

IVUS Assessment of Late Complications: Malapposition, Stent Fracture, and Aneurysm Formation

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Disclosure Statement of Financial Interest

Within the past 12 months, I have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship

- Grant/Research Support
- Grant/Research Support
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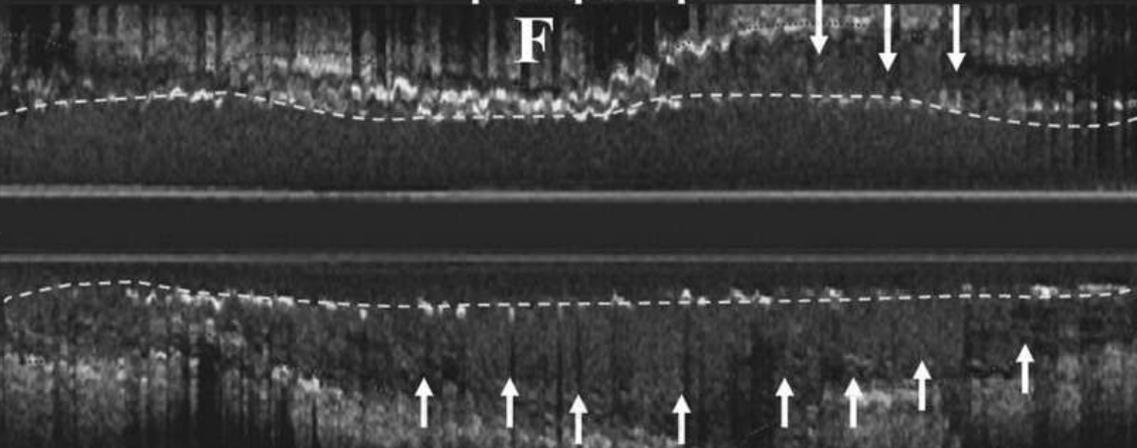
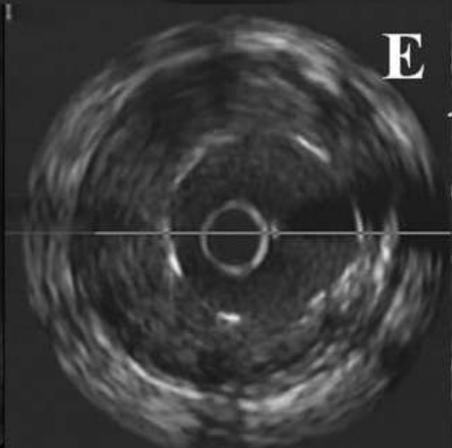
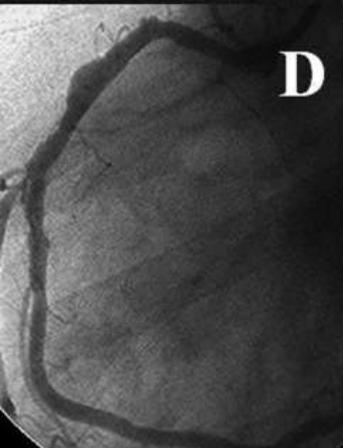
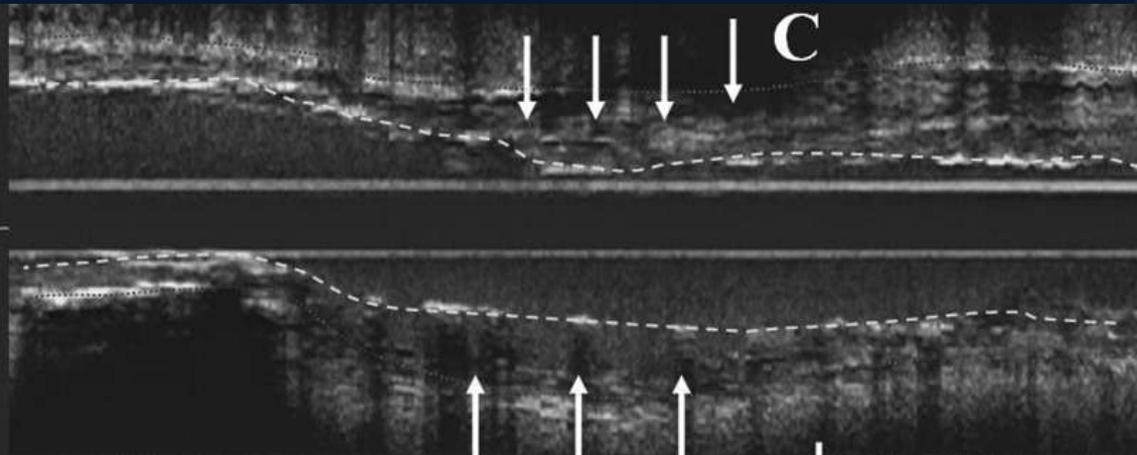
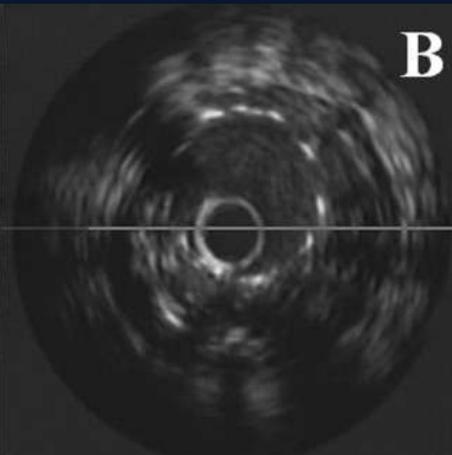
Company

- Volcano
- BostonScientific
- Volcano
- BostonScientific
- Terumo
- Prescient
- LightLab

Two Cases of Very Late Stent Thrombosis after DES Implantation

- LSM @ 6 months occurred in 10/195 (5.1%) lesions overall
 - 7/175 sirolimus-eluting stents
 - 3/20 paclitaxel-eluting stents
- Subsequent follow-up of 19 ± 9 months
- ***Two patients developed late stent thrombosis (331 and 1152 days). These patients had a 20% (50mm^3) and a 39% (135mm^3) increase in EEM volume and, presumably, severe LSM***

(Siquiera et al. J Am Coll Cardiol 2006;47:365A)
(Feres et al. Cath Cardiovasc Intervent 2006;68:83-8)
(Siquiera et al. Eur Heart J 2007;28:1304-9)

