Clinical Evidences of Neoatherosclerosis:
ISR and Late Stent Thrombosis

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Conventional Thought

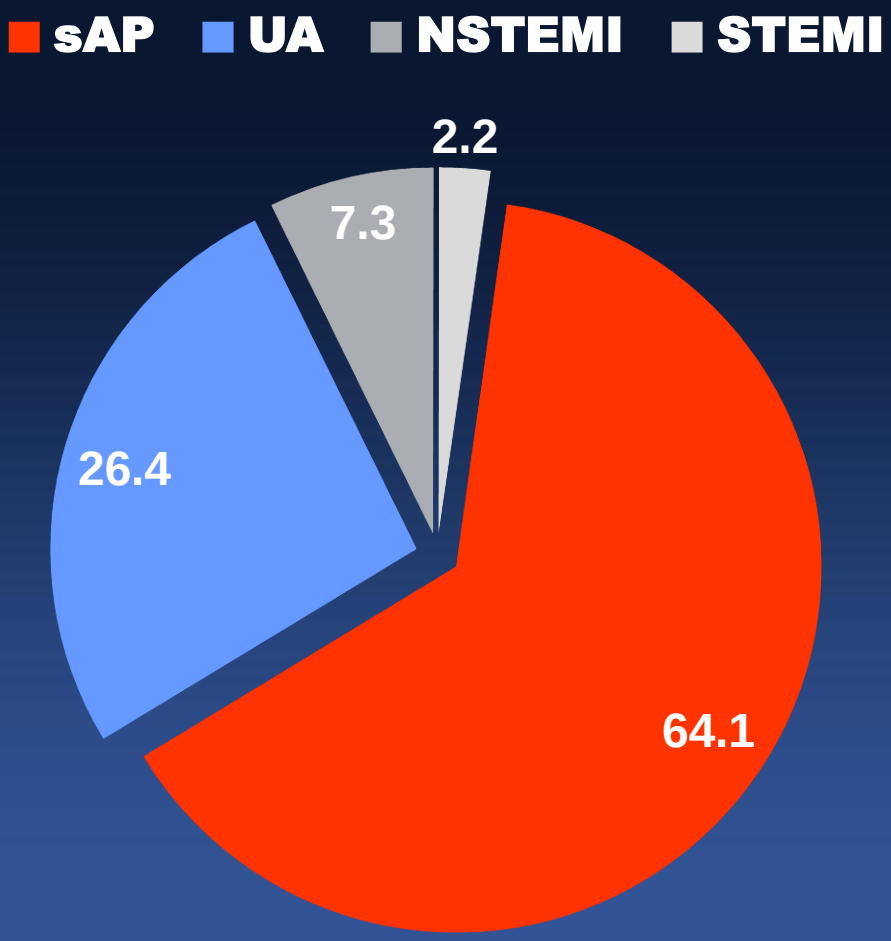
- Restenosis **Does Not** present as an **ACS**.
- Symptomatic restenosis presents as **Progressive Exertional Angina** over time.

1) Levine GN, Chodos AP, Loscalzo J. Restenosis following coronary angioplasty: clinical presentations and therapeutic options. Clin Cardiol 1995;18:693–703.

2) Schatz RA, Baim DS, Leon M, et al. Clinical experience with the Palmaz–Schatz coronary stent. Initial results of a multicenter study. Circulation 1991;83:148–61.

Clinical Presentation of BMS ISR

1186 cases of bare metal ISR in 984 patients

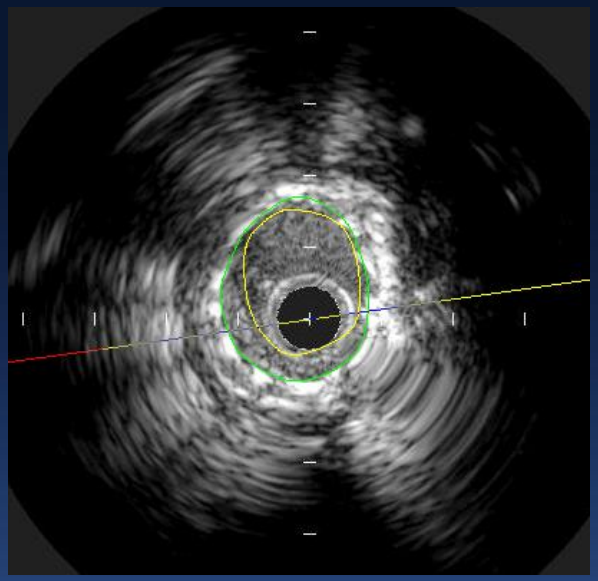


Am Heart J 2006;151:12602

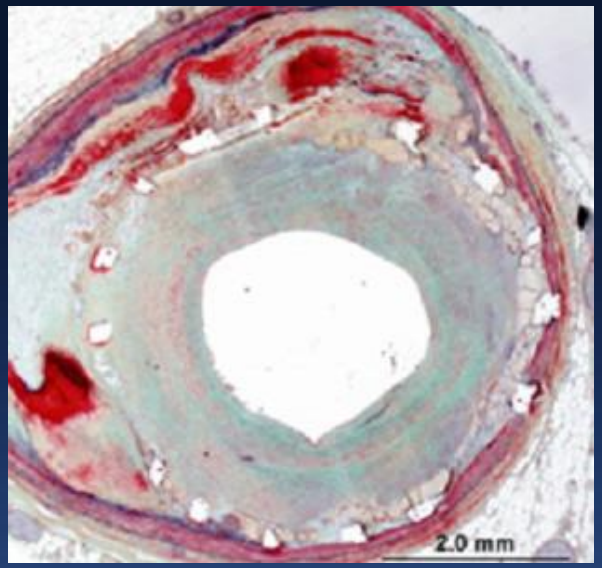
Mechanism of Stent Failure<1 year

Patient, Device and Procedure–related Multi-factors

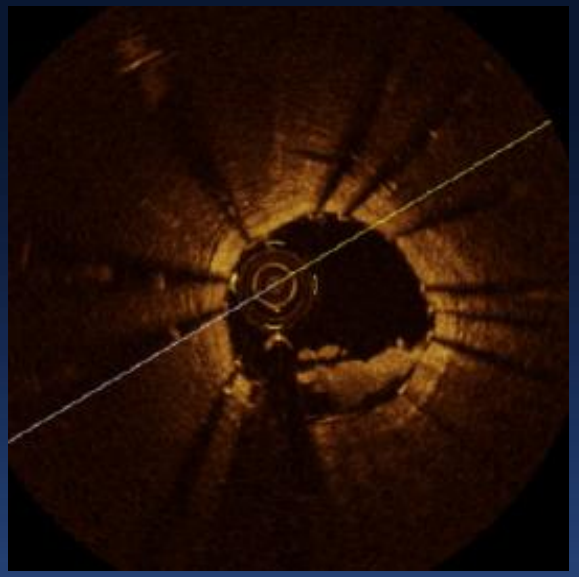
ISR (9 months)



ISR (6 months)



