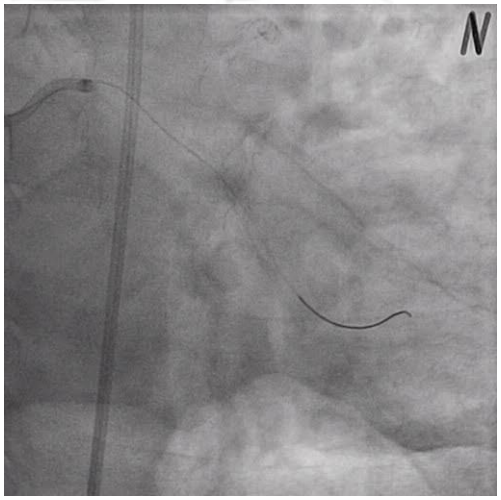
"Neo-atherosclerosis"

Featured Insights from OCT Studies

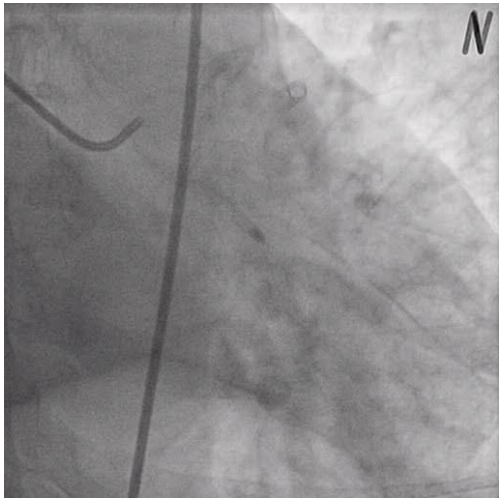
So-Yeon Choi, MD., PhD.
Department of Cardiology
Ajou University School of Medicine

Case #1

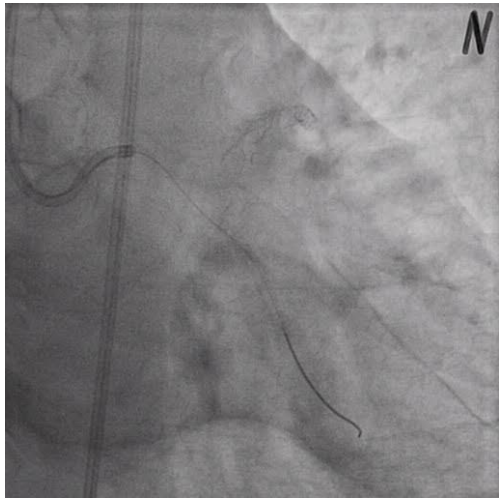
M/56 with AMI (lat)
PCI with Endeavor stent 2.75 x 12mm at OM 18 months ago