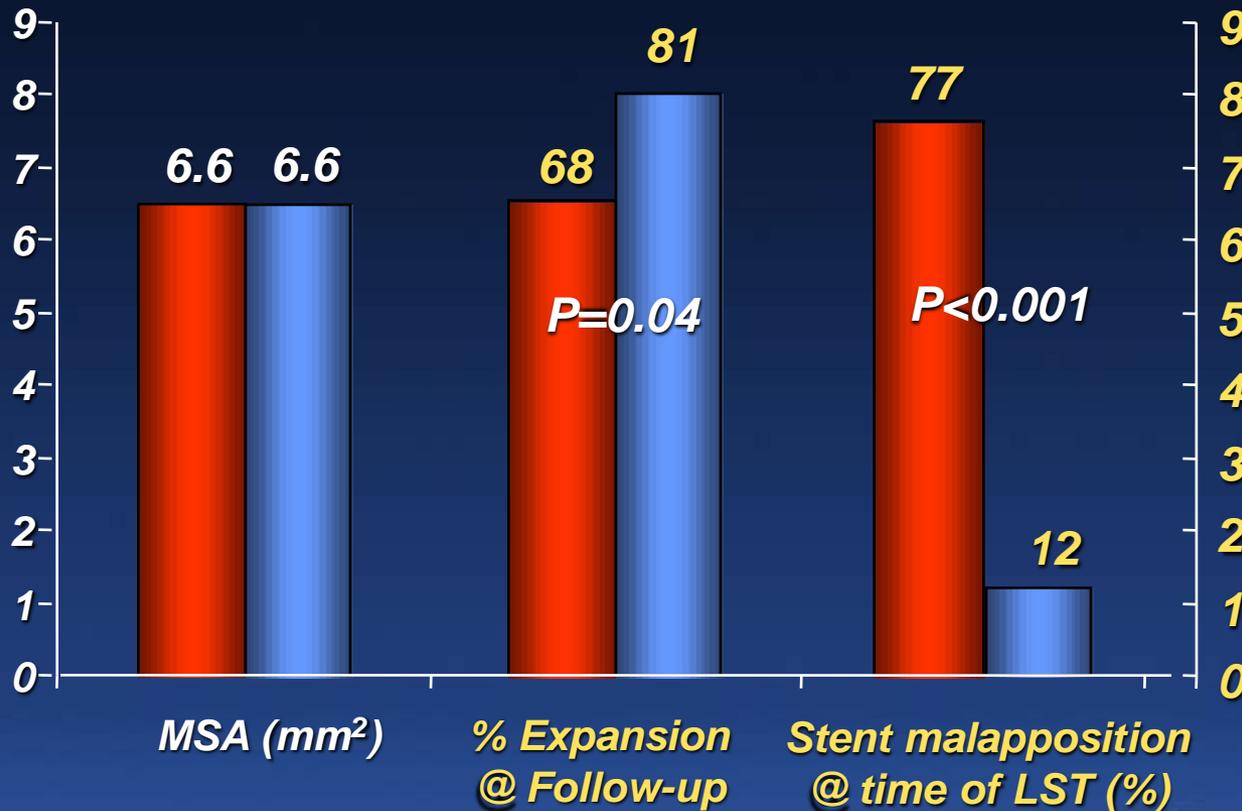


IVUS Predictors of Very Late (>12 months) DES Thrombosis

	Very Late ST	Controls	P
N	13	144	
ACS	69%	50%	NS
Diabetes	0	18%	0.13
Lesion length (mm)	23.9±16.0	13.3±7.9	<0.001
Stent length (mm)	34.6±22.4	18.6±9.5	<0.001
Stent overlap	39%	8%	<0.001

IVUS Predictors of Very Late DES Thrombosis

- Late DES Thrombosis (n=13)
- Controls (n=175)



Expansion was assessed at follow-up. "Underexpansion" probably represented an increase in reference vessel size (positive remodeling) rather than true underexpansion.

Meta-Analysis of Late Stent Malapposition (LSM) Frequency

- 17 studies with 4648 patients
 - 2453 BMS and 2195 DES
 - 4 SES, 4 PES, 1 EES, 2 ZES, 3 DES vs DES, and 3 BMS only
- LSM more common in DES than BMS
 - OR=2.5, p=0.02 when both RCT and observational studies were included
 - OR=4.4, p=0.002 when only RCT were included
 - SES > PES > ZES > EES

Meta-Analysis of Very Late ST in LSM

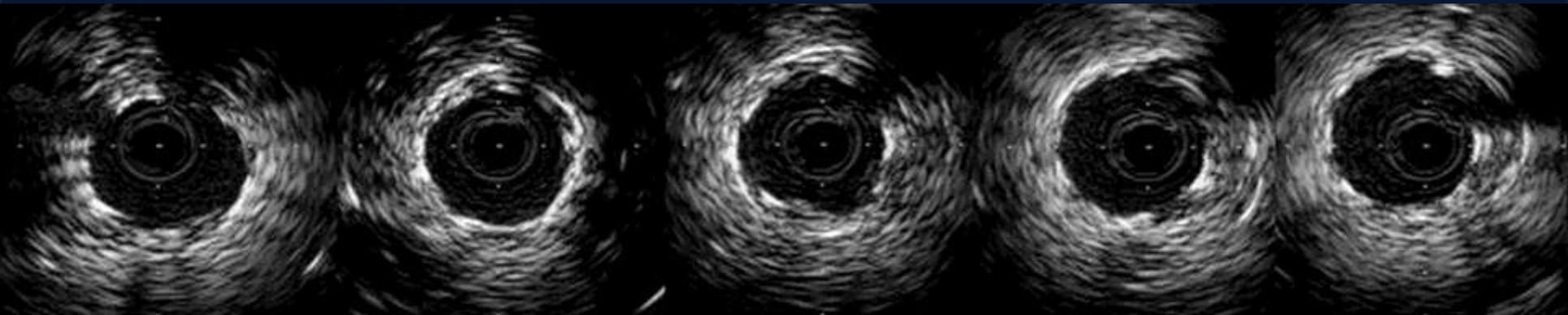
- 5 studies with 2080 patients
 - 228 LSM and 1852 no LSM
 - 3 Late ST (<12 mos), none in LSM
 - 6 Very late ST (>12 mos), 4 in LSM
- Risk of very late ST was higher in LSM patients (OR=6.5, p=0.02).
- Based on the expected numbers of very late ST, 3 of 5 studies favored the relationship between LSM and very late ST.

LSM in acute myocardial infarction

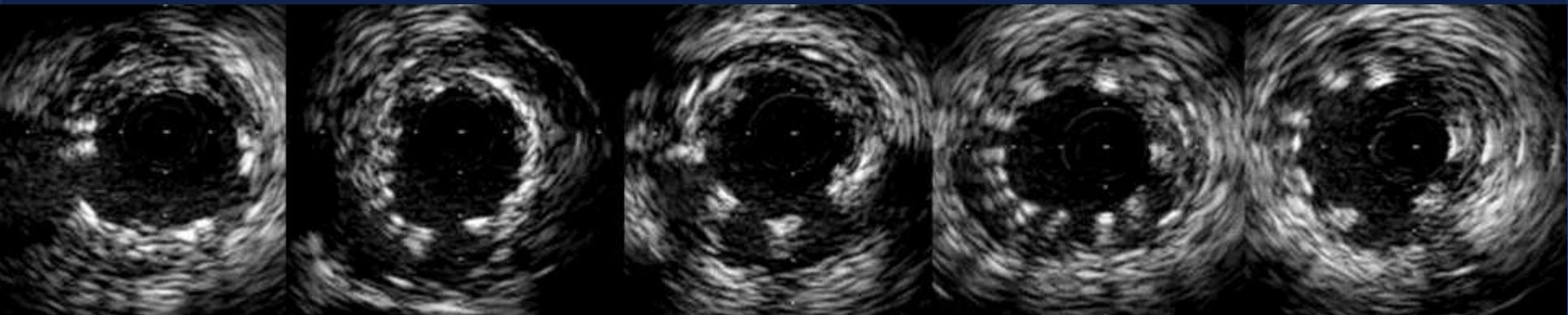
	Mission (AMI)		HORIZONS (AMI)	
	SES	BMS	TAXUS	BMS
Any malapposition at follow-up	37.5%	12.5%	46.3%	29.0%
Late acquired stent malapposition	25.0%	5.0%	30.8%	8.1%

