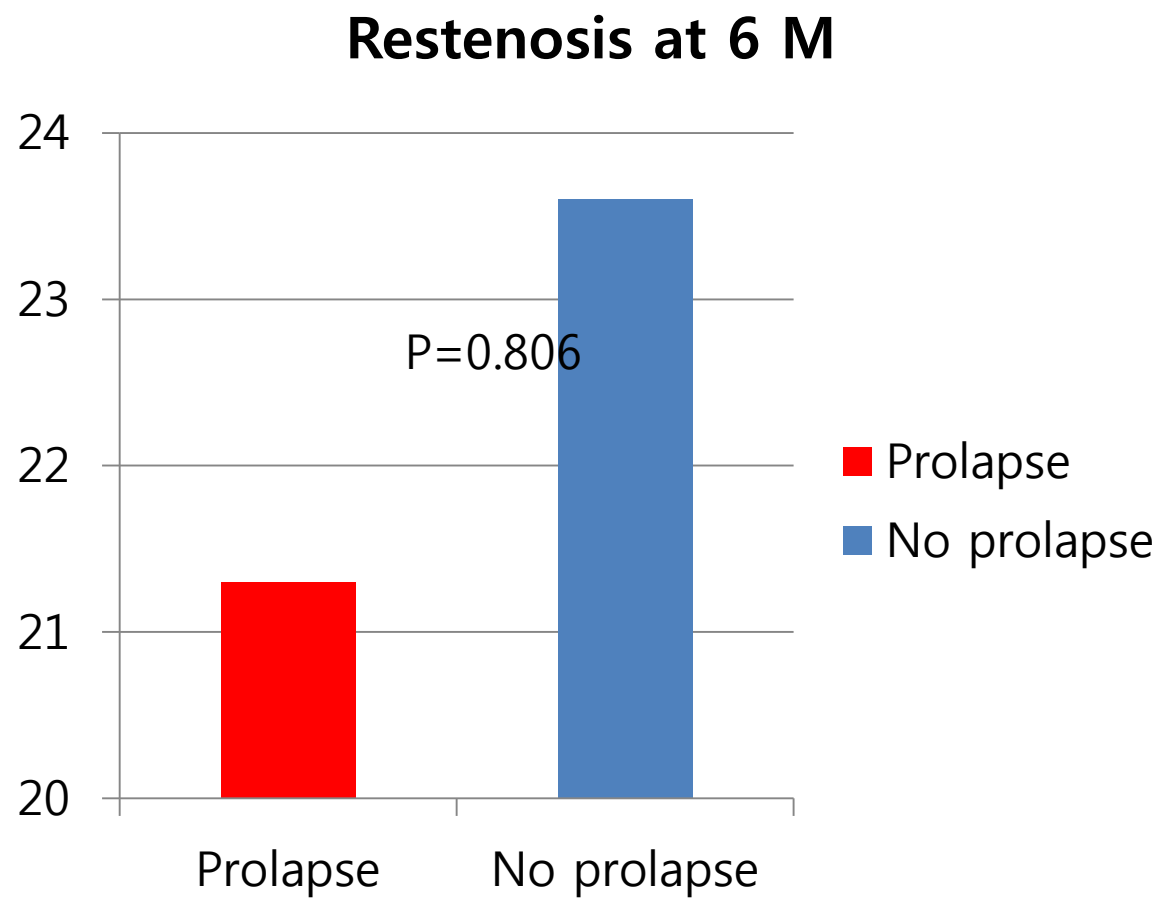
Doi et al., Am J Cardiol 2009;103:818–823)

Tissue (Plaque/thrombus) Prolapse



- IVUS cannot discriminate thrombus from plaque protrusion through stent struts because of its limitation of resolution.
- In the setting of PCI for AMI showed that tissue prolapse after stenting was seen more often than in SA.

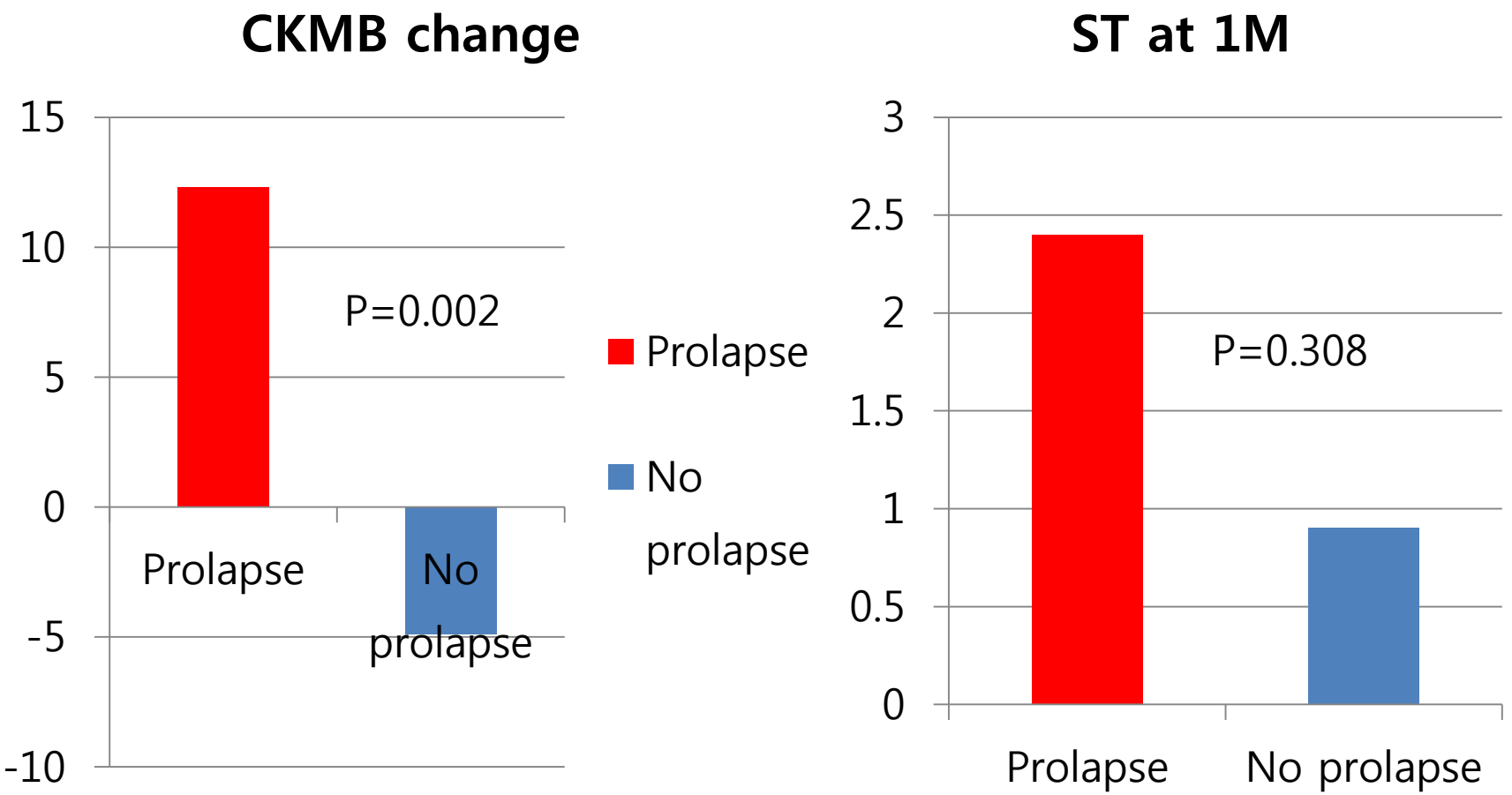
Long-Term Outcomes of Plaque Prolapsed Within BMS Stents (SA)



- 384 patients with 407 coronary lesions.
- Minor plaque prolapsed within the stent was found in 75 of 334 lesions (22.5%).
- The development of minor plaque prolapse was significantly associated with infarct-related artery (*P=0.000) and small pre-intervention minimal lumen diameter* (*P=0.001).*

Hong et al. Cathet. Cardiovasc. Intervent. 2000;51:22–26

Short-Term Outcomes of Plaque Prolapsed Within DES Stents (AMI)



Hong et al. JACC Imaging 2008;4:489

DES Stent Thrombosis

- ST occurs in patients after implantation of either a BMS or a DES.
- The risk of early ST is similar between BMS and DES, but very late ST occurs more frequently in patients receiving DES because of its biologic response.

