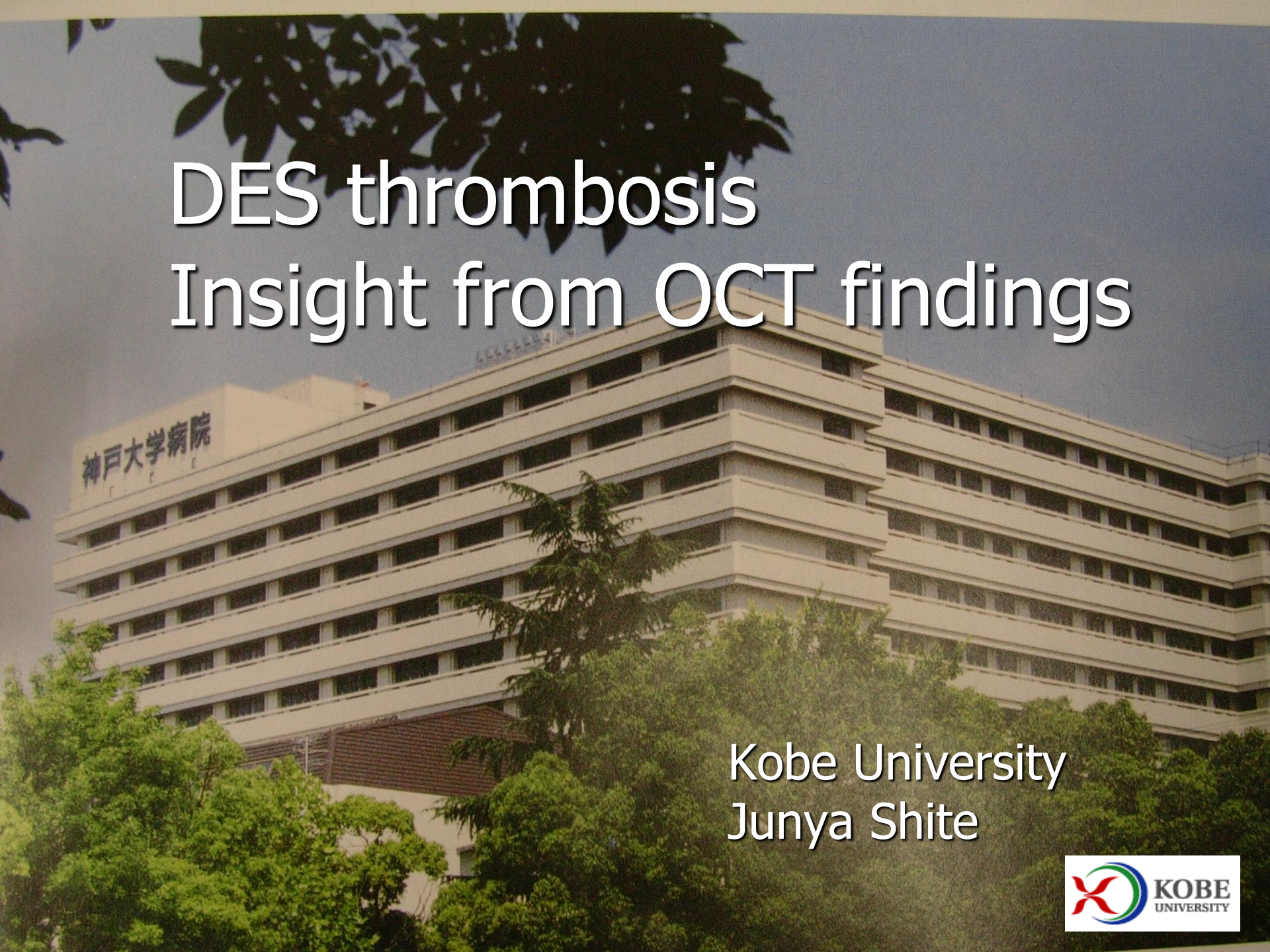


