In-Stent Neoatherosclerosis

A Common Pathway of Late Stent Failure

Soo-Jin Kang MD., PhD.

University of Ulsan College of Medicine, Heart Institute
Asan Medical Center, Seoul, Korea

Disclosure

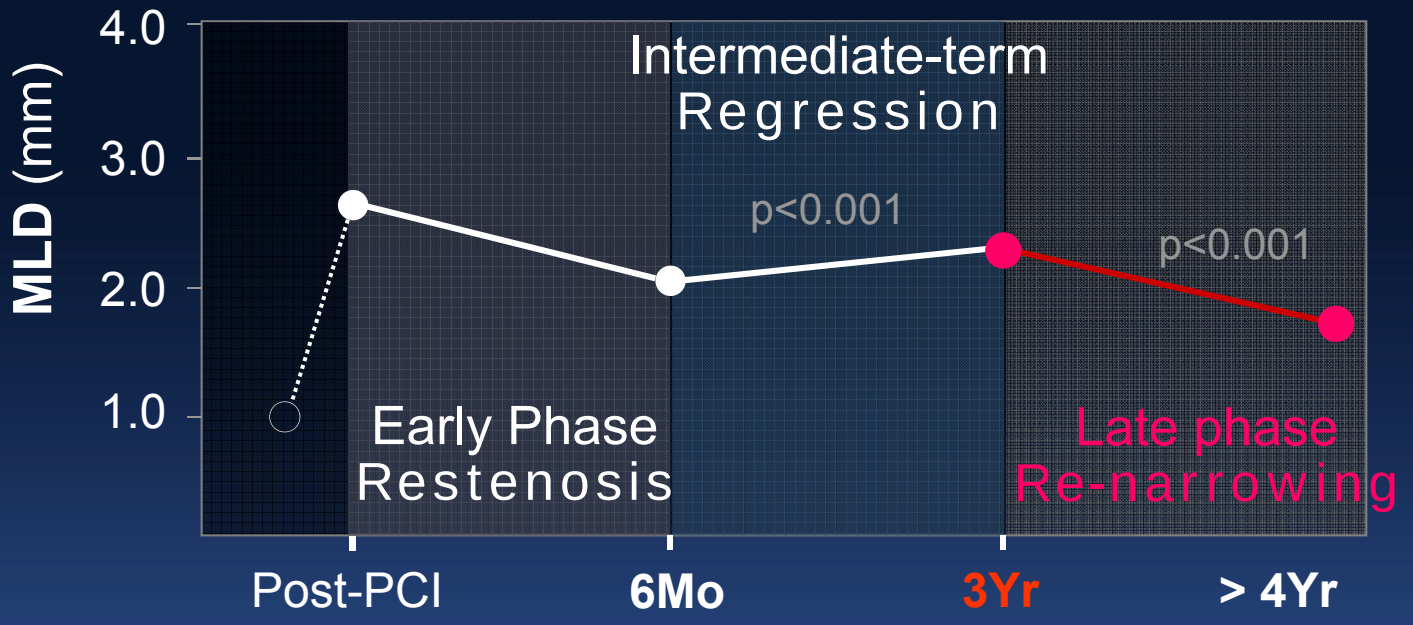
I have nothing to disclose

Neoatherosclerosis

As a Mechanism of

Late In-stent Restenosis

Luminal Response in BMS

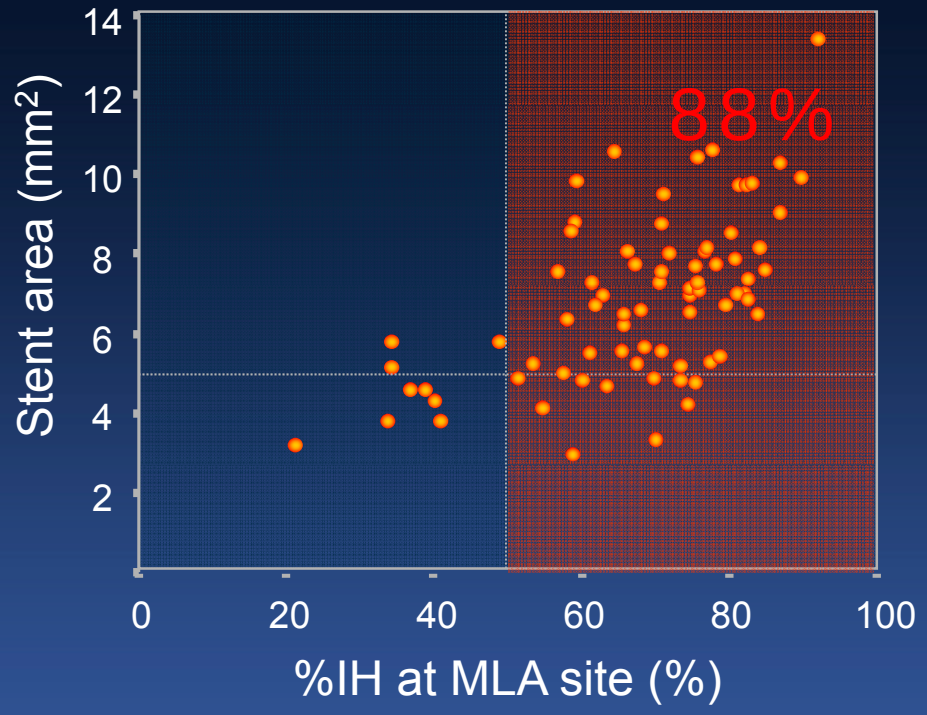


"*De-novo* Neoatherosclerosis"

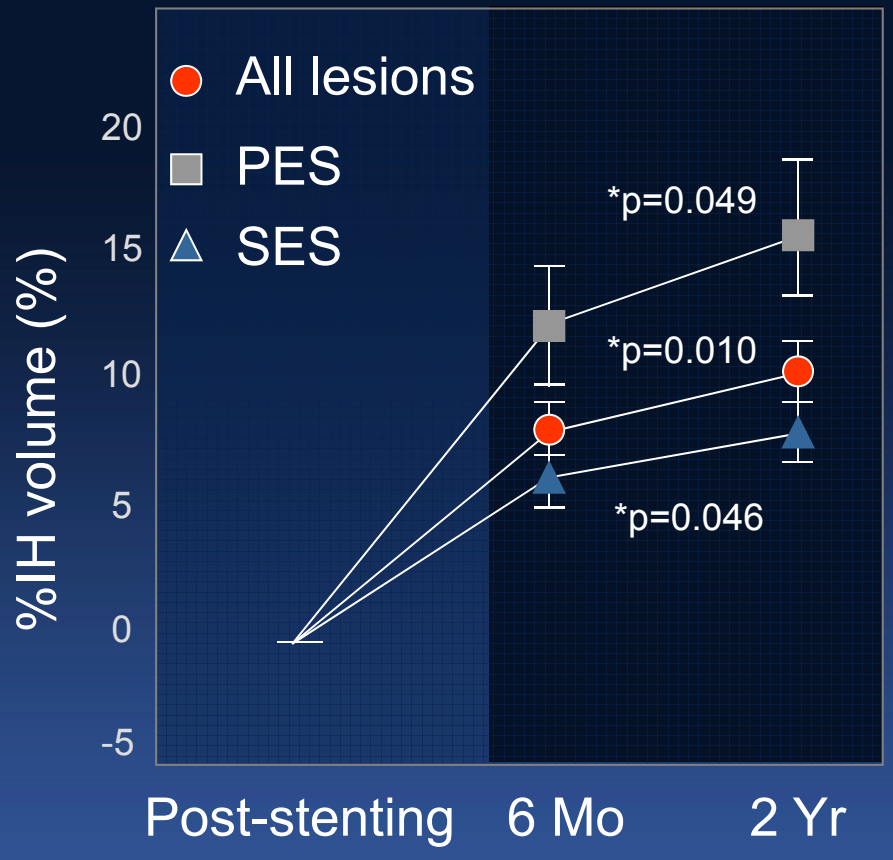
Kimura et al. N Engl J Med 1996;334:561-6
Kimura et al. Circulation 2002;105:2986-91

"Late Catch-up" in DES

Mechanism of DES-ISR



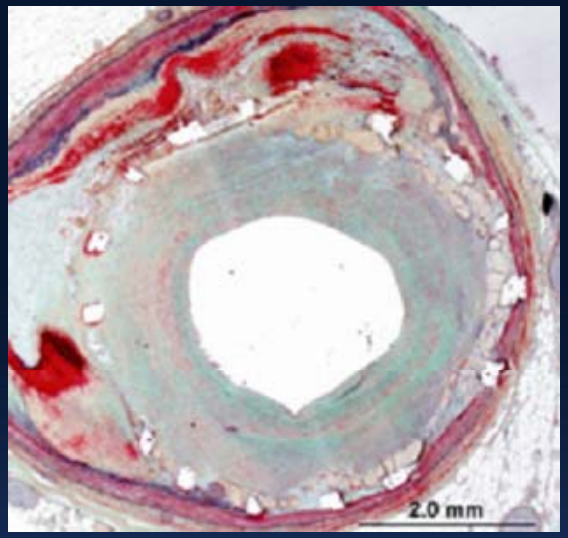
Serial F/U %IH

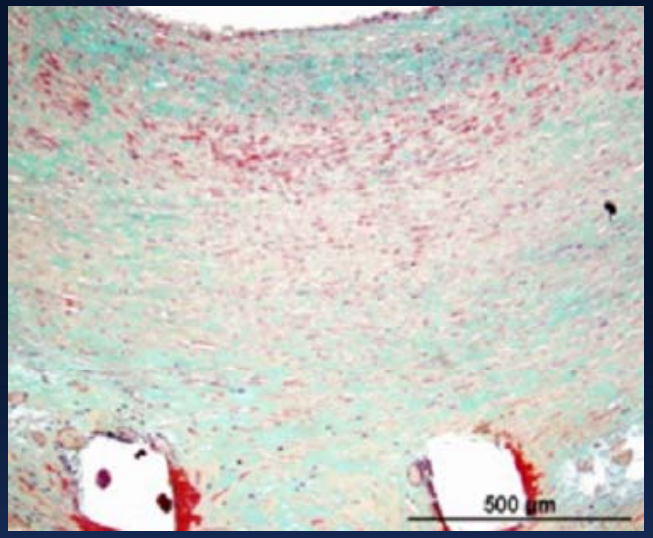


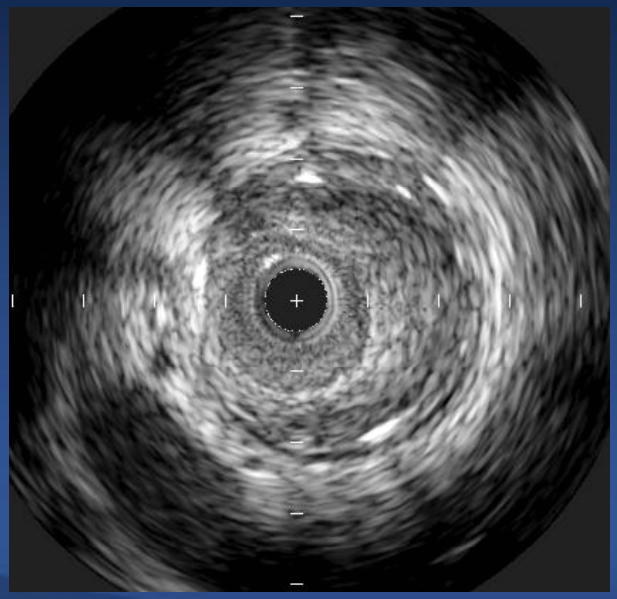
Kang et al. Circ Cardiovasc Interv 2011;4:9-14