Incidence of ST in RCTs

	Stable Angina	UA/NSTEMI	STEMI
BMS	**0-0.5%**	**1.4-1.6%**	**2.9%**
DES	**0.3-0.4%**	**1.2-1.9%**	**3.1%**

Cook S. et al, *Circulation 2009; 120:391-9*
Cook S. et al, Circulation 2009;119:657-9

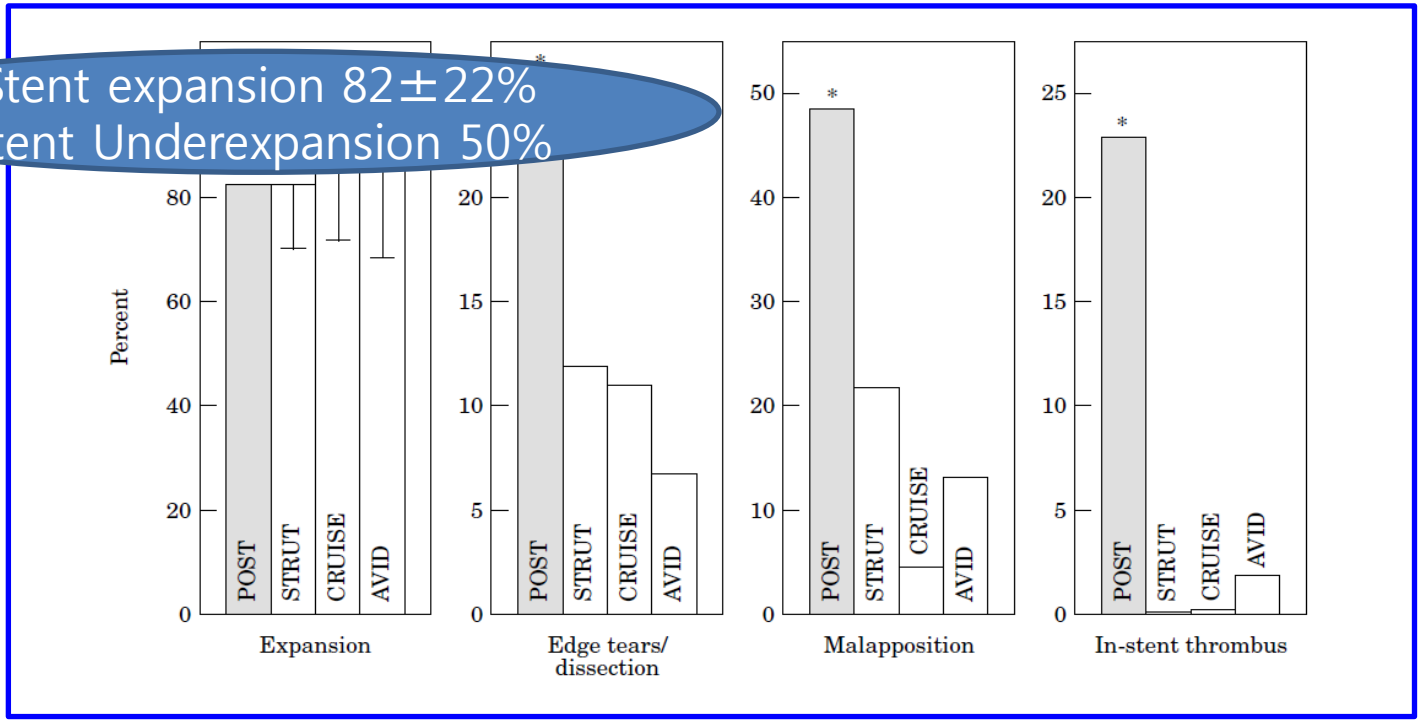
IVUS Predictors of DES Stent Thrombosis

- Small stent lumen area and residual inflow/outflow disease have been reported as the strongest IVUS predictors of ST in patients with stable angina.

Predictors of early ST in BMS
POST Registry investigator

53 patients c early ST:
Overall, 94% of cases demonstrated one abnormal ultrasound finding (under-expansion, malapposition, inflow/outflow disease, dissection, or thrombus).

Stent expansion 82±22%
Stent Underexpansion 50%

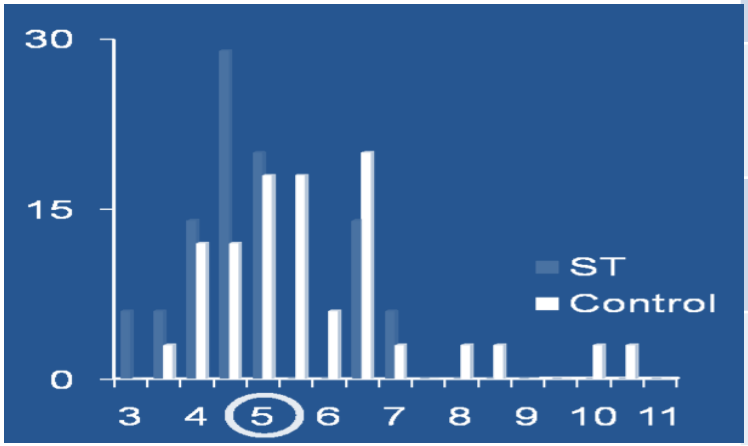


N. G. Uren, Eur Heart J 2002; 23: 124–132

MSA and RD are associated with ST in DES (SES, PES):

