Late DES failure

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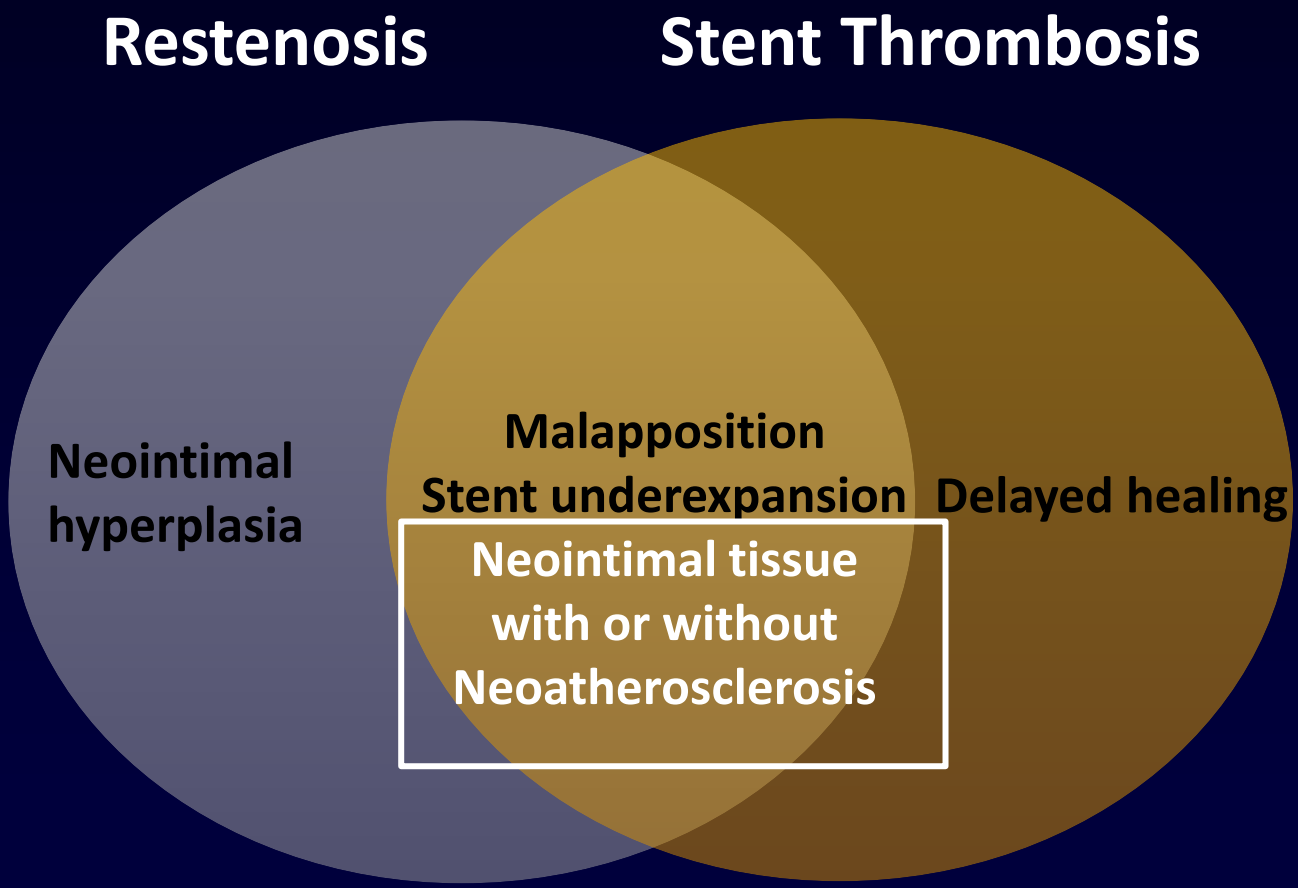
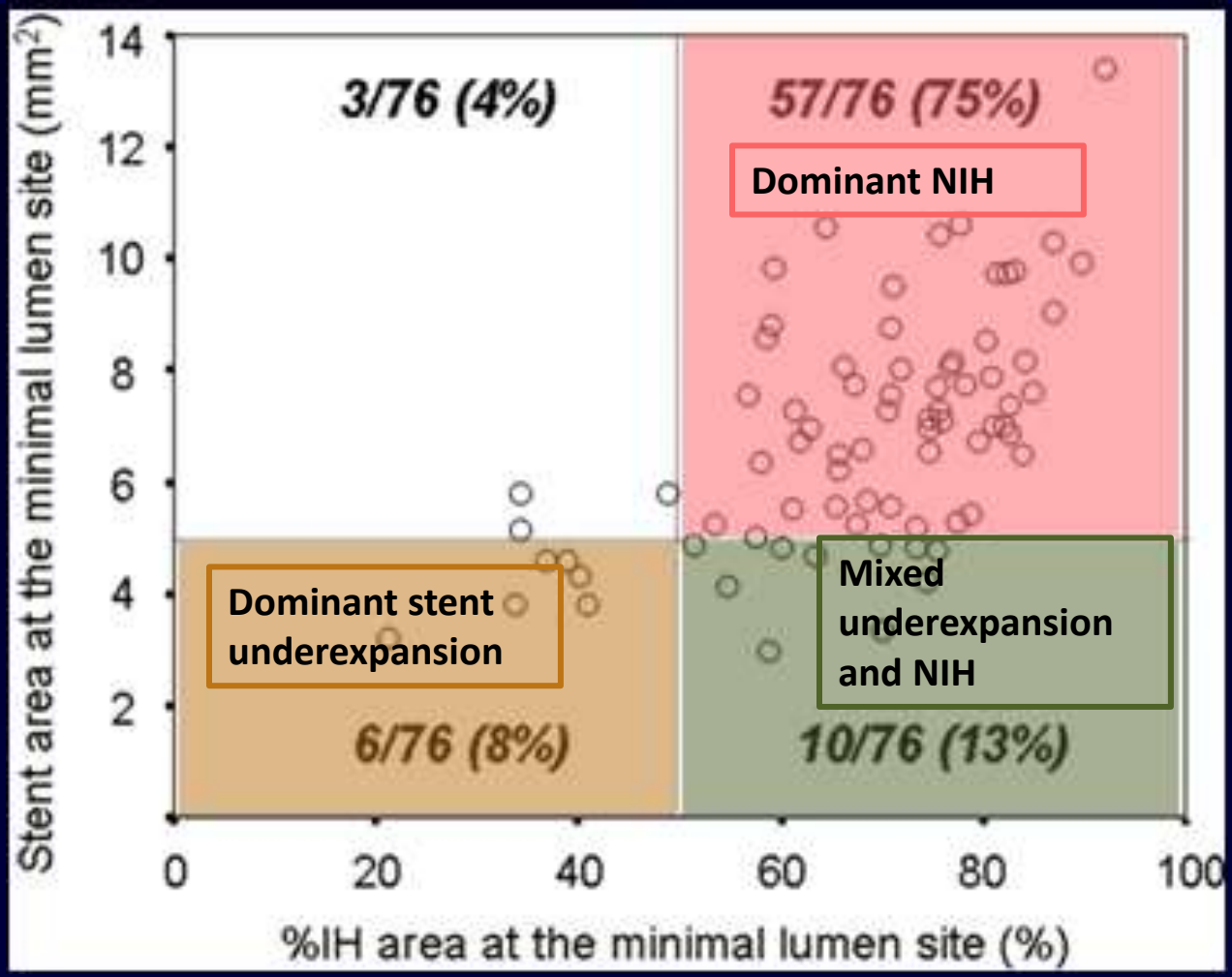
Mechanisms of DES ISR and stent thrombosis



Stent underexpansion and NIH proliferation (n=76 DES ISR)

