Assessment of DES Failure Using IVUS

Gary S. Mintz, MD
Cardiovascular Research Foundation
New York, NY

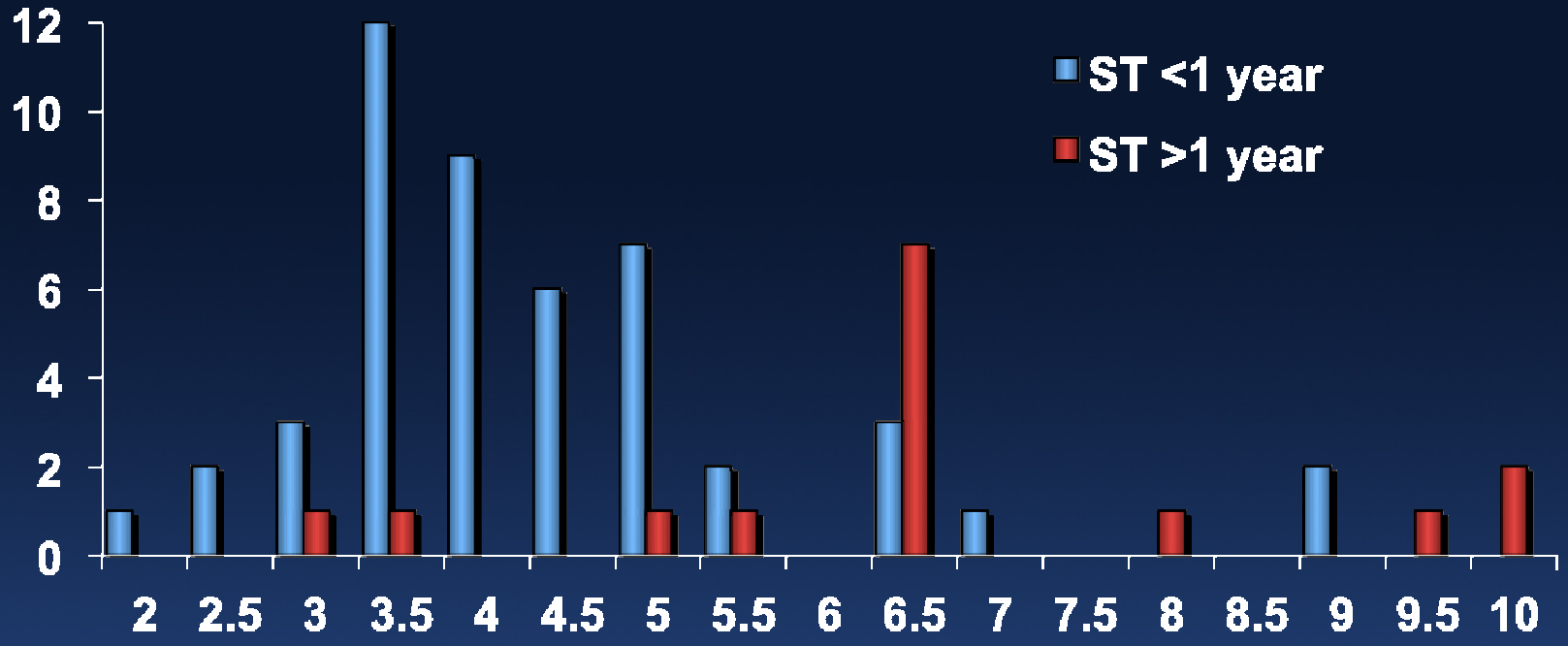
Findings in DES Failure

DES Restenosis		Early/Late DES Thrombosis	Very Late DES Thrombosis
+	Underexpansion	+	
+	Intimal hyperplasia		
	Thrombus	+	+
	Acute malapposition	±	
	Late acquired malapposition		+
+	Strut fracture	±	+
+	Muscle bridge		
+ (Late catch-up)	Neoatherosclerosis		+

DES Underexpansion and Restenosis and Early/Late, but Not Very Late Thrombosis

Early/Late DES Thrombosis	DES Restenosis
•*Fujii et al. J Am Coll Cardiol 2005;45:995-8)* •*Okabe et al., Am J Cardiol. 2007;100:615-20* •*Liu et al. JACC Cardiovasc Interv. 2009;2:428-34* •*Choi et al. Circ Cardiovasc Interv (in press)*	•*Sonoda et al. J Am Coll Cardiol 2004;43:1959-63* •*Hong et al. Eur Heart J 2006;27:1305-10* •*Doi et al JACC Cardiovasc Interv. 2009;2:1269-75* •*Fujii et al. Circulation 2004;109:1085-1088* •*Kang et al. Circ Cardiovasc Interv 2011;4:9-14* •*Choi et al. HORIZONS, unpublished*

with DES Thrombosis



(Okabe et al. Am J Cardiol 2007;100:615-20)
(Liu et al. JACC Cardiovasc Interv. 2009;2:428-34)
(Cook et al. Circulation 2007;115:2426-34)
(Choi et al. Circulation Cardiovasc Interven, in press)

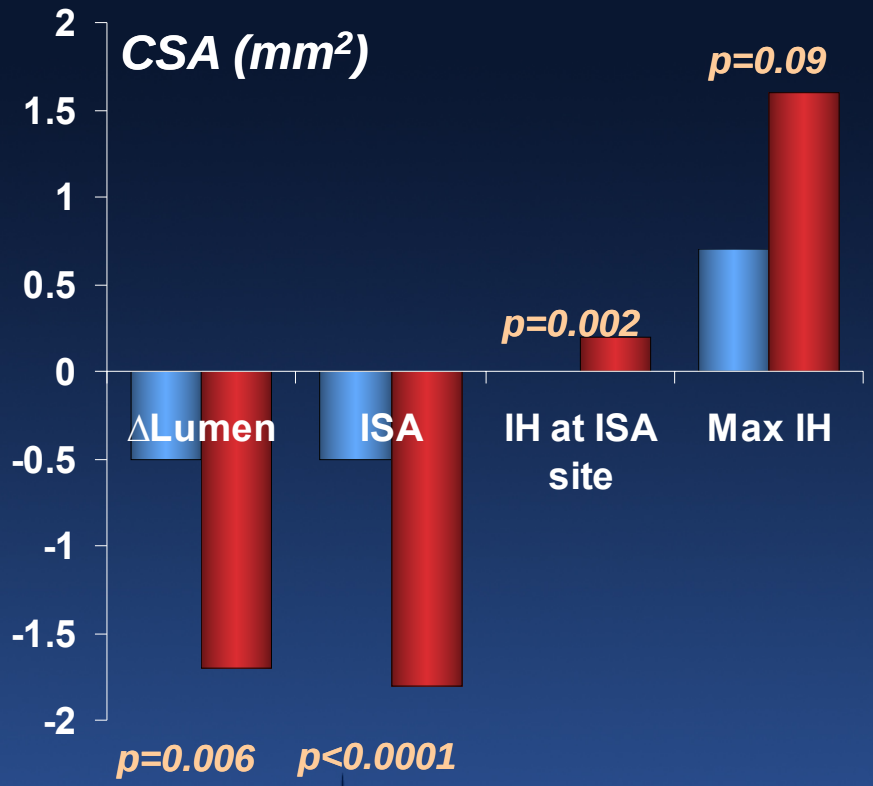
What about acute stent malapposition?

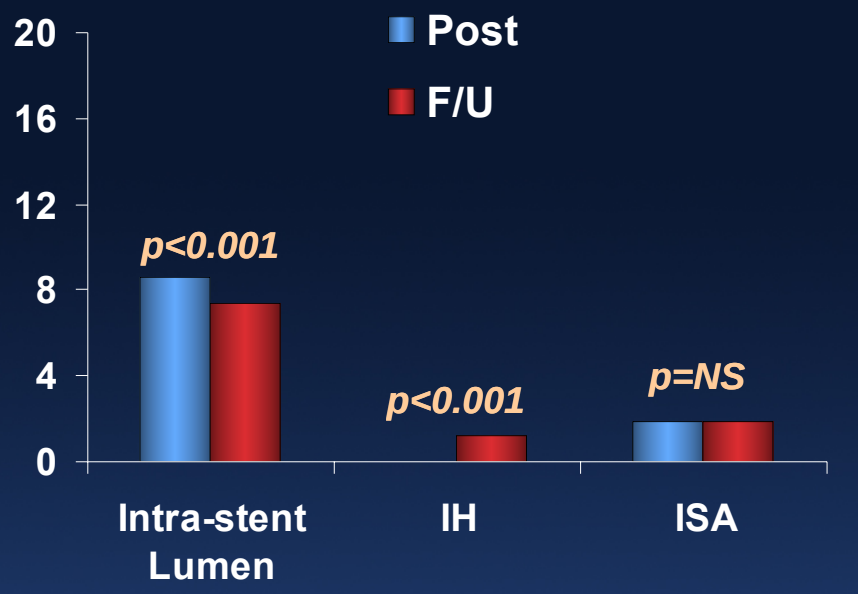
Although it was one of the original Colombo criteria, there is little or no data linking *isolated* acute stent malapposition to adverse clinical events including DES thrombosis.

