

Update - Clinical Implication of Neoatherosclerosis

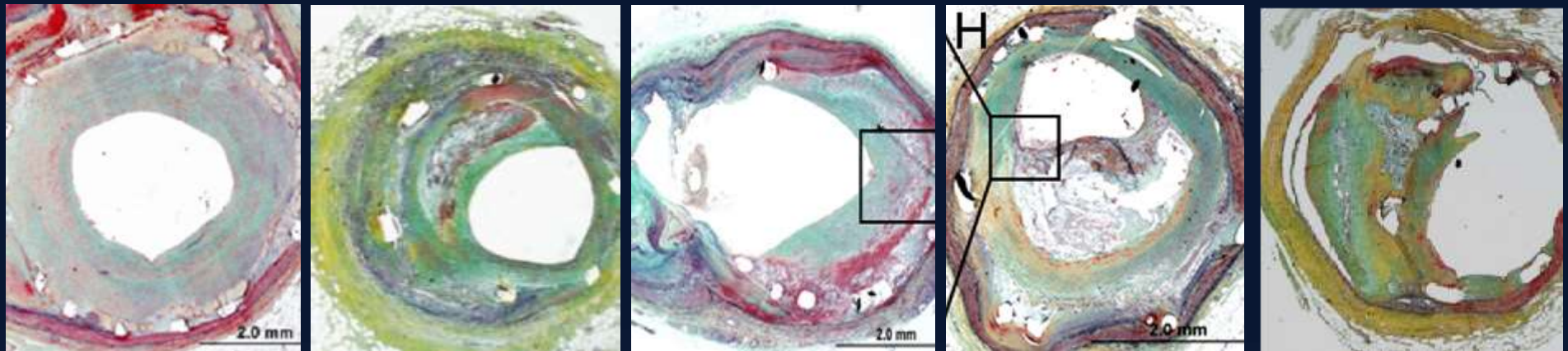
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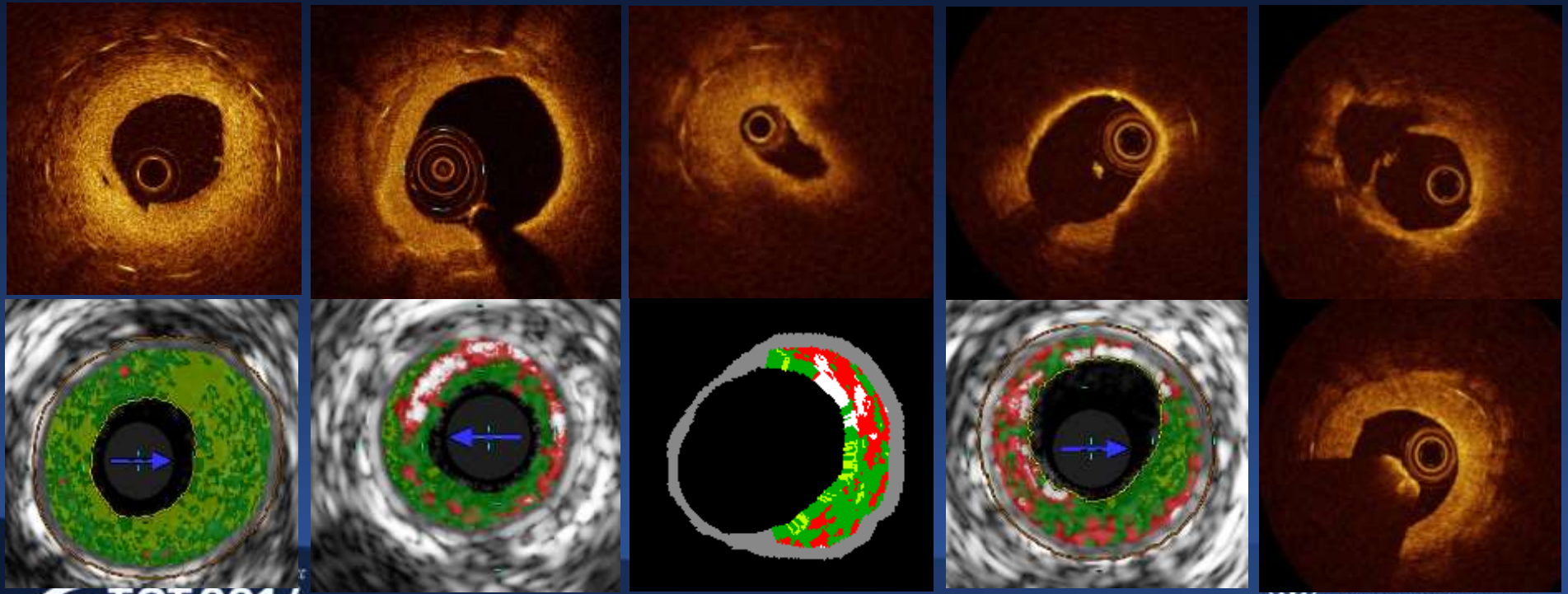
Disclosure Statement of Financial Interest