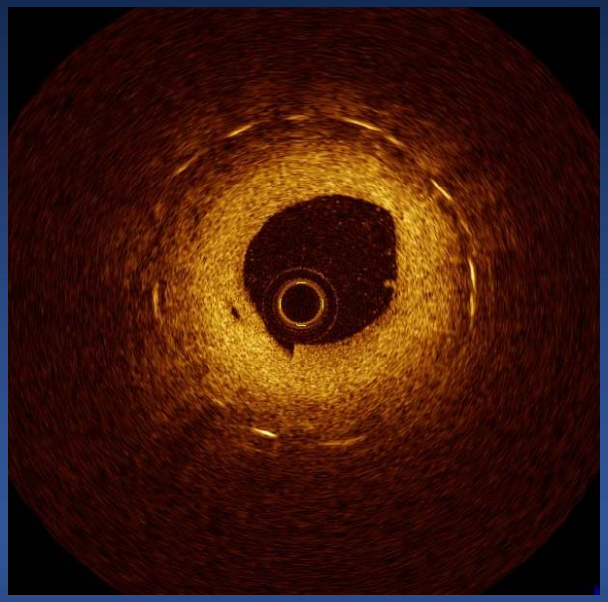
Kang et al. Am J Cardiol 2010;105:1402-8

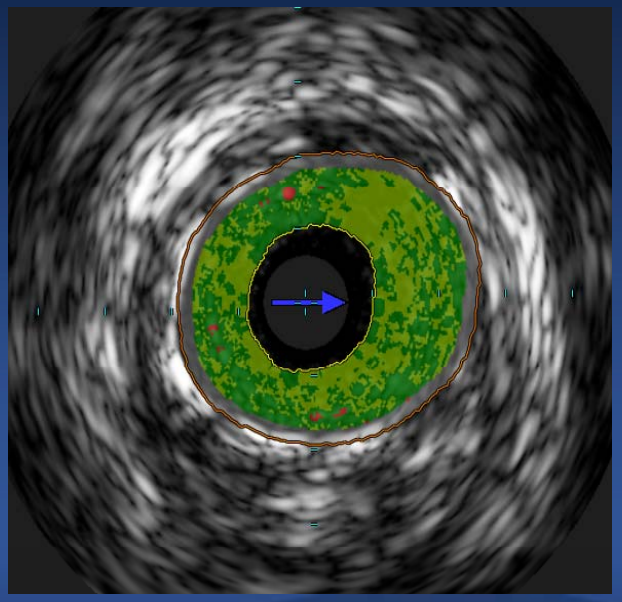
Early Neointima







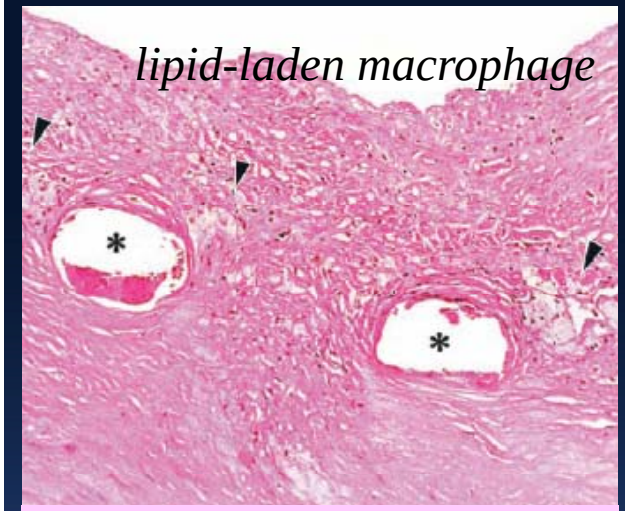




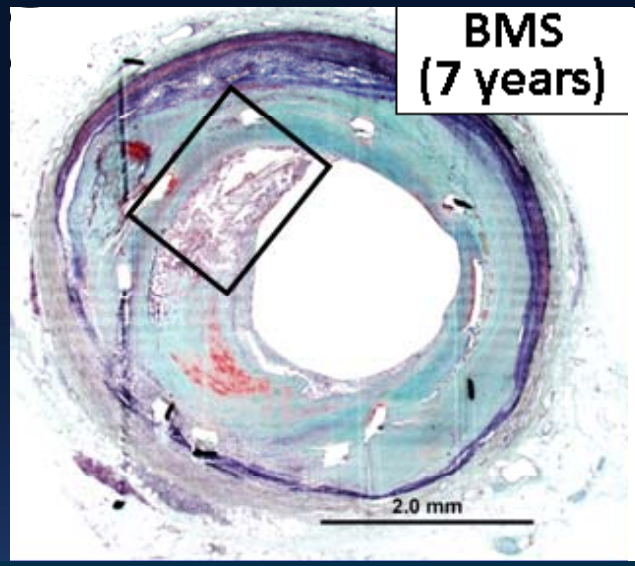
Chieffo et al. Am J Cardiol 2009;104:1660–7
Nakazawa et al. JACC Cariovasc Imaging 2009;2:625-8

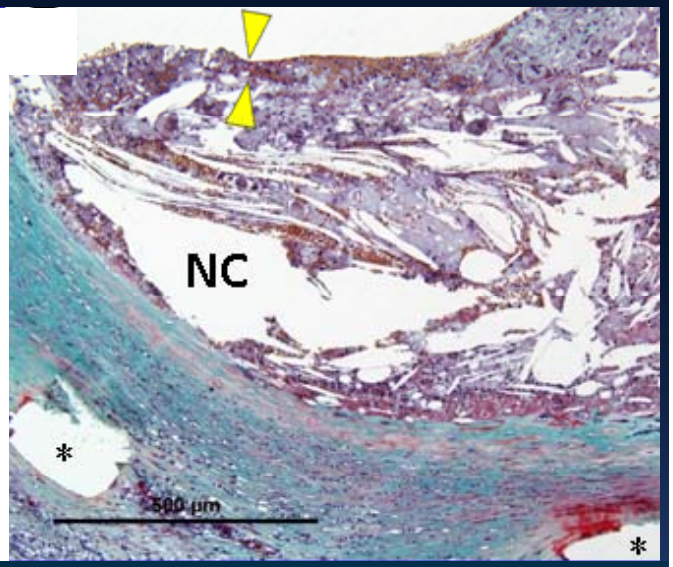
Neoatherosclerosis

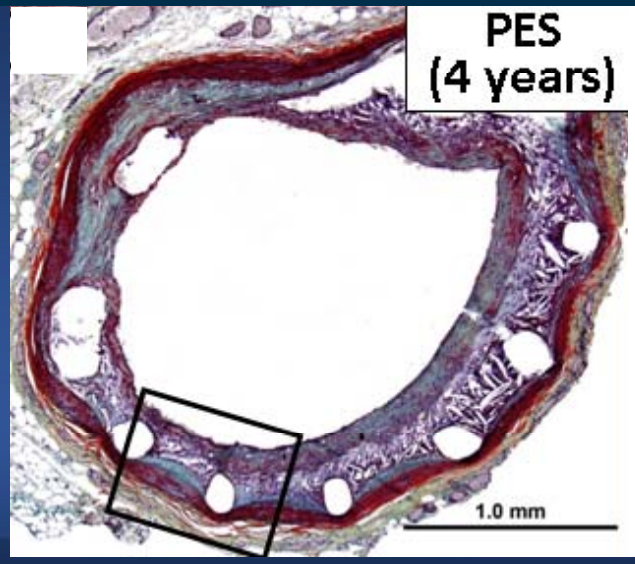
Defined as Infiltration of Foamy Macrophage Clusters