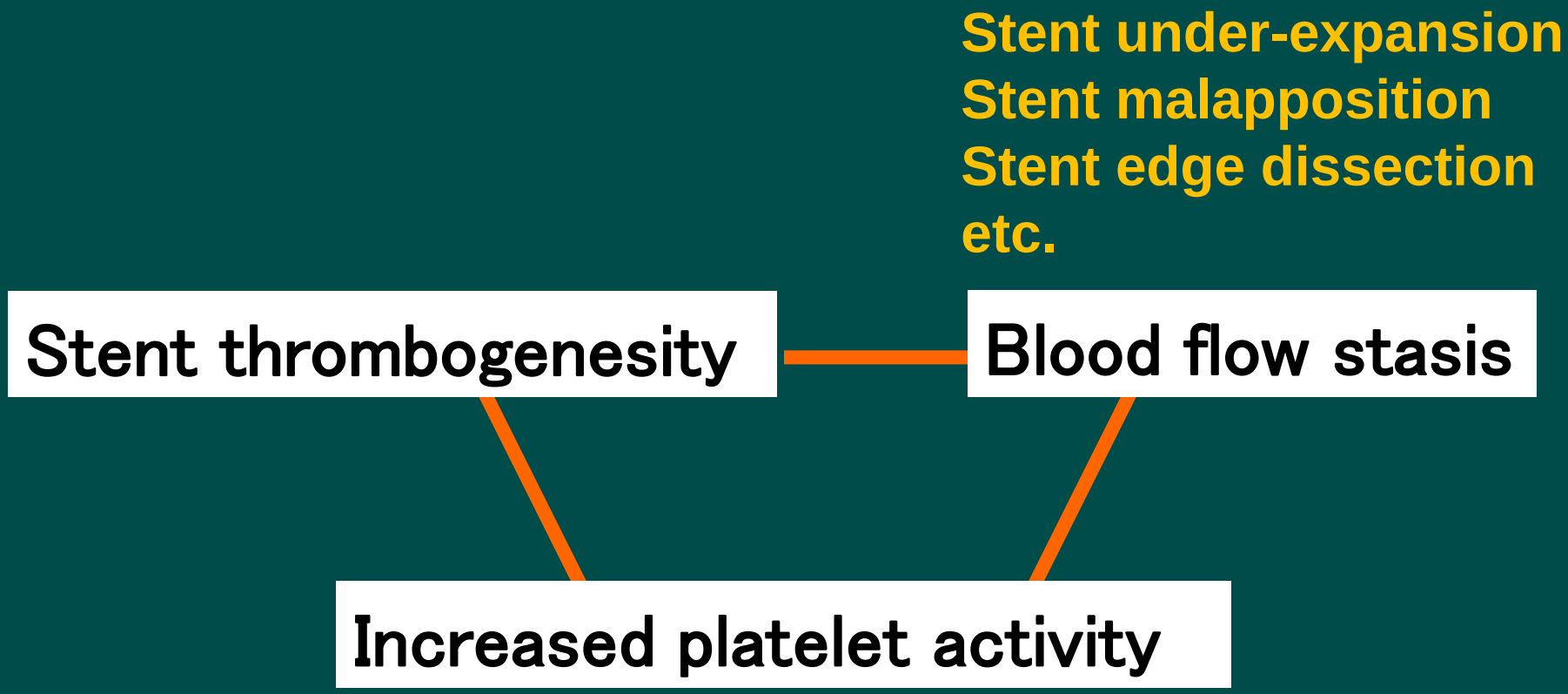
DES thrombosis
Insight from OCT findings