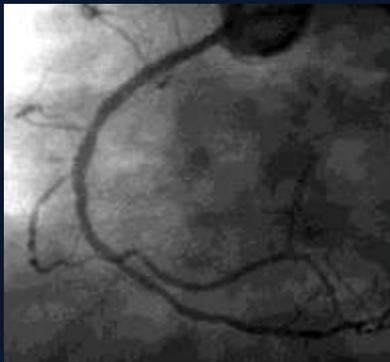
Frequency of late acquired stent malapposition in BMS presumably related to thrombus dissolution

Increased frequency of late acquired stent malapposition in DES vs BMS related to positive remodeling (77% of DES with LSM)



0 → 2.5 → 10.0mm





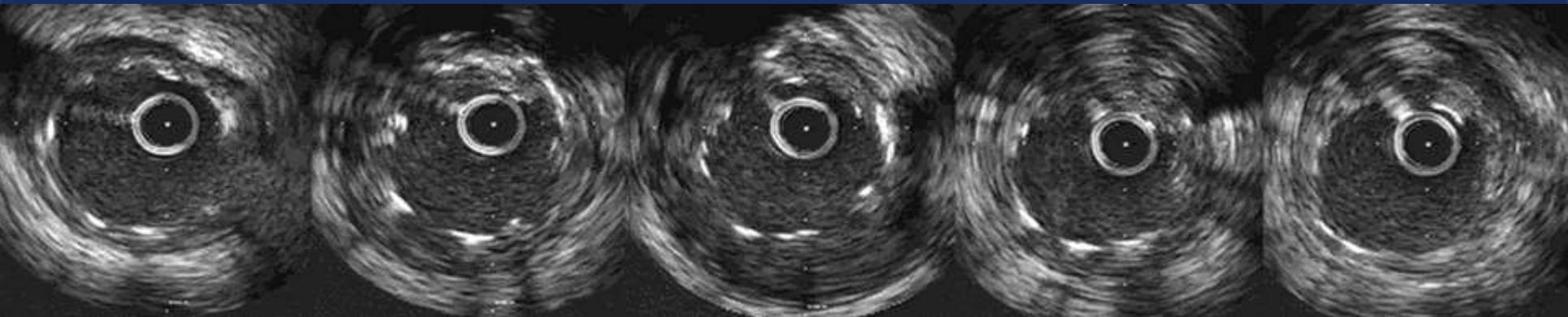
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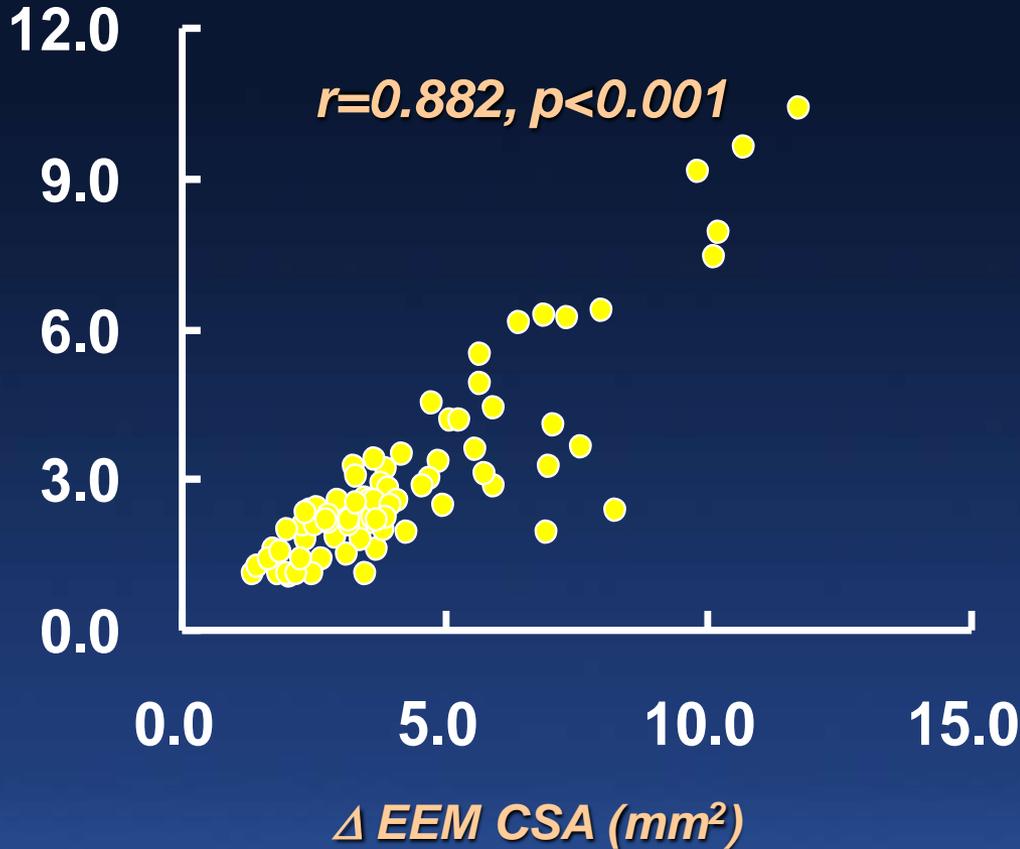
3.0



12.0mm



LSM CSA (mm²)



- **Remodeling**

- Increased EEM area greater than the increase in plaque area or in the absence of an increase in plaque