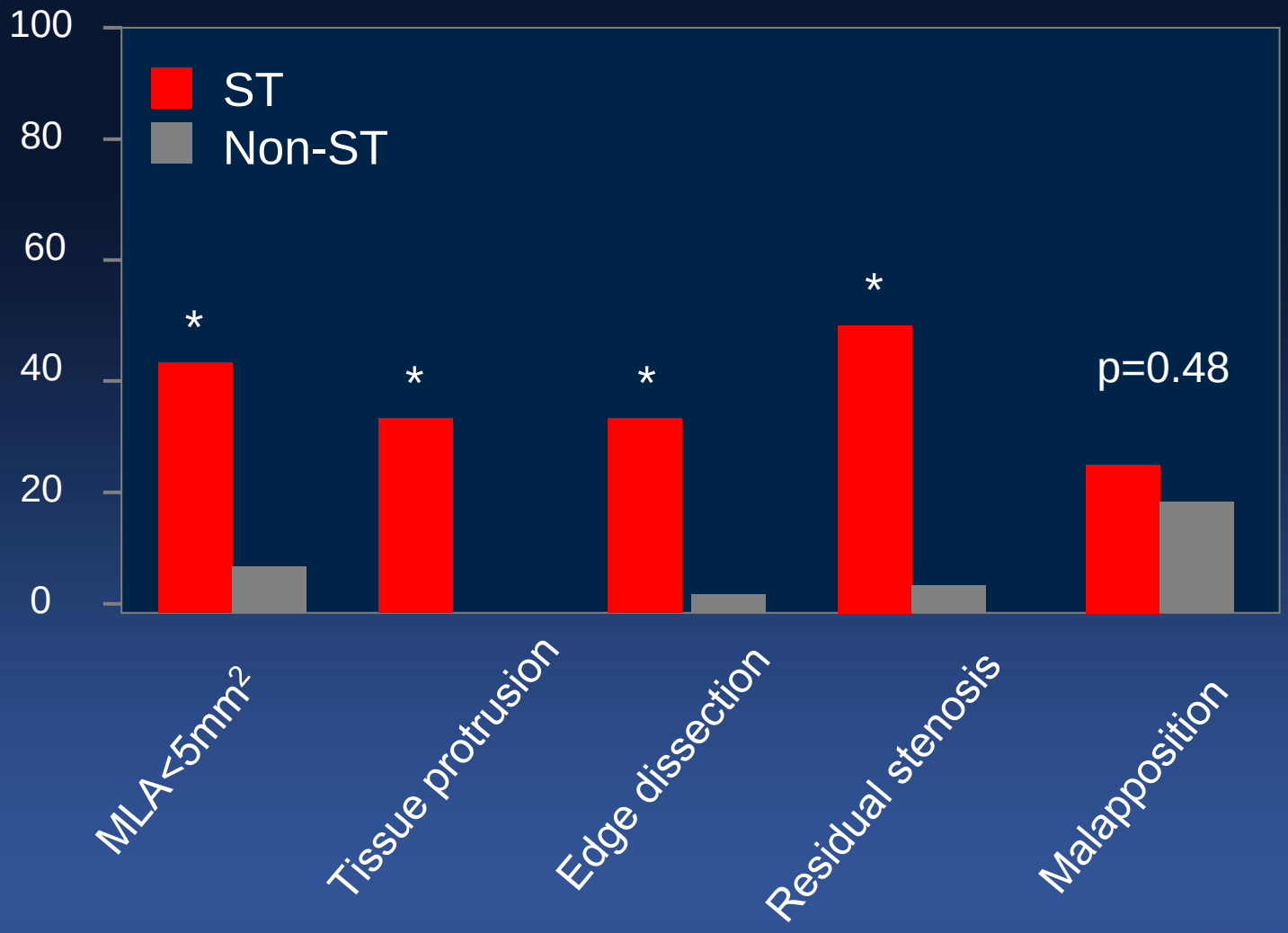
Acute ST



- Procedural – underexpansion, edge problems
- Thrombogenicity of stent or underlying plaque
- Inadequate antithrombotic drugs
- DES effects on arterial healing

Predictors for Early ST

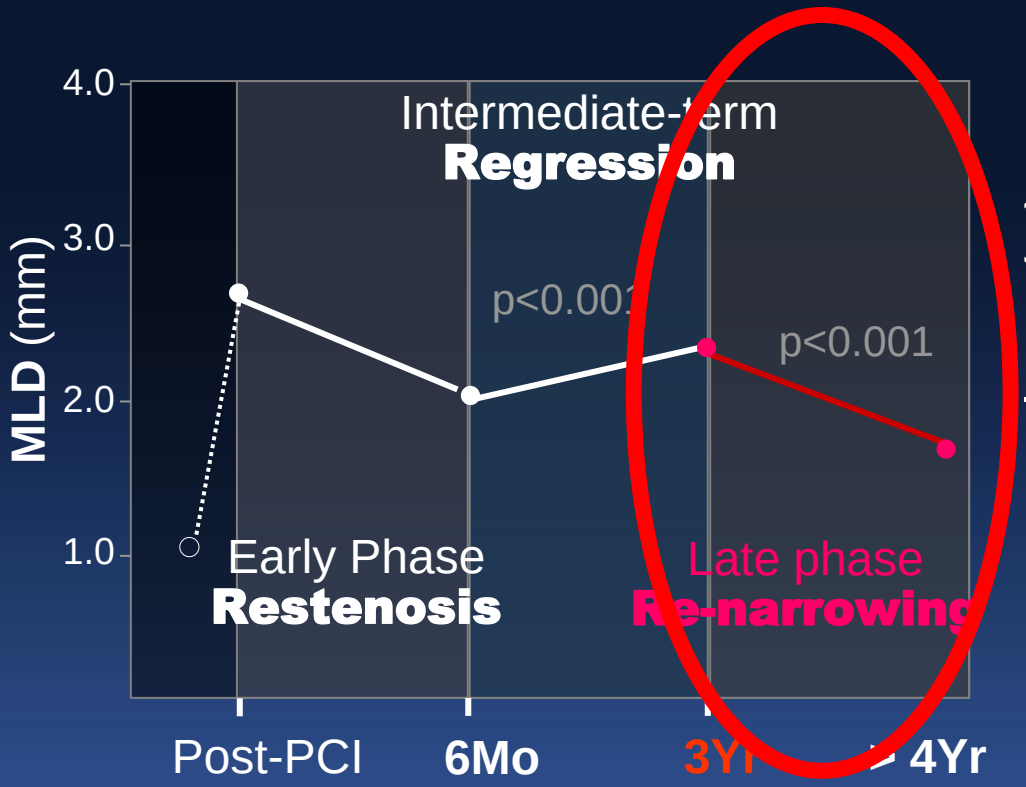
HORIZONS-AMI Substudy (Primary PCI)



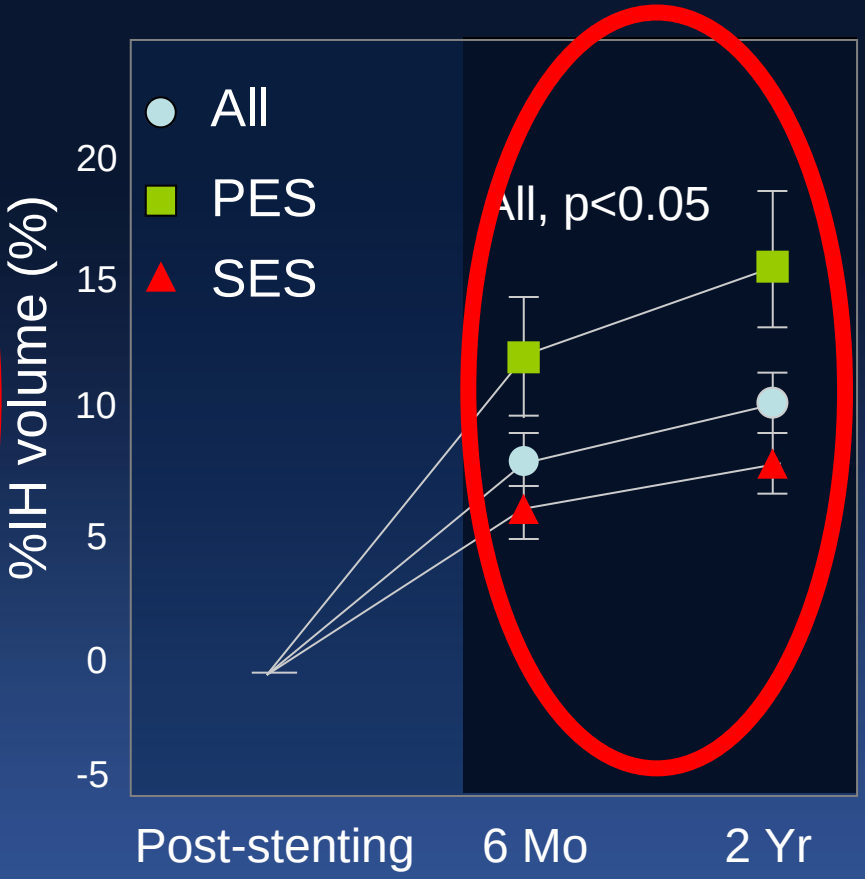
Choi et al. Circ Cardiovasc Interv 2011;4:239-47

"Late Catch-up"