Kobe University
Junya Shite

KOBE UNIVERSITY

Three major factors for stent thrombosis

Major factors or stent thrombosis

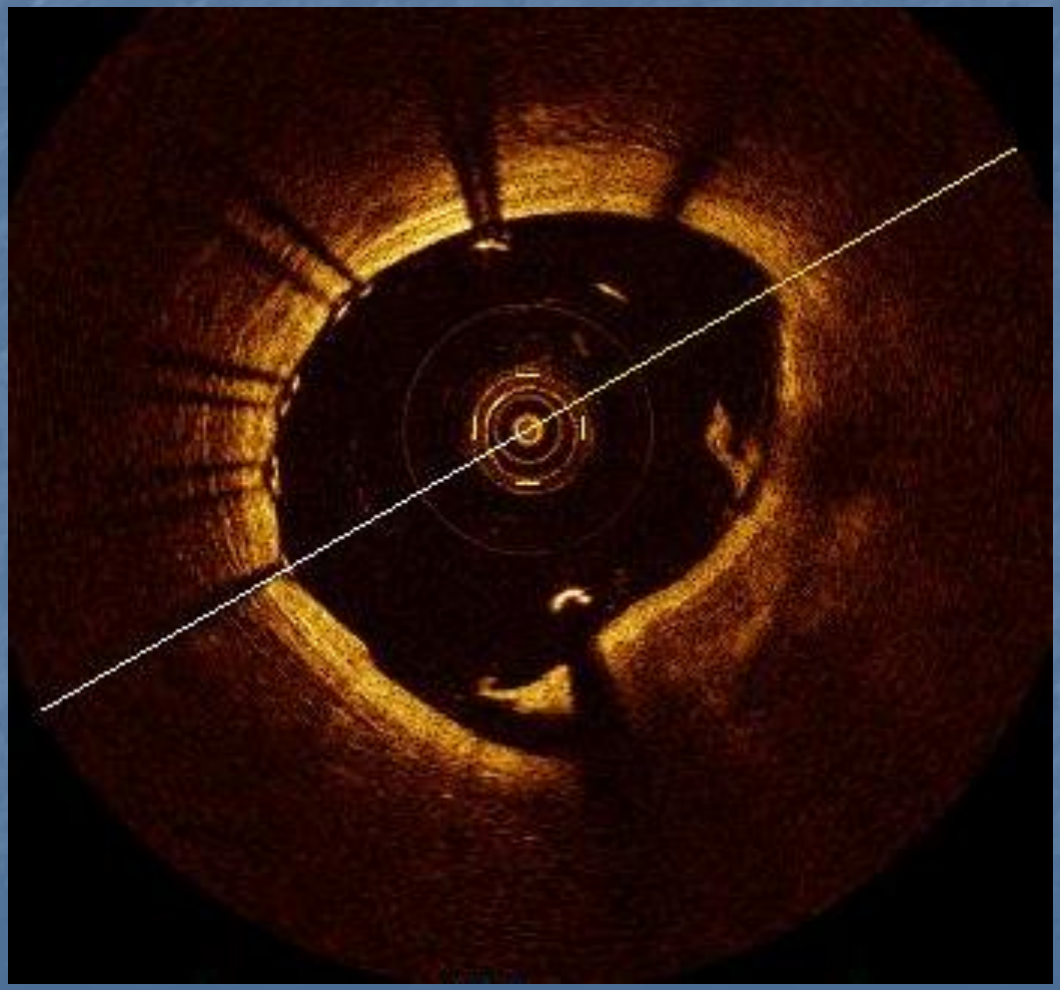


Frequency of post-stent abnormality visualized by OCT and IVUS

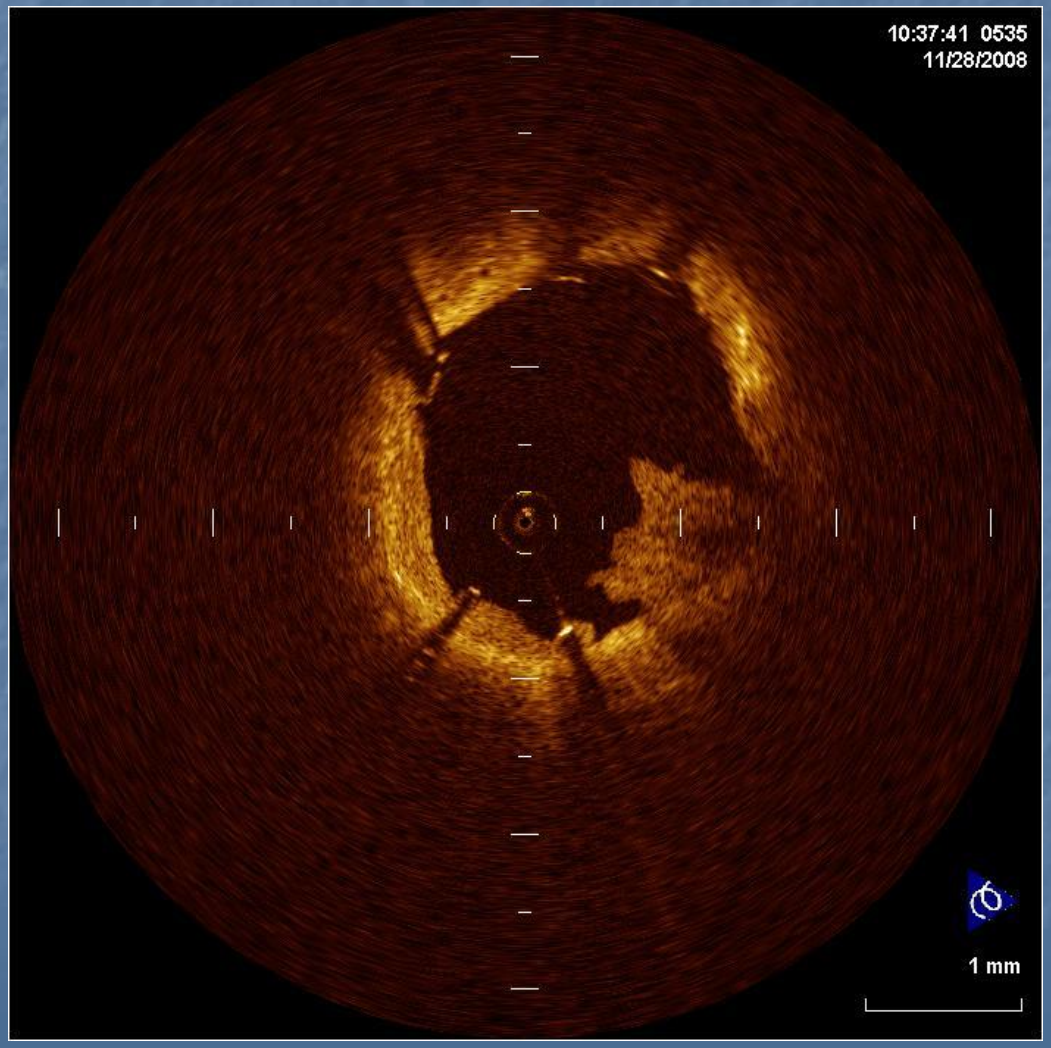
	OCT-image	IVUS-image
Stent malapposition		
Immediate after stent deployment	70%	40%
Final result	30 %	5%
Stent edge dissection	10%	0%
Tissue prolapse	100%	5%
Thrombus	15%	5%

Kawamori H, Shite J et al. J Invasive Cardiol 2010, 22 541–545.