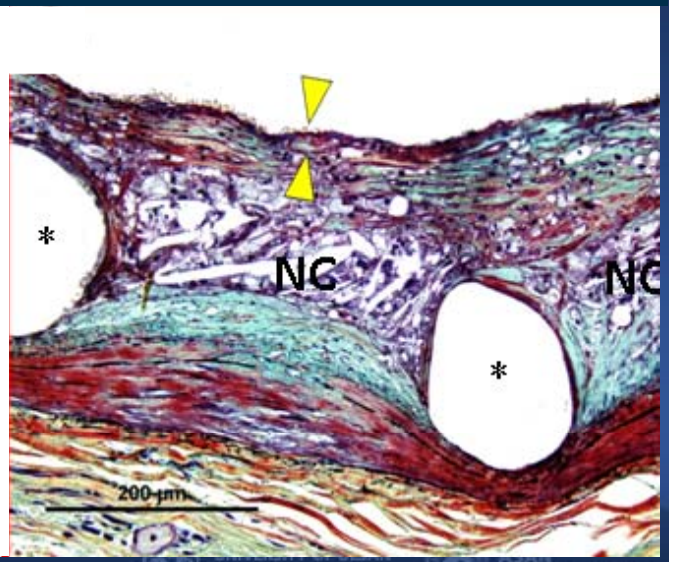


5-year Palmaz-Schatz

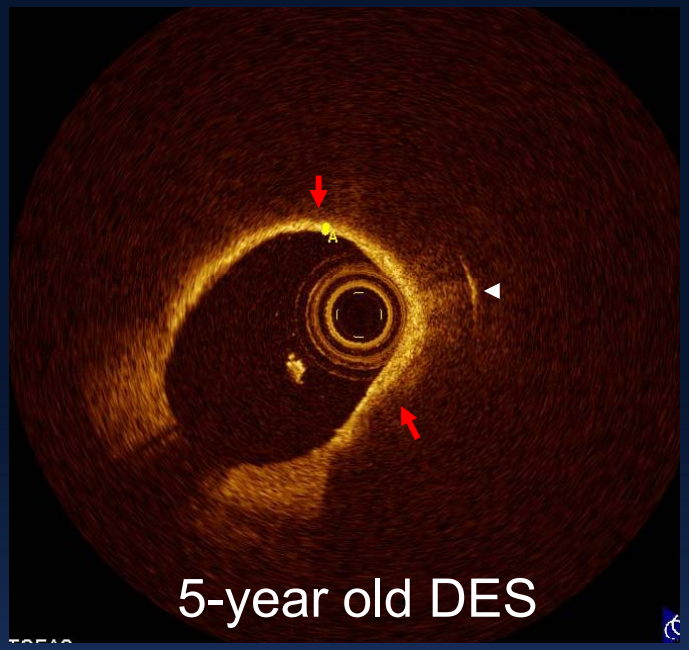


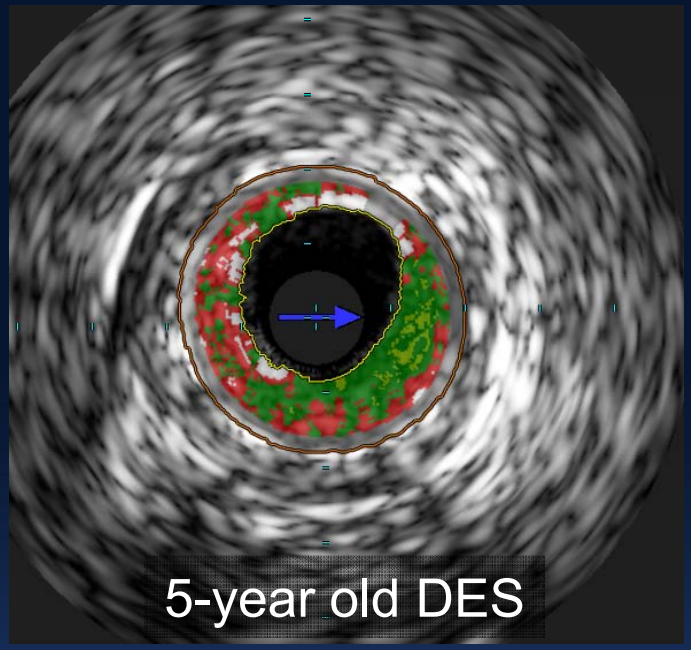


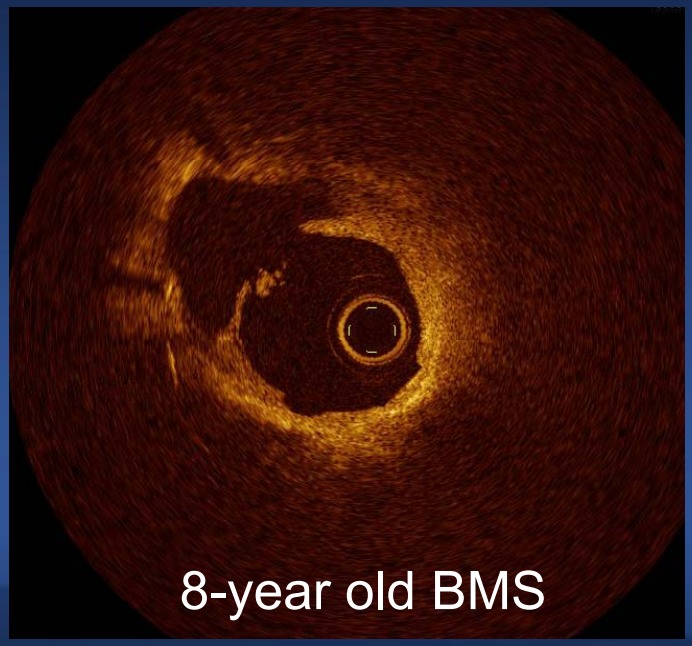


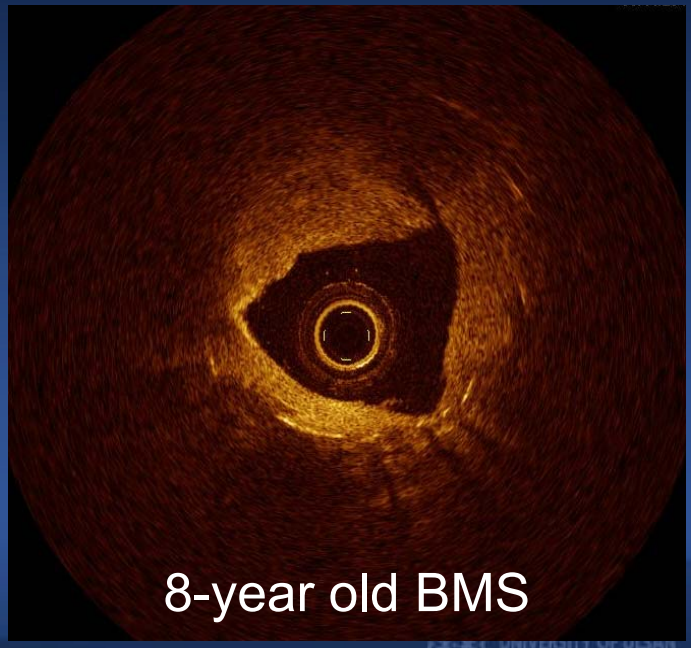


Nakazawa et al.
JACC 2011;57:1314–22

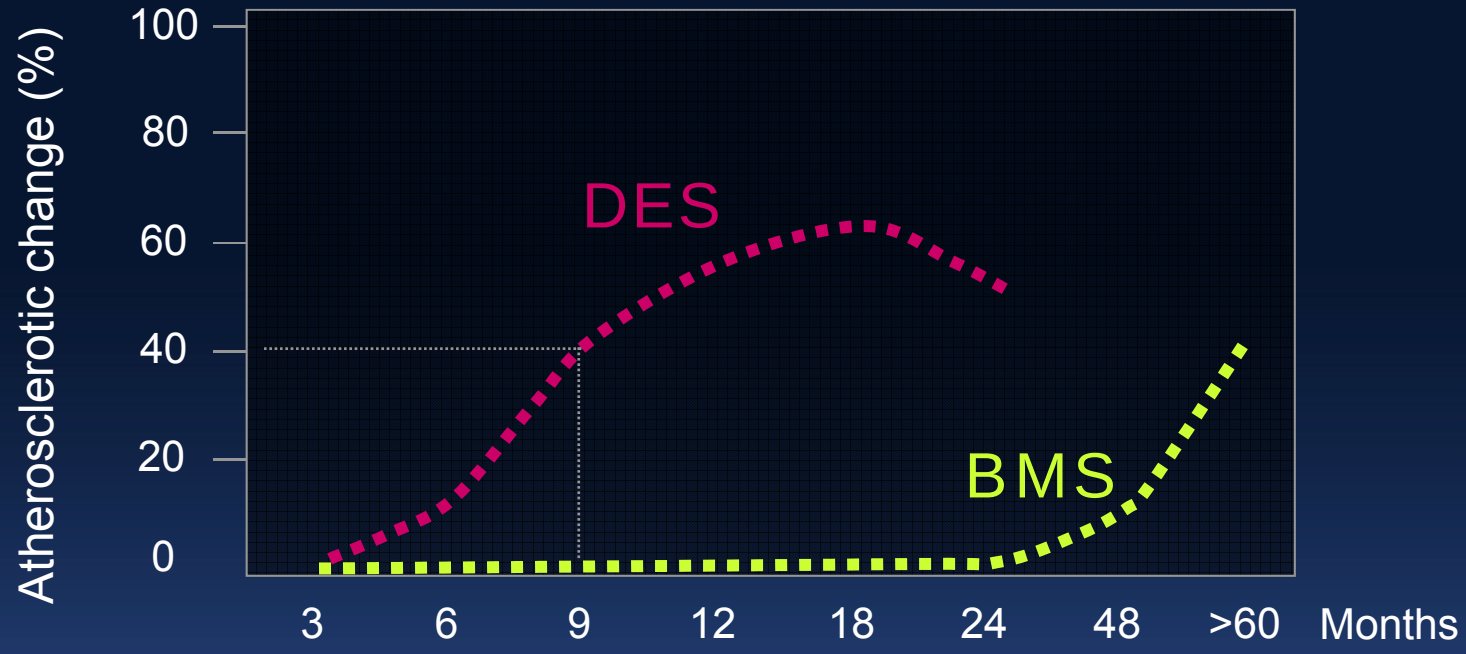

5-year old DES


5-year old DES


8-year old BMS


8-year old BMS

Different Timing DES vs. BMS

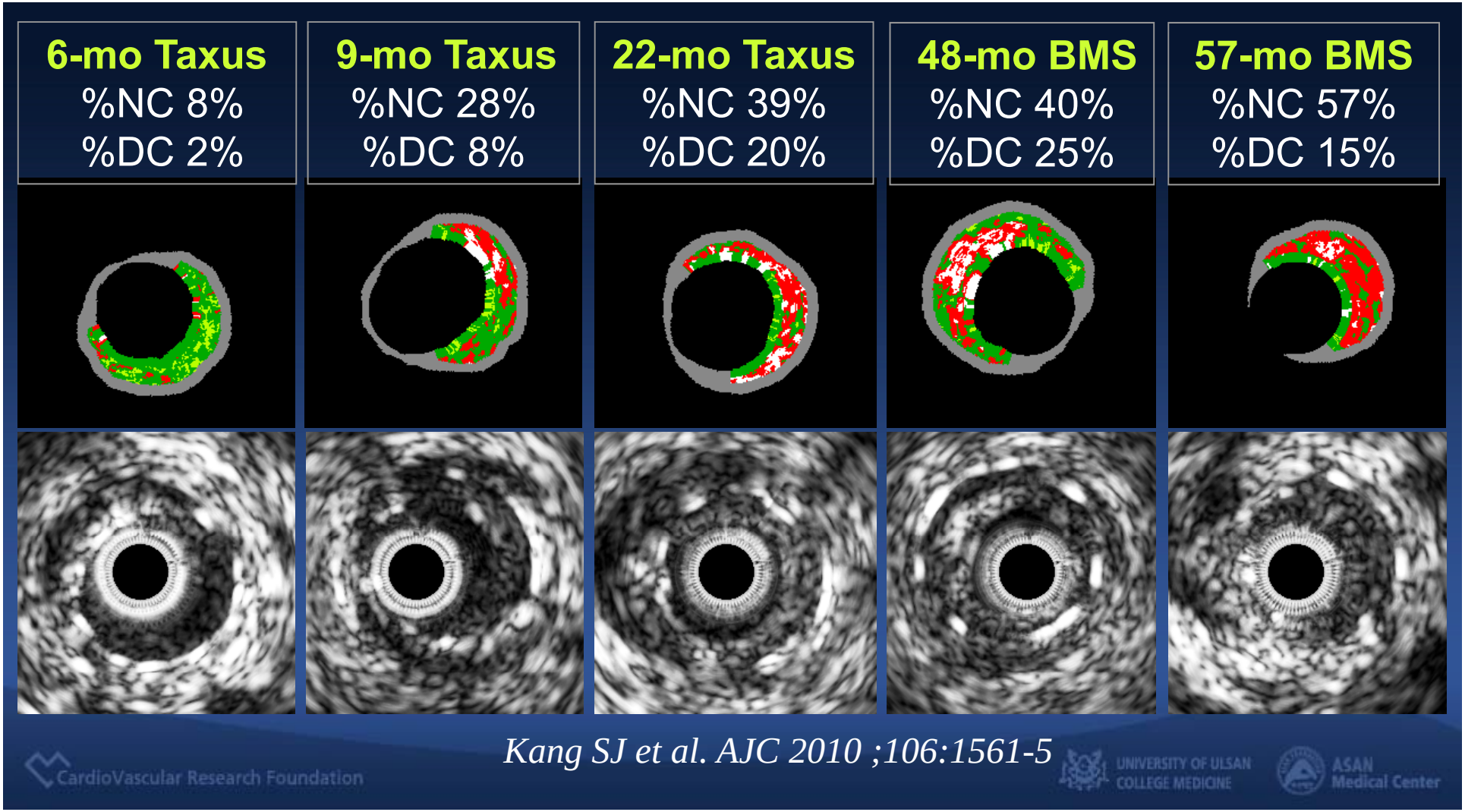


	<2 years		2-6 years	
	DES	BMS	DES	BMS
Neoatherosclerosis	29%	0%	41%	22%
Fibroatheroma (NC)	13%	0%	22%	15%