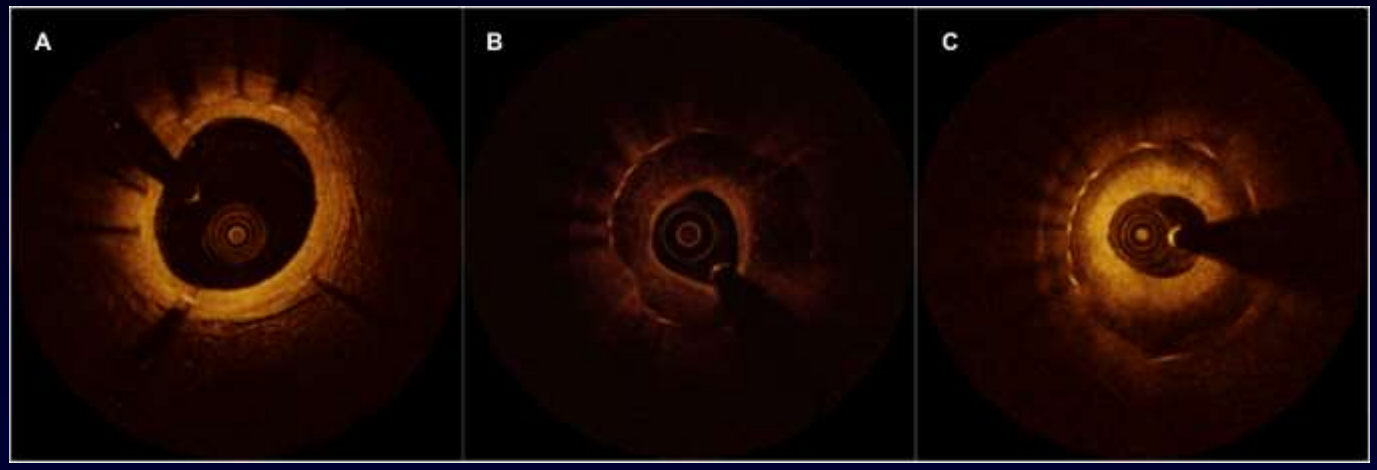


Asan Medical Center, Circ Cardiovasc Interv. 2011;4:9-14

Neointimal pattern assessed by OCT

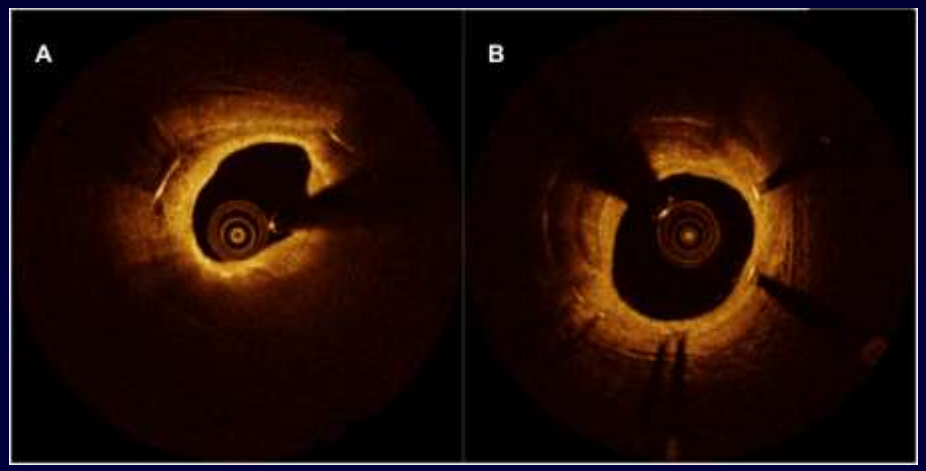
Homogeneous | Heterogeneous | Layered

Neointima without neoatherosclerosis

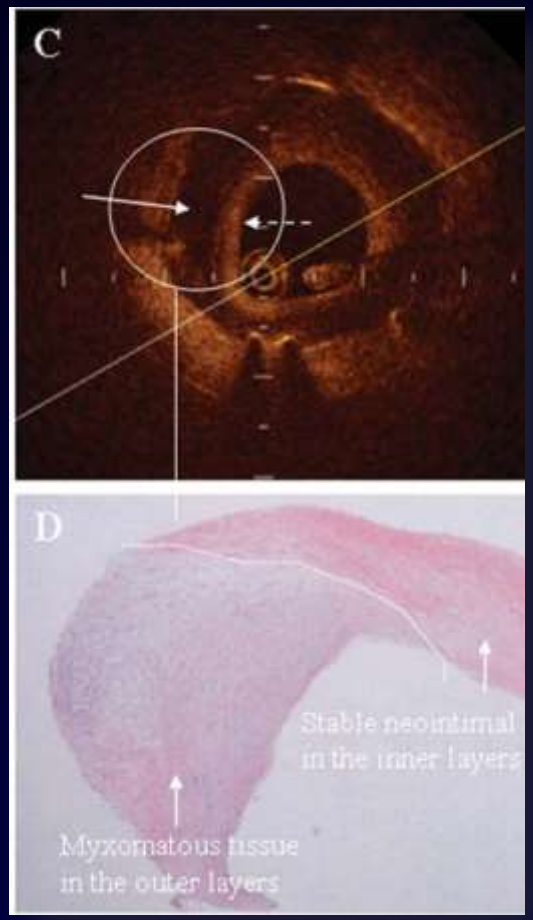


Lipidic neointima | Calcification

Neoatherosclerotic neointima



Dark areas in restenotic tissue on OCT



Layered feature:

bilayer structure of hyperechoic outer layers (dotted arrow) and highly echolucent inner layers (arrow)

Hyperechoic regions on the OCT

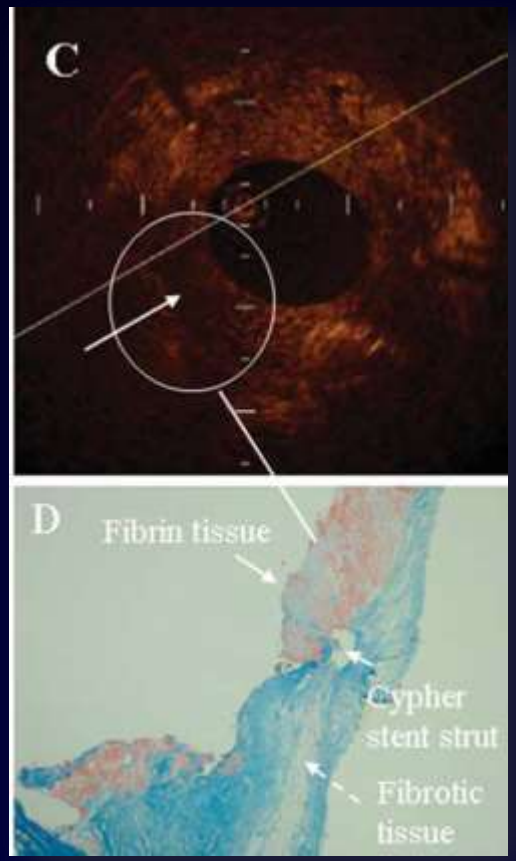
: smooth muscle cells

Highly echolucent region

: myxomatous tissue

Nagai et al, Catheter Cardiovasc Interv 75:961–963 (2010)

