IVUS Assessment of the Mechanism of In-stent Restenosis?

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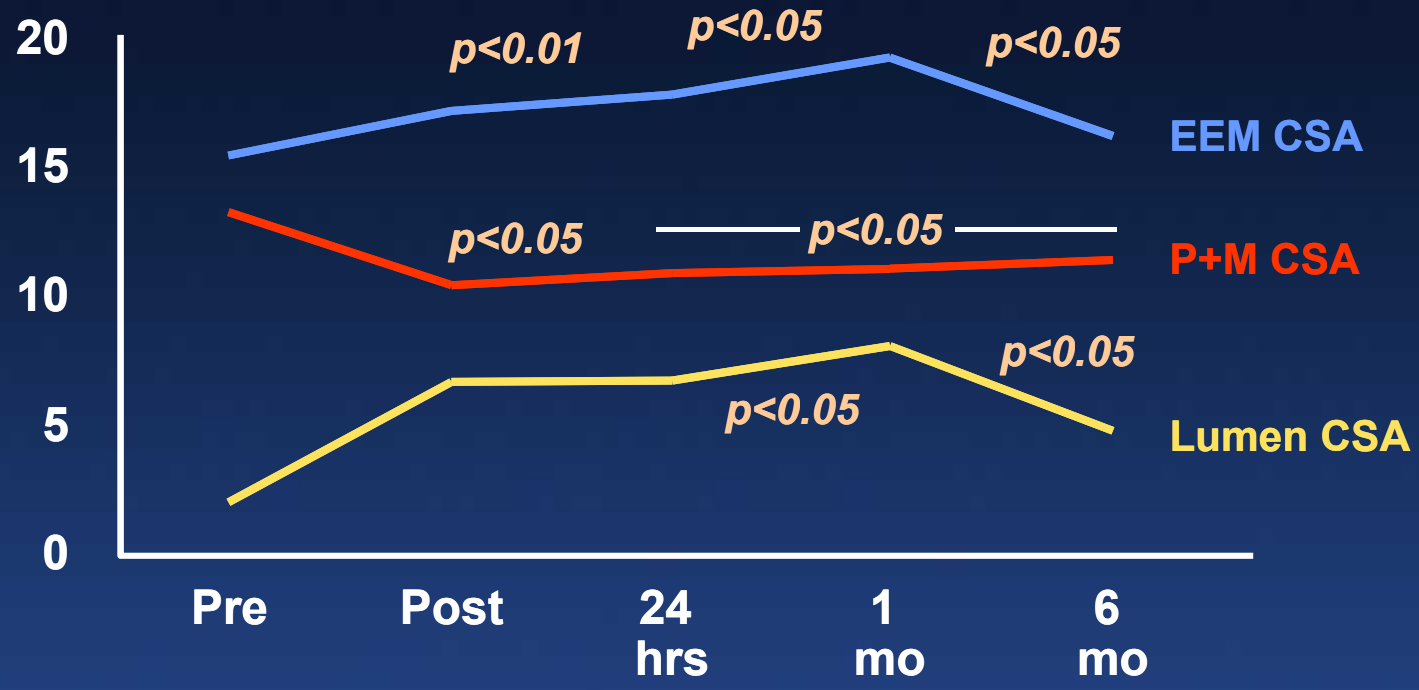
SURE Trial: Restenosis in non-stented lesions

Average of the two image slices with the smallest pre-intervention and follow-up lumen CSA



61 native vessel lesions (26 DCA, 35 PTCA) with complete serial IVUS studies (out of 79 lesions enrolled in the study)

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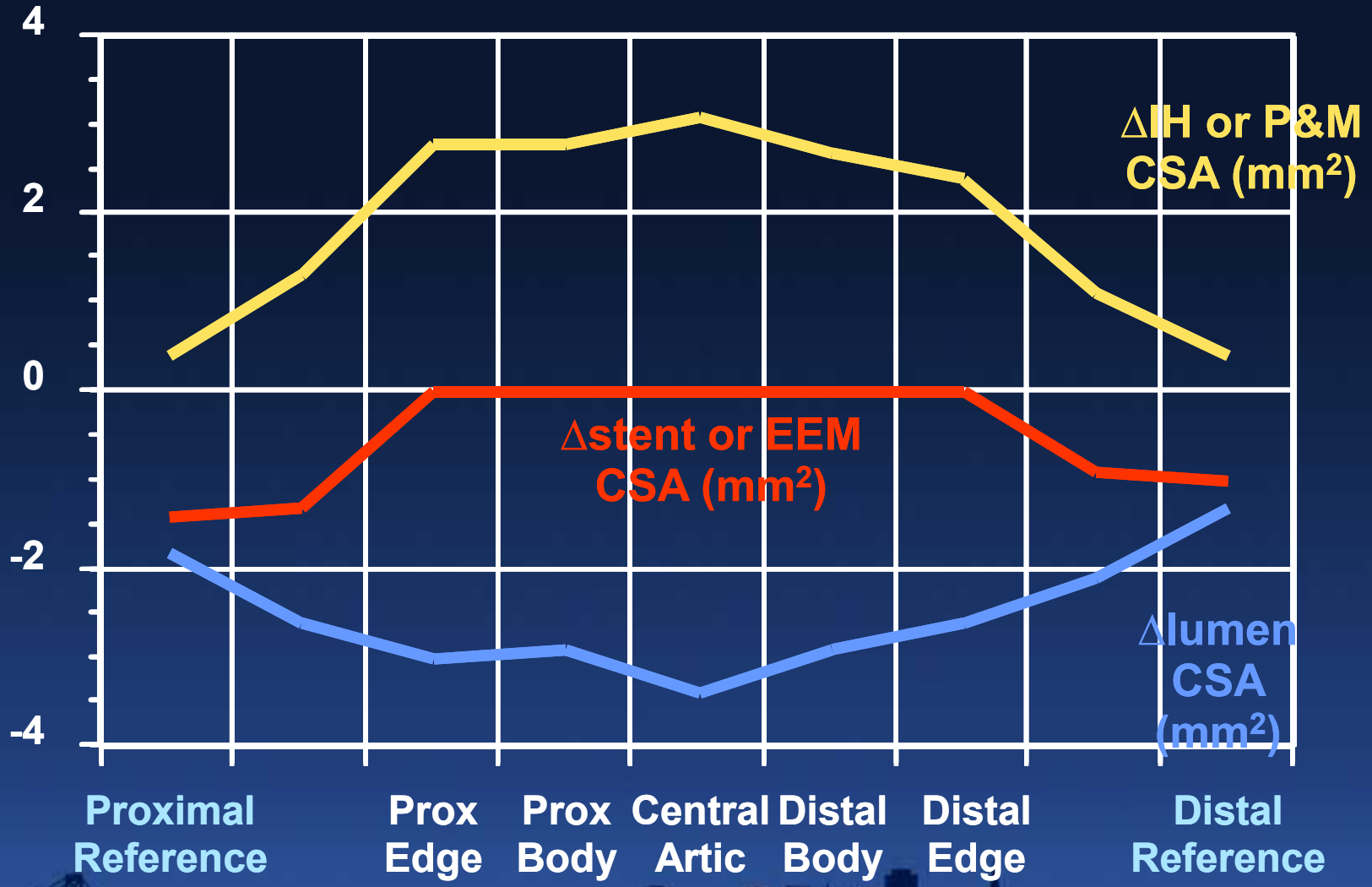
Kimura et al. Circulation 1997;96:475-83

Restenosis in Stented Lesions



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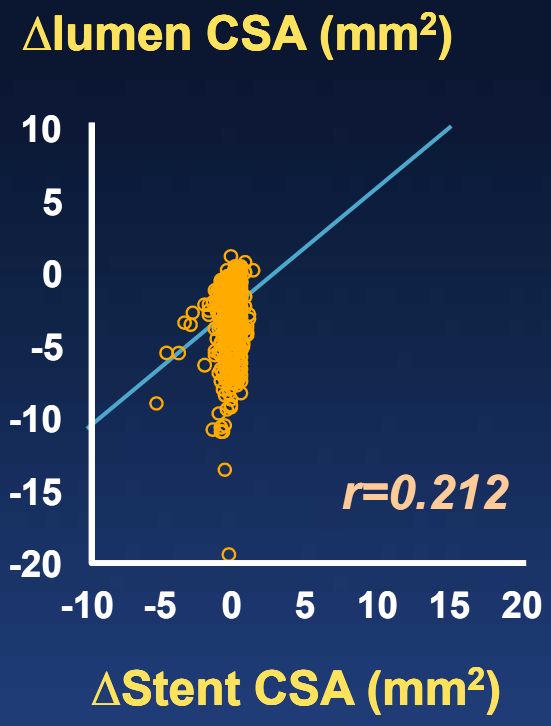
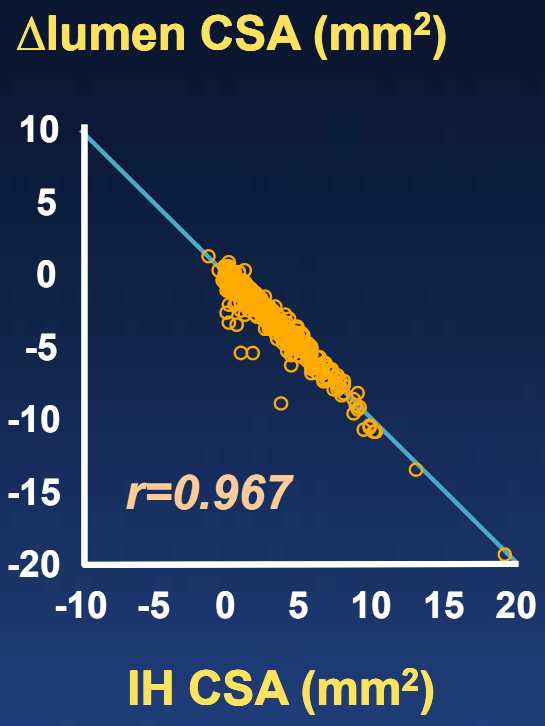
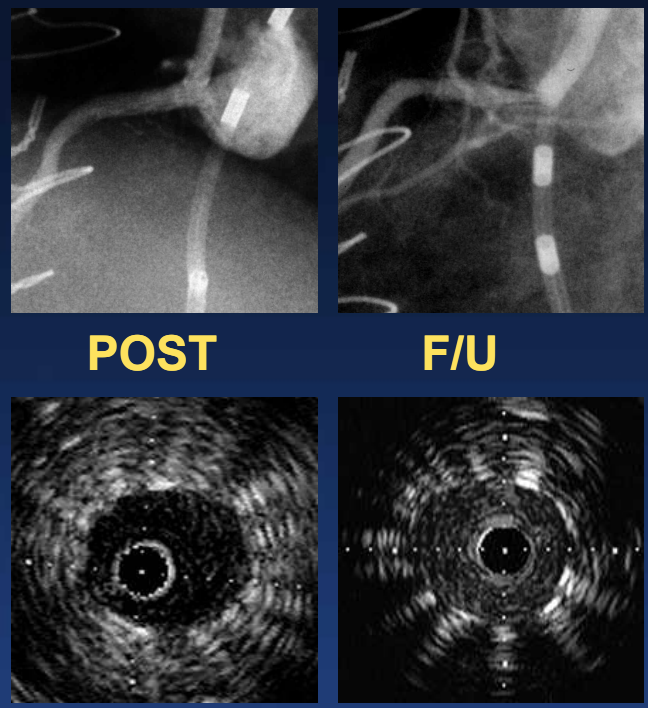
Hoffmann et al. Circulation 1996;94:1247-54