3 acute, 5 subacute, and 5 late ST

MSA <5.0 mm²,
ST (n=11, 79%) vs. Control (n=12, 40%), p<0.05

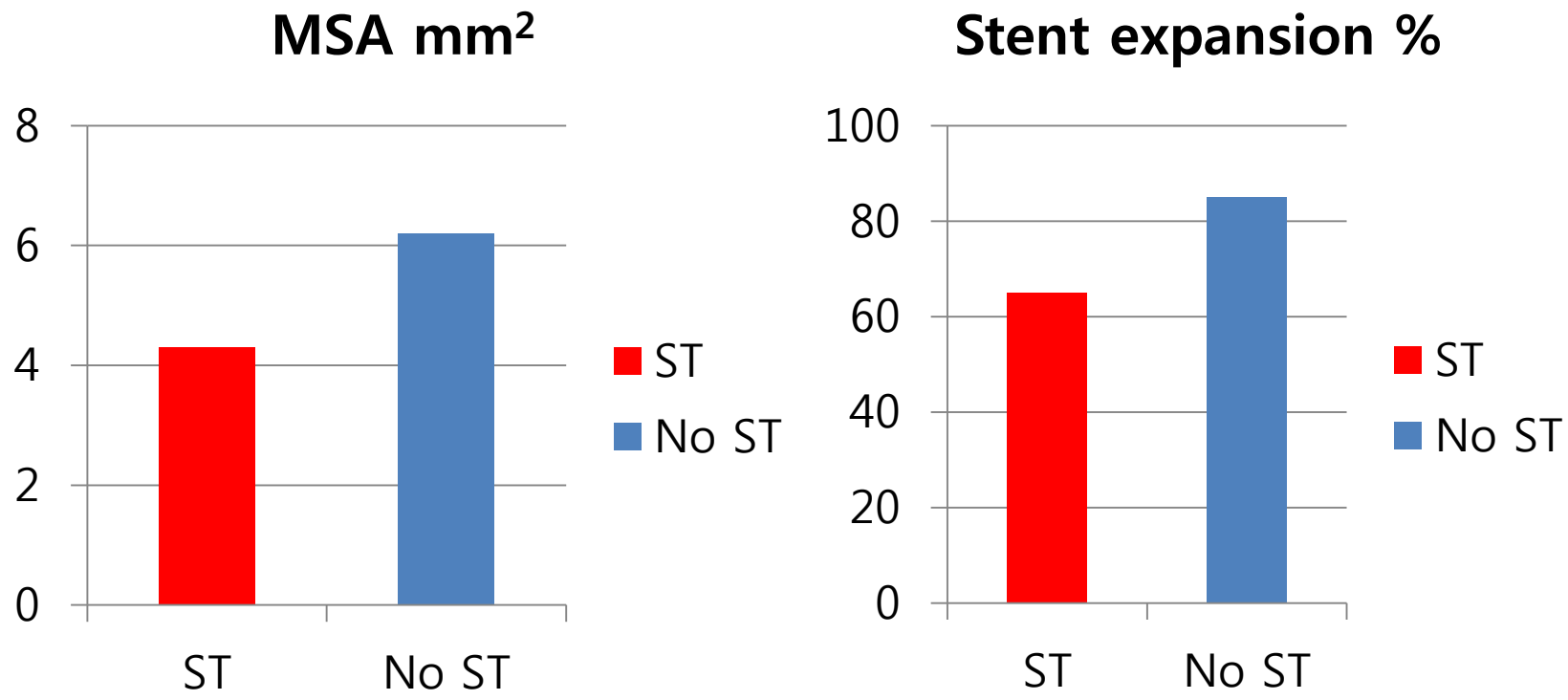


Variables	ST (n=14)	Control (n=30)	p-Value
Proximal reference segment			
PB%	**0.66±0.08**	**0.56±0.10**	**0.002**
Stented segment			
MSA (mm²)	**4.6±1.1**	**5.6±1.7**	**0.049**

Okabe T, Am J Cardiol 2007;100:615-620

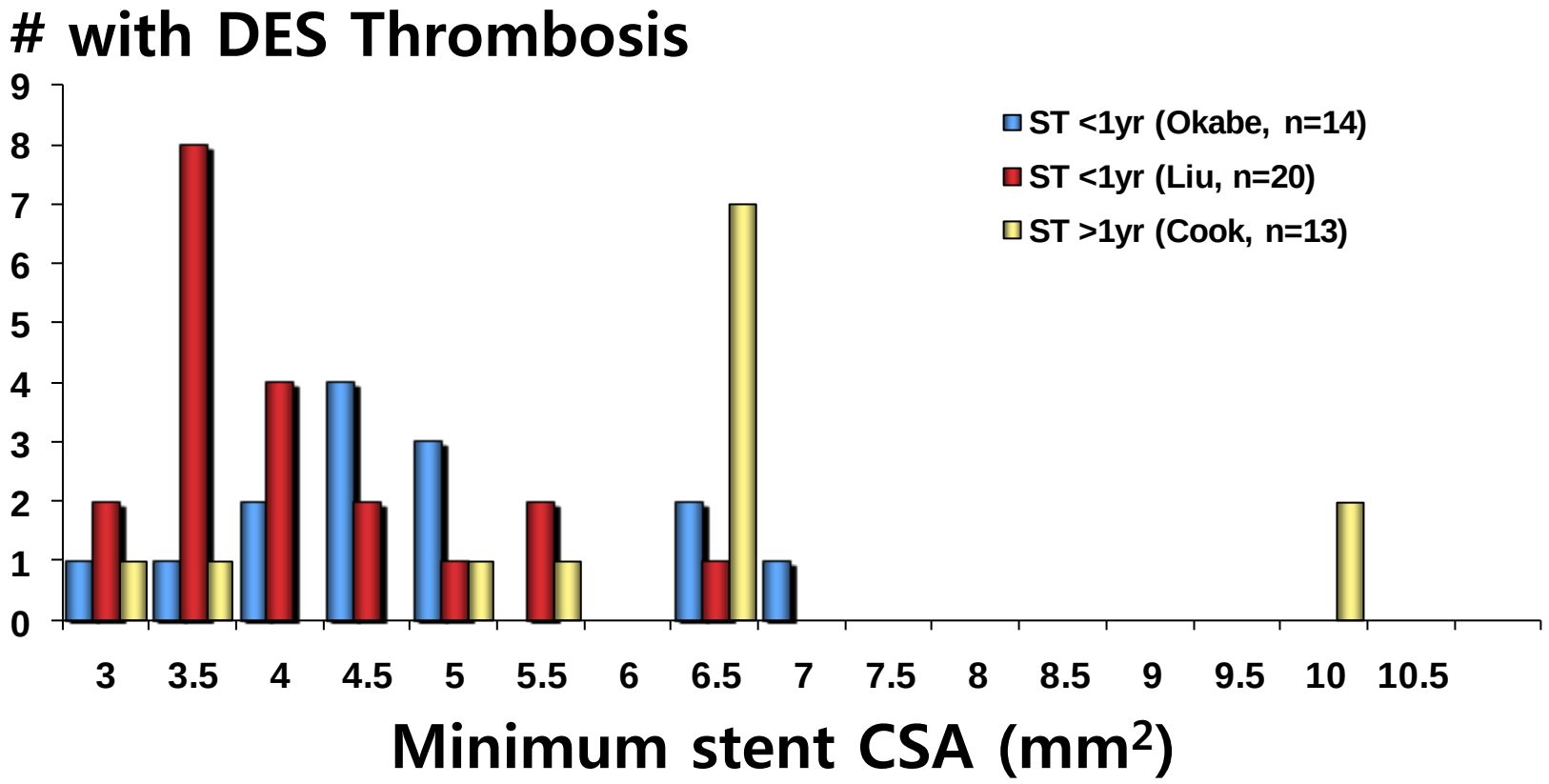
Stent underexpansion and RD are related with early ST in SES

15 patients with ST vs 45 matched controls



Kenichi Fujii, Am Coll Cardiol 2005;45:995– 8)

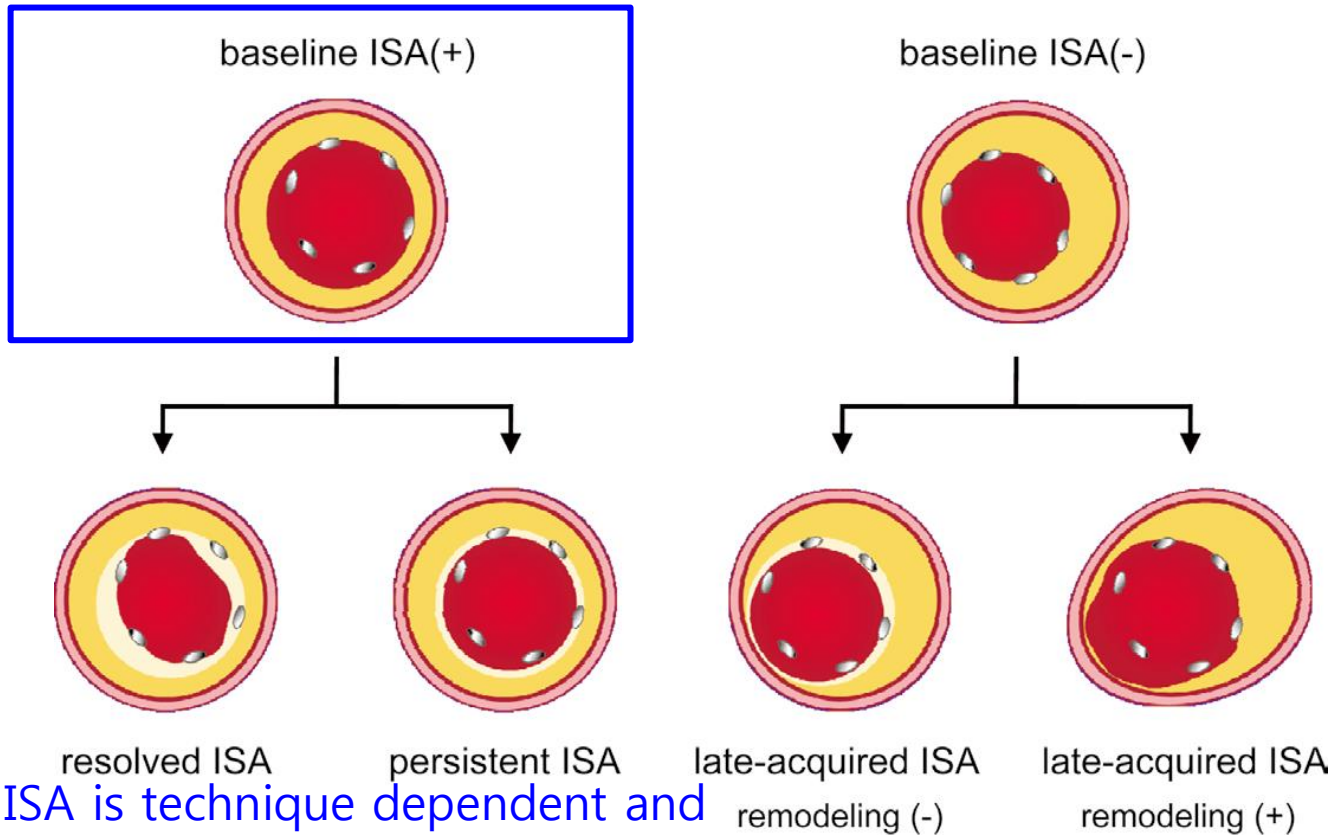
Stent Underexpansion in Early (<1 year) vs Very Late (>1 year) DES Thrombosis