- **Persistent stent malapposition is associated with *less* intimal hyperplasia – the drugs can cross small stent vessel-wall gaps**
  - *Hong et al, Circulation. 2006;113:414-9*
  - *Balakrishnan et al. Circulation 2005;111:2958-65*
  - *Kimura et al. Am J Cardiol . 2006;98:436-42*
  - *Guo et al. Circulation. 2010;122:1077-1084*
- **In the integrated analysis of slow release formulation PES in TAXUS IV, V, and VI and TAXUS ATLAS Workhorse, Long Lesion, and Direct Stent Trial, there was no effect of acute stent malapposition on MACE (or stent thrombosis within the first 9 months) – whether BMS or DES**
  - *Steinberg et al, JACC Cardiovasc Intervent 2010;3:486-94*
- **In HORIZONS-AMI, post-intervention acute stent malapposition was detected in 33.8% of 68 lesions treated with PES and 38.7% of 24 lesions treated with BMS (p=0.7). There was no difference in MACE between patients with versus without acute stent malapposition in either BMS or PES cohorts.**
  - *Guo et al. Circulation. 2010;122:1077-1084*

Late incomplete SES Apposition and IH

- *Persistent ISA (n=40, 83% decreased in size)*
- *Completely resolved ISA (n=15)*





Kimura, et al. Am J Cardiol 2006;98:436-42
Hong et al. Circulation 2006;113:414-9

CARDIOVASCULAR RESEARCH FOUNDATION
A Passion for Innovation

Columbia University Medical Center
NewYork-Presbyterian
The University Hospital of Columbia and Cornell

IVUS Meta-Analysis of Late Stent Malapposition (LSM) and VLST (>12 mos)

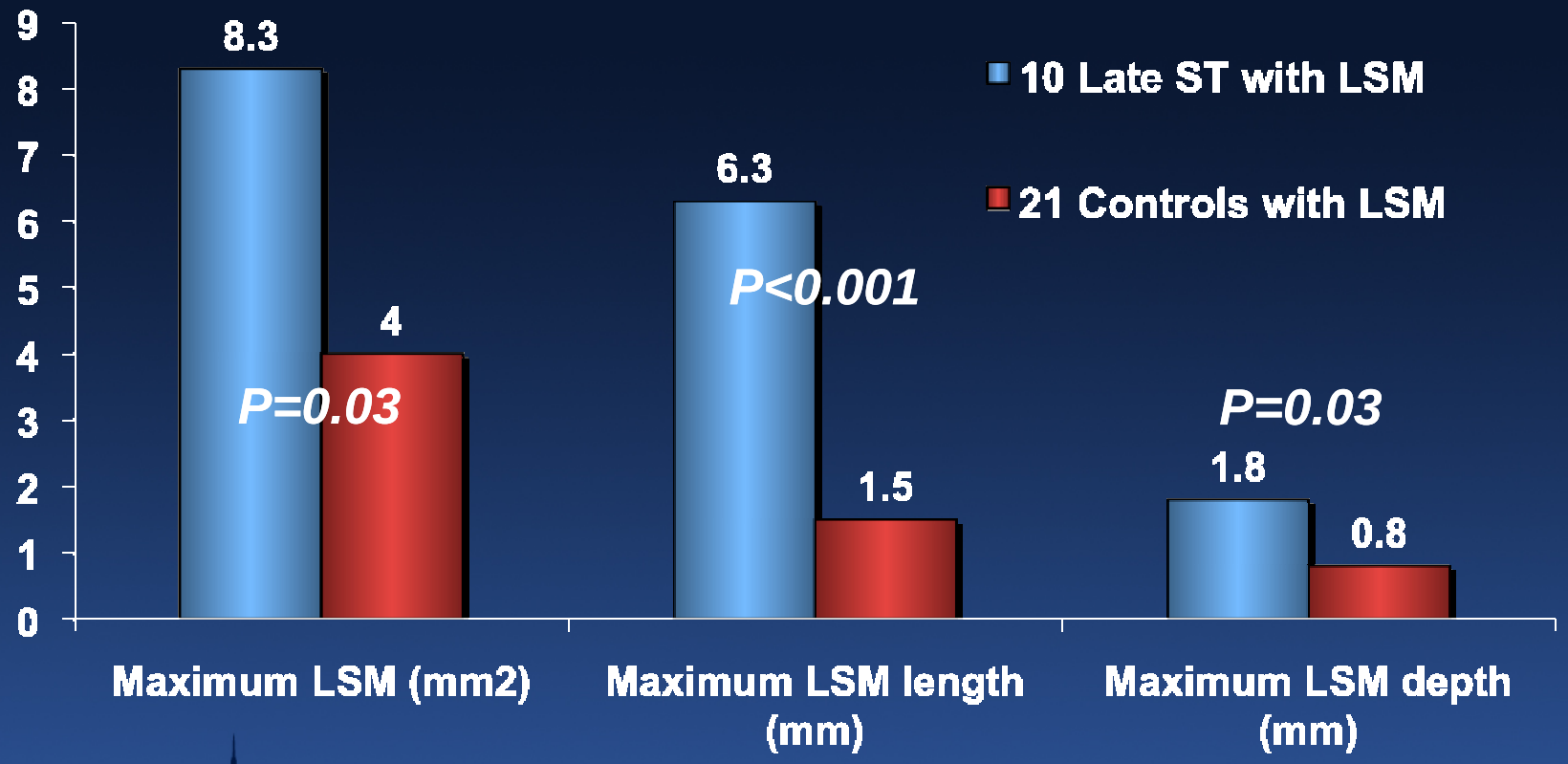
- LSM: 17 studies with 4648 patients (2453 BMS and 2195 DES)
  - LSM more common in DES than BMS (OR=2.5, p=0.02)
  - SES > PES > ZES > EES
- VLST: 5 studies with 2080 patients (228 LSM and 1852 no-LSM)
  - 6 Very late ST (>12 mos), 4 in LSM
  - Risk of very late ST was higher in LSM patients (OR=6.5, p=0.02), but only based on the expected numbers of very late ST

(Hassan et al. Eur Heart J 2010;31:1172-80)

	Clinical F-Up	Stent Type	LSM?	#	Observed LSM (#)		Expected VLST (#)
					LST	VLST	
Hoffmann	48 mos	SES+BMS	Y	57	0	1	0.18
			N	268	0	0	0.82
Tanabe	12 mos	PES+BMS	Y	46	0	NA	0.2
			N	423	2	NA	1.8
Hong	36 mos	SES+PES	Y	82	NA	1	0.44
			N	475	NA	2	2.56
Siqueira	29 mos	SES+PES	Y	10	0	2	0.11
			N	172	0	0	1.89
Weissman	24 mos	PES+BMS	Y	33	0	0	0.06
			N	514	1	0	0.94

Hassan et al. Eur Heart J 2010;31:1172-80

LSM was found in 77% of 13 VLST pts vs 12% of controls (p<0.0001)

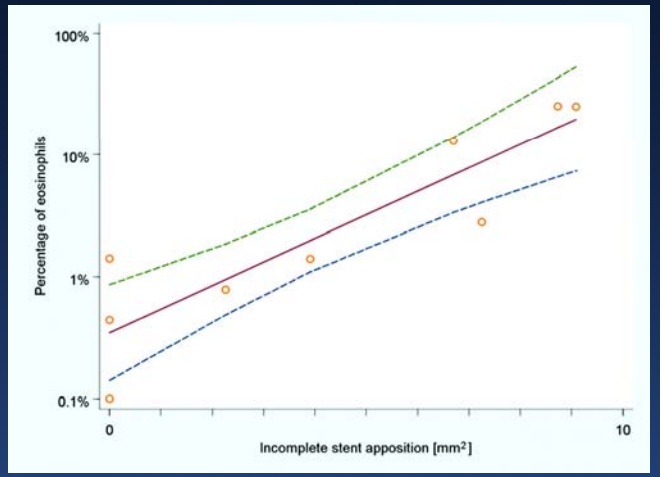


(Cook et al. Circulation 2007;115:2426-34)

Correlation of IVUS Findings With Aspirates in 28 Pts with Very Late DES Thrombosis

- **28 pts with very late DES ST and 26 controls**
- **LSM in 73% of very late DES ST segments. Maximal LSM area measured 6.2±2.4mm², and length measured 9.4±9.5mm. LSM area exceeded 5.0mm² in 5 of 8 segments (63%)**