stent malapposition and edge dissection

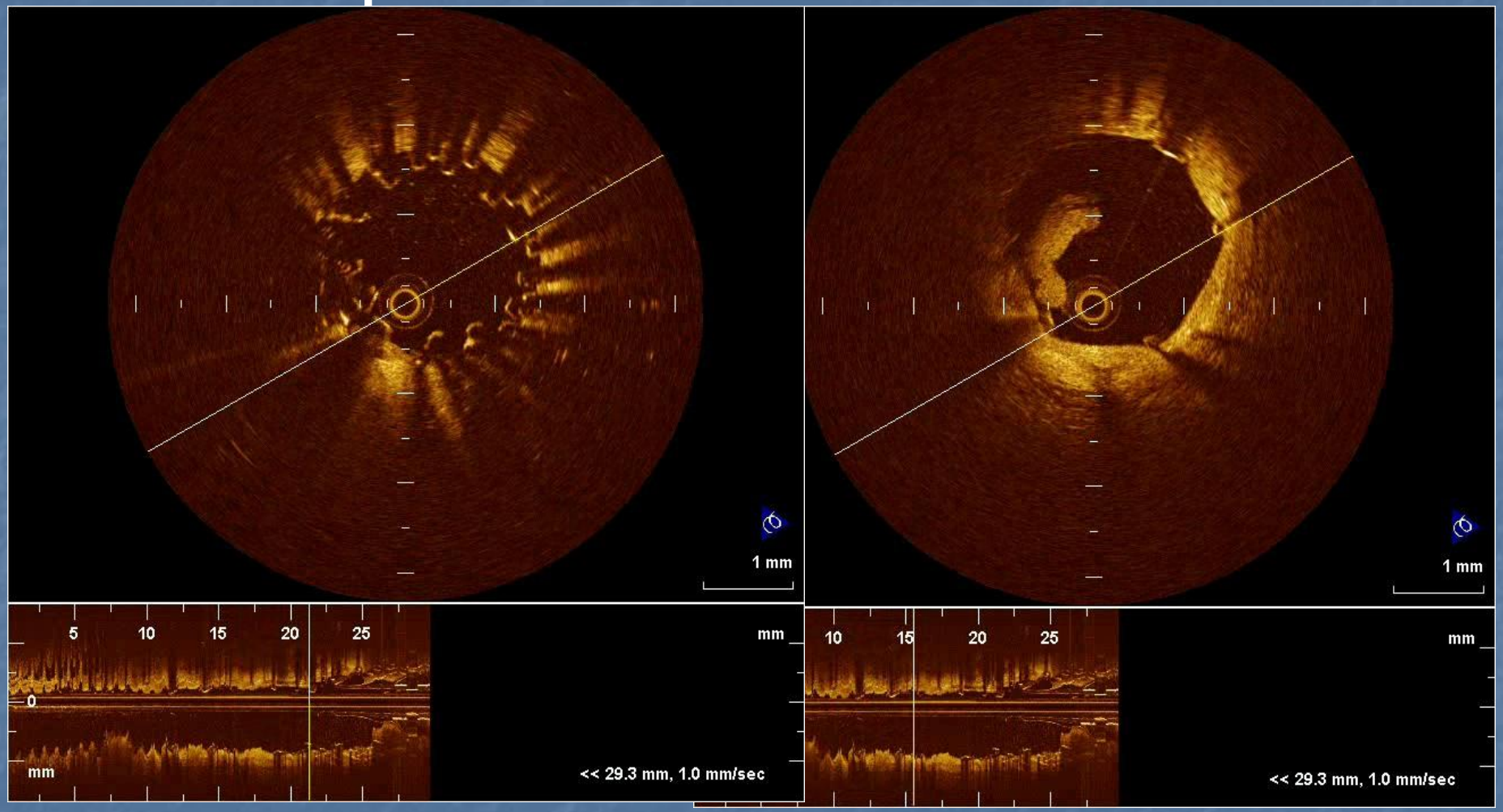


Tissue prolapse during stent strut



Stent overlap under expansion

Intra stent thrombus



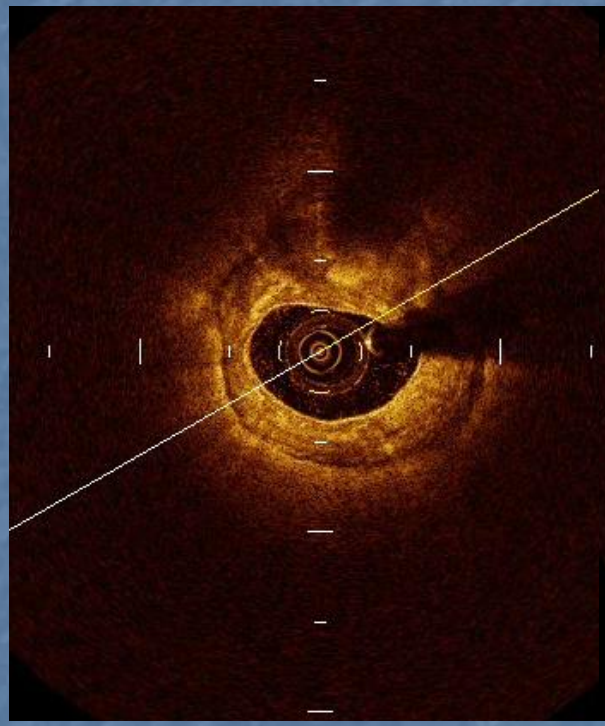
TOPIC 2008 Live　Courtesy by Saiseikai Yokohamashi Toubu Hosp