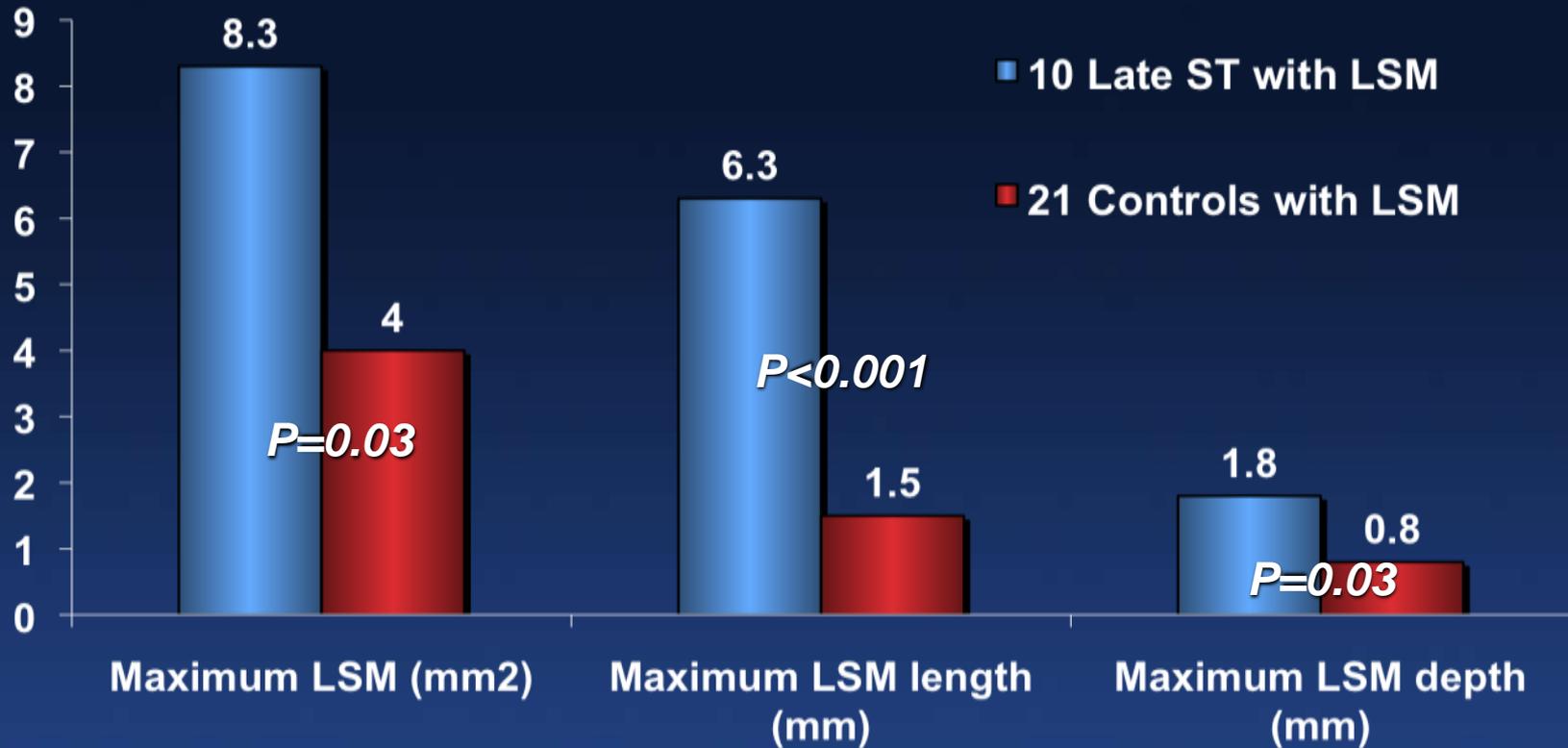
- **Thrombus dissolution**

Serial (post-stenting and 6-month and 2-year follow-up) IVUS analysis of LSM at Asan Medical Center

- Among 250 patients with complete serial IVUS data, LSM was identified at 6 months in 19 (7.6%). An additional 23 LSM were identified at 2 years. Because no LSM resolved between 6 months and 2 years, the LSM at 2 years was 12.8%.
- LSM noted at 6 months continued to increase from 6 months to 2 years and correlated to the ongoing increases in EEM.

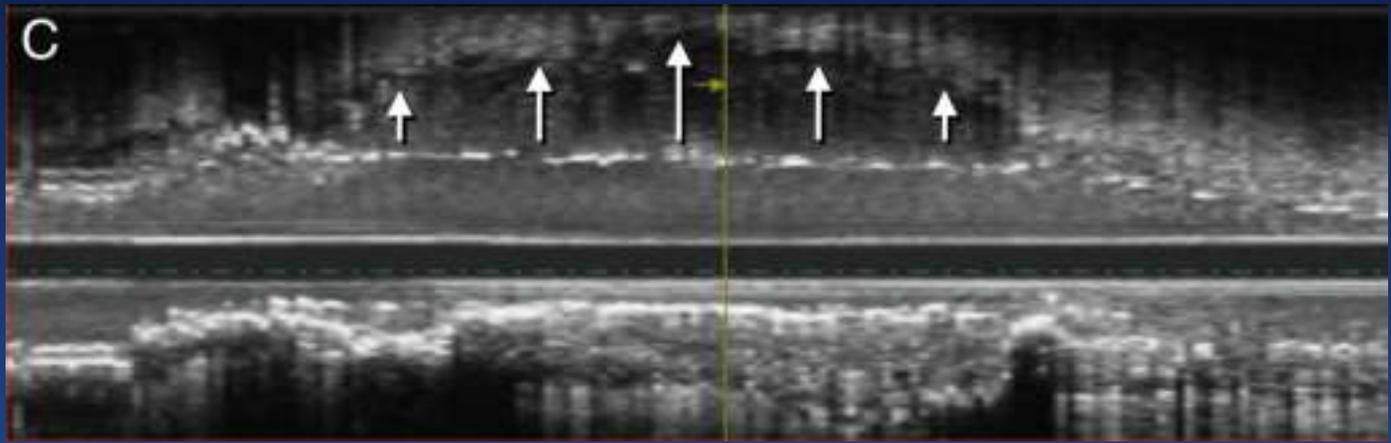
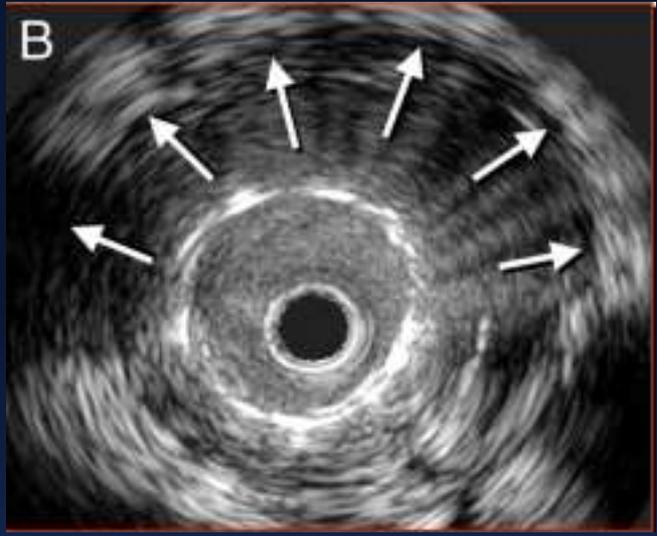
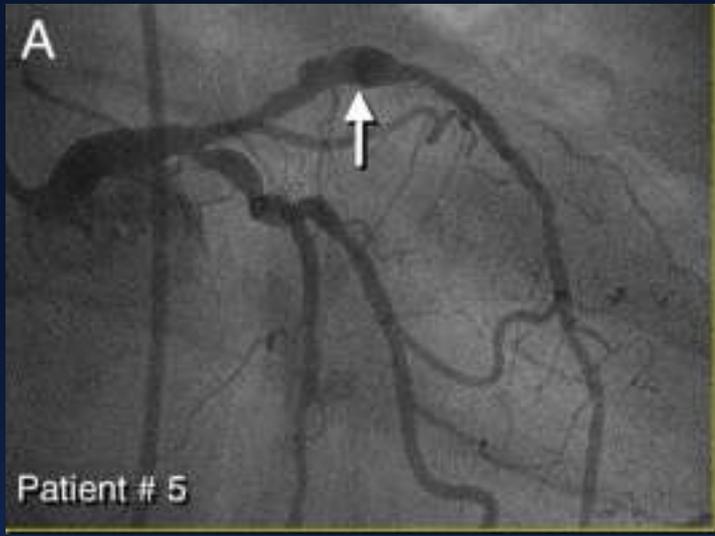
	# (%) in IVUS substudy	% With LSM	LSM	Events
CYPHER				
RAVEL	48 (40%)	21% @ follow-up	3mm ² (mean area)	0
SIRIUS	80 (15%)	7.5% persistent 8.7% late acquired	0.4±0.1mm (max depth) 0.7±0.3mm (max depth)	0
TAXUS	(85%)			
II-MR	116	0% persistent 9.5% late acquired	- 3.4±2.6mm ² (max area)	0
II-SR	113	4.4% persistent 8.0% late acquired	- 5.1±1.8mm ² (max area)	0
IV,V, and VI	(20%)			
MR	78	10.3% persistent 16.7% late acquired		0
SR	209	2.5% persistent 5.3% late acquired		0
AMC Experience	705	12.1% late acquired	3.0±1.9mm ² (max area)	0