	WBCs	p	Eos	p
Controls				
Spontaneous MI	291±94		7±10	
Early ST-BMS	146±117		1±1	
Early ST-DES	73±117		1±2	
Very late ST-BMS	84±50	0.0001	2±3	0.038
Very late ST-DES	283±149		20±24	



LSM area correlated with total eosinophil count (p=0.008)

(Cook et al. Circulation 2009;120:391-9)

Nordic IVUS Study (NIDUS): A registry of 124 stent thrombosis cases (87 DES, 37BMS)

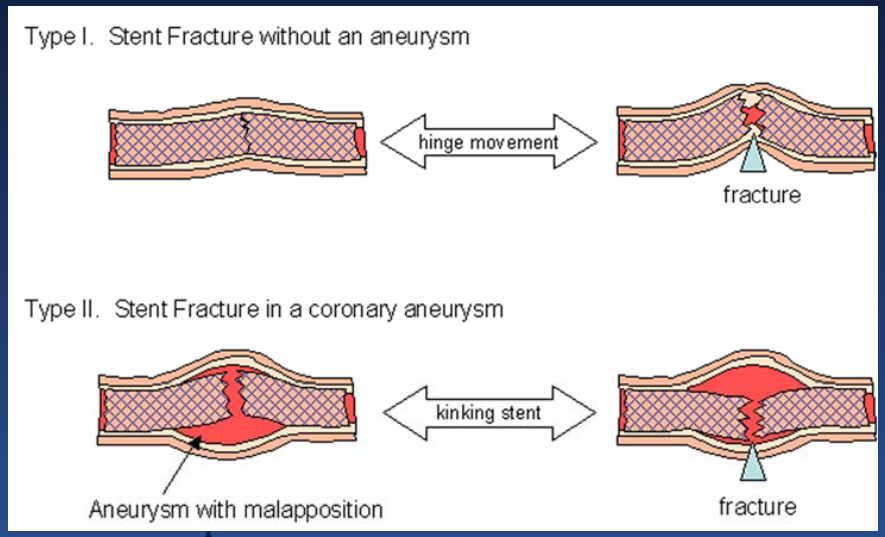
	Early/Late DES Thrombosis	Very Late DES Thrombosis
#	26	61
Stent fracture	4	10
Stent malapposition	7	30

Both stent fracture and malapposition were seen in 4 pts (7%); neither one was noted in 25 pts (41%)

(Kosonen et al. EuroPCR 2010)

Analysis of 20 DES fractures in 17 patients

- 15 stent fractures in 13 pts were associated with in-stent restenosis (all focal); and 2 stent fractures in 2 pts were associated with very late stent thrombosis
- Five stent fractures occurred within a coronary aneurysm accompanied by malapposition despite the absence of a coronary aneurysm at index.



Comparing stent fractures with vs without an aneurysm, complete stent fracture was more frequent (100% vs. 27%, p=0.008), and all presented >1 year post-stenting (vs. 33%, p=0.03).

Doi et al. Am J Cardiol 2009;103:818-23

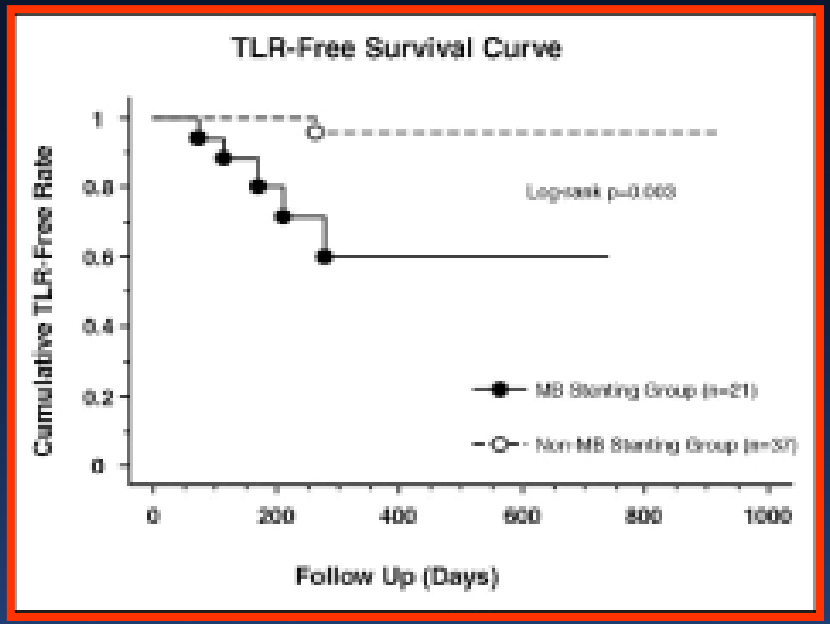
Meta-analysis of incidence, clinical characteristics and implications of stent fracture.

- Eight studies with 108 stent fractures in 5,321 patients
- The mean incidence of stent fracture per patient was 4.0%. All cases except one were reported with SES.
- The probability of stent fracture was significantly higher in
  - RCA than in the LAD and LCX lesions ($p<0.01$).
  - Overlapping stents (7.5% vs 2.1%, $p=0.01$) and long stents (46 vs 32.5mm, $p<0.01$).
- *Lesions with stent fractures had higher rates of ISR (38% vs 8.2%, $p<0.01$) and TLR (17% vs 5.6%, $p<0.01$); and the probability of stent fractures was higher in patients with ISR (12.8% vs 2.1%, $p<0.01$) and TLR (8.8% vs 2.7%, $p<0.01$).*

Chakravatny et al. Am J Cardiol 2010;106:1075-80

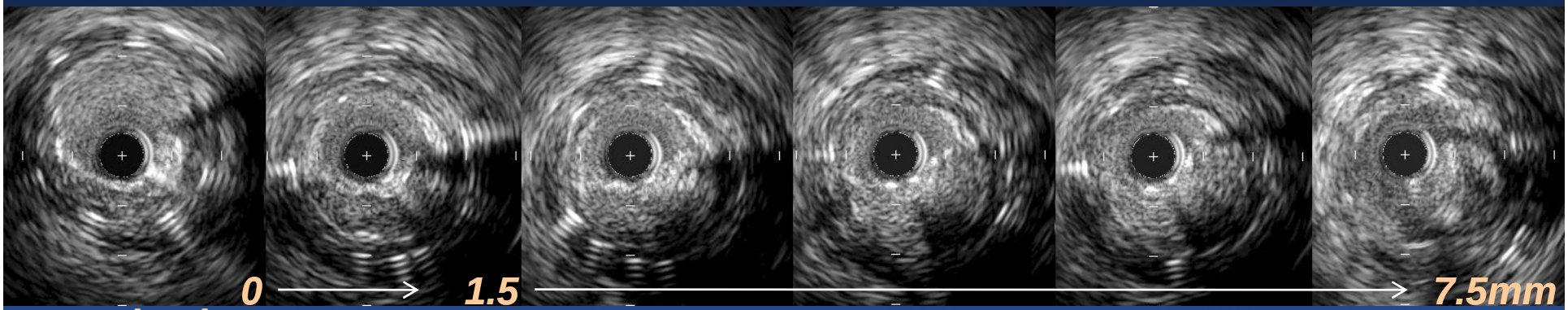
Impact of muscle bridge on DES restenosis

- IVUS identified muscle bridges in 70/317 patients undergoing LAD DES implantation.
- DES extended into the MB segment beyond the obstructive lesion in 24 pts(34%), although significant plaque was not observed within any muscle bridge segment.
- MSA was significantly smaller in the MB stent group than non-MB stent group: 4.8±1.1 vs 5.8±1.8mm^2 (p=0.02).
- At a mean follow-up of 358 days, TLR, TVR, and MACE were more common in pts with versus without MB stent placement.