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

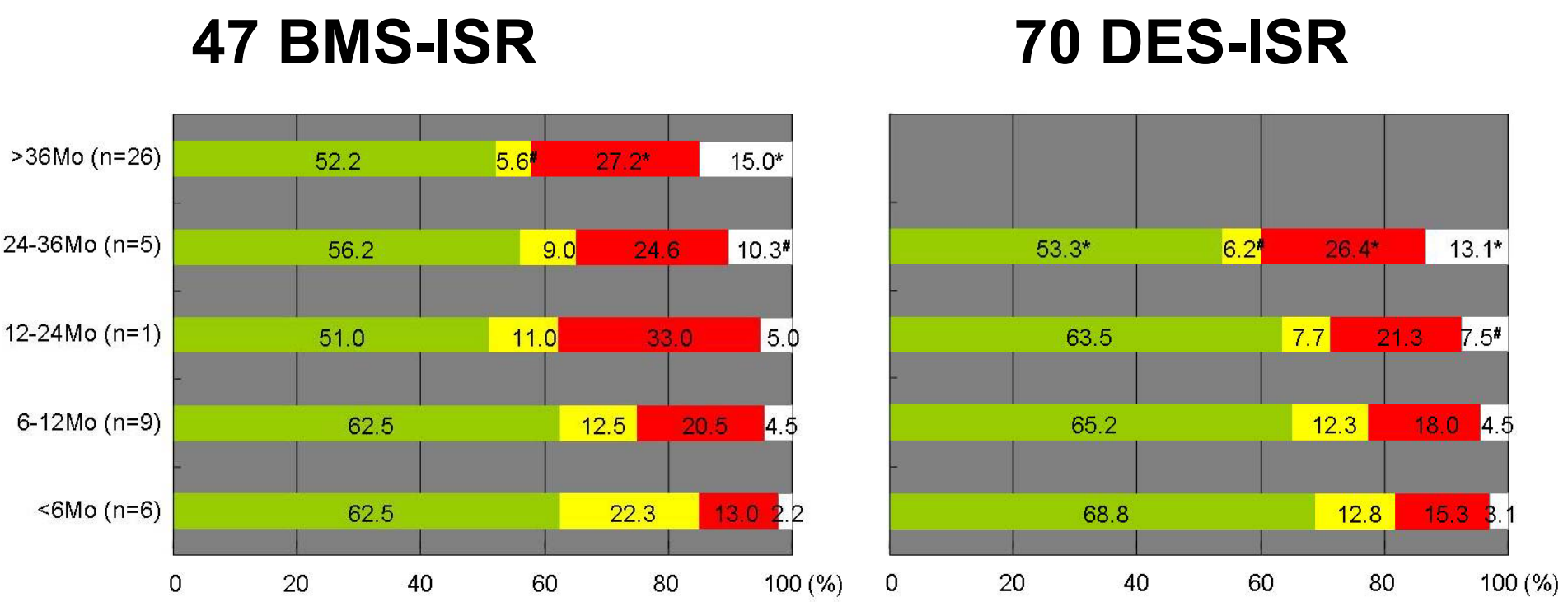
Tissue Characterization of In-Stent Neointima Using Intravascular Ultrasound Radiofrequency Data Analysis

Soo-Jin Kang, MD[a], Gary S. Mintz, MD[b], Duk-Woo Park, MD[a], Seung-Whan Lee, MD[a], Young-Hak Kim, MD[a], Cheol Whan Lee, MD[a], Ki-Hoon Han, MD[a], Jae-Joong Kim, MD[a], Seong-Wook Park, MD[a], and Seung-Jung Park, MD[a,*]



Kang SJ et al. AJC 2010 ;106:1561-5

Neointimal VH Composition



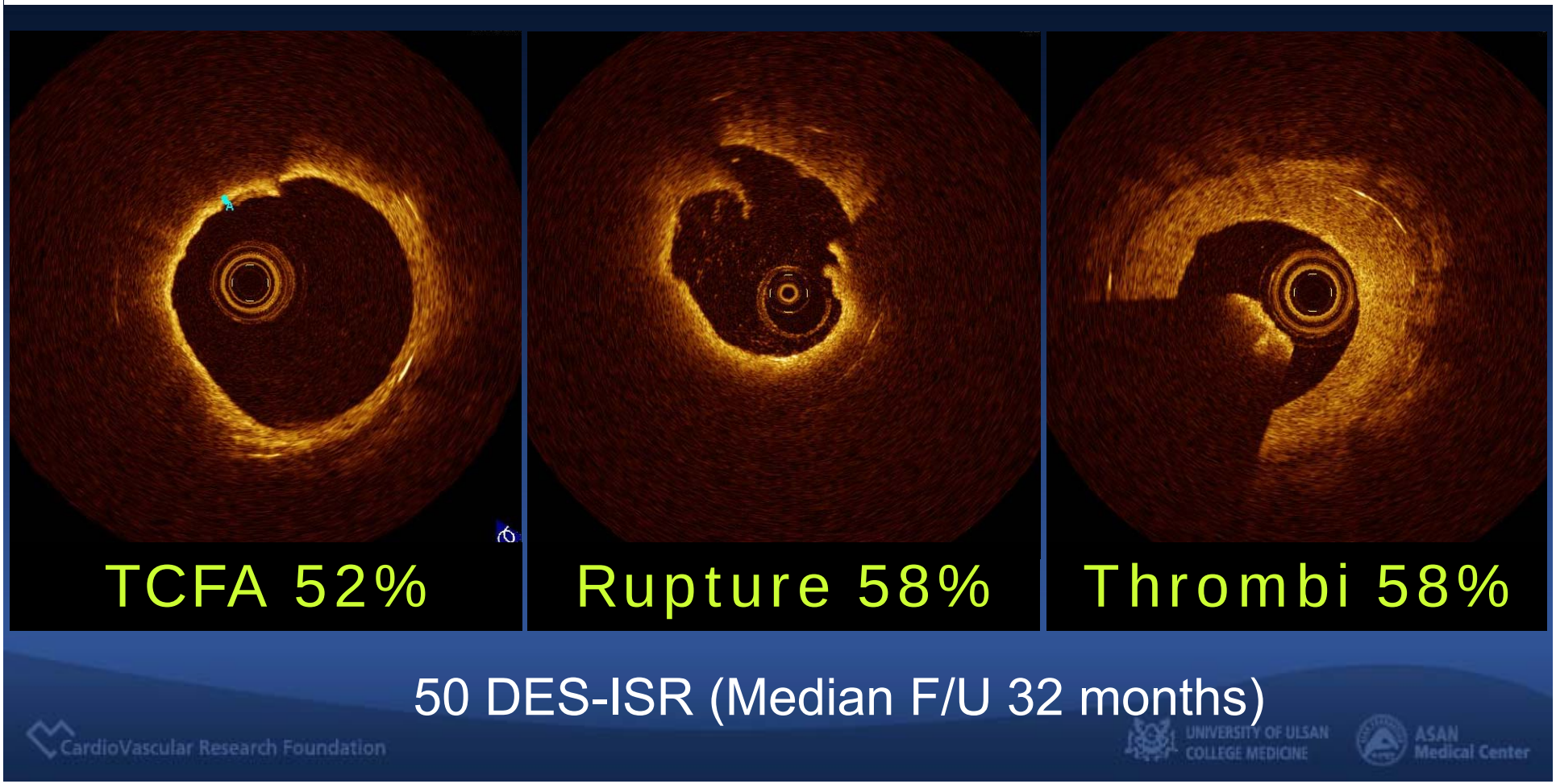
*p<0.01 and #p<0.05, vs. lesions at follow-up time <6 months

Kang SJ et al. AJC 2010 ;106:1561-5

Optical Coherence Tomographic Analysis of In-Stent Neoatherosclerosis After Drug–Eluting Stent Implantation

Soo-Jin Kang, MD; Gary S. Mintz, MD; Takashi Akasaka, MD, PhD; Duk-Woo Park, MD, PhD; Jong-Young Lee, MD; Won-Jang Kim, MD; Seung-Whan Lee, MD, PhD; Young-Hak Kim, MD, PhD; Cheol Whan Lee, MD, PhD; Seong-Wook Park, MD, PhD; Seung-Jung Park, MD, PhD