Lumen Response in BMS



Serial %IH in DES



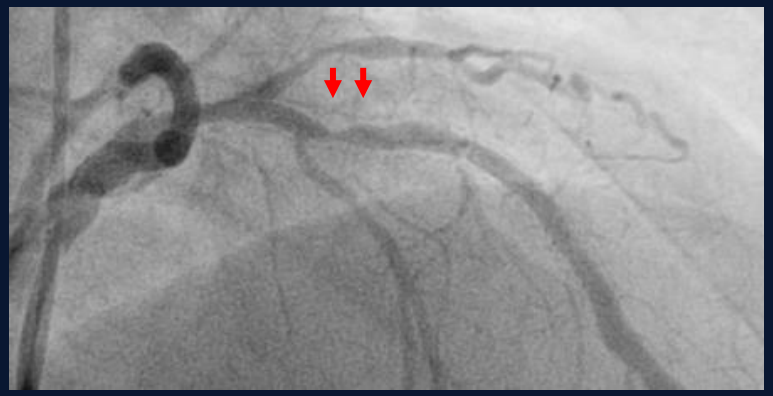
subsequent progression of IH

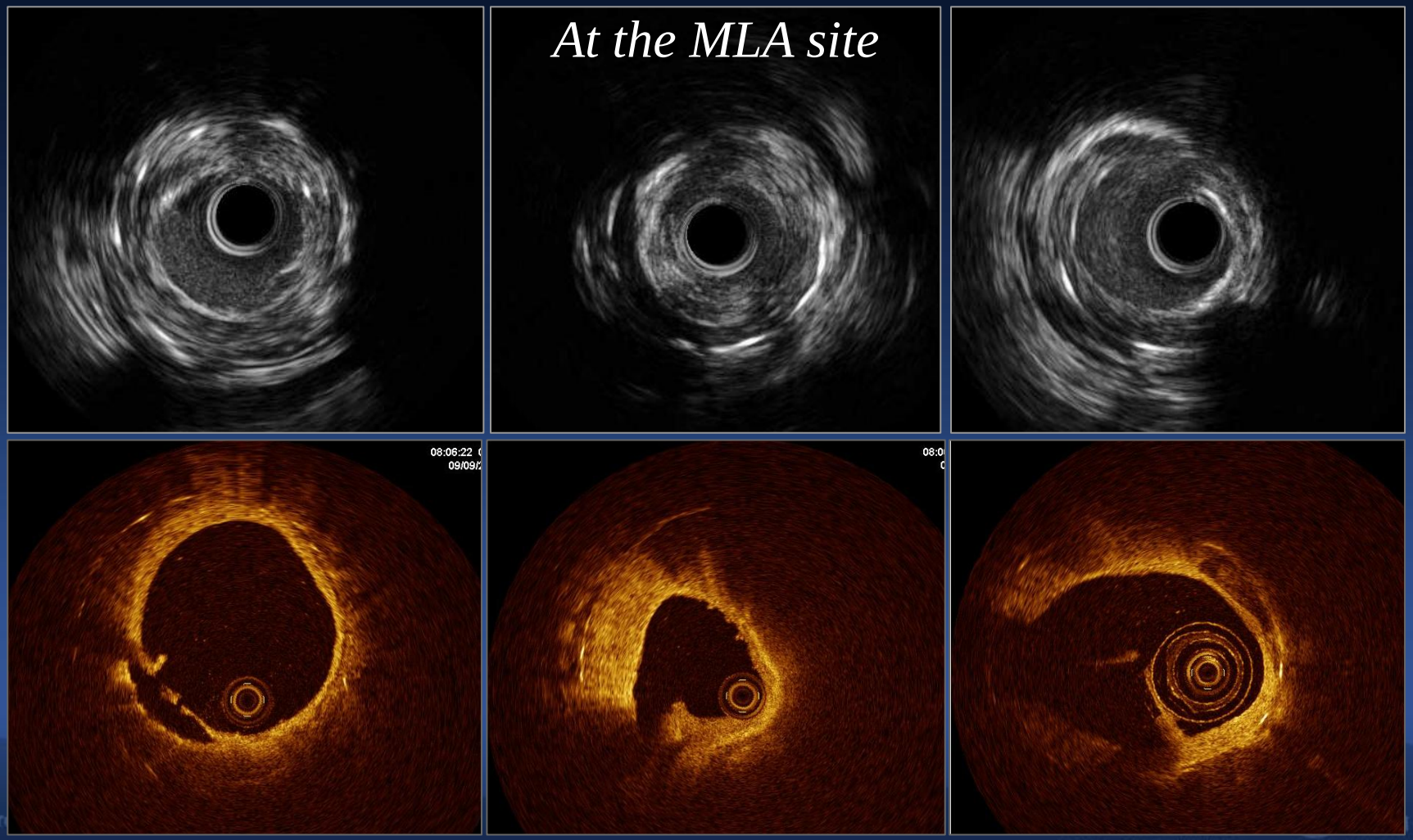
Kimura et al. Circulation 2002;105:2986-91