Quantification of LSM in Patients with Very Late DES Thrombosis



Coronary Aneurysm Formation

- **Coronary aneurysms developed in 15/1,197 (1.25%) consecutive pts with late angiographic follow-up after DES implantation.**
 - **Coronary aneurysms were more frequently implanted during acute myocardial infarction and use of longer stents.**
 - **On IVUS, LSM area measured $12.1 \pm 8.6 \text{mm}^2$.**
 - **Two patients presented with acute myocardial infarction secondary to DES thrombosis, and 4 additional patients presented with unstable angina and underwent repeat PCI with a significant reduction in LSM area ($11.6 \pm 3 \text{mm}^2$ to $5.5 \pm 0.6 \text{mm}^2$, $p < 0.05$).**
 - **Dual antiplatelet therapy was recommended in the remaining 9 patients who were asymptomatic at CAN diagnosis**
- **After a mean follow-up of 399 ± 347 days, the 1-year event-free survival was $49 \pm 14\%$ and was related to aneurysm size on IVUS. In 2 pts aneurysms disappeared and IVUS showed abluminal thrombosis.**





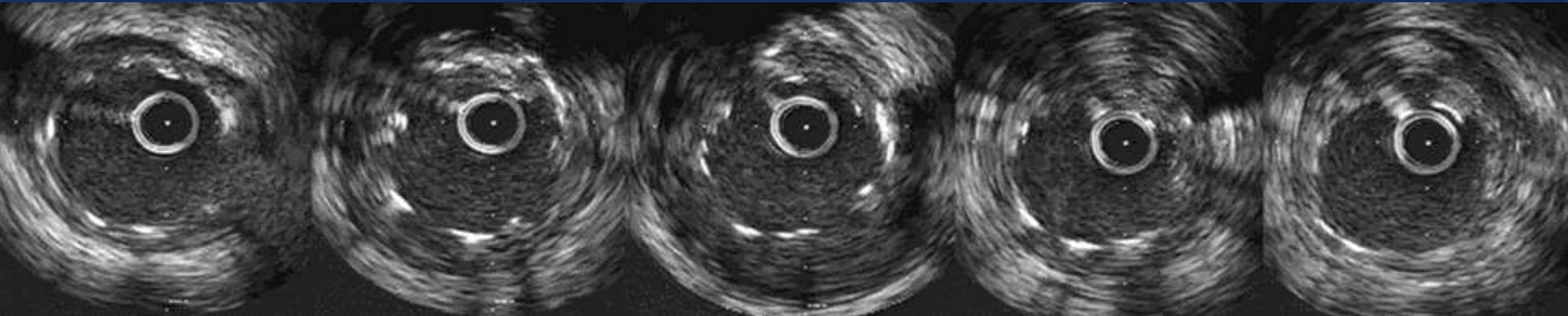
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3.0



12.0mm



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

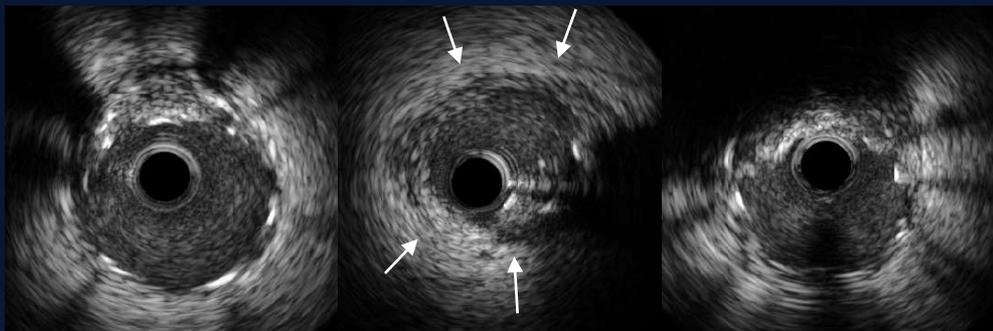
- 28 pts with very late DES ST and 26 controls (7 spontaneous MI, 4 early BMS thrombosis, 5 late BMS thrombosis, and 10 early DES thrombosis).
- LSM was present in 73% of very late DES ST segments. Maximal LSM area measured $6.2 \pm 2.4 \text{mm}^2$, and length measured $9.4 \pm 9.5 \text{mm}$. LSM area exceeded 5.0mm^2 in 5 of 8 segments (63%)
- LSM area was associated with total eosinophil count ($p=0.008$)

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

“We have shown that in humans delayed healing is common with current DES and that in those that thrombose, other factors, such as hypersensitivity reaction, bifurcating and ostial stenting, penetration of a necrotic core, stent malapposition, and restenosis, may also be important predictors of thrombosis.”

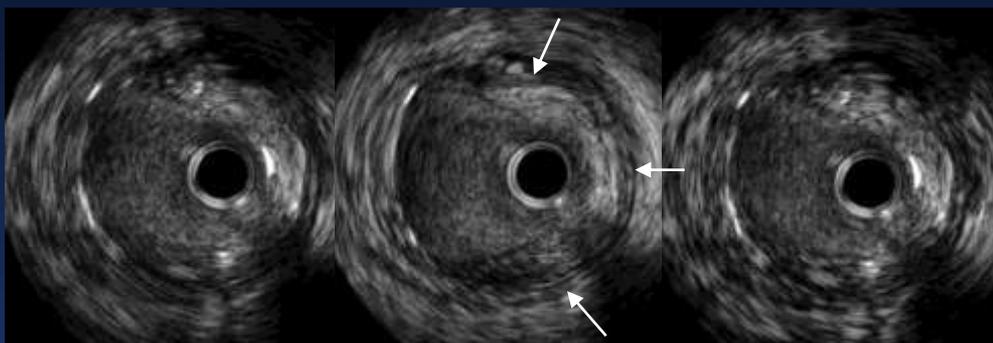
IVUS Classification of stent fractures

Complete fracture

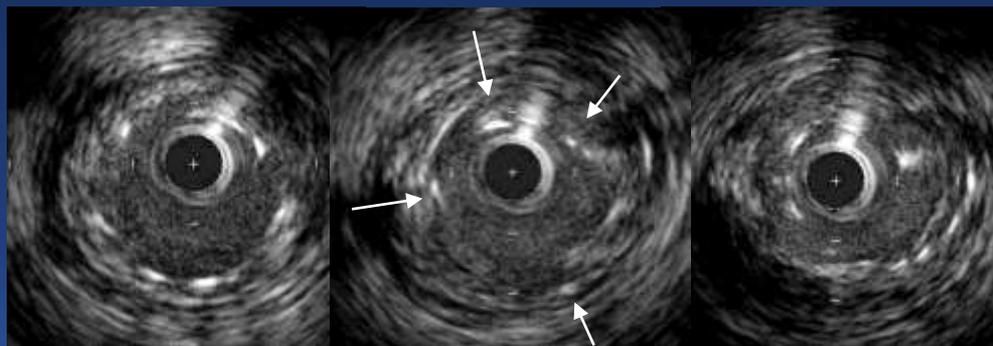


Partial fracture

Absence of strut $> 120^\circ$
(Max angle in control $65 \pm 12^\circ$)