Therefore, in-stent restenosis is all intimal hyperplasia







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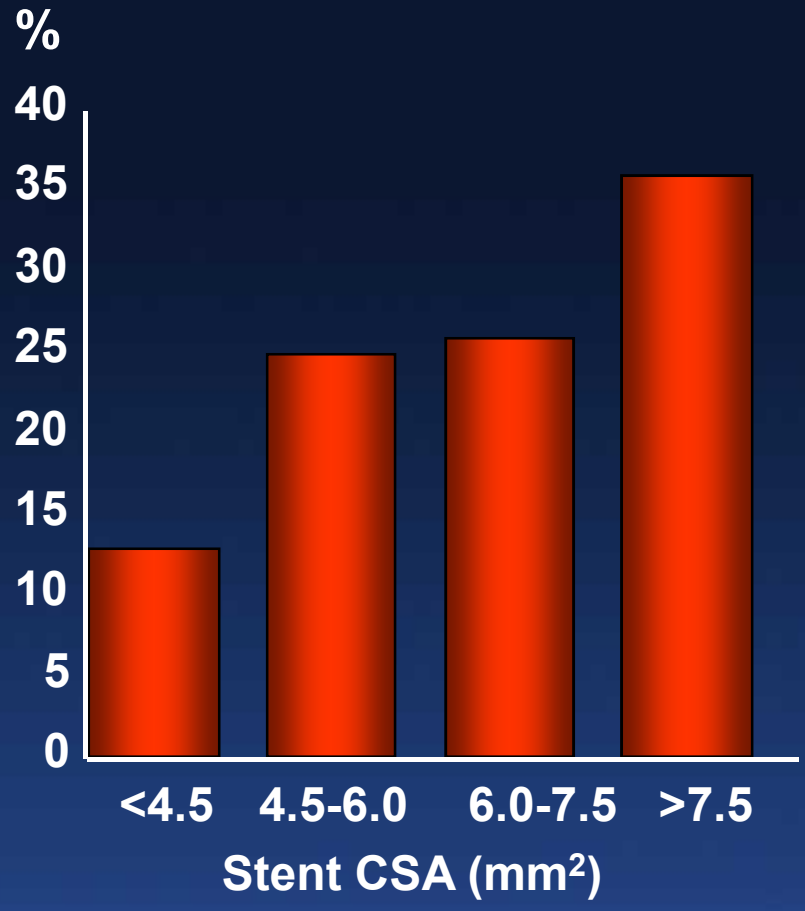
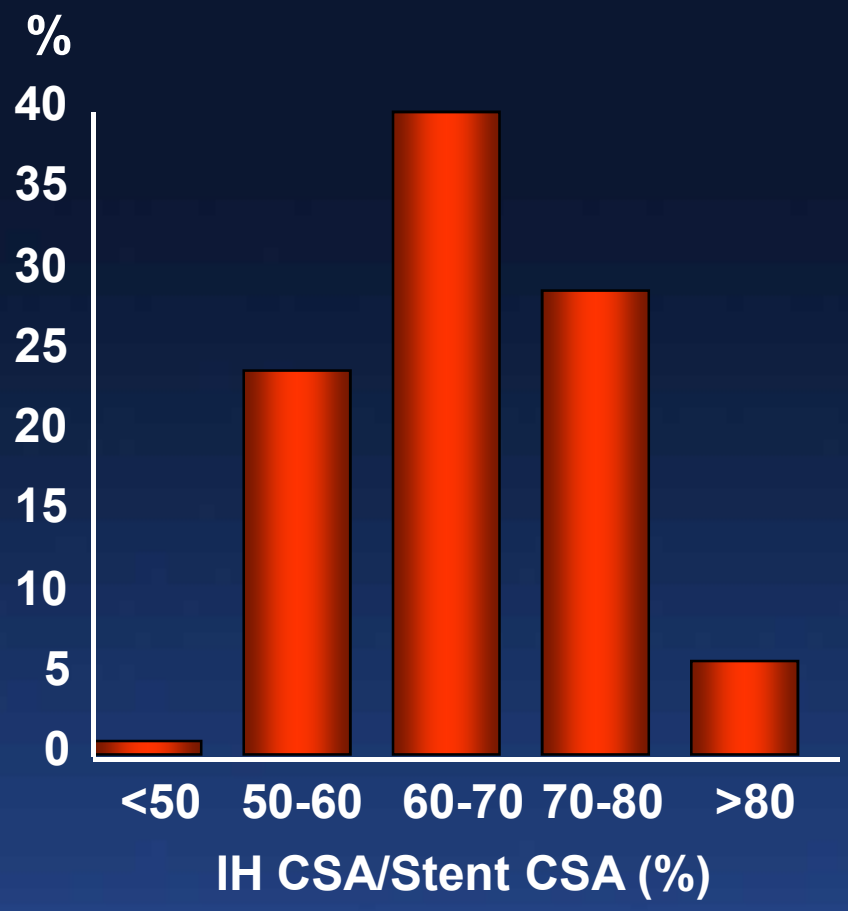
Hoffmann et al. Circulation 1996;94:1247-54

Analysis of 1089 Consecutive Patients With Bare Metal In-stent Restenosis





4.4% of cases had "unrecognized mechanical complications"
12% had severe chronic stent underexpansion (<4.5mm²)

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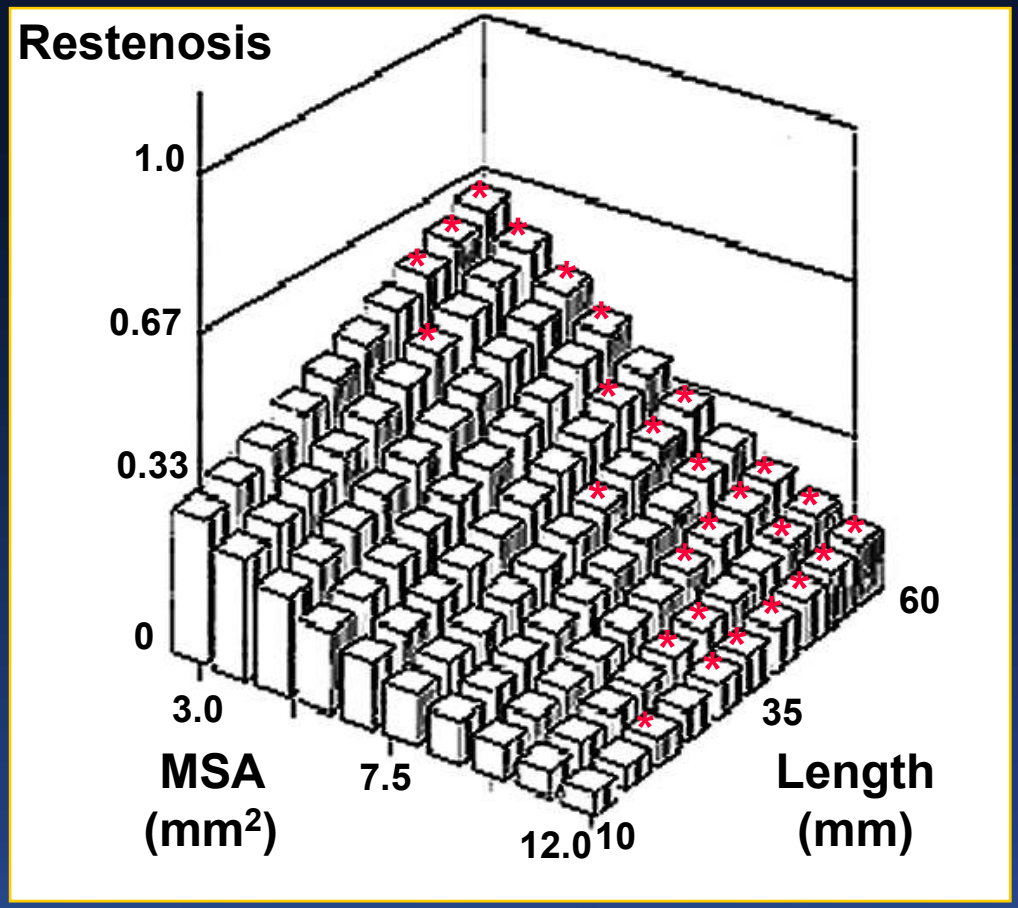
Castagna et al. AHJ 2001;142:970-4