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

ISR in Late Phase

63-year old male, stable angina
10 YA BMS at pLAD





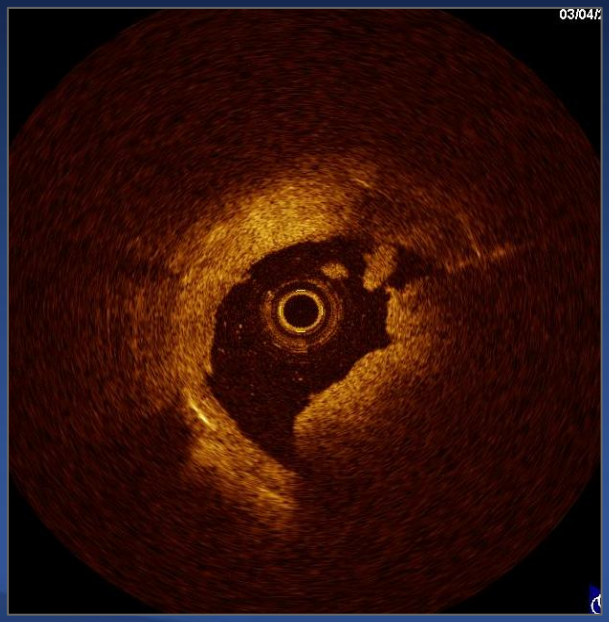
Very Late Stent Thrombosis

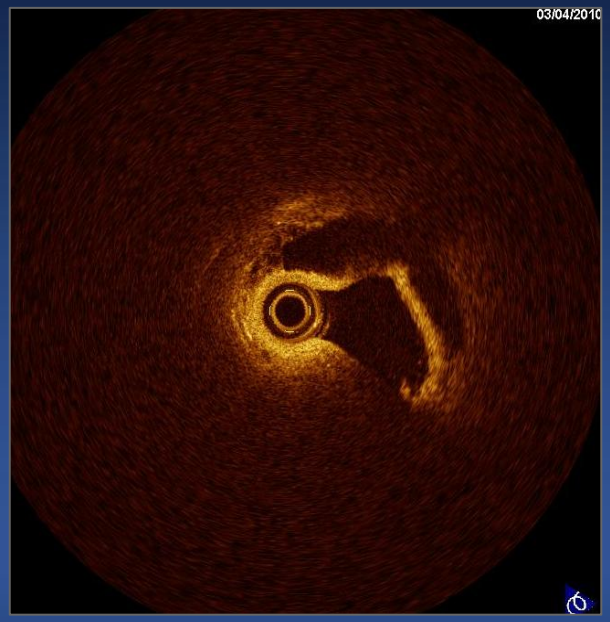
59-year old male

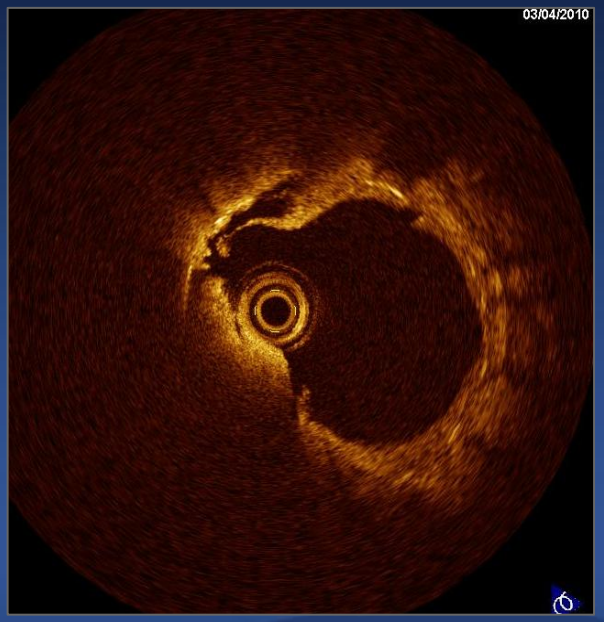
7YA Cypher implantation at OM

NSTEMI with very late ST

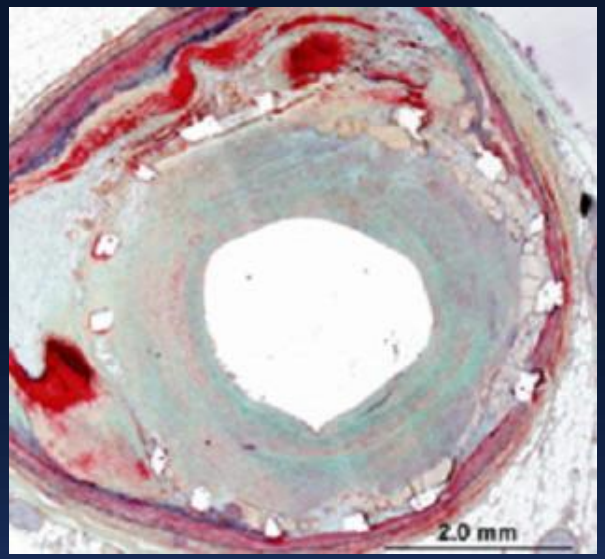
At MLA site

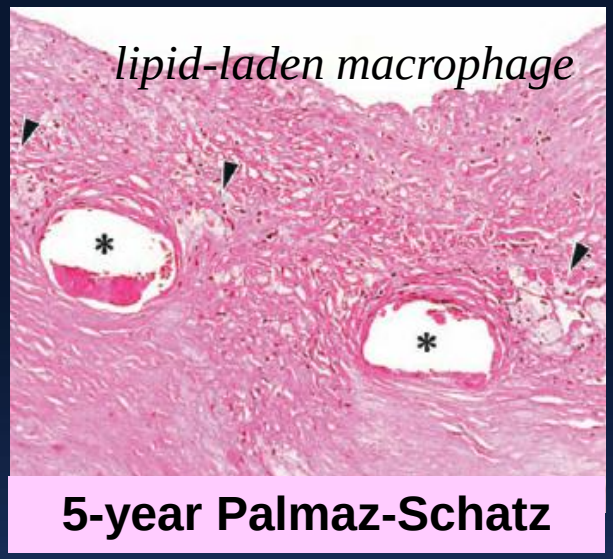




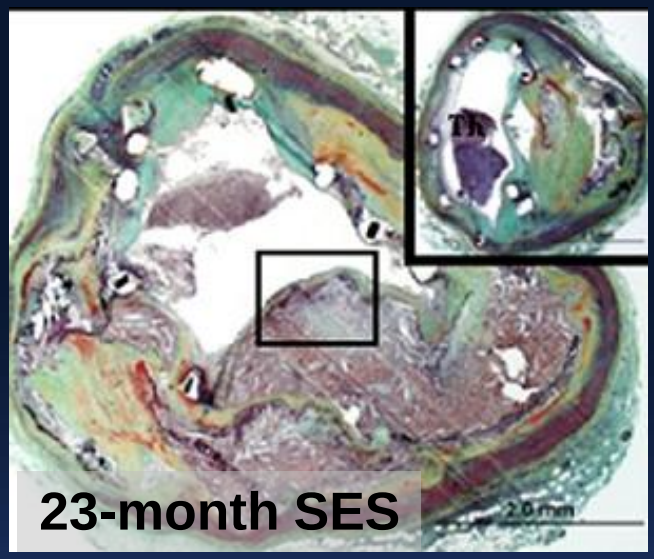


Early Neointima → Neoatherosclerosis

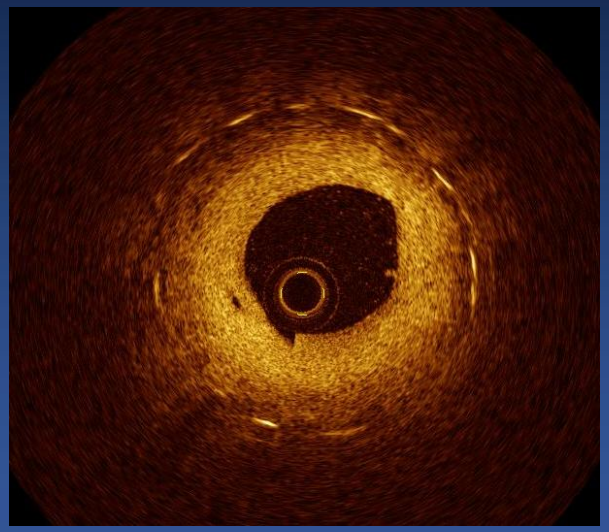


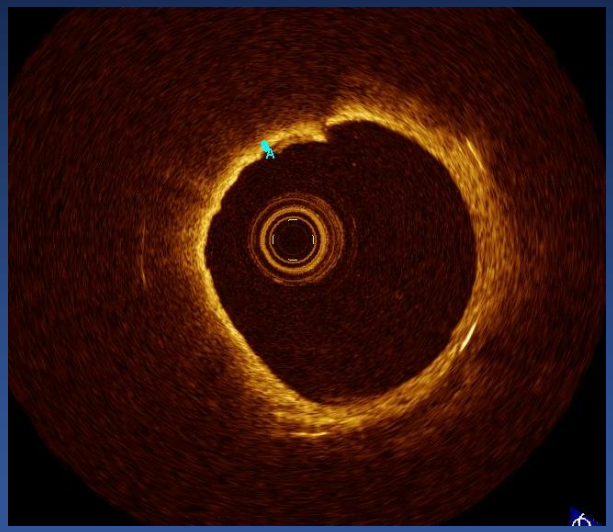


5-year Palmaz-Schatz



23-month SES





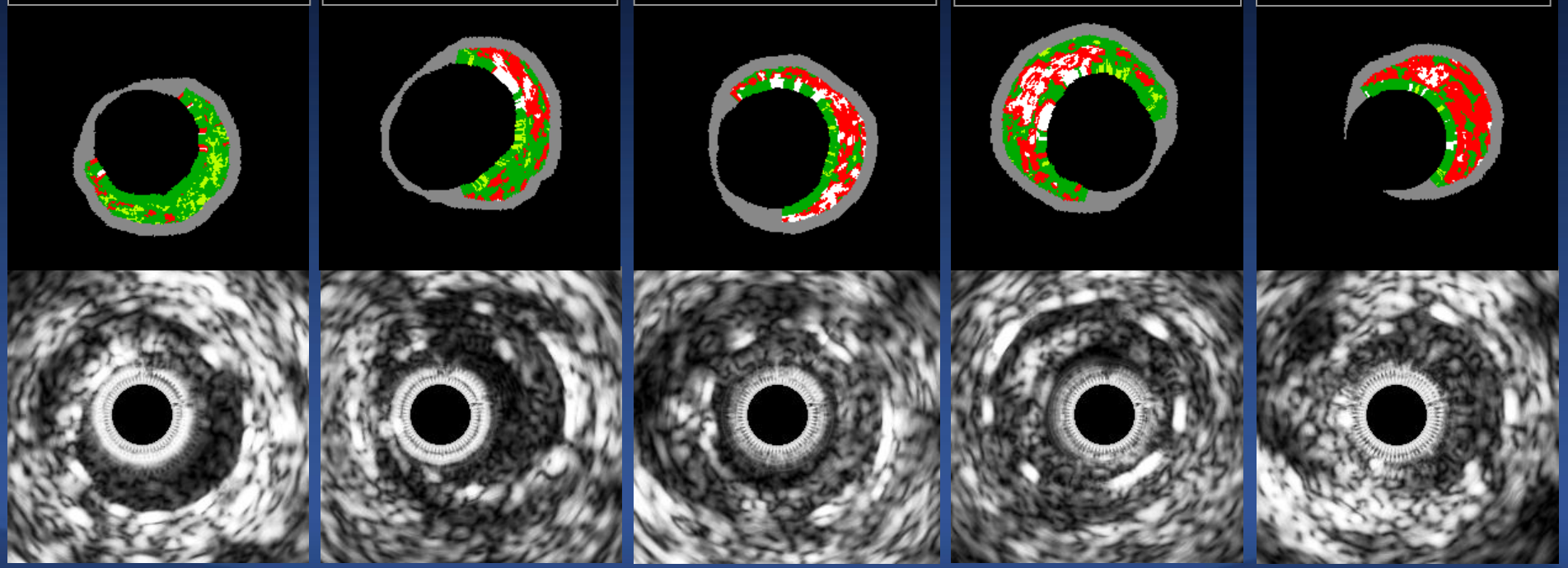
Chieffo et al. Am J Cardiol 2009;104:1660–7
Nakazawa et al. JACC Cariovasc Imaging 2009;2:625-8