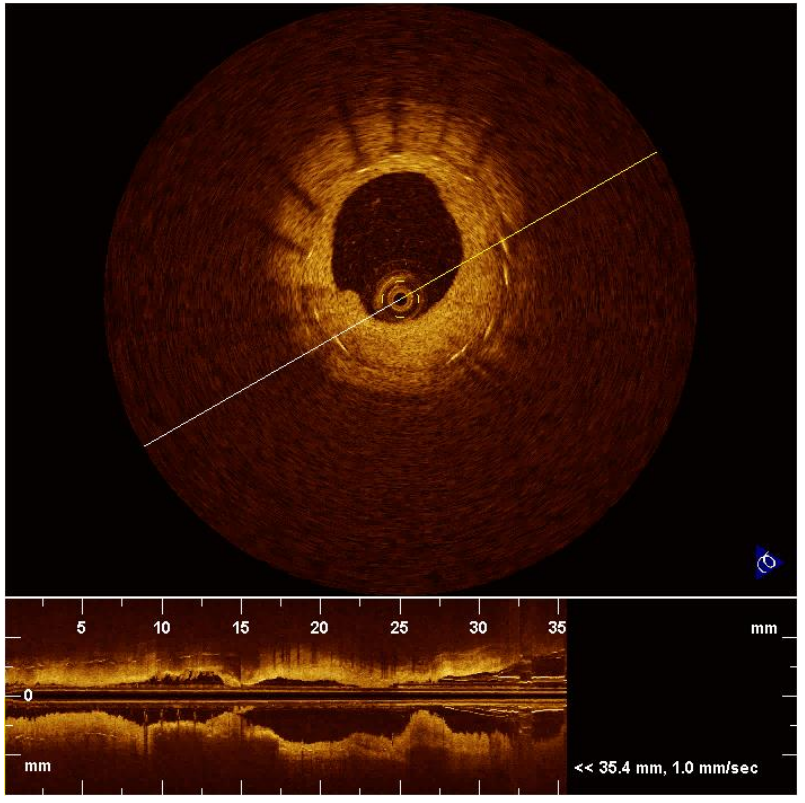
18mo ago

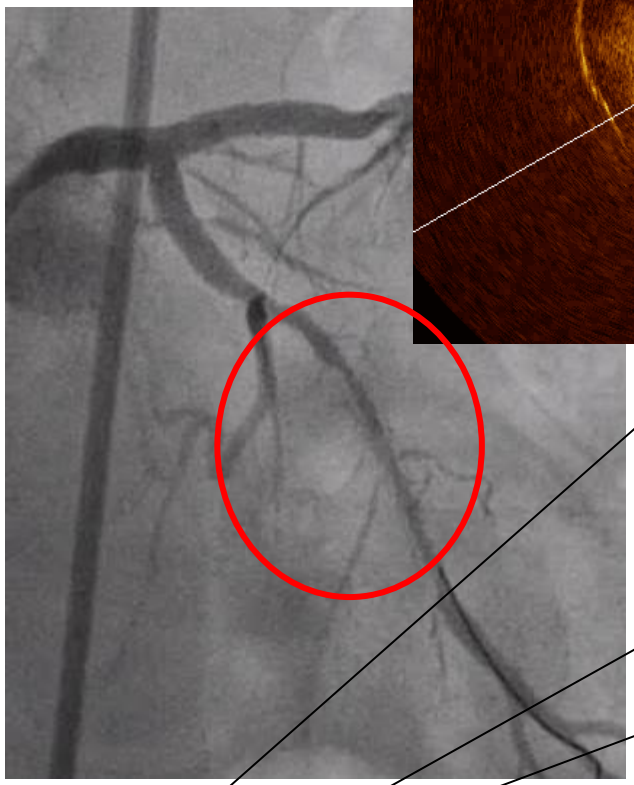


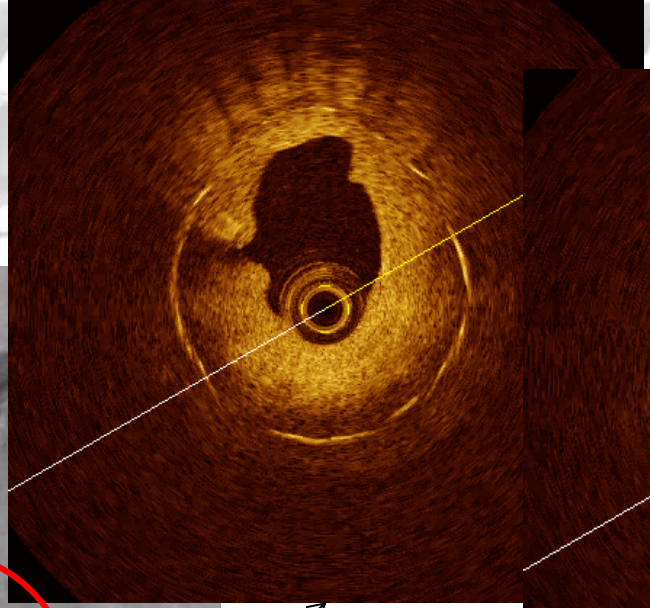
Baseline

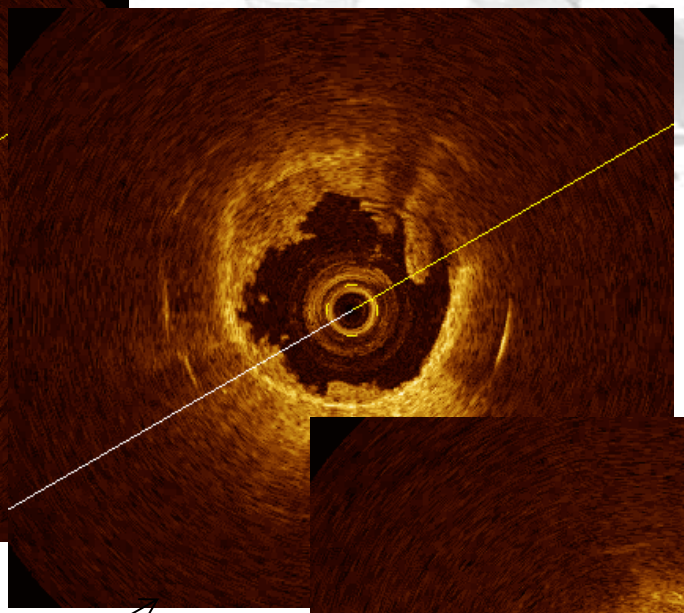


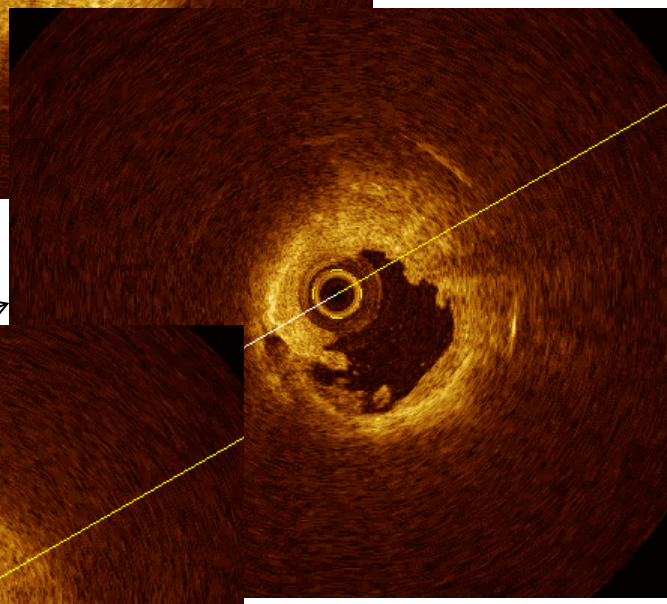
After thrombosuction

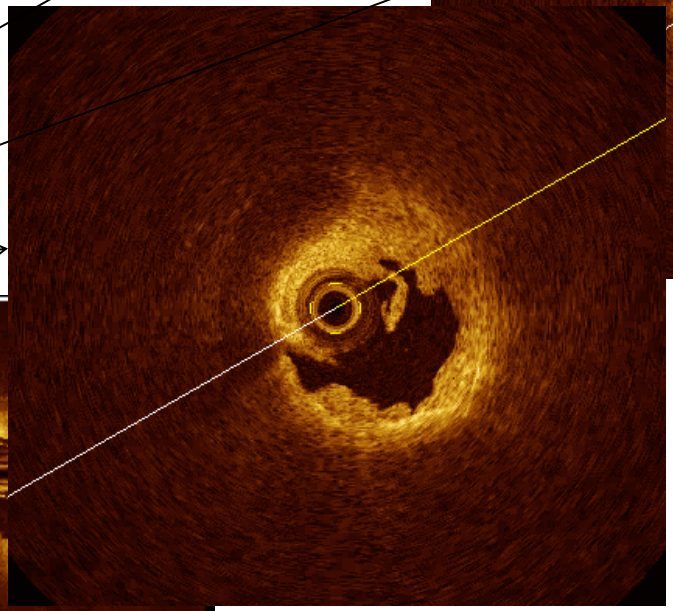


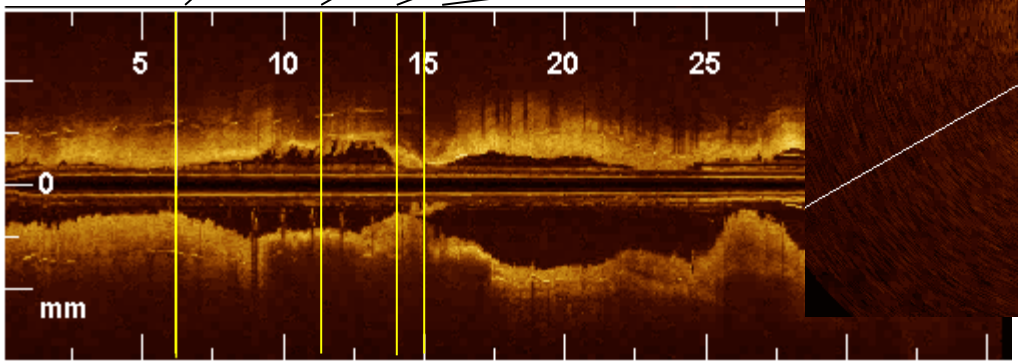








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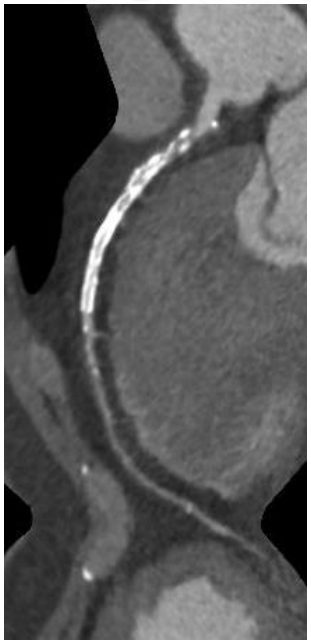
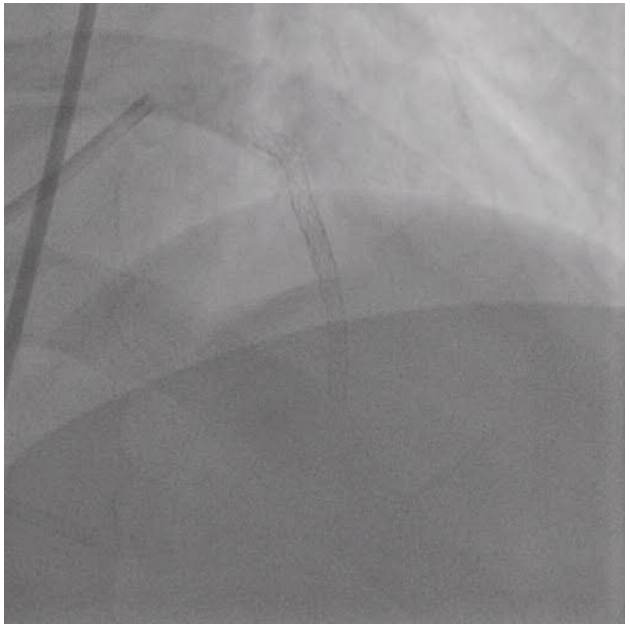
Case #2

M/67 with UAIB (recent exertional chest pain)
PCI with BMS at mLAD on Mar.1998

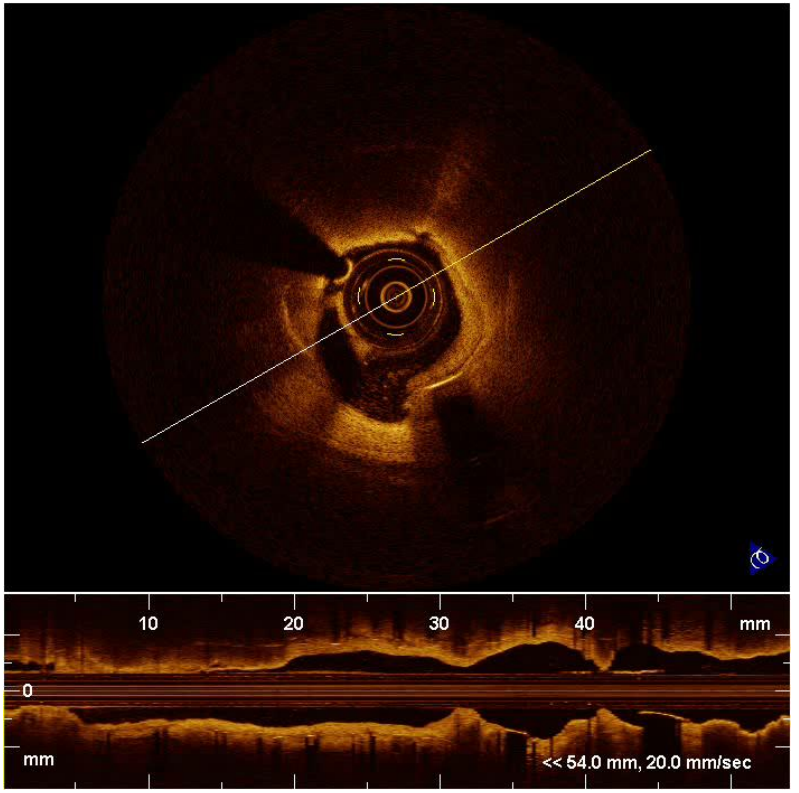
A Live Case presented by Dr YJ Hong in 2011GICS