(Okabe et al. Am J Cardiol 2007;100:615-20)
(Liu et al. JACC Interventions,
Cook et al. Circulation 2007;115:2426-34)

Classification of Incomplete stent apposition (ISA)

The incidence of acute ISA is similar in BMS/ DES-treated lesions, but is higher in STEMI than in SA



Acute ISA is technique dependent and usually resolves at follow-up.

Acute Incomplete Stent Apposition

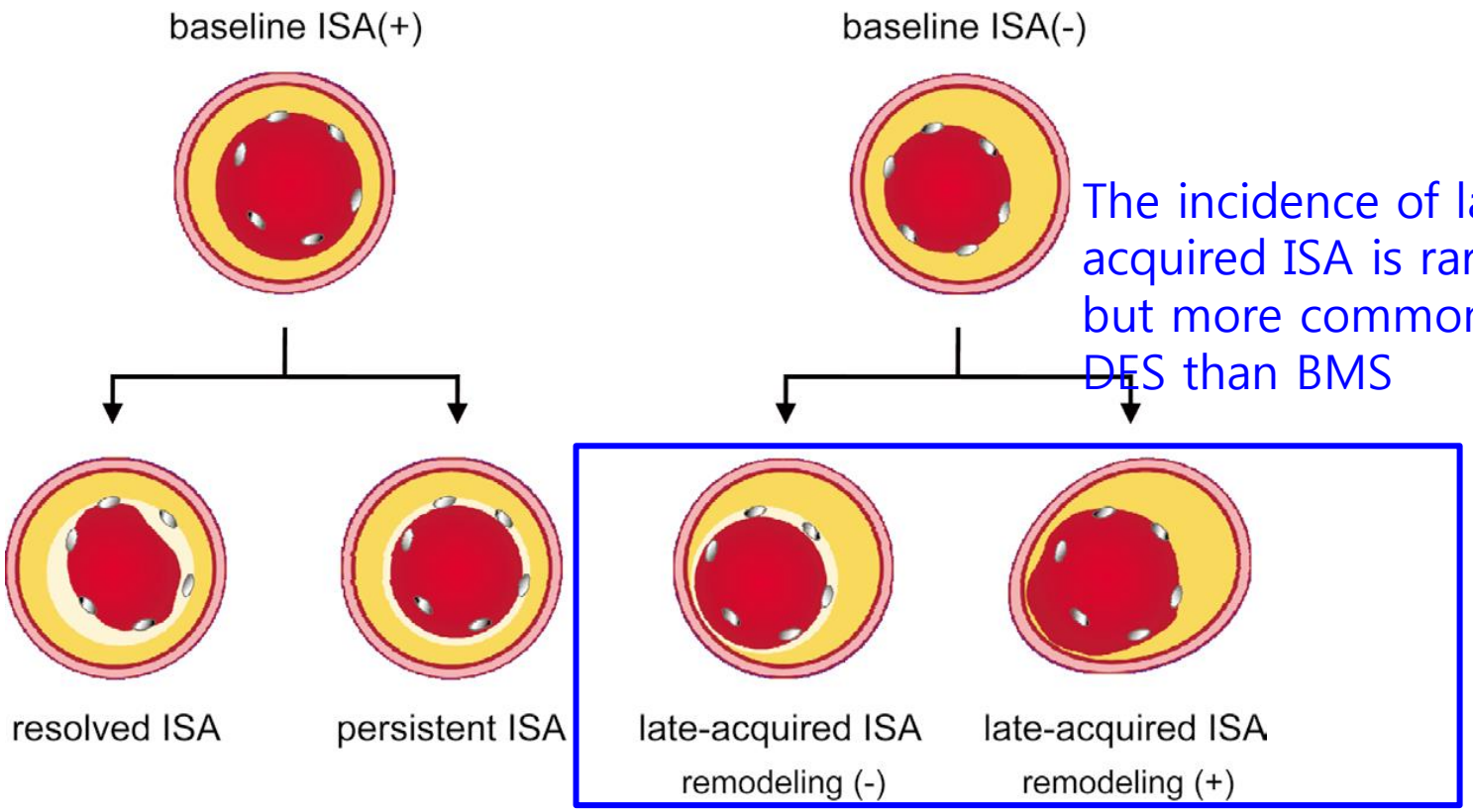
- There is little or no data linking *isolated* acute ISA to adverse clinical events including DES thrombosis.

- Persistent ISA is associated with *less* intimal hyperplasia – the drug can cross small stent vessel-wall gaps. *Balakrishnan et al., Circulation 2005;111:2958-65*

- Integrated analysis of slow release formulation PES in TAXUS IV, V, and VI and TAXUS ATLAS Workhorse, Long Lesion, and Direct Stent Trials
  - No effect of acute ISA on MACE or ST within the first 9 months whether BMS or DES

Doi et al. Circ Cardiovasc Intervent. 2008;1:111-118.

Classification of Incomplete stent apposition (ISA)



The incidence of late acquired ISA is rare but more common in DES than BMS

Late ISA in AMI

	Mission (AMI)		HORIZONS (AMI)	
	SES	BMS	TAXUS	BMS
Any malapposition at follow-up	37.5%	12.5%	44.4%	28.6%
Late acquired stent malapposition	25.0%	5.0%	28.3%	7.9%