Circulation 2011;123:2954-63

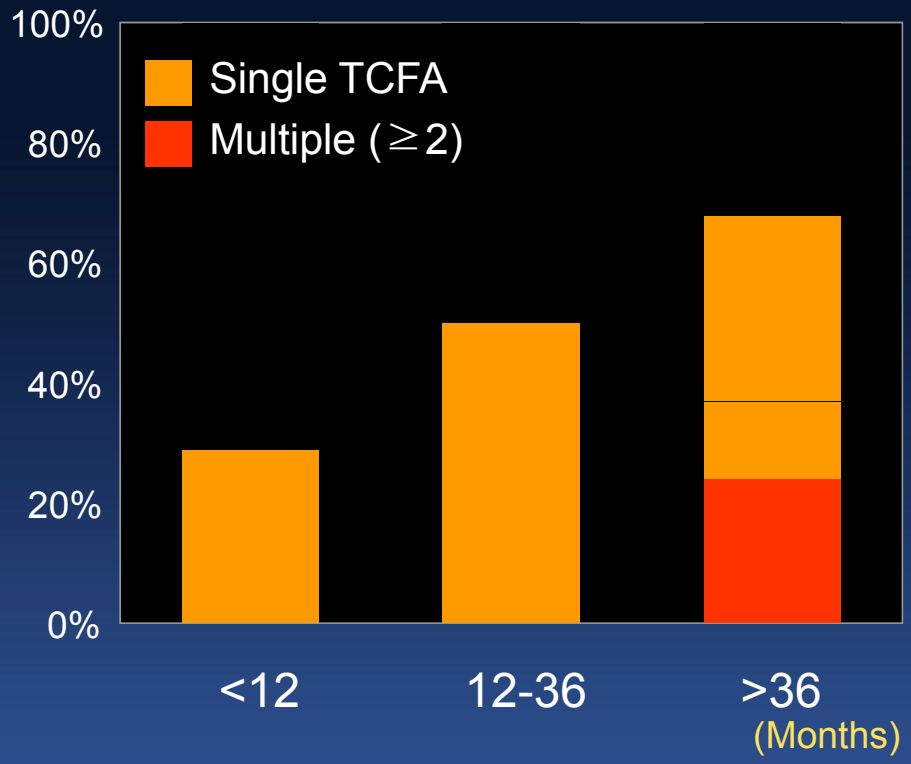


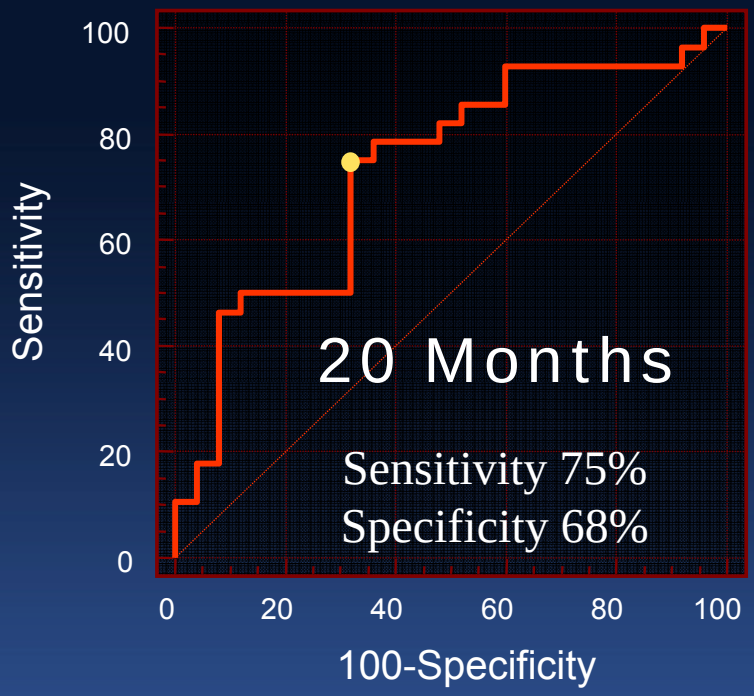
Stable vs. Unstable Angina

	Stable N=30	Unstable N=20	P
Fibrous cap thickness, μm	100 (60-205)	55 (42-105)	0.006
Incidence of thrombi	13 (43%)	16 (80%)	0.010
Incidence of red thrombi	1 (3%)	6 (30%)	0.012
Incidence of rupture	14 (47%)	15 (75%)	0.044
Incidence of TCFA	11 (37%)	15 (75%)	0.008

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

DES Duration >20 Months
Best Predict TCFA-Containing Neointima

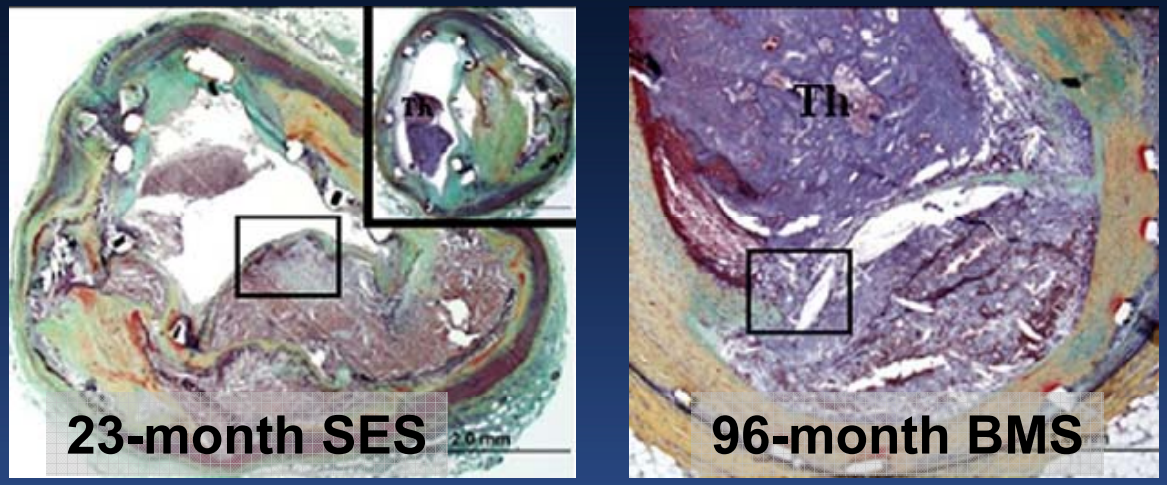




Kang et al. Circulation 2011;123:2954-63

More Advanced Neoatherosclerosis

TCFA-Containing Intimal Rupture Thrombosis

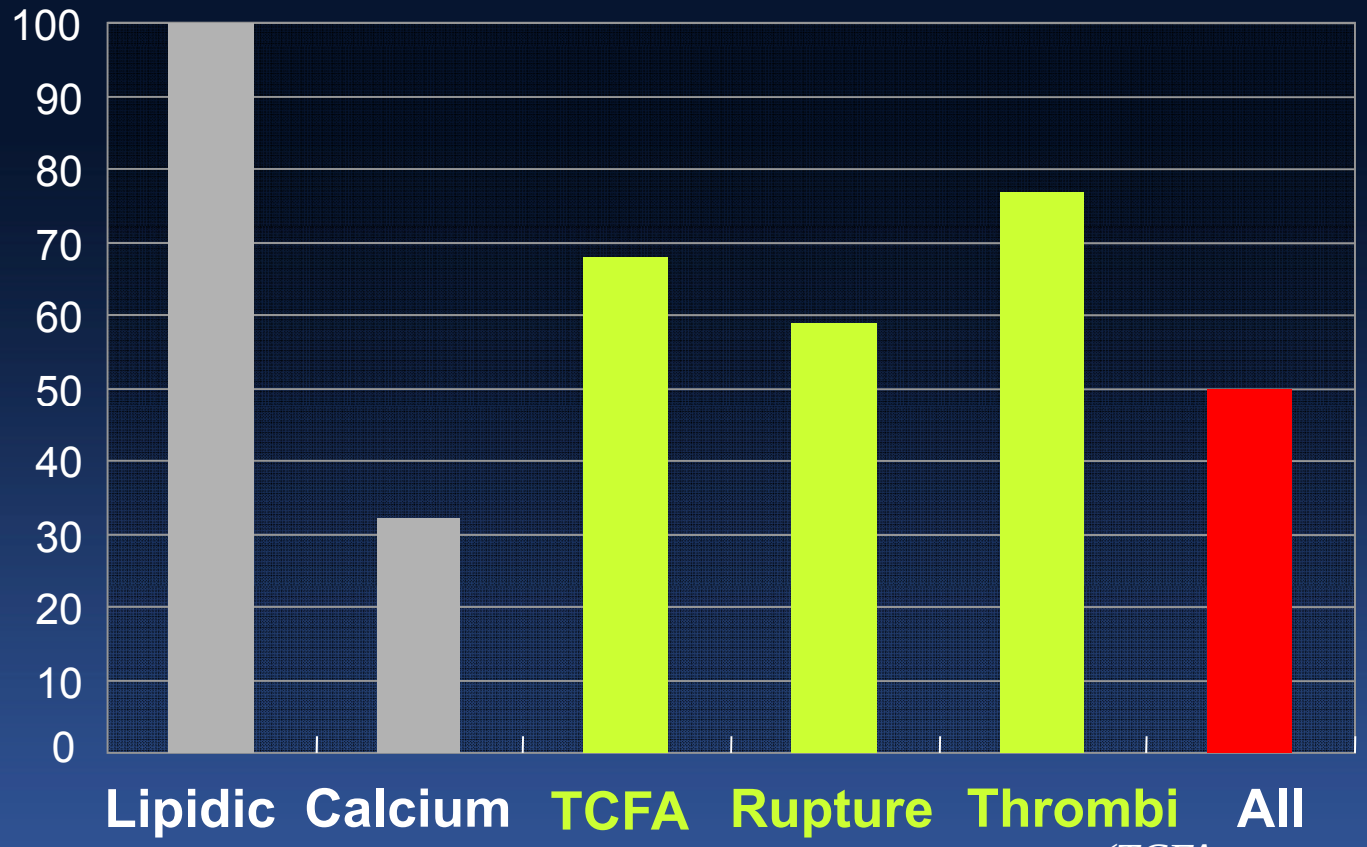


Although uncovered struts remain the cause of DES-VLST, neoatherosclerosis is added as another factor

Nakazawa et al. JACC 2011;57:1314-22

OCT Findings of BMS-ISR at 10 Years

Clinically-driven TLR, Median F/U time 11 years [9–14]