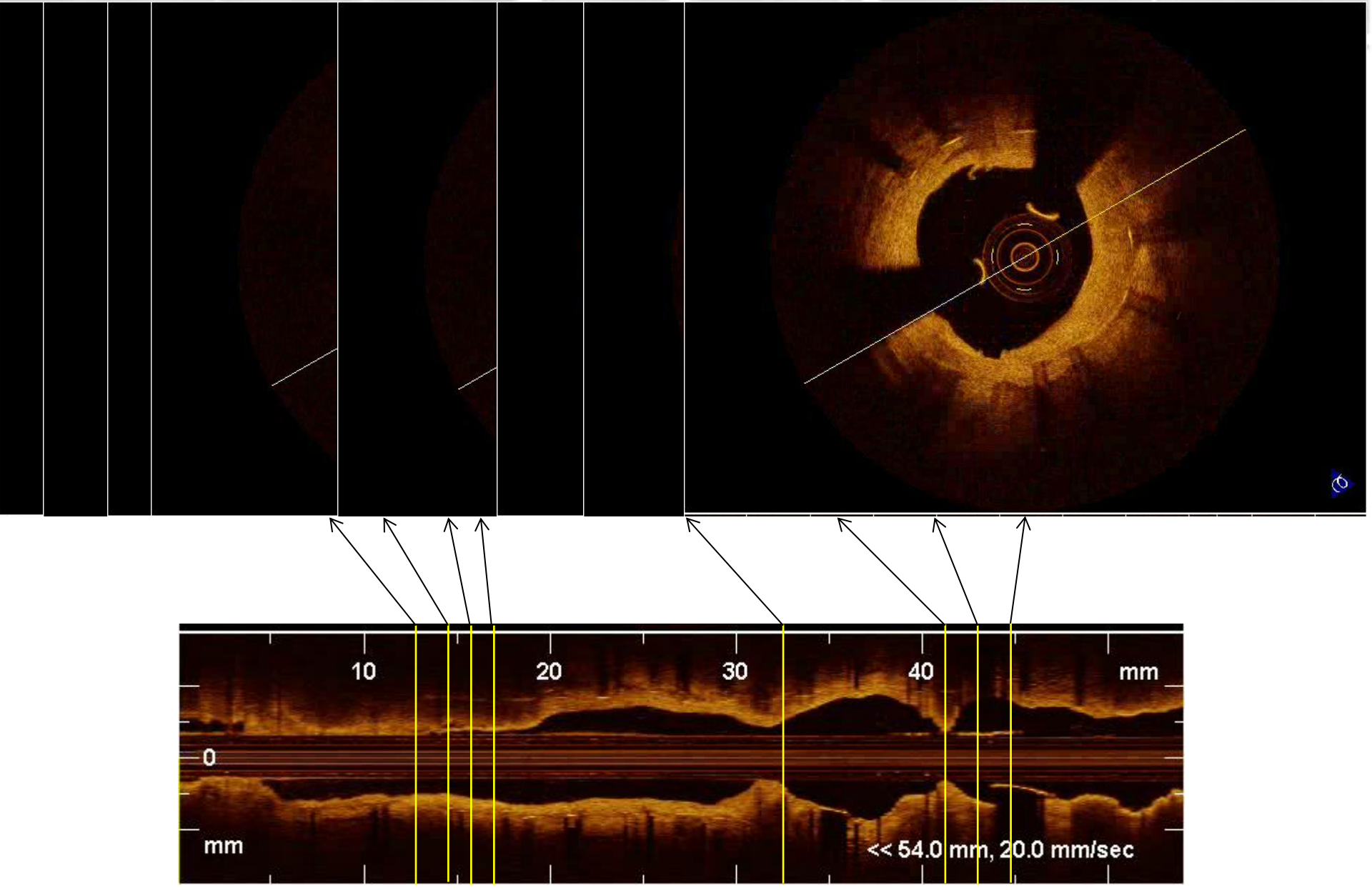


Cardiac CT on Jan 2011



Coronary angiogram and OCT on Jun 2011

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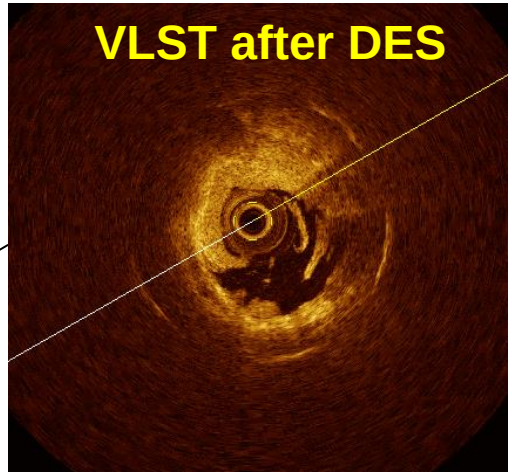
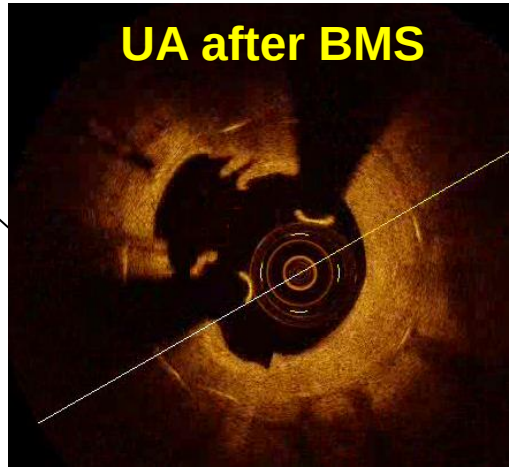
<< 54.0 mm, 20.0 mm/sec

Neo-atherosclerosis

Nouveau Atherosclerosis





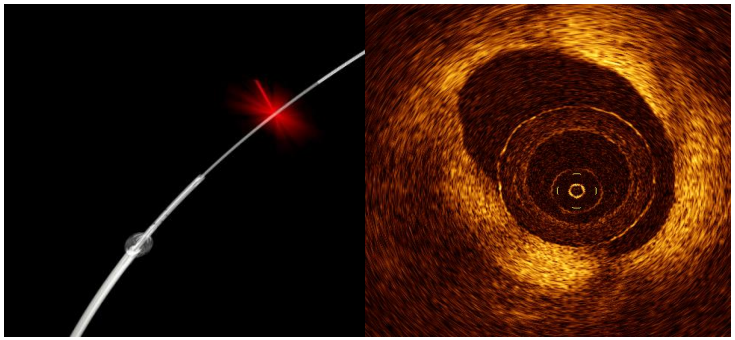
What is Neo-atherosclerosis?

Nouveau(=new) atherosclerosis

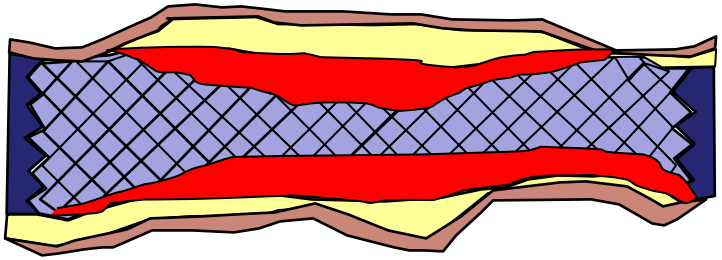
Ruptured Neointima

Lipid-laden (lipid-rich) neointima

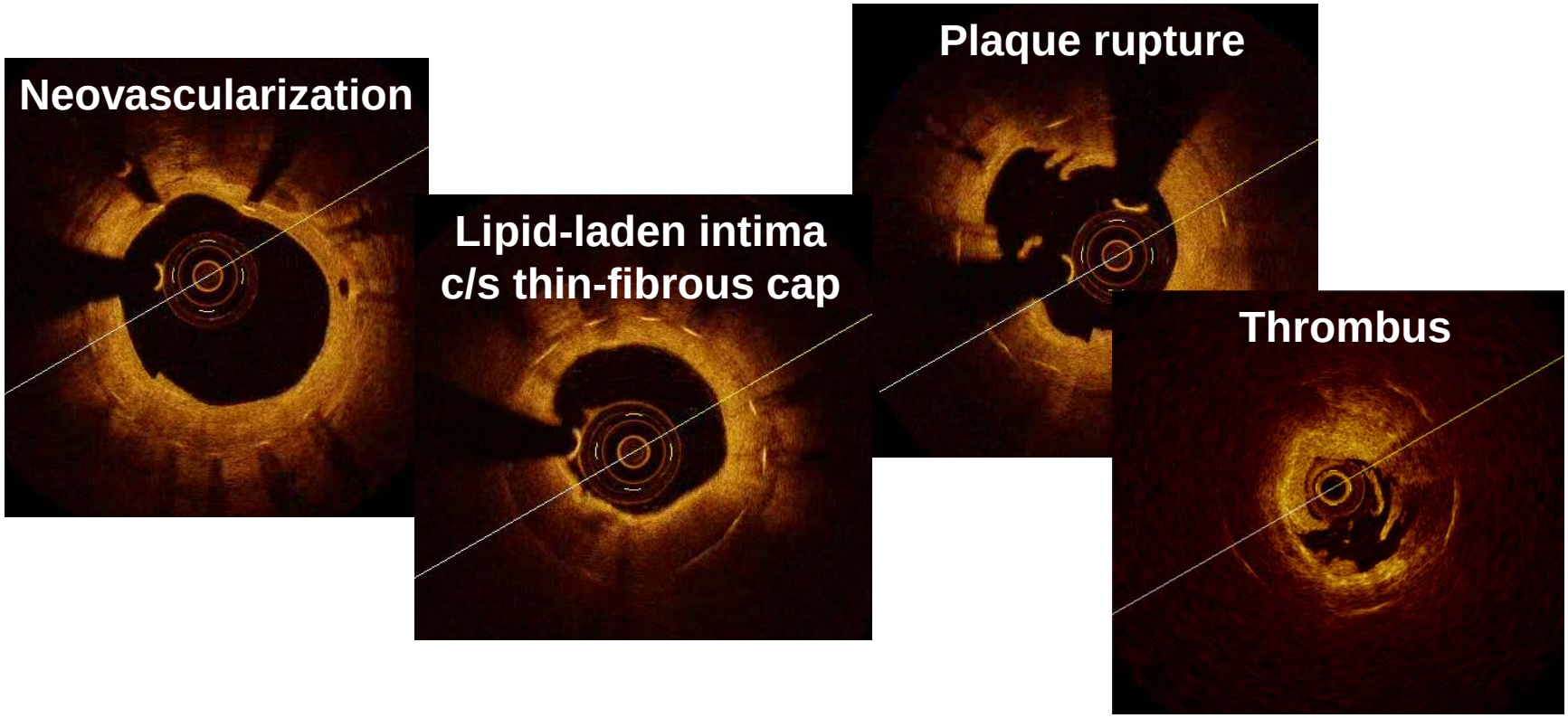
Neo-atherosclerosis (NAS) in OCT Studies



A high resolution imaging technology provides new understanding of the progression intima or the genesis of new atherosclerosis over the time sequence after stenting.



Neo-atherosclerosis (NAS) in OCT Studies

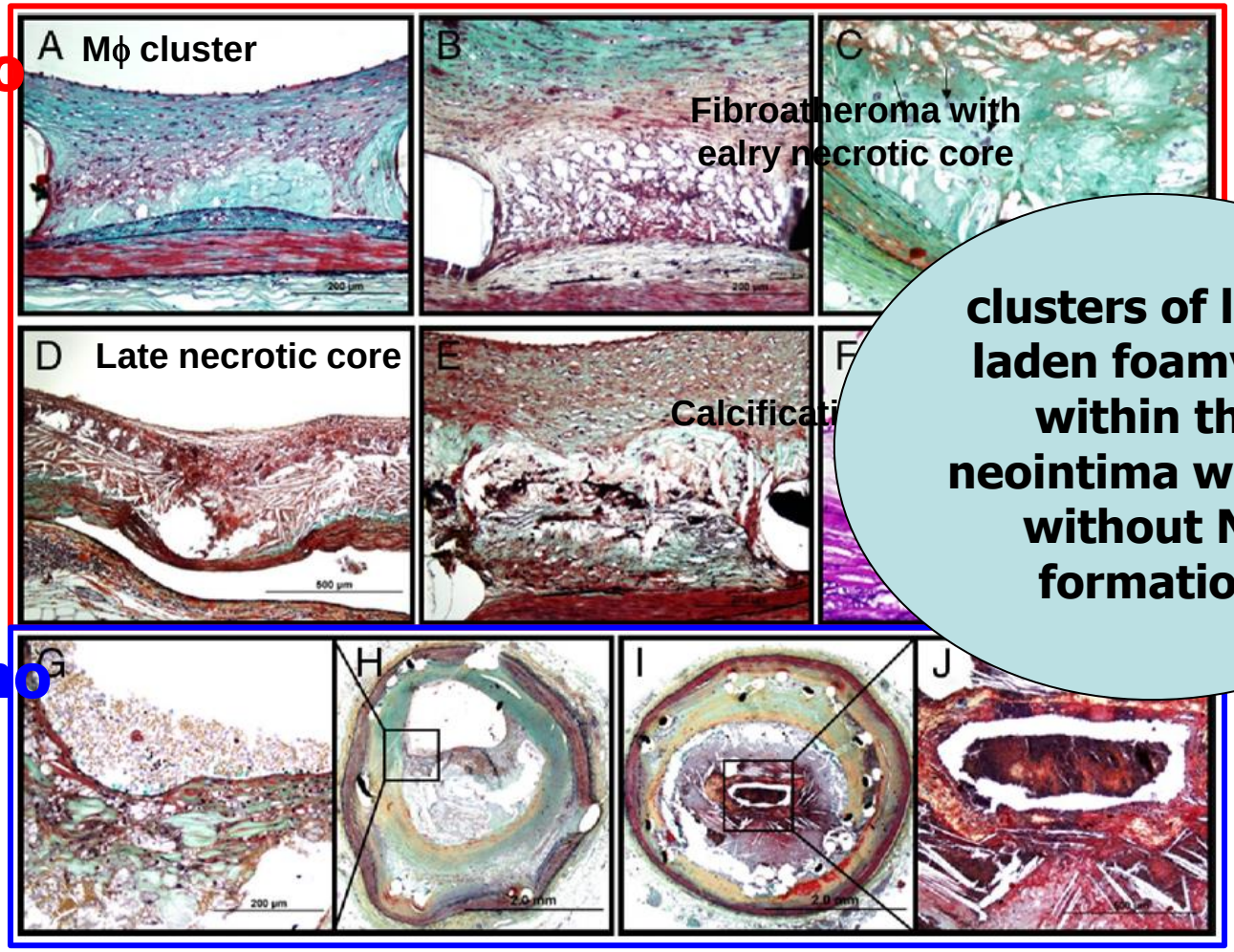


Neo-atherosclerosis (NAS) in Pathologic Studies

Representative Images of Various Stages of Newly Formed Atherosclerosis Within Neointima After Stent Implantation

