Clinical Impact of Neoatherosclerosis

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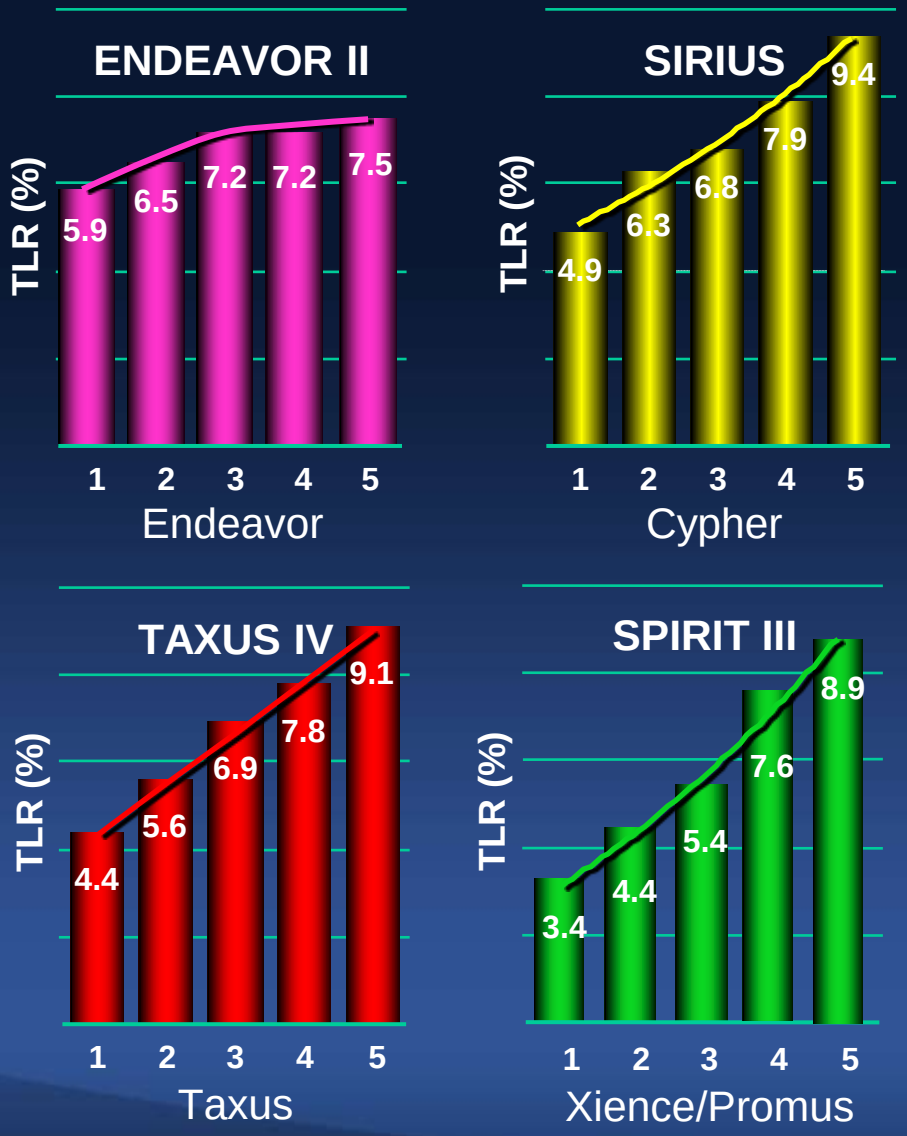
Disclosure Statement of Financial Interest

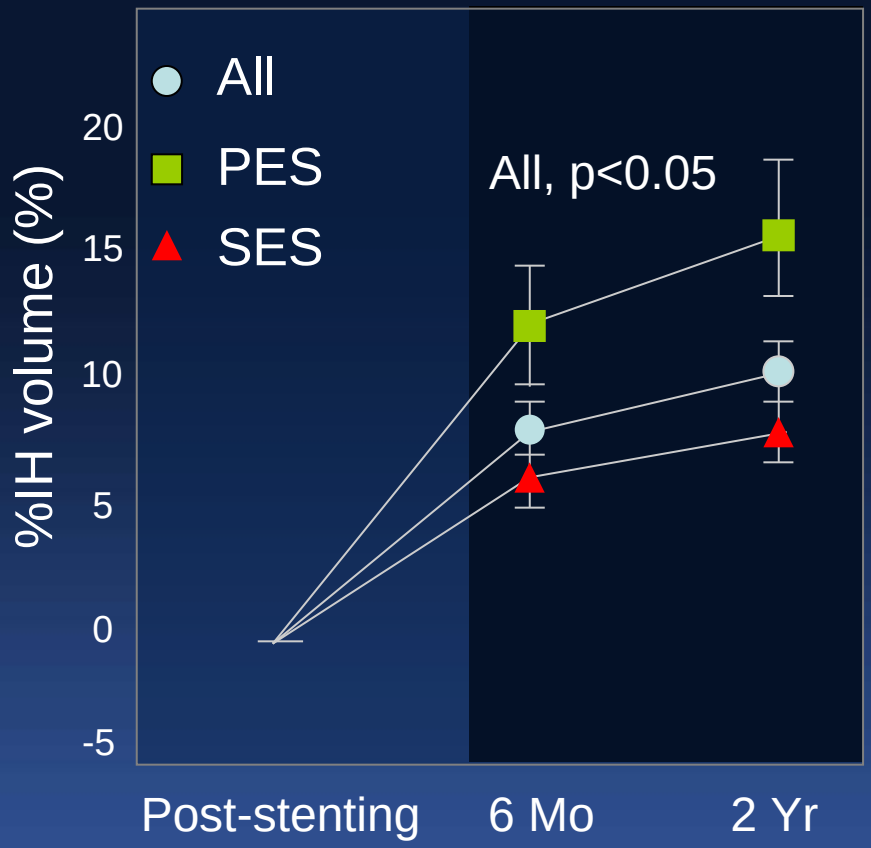
I, Soo-Jin Kang DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation

Cumulative Risk of TLR



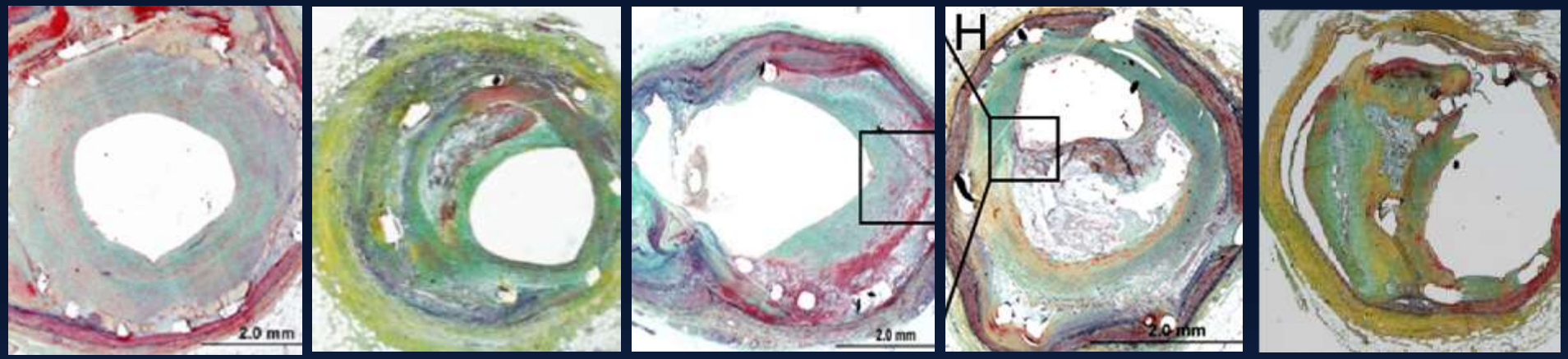
"Late Catch-up"