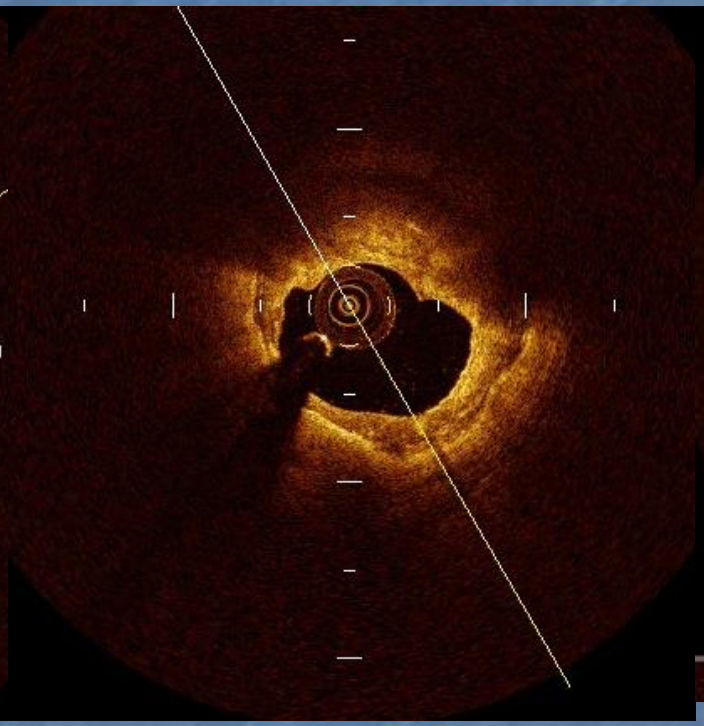
Calcified lesion

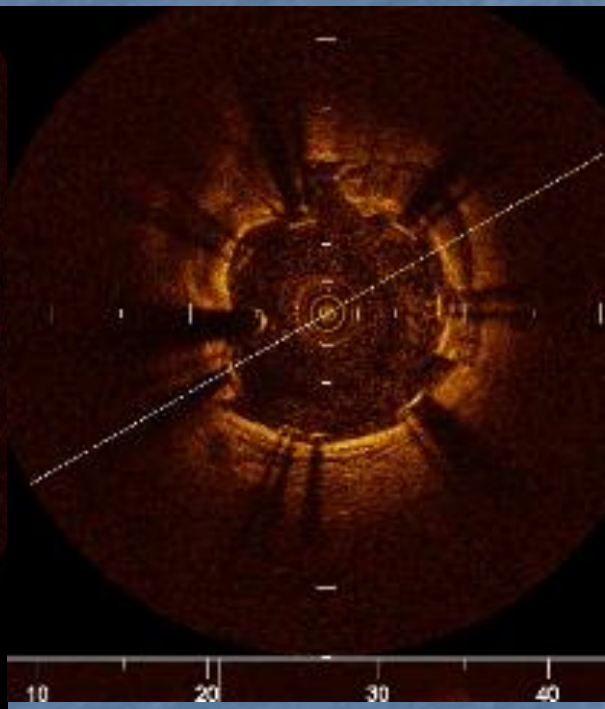
Before Rota

After Rota