SES 13mo

BMS 61mo

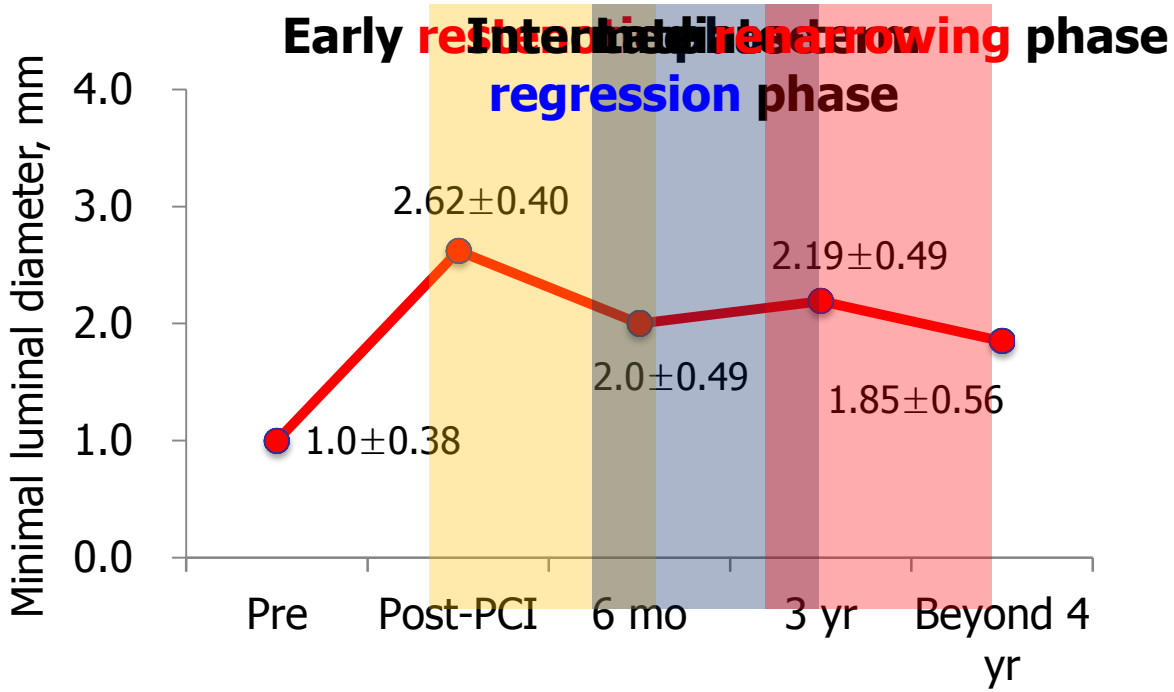


Nakazawa et al, J Am Coll Cardiol 2011;57:1314–22

Onset, Prevalence and Mechanism

Serial Changes in MLD after BMS

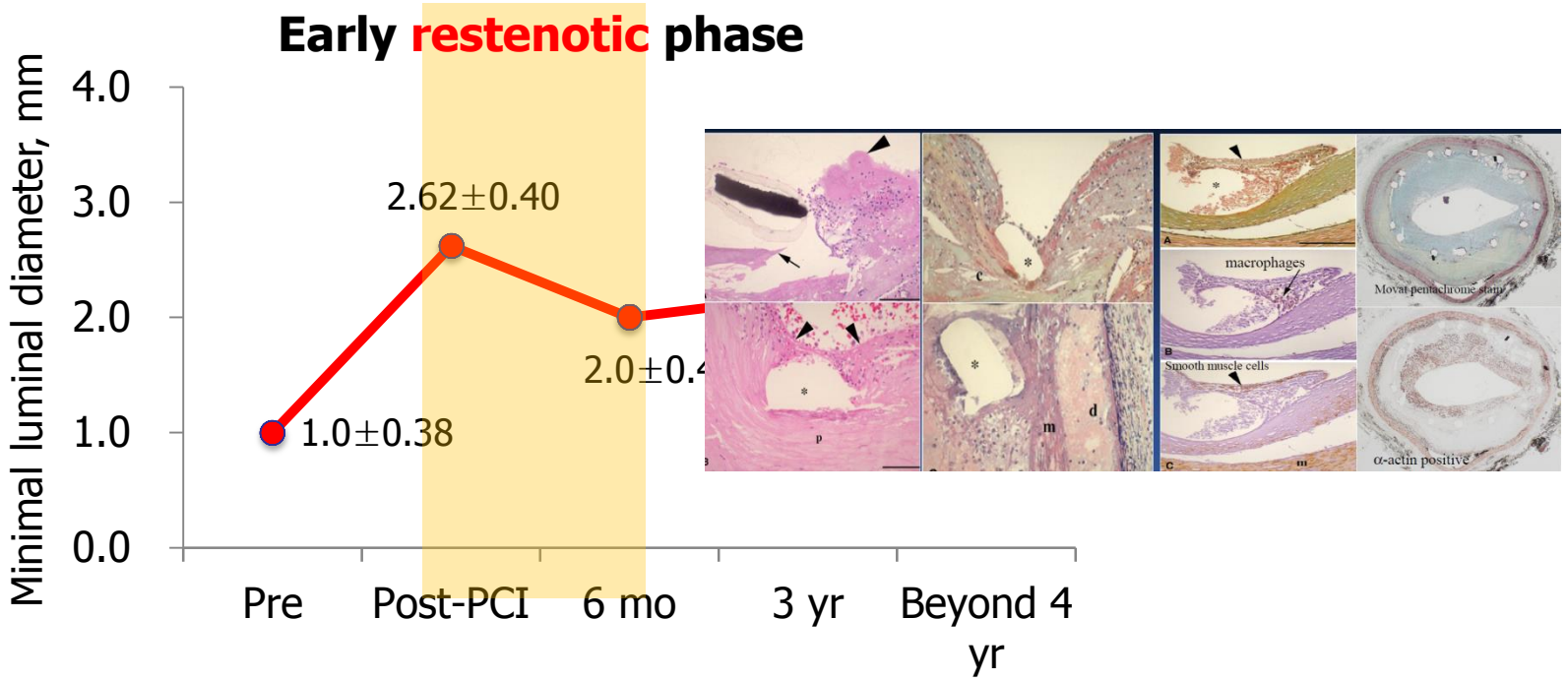
3 phasic response of neo-intimal haperplasia within the stent after BMS implantation over long term follow-up



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

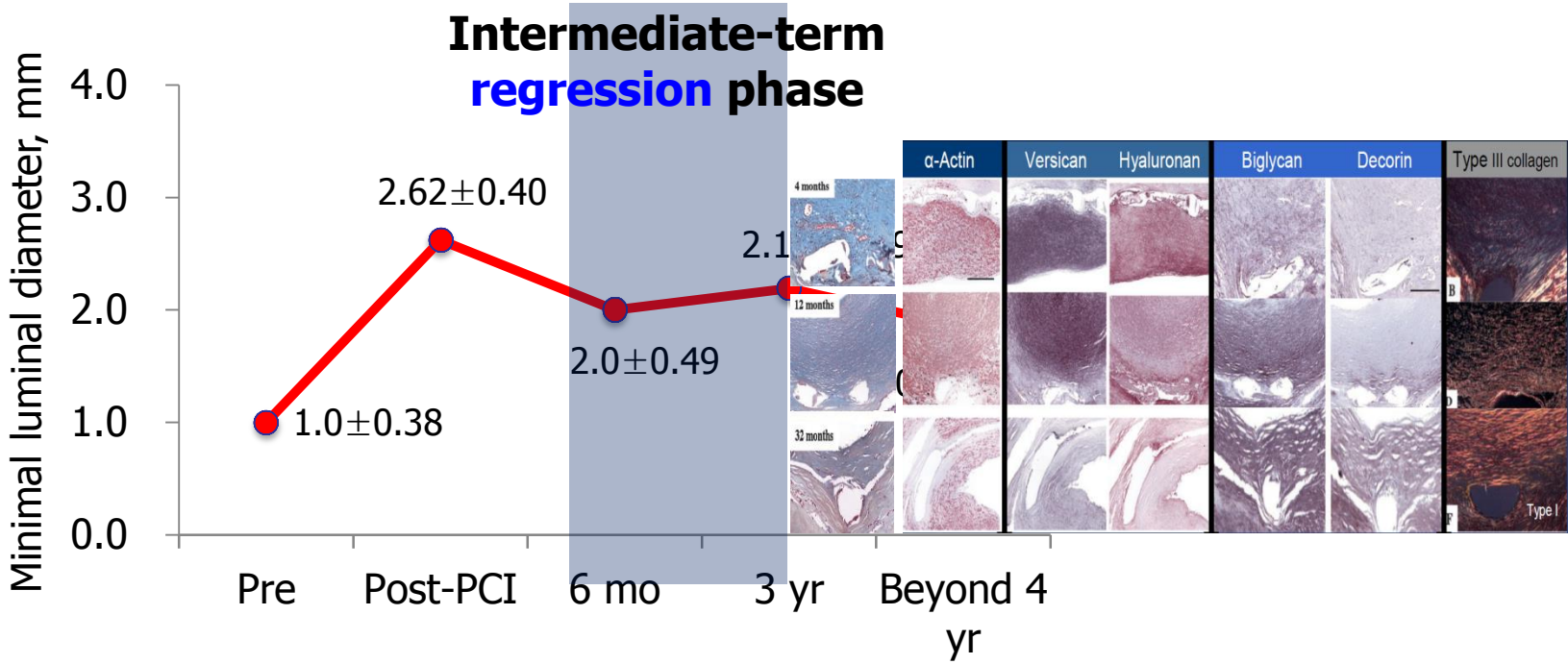
Early Restenotic Phase: Healing Phase

Thrombus and fibrin deposition existed in peri-stent area, acute inflammationory cells appeared, granulation tissue response (smooth muscle cell and matrix deposition) occurred.