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,*]

The longer f/u duration, the greater atherosclerotic change

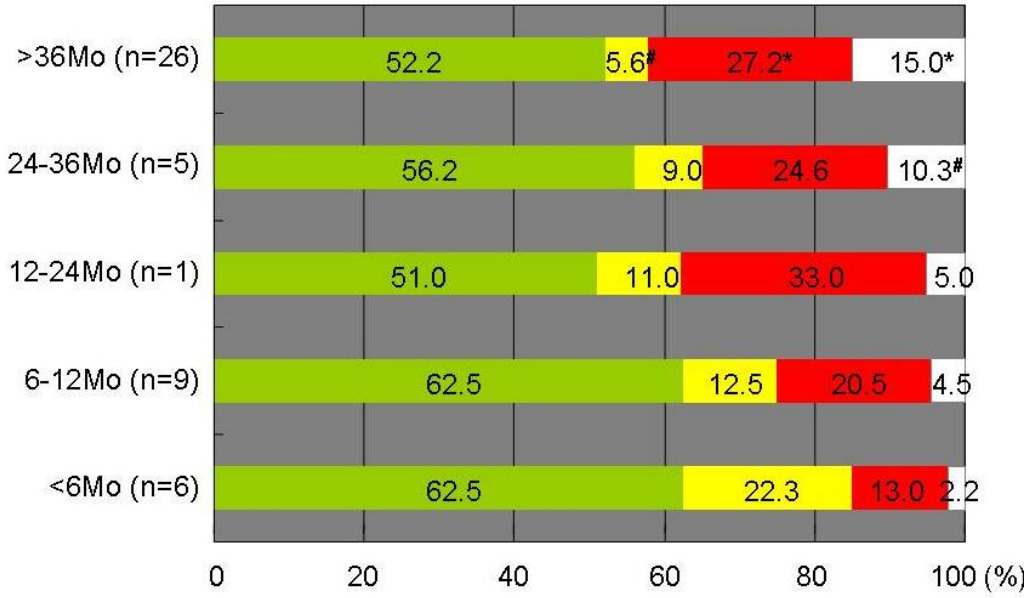
6-mo Taxus	9-mo Taxus	22-mo Taxus	48-mo BMS	57-mo BMS
%NC 8%	%NC 28%	%NC 39%	%NC 40%	%NC 57%
%DC 2%	%DC 8%	%DC 20%	%DC 25%	%DC 15%



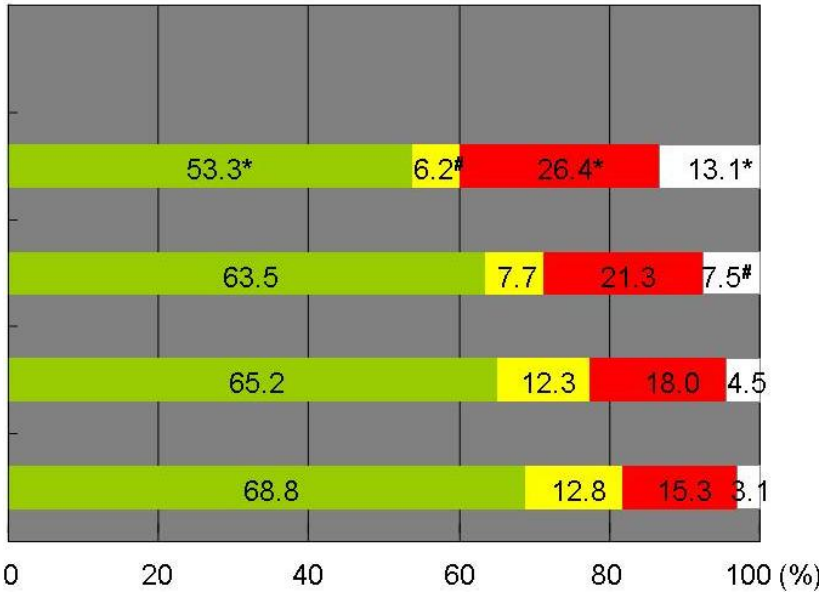
Kang SJ et al. AJC 2010 ;106:1561-5

Neointimal VH Composition

47 BMS-ISR



70 DES-ISR



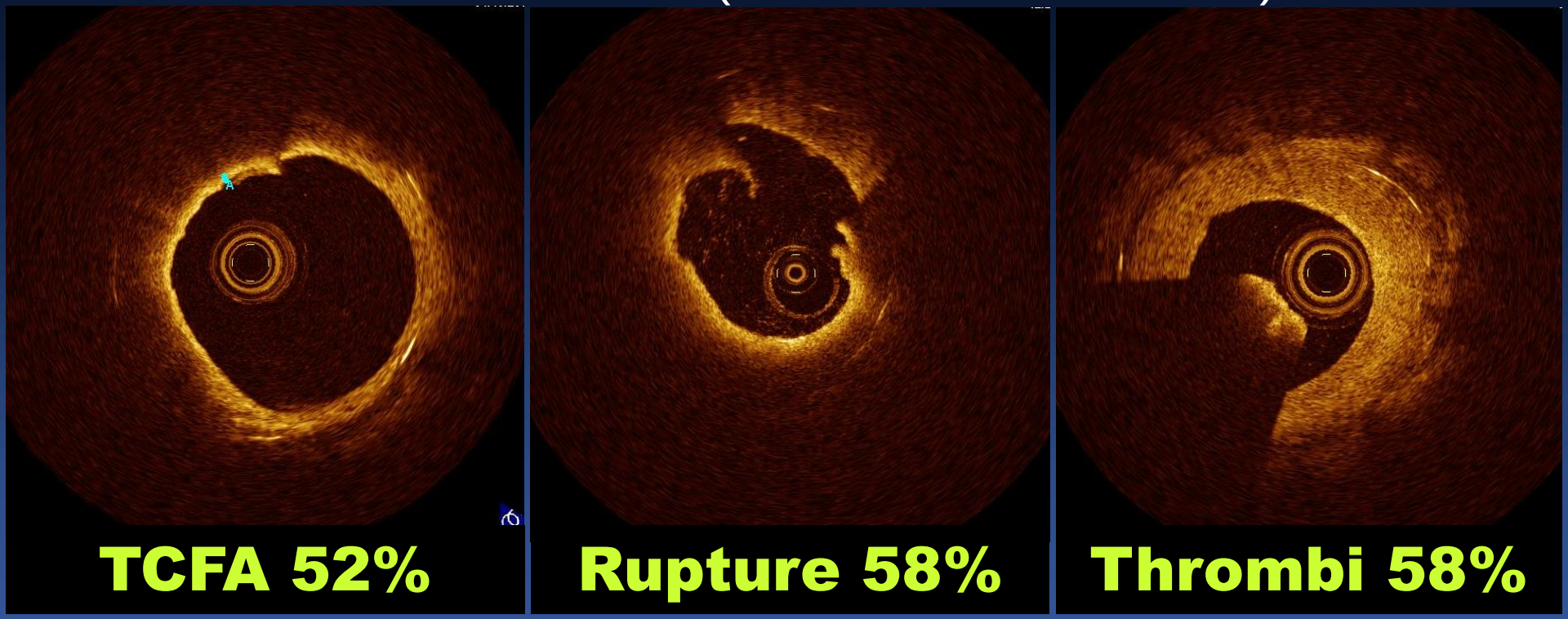
*p<0.01 and #p<0.05, vs. lesions at follow-up time <6 months