Dark areas in restenotic tissue on OCT

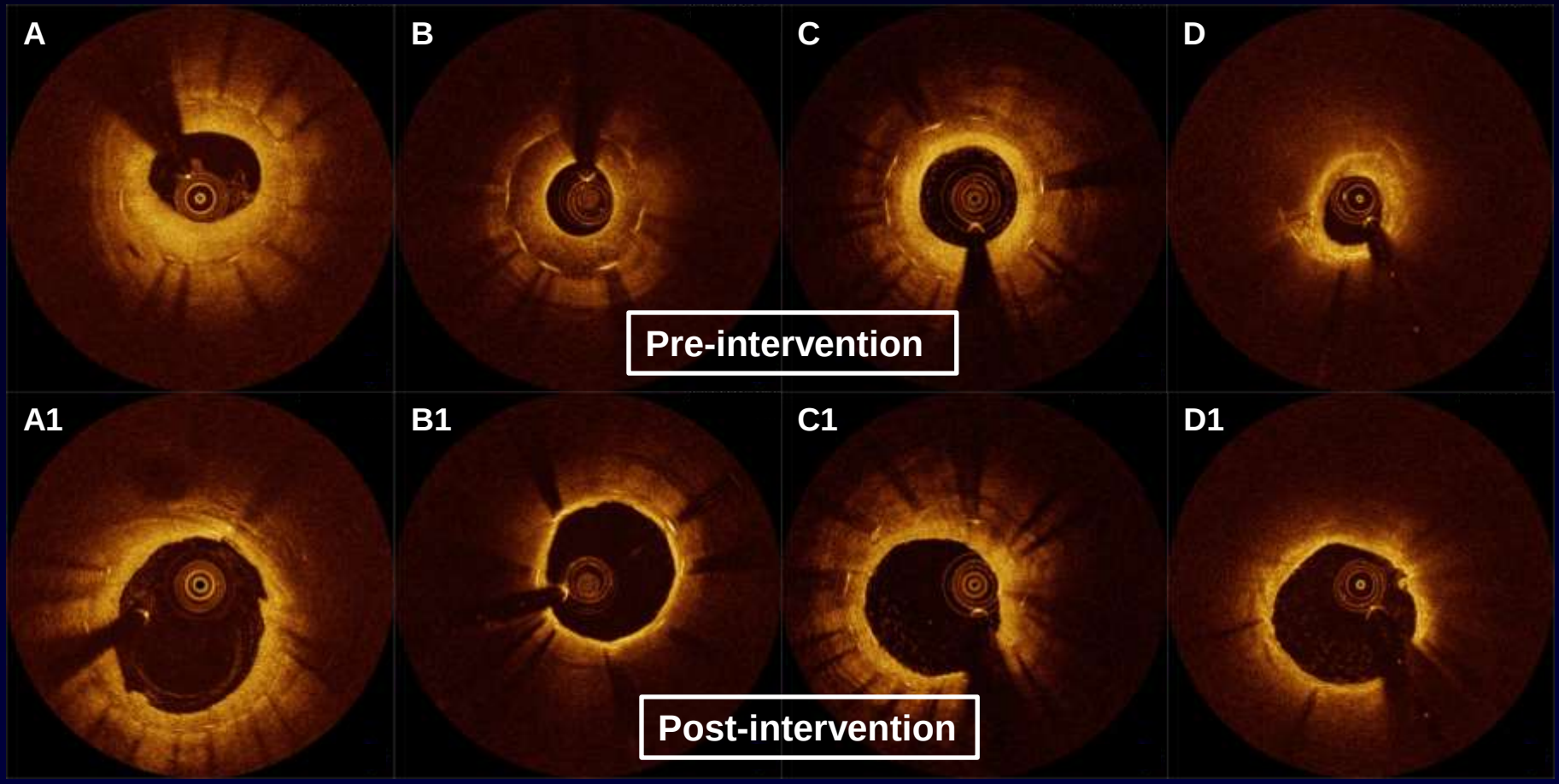


Heterogeneous feature:
patchy and highly echolucent regions throughout the layers

Highly echolucent region on the OCT
: organizing fibrin thrombus

Nagai et al, Catheter Cardiovasc Interv 75:961–963 (2010)

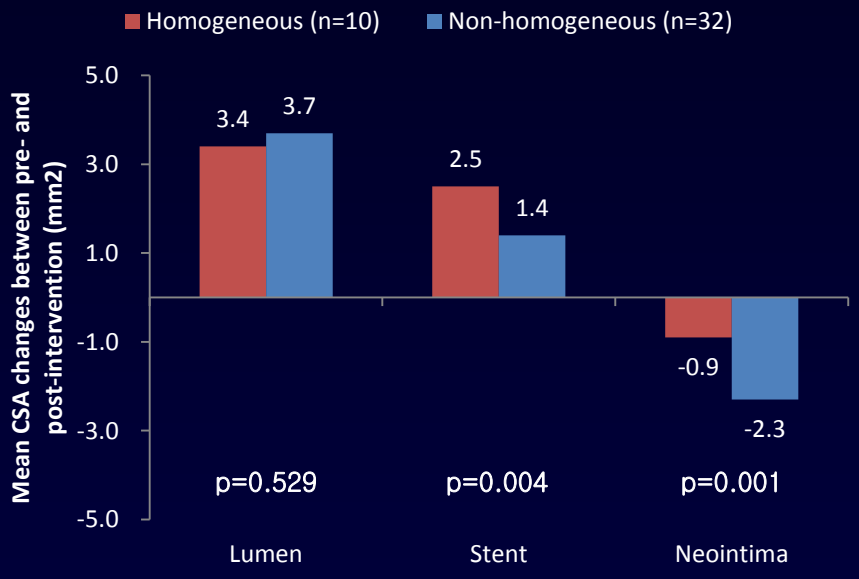
Mechanisms of post-intervention and 9-month lumen enlargement after treatment of DES ISR with a drug-eluting balloon (n=42 DES ISR lesions)



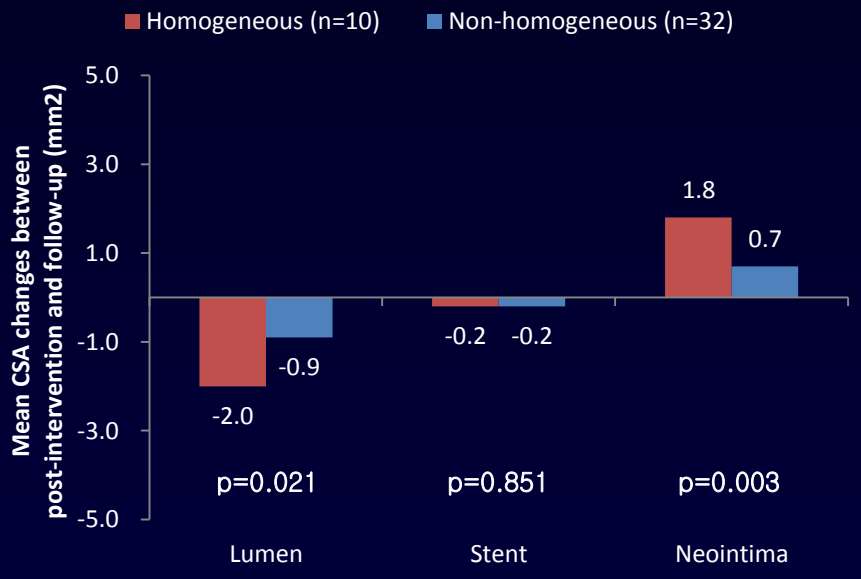
Lee SY, Hong MK (corresponding author). *Am J Cardiol* 2014;113:1468-1473

Mechanisms of post-intervention and 9-month lumen enlargement after treatment of DES ISR with a drug-eluting balloon (n=42 DES ISR lesions)