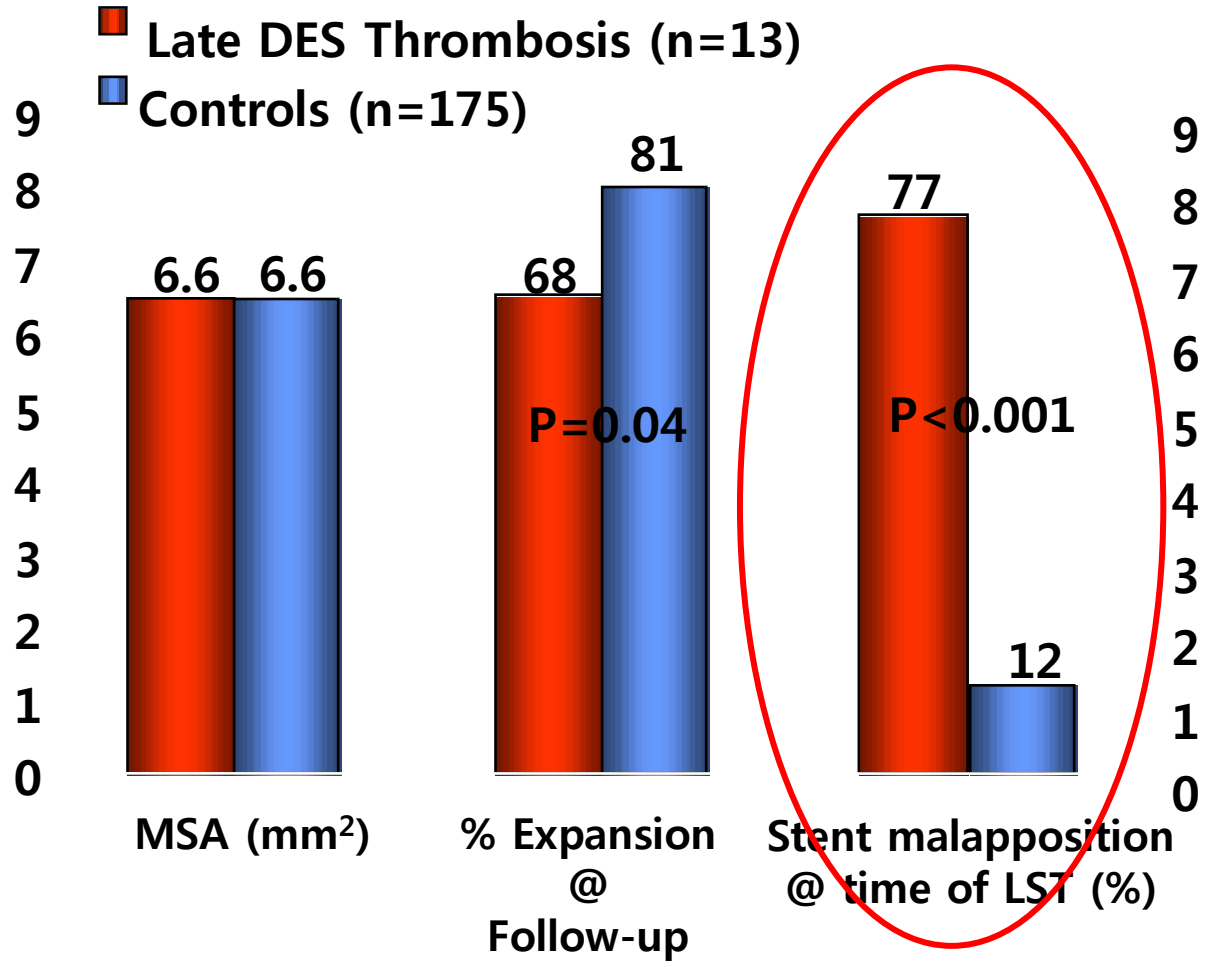
Frequency of late acquired ISA in BMS presumably related to thrombus dissolution

Increased frequency of late acquired ISA in DES presumably related to positive remodeling

(van der Hoeven et al. J Am Coll Cardiol 2008;51:618-26)

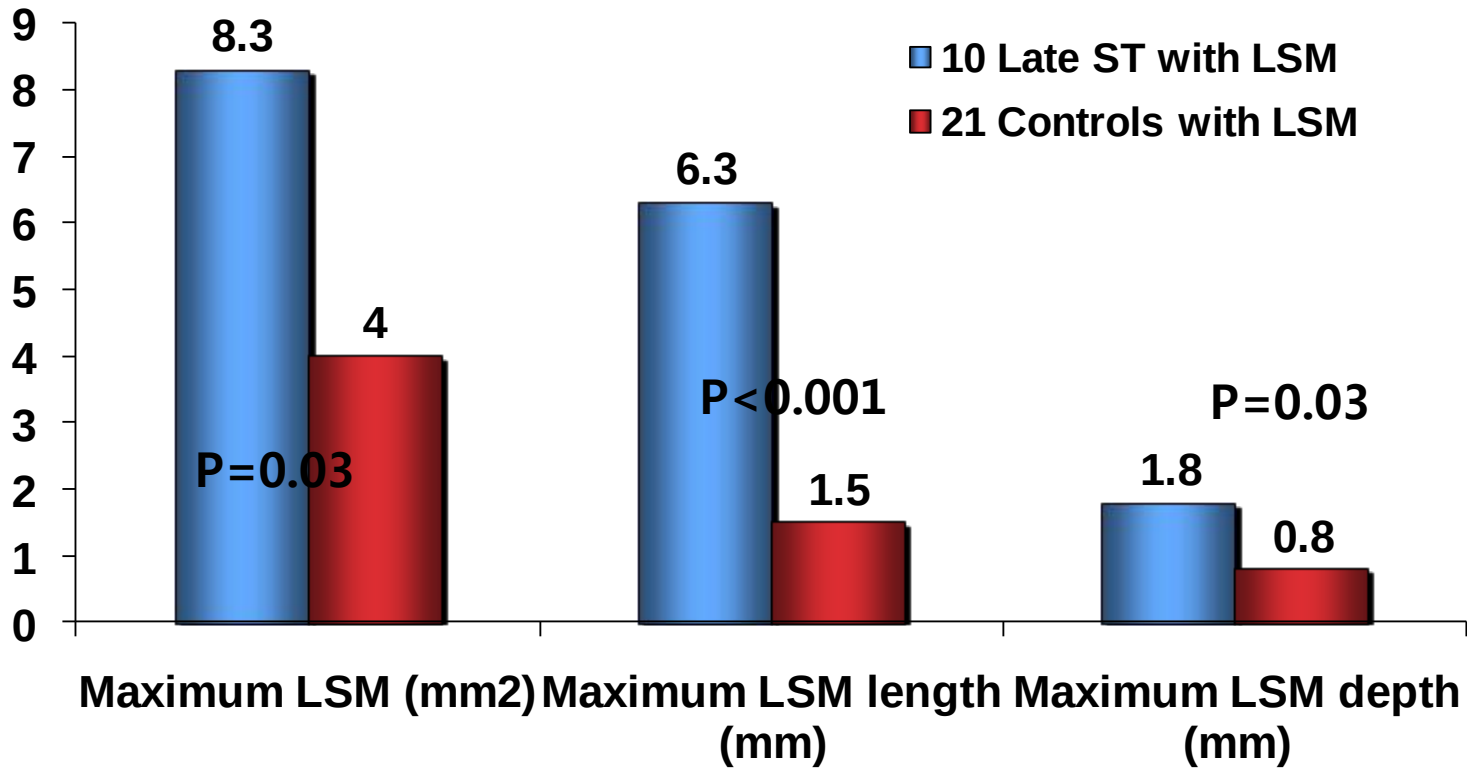
(Guo et al. Circulation. 2010;122:1077-1084.)