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

50 DES-ISR (Median F/U 32 months)



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

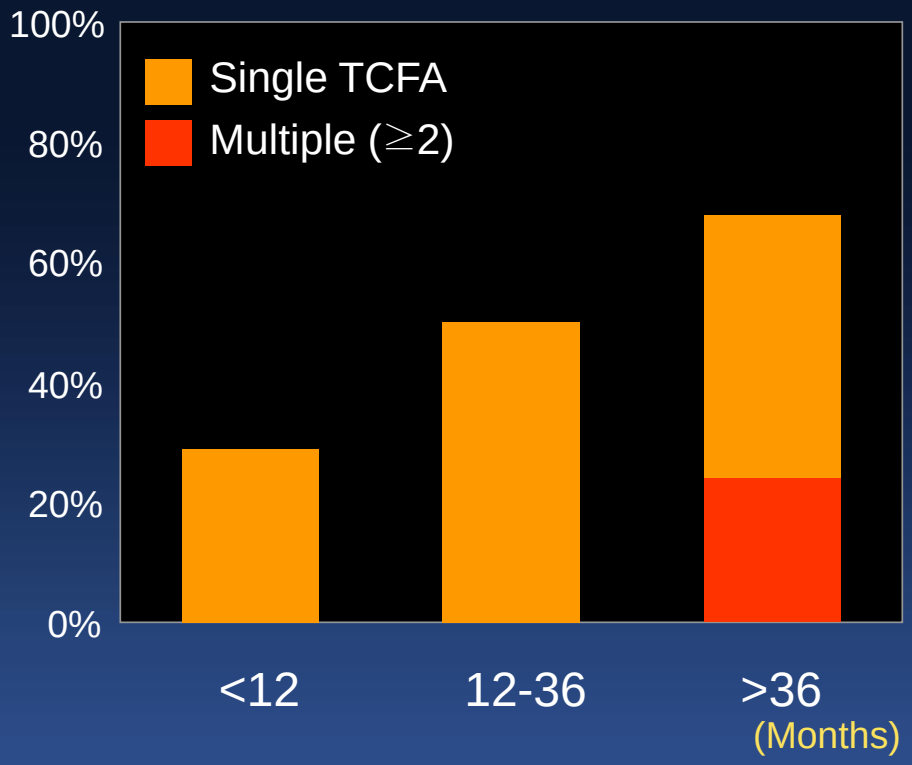
Stable vs. Unstable Angina

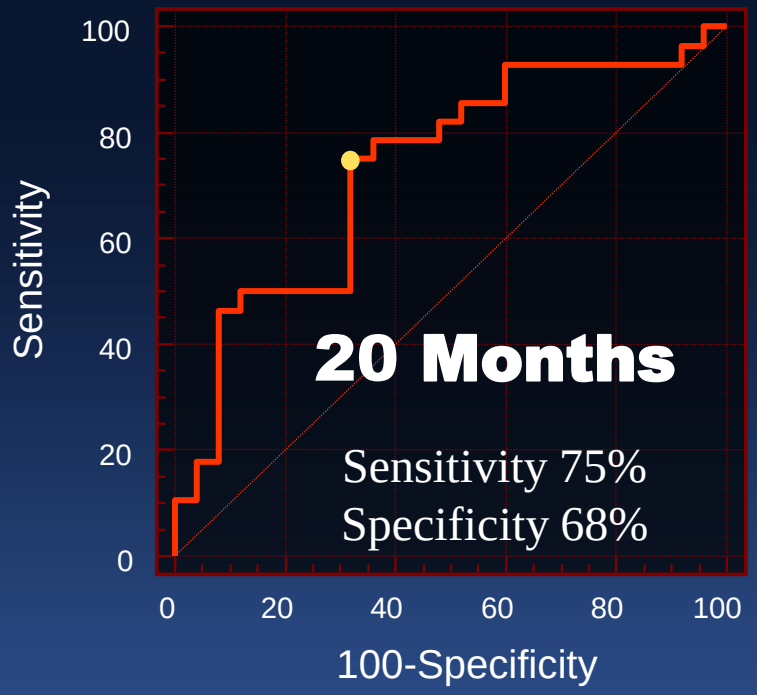
	Stable N=30	Unstable N=20	P
Fibrous cap thickness, μm	100 (60-205)	55 (42-105)	0.006
Incidence of thrombi	13 (43%)	16 (80%)	0.010
Incidence of red thrombi	1 (3%)	6 (30%)	0.012
Incidence of rupture	14 (47%)	15 (75%)	0.044
Incidence of TCFA	11 (37%)	15 (75%)	0.008