Intermediate-term Regression

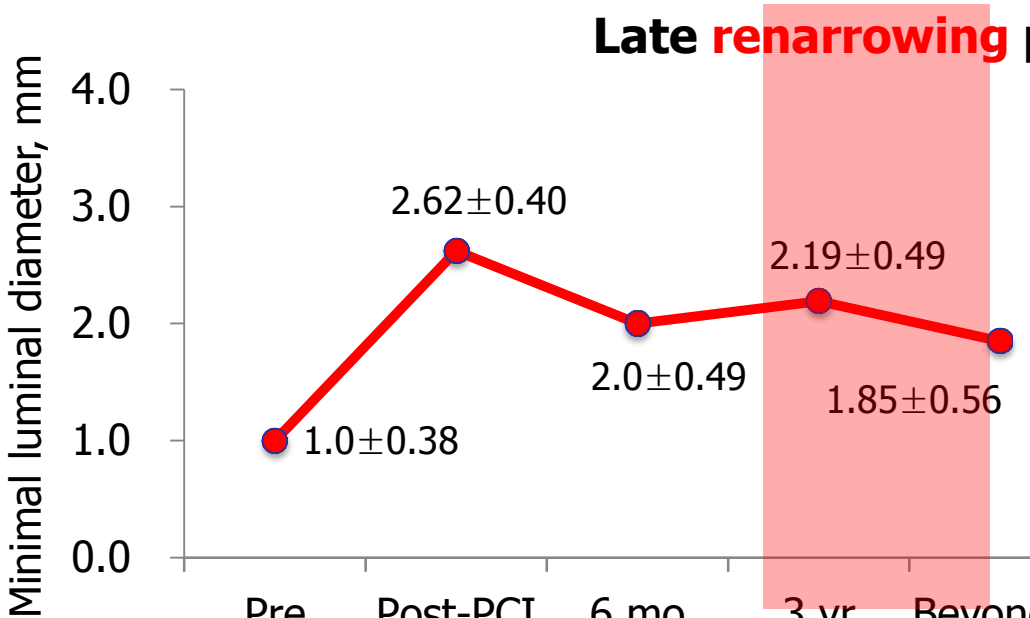
Number of smooth muscle decreased (reduction of cellularity) and change of contents of ECM (reduced versican/hyaluronan, increased biglycan/decorin, replaced with type III collagen) occurred.

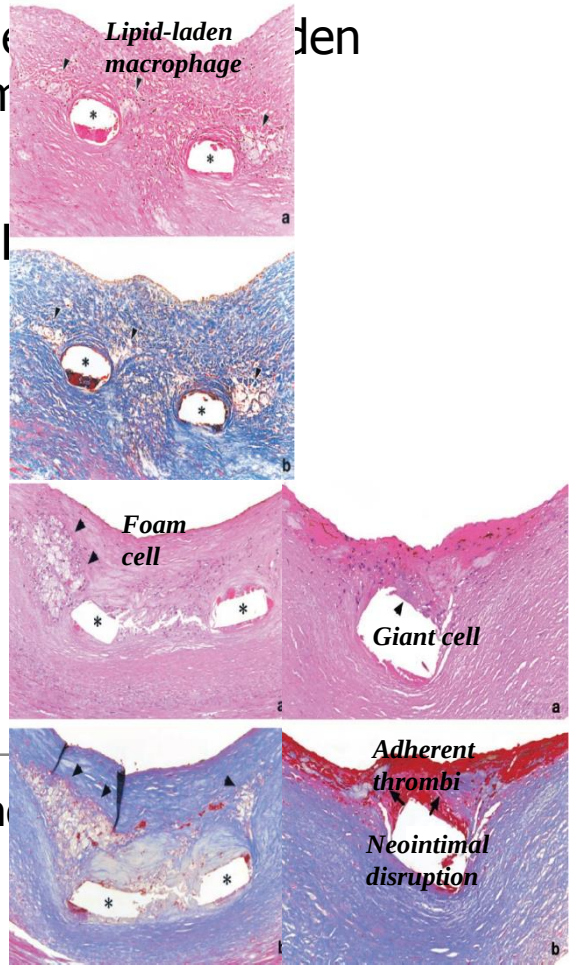


Farb A et al, Circulation, 2004;110:940-947

Late Renarrowing Phase

SMC decreased and collagen fiber became to be de den macrophage in peri-stent area at 3-yr FU and foam appeared at 7-yr FU



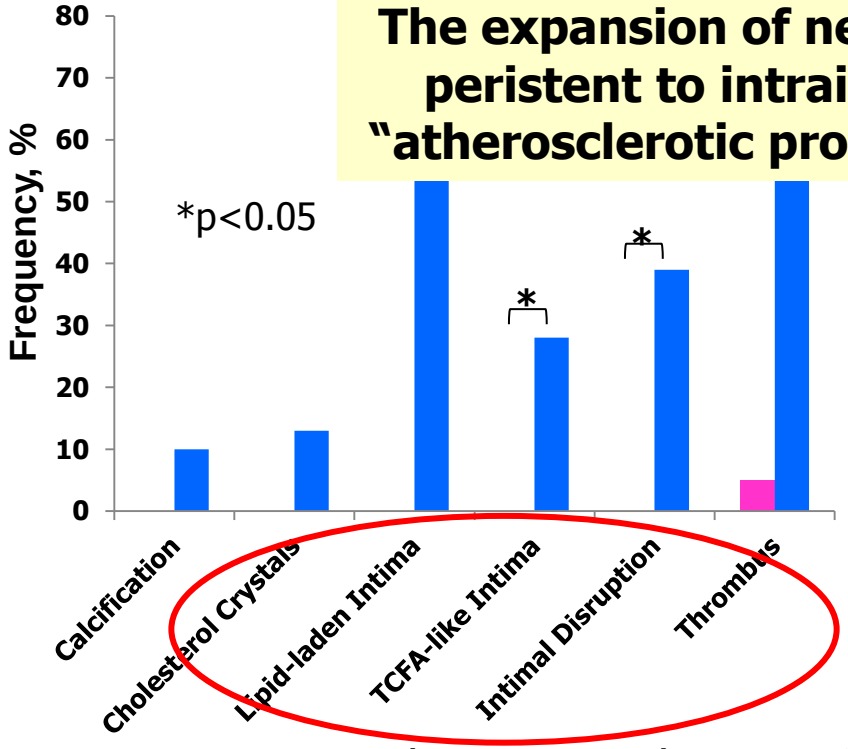


Inoue et al. Cardiovasc Pathol 2004;13(2):109-15

Lipid-Laden Intima and Neovascularization After BMS

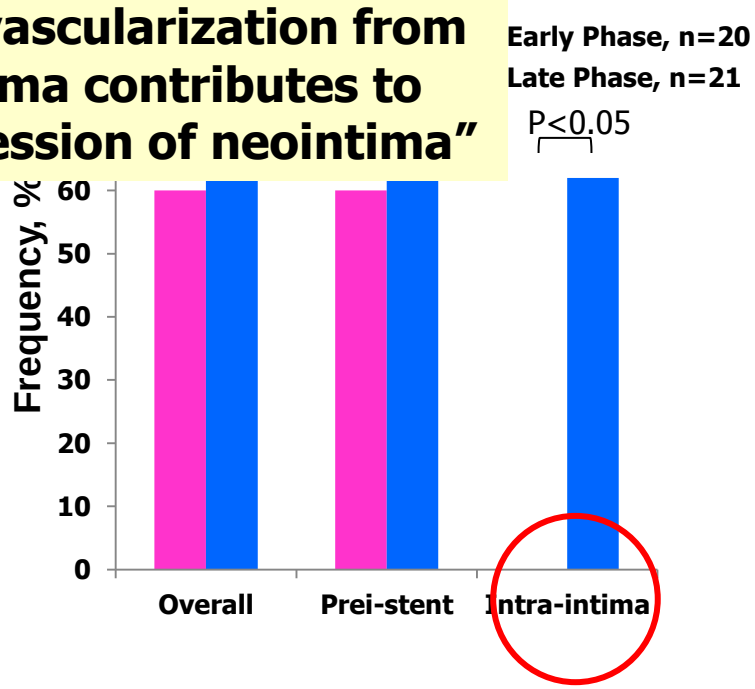
Early phase (<6mos, n=20) vs late phase (≥5 yrs, n=21) observation by OCT

Atherosclerotic Findings



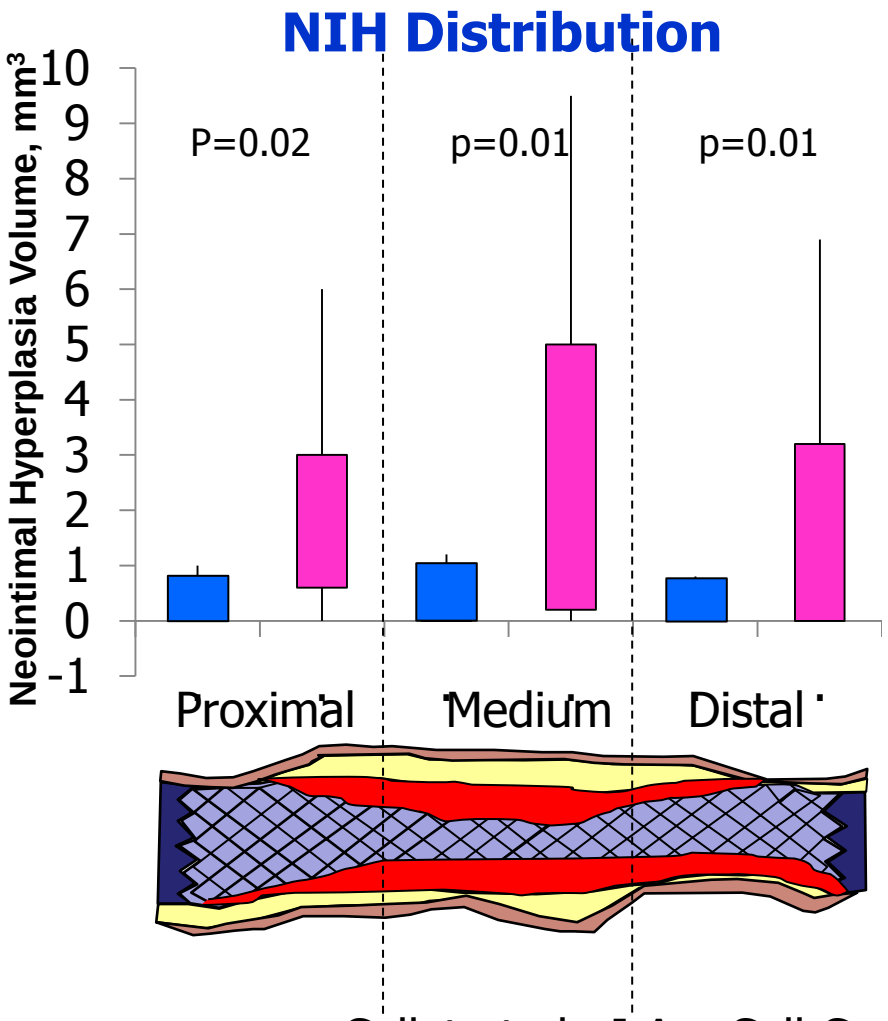
The expansion of neovascularization from peristent to intraintima contributes to "atherosclerotic progression of neointima"