Serial %IH in DES

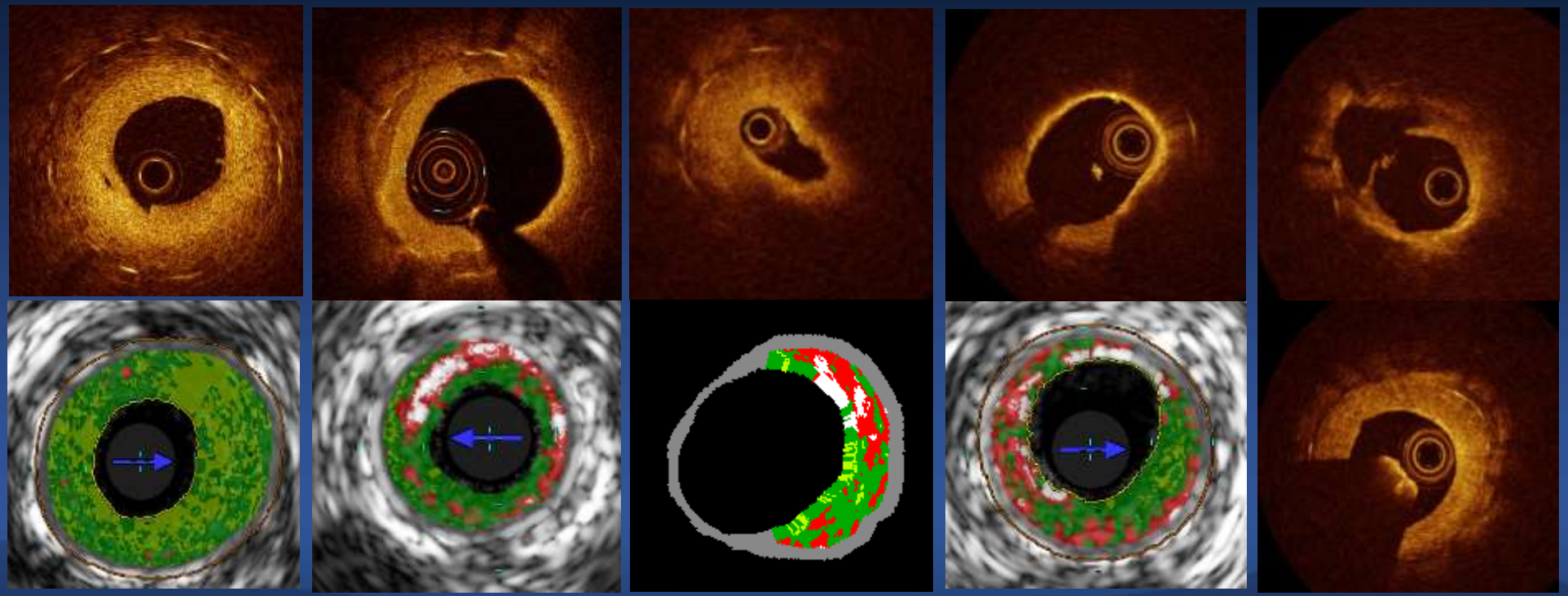


Kang et al. Am J Cardiol 2010;105:1402-8

Early neointima | Fibrocalcific | ThCFA | TCFA | Intimal rupture



Nakazawa et al. JACC Cariovasc Imaging 2009;2:625-8



How Frequent is Neoatherosclerosis the Mechanism of Stent Failure?

Stent failure OCT data from AMC

	DES-ISR[1]	BMS-ISR[2]	VLST[3]	
Lesion	50 DES	51 BMS	6 BMS	27 DES
Median F/U	32 Mo	132 Mo	109 Mo	62 Mo
Lipid or NC	90%	100%	100%	100%
OCT-TCFA	**52%**	**68%**	**100%**	**56%**
OCT-rupture	**58%**	**59%**	**100%**	**63%**
TLR	98%	all	all	all

1. *Kang et al. Circulation 2011;123:2954-63*
2. *Kang et al. JACC Cardiovasc Imaging 2012;5:1267-8*
3. *Kang et al. JACC Cardiovasc Imaging 2013;6:695-703*

Old vs. Newer DES

New anti-proliferative drugs
Biodegradable polymer
Thinner struts
Better strut coverage

→ *Expected to reduce neoatherosclerosis…*

	73 **SES**	85 **PES**	46 **EES**	P vs. SES	P vs. PES
Median F/U	9 months	7 months	7 months		
Uncovered strut, %	18.0 (0-51.4)	18.7 (7.1-44.4)	2.6 (0-7.1)	<0.001	<0.001
Fibrin deposition,%	29.9 (12.1–59.9)	51.1 (36.9–72.9)	8.5 (0-28.2)	0.001	<0.001
Inflammatory score	1.0 (0.3–2.0)	1.0 (0.1–1.4)	0.26 (0-0.6)	<0.001	0.006
Neoatherosclerosis	**25 (35%)**	**15 (19%)**	**12 (29%)**	**0.91**	**0.19**

Otsuka, Virmani et al. Circulation 2014;129:211-23

Predictors of Neoatherosclerosis

MGH OCT Registry

	A-OR	p
PES	24.17	<0.001
SES	2.86	0.07
ZES	7.18	0.013
EES	6.46	0.007
Stent age>4 yrs	10.45	<0.001
Age >65 years	1.84	0.121
Current smoking	7.03	<0.001
Chr renal disease	3.69	0.035
ACE-I / ARB use	0.39	0.028

Yonetu et al. Circ Imaging 2012;5:660-6

Korean OCT registry

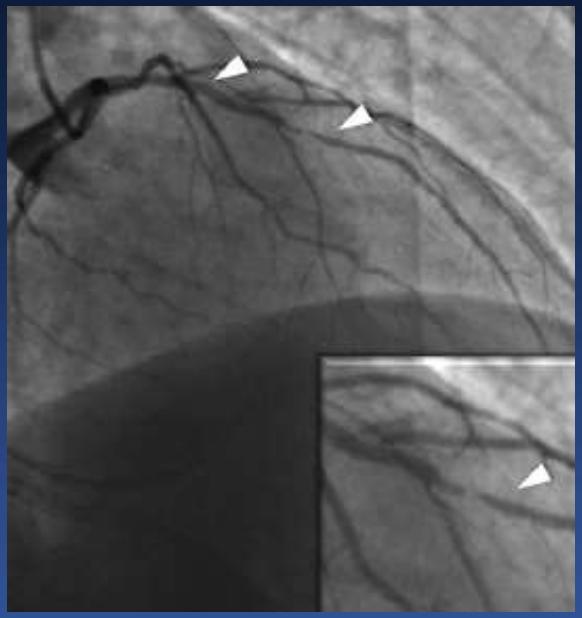
	OR	p
Stent duration	1.7	0.001
LDL >70 mg/dl	2.5	0.038
Chr renal disease	4.1	0.037
Diabetes	1.0	0.99
Newer DES	0.5	0.23
ACE inh/ARB	1.6	0.33
Statin	0.5	0.29