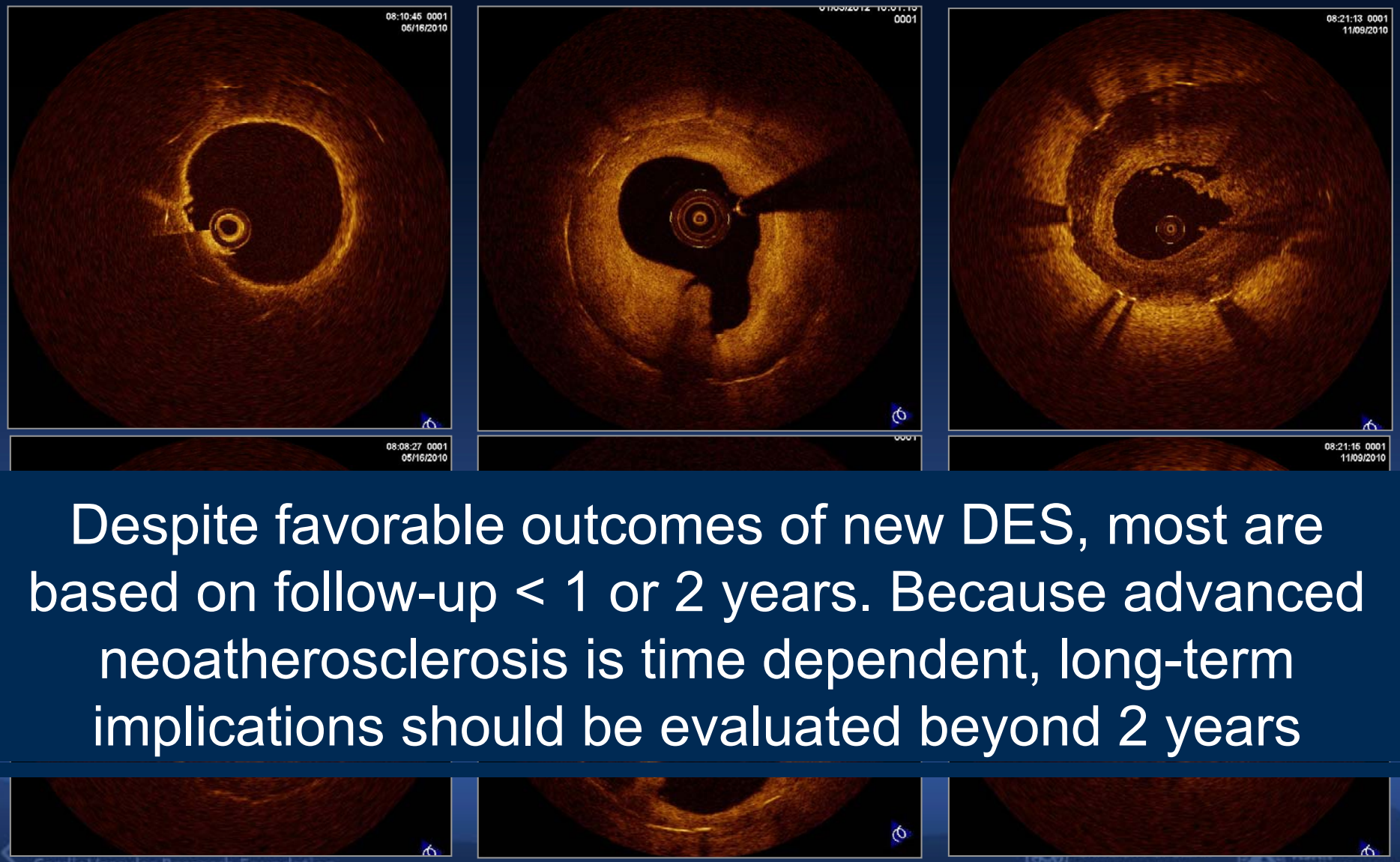


(TCFA, rupture, thrombi)

Kang et al. JACC Cardiovasc Imaging 2012 (in press)

2nd Generation DES-ISR

37-month Endeavor ***23-month*** Xience ***6-month*** Promus-E



Despite favorable outcomes of new DES, most are based on follow-up < 1 or 2 years. Because advanced neoatherosclerosis is time dependent, long-term implications should be evaluated beyond 2 years

New Generation DES-ISR

16 patients with clinically-driven TLR

(5 EES, 5 ZES, 3 Coroflex Please, 2 Cilotax, 1 Nobori)

- Median duration 14.0 months (IQR 8.5–32.9)
- Unstable angina 25%
- Lipidic neointima 88%
- TCFA-containing neointima 25%
- Intimal rupture 44%
- Intraluminal thrombi 38%

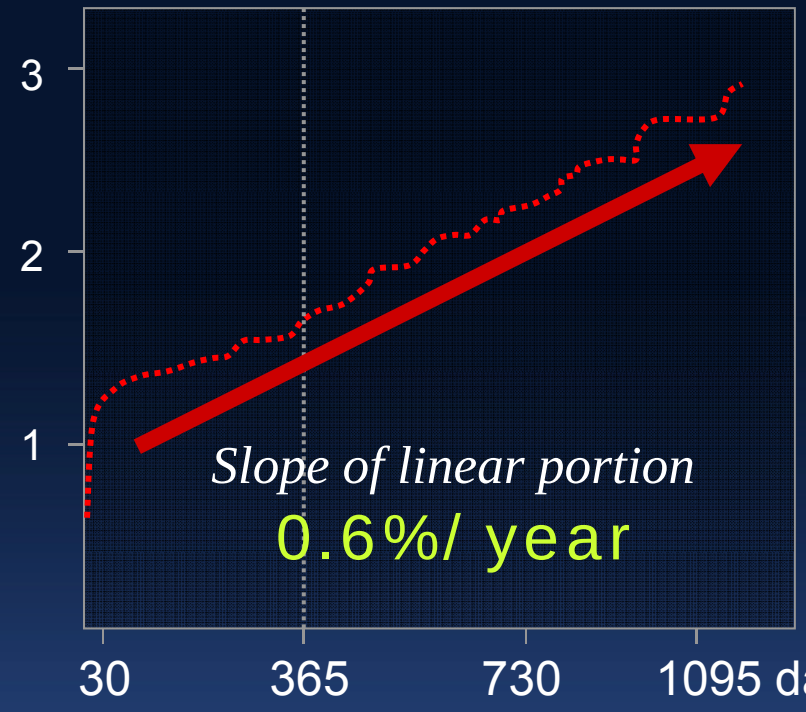
AMC preliminary

Neoatherosclerosis

As a Mechanism of

Very Late Stent thrombosis

Cumulative Incidence of DES Thrombosis

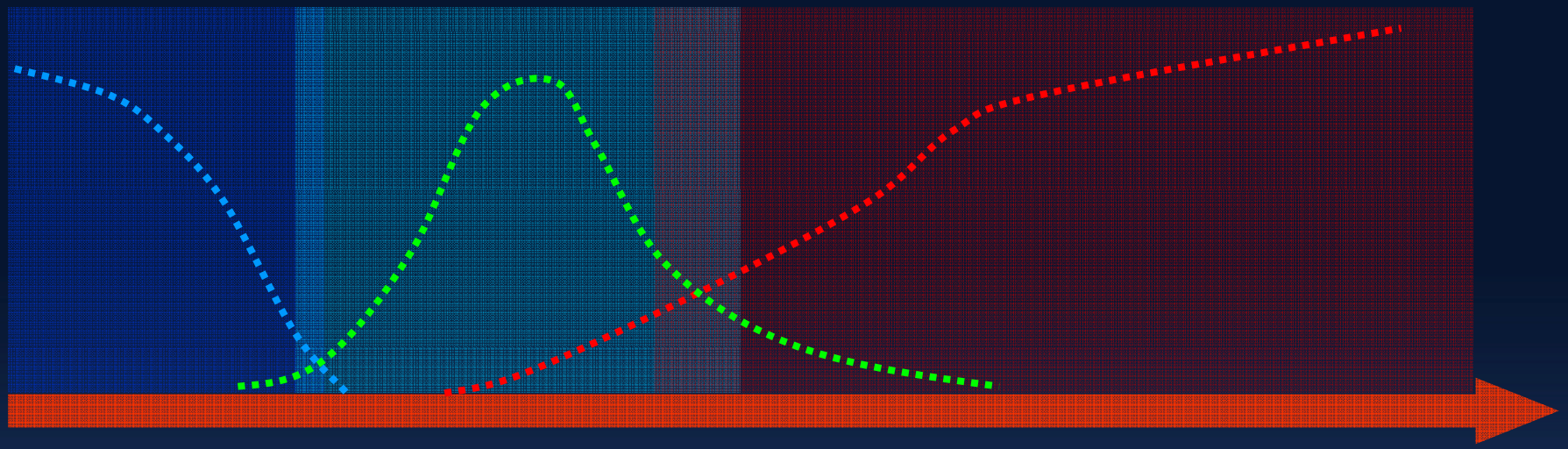


	30	365	730	1095 days
Cumulative incidence	**1.2%**	**1.7%**	**2.3%**	**2.9%**

Although the majority of DES showed good stent coverage beyond 1 year, a steady increase in very late stent thrombosis (0.6% / year) have demonstrated thereafter

Daemen et al. Lancet 2007;369:667—78

Timing and Mechanism of DES Thrombosis



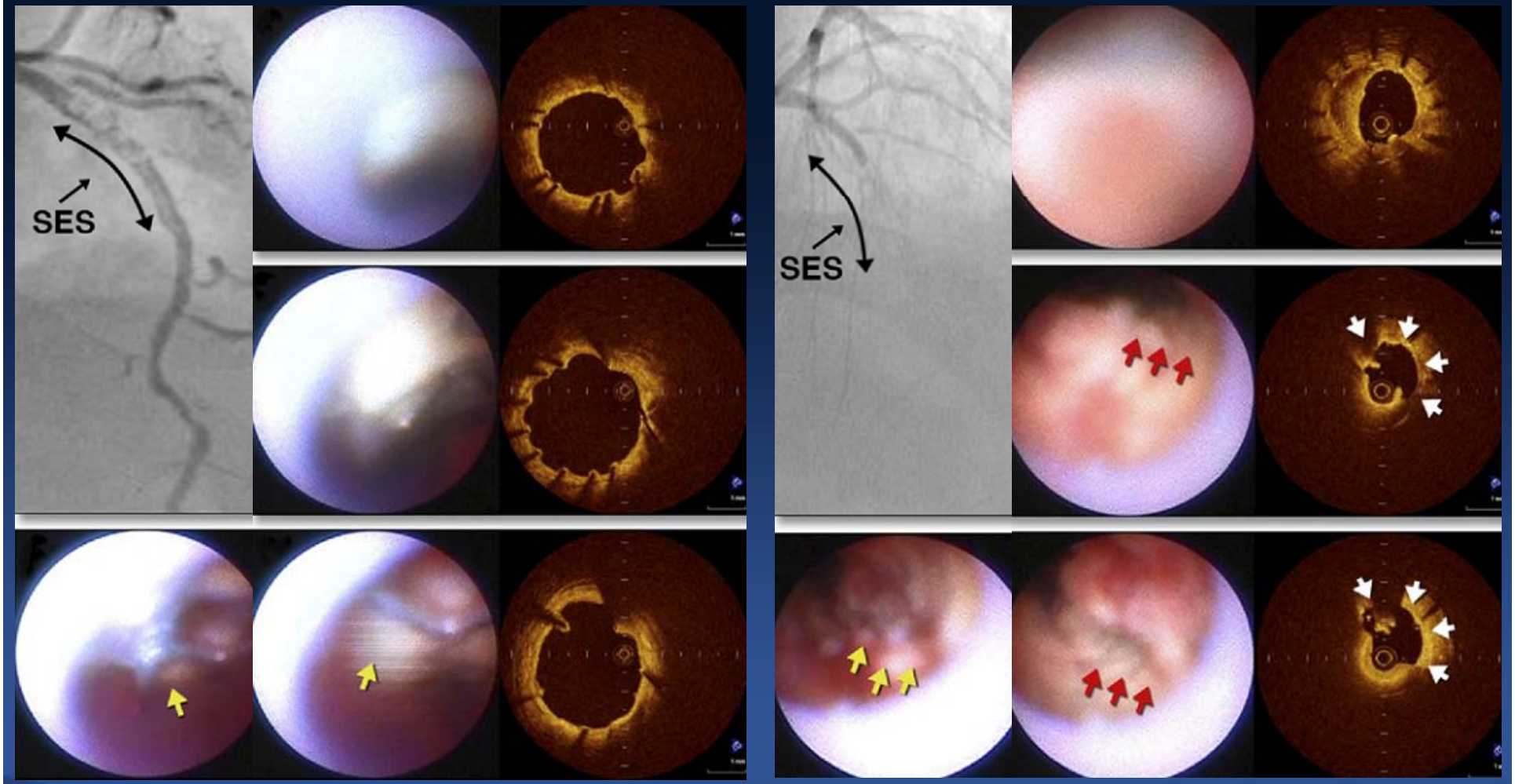
Early (<30d)	Late (1-12 Mo)	Very late (>12 Mo)
Procedural	Delayed healing	Abnormal vascular response
Underexpansion Edge dissection Residual plaque	Uncovered struts Fibrin deposition	Hypersensitivity Extensive fibrin deposition Late malapposition? Neoatherosclerosis