Pre-intervention vs. post-intervention

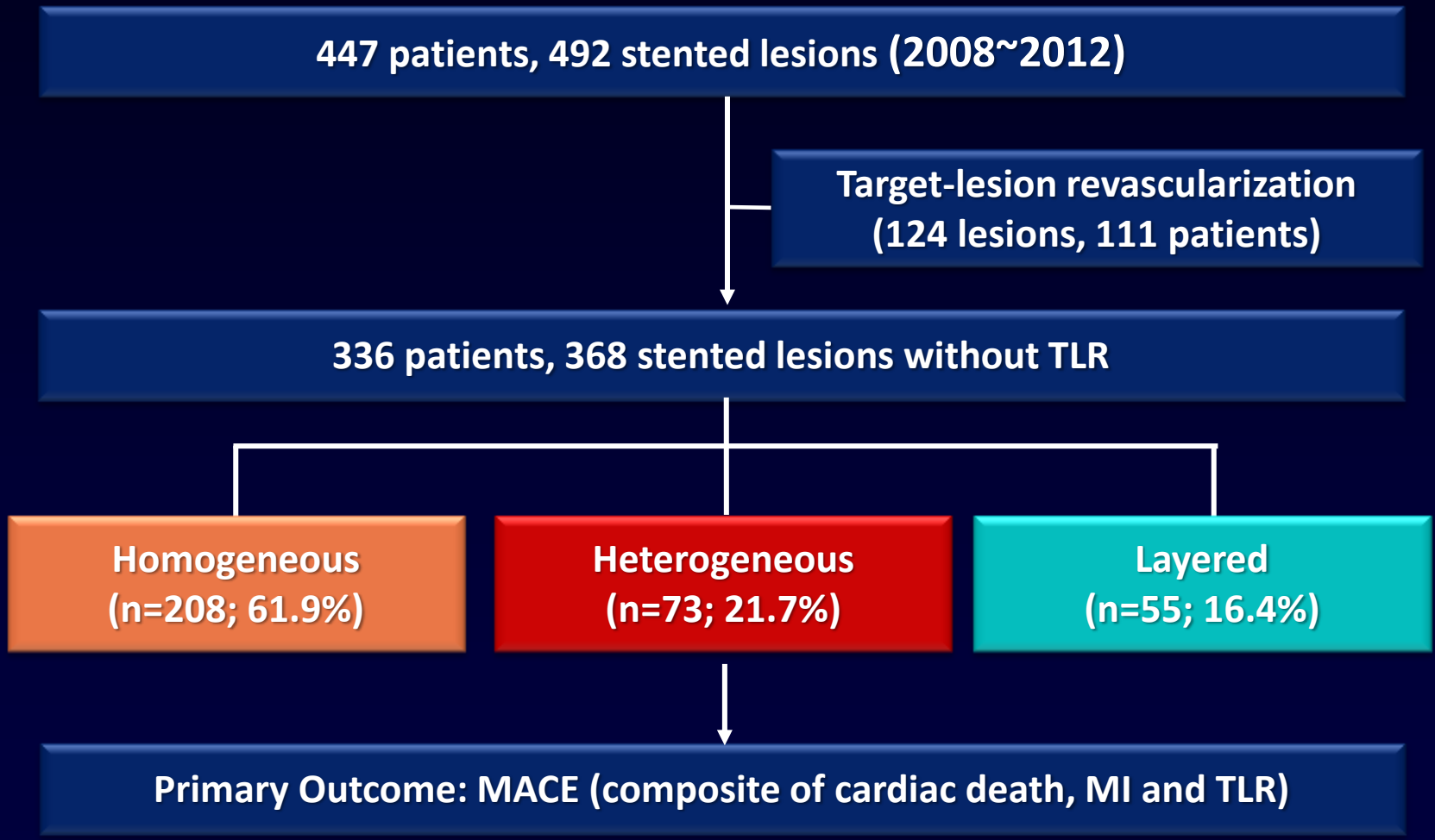


Post-intervention vs. follow-up



Lee SY, Hong MK (corresponding author). *Am J Cardiol* 2014;113:1468-1473

Long-term clinical outcomes of neointima without neoatherosclerosis



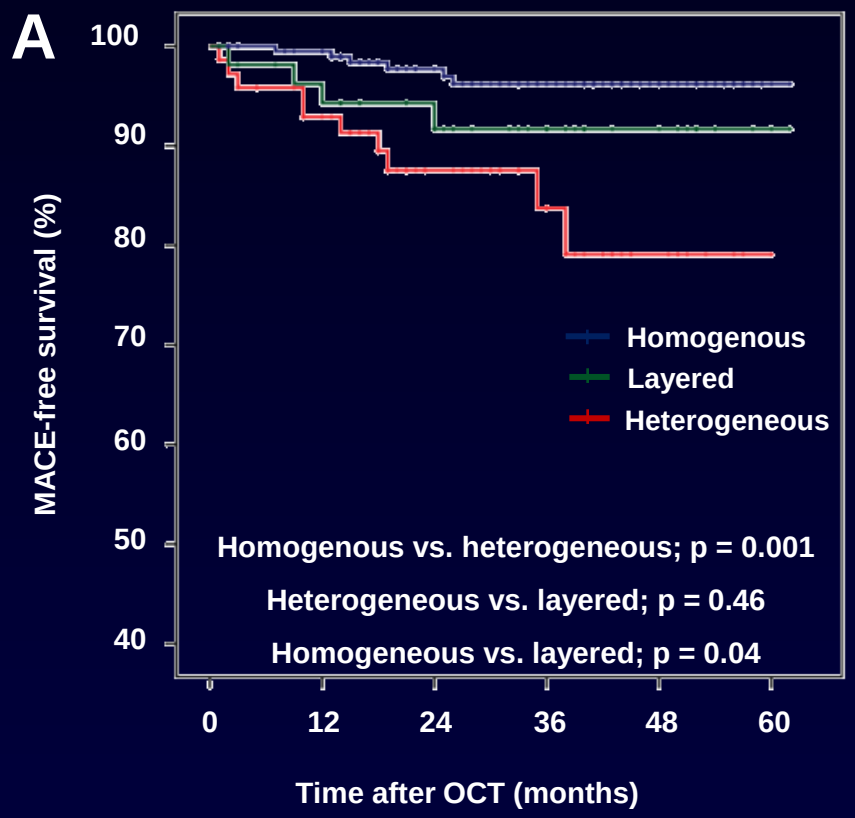
Kim JS, Lee JH, Hong MK (corresponding author). *J Am Coll Cardiol Img* 2014;7:788-795