IVUS Predictors of Very Late (>12 months) DES ST



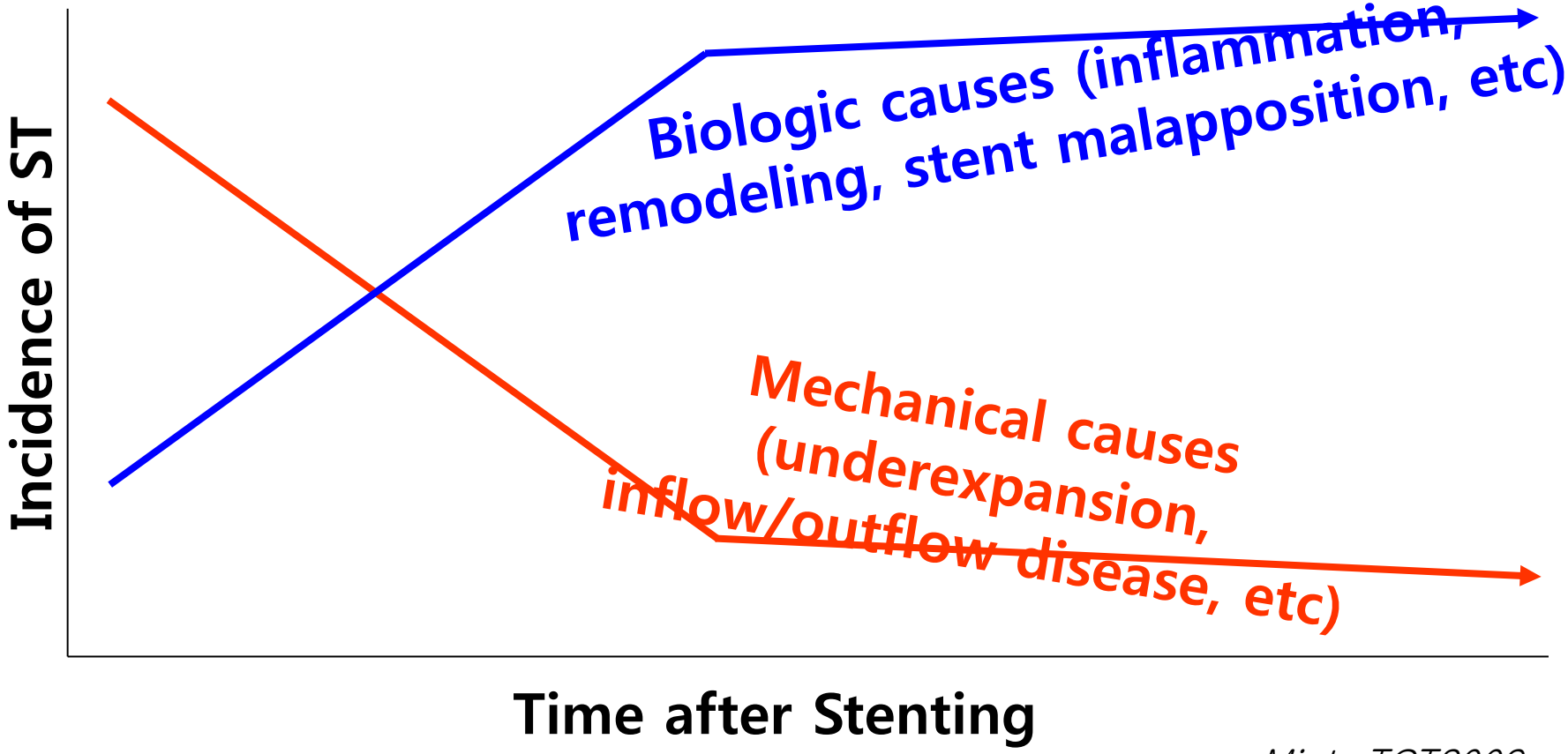
(Cook et al. Circulation 2007;115:2426-34)

Quantification of LSM in Patients with Very Late DES Thrombosis



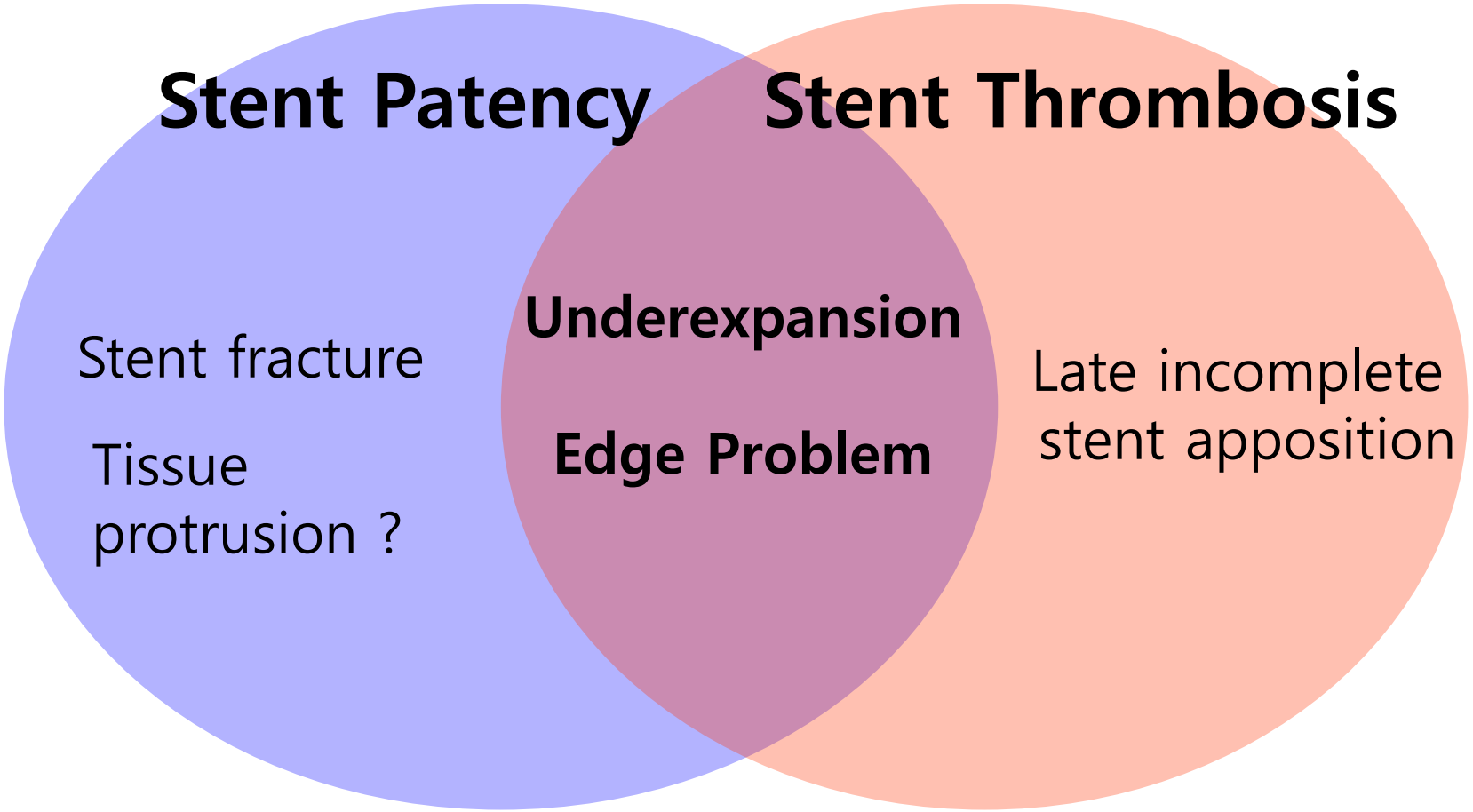
(Cook et al. Circulation 2007;115:2426-34)