Impact of lesion length and final minimum stent area (MSA) on restenosis



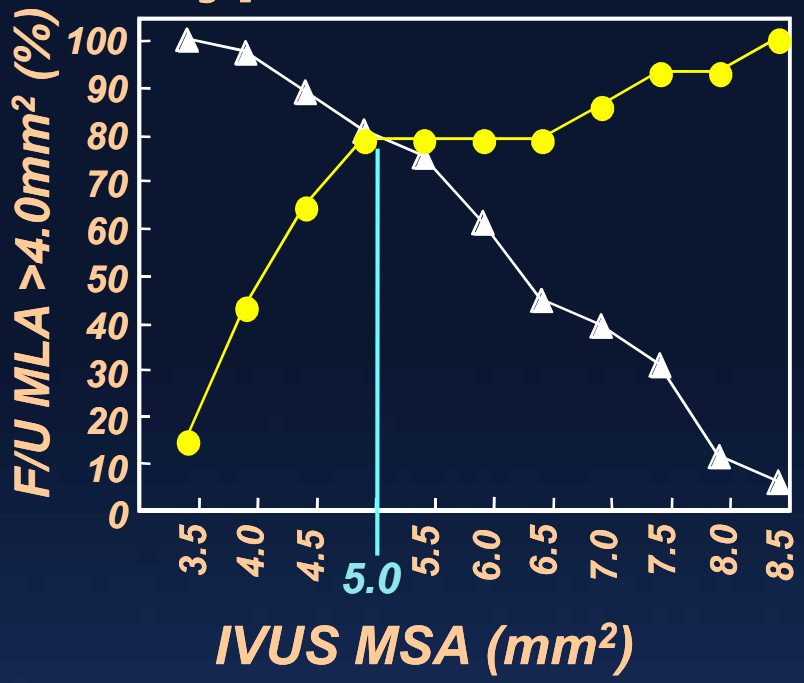
*No actual observations in this range

de Feyter et al. Circulation 1999;100:1777-83

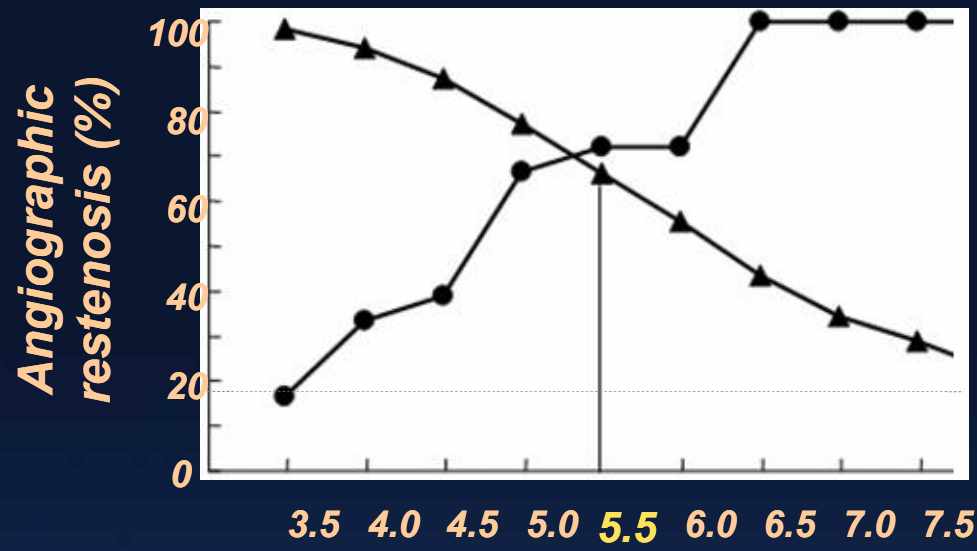
Predictors of DES Thrombosis & Restenosis

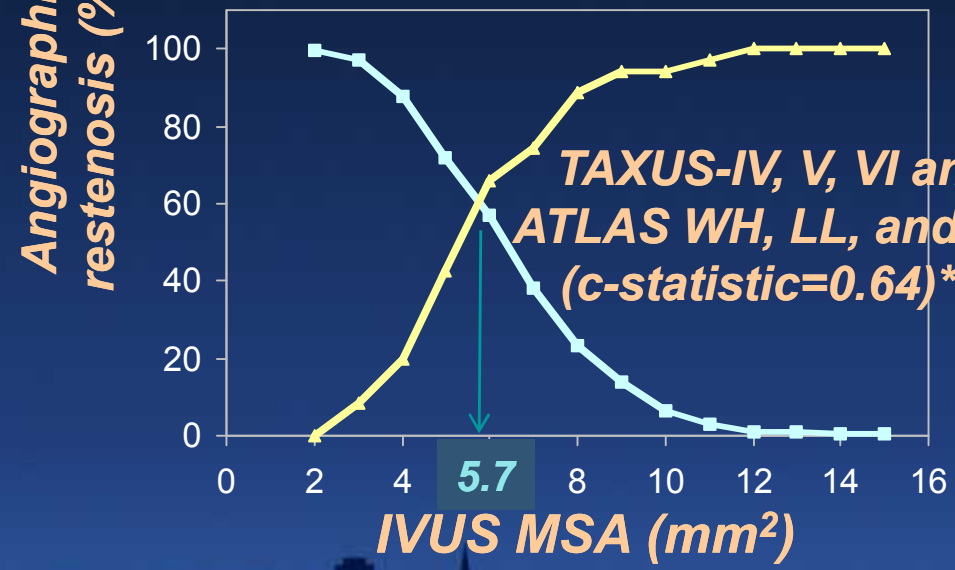
	DES Thrombosis	DES Restenosis
Underexpansion	•*Fujii et al. J Am Coll Cardiol 2005;45:995-8)* •*Okabe et al., Am J Cardiol. 2007;100:615-20* •*Liu et al. JACC Cardiovasc Interv. 2009;2:428-34*	•*Sonoda et al. J Am Coll Cardiol 2004;43:1959-63* •*Hong et al. Eur Heart J 2006;27:1305-10* •*Doi et al. JACC Cardiovasc Interv. 2009;2:1269-75* •*Fujii et al. Circulation 2004;109:1085-1088* •*Rathore et al. EuroIntervention 2009;5:349-54.*
Edge problems (geographic miss, secondary lesions, large plaque burden, etc)	•*Fujii et al. J Am Coll Cardiol 2005;45:995-8)* •*Okabe et al., Am J Cardiol. 2007;100:615-20* •*Liu et al. JACC Cardiovasc Interv. 2009;2:428-34*	•*Sakurai et al. Am J Cardiol 2005;96:1251-3* •*Liu et al.Am J Cardiol 2009;103:501-6* •*Costa et al, Am J Cardiol, 2008;101:1704-11*

Cypher in SIRIUS*



Cypher at AMC**





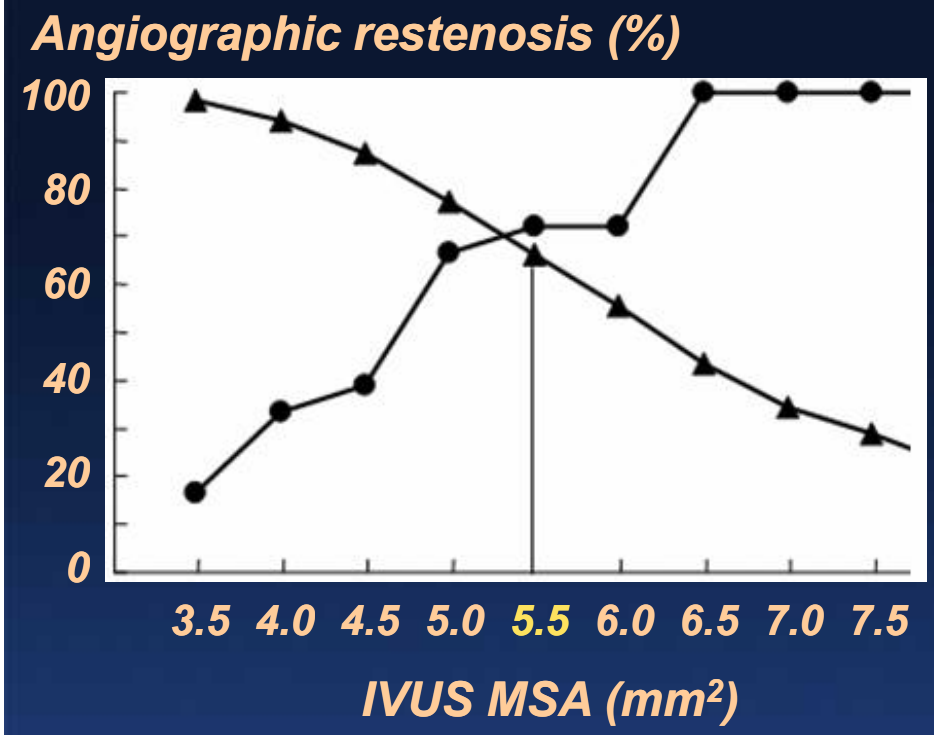
By definition, sensitivity/specificity curve analysis "must" identify a single MSA that best separates restenosis from no restenosis

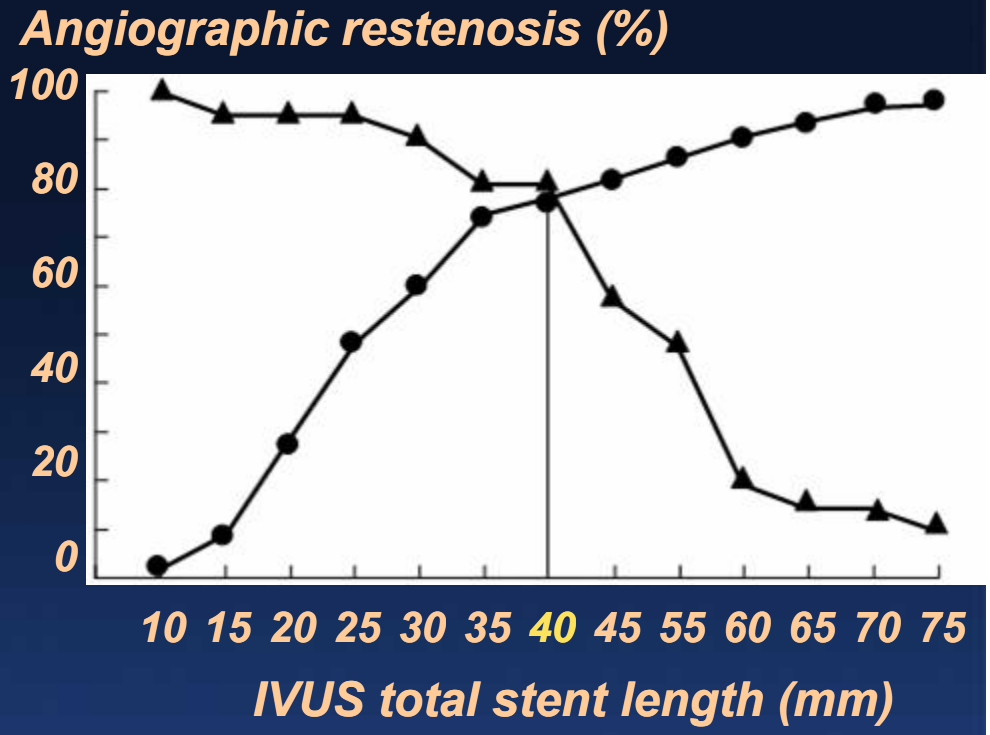
<u>This does NOT mean that 5.0-5.5mm² suffices in all pts/lesions.</u>

TAXUS-IV, V, VI and ATLAS WH, LL, and DS (c-statistic=0.64)***

*Sonoda et al. J Am Coll Cardiol 2004;43:1959-63
**Hong et al. Eur Heart J 2006;27:1305-10
***Doi et al. J Am Coll Cardiol Intv 2009 2: 1269-75
Honda & Fitzgerald. J Am Coll Cardiol Intv 2009 2: 1276-8

Predictors of angiographic restenosis in 550 pts with 670 native lesions treated with Cypher stents