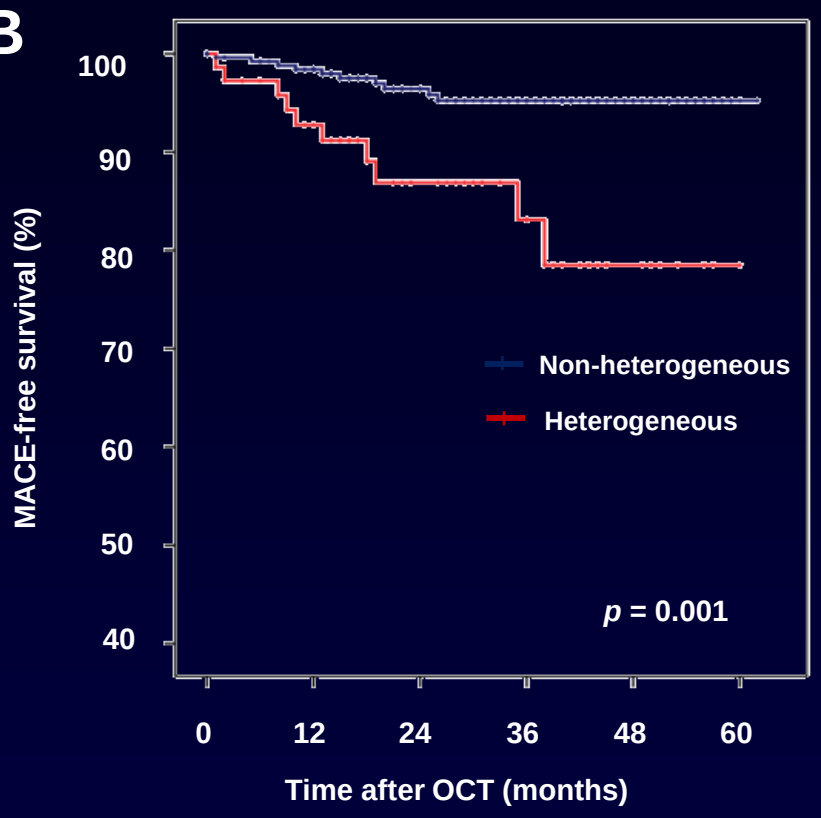
Cox regression analysis for MACE

	Univariate analysis		Propensity score adjusted Cox regression analysis	
	HR (95% CI)	p	HR (95% CI)	p
Age (per years)	1.006 (0.959-1.055)	0.81		
Gender (male)	0.931 (0.371-2.333)	0.88		
Hypertension	0.688 (0.286-1.652)	0.40		
Diabetes mellitus	1.881 (0.779-4.539)	0.16		
Initial ACS dx	1.586 (0.648-3.884)	0.31		
1st gen. DES	2.440 (0.980-6.075)	0.06		
Time interval to OCT (months)	1.018 (1.003-1.033)	0.017		
Minimal lumen CSA (per mm^2)	0.325 (0.211-0.501)	<0.001	0.368 (0.242-0.560)	<0.001
Stent diameter (per mm)	1.207 (0.322-4.523)	0.78		
Stent length (per mm)	1.024 (0.954-1.098)	0.51		
Heterogeneous group	4.236 (1.759-10.200)	0.001	3.925 (1.445-10.662)	0.007

Kim JS, Lee JH, Hong MK (corresponding author). *J Am Coll Cardiol Img* 2014;7:788-795

Long-term outcomes of neointimal hyperplasia without neoatherosclerosis after drug-eluting stent implantation



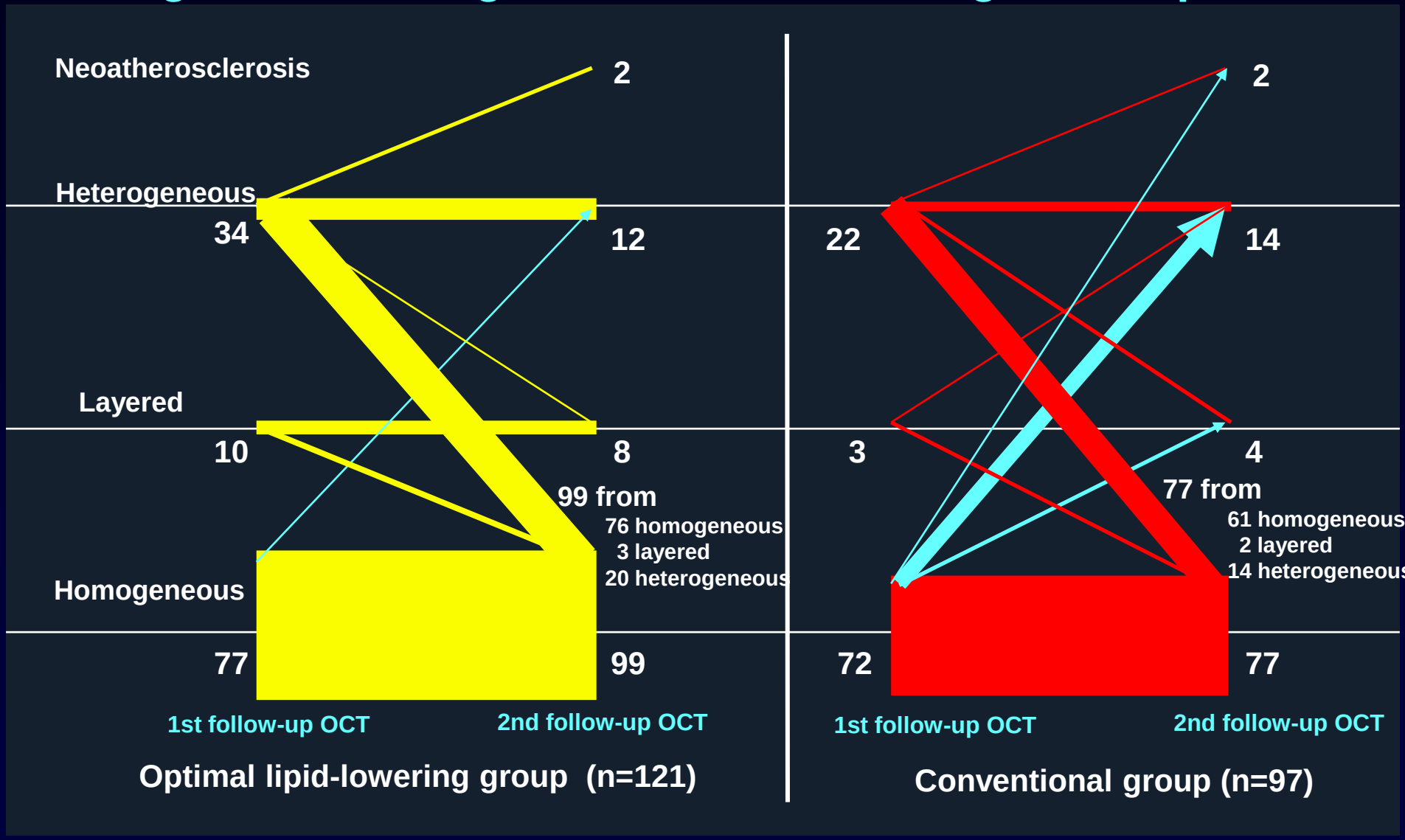


Homogeneous (n)	208	193	140	108	64	21
Layered (n)	55	50	36	24	11	1
Heterogeneous (n)	73	62	34	24	12	2

Non-heterogeneous (n)	263	243	176	132	75	22
Heterogeneous (n)	73	62	34	24	12	2

Kim JS, Lee JH, Hong MK (corresponding author). *J Am Coll Cardiol Img* 2014;7:788-795