After Stenting





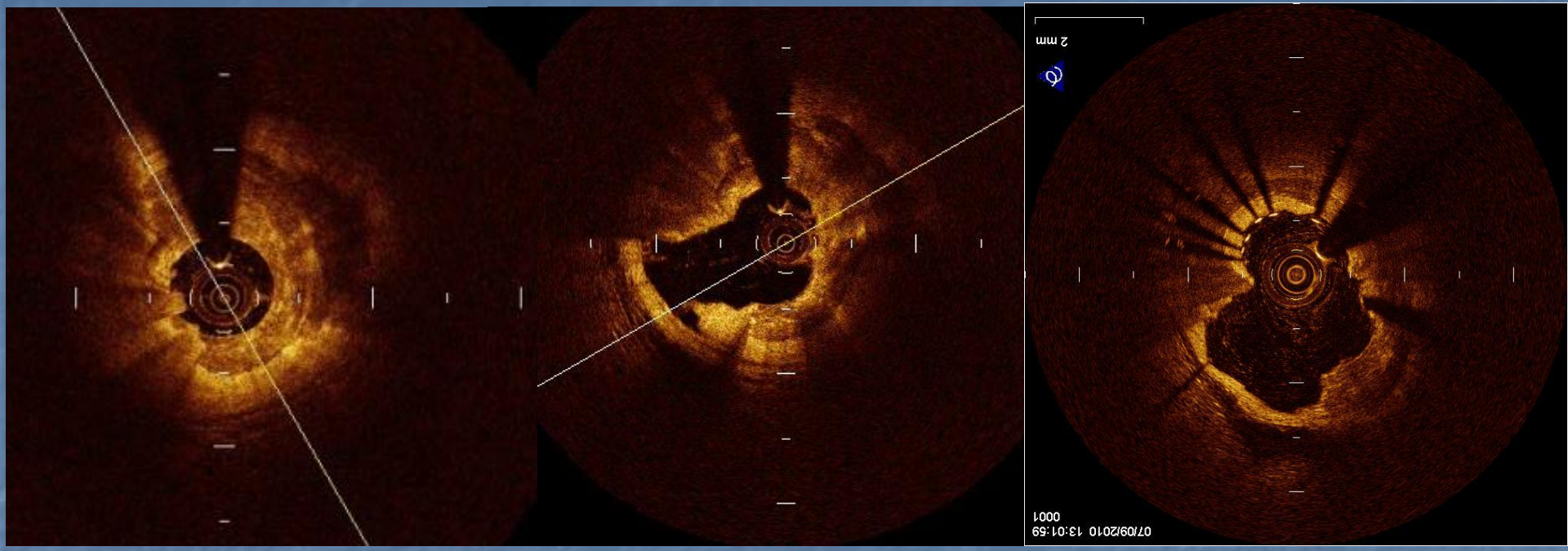


If the ablation area is enough, stent will well expand.