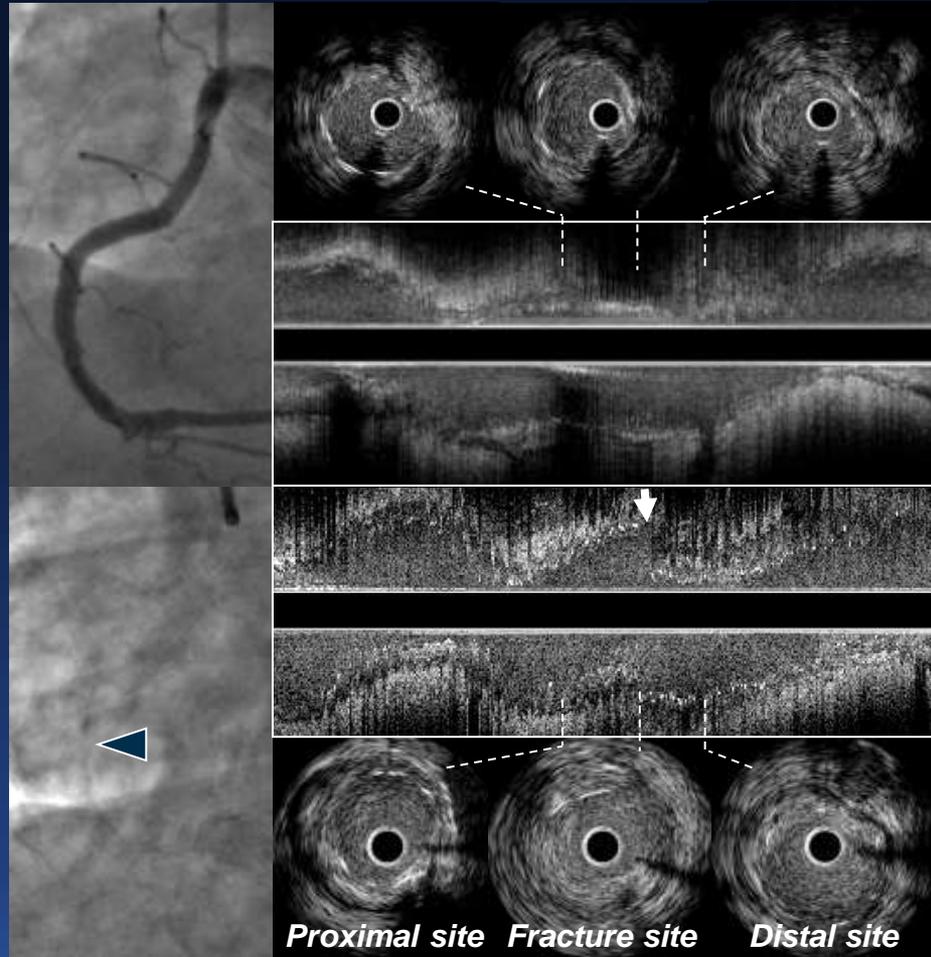


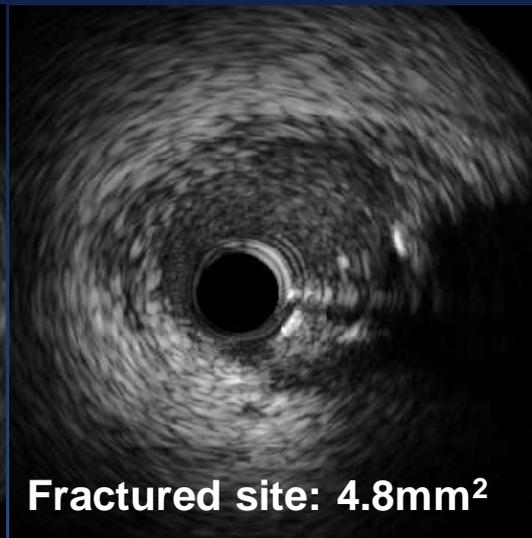
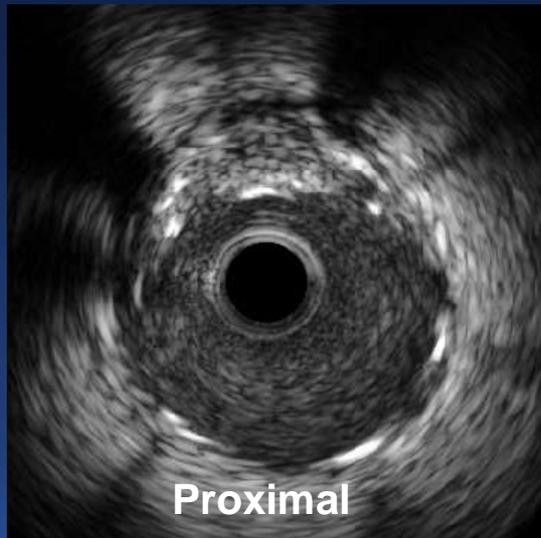
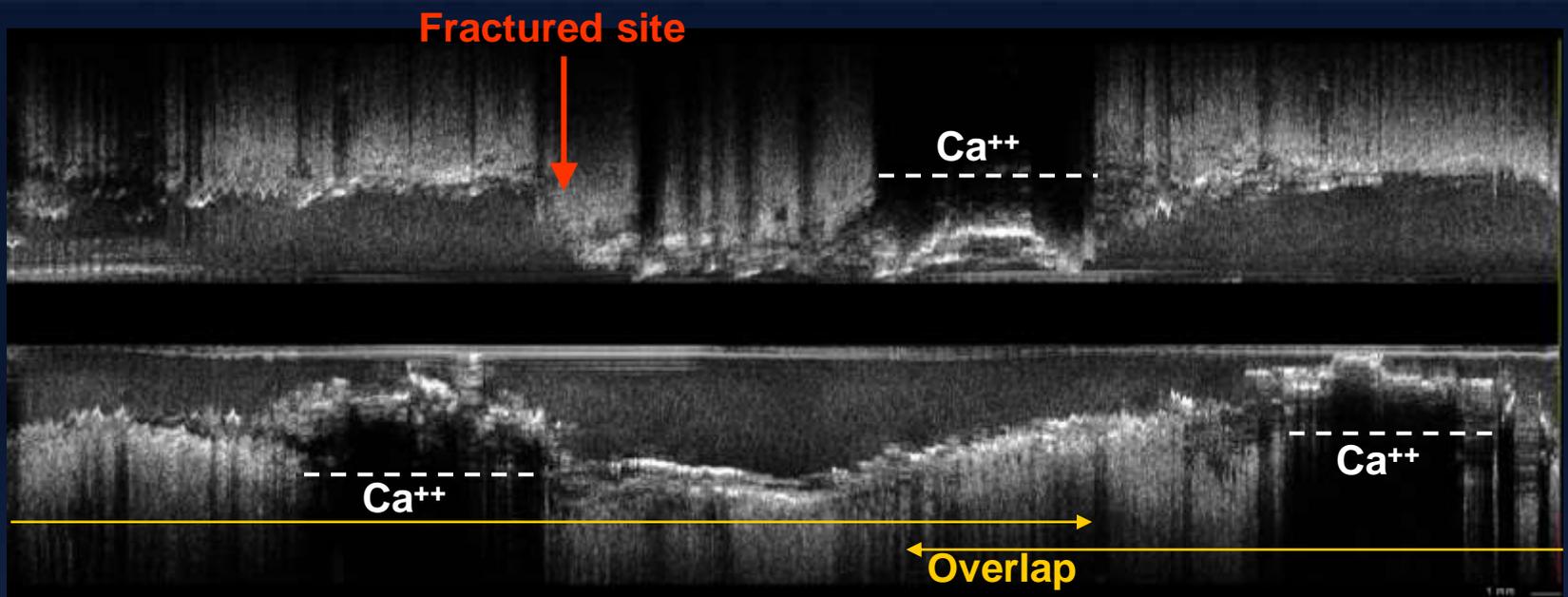
Mal-alignment