Different Mechanism of ST According to Time-Pass



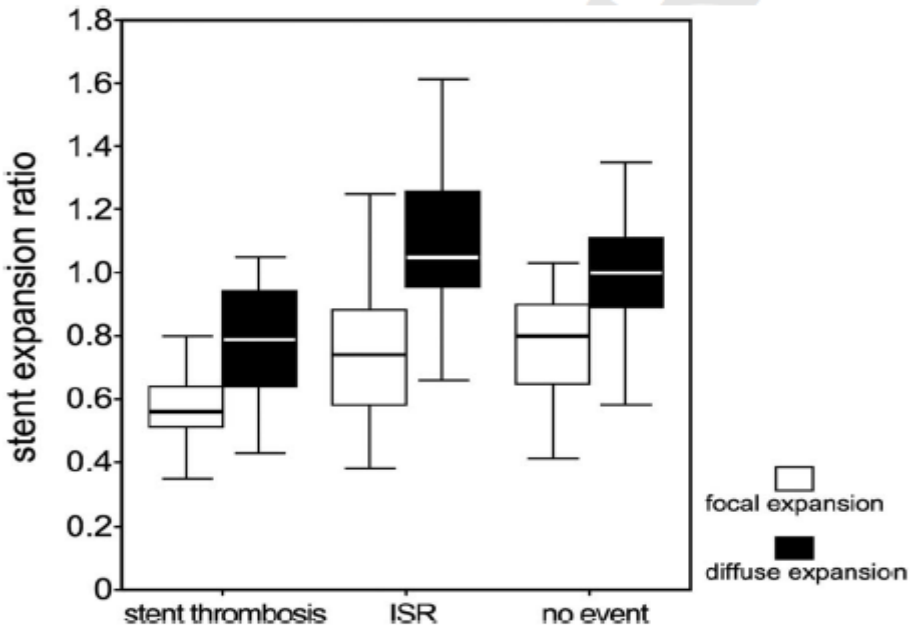
Mintz TCT2009

IVUS Predictors of Restenosis and Stent Thrombosis

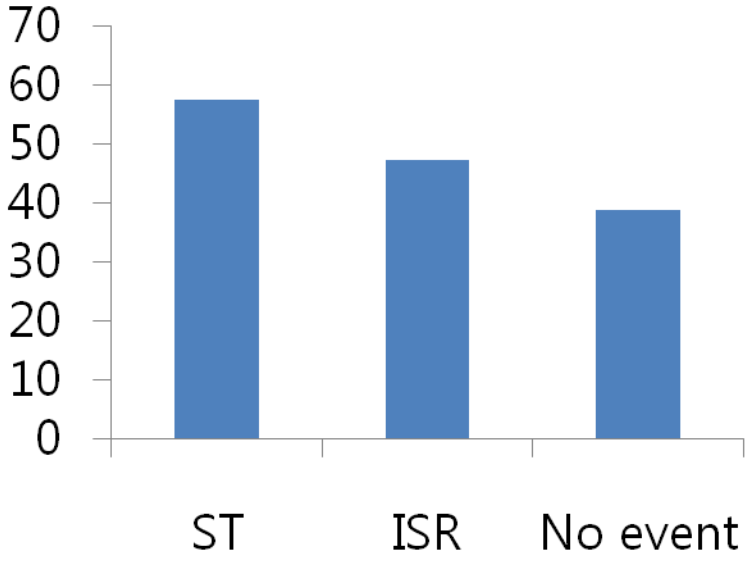


IVUS Findings in Restenosis vs ST

Stent Expansion



Reference Plaque burden Most disease slice

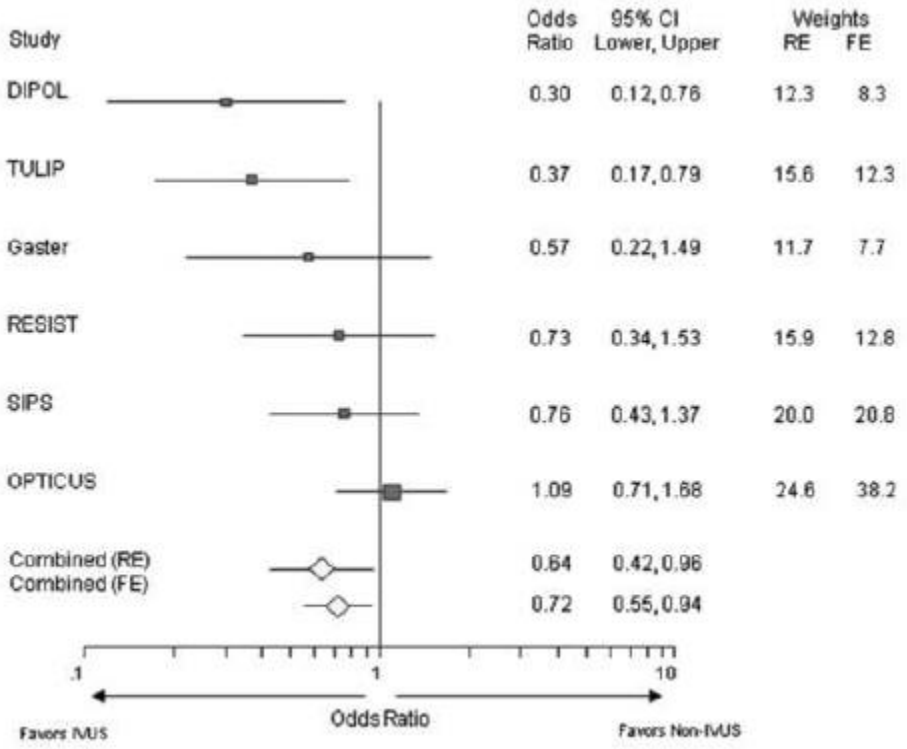


Liu et al. JACC Interventions 2009;2:428-34

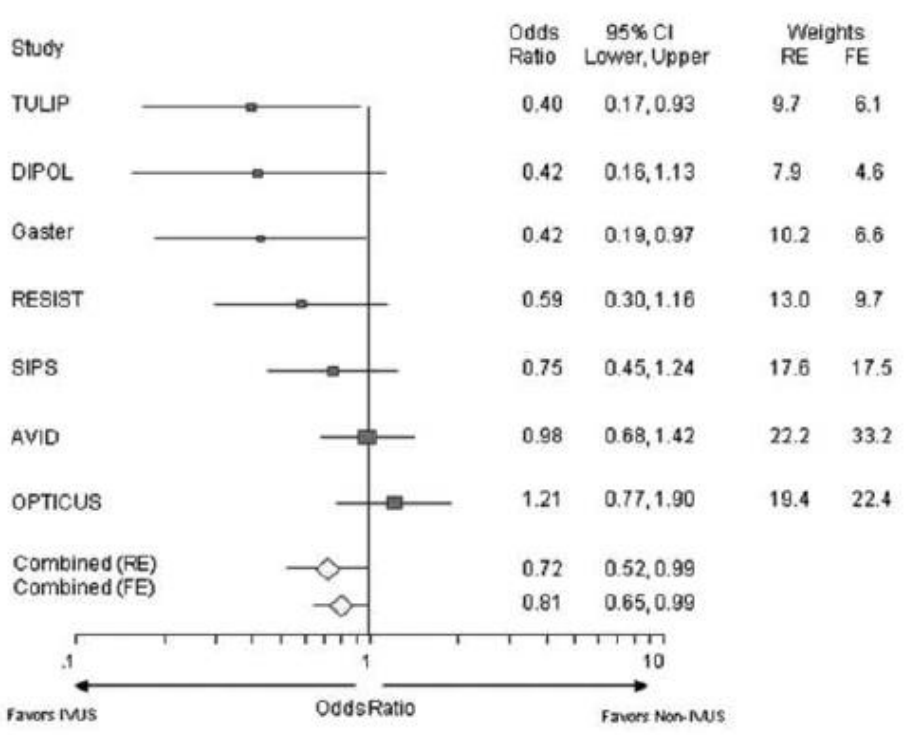
IVUS Guided PCI

A Meta-Analysis of 7 RCTs Comparing IVUS vs Angiographic Guidance of PCI in the Pre-DES