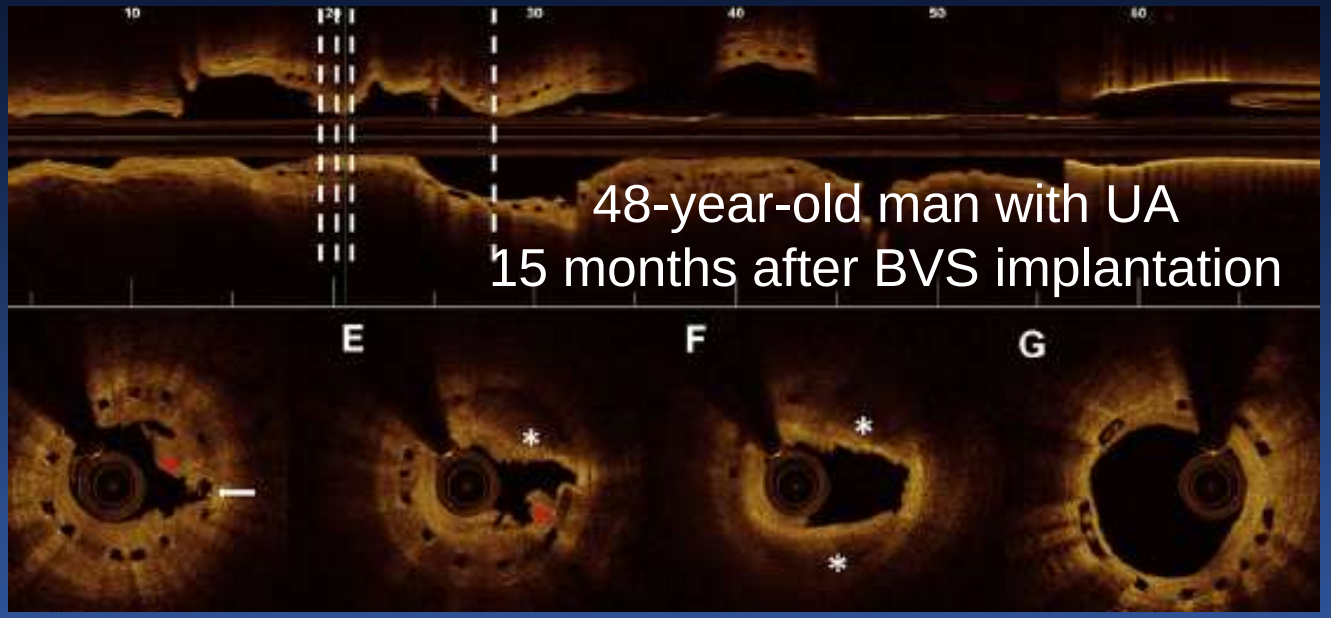
Newer DES is not protective against NA. Endothelial maturation is still insufficient in both old and newer DES

Lee SY et al. Circ Cardiovasc Interv 2015;8:e001878

Neoatherosclerosis as a Cause of Late Restenosis of BVS

- BVS eliminates permanent vessel caging
- Promote late lumen enlargement
- Stabilize vulnerable plaques by uniform neointimal layers



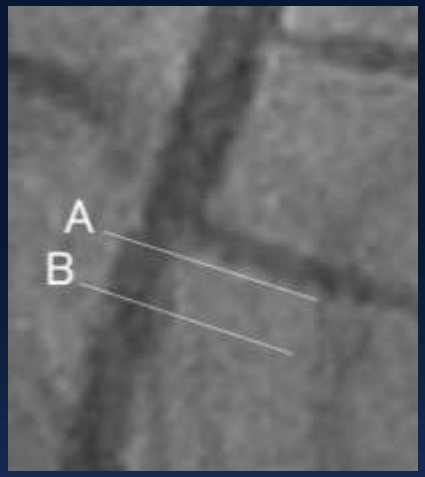


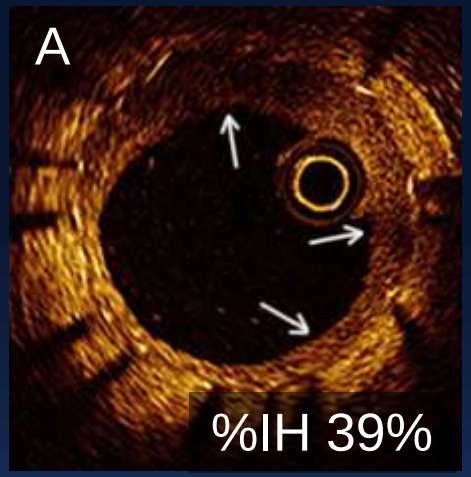
BVS has not eliminated the early- and mid-term presence of polymer and drugs with a pro-inflammatory action

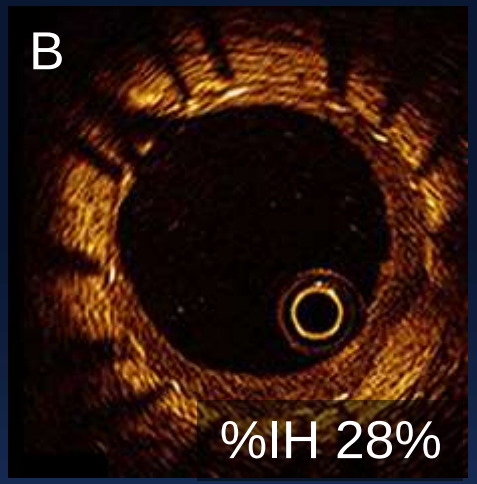
Mangiameli et al. JACC Cardiovasc Interv 2015