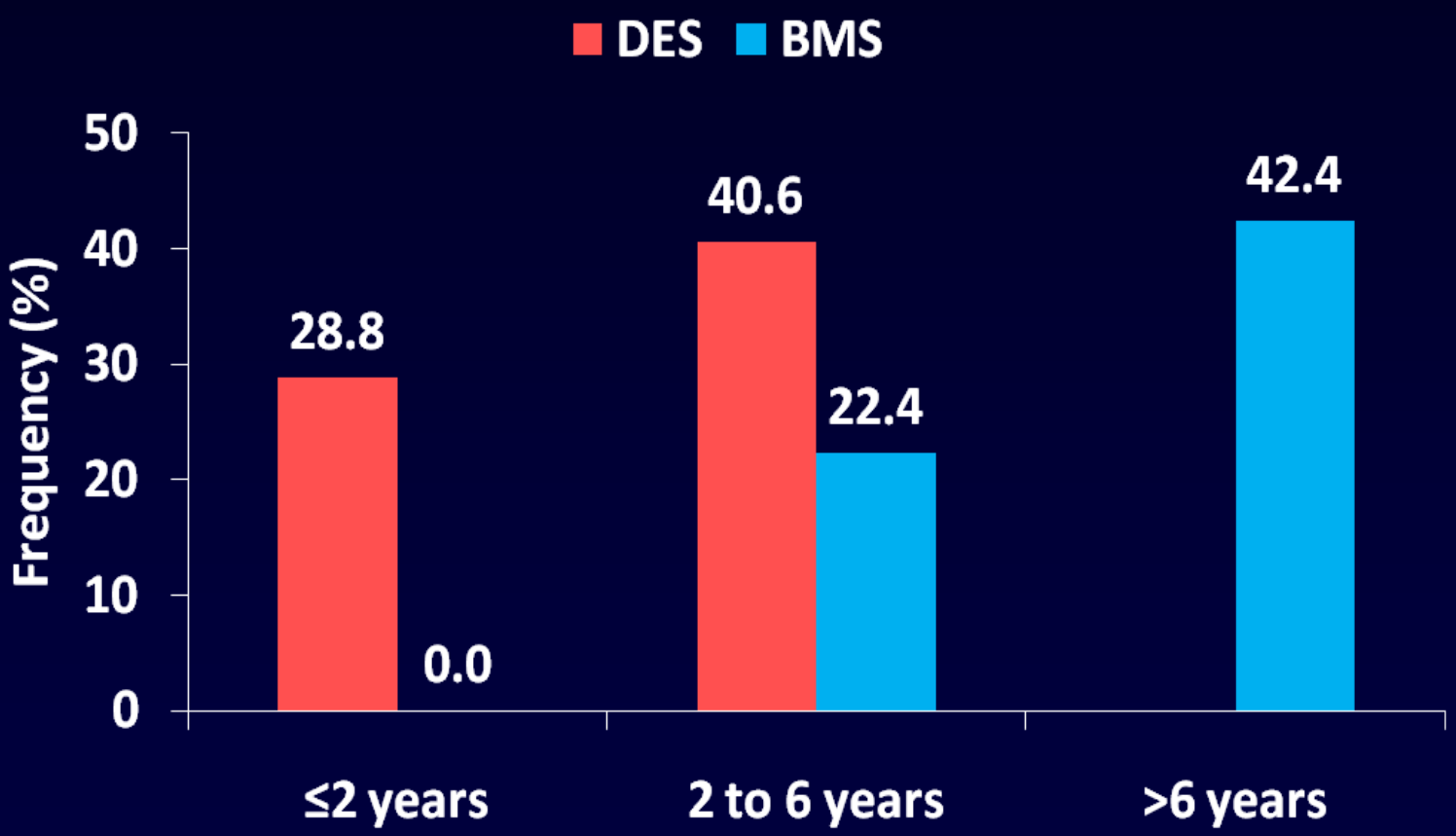
Optimal lipid-lowering treatment can prevent neointimal change from homogeneous to non-homogeneous pattern



Jang JY, Kim JS, Hong MK (corresponding author). *Atherosclerosis* 2015;242:553-559

Neoatherosclerosis in pathologic study

Incidence of Atherosclerotic Change With Time After Implantation of BMS (n=197) versus DES (n=209)



Nakazawa et al, JACC, 2011;57:1314-1322

OCT-based predictors for CK-MB elevation after elective PCI for ISR (n=125 ISR lesions)

Post-PCI CK-MB elevation was observed in 20 (16.0%) patients.

Independent predictors for post-PCI CK-MB elevation in multivariate analysis

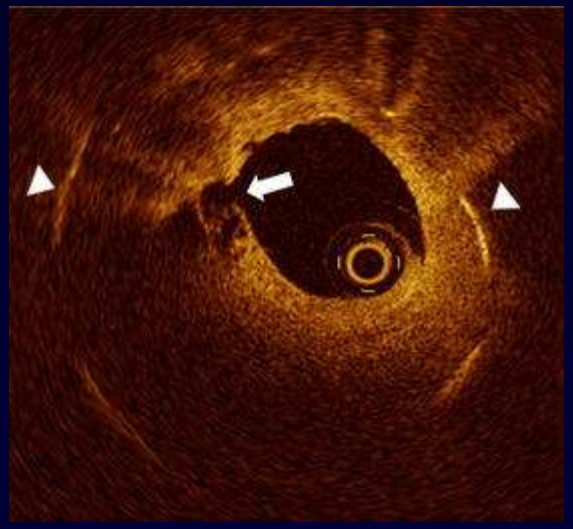
1) Maximum length of segments with neoatherosclerosis (OR, 1.463; 95% CI, 1.090–1.962; p=0.011),

2) Thin-cap fibroatheroma (OR, 14.328; 95% CI, 1.118–183.628; p=0.041) were

Lee SY, Hong MK (corresponding author). *Cathet Cardiovasc Intervent* 2015;85:564-572

Very late stent thrombosis after 1st-generation DES implantation (n=18)

Neointimal rupture



	VLST with rupture (n = 4)	VLST without rupture (n = 14)	P
Uncovered struts	0 (0.0)	9 (64.3)	0.082
Malapposed struts	0 (0.0)	7 (50.0)	0.092
Lipid-laden neointima	4 (100.0)	4 (28.6)	0.023

Neoatherosclerosis (44%, 8/18) is partly attributable to very late stent thrombosis in DES-treated patients

Ko YG, Hong MK (corresponding author). *Int J Cardiovasc Imaging* 2012;28:715-23

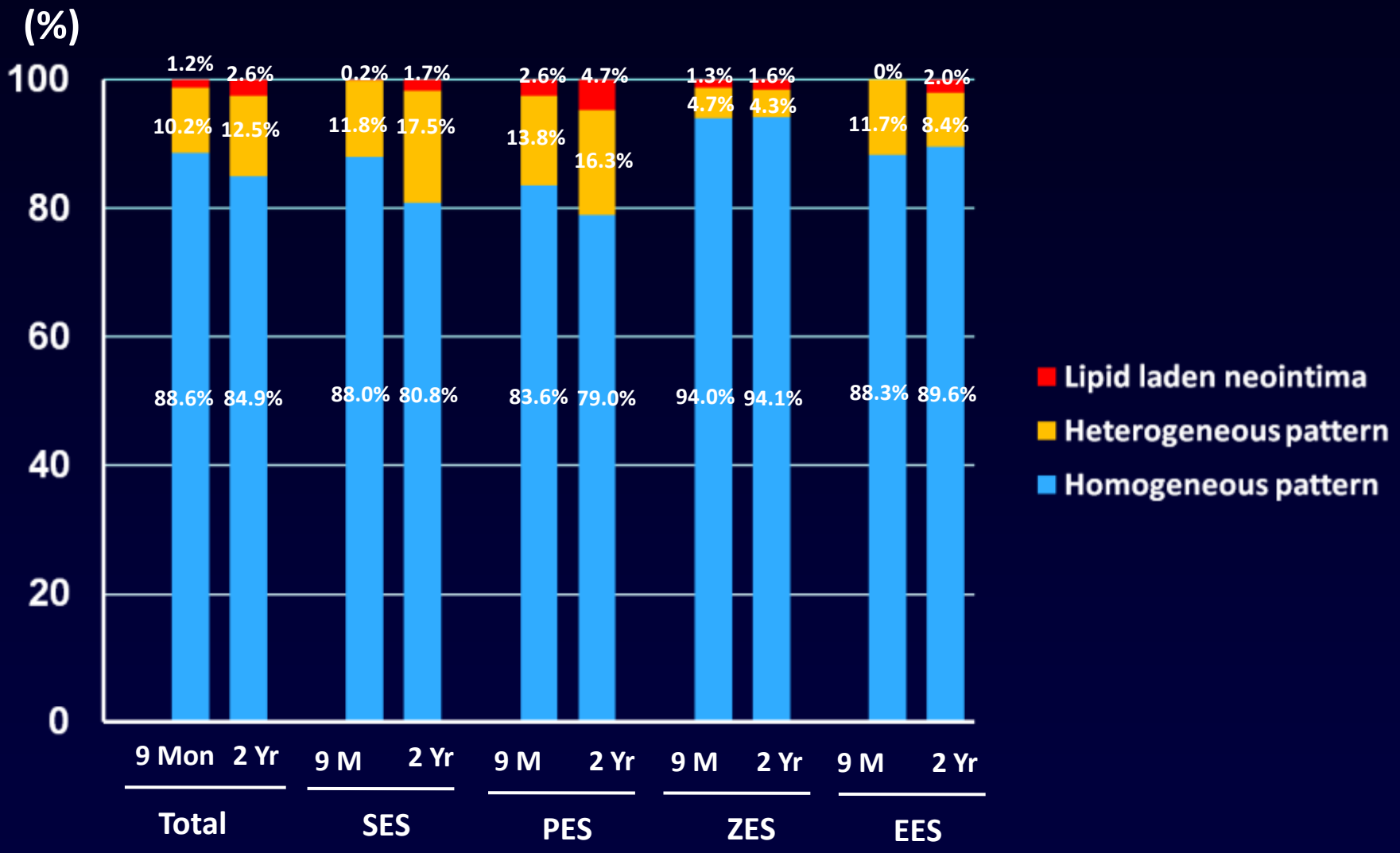
Serial OCT : DES

Neoatherosclerosis is a time dependent process.