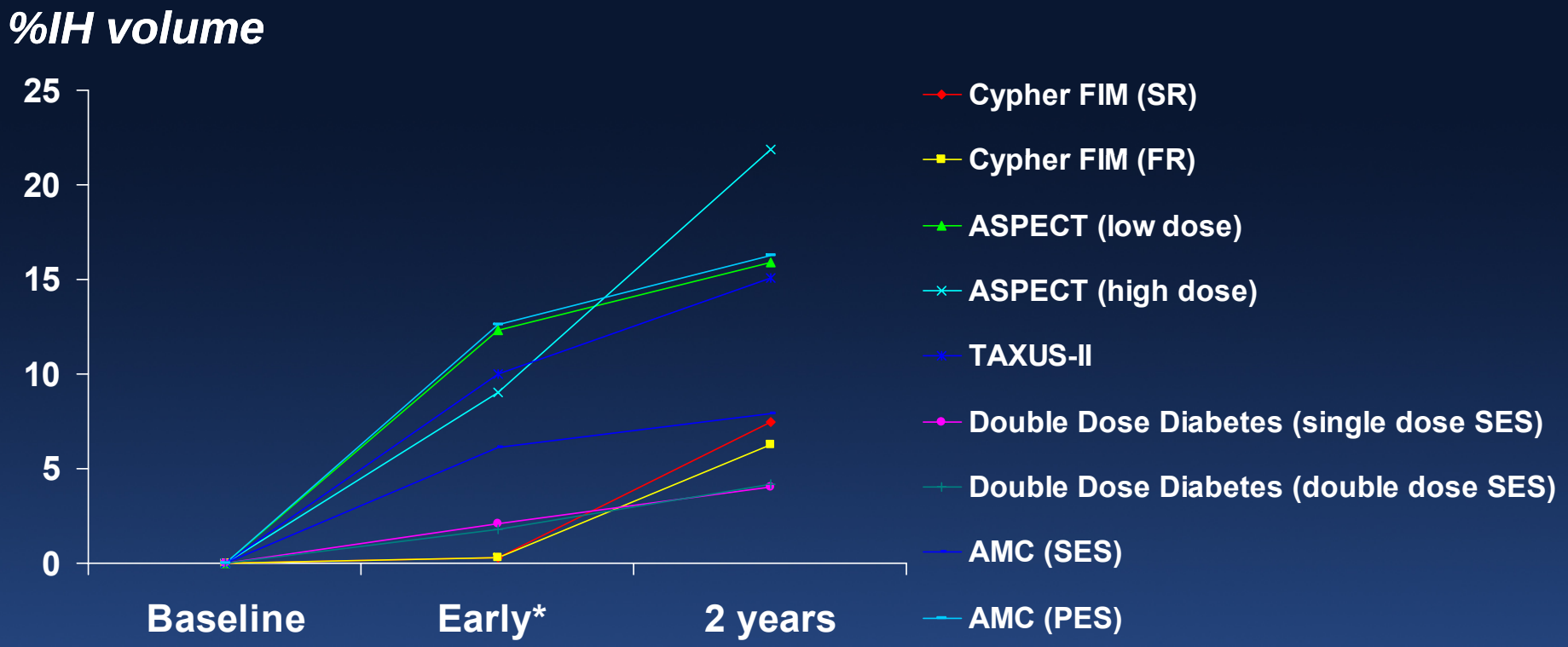
IVUS analysis of 23 very late DES thrombosis cases at Asan Medical Center

- LSM was observed in 17 DES pts (73.9%)
- In-stent neointimal rupture or peri-stent reference segment plaque rupture was observed in 15 DES pts (65.2%)



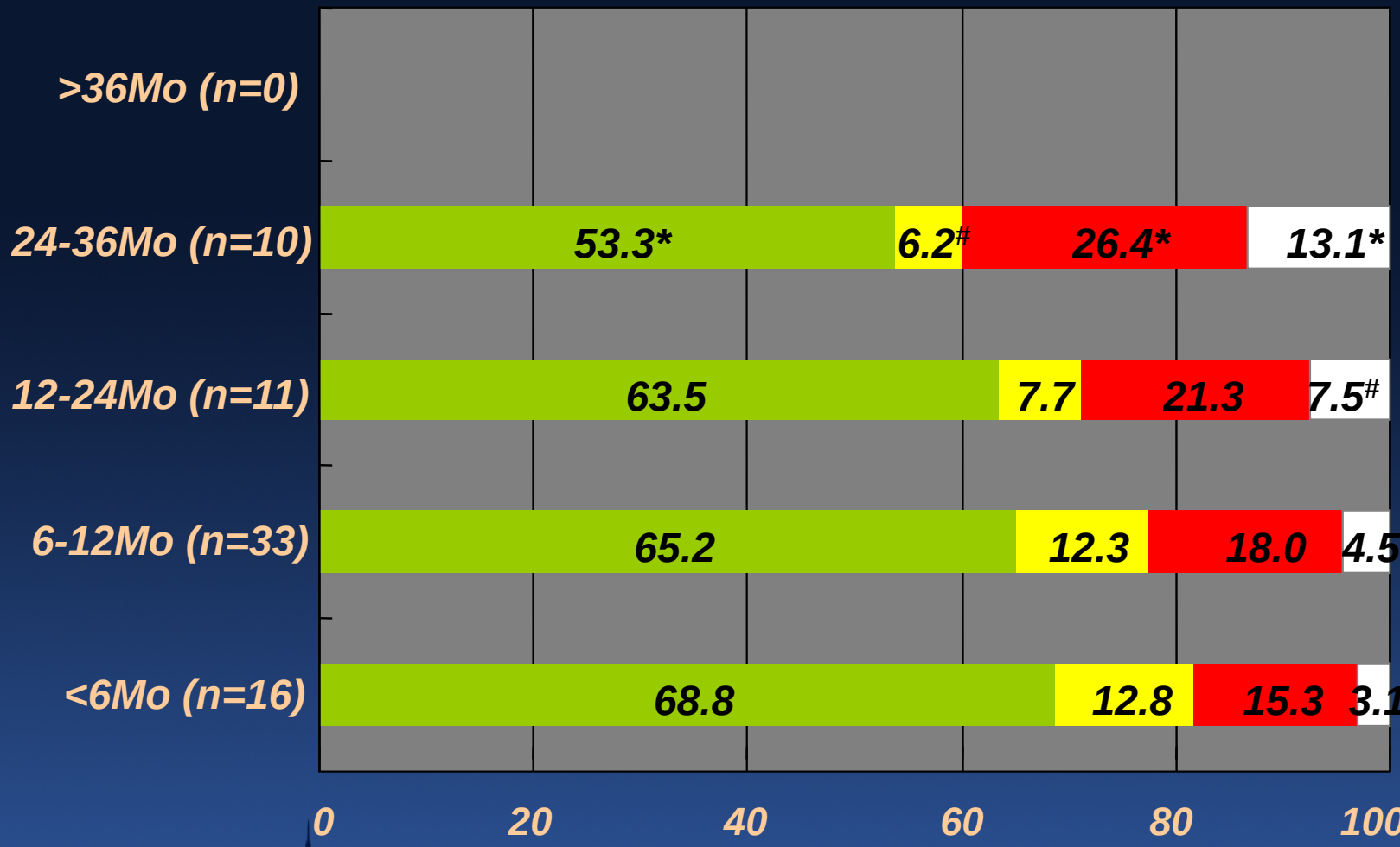
(Lee et al. J Am Coll Cardiol. 2010;55:1936-42)

Late DES Catch-Up Among IVUS Substudy Patients



**defined as 4-9 months*

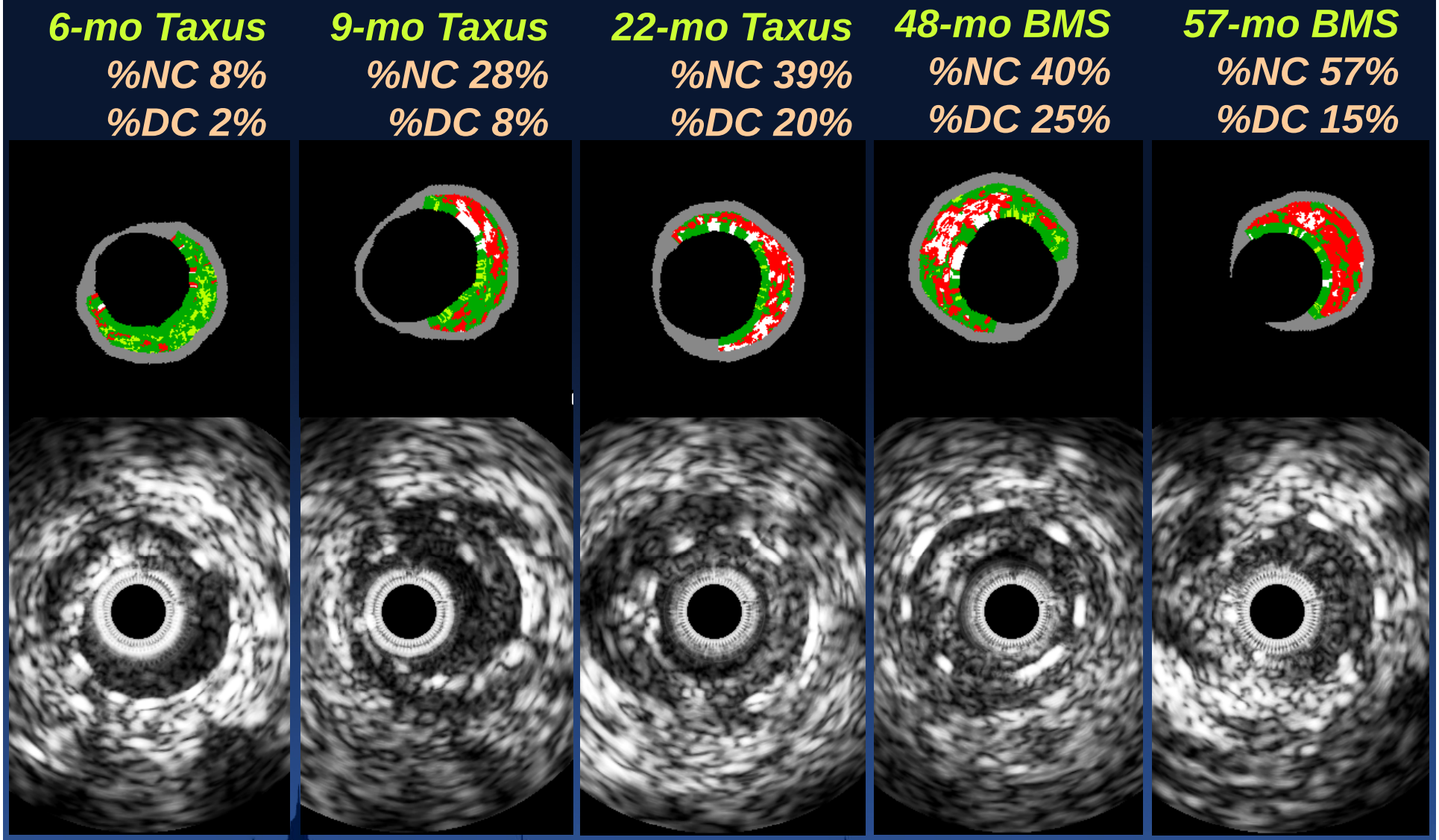
VH Composition of Neointima at Various Follow-Up Times in 70 DES Restenosis Lesions