Natural History of Low-intensity Neointima After EES Implantation

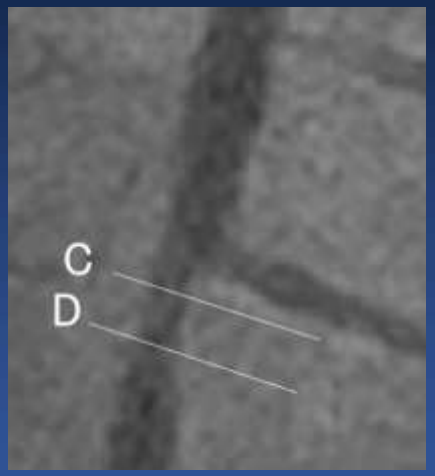
6 months

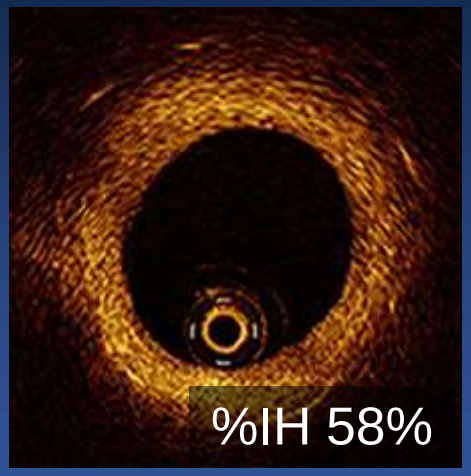


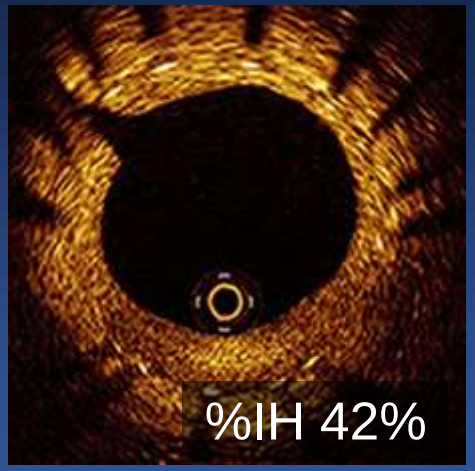




17 months







Low-intensity intima may be a morphometric predictor of late neointimal growth

Shibuya et al. Heart Vessel 2015;30:136-9

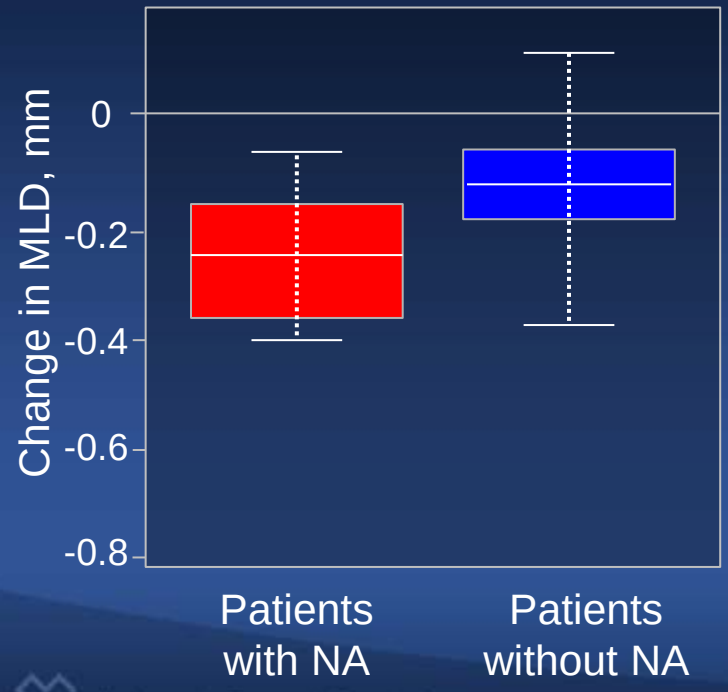
Association Between In-stent NA vs. Native Coronary Atherosclerosis Progression

SIRTAX-LATE OCT study

OCT assessment of DES at 5 years

→ Clinical follow-up at 9 years

Change in MLD in native coronary artery



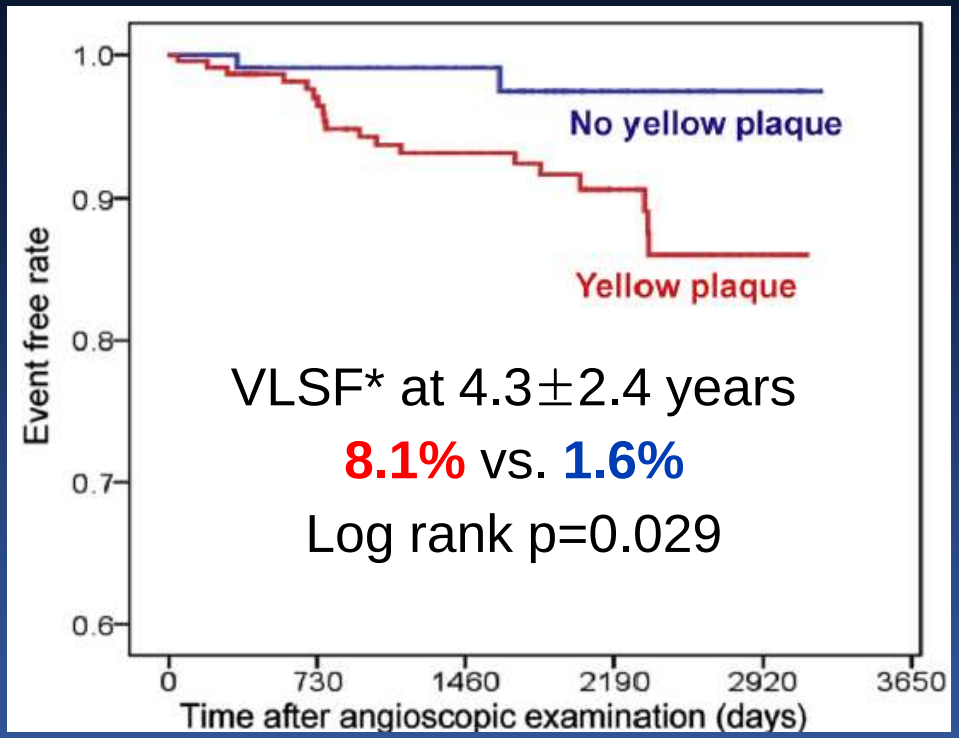
Clinical events over 5 years

	Patients with NA	Patients without NA	OR	p
Non-target vessel revascularization	71.4%	43.2%	3.28	0.06
Non-target lesion revascularization	78.6%	44.6%	4.56	0.03
Any revascullariz	78.6%	50.0%	3.67	0.06

Taniwaki et al. Eur Heart J 2015;36:2167–76

In-Stent Yellow Plaque as a Predictor of Future Event of Very Late Stent Failure

DESNOTE Study 360 consecutive pts who received angioscopy at 1 year after DES implantation were clinically followed up



Independent predictors

- Presence of yellow plaque (HR: 5.38; p=0.02)
- Absence of statin therapy (HR: 3.25; p=0.02).