Total (n = 76)	9 months FU	2 years FU	P
Qualitative analysis			
Intracoronary thrombus	8 (10.5%)	7 (9.2%)	0.79
Lipid-laden neointima	11 (14.5%)	21 (27.6%)	0.047
TCFA-like neointima	3 (3.9%)	10 (13.2%)	0.04
Neovascularization	34 (44.7%)	56 (73.7%)	<0.001
Extrastent lumen	15 (19.7%)	21 (27.6%)	0.25

Kim JS, Hong MK (corresponding author) et al. *JACC Cardiovasc imaging* 2012;5:1145-55

Serial OCT : DES



Kim JS, Hong MK (corresponding author) et al. *JACC Cardiovasc imaging* 2012;5:1145-55

Clinical implication of neoatherosclerosis: TLR and stent thrombosis

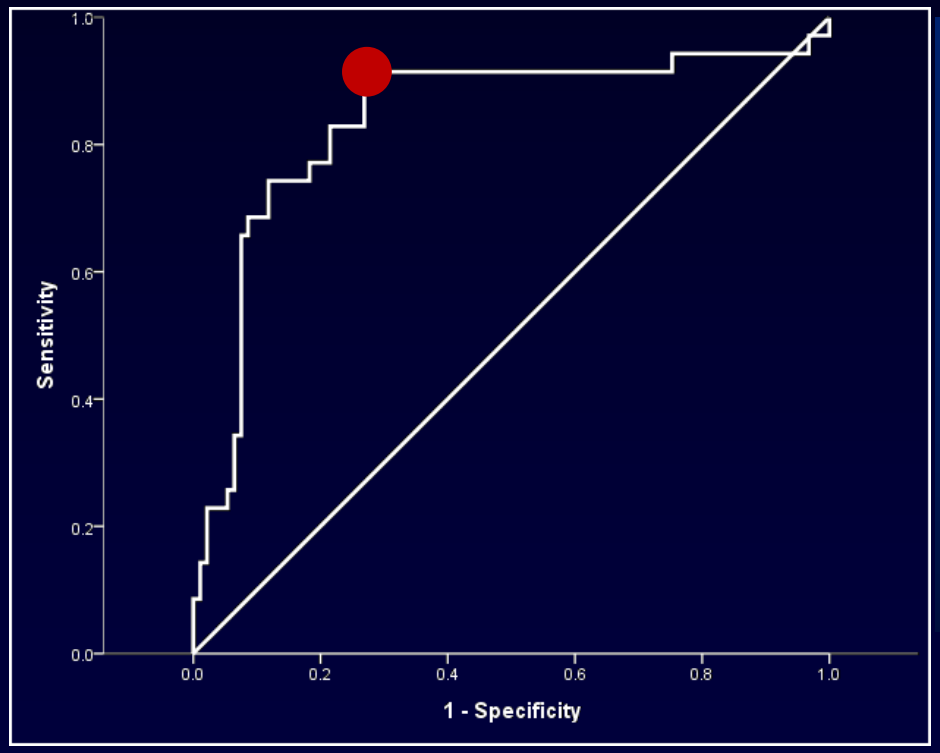
152 lesions (24 BMS, 74 first-generation DES and 54 second-generation DES) with NIH > 50% of stent area

	Presence of neoatherosclerosis (n = 54)	Absence of neoatherosclerosis (n = 98)	p
Time interval to follow-up OCT (months)	70.7 (54.4 – 120.4)	13.4 (10.6 – 39.6)	< 0.001
Clinical presentation at follow-up OCT, # (%)			< 0.001
Asymptomatic	4 (7.4)	22 (22.4)	
Stable angina	33 (61.1)	72 (73.5)	
Acute coronary syndrome	17 (31.5)	4 (4.1)	
Target lesion revascularization, # (%)	50 (92.6)	76 (77.6)	0.018
Stent thrombosis, # (%)	8 (14.8)	0 (0)	< 0.001

Lee SY, Hong MK (corresponding author). *EuroIntervention 2013;9:945-951*

Cut-off time to predict neoatherosclerosis in DES-treated lesions

Cross-sectional design
152 ISR lesions with intimal hyperplasia > 50% of stent area



Optimal cut-off time: 30 months

AUC: 0.839
95% CI: 0.764 to 0.898

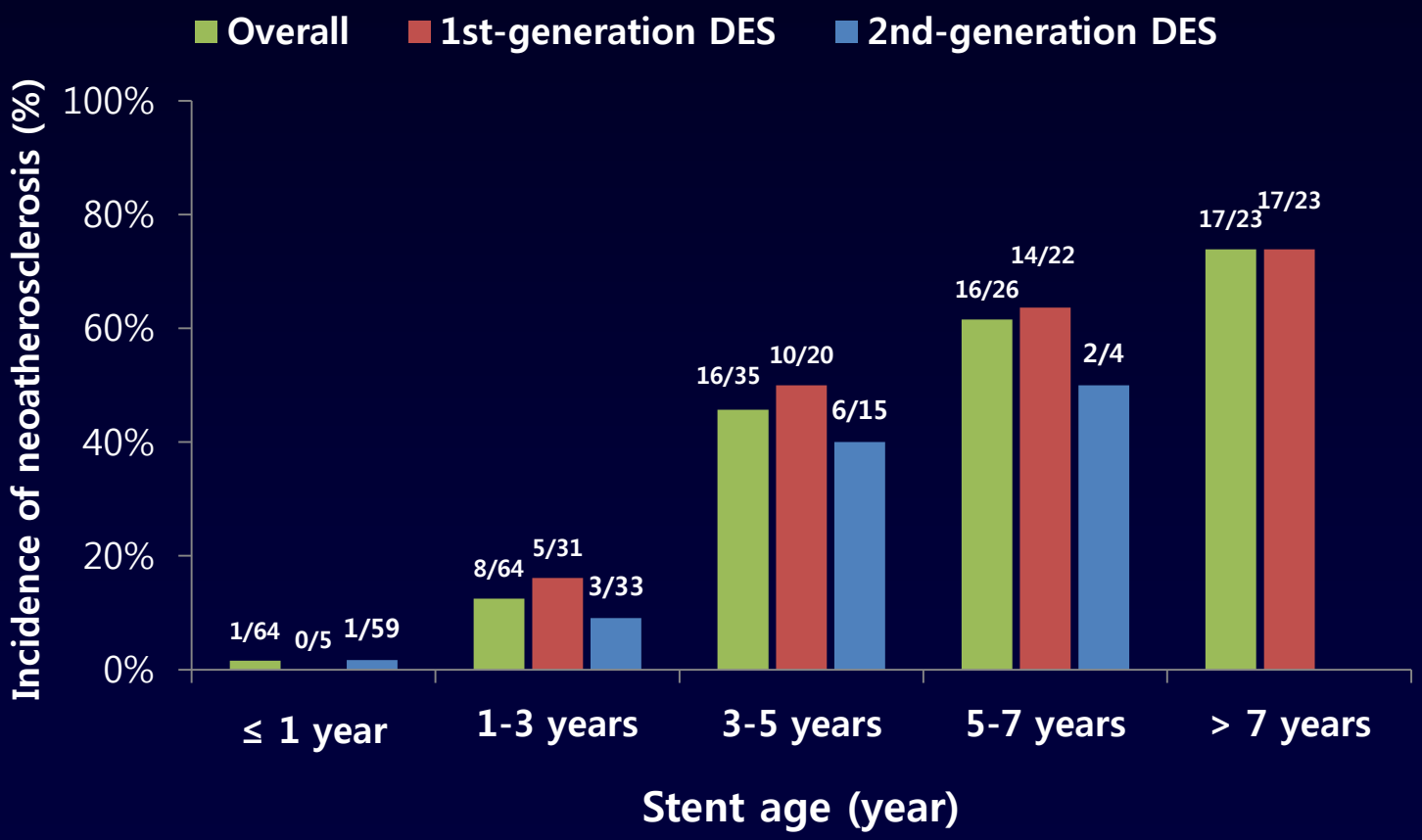
Sensitivity: 91.4%
Specificity: 72.0%
Negative predictive value: 95.7%
Positive predictive value: 55.2%