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

Early neointima Fibrocalcific ThCFA TCFA Intimal rupture



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



Late ISR

63-year old male
Stable angina

VLST

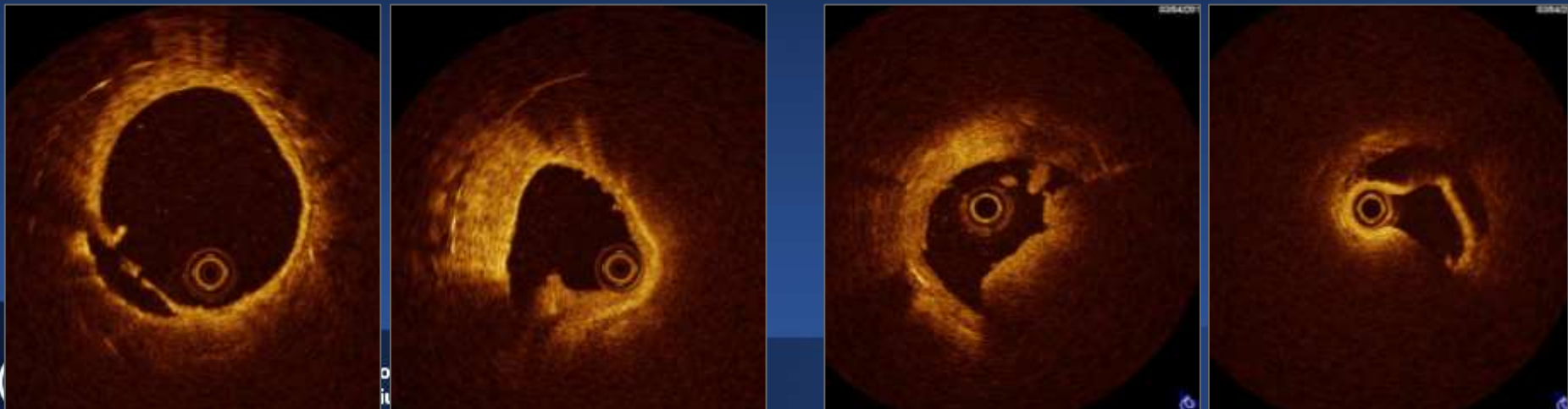
60-year old male
AMI with VLST

IMAGES IN CARDIOLOGY

Neoatherosclerosis:

The Missing Link Between Very Late Stent Thrombosis and Very Late In-Stent Restenosis

Fernando Alfonso, MD, Federico Fernandez-Viña, MD, Miguel Medina, MD, Rosana Hernandez, MD
Madrid, Spain



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

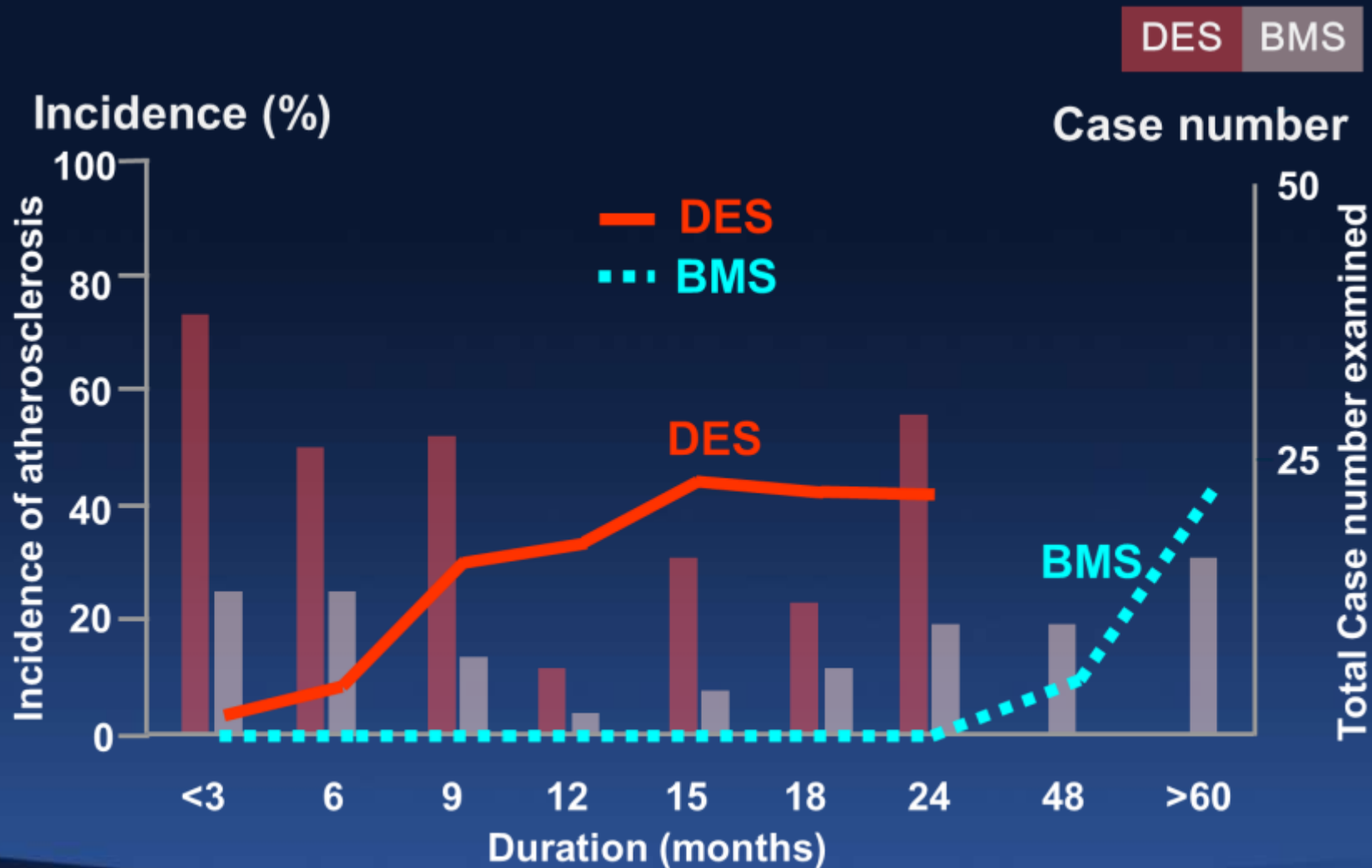
Update of Neoatherosclerosis

Frequency

- Stent duration
- Stent type (DES vs. BMS)
- Population (stent failure, routine f/u, SCD...)
- Definition of neoatherosclerosis