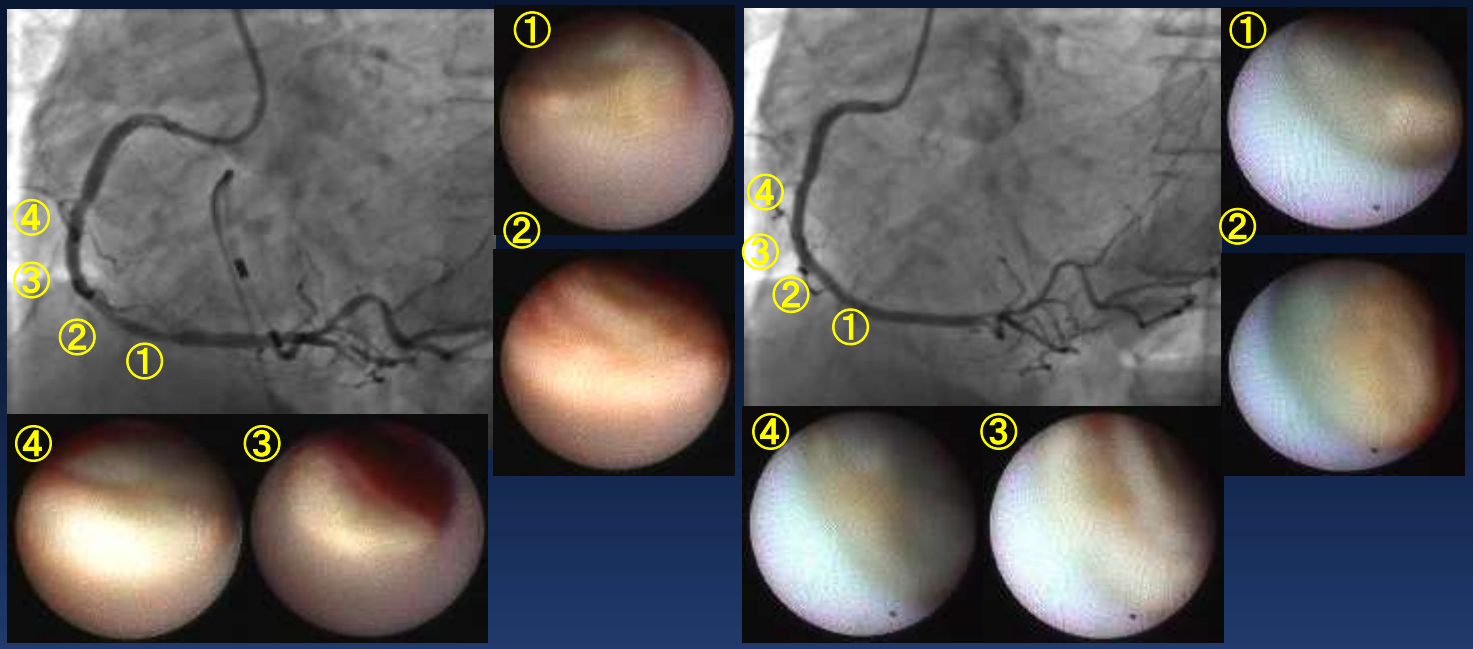
*VLSF defined as cardiac death, ACS, and need for TLR

Ueda et al. JACC Intv 2015;8:814–21

Regression of Yellow Plaque with Statin

Before

80-week atorvastatin (10mg/d)



Ueda TCT 2013

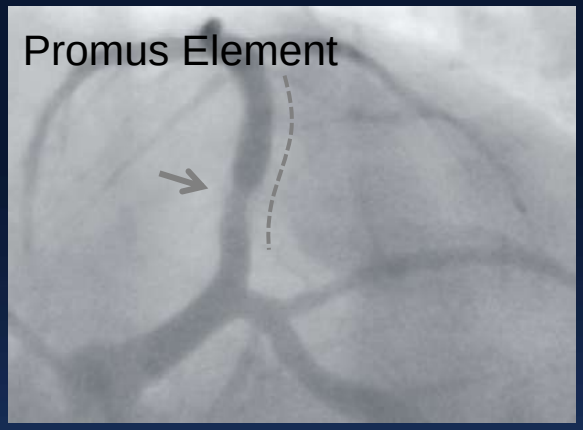
Independent predictors of serial follow-up OCT change from homogeneous to non-homogeneous neointima

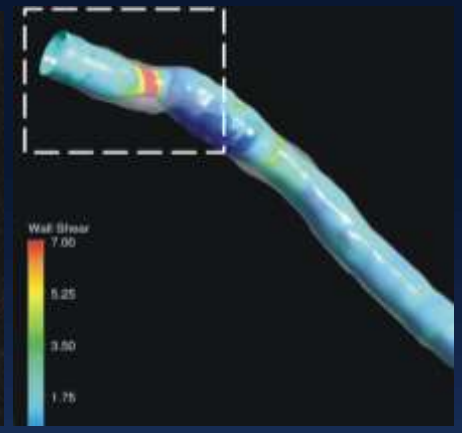
- Age *(OR=1.11, p=0.08)*
- Optimal LDL control *(OR=0.05, p=0.008)*

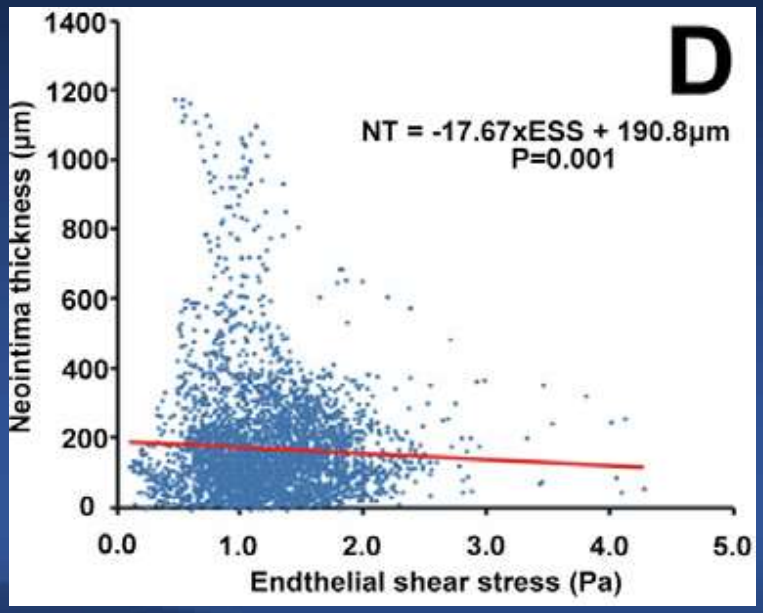
Jang et al. Atherosclerosis 2015;242:553-9

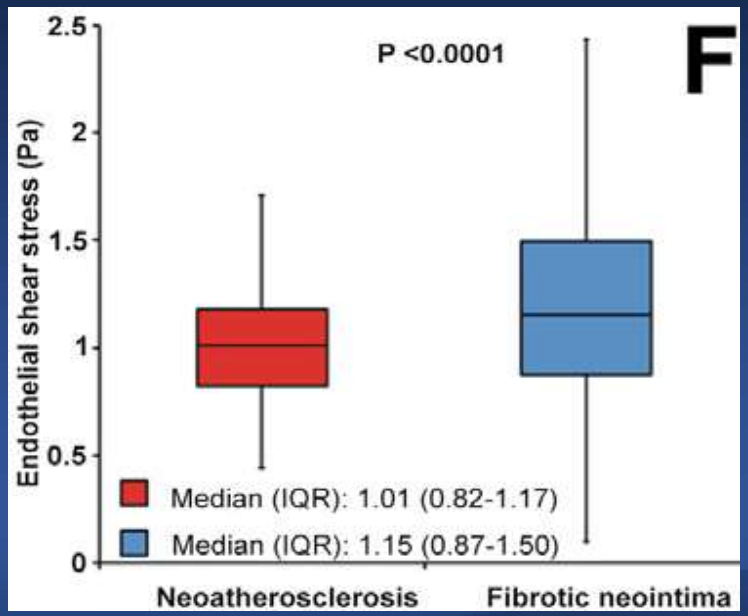
Local Endothelial Wall Shear Stress

An Innocent Bystander or a Critical Factor Regulating Neoatherosclerotic Evolution?