Restenosis

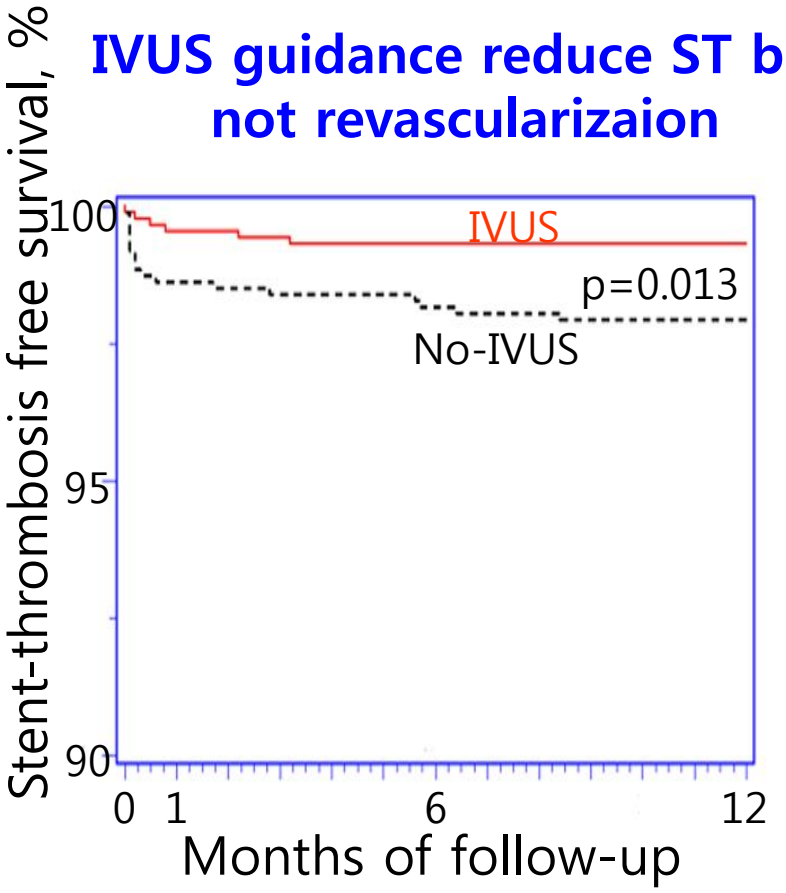


MACE



1296 IVUS-guided, DES-treated lesions in 884 pts vs 1312 propensity-score-matched, angio-guided, DES-treated lesions in 884 pts

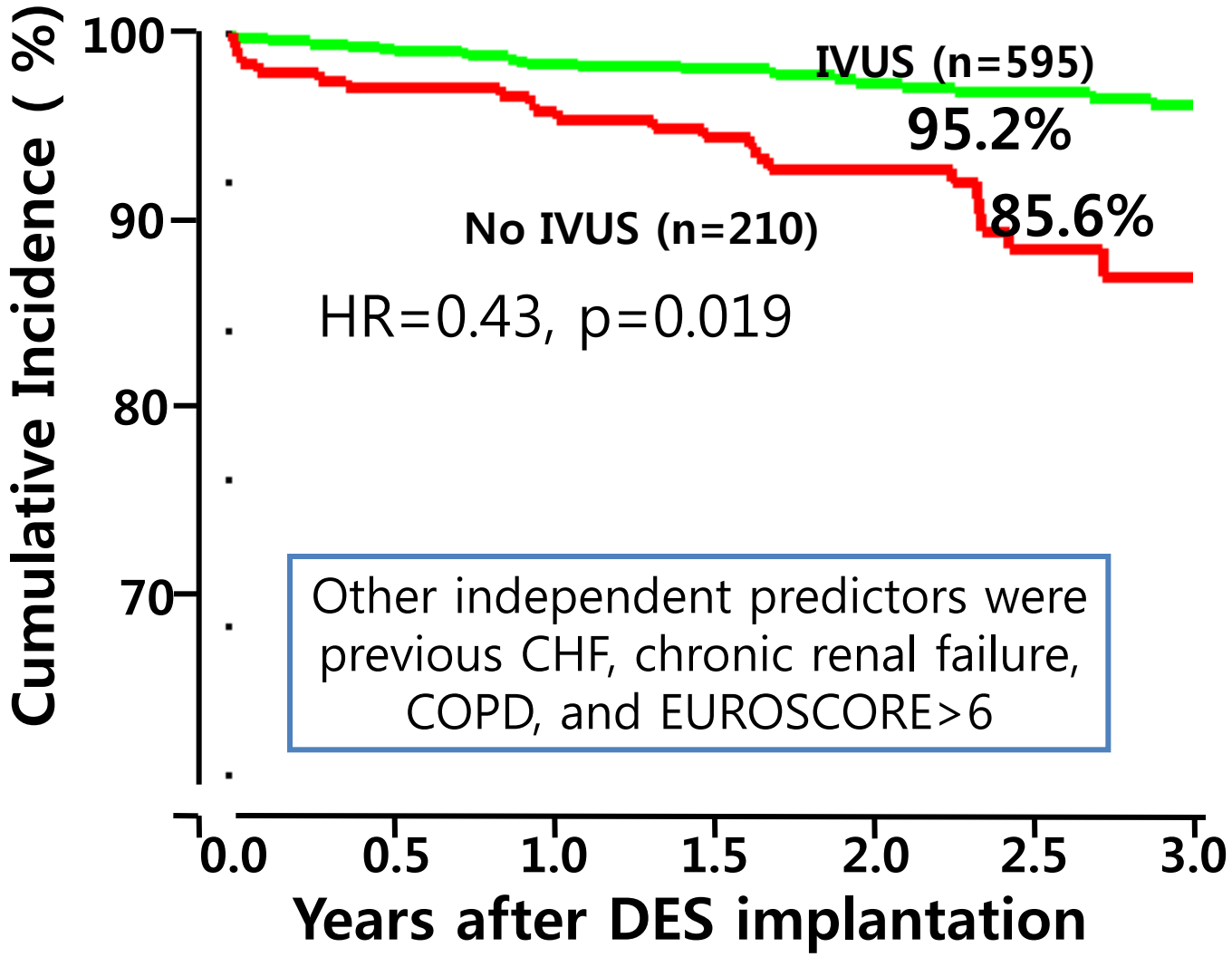
IVUS guidance reduce ST but not revascularizaion



	IVUS-guided	Angio-guided	p
30 day			
MACE	2.8%	5.2%	0.01
Stent thrombosis	0.5%	1.4%	0.045
TLR	0.7%	1.7%	0.045
1 year			
MACE	14.5%	16.2%	0.3
Definite stent thrombosis	0.7%	2.0%	0.014
Probably stent thrombosis	4.0%	5.8%	0.08
TLR	5.1%	7.2%	0.06
Late definite stent thrombosis	0.2%	0.7%	0.3

Roy et al. Eur Heart J 2008;29:1851-7

All-Cause Mortality After LMCA DES Implantation: Impact of IVUS Guidance



(Park et al. Circ Cardiovasc Interv. 2009;2:167-77)

IVUS Guidance PCI

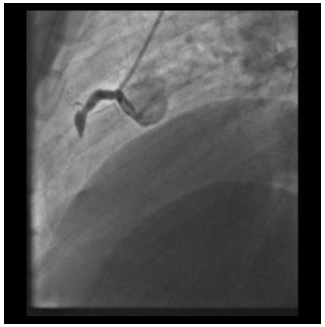
- It is not clear why IVUS guidance improves clinical outcomes after BMS or DES implantation in stable angina, but not in AMI patients even though the MSA is strongly predictive of restenosis in both lesion subsets.

Take Home Messages

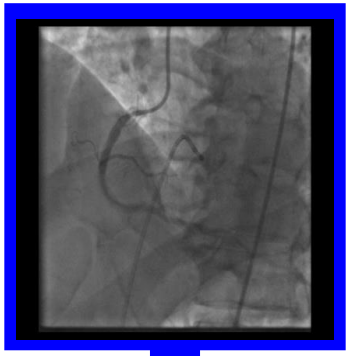
- Stent underexpansion, edge problems has been known as common IVUS predictors of restenosis and ST.
- Late ST has different mechanism compared to early ST.
- The current main cause of DES-ISR is stent under-expansion in difficult lesions such as calcified, long, small vessels.
- Late ISA could not be prevented by coronary imaging system.
- For complex lesions, IVUS guided tailor-made PCI strategy is important.

To best predict the outcome is not the same as to predict the best outcome!

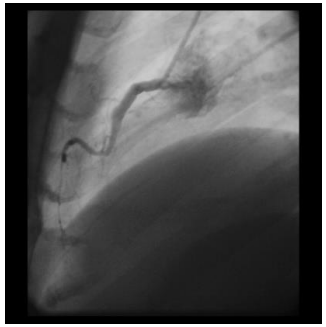
41/M
Inf. AMI
smoking,
dyslipidemia
FHx



Pre



Post



ST 2 days later