Lee SY, Hong MK (corresponding author). *EuroIntervention 2013;9:945-951*

Neoatherosclerosis in 2nd generation DES

212 DES-treated lesions (101 first-generation DES and 111 second-generation DES) with NIH > 50% of stent area

Neoatherosclerosis is a time dependent process.



Lee SY, Hong MK (corresponding author), et al. *Circ Cardiovasc Interv* 2015;8:e001878

Neoatherosclerosis in 2nd generation DES

212 DES-treated lesions (101 first-generation DES and 111 second-generation DES) with NIH > 50% of stent area

Multivariable analysis

	Odds ratio	95% CI	p
Baseline			
Age (years)	1.017	0.969 – 1.067	0.50
Male	1.077	0.393 – 2.947	0.89
Chronic kidney disease	4.113	1.086 – 15.575	0.037
2nd DES	0.538	0.196 – 1.481	0.23
Follow-up			
LDL >70 mg/dL	2.532	1.054 – 6.084	0.038
Stent age (years)	1.710	1.403 – 2.084	<0.001

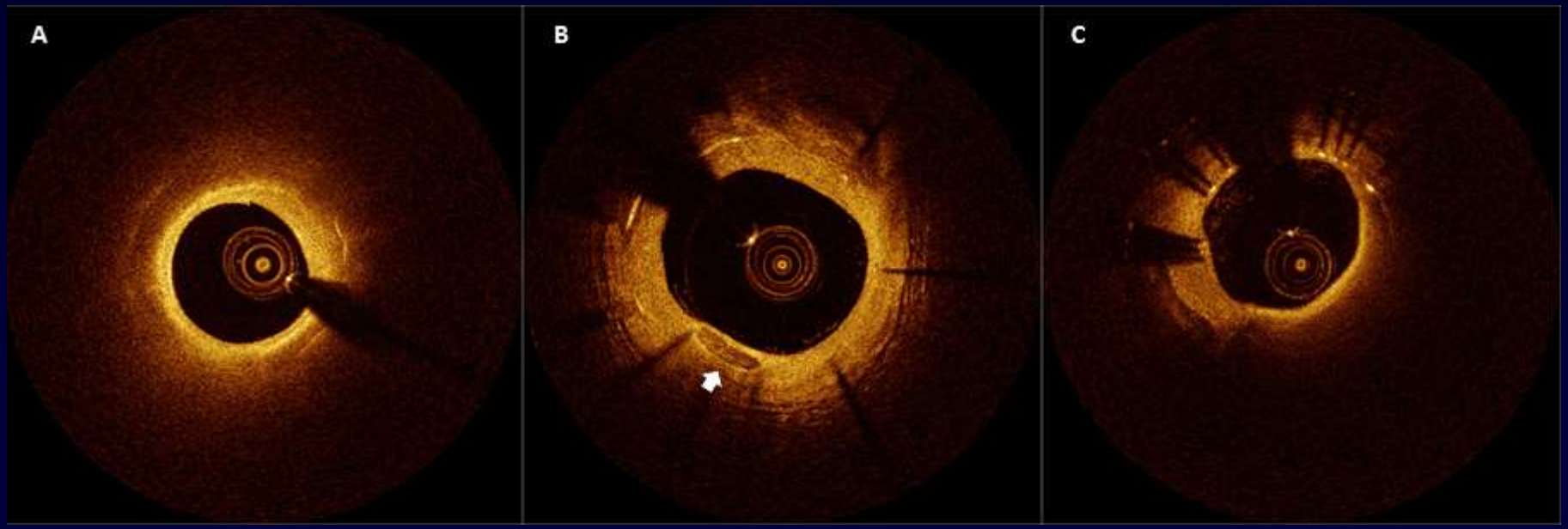
Compared to 1st DES, 2nd DES is not more protective against neoatherosclerosis.

CKD at index procedure and LDL cholesterol at follow-up may be associated with neoatherosclerotic restenosis

Lee SY, Hong MK (corresponding author), et al. *Circ Cardiovasc Interv* 2015;8:e001878

Early neoatherosclerosis within 1 year after DES implantation

- 449 patients (482 lesions ≤12 months after DES with mean neointimal thickness >100μm)
- Incidence of neoatherosclerosis: 6.4% (31/482 lesions)



Kim C, Kim BK, Hong MK (corresponding author). *Am Heart J* 2015;170:591-597

Predictor of early neoatherosclerosis

Variables	Univariate Models		Multivariate Model	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Male	1.27 (0.58-2.77)	0.549		
Age >65 y	1.09 (0.51-2.34)	0.819		
Hypertension	2.61 (1.10-6.19)	0.029	3.20 (1.32-7.78)	0.010
DM	1.02 (0.47-2.21)	0.97		
Current smoker	1.08 (0.45-2.58)	0.865		
ACS at index procedure	0.75 (0.36-1.58)	0.452		
Fasting glucose >100 mg/dL	0.88 (0.32-2.37)	0.792		
Estimated GFR <60 mL/min/1.73 m^2	1.14 (0.48-2.72)	0.771		
LDL-cholesterol <100 mg/dL	Reference		Reference	
LDL-cholesterol 100-129 mg/dL	1.42 (0.53-3.83)	0.489	1.63 (0.59-4.51)	0.350
LDL-cholesterol ≥130 mg/dL	3.10 (1.33-7.21)	0.009	3.89 (1.62-9.36)	0.002
Statin	0.50 (0.14-1.77)	0.284		
ACE-i or ARB	0.98 (0.45-2.12)	0.949		
1st generation DES	Reference		Reference	
Next-generation DES	0.57 (0.26-1.25)	0.158		
EES	0.44 (0.13-1.44)	0.174	0.40 (0.12-1.36)	0.141
ZES	0.51 (0.22-1.23)	0.135	0.49 (0.20-1.20)	0.119
BES	1.12 (0.36-3.46)	0.849	1.35 (0.41-4.43)	0.622
Stent diameter >3 mm	0.83 (0.36-1.93)	0.669		
Total stent length >35 mm	1.62 (0.73-3.60)	0.233		
Time to OCT, per 1 month	1.08 (0.95-1.23)	0.258	1.11 (0.97-1.26)	0.121

Kim C, Kim BK, Hong MK (corresponding author). *Am Heart J* 2015;170:591-597

Conclusions

- **OCT is an useful tool to evaluate the status of neointimal tissue which may be associated with occurrence of late DES failure.**

- **Optimal lipid control might be beneficial to improve the DES-related neointimal characteristics.**


Dreams will
come true