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

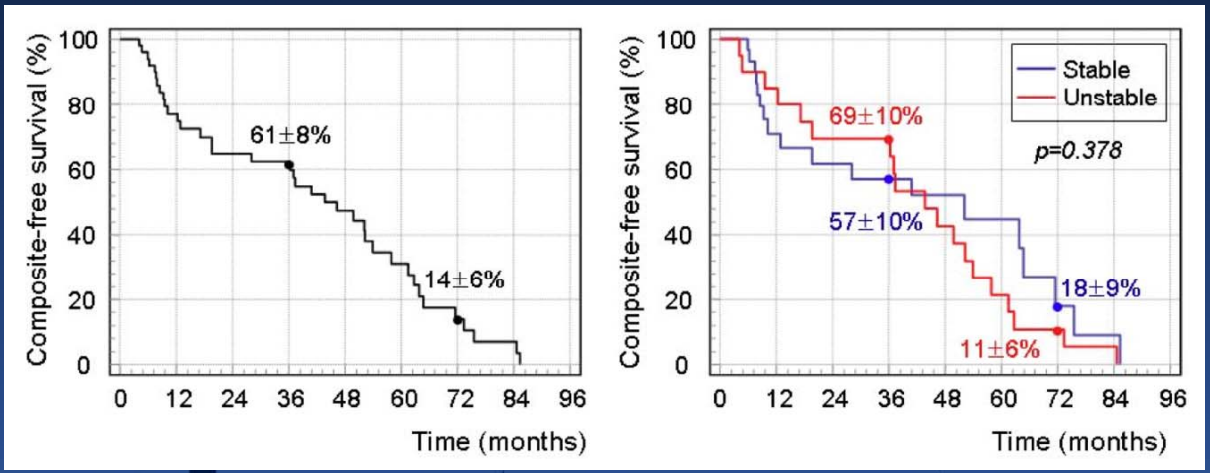
Kang et al. Am J Cardiol. 2010;106:1561-5

Neointimal VH Composition at the Maximal %IH Sites



In-stent Neoatherosclerosis after DES (n=50, median follow-up of 32 months)

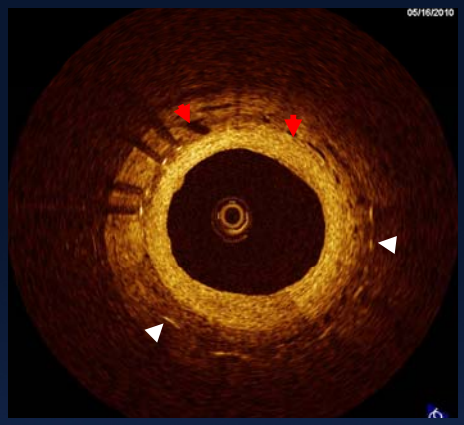
- 52% lesions had at least one in-stent TCFA-like neointima
- 58% had at least one in-stent neointimal rupture.
- Fibrous cap thickness negatively correlated with follow-up time (r=-0.318, p=0.024).
- 20 months post-implantation was the best cut-off to predict TCFA-like neointima). DES ≥20 months post-implantation had
  - Higher incidence of TCFA-like neointima (69% vs. 33%, p=0.012)
  - Higher incidence of red thrombi (27% vs. 0%, p=0.007).