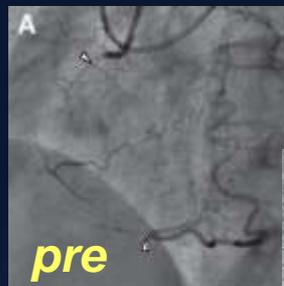
Comparing PES vs SES fractures

- Similar frequency of complete stent fracture (17% vs. 21%)
- Better angiographic detection (110% vs. 71%)
- Similar frequency of fracture adjacent to calcified plaque or stent metal overlap (86% vs. 100%)
- Similar stent lengths (45.2mm vs. 39.3mm)
- More frequent complete malalignment of proximal and distal fragments in PES-strut fractures compared to SES fractures (83% vs. 7%)

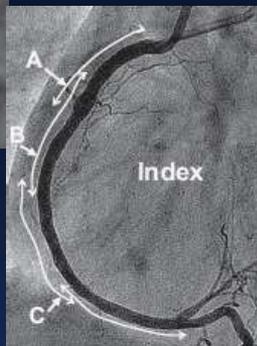




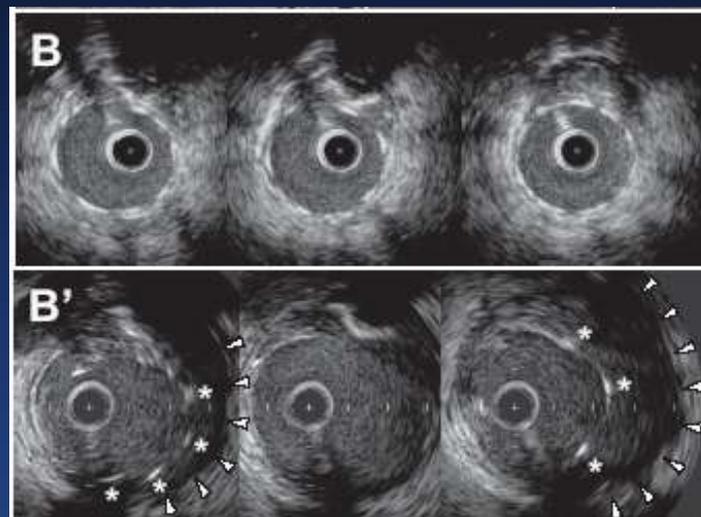
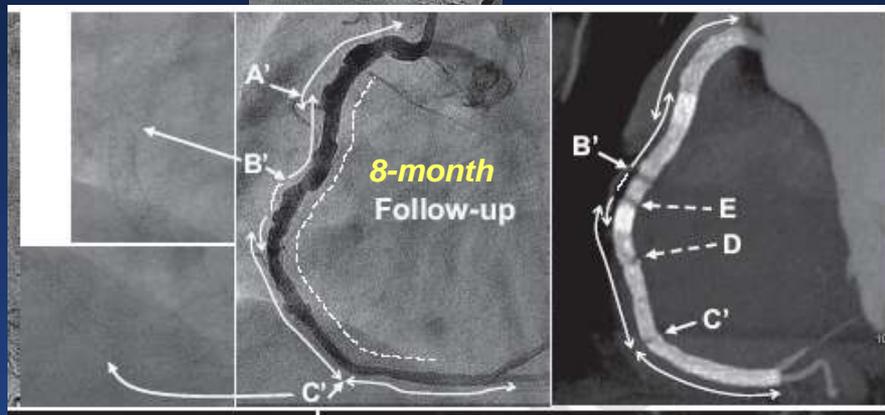
Multiple Taxus stent fractures accompanied by malapposition after successful CTO recanalization



- A 50-year-old male with CTO of the proximal RCA



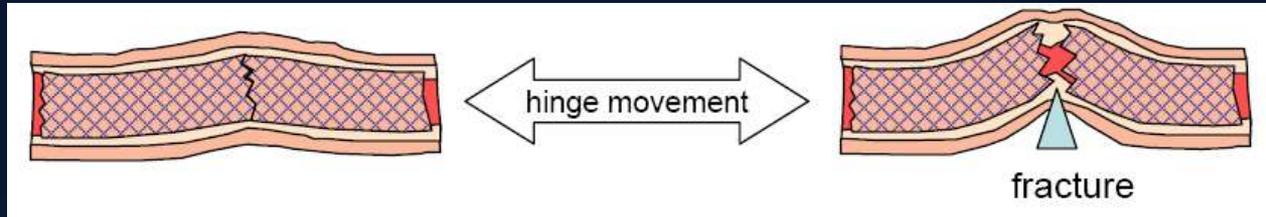
- The guidewire passed through the occluded lesion in the retrograde direction
- PES were successfully implanted (2.75-32, 3.0-32, 3.0-32, and 3.5-28).



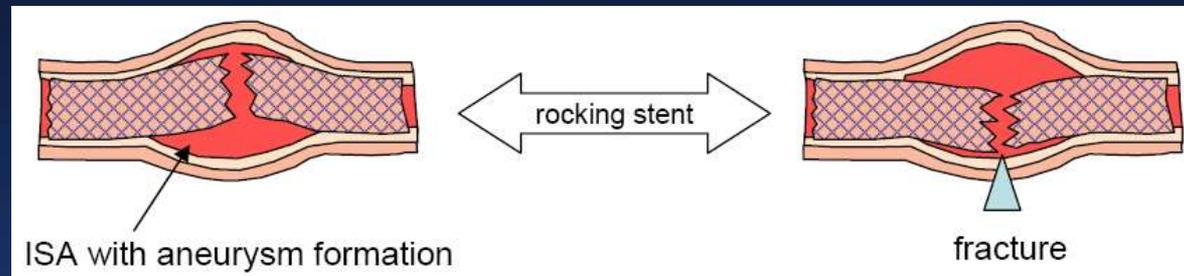
- There were 2 stent fractures (B' and E) identified by Angio, IVUS and MDCT.