Incidence and Time Course

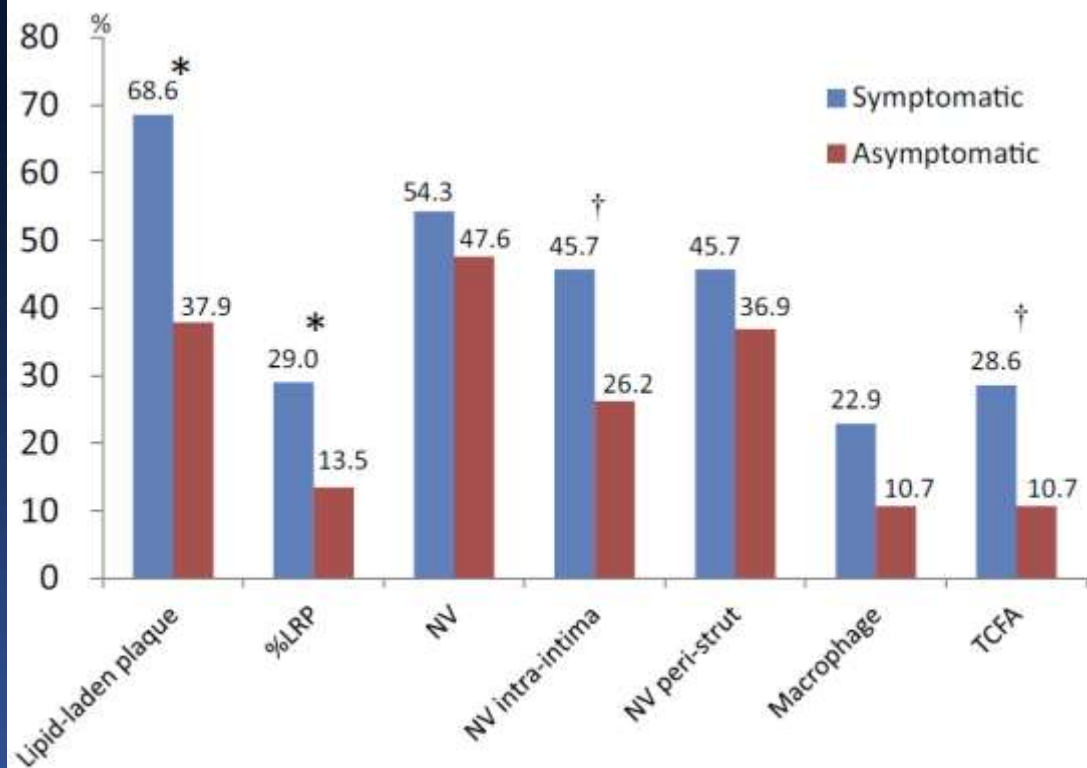
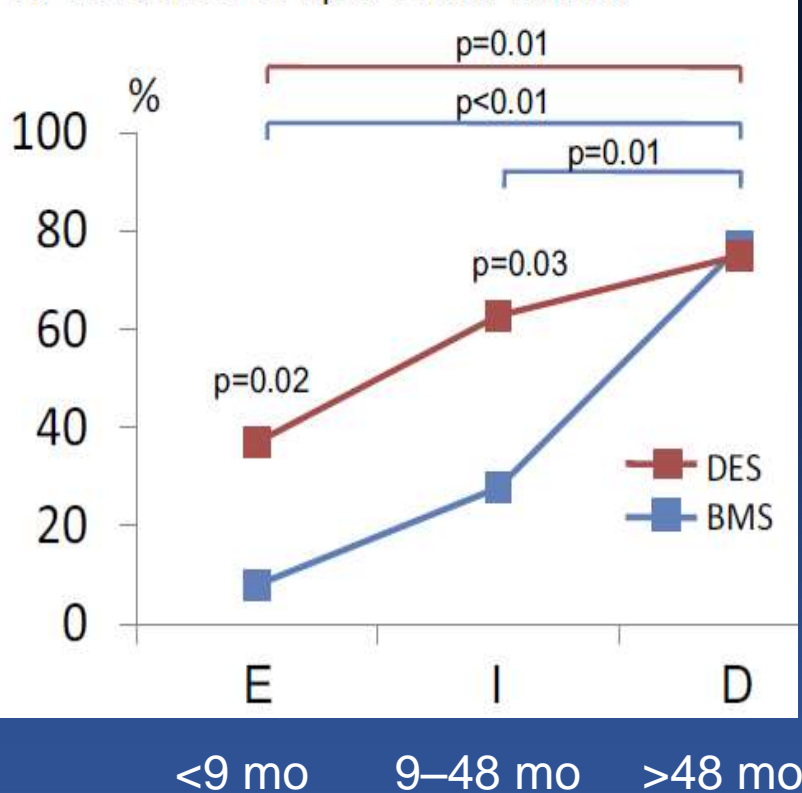
Autopsy data from CVpath



Incidence and Time Course

In Vivo data from MGH OCT registry

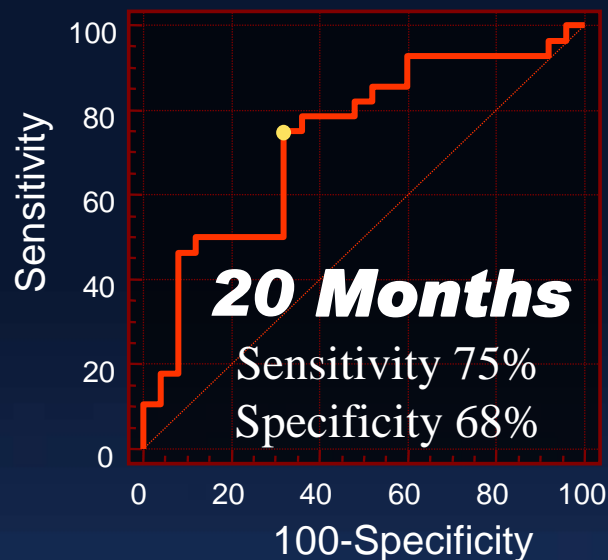
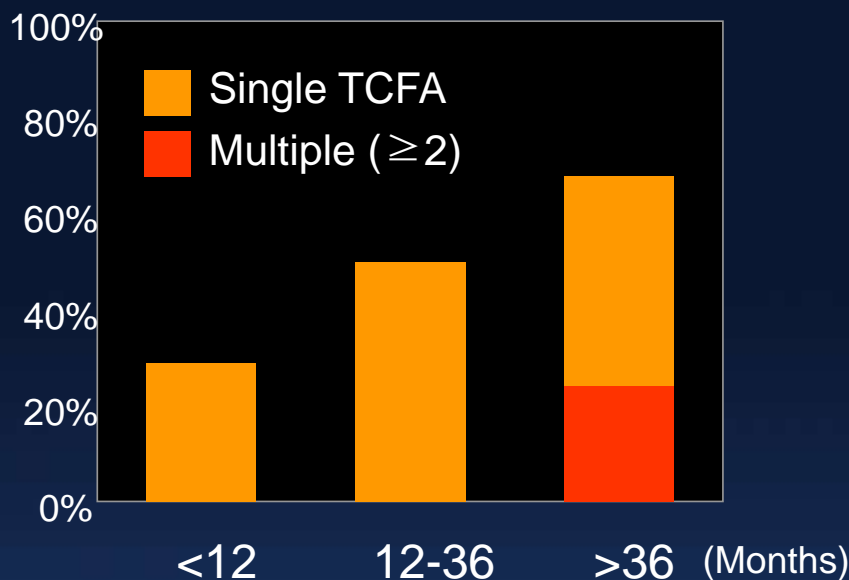
A. Incidence of lipid-laden intima