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

DES Duration >20 Months

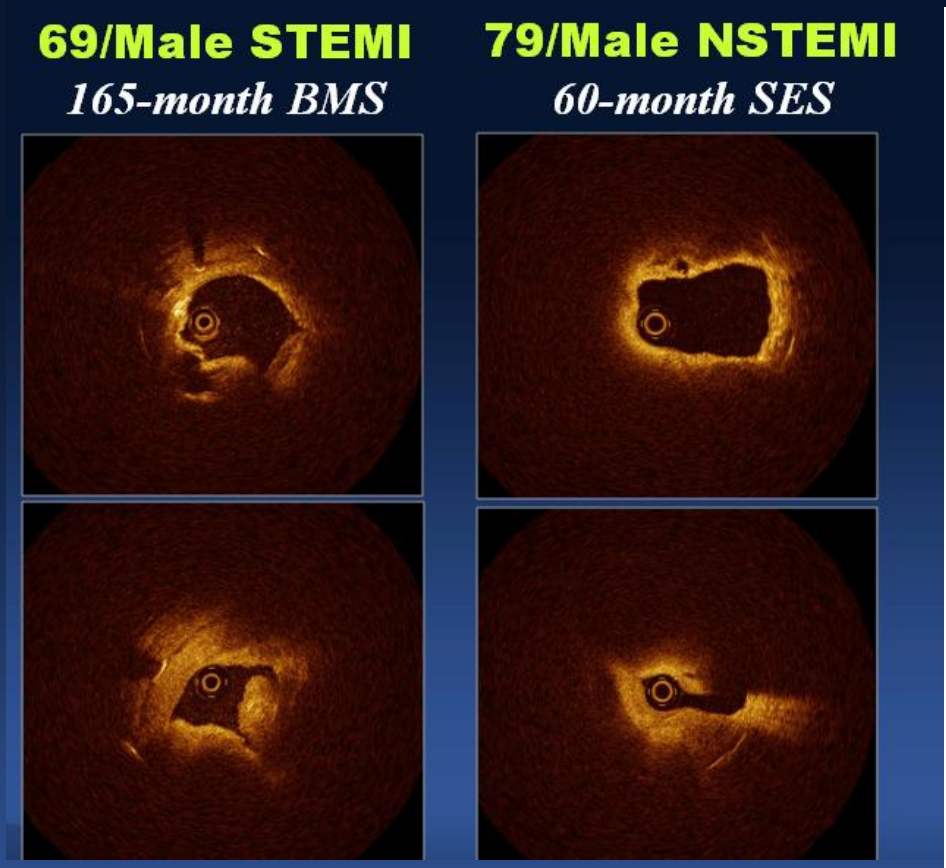
Best Predict TCFA-Containing Neointima

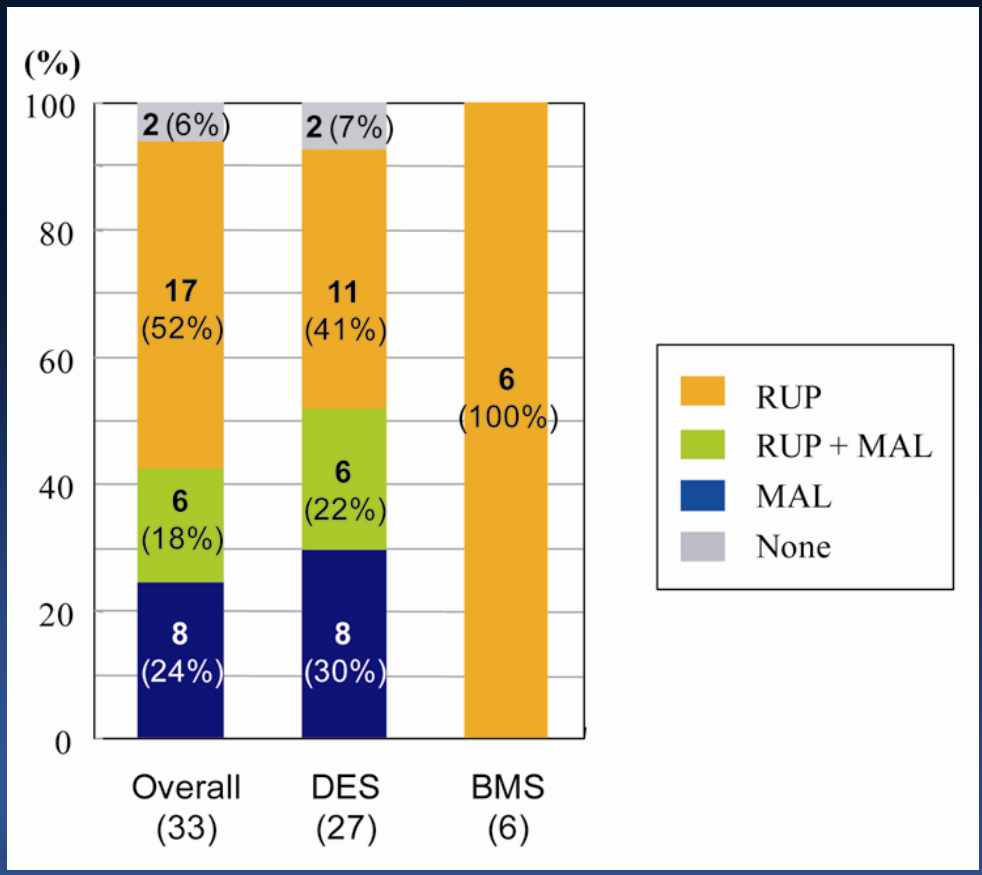




Kang et al. Circulation 2011;123:2954-63

OCT Analysis in Definite VLST



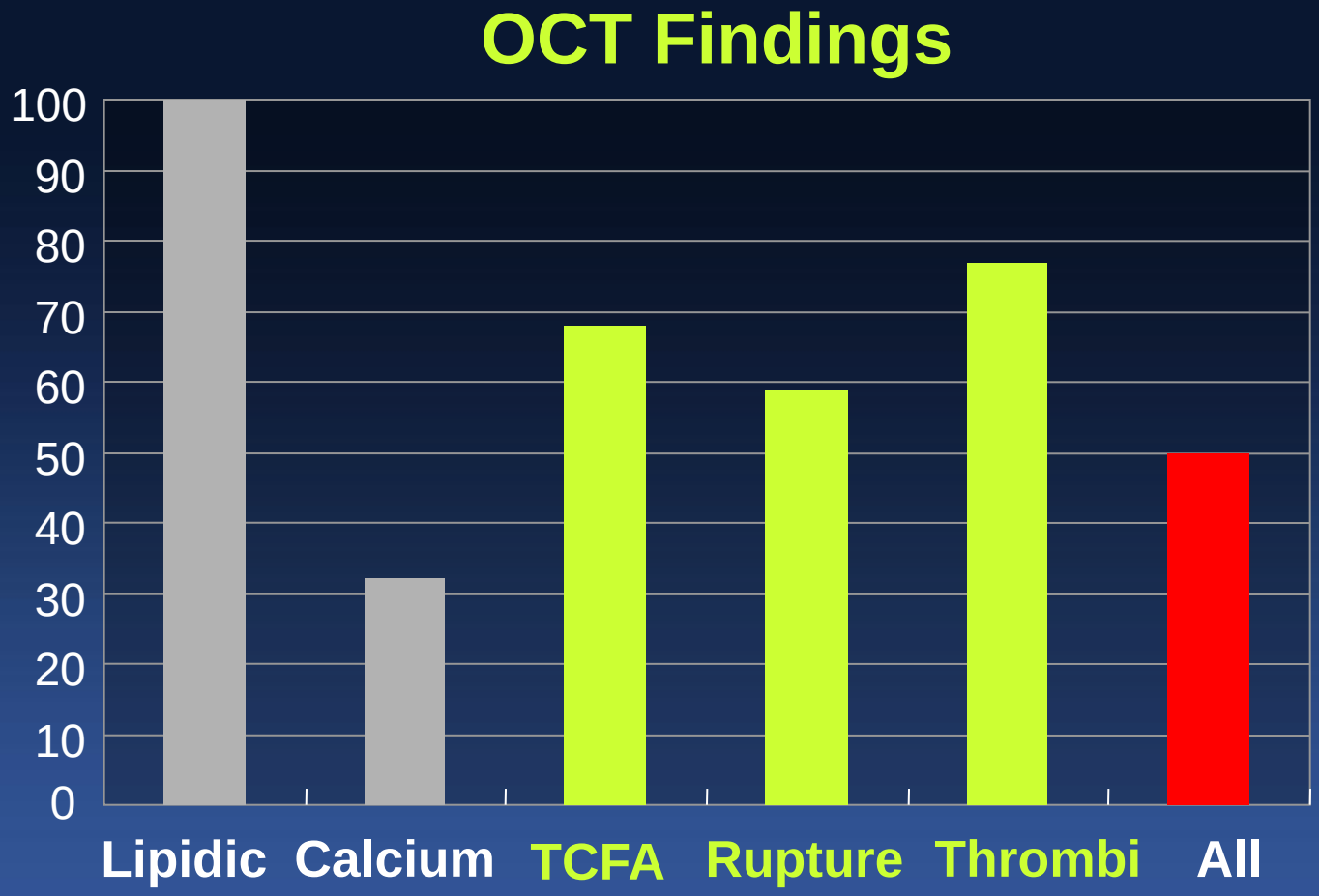


TCFA: DES 56%, BMS 100%

Kang et al. JACC Cardiovasc imaging 2013 in press

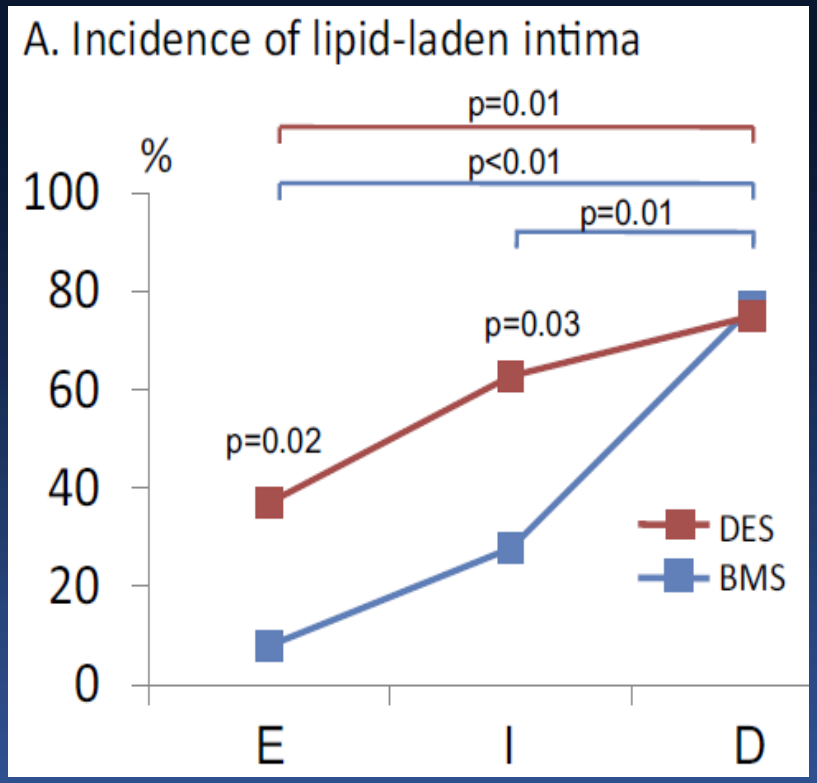
BMS-ISR at 10 Years

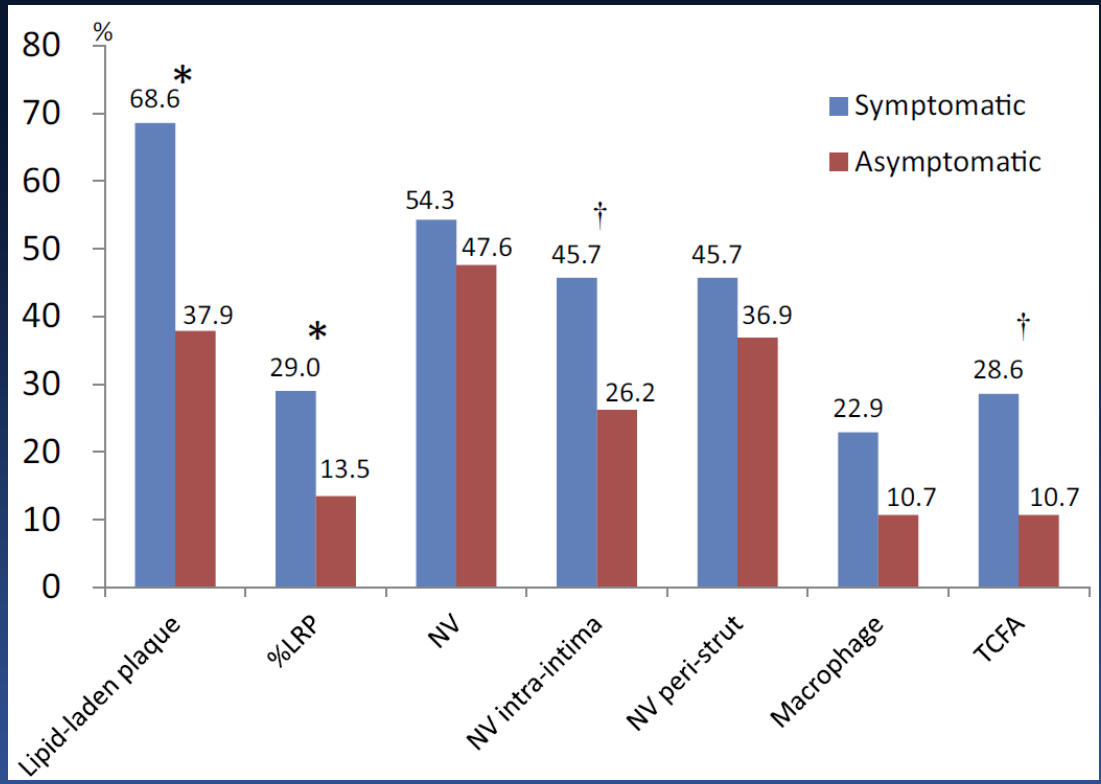
Clinically-driven TLR, Median F/U 11 years



Kang et al. JACC Cardiovasc Imaging 2012;5:1267-8

Incidence and Time Course of Neoatherosclerosis; from MGH OCT registry





<9 mo 9–48 mo >48 mo

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

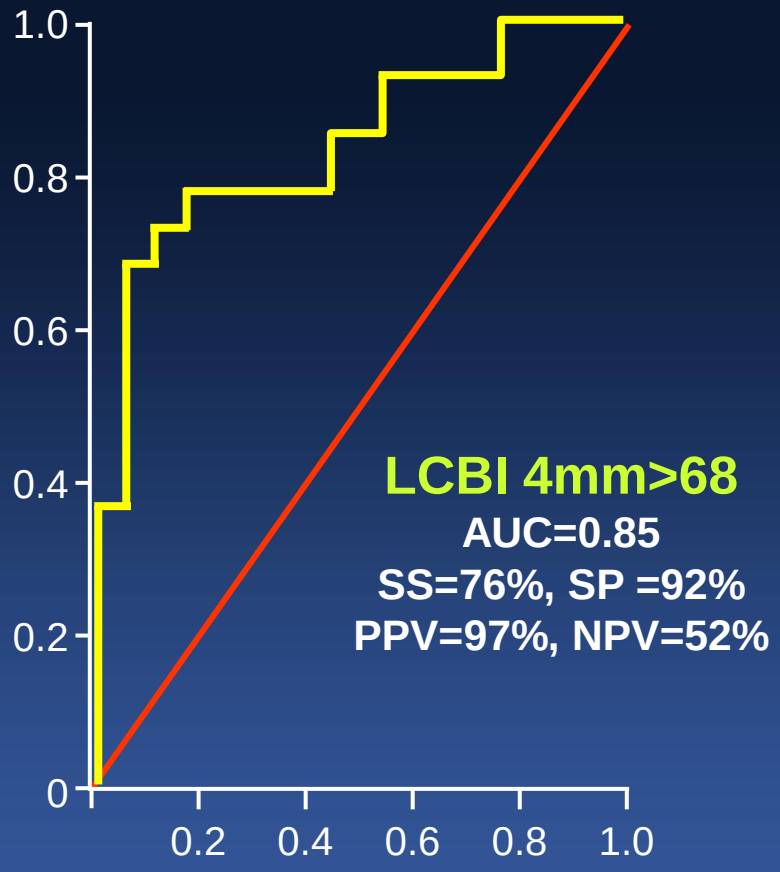