Kang et al. Circulation, in press

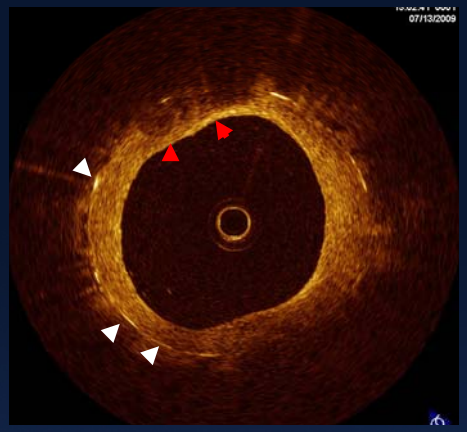
Late in-stent neoatherosclerosis in DES

Microvessel



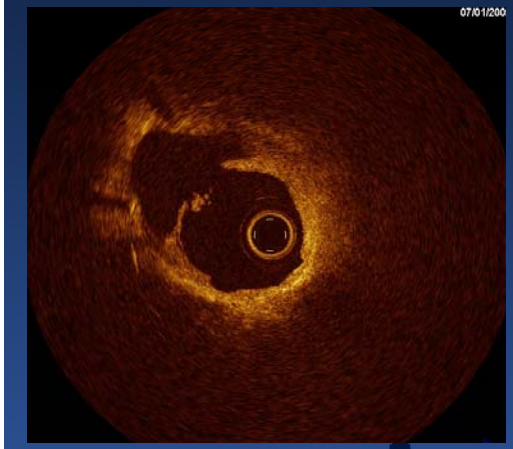
TCFA-like neointima

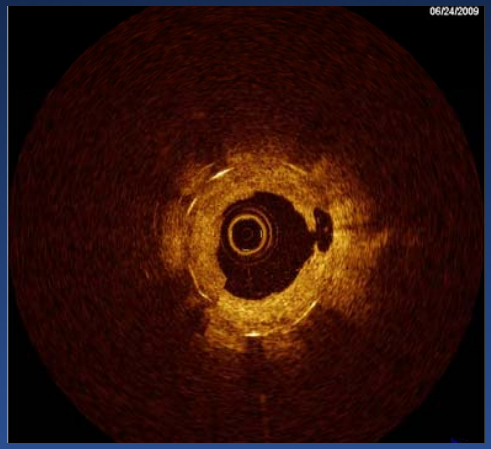
Calcium



Red thrombus

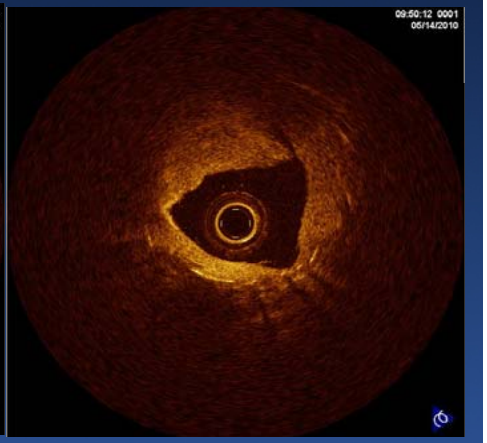
Neointimal rupture





Mixed thrombus

White thrombus

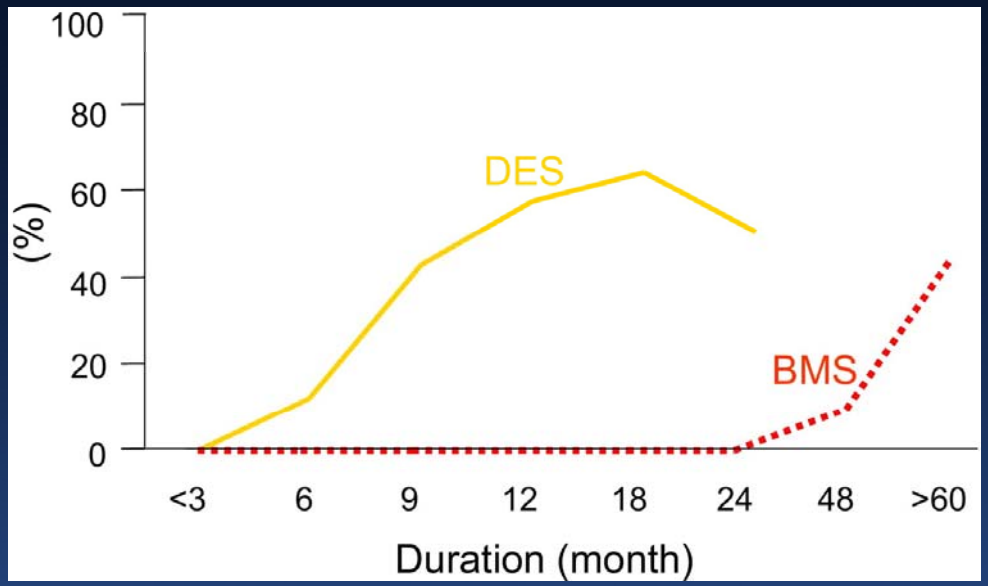


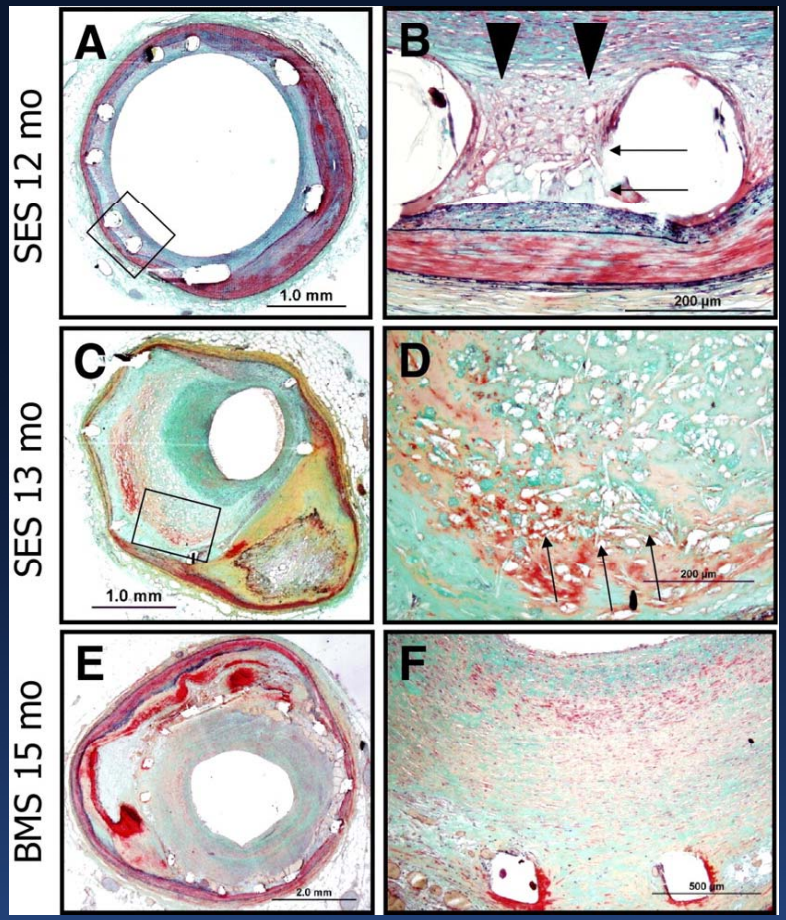
Kang et al. Circulation, in press

CARDIOVASCULAR RESEARCH FOUNDATION
A Passion for Innovation

COLUMBIA UNIVERSITY MEDICAL CENTER
NewYork-Presbyterian
The University Hospital of Columbia and Cornell

Percentage of Patients With Atherosclerotic Changes in DES Versus BMS in Relation to Duration of Implant at Autopsy





Nakazawa et al. J Am Coll Cardiol Img 2009;2:625-8

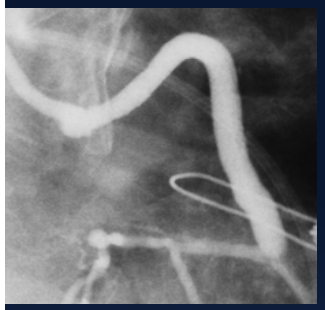
Pathology of In-stent Neoatherosclerosis in

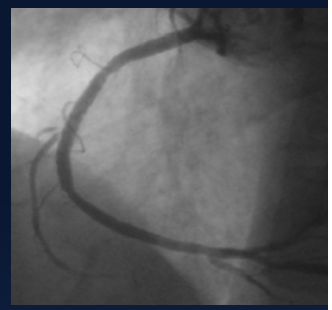
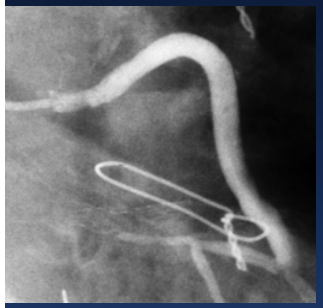
- 197 BMS, 103 SES, and 106 PES with implant duration >30 days
- The incidence of neoatherosclerosis was significantly greater in DES (31%) than BMS (16%; p < 0.001).
- Median stent duration with neoatherosclerosis was shorter in DES than BMS (420 days v 2,160 days, p < 0.001).

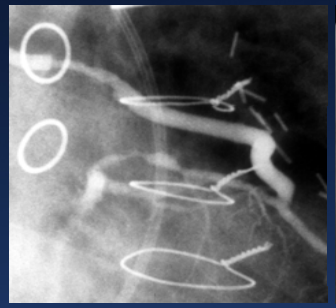
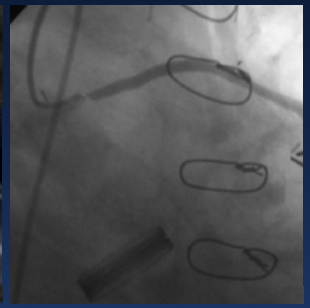
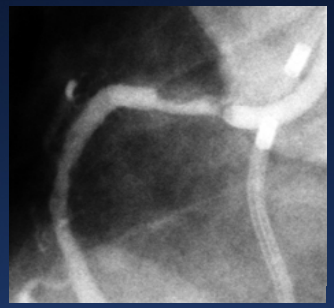
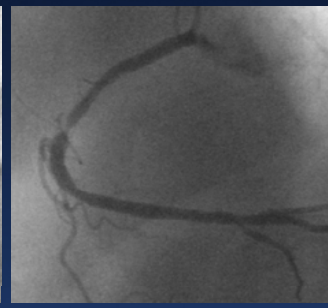
	≤2yrs	2-6yrs	>6yrs
BMS	0%	22%	42%
DES	29%	41%	

  - 7 BMS and 3 DES had TCFA or plaque rupture occurring with shorter implant durations for DES (1.5±0.4 years) compared to BMS (6.1±1.5 years).