Yonetsu et al. Am J Cardiol 2012;110:933-9

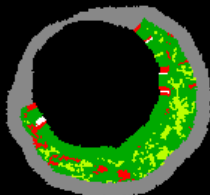
DES Duration >20 Months

Best Predict TCFA-Containing Neointima

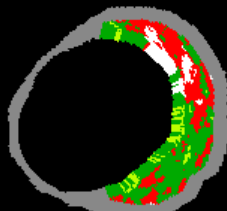


Kang et al. Circulation 2011;123:2954-63

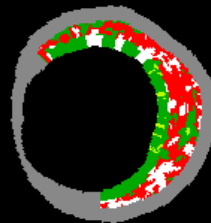
6-mo Taxus



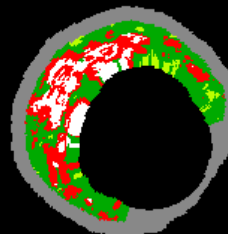
9-mo Taxus



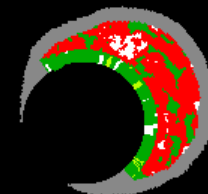
22-mo Taxus



48-mo BMS



57-mo BMS



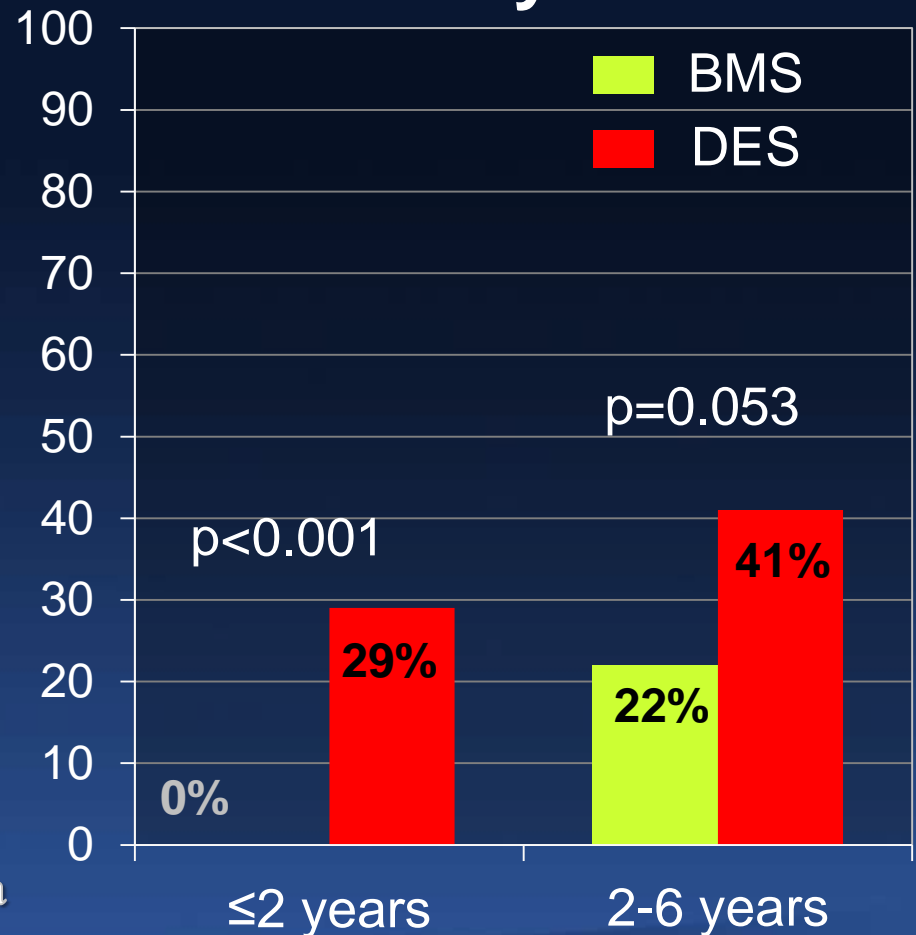
Frequency of Neoatherosclerosis

Autopsy Data from CVpath

	Nakazawa (CVPath) ¹	
Lesion	197 BMS	209 DES
F/U duration	72 Mo	14 Mo
Stent failure	ISR 27% ST 4%	ISR 6% ST 20%
Neoatherosclerosis*	16%	31%

* foamy macrophage infiltration within intima

Stratified by Duration



Pathology of EES vs. SES vs. PES

	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

Old vs. Newer Generation DES-ISR

Propensity matching groups

	Old DES (n=51)	Newer DES (n=35)	p
Age	61.80±10.82	61.03±8.93	0.727
Sex	41 (80.4%)	26 (74.3%)	0.502
Stent duration, days	693±447	546±339	0.087
DM	21 (41.2%)	13 (37.1%)	0.707
HTN	28 (54.9%)	25 (71.4%)	0.122
Dyslipidemia	42 (82.4%)	30 (85.7%)	0.678
ACS	10 (29.4%)	3 (20.0%)	0.130
DES types	SES 31%, PES 69%	ZES 11%, ZES-R 14%, EES 60%, Nobori 6%, Cilotax 8%	

AMC preliminary

Old vs. Newer Generation DES-ISR

Propensity matching groups

	Old DES (n=51)	Newer DES (n=35)	p
Stent duration, days	693±447	546±339	0.087
Lipidic neointima	47 (92.2%)	30 (85.7%)	0.338
Calcific neointima	5 (9.8%)	2 (5.7%)	0.847
In-stent TCFA	18 (35.3%)	4 (11.4%)	0.013
Intimal rupture	23 (45.1%)	8 (22.9%)	0.035
Intimal rupture at MLA	17 (33.3%)	5 (14.3%)	0.047