Predictors for Neoatherosclerosis

Retrospective Study 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
Age >65 years	1.84	0.85 – 3.97	0.121
Stent age >48 months	10.45	3.71 – 29.41	<0.001
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

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

NIRS vs. OCT
to Predict Neoatherosclerosis



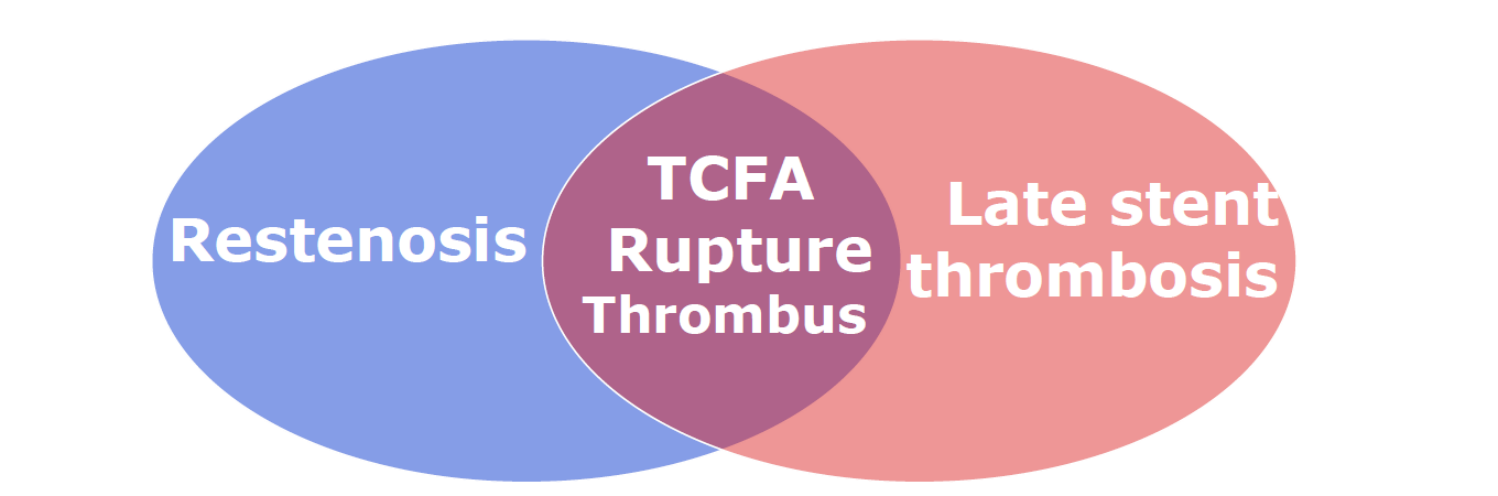
- **LCBI-4mm > 68** was the best threshold for OCT-visualized lipid core within neointima
- Inverse correlation between LCBI and cap thickness (0.22, 95% CI 0.05-0.39; P=0.01)

Ali ZA et al. Circ Interv 2013;6:507-17

Summary

Neoatherosclerosis is a common mechanism of late restenosis and very late stent thrombosis

Late Stent Failure



In-stent Neoatherosclerosis