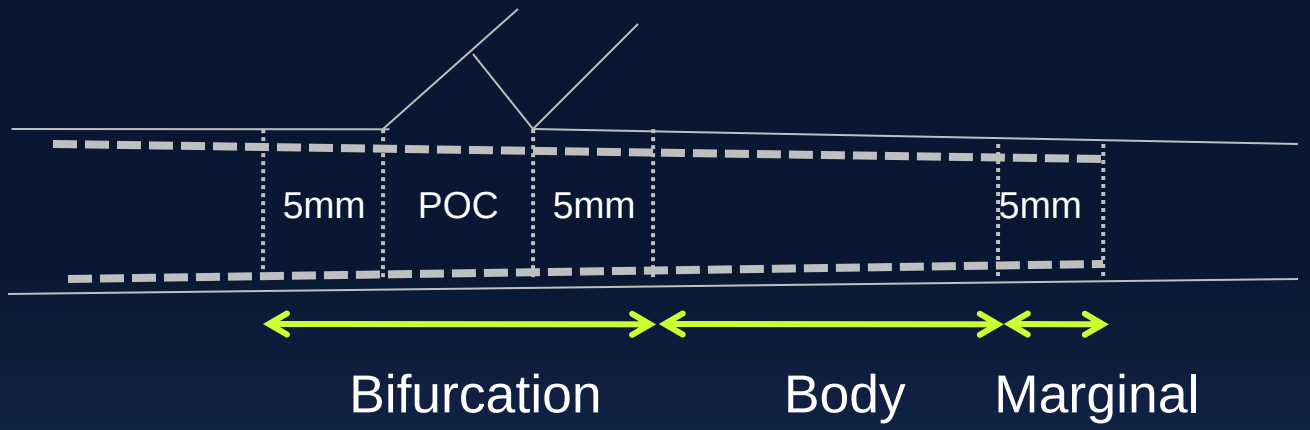


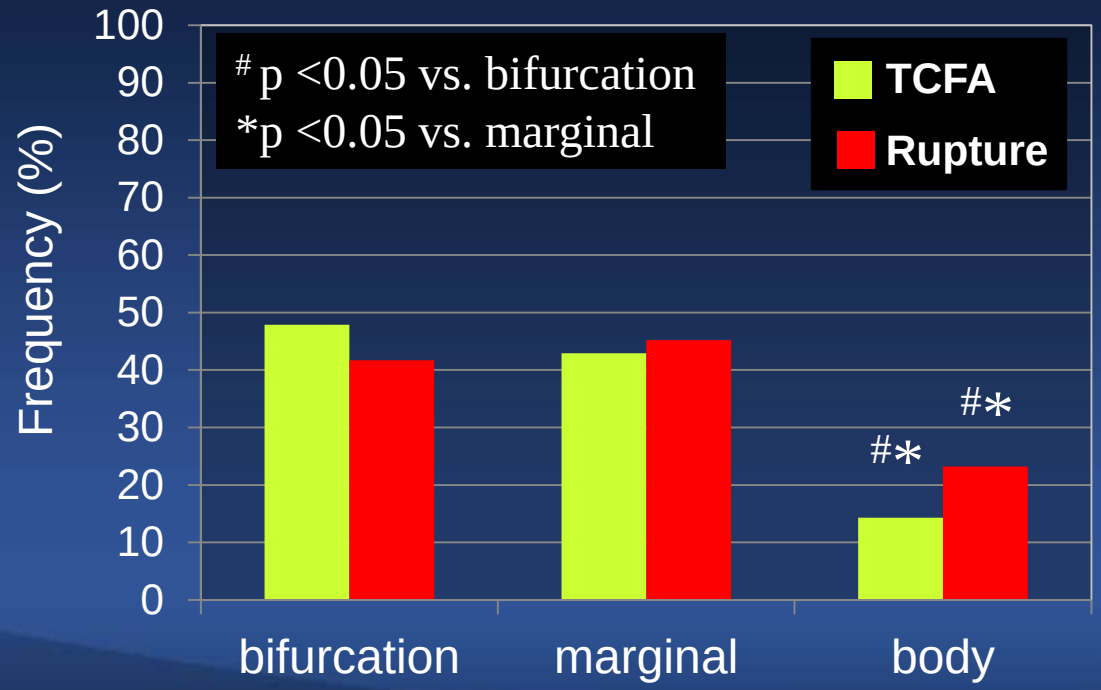


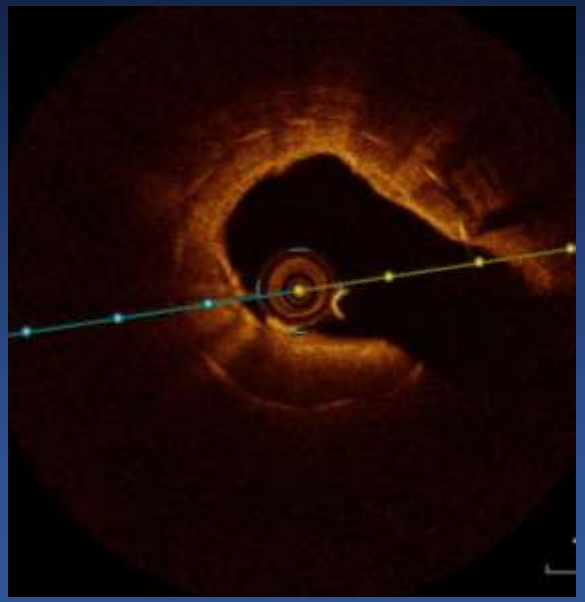
Michail et al. JACC Cardiovasc Interv 2015;8:e149-50

Site-specific Neoatherosclerosis

Sites of in-stent MLA in 146 ISR lesions (39 BMS, 107 DES)