AMC preliminary

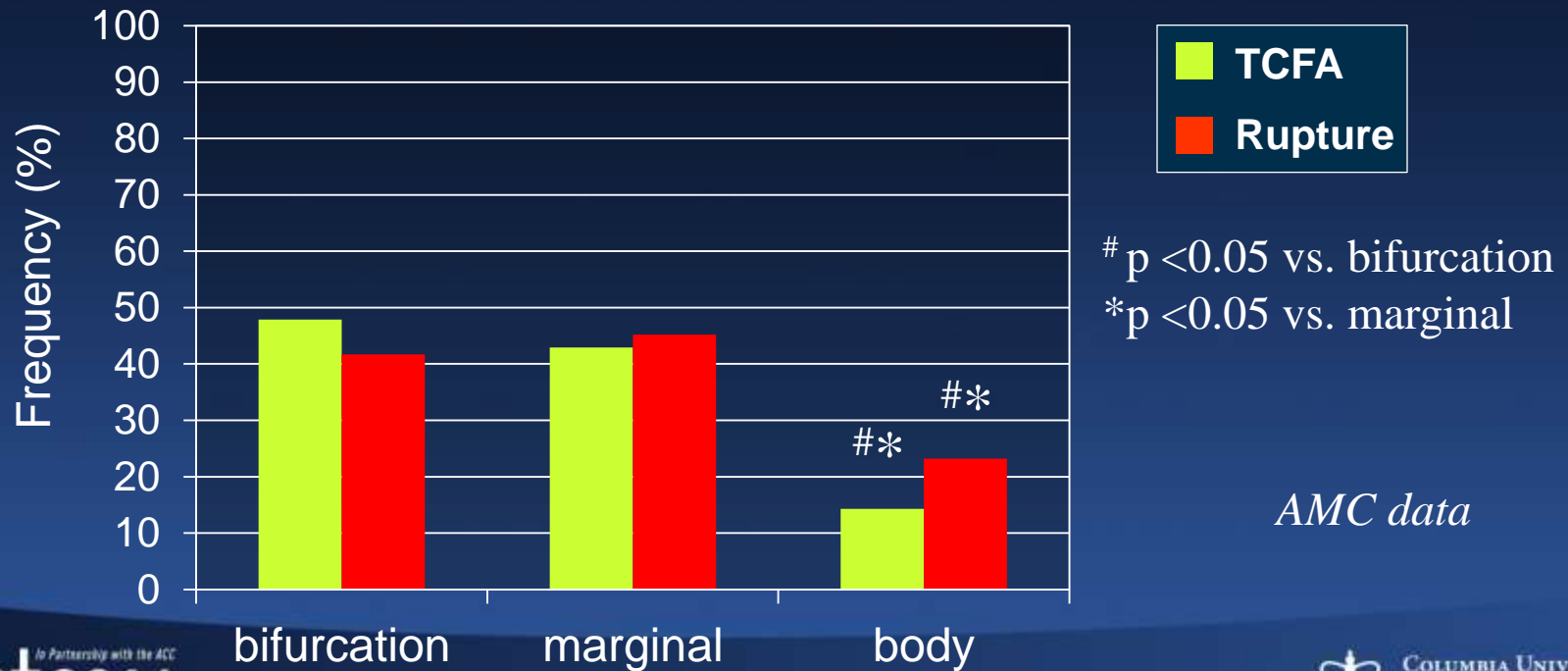
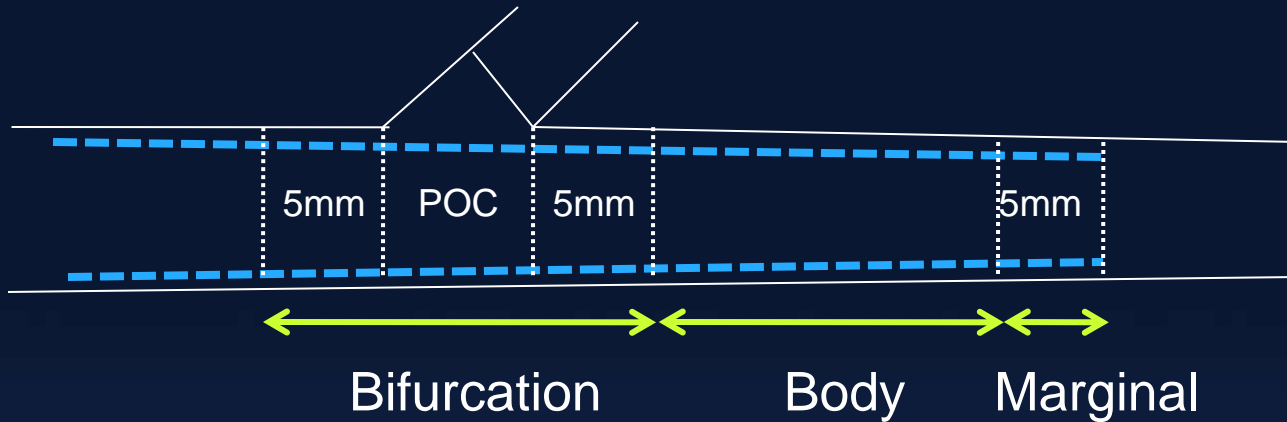
Predictors for Neoatherosclerosis

Retrospective Data from MGH OCT Registry

Multivariable Analysis			
	Adjusted OR	95% CI	p
SES	3.86	1.44 – 10.38	0.007
PES	24.17	6.02 – 97.02	<0.001
ZES	7.18	1.51 – 34.21	0.013
EES	6.46	1.65 – 25.34	0.007
Stent age >48 months	10.45	3.71 – 29.41	<0.001
Age >65 years	1.84	0.85 – 3.97	0.121
Current smoking	7.03	2.46 – 20.04	<0.001
Chronic renal disease	3.69	1.10 – 12.35	0.035
ACE-I / ARB use	0.39	0.17 – 0.91	0.028