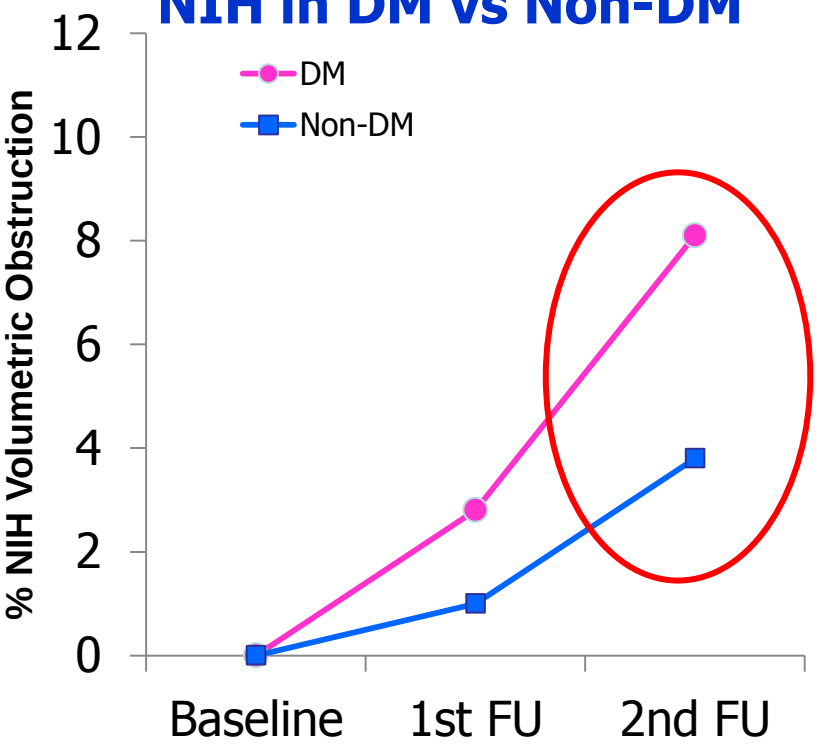
Neovascluarization



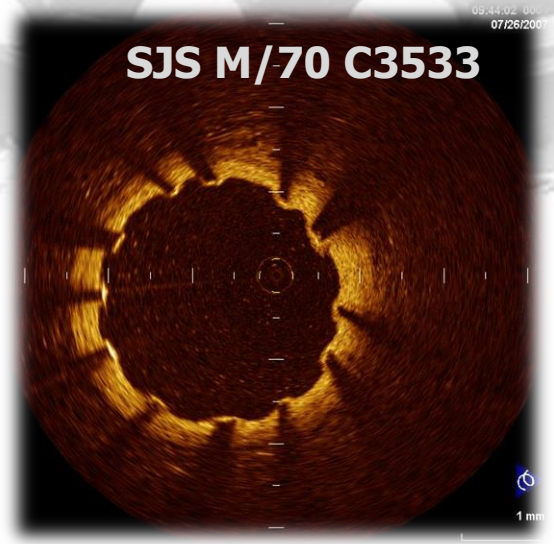
Takano M et al., J Am Coll Cardiol 2010;55:26–32

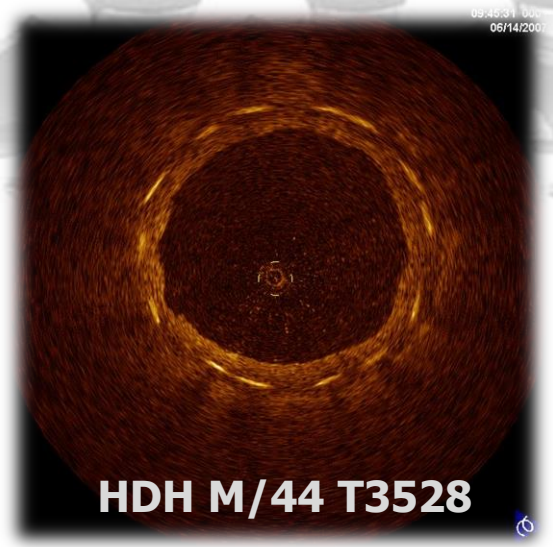
Temporal Course of NIH after DES

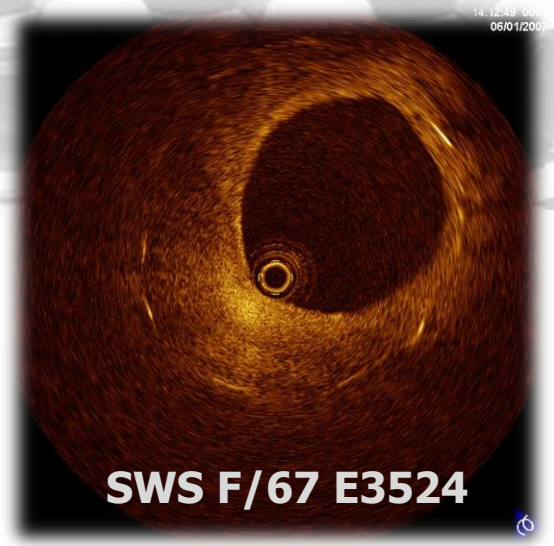


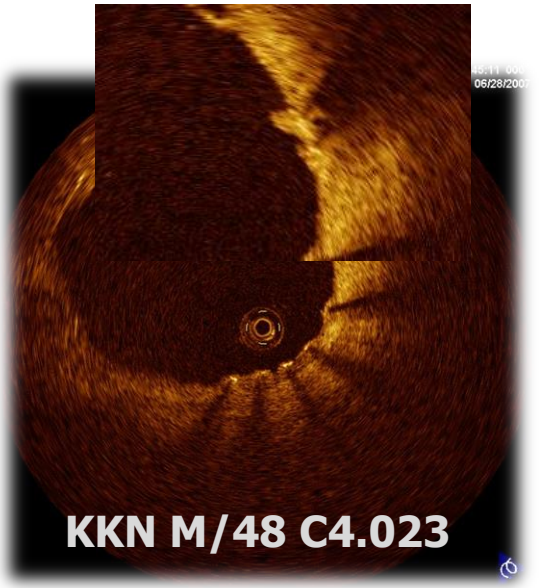


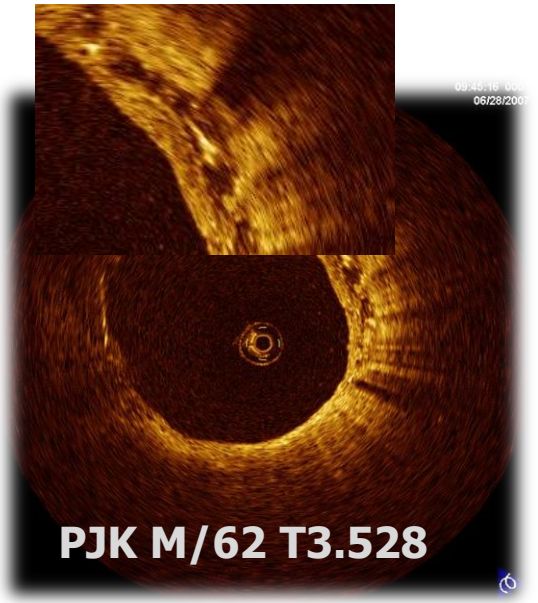
Collet et al., J Am Coll Cardiol Intv 2011;4:1067–74