Nakazawa et al. J AM Coll Cardiol 2011;57:1314-22

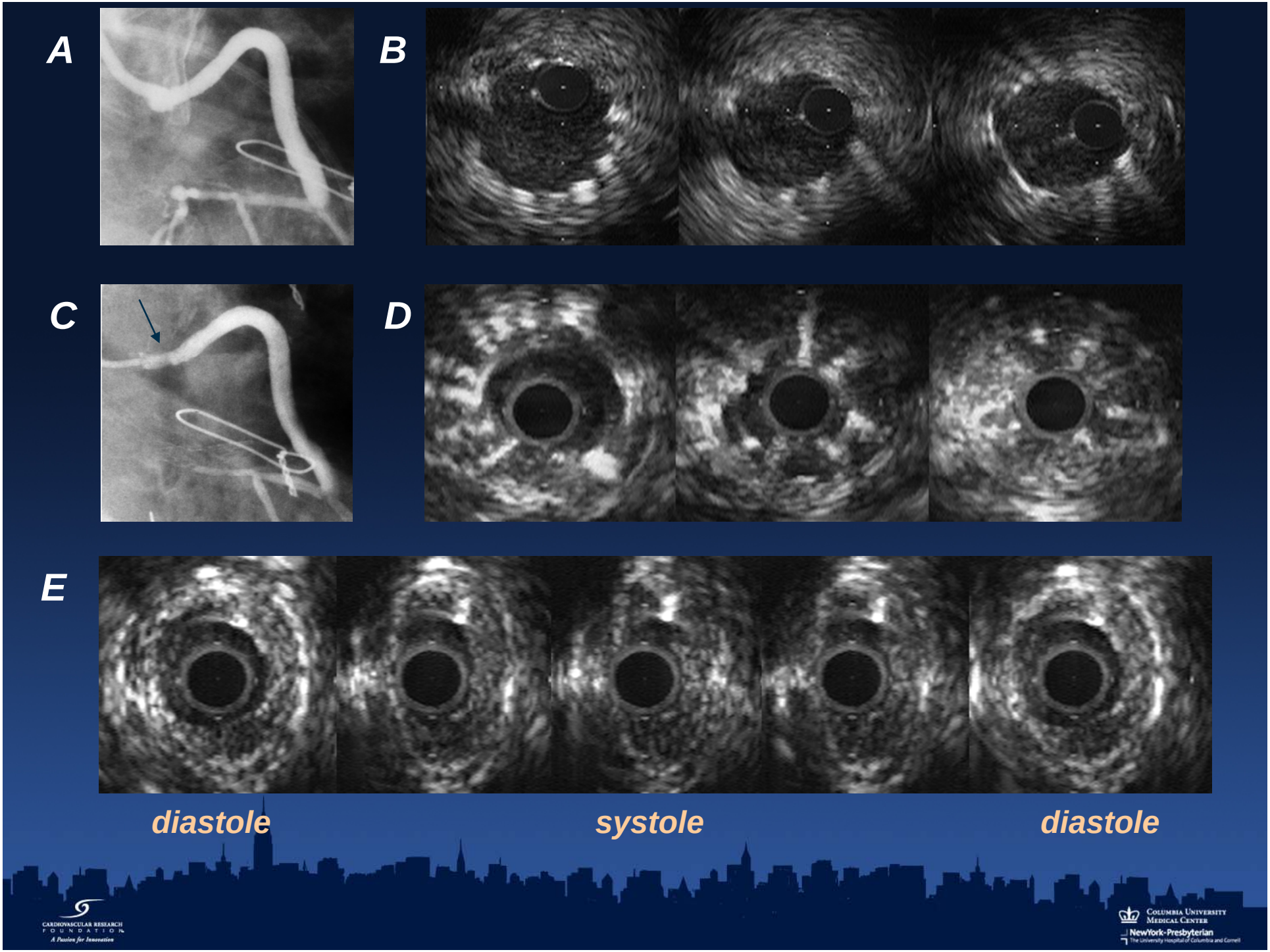


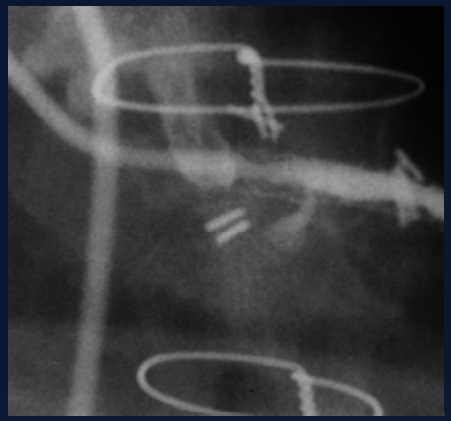



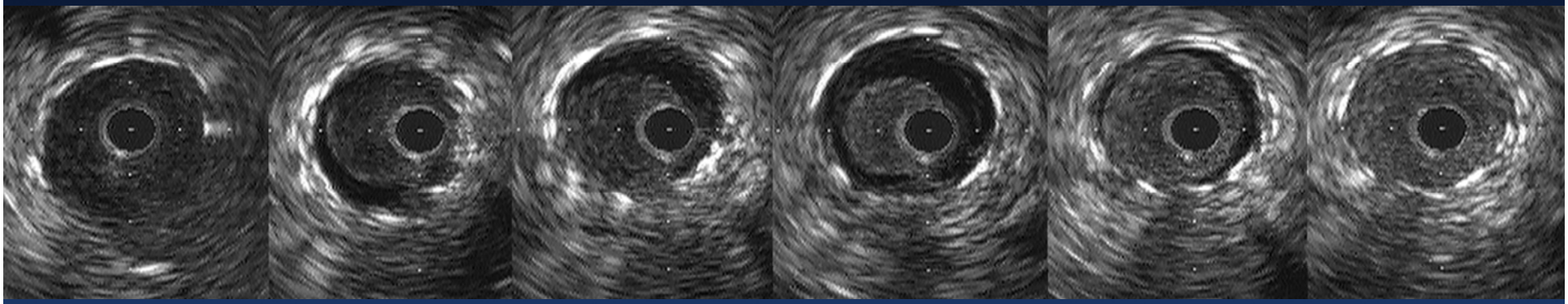





CARDIOVASCULAR RESEARCH FOUNDATION
A Passion for Innovation

COLUMBIA UNIVERSITY MEDICAL CENTER
NewYork-Presbyterian
The University Hospital of Columbia and Cornell


A
B
C
D
E
diastole
systole
diastole
CARDIOVASCULAR RESEARCH FOUNDATION
A Passion for Innovation
COLUMBIA UNIVERSITY MEDICAL CENTER
NewYork-Presbyterian

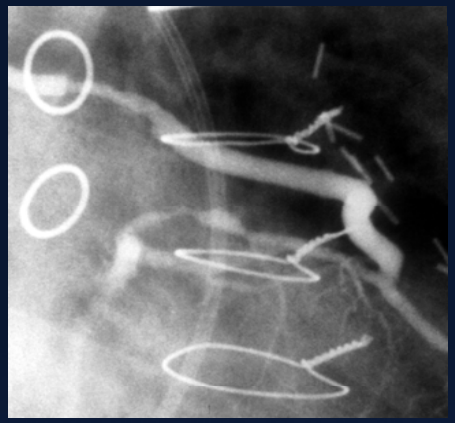


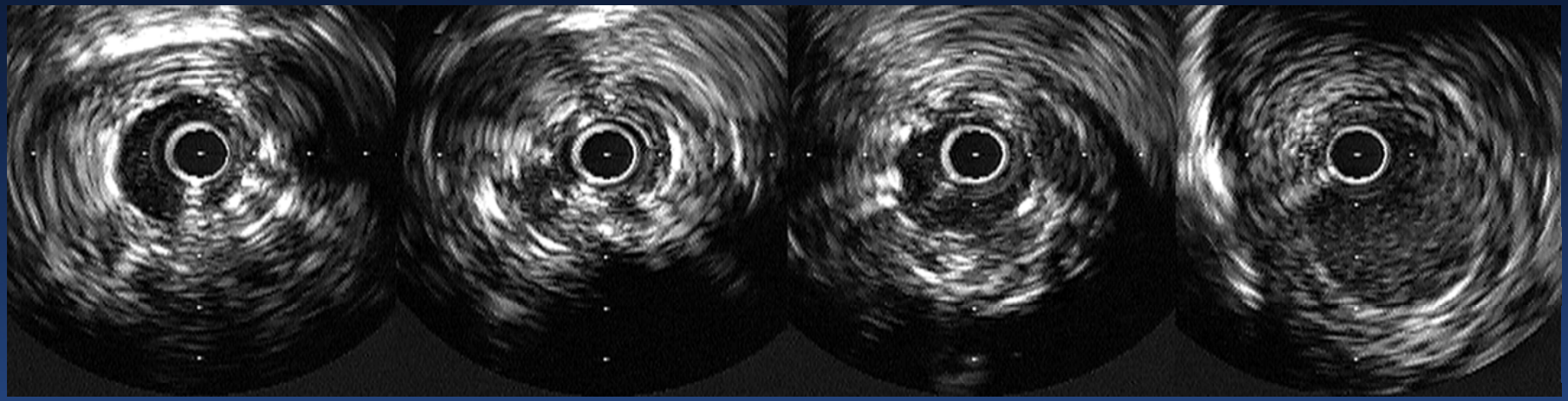


0 → 2.5 → 12.5mm

CARDIOVASCULAR RESEARCH FOUNDATION
A Passion for Innovation

COLUMBIA UNIVERSITY MEDICAL CENTER
NewYork-Presbyterian
The University Hospital of Columbia and Cornell