Site-specific Neointimal Hyperplasia

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



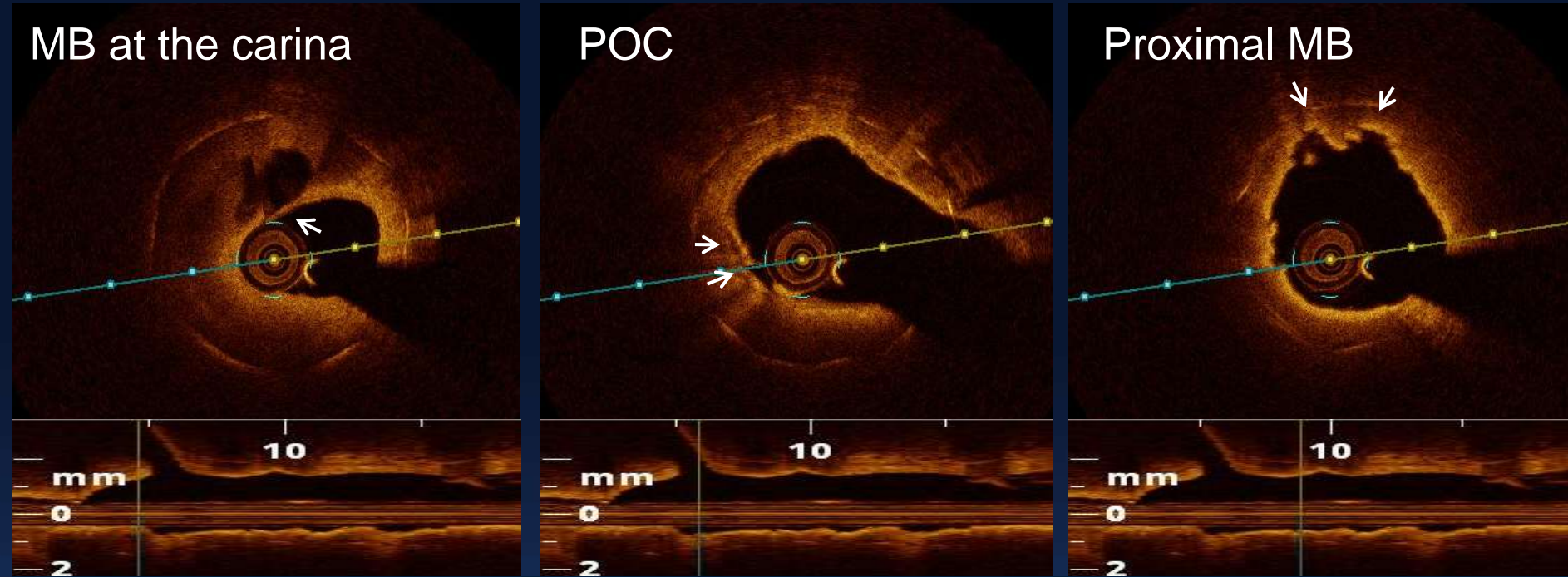
AMC data

ISR at bifurcation

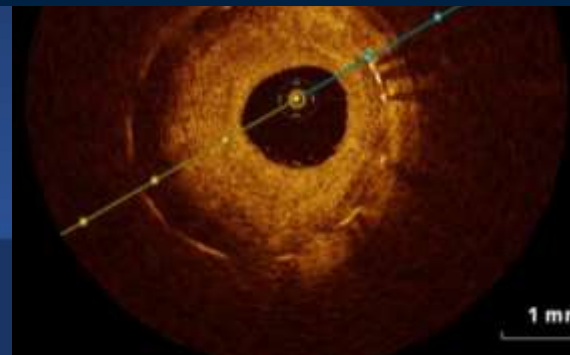
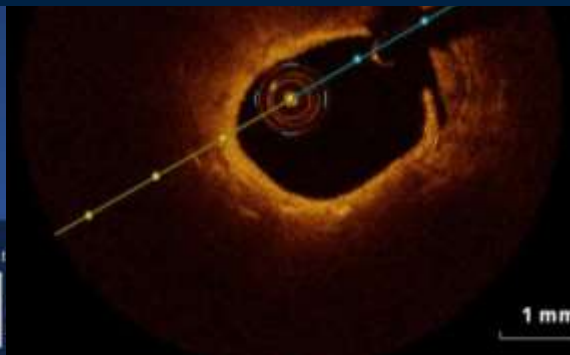
MB at the carina