	<5.5mm²	≥5.5mm²
≤40mm	2.4%	0.4%
>40mm	17.7%	8.6%

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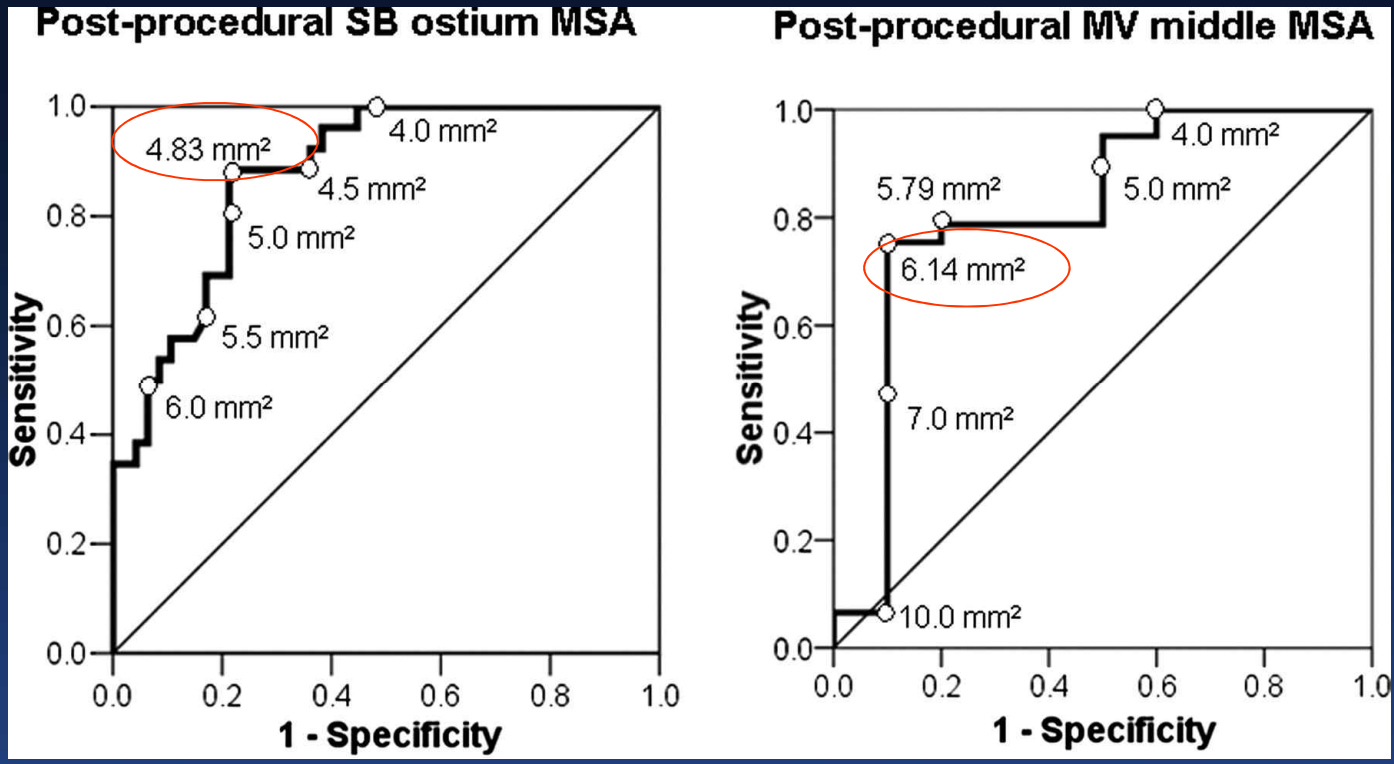
Hong et al. Eur Heart J 2006;27:1305-10

The Optimal Cutoff Value of Post-Procedural MSA to Predict a Follow-up MLA ≥4mm² After Bifurcation T-Stenting



AUC=0.88
(95%CH=0.80-0.95)

AUC=0.81
(95%CH=0.64-0.99)

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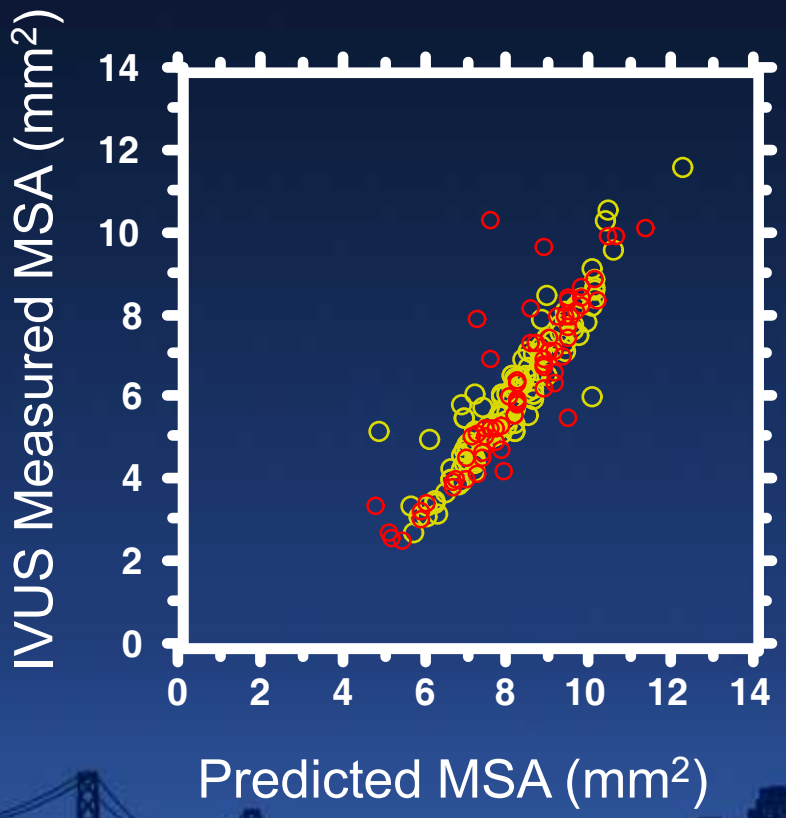
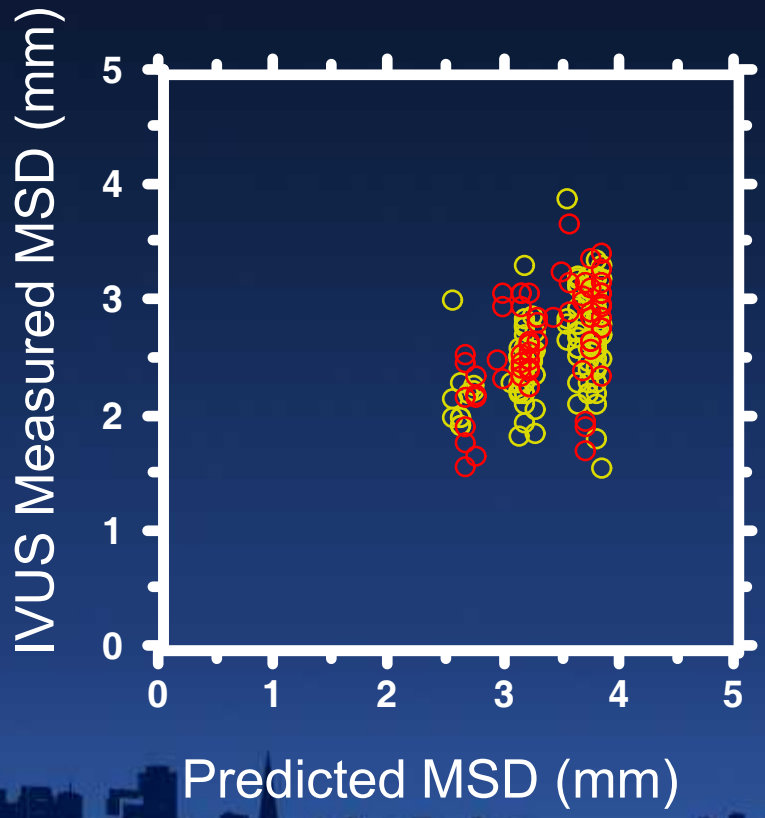
Hahn et al. J Am Coll Cardiol 2009;54:110-7

Manufacturer's Compliance Charts Cannot Be Used to Guarantee Adequate Stent Expansion

Comparison of IVUS-measured minimum stent diameter (MSD) and minimum stent area (MSA) with the predicted measurements from Cordis (Cypher in yellow, n=133) and BSC (Taxus in red, n=67). DES achieve an average of only 75% of the predicted MSD (66% of MSA)





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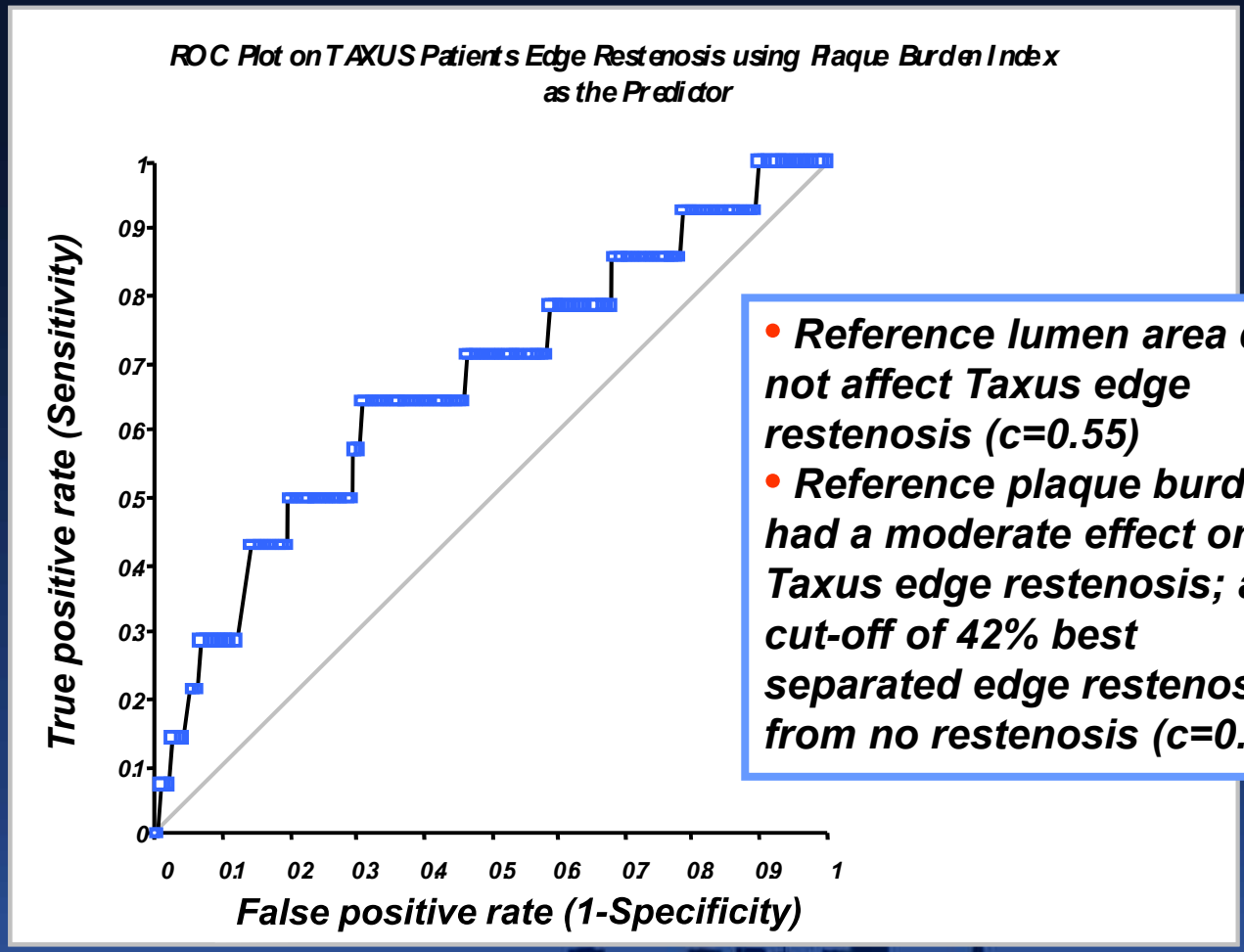
(de Rebamar Costa et al, Am Heart J 2007;153:297-303)