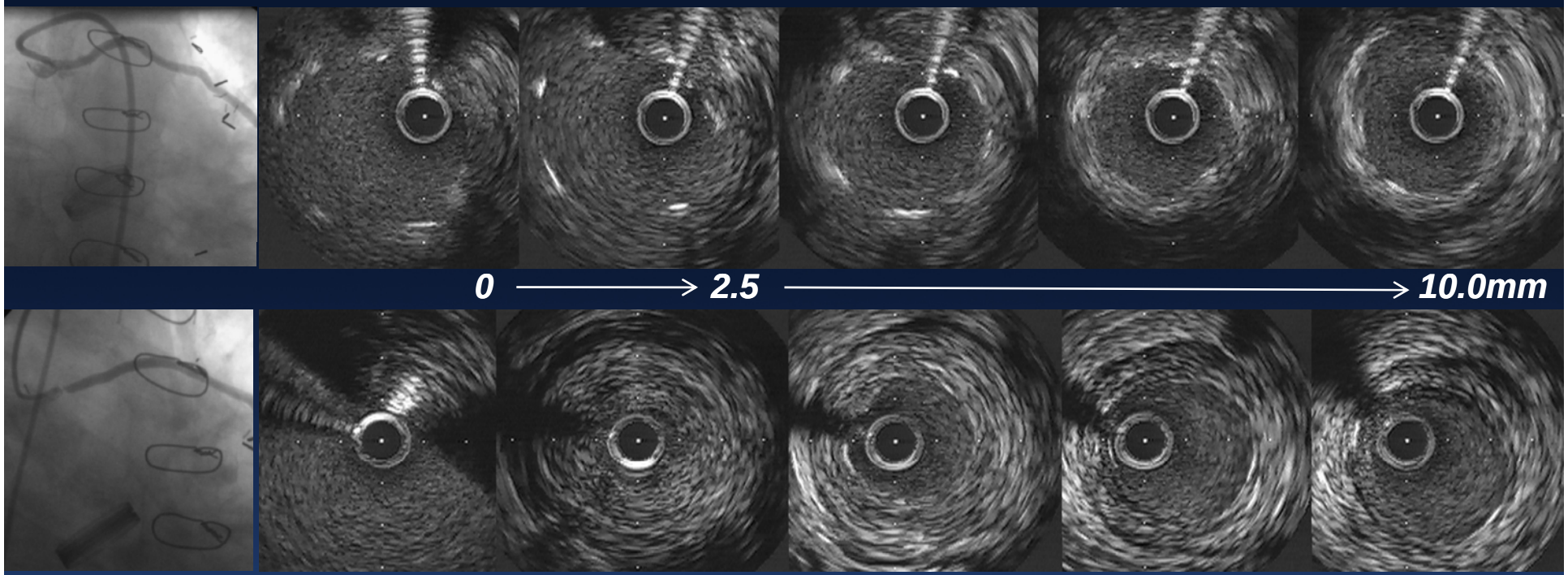


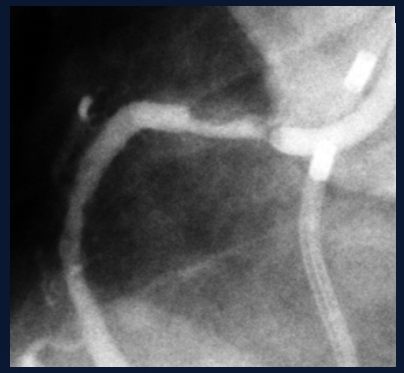


0 → *5.0* → *15.0mm*

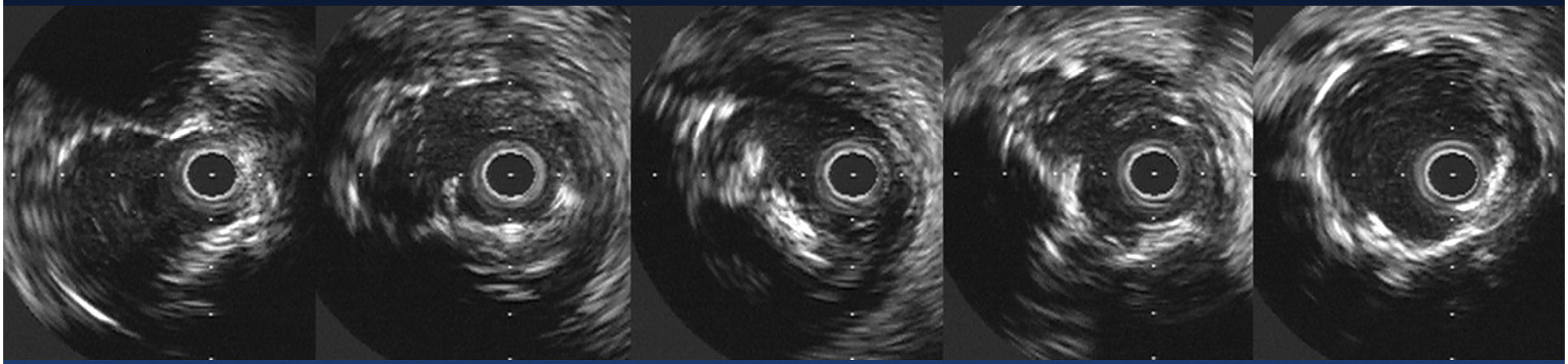
CARDIOVASCULAR RESEARCH FOUNDATION
A Passion for Innovation

COLUMBIA UNIVERSITY MEDICAL CENTER
NewYork-Presbyterian
The University Hospital of Columbia and Cornell

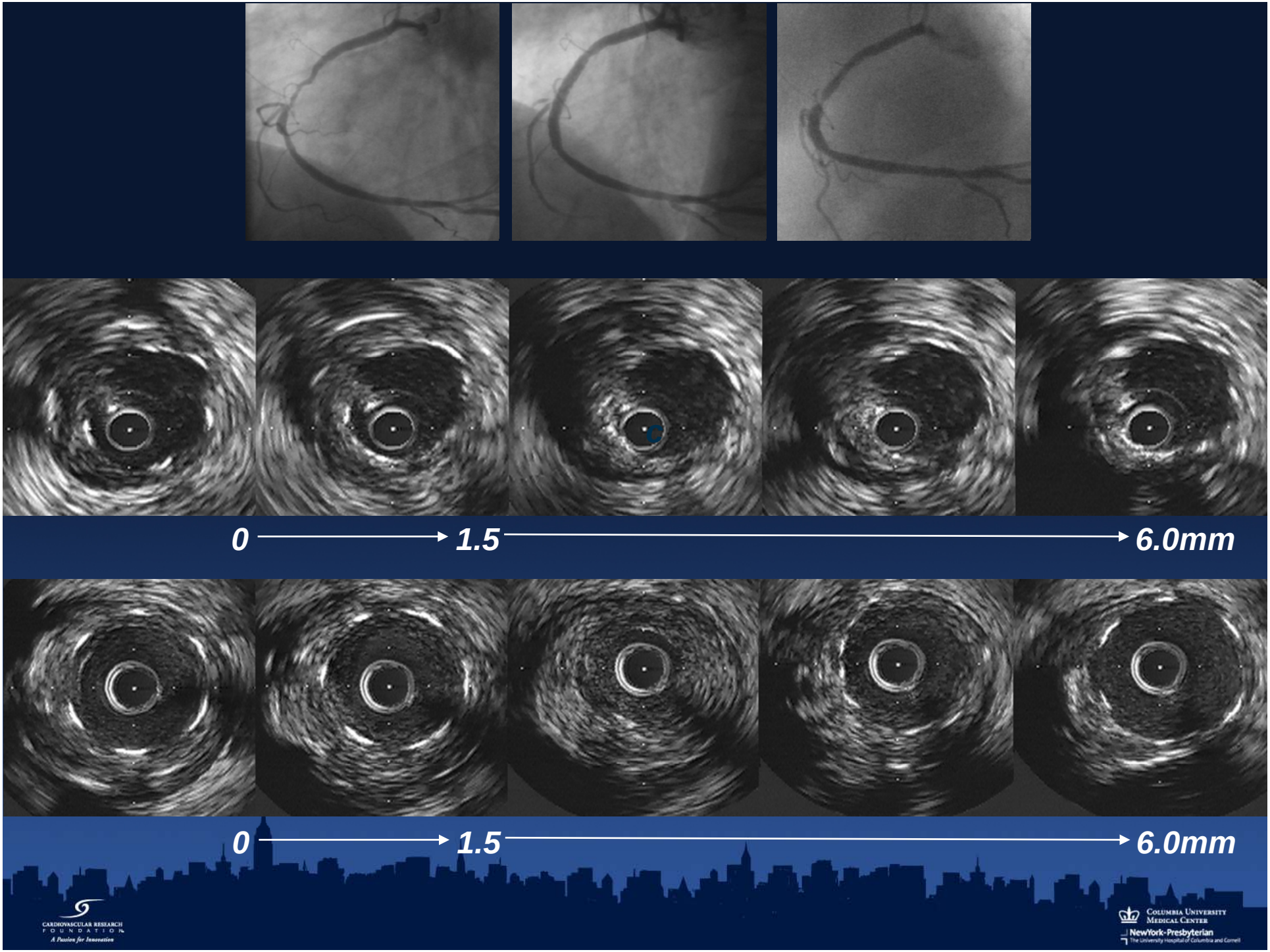




Proximal



0 → ***2.5mm*** → ***10.0mm***


0
1.5
6.0mm
0
1.5
6.0mm
CARDIOVASCULAR RESEARCH FOUNDATION
A Passion for Innovation
COLUMBIA UNIVERSITY MEDICAL CENTER
NewYork-Presbyterian