POC

Proximal MB

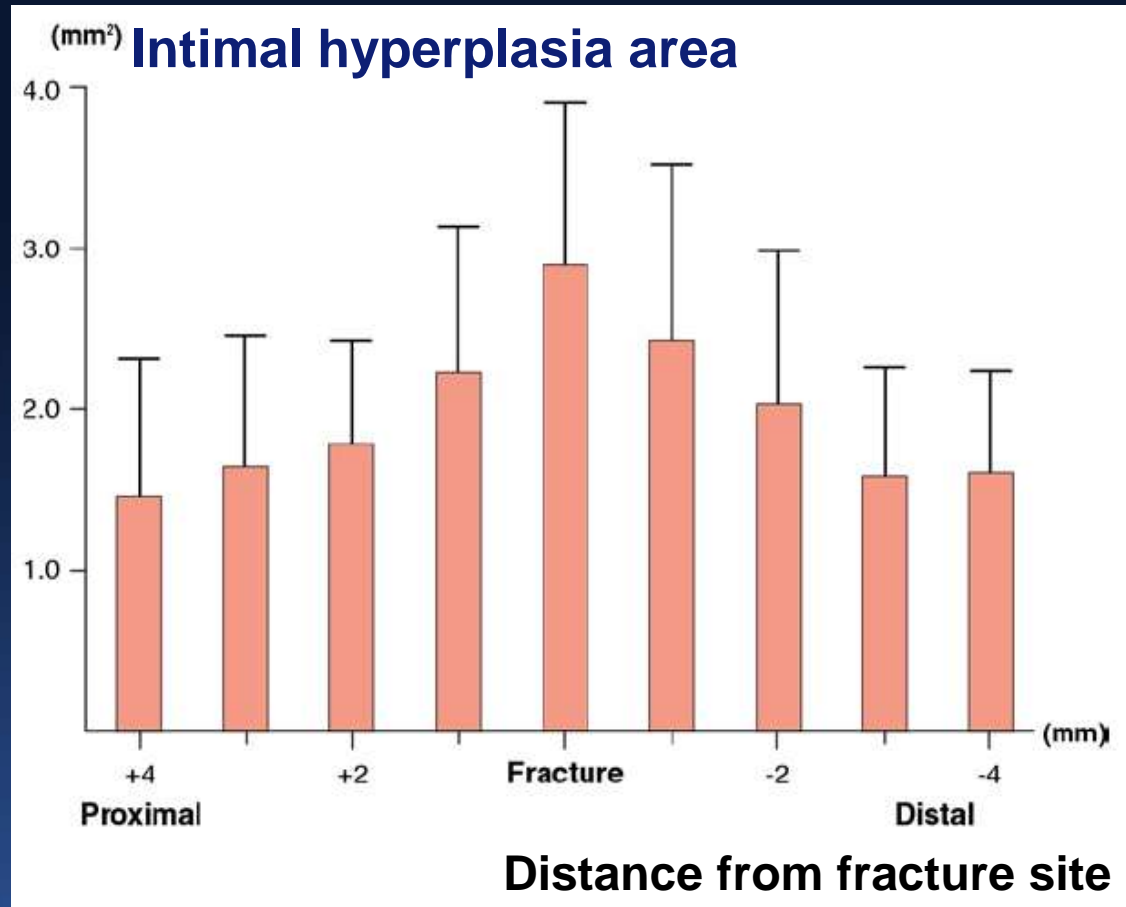
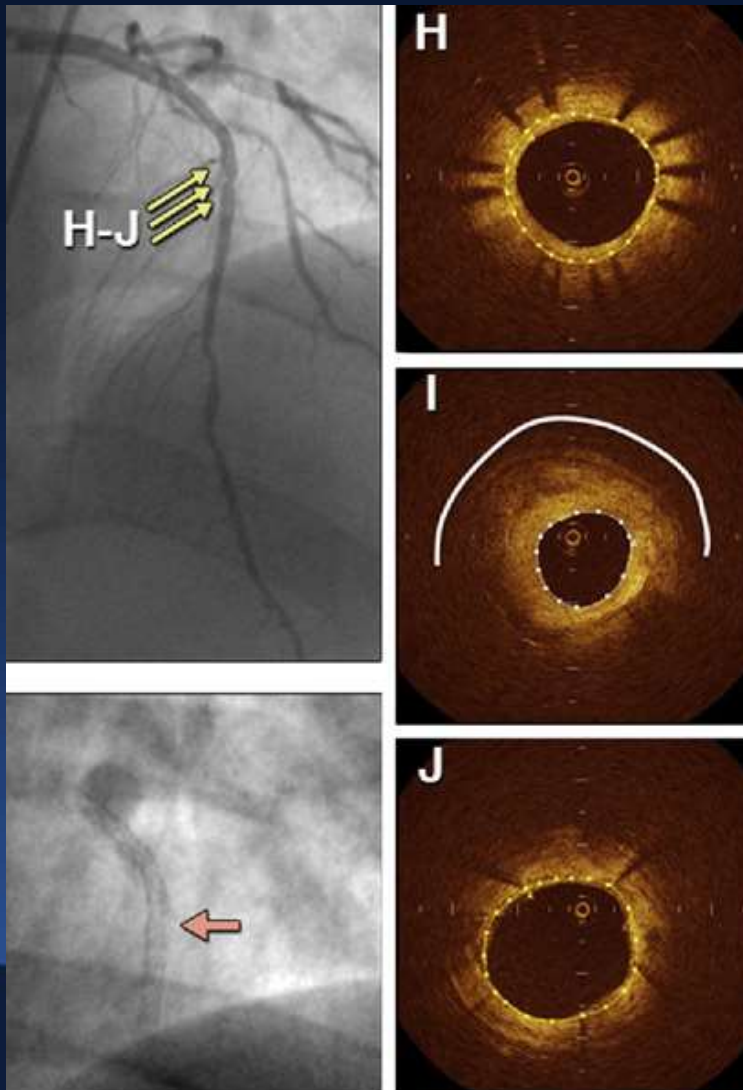


Neoatherosclerosis is common when ISR is located at bifurcation, stent margin and fracture site



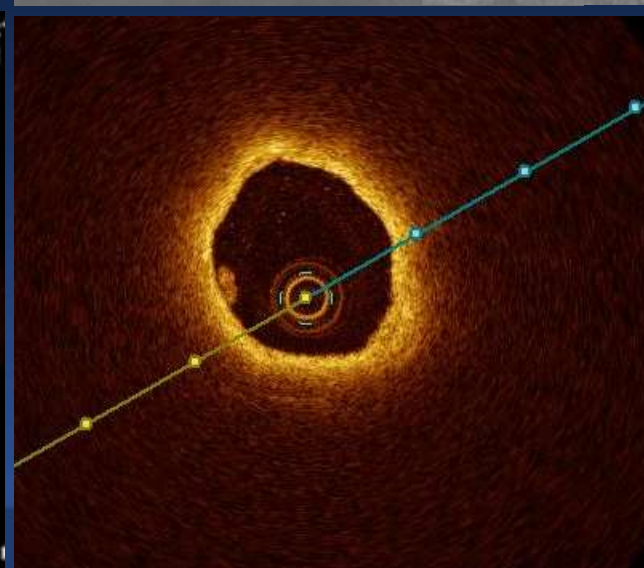
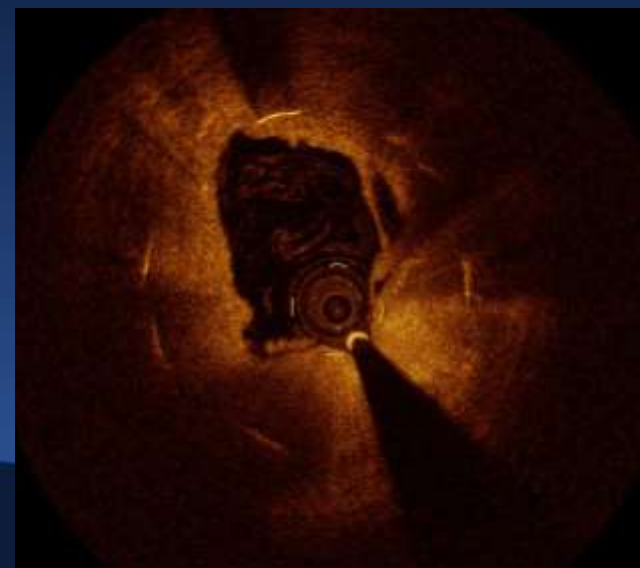
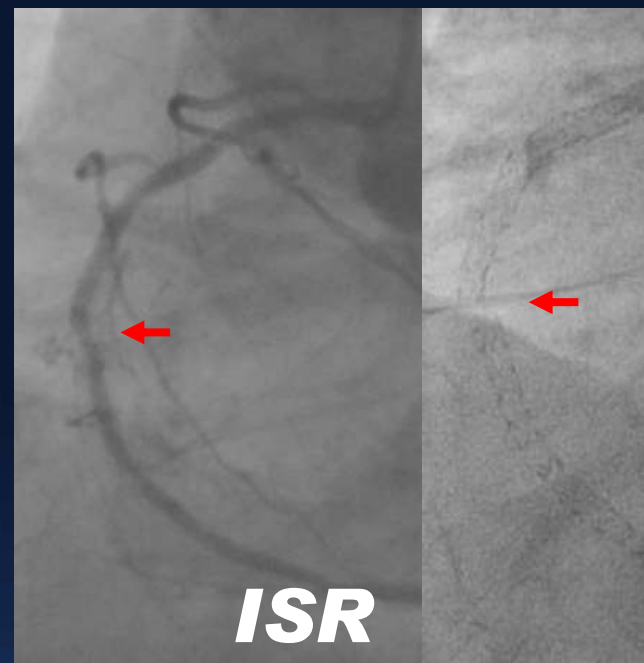
Effect of Stent Fracture