Comparison of 9-month QCA edge restenosis vs reference lumen area and plaque burden in TAXUS-IV, V, and VI (n=810)



- *Reference lumen area did not affect Taxus edge restenosis (c=0.55)*
- *Reference plaque burden had a moderate effect on Taxus edge restenosis; a cut-off of 42% best separated edge restenosis from no restenosis (c=0.67)*

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

Underexpansion is often lumped with malapposition - even by people who should know better

Stent Thrombosis – No single set of predictors

	JEREMIAS (registry)	IAKOVOU (registry)	MORENO (R.C.T's)	e-CYPHER (registry)	ARRIVE 1 (registry)	Cheneau et al. (registry)
Advanced age				Yes		
Plus Non-compliance	Yes	Yes				
Diabetes		Yes		Yes	Yes	
ACS/AMI				Yes		
Renal failure		Yes				
Low LVEF		Yes				
Bifurcation		Yes				
Calcifications				Yes		
Total occlusion				Yes		
MVD				Yes		
Total stent length			Yes			
Malapposition						Yes
Number of stents			Yes			

AMI = acute myocardial infarction; LVEF = left ventricular ejection fraction; RCT = randomized clinical trial; MVD = multivessel disease.
Modified from Urban. EuroPCR, 2006. Oral presentation; Cheneau et al. *Circulation*. 2003; 108:43.

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Summary

- **Stent thrombosis is multifactorial**
  - Anatomic, clinical, pharmacologic
- ***Early* stent thrombosis (~ 0.6%) is related to:**
  - Lesion complexity
  - Stent malapposition
  - Variable anti-platelet agent responsiveness
  - Early discontinuation of anti-platelet therapy (strongest risk factor)
- **LST and VLST are rare but serious complications of DES**
  - It was not seen in patients who remain on dual anti-platelet therapy in the RESEARCH/TSEARCH analysis by Qng et al, or the TAXUS meta-analysis (1 patient only)
- **Current ESC PCI guidelines now recommend 6-12 months of dual anti-platelet therapy after DES**
  - The TAXUS® Express²™ DFU recommends 6 months of dual anti-platelet therapy

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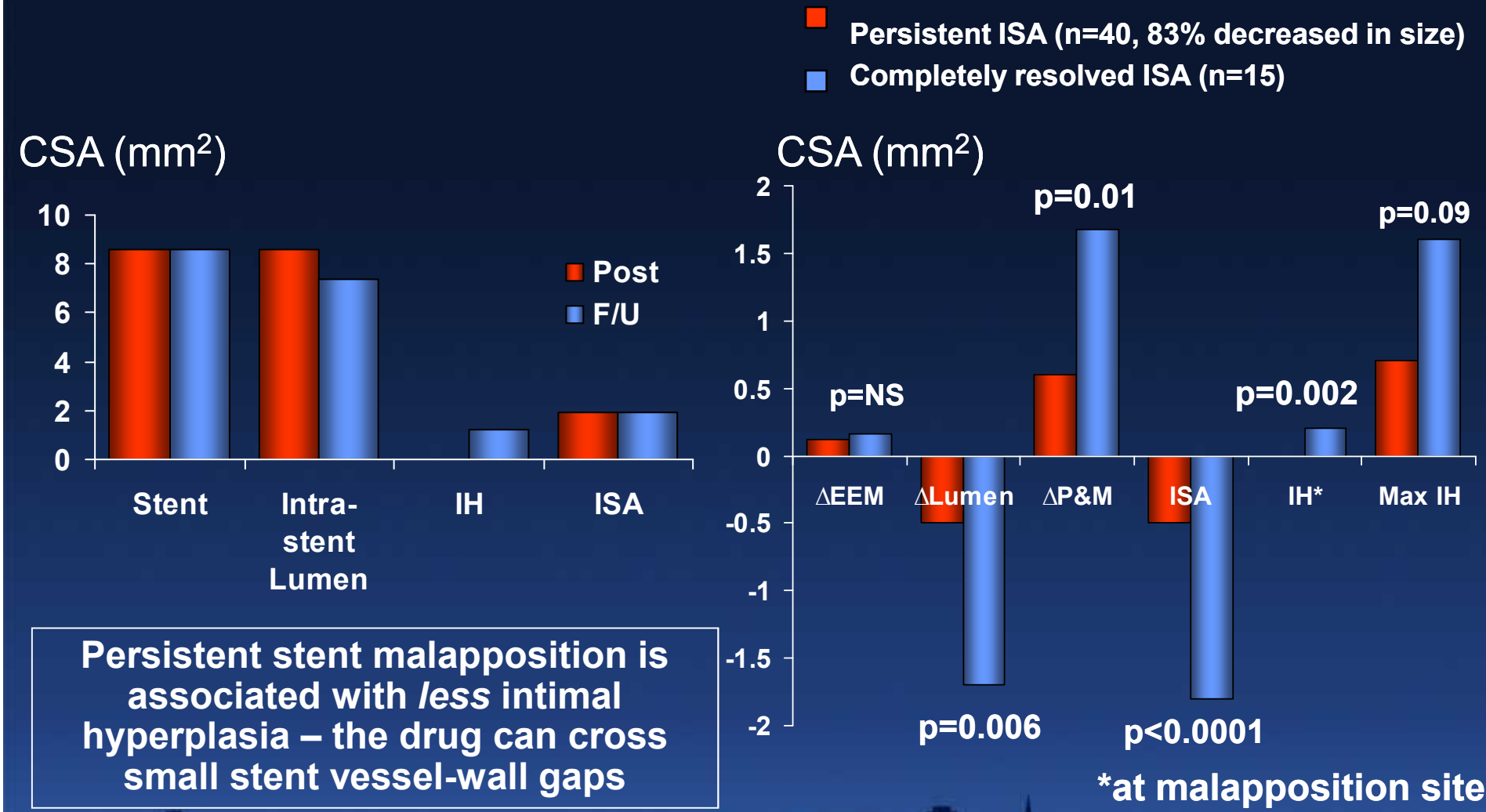
Acute Incomplete DES Apposition and IH



Persistent stent malapposition is associated with *less* intimal hyperplasia – the drug can cross small stent vessel-wall gaps

(Hong et al. Circulation 2006;113:414-9)
(Kimura, et al. Am J Cardiol 2006;98:436-42)
(Balakrishnan et al., Circulation 2005;111:2958-65)

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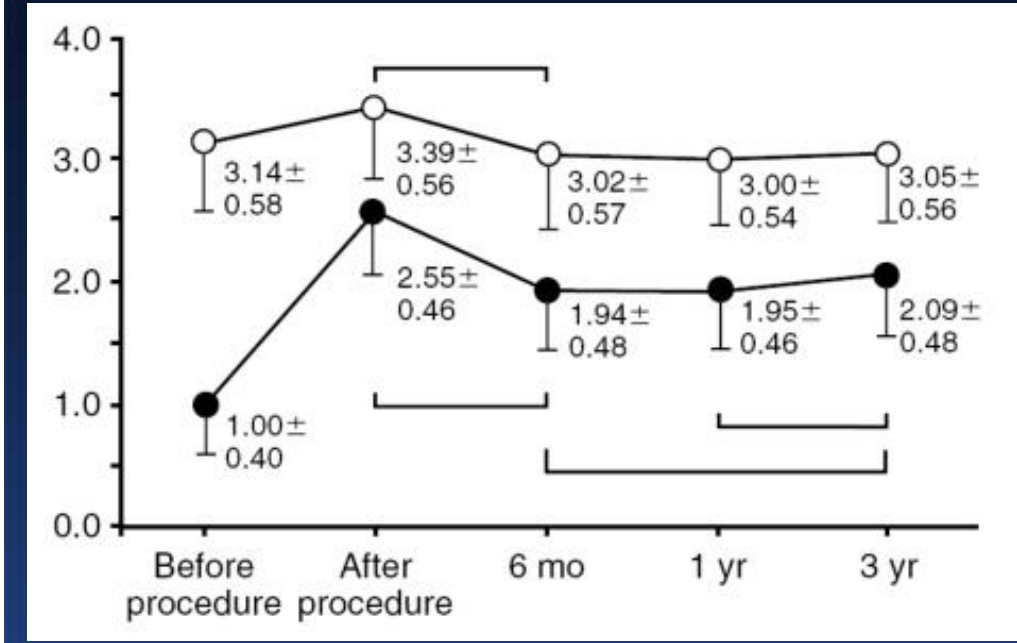
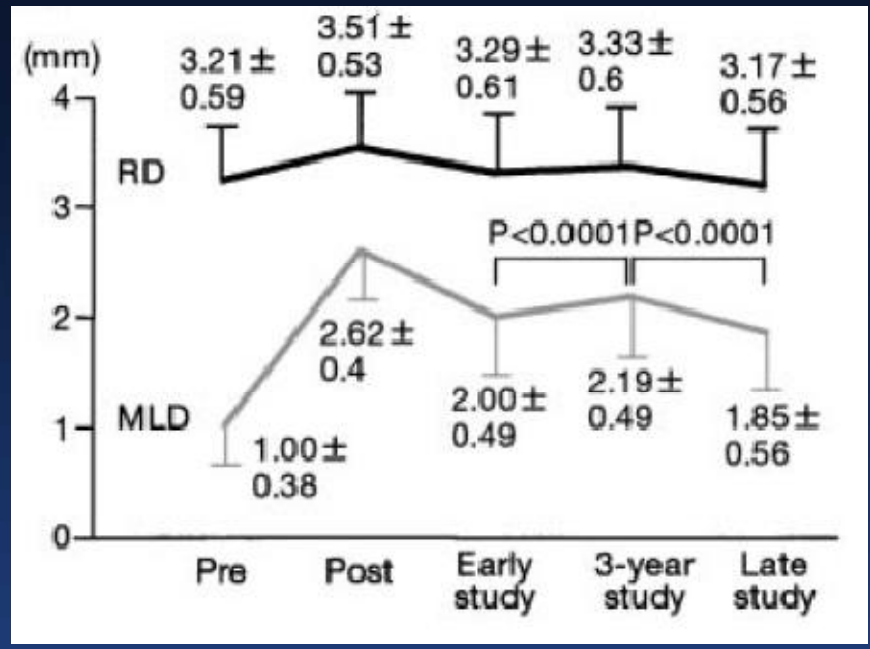
Serial angiographic FU of Palmaz-Schatz stents