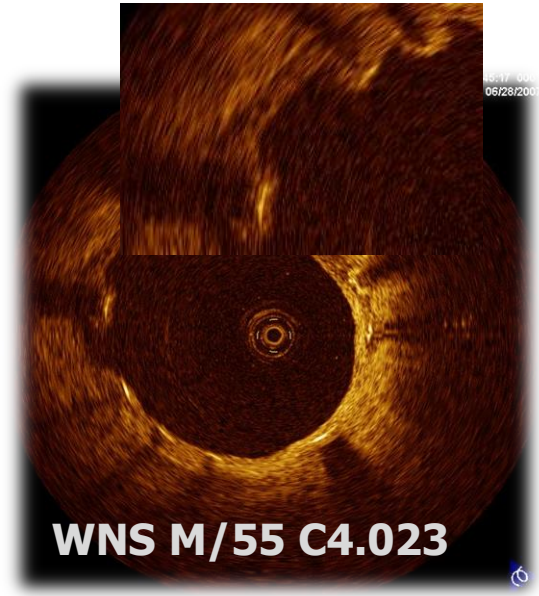






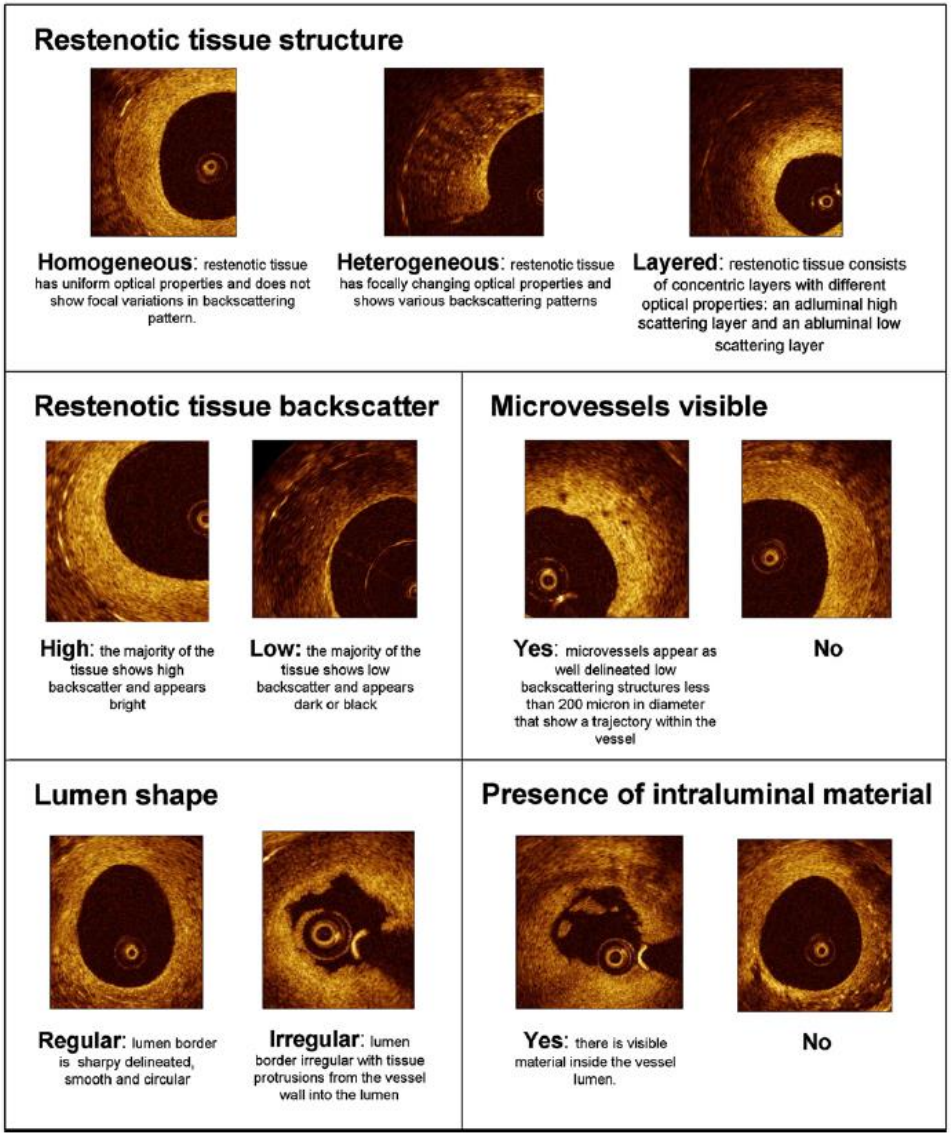






The amount and/or characteristics of neointima after DES implantation are different among various stent types

OCT Patterns of Stent Restenosis



- 24 patients with 24 lesions presenting angiographic stent restenosis (50%)
- 16% BMS and 84% various DES
- The median time from stent implantation was 12 months (4-42 months).
- Restenosis patients with UA Sx presented more frequently irregular lumen shape (60 vs 6.7%, p=0.007).

Gonzalo et al.,
Am Heart J 2009;158:284-93

Neointima in ISR lesion with DES

50 ISR lesions with DES implantation
Median follow-up time was 32.2 months

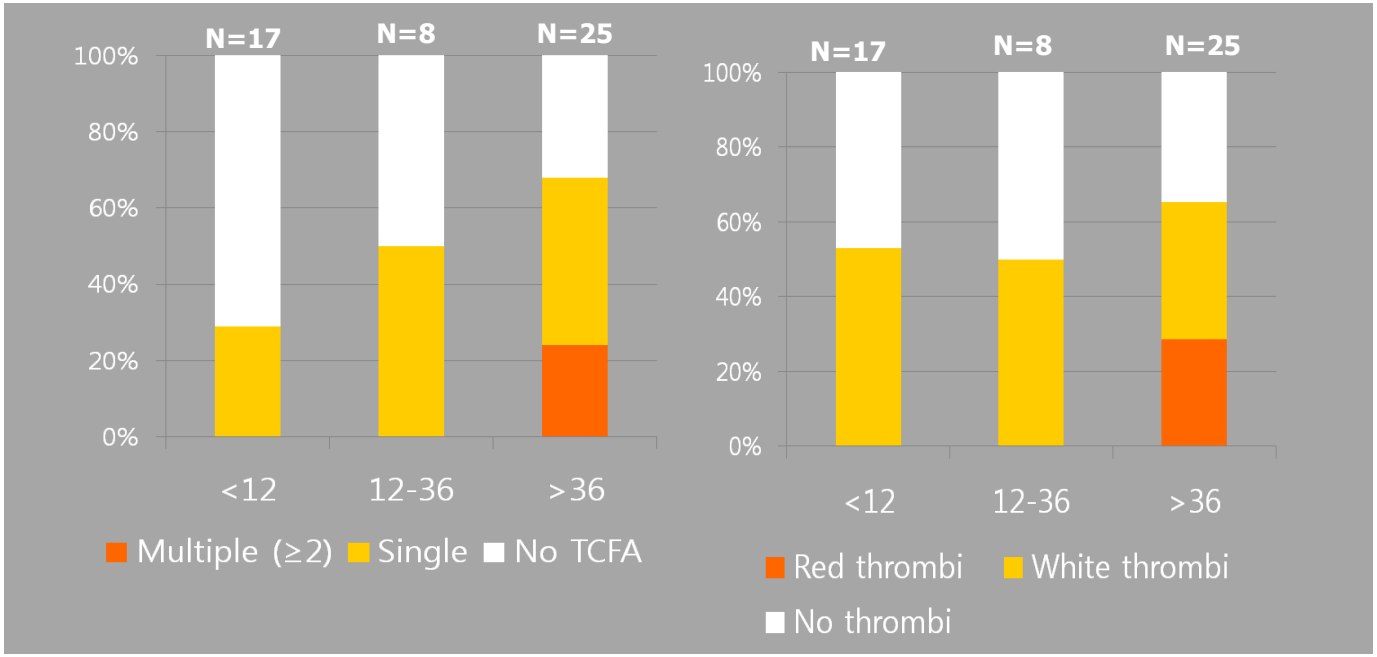
26 lesions (52%) had at least 1 OCT-defined in-stent thin-cap fibroatheroma (TCFA)–containing neointima and 29 (58%) had at least 1 in-stent neointimal rupture.

	Stable	Unstable	p
Fibrous cap thickness, μm	100 (60-205)	55 (42-105)	0.008
Intimal rupture	47%	75%	0.044
Thrombi	43%	80%	0.007
Red thrombi	3%	30%	0.012
Lipid neointima	83%	100%	0.067
TCFA	37%	75%	0.008
Neovascularization	50	75%	0.069

Kang SJ et al., Circulation. 2011;123:2954-2963.)

Neointima in ISR lesion with DES

Frequency of OCT-defined TCFA-neointima and thrombi according to FU time



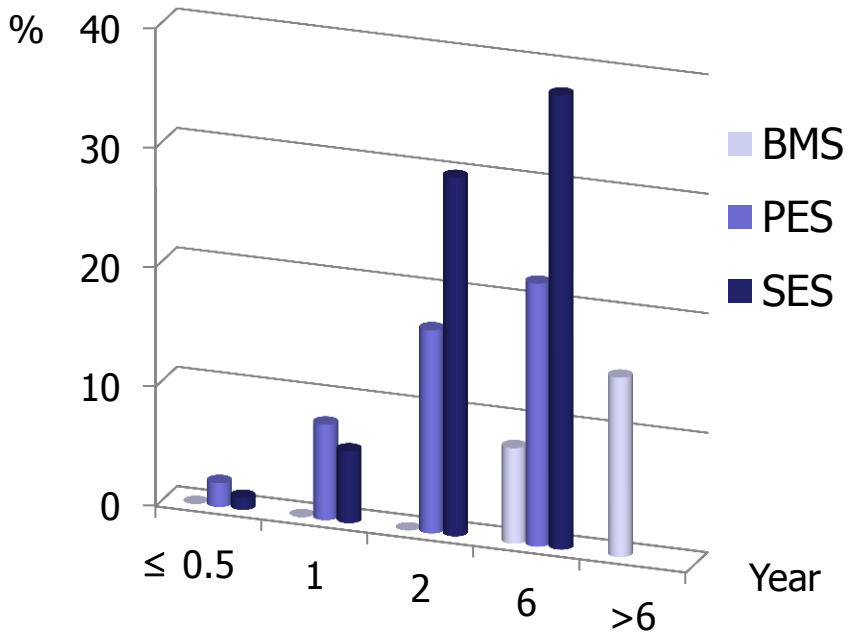
	FU <20mo	FU ≥ 20m	p
Fibrous cap thickness, μm	100 (60-220)	60 (50-122.5)	0.020
Red thrombi, n (%)	0 (0)	7 (27)	0.007
TCFA, n (%)	8 (33)	18 (69)	0.012

Kang SJ et al., Circulation. 2011;123:2954-2963.)

Neo-atheroma within stent in Pathology study

- The incidence of NAS was significantly greater in DES lesions (31%) than BMS lesions (16%; p<0.001).
- The median stent duration was shorter in DES than BMS (DES, 14 [12, 23] mo vs BMS, 72 [60, 96] mo, p<0.001)
- Unstable features are identified for both BMS and DES with shorter implant durations for DES (1.5 ± 0.4 years) compared to BMS (6.1 ± 1.5 years).