Nakazawa et al. J Cardiol 2011;58:84-91

Different Mechanisms of DES-VLST

VLST of 34-month SES

VLST 54-month SES



Ikenaga et al. JACC Cardiovasc Imaging 2011;4:1217-9

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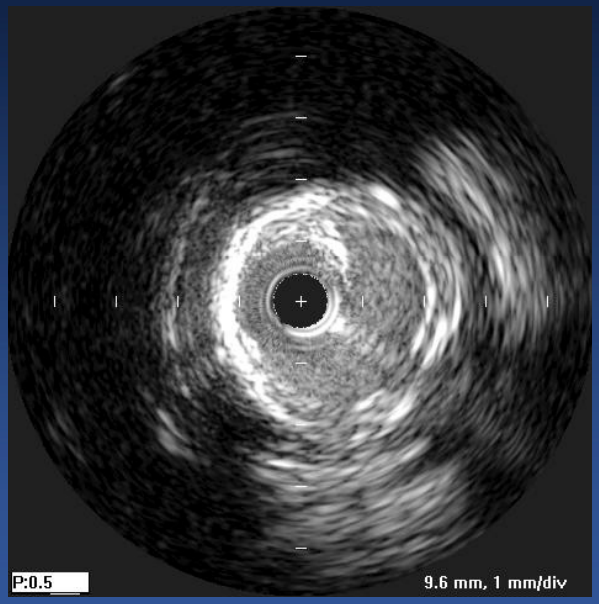
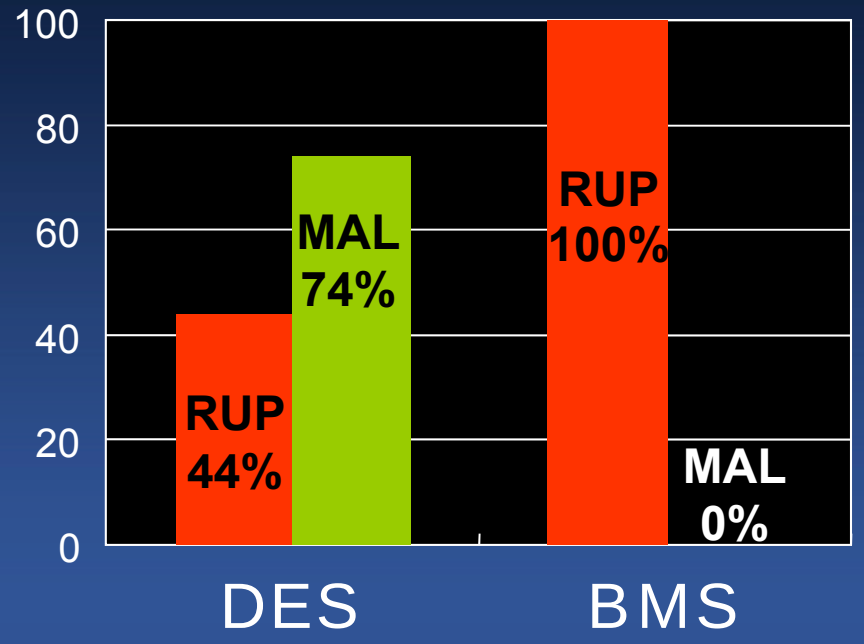
doi:10.1016/j.jacc.2009.10.077

Intravascular Ultrasound Findings in Patients With Very Late Stent Thrombosis After Either Drug-Eluting or Bare-Metal Stent Implantation

30 AMI with VLST (Mean F/U 33 Mo in DES, 108 Mo in BMS)





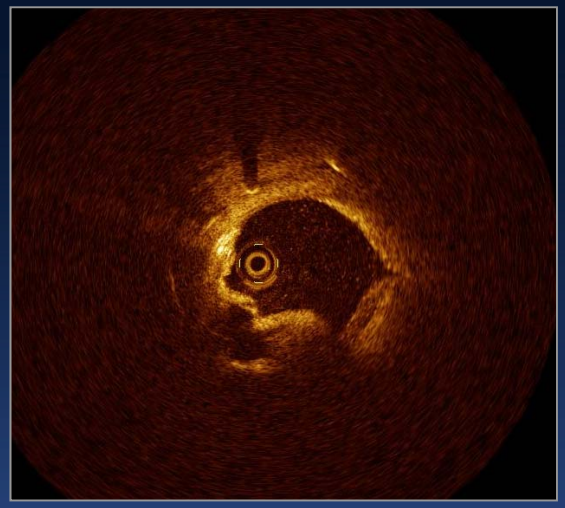
Lee et al. J Am Coll Cardiol 2010;55:1936-42

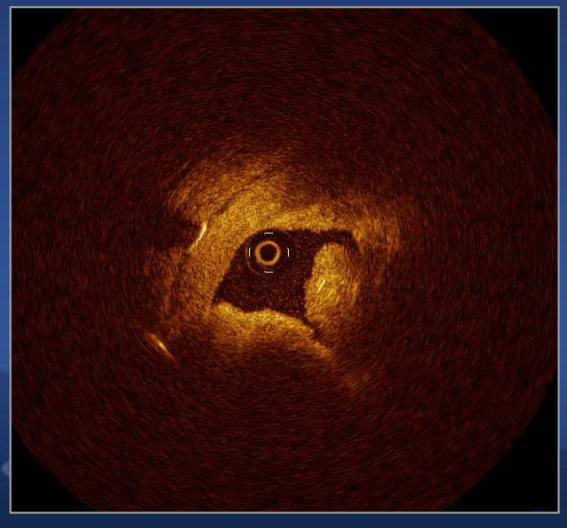
Definite VLST (27 DES, 6 BMS)