3 yr FU



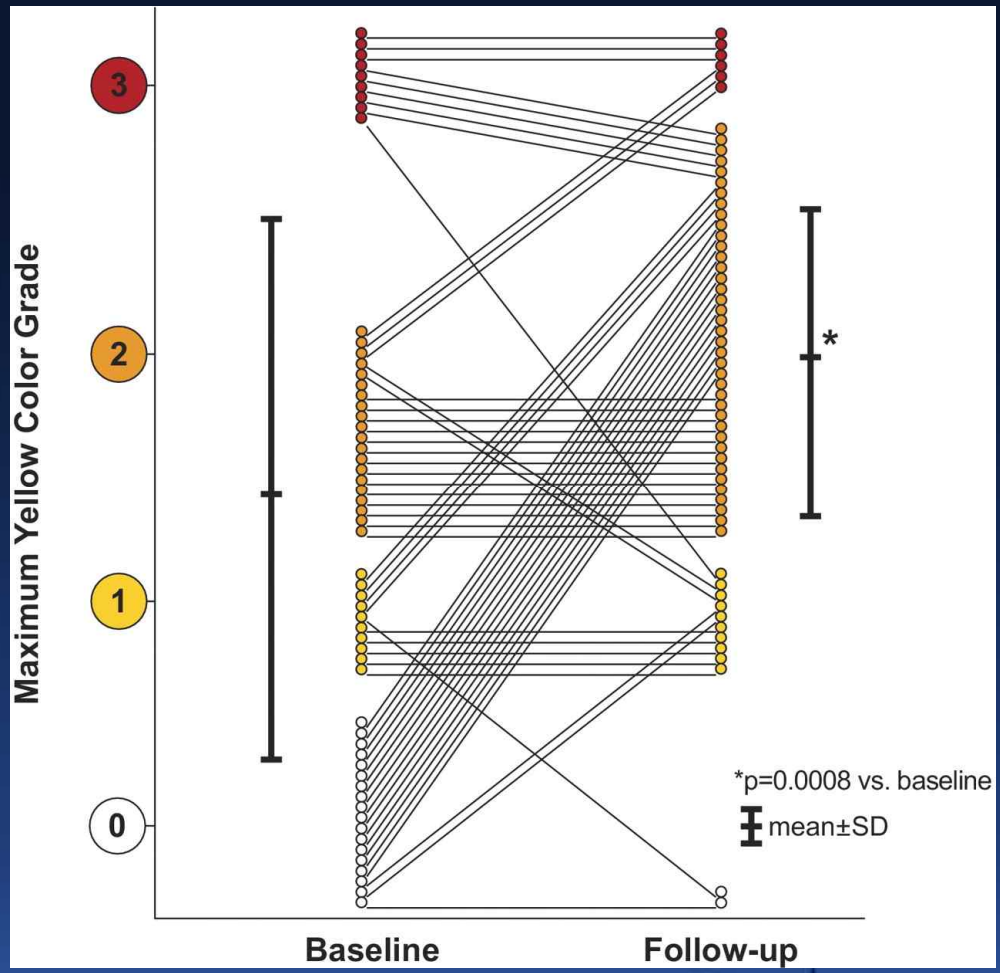
Kimura et al., N Engl J Med 1996;334:561-6

Extended FU (7 – 11 yrs)

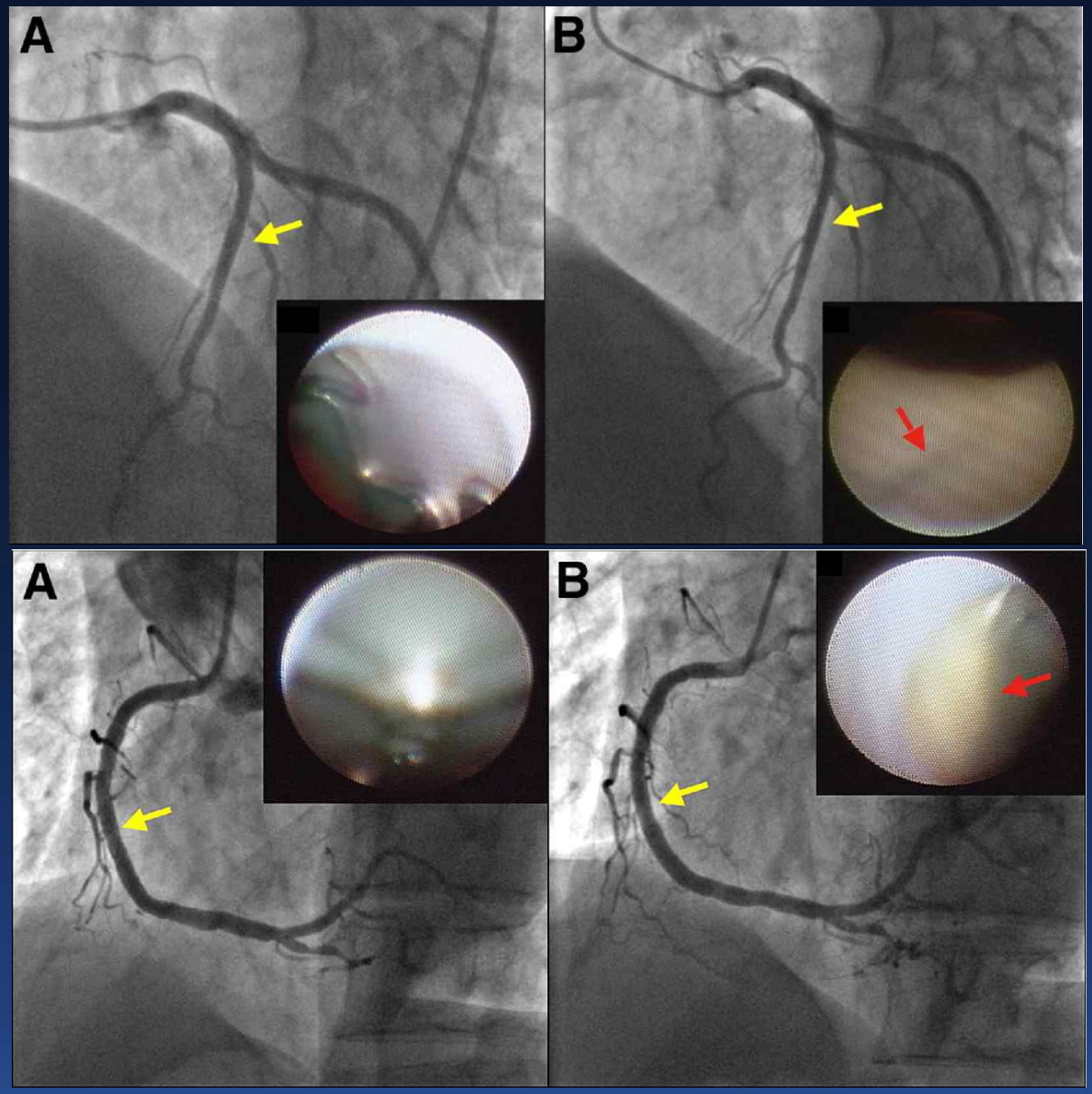


Kimura et al., Circulation 2002;105:2986-91

Changes in Maximum Yellow Color Grade From Baseline to Follow-Up in DES



Higo et al. J Am Coll Cardiol Img 2009;2:616-24



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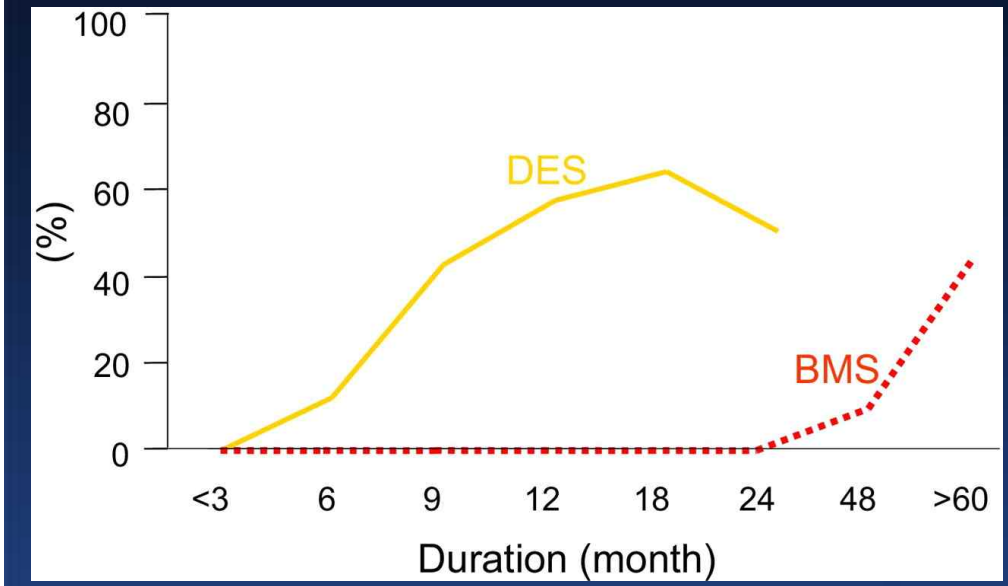
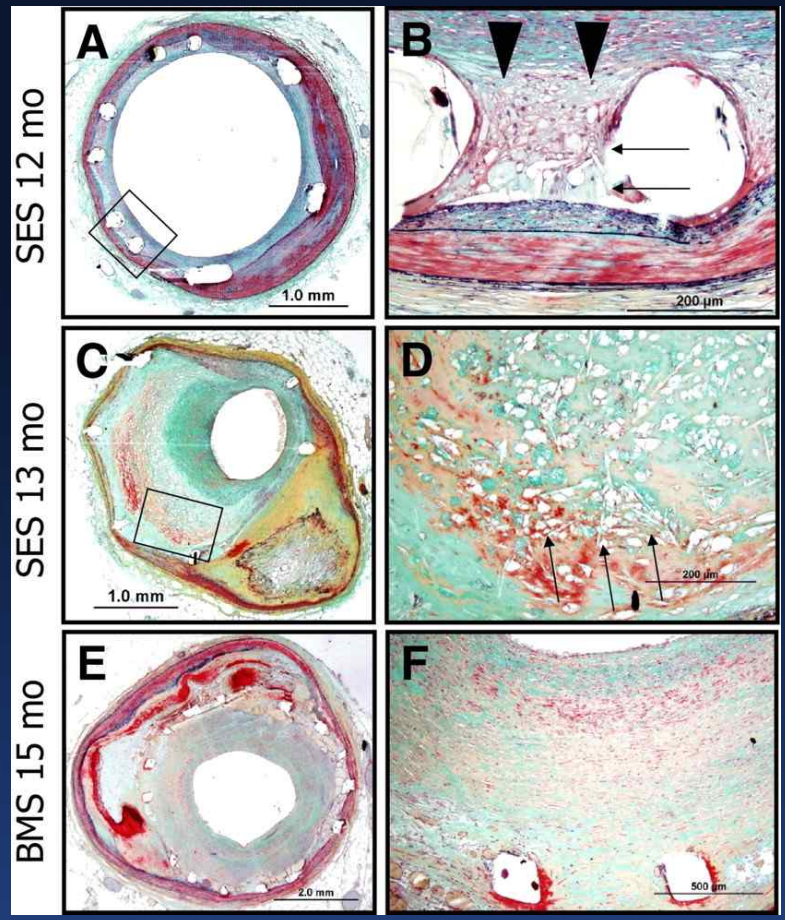
Higo, T. et al. J Am Coll Cardiol Img 2009;2:616-624