197 BMS, 209 DES (103 SES, 106 PES)



Cumulative Incidence of Atherosclerotic Change With Time After Implantation of BMS Versus SES and PES

Nakazawa et al, J Am Coll Cardiol 2011;57:1314–22

Neo-atherosclerosis (NAS) in Pathologic Studies

Independent risk factors for neoatherosclerosis

Variable	OR	95% CI	P Value
Age, per yr	0.963	0.942-0.983	<0.001
Stent duration, per month	1.028	1.017-1.041	<0.001
SES usage	6.534	3.387-12.591	<0.001
PES usage	3.200	1.584-6.469	0.001
Underlying unstable lesion	2.387	1.326-4.302	0.004

Nakazawa et al, J Am Coll Cardiol 2011;57:1314–22

Mechanism of Neo-atherosclerosis

New atherosclerosis superimposed on a stable neointimal platform

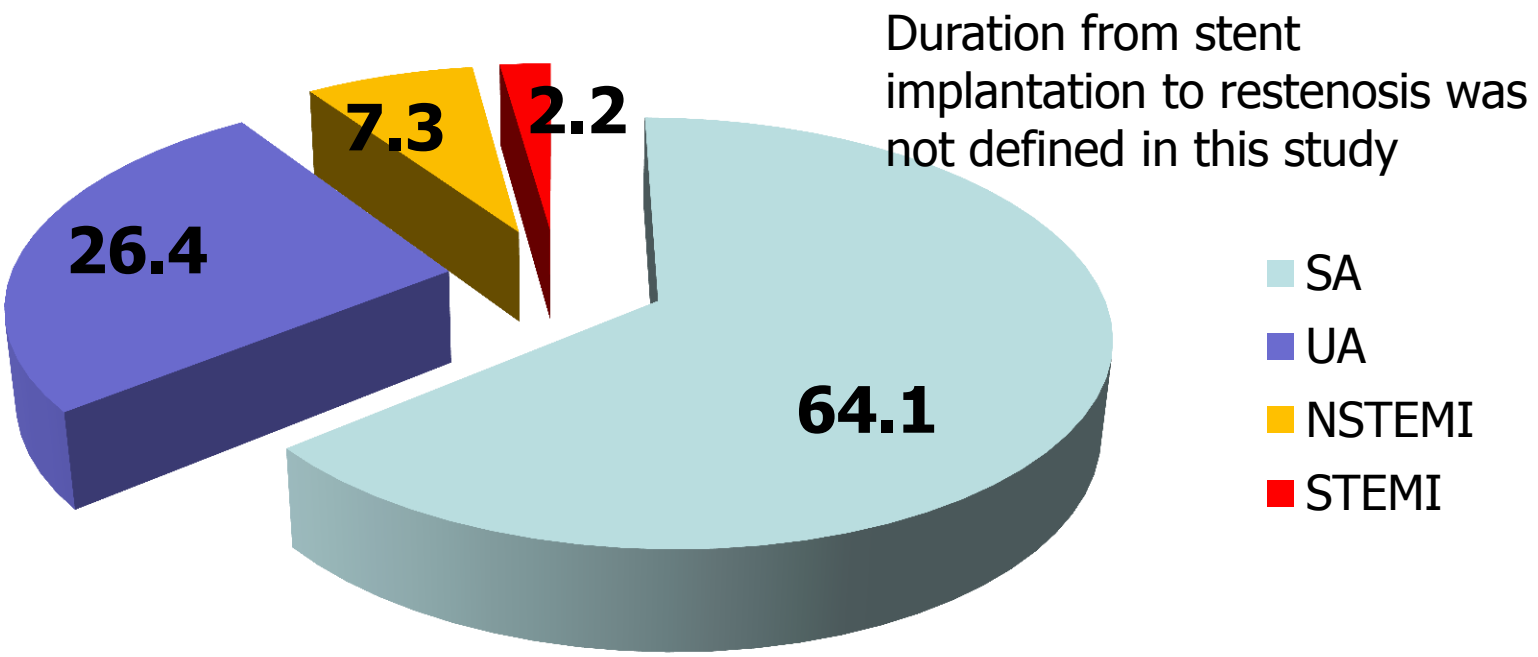
Atherosclerotic neointimal degenerative changes over time

Clinical outcomes

BMS Restenosis is not a benign

1186 cases of BMS-ISR in 984 patients

Clinical Presentation of BMS ISR



Chen MS et al., Am Heart J 2006;151:1260-24

IC Imaging Predictors of Stent Thrombosis

PARAMETERS		
Small stent CSA or stent underexpansion	Fujii et al. J Am Coll Cardiol 2005;45:995-8)	Early, DES
	Okabe et al., Am J Cardiol. 2007;100:615-20	Early and late, DES
	Liu et al. JACC Interventions 2009;2:428-34	Early and late, DES
	Choi et al. Circ Cardiovasc Interv 2011:4 ;239-47	Early, DES/BMS. STEMI
Residual inflow/outflow disease (dissection, residual stenosis)	Fujii et al. J Am Coll Cardiol 2005;45:995-8)	Early, DES
	Okabe et al., Am J Cardiol. 2007;100:615-20	Early and late, DES
	Liu et al. JACC Interventions 2009;2:428-34	Early and late, DES
	Choi et al. Circ Cardiovasc Interv 2011:4 ;239-47	Early, DES/BMS. STEMI
Stent malapposition	Cook et al, Circulation 2007;115:2426-34	VLST, DES
	Lee et al, JACC 2010;55:1936-42	VLST, DES/BMS
	Ko et al, Int J Cardiovasc Imaging, in press	VLST, DES
Coronary aneurysm		
New atheroma	Ko et al, Int J Cardiovasc Imaging, 2011	VLST, DES
	Lee et al, JACC 2010;55:1936-42	VLST, DES/BMS
Stent fracture?	Lee et al, Cath Cardiov Int , in press	VLST, DES

Neoatheroma and VLST after DES or BMS

- 30 VLST patients with AMI (23 DES and 7 BMS)

	DES	BMS	p
Months after index procedure	33.2±12.5	108.4±26.5	<0.001
Stent length, mm	32.9±13.0	18.6±4.2	0.001
Minimum stent CSA, mm^2	6.2±1.6	7.4±3.8	0.413
Mean EEM CSA, mm^2	19.6±6.1	18.3±4.2	0.774
Malapposition, %	73.9	0	0.001
Neo-intimal rupture, %	43.5	100	0.010

Lee et al, Am Coll Cardiol 2010;55:1936–42

OCT for VLST after DES implantation

- 22.2% (4/18) patients with VLST had ruptured and lipid-laden neointima inside DESs without uncovered or malapposed stent struts.
- 14 patients without neointimal rupture, uncovered and malapposed struts were observed in nine and seven patients, respectively, and lipid-laden neointima in four patients.
- Time to OCT study after DES implantation was significantly longer in the eight patients with lipid-laden neointima than in 49 patients without lipid-laden neointima (45.5±17.7 months vs. 11.7±7.2 months, respectively, $P<0.001$).

Ko YK, SY Choi et al,
Int J Cardiovasc Imaging, 2011 June 8 [Epub ahead of print]

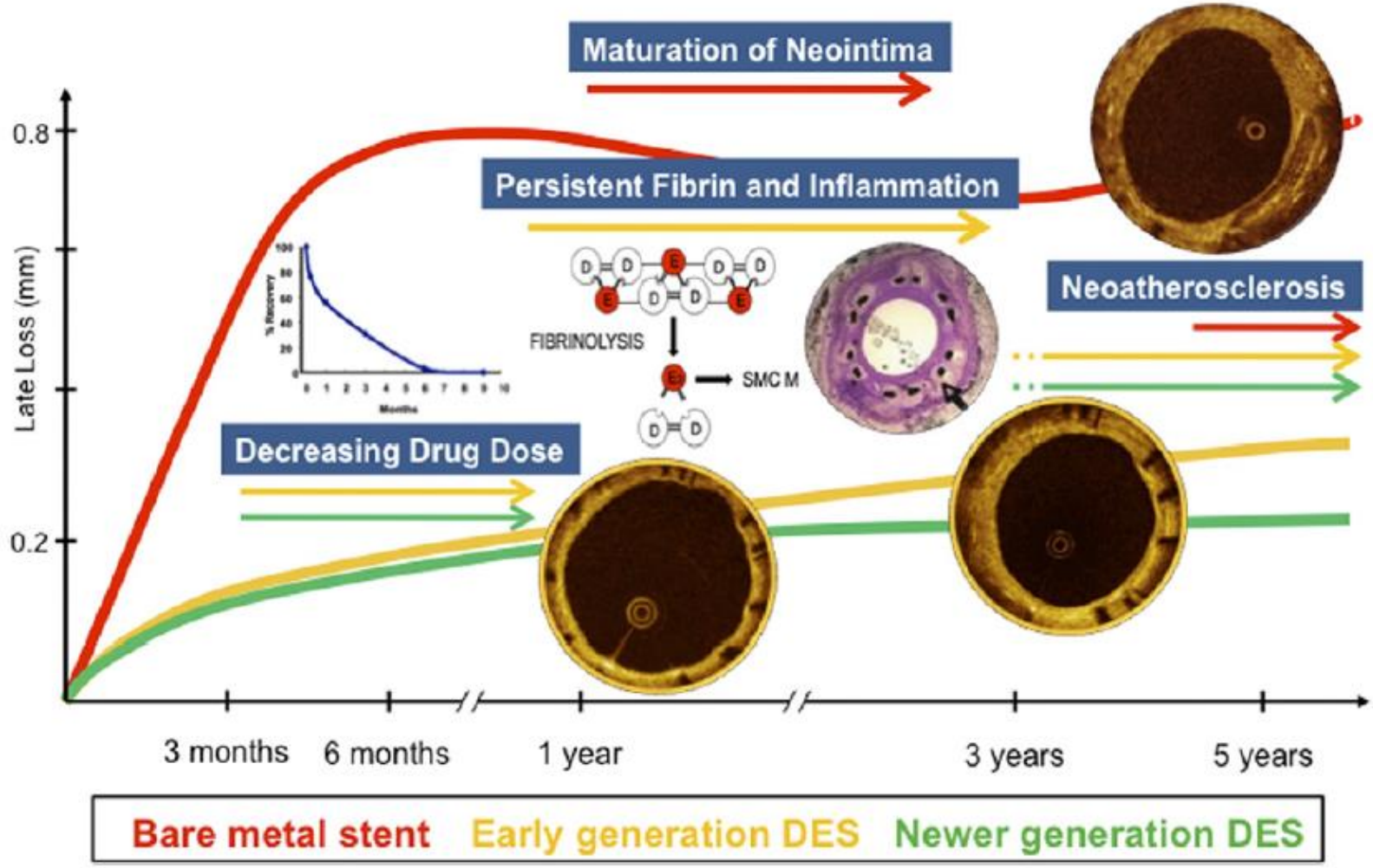
Lessons from Current Experiences

- Neo-atherosclerosis is identified in patients with both BMS and DES implantation.
- Neo-atherosclerosis occurs earlier after DES implantation than after BMS implantation (>1.5 yr in DES, >5~6 yr in BMS).
- Neo-atherosclerosis frequently presents unstable features containing lipid-laden intima, large necrotic core, thin fibrous cap, TCFA, intimal rupture and thrombi.

Lessons from Current Experiences

- In-stent neo-atherosclerosis may be an important mechanism of stent failure, especially late after implantation.
- The (late) neo-atherosclerosis might be related with unstable clinical presentation like ACS or stent thrombosis.
- OCT is the best modality to detect neo-atherosclerosis and predict unstable clinical outcomes. Furthermore, OCT can provide better information for understanding the mechanism of disease progression after stent implantation.

Mechanism of Intimal Growth after Stent Implantation



Räber et al. J Am Coll Cardiol Intv 2011;4:1075-8