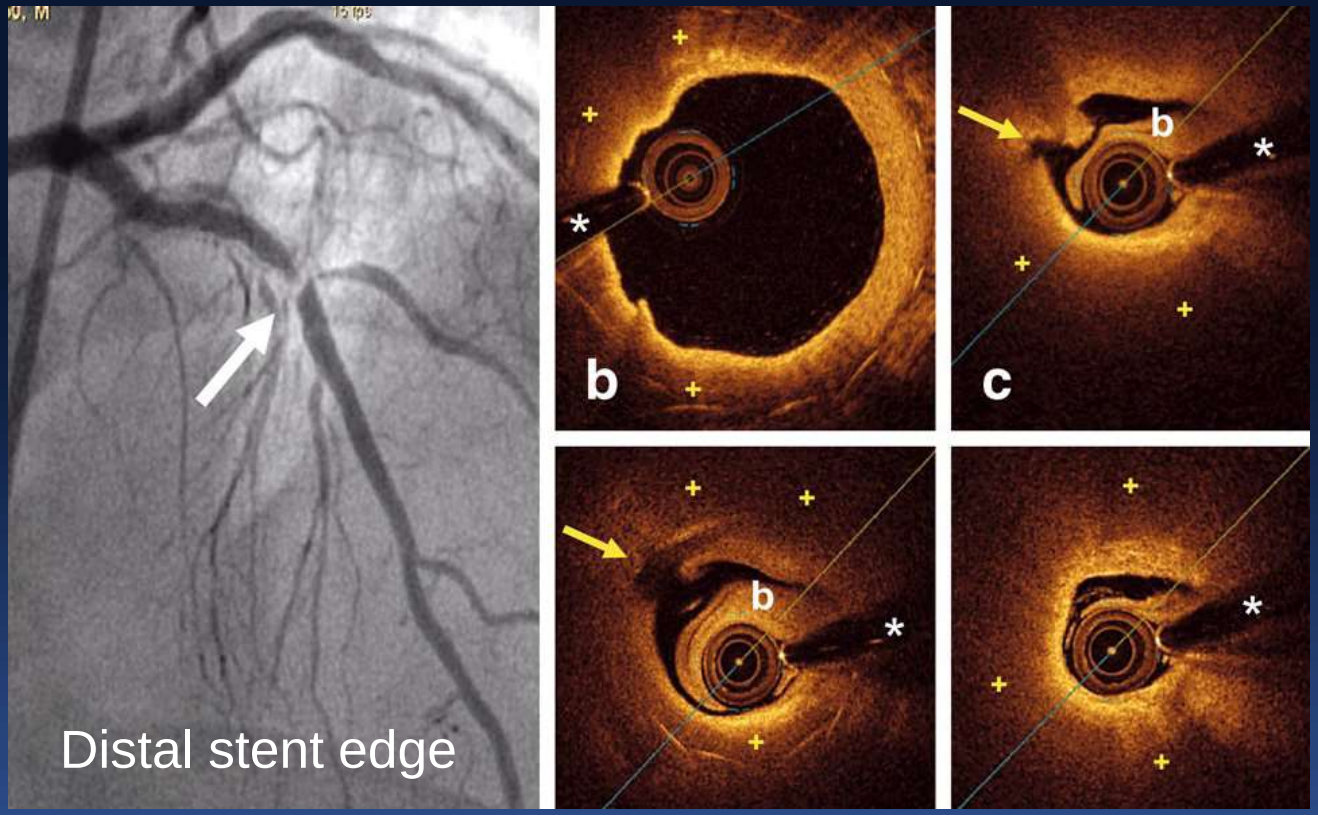






Kang et al. AsiaIntervention 2015 in press

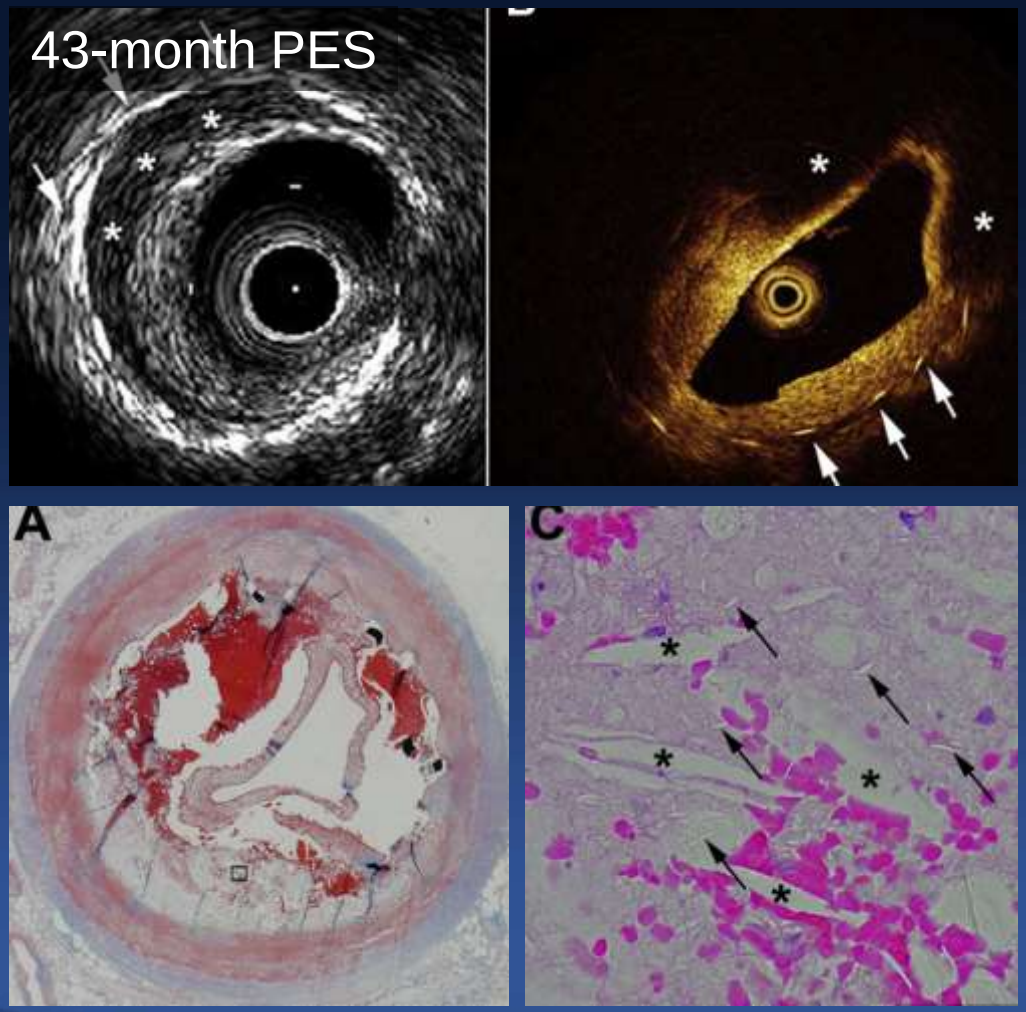
Neoatherosclerosis Causing Edge ISR



Alfonso et al. Neth Heart J 2015;23:287-8

Neointimal Hemorrhage

Possible Role for Development of Neoatherosclerosis

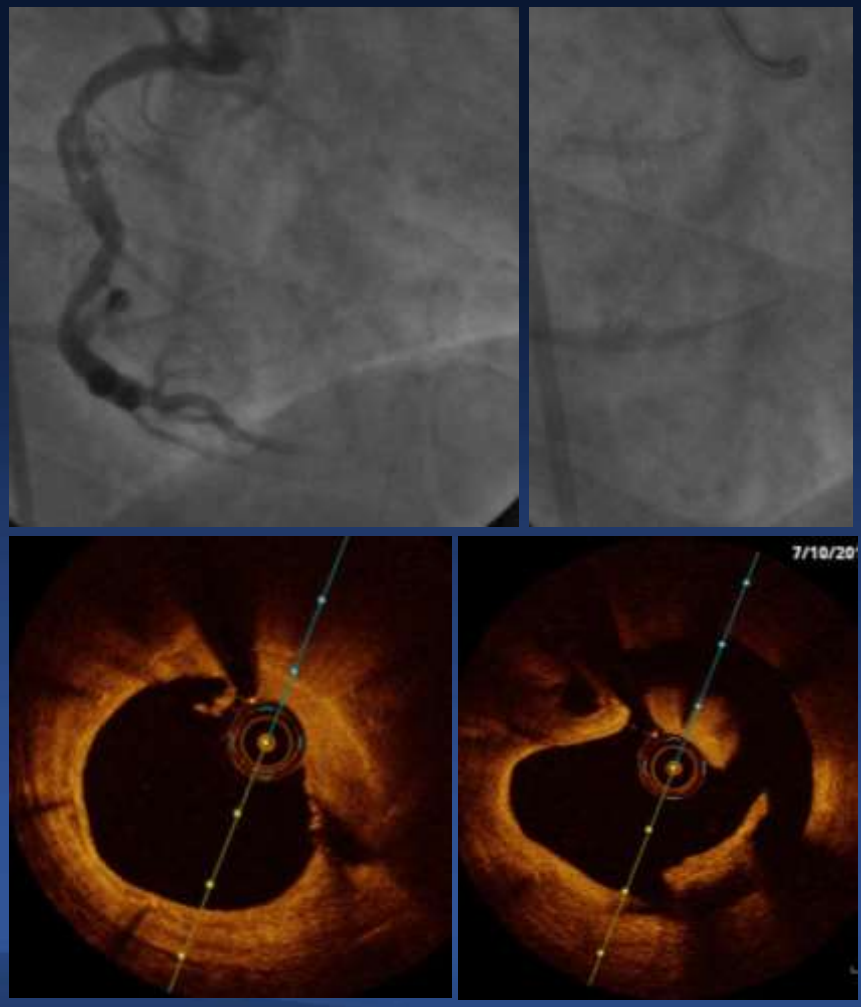


- massive hemorrhage
- foam cell and RBC infiltration adjacent to the tiny cholesterol clefts
- RBC membrane as the source of chol-esters

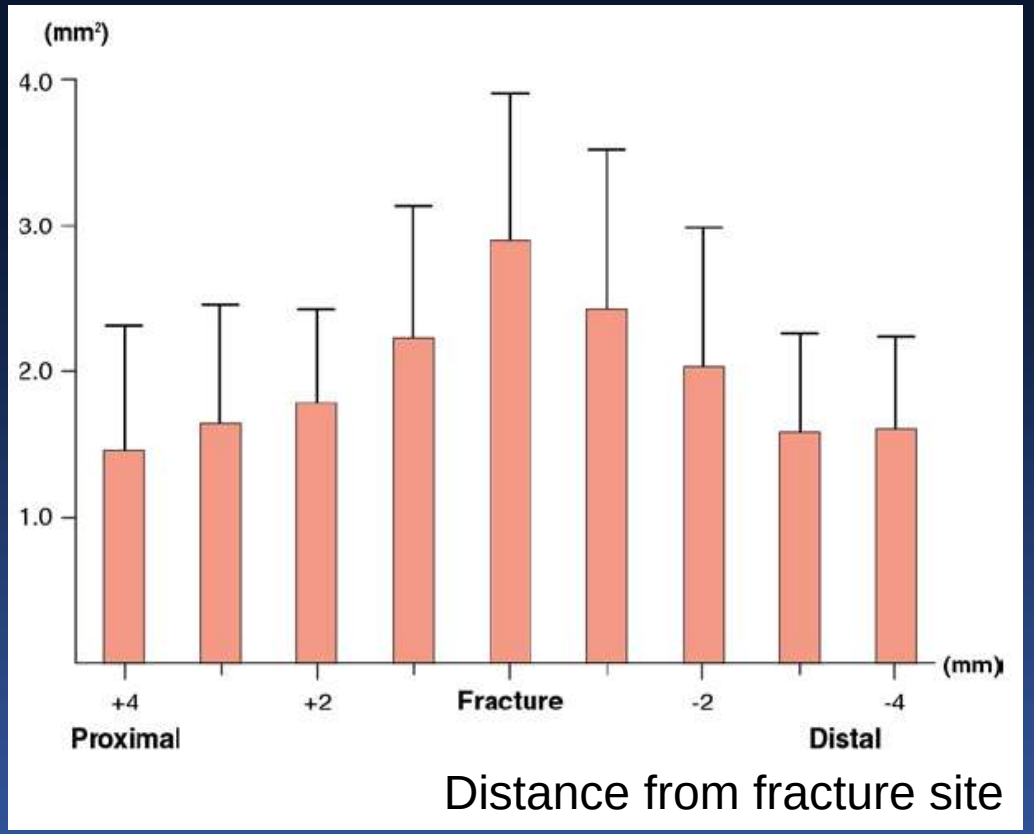
Hao et al. JACC Cardiovasc Interv 2014;7:1196-7

Mechanical Injury from Stent Fracture

- 7YA SES at RCA
- ISR with stent fracture



Increased intimal hyperplasia area at the fracture site



Distance from fracture site

Kashiwagi et al. JACC Cardiovasc Img 2012;5:232-3

Predictor of Peri-procedural MI

Treatment of ISR in 152 patients
Median F/U 52.8 months