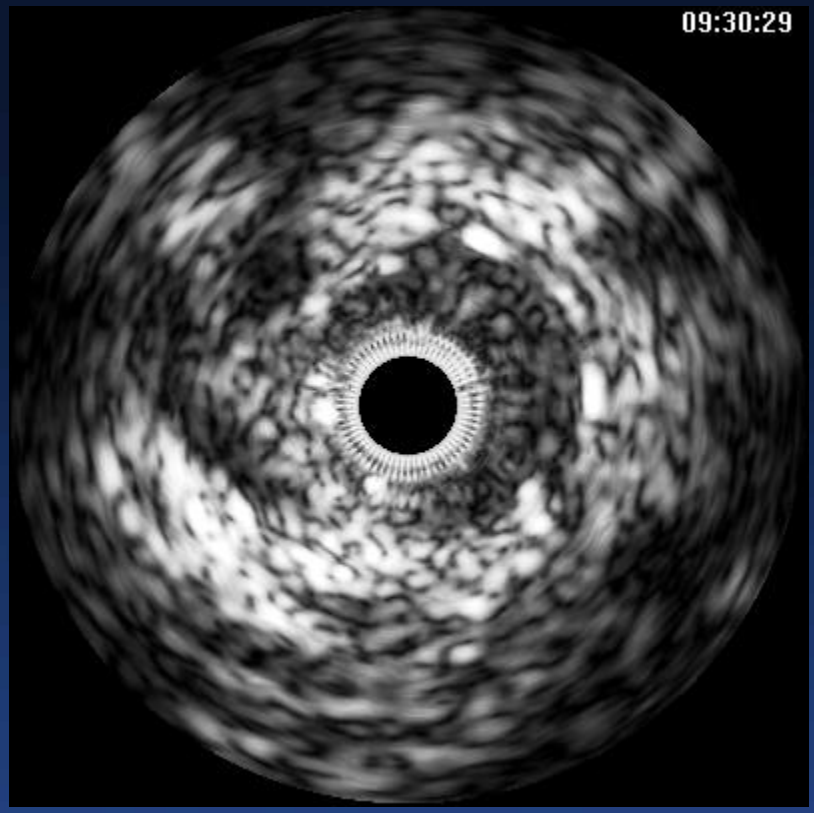
Percentage of Patients With Atherosclerotic Changes in DES Versus BMS in Relation to Duration of Implant at Autopsy

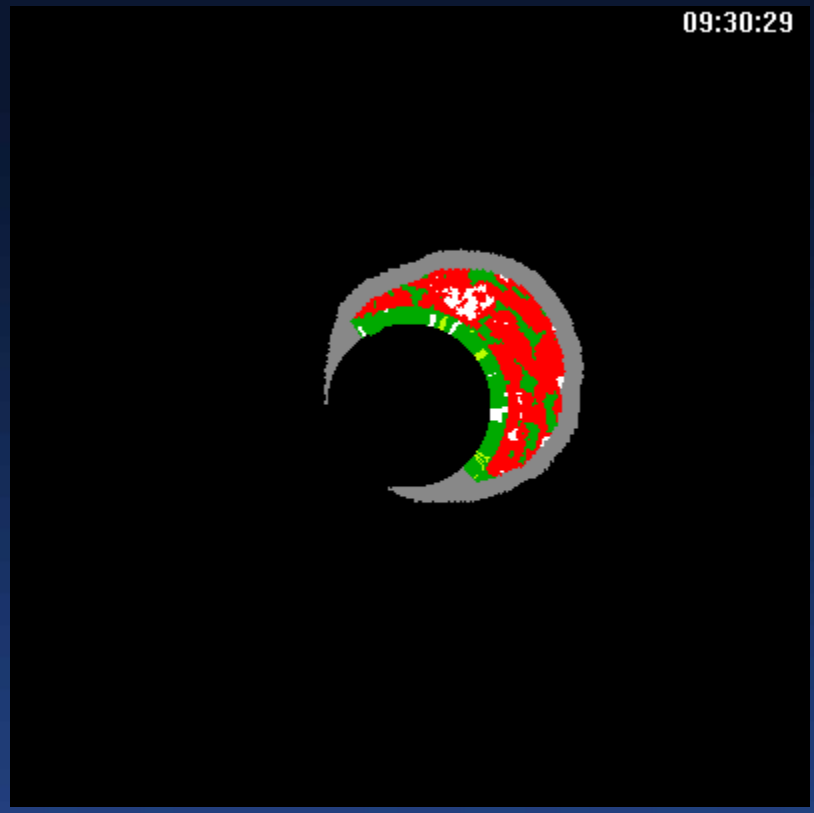




Nakazawa et al. J Am Coll Cardiol Img 2009;2:625-8

BMS 57-month follow-up





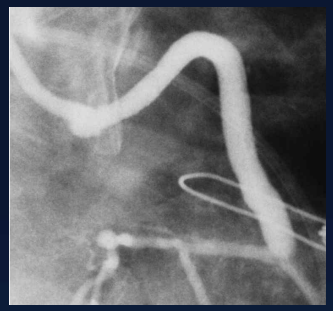
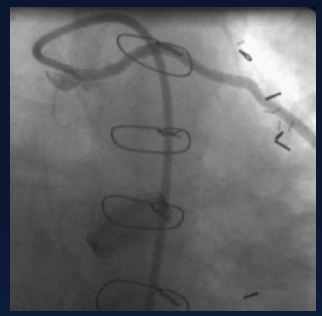
Analysis of 20 stent fractures in 17 patients

- 15 stent fractures were detected by angiography and IVUS, and 5 were detected only by IVUS
- 15 stent fractures in 13 patients were associated with in-stent restenosis (all focal); and 2 stent fractures in 2 patients were associated with very late stent thrombosis
- Five stent fractures occurred within a coronary aneurysm accompanied by malapposition despite the absence of a coronary aneurysm at index stenting.
  - Comparing stent fractures associated with an aneurysm to ones that did not occur in association with an aneurysm, complete stent fracture was more frequent (100% vs. 27%, p=0.008), and all presented >1 year after index stenting (vs. 33%, p=0.03).

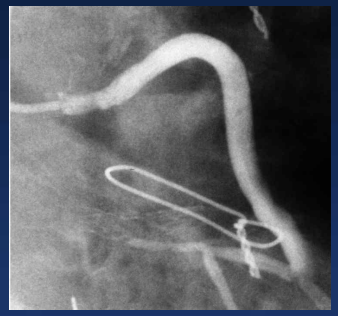
(Doi et al. Am J Cardiol 2009;103:818-23)

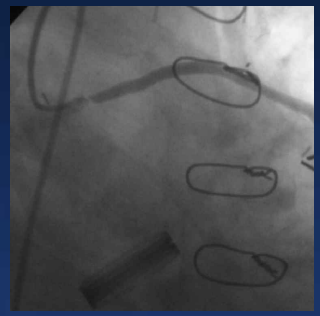
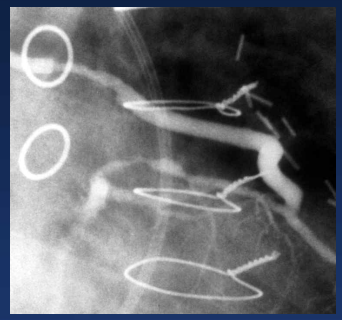
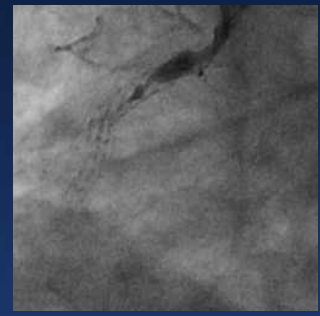
Assessment of causes of in-stent restenosis