Increased intimal hyperplasia at the fracture site



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

DES Failure Associated with Fracture



Predictor of Peri-procedural MI

152 Patients with ISR, Median F/U 52.8 months

Treatment of ISR	
Balloon, N (%)	9 (6%)
Cutting, N (%)	24 (16%)
DEB, N (%)	9 (6%)
DES, N (%)	94 (62%)
Cutting+DEB, N (%)	16 (11%)

Thin-cap thickness <60um

To predict 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

Neoatherosclerosis (NA) Predicts CK-MB elevation after PCI for ISR

	CK-MB elevation		P value
	Yes (N=20)	No (N=105)	
%IH, %	44.7 (33.0 – 60.3)	33.1 (25.3 – 46.1)	0.020
Max length of NA, mm	8.8 (1.5 – 10.4)	0 (0-1.0)	<0.001
NA neointima, %	51.1 (8.1 – 74.2)	0 (0-8.0)	<0.001
Cap thickness, μ m	60.0 (50.0 – 60.0)	240 (170 – 430)	<0.001
TCFA, %	11 (55%)	2 (2%)	<0.001

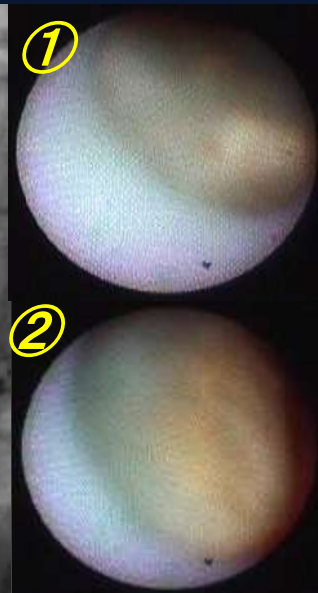
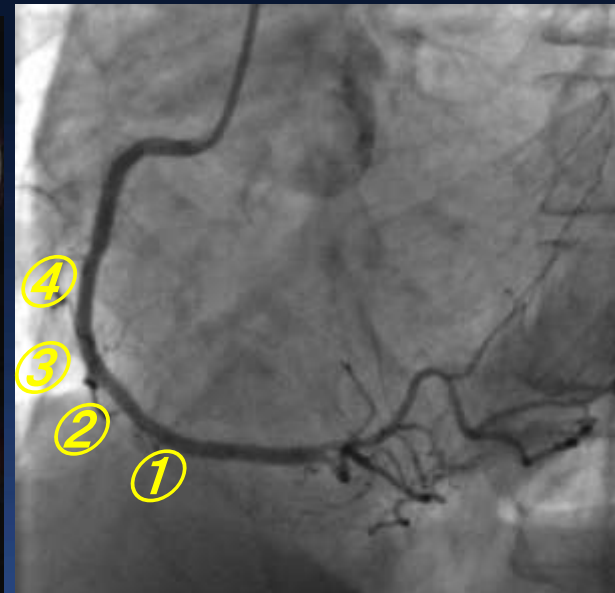
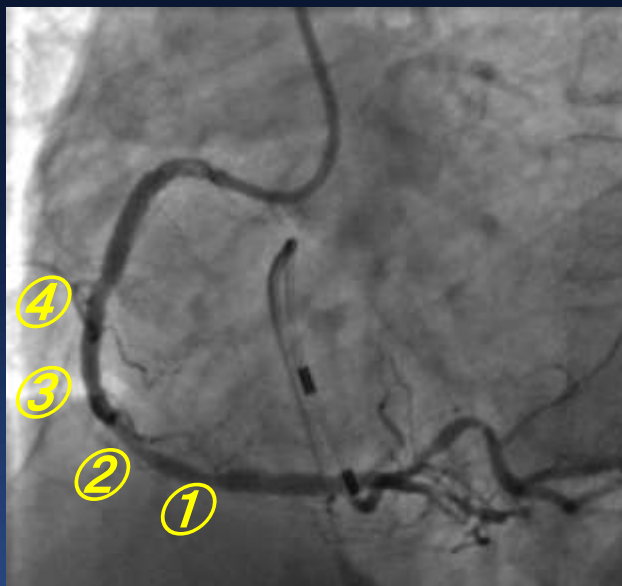
Predictors of post-PCI CK-MB elevation

- Maximal length of NA (OR=1.46, 95% CI=1.09-1.96)
- TCFA at MLA (OR=14.32, 95% CI=1.11-183.6)

Regression of Yellow Plaque with Statin Therapy

Before

After 80 weeks
Atorvastatin (10mg/day)



Ueda TCT 2013

Summary

- Intravascular imaging is useful for assessing neointimal characteristics
- Neoatherosclerosis is a common mechanism of late stent failure
- To see general incidence of neoatherosclerosis, natural history and treatment, we need more data