Thin-cap thickness <60um

For the prediction of peri-procedural MI *(CK-MB>15ng/ml)*
Sensitivity 91%, Specificity 58%

	TCFA			Intimal rupture		
	Yes (N=68)	No (N=84)	P	Yes (N=71)	No (N=81)	P
Pre-PCI CK-MB	1.1 (0.5–2.3)	0.8 (0.5–1.5)	0.110	1.1 (0.4–2.2)	0.9 (0.6–1.7)	0.659
Post-PCI CK-MB	2.0 (1.0–5.0)	1.4 (0.8–2.2)	0.012	2.0 (0.9–4.1)	1.3 (0.9–2.4)	0.017
CK-MB>15ng/ml	9 (13%)	2 (2%)	0.010	9 (13%)	2 (3%)	0.015
MACE at 2 years	5 (7%)	5 (6%)	0.729	5 (7%)	5 (6%)	0.829

Kang et al. JACC Cardiovasc Imaging 2015 in press

Summary

- Neoatherosclerosis is a common substrate of late restenosis and has a prognostic implication
- Either newer DES or BVS failed to fully protect the vessels from neoatherosclerosis
- Abnormal ESS, intimal hemorrhage, stent fracture or deformation may contribute to lesion progression
- Vulnerable neointima may increase the risk of PMI