Three Mechanisms of Stent Fracture

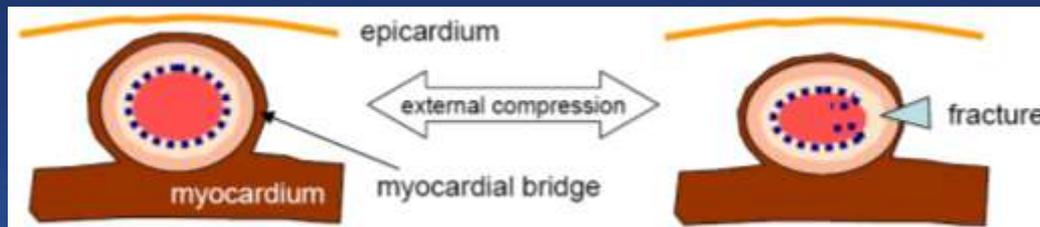
Type I: Stent fracture in lesion with neither aneurysm nor myocardial bridge



Type II: Stent fracture in an aneurysm with incomplete apposition



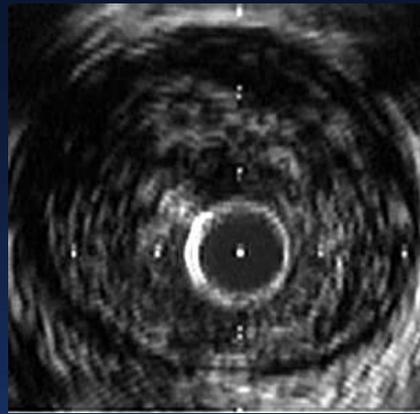
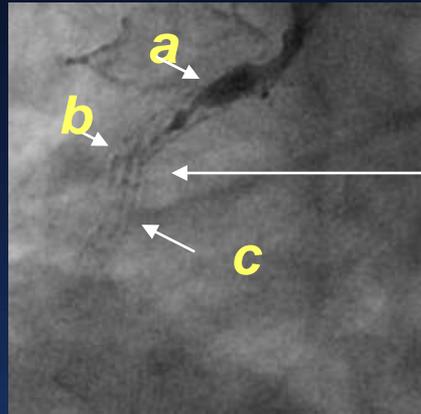
Type III: Stent fracture in a myocardial bridge



Analysis of 20 stent fractures in 17 patients

- 15 stent fractures were detected by angiography and IVUS, and 5 were detected only by IVUS
- 15 stent fractures in 13 patients were associated with in-stent restenosis (all focal); and 2 stent fractures in 2 patients 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 stenting.
 - Comparing stent fractures associated with an aneurysm to ones that did not occur in association with an aneurysm, complete stent fracture was more frequent (100% vs. 27%, $p=0.008$), and all presented >1 year after index stenting (vs. 33%, $p=0.03$).

***DES after VBT
failure for Rx of
BMS Restenosis***



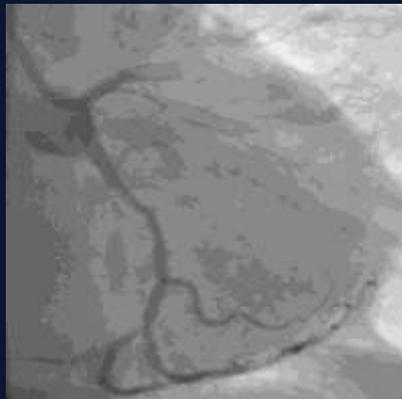
2 years later



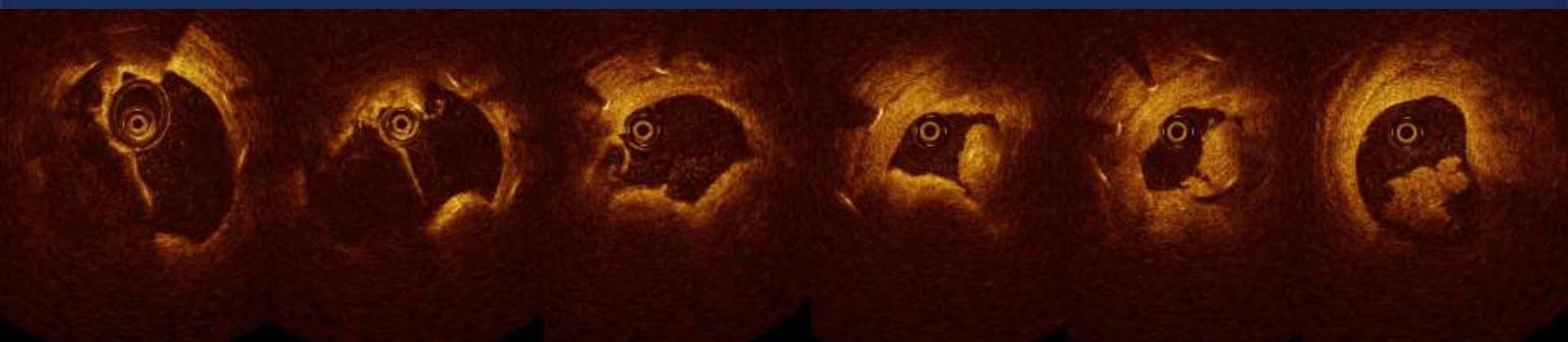
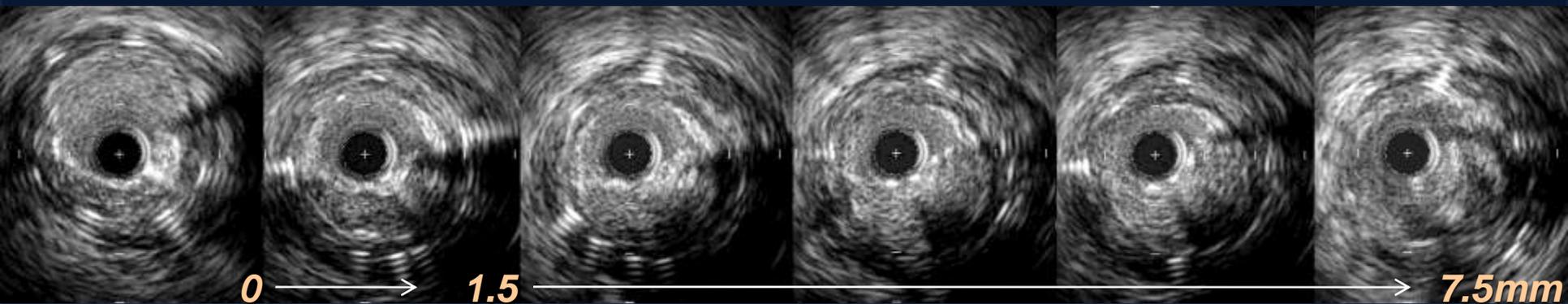
IVUS analysis of 23 very late DES thrombosis cases at Asan Medical Center

- LSM was observed in 17 DES patients (73.9%)
- Disease progression with neointimal rupture within the stent was observed in 10 DES patients (43.5%) and reference segment plaque rupture in another 5 DES patients (21.7%)
- Only two very late DES thrombosis patients had neither of these findings

Proximal



Distal



Conclusions

- LSM is common, occurring in 10-20% of DES and is higher in Cypher compared to Taxus and BMS
- Positive remodeling continues beyond 6 months to increase the frequency of very late stent malapposition at 2 years vs 6 months
- Routine follow-up detects LSM that is modest in size and has not been associated with very late ST
- The size of LSM that has been reported in cases of very late ST is much larger than detected at routine follow-up.
- Aneurysm formation is an exaggerated form of LSM and is associated with increased vessel wall inflammation, delayed healing, hypersensitivity, inflammation, etc. and, therefore, very late ST
- We postulate that the increased frequency of DES fracture (compared to the rare stent fracture in the equivalent BMS) is partly related to suppression of neointima that helps to stabilize BMS. This would explain the finding that malapposition or aneurysm formation appears to increase the frequency of DES strut fracture by destabilizing the stent structure.
- Although still relatively uncommon, DES fracture is associated with increased restenosis and ST
- Neoatherosclerosis can develop within DES leading to vulnerable plaques, plaque rupture, and thrombosis