STEMI 52%, NSTEMI 33%, UA 15%

69/Male STEMI

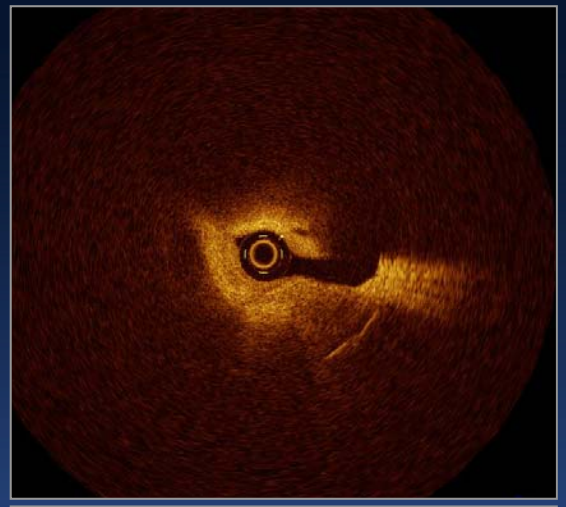
165-month BMS

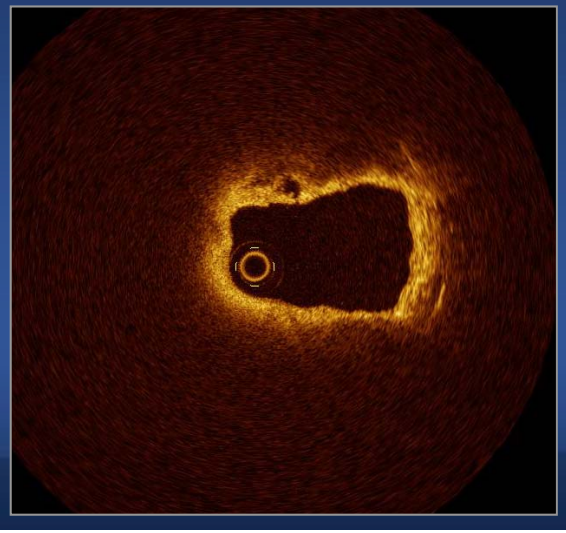




79/Male NSTEMI

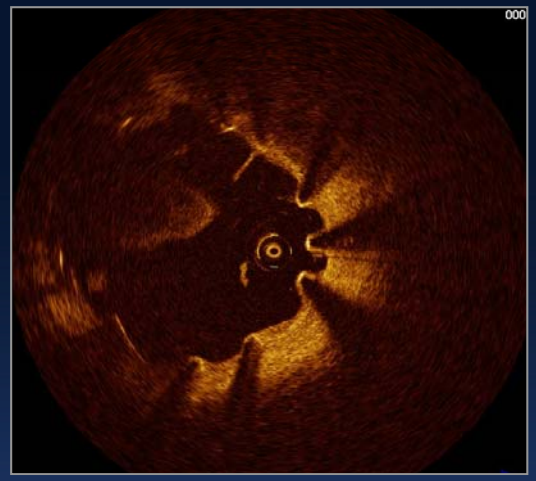
60-month SES





51/Male STEMI

75-month SES



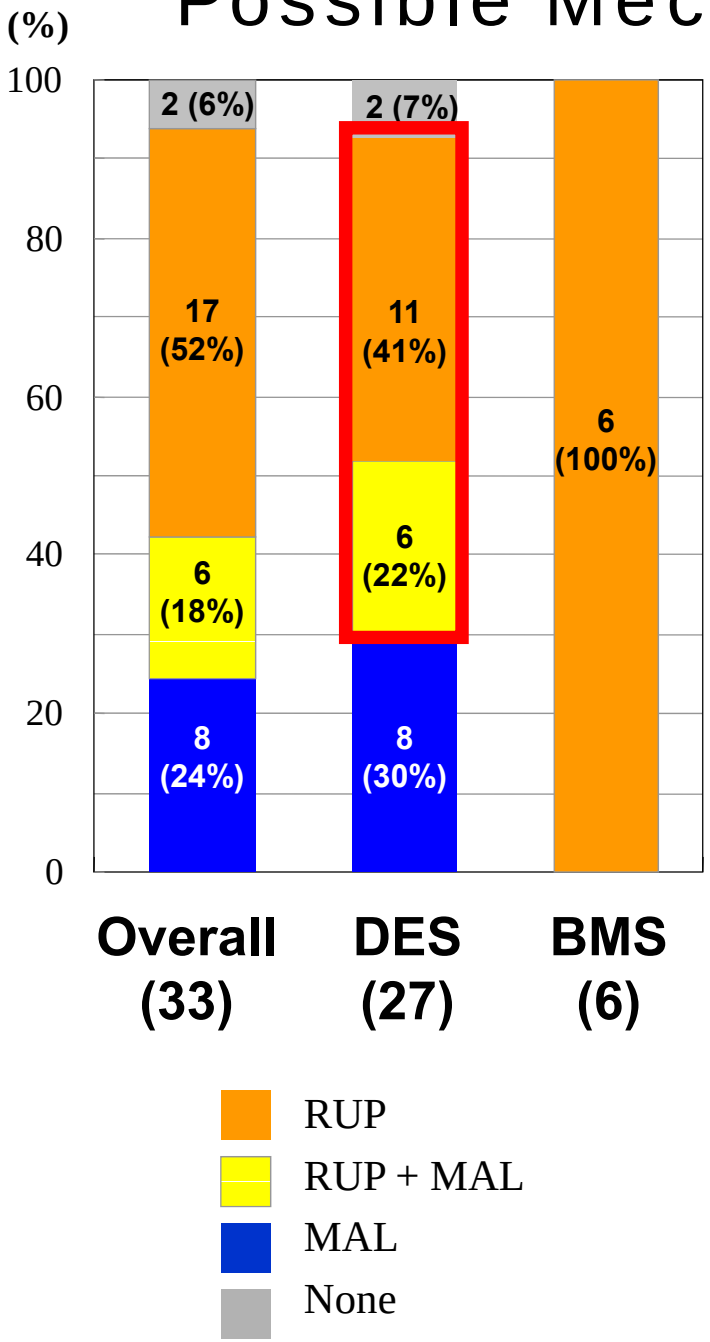
69/Male NSTEMI

53-month SES

OCT Characteristics

N	DES 27	BMS 6	P
Thrombi	25 (93%)	6 (100%)	0.665
Lipid neointima, N (%)	22 (82%)	6 (100%)	0.252
Intimal rupture, N (%)	17 (63%)		0.074
TCFA-containing, N (%)	15 (56%)		0.041
Proportion of lesions with at least one frame with			
Uncovered strut, %	15 (56 %)	1 (17%)	0.085
Malapposed strut, %	14 (52%)	0 (0%)	0.020
Proportion of lesions with at least >10% of frame with			
Uncovered strut, %	12 (44%)	0 (0%)	0.041
Malapposed strut, %	8 (30%)	0 (0%)	0.126

Possible Mechanisms of VLST

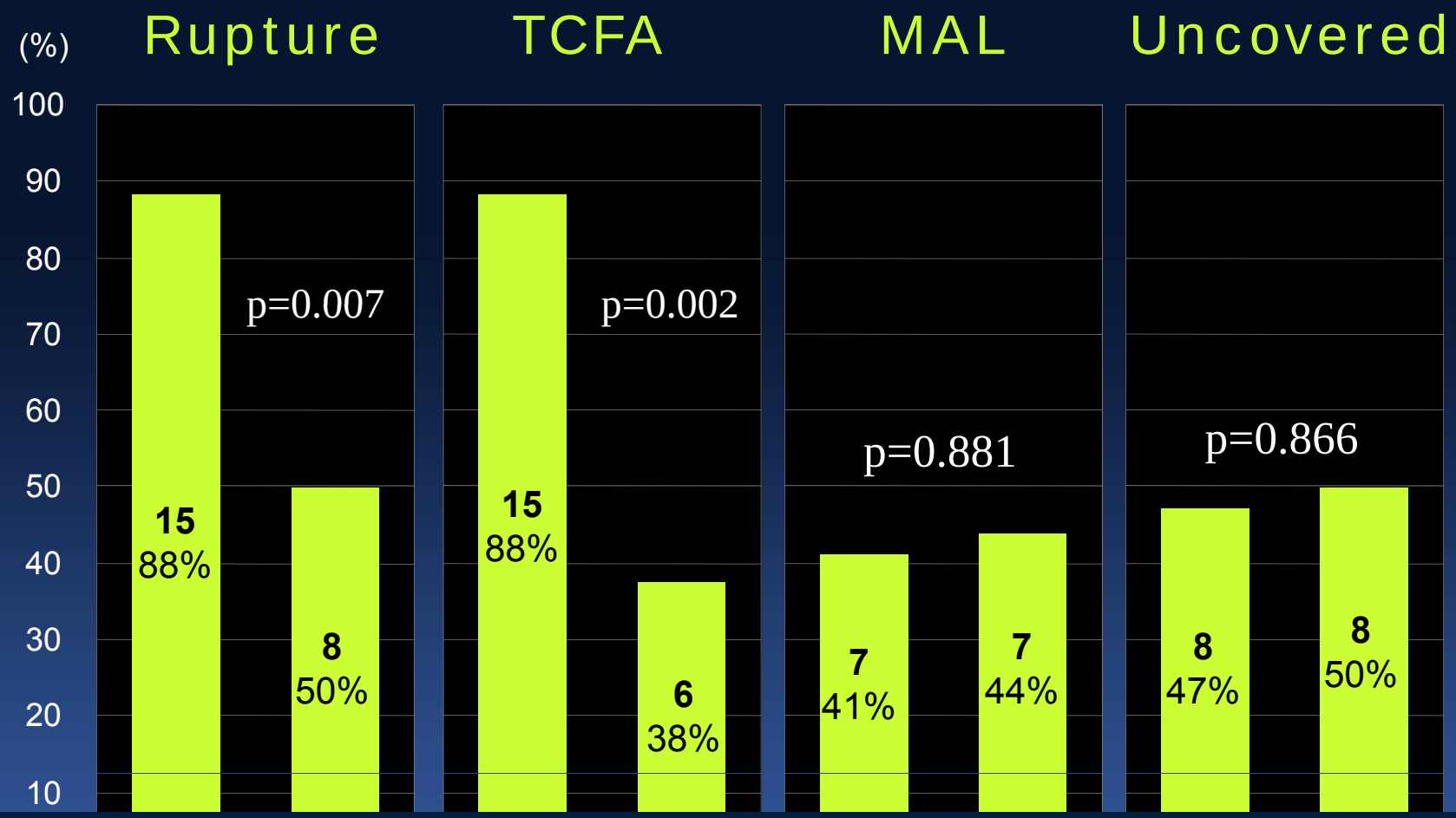


63%

Intimal rupture

direct mechanism of VLST

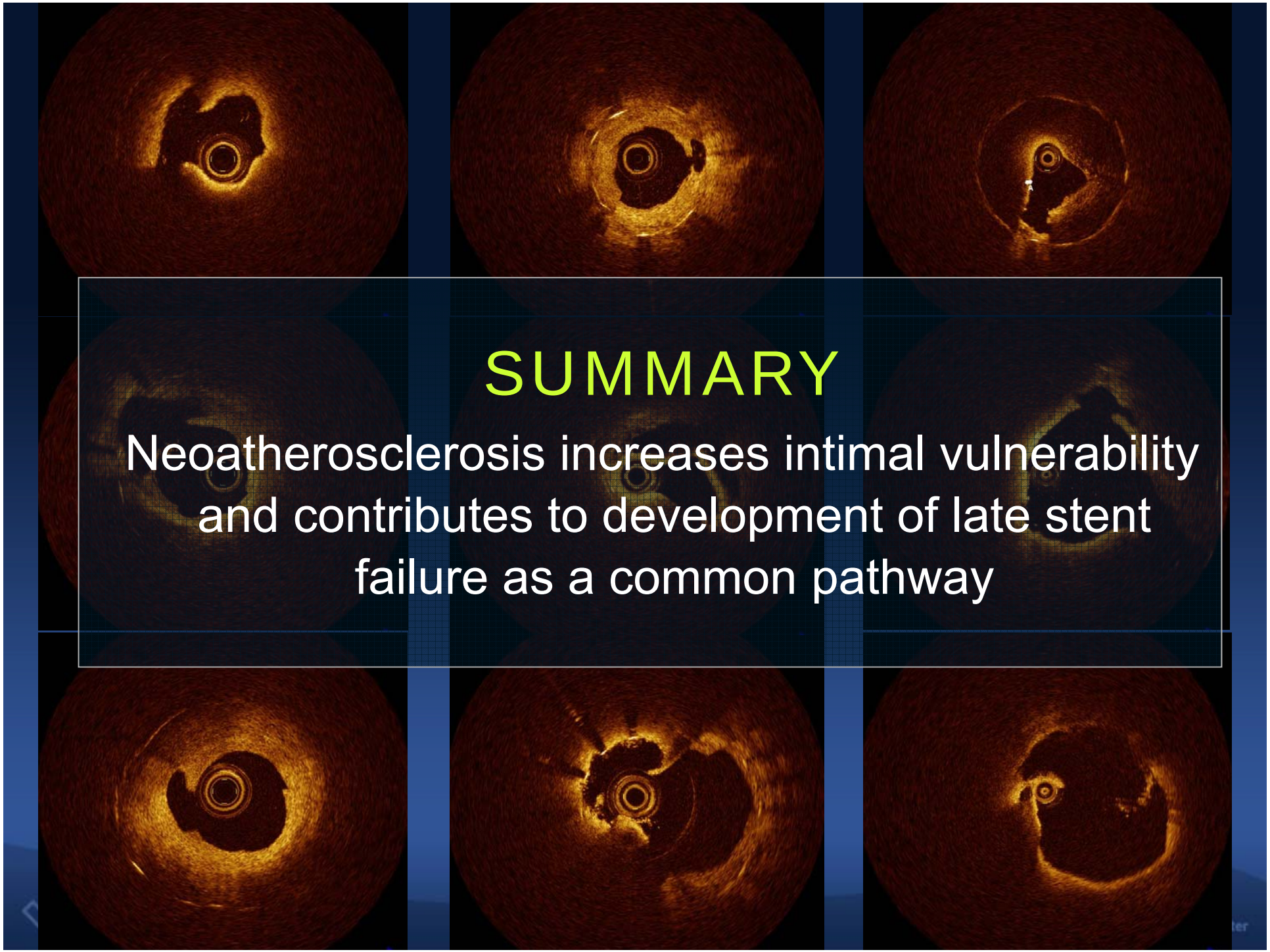
VLST Presented with STEMI vs. Without



Advanced neoatherosclerosis is a common and more aggressive mechanism of definite VLST

OCT Data in VLST

	Hong et al.	Guagliumi et al.	AMC
Published	*Int J Cardiovasc Imaging 2011*	*JACC interv 2012*	*Preliminary*
Population	18 DES-VLST	18 DES-LST (15 VLST, 3 LST)	33 VLST (27 DES, 6 BMS)
Stent duration	**41±18 mo**	**21 mo** (13 – 40)	**74 mo** (46 – 90)
Thrombectomy	**Before OCT, all**	**Before OCT, all**	**After OCT**
Thrombi	Aspirated	Aspirated	White 94% Red 79%
Intimal rupture	22%	17%	DES 63% BMS 100%
Malapposition	39%	78%	DES 52%
Uncovered struts	50%	72% (with >30%)	DES 56%



SUMMARY

Neoatherosclerosis increases intimal vulnerability and contributes to development of late stent failure as a common pathway