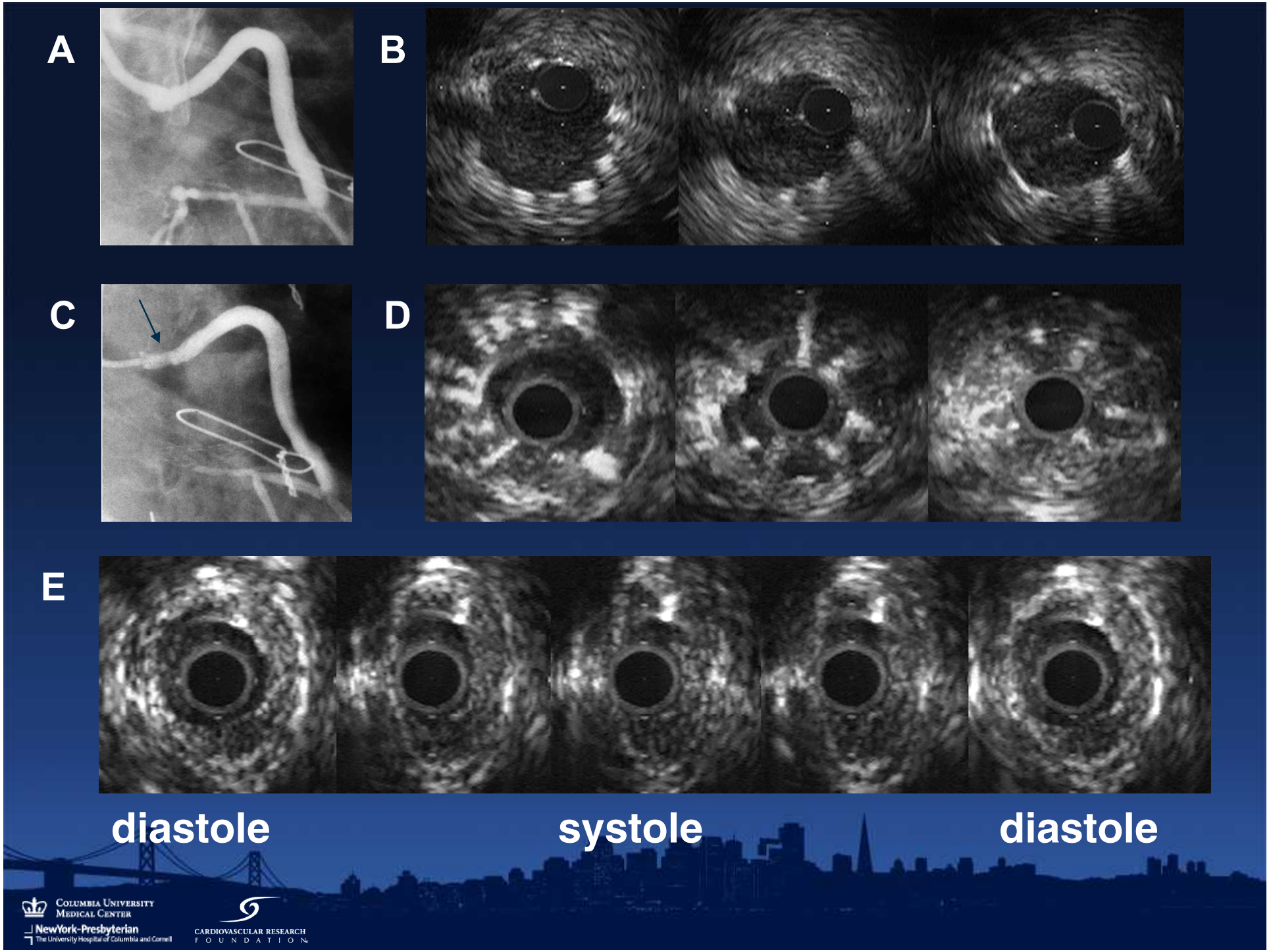
Baseline


Follow-up

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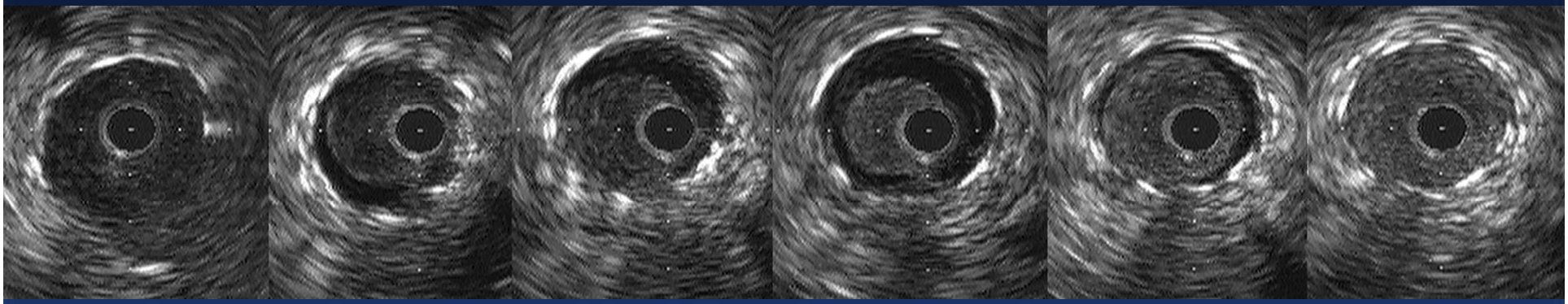

0 → 2.5 → 12.5mm

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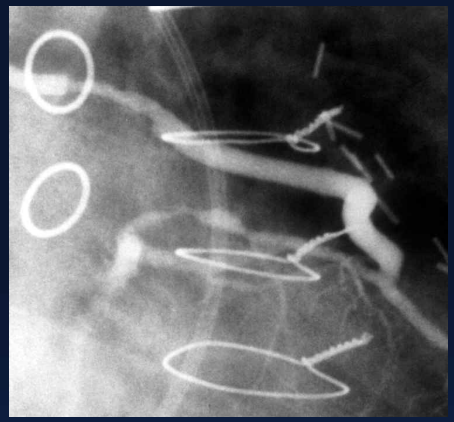

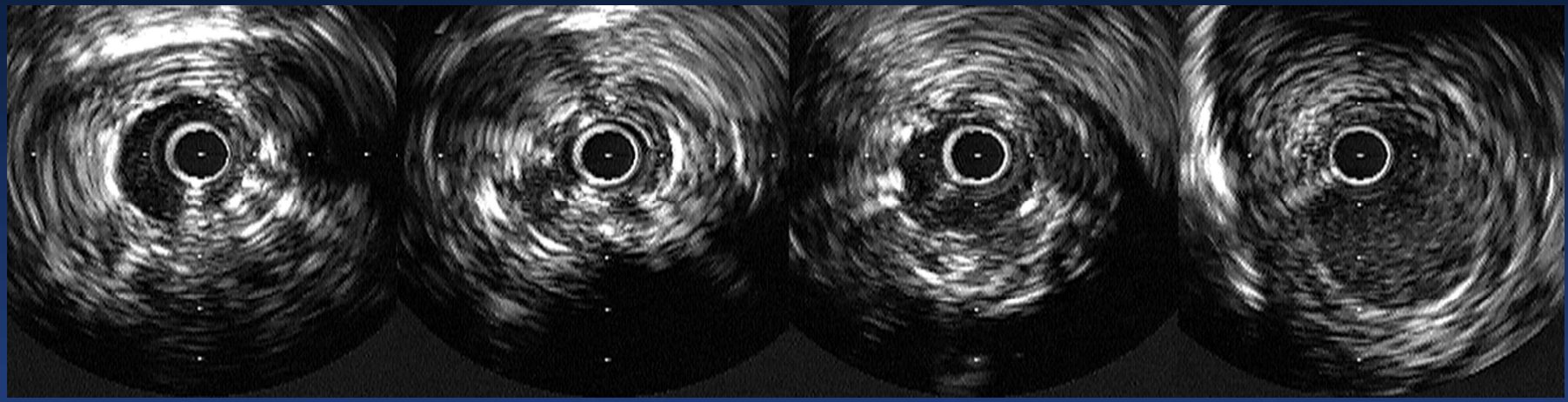

0 → 5.0 → 15.0mm

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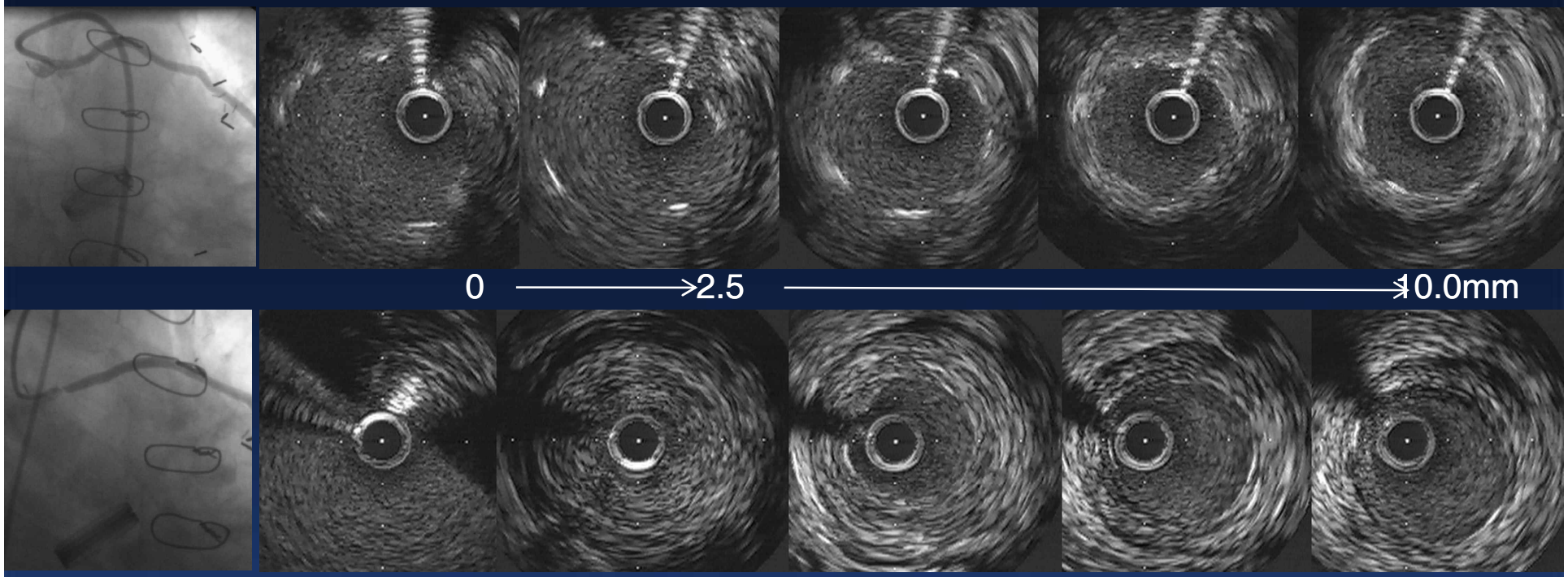

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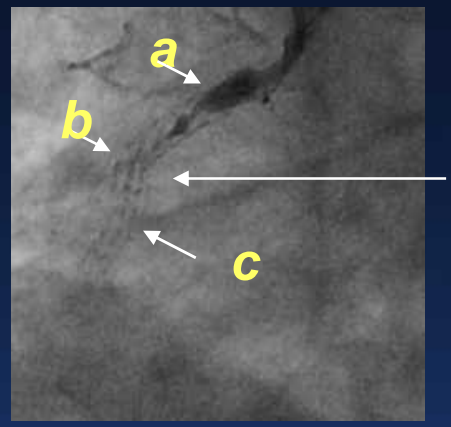
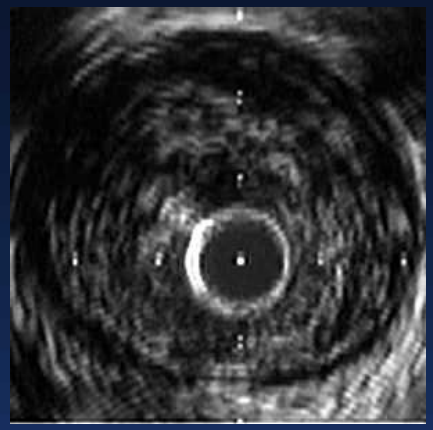
DES after VBT failure for Rx of BMS Restenosis





2 years later

9-month minimum lumen area that predicts 3-year MACE-free survival in patients from TAXUS IV, V, and VI

n=348	BMS	
	C-statistic	Cutoff
Minimum lumen area	0.73	4.0mm^2

n=351	Taxus	
	C-statistic	Cutoff
Minimum lumen area	0.75	4.2mm^2

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Doi et al. Circ Cardiovasc Intervent 2008;1:111-8