After Rota

After POBA

After Stenting

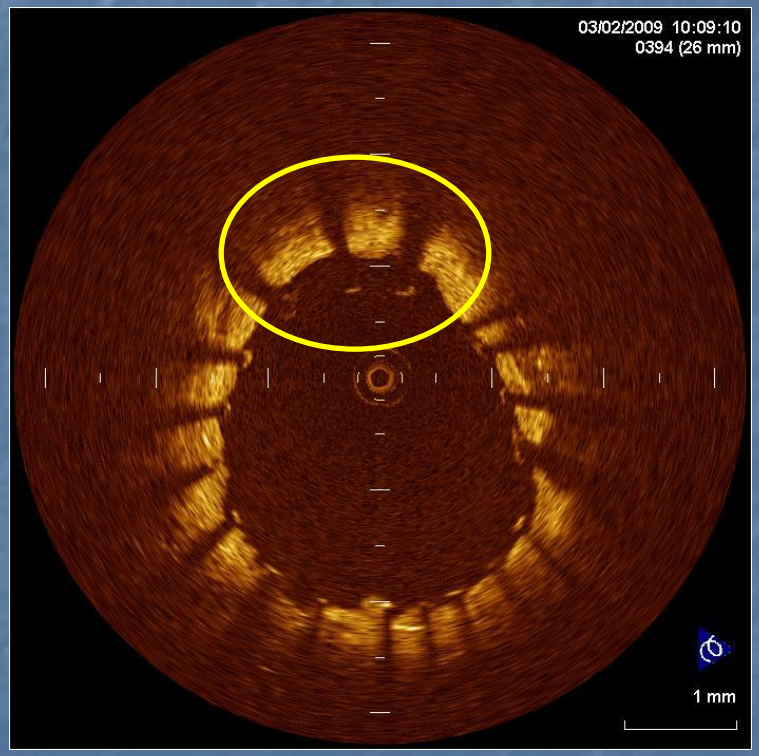


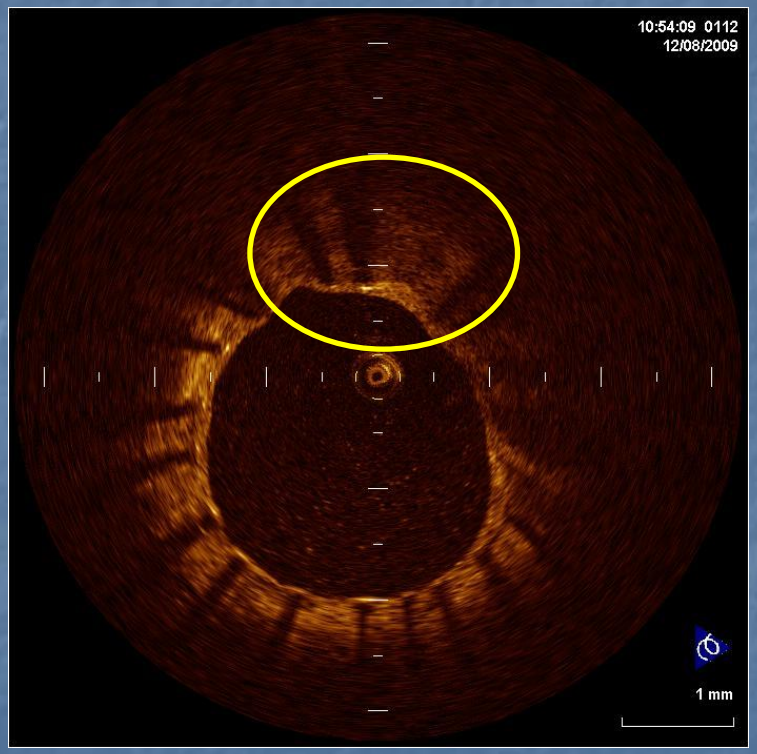
If the ablation area is not enough, stent will not well expand and sometimes becomes irregular shape or underexpansion.

These OCT findings may have a risk for acute and subacute stent thrombosis.

How about time course of OCT abnormal findings?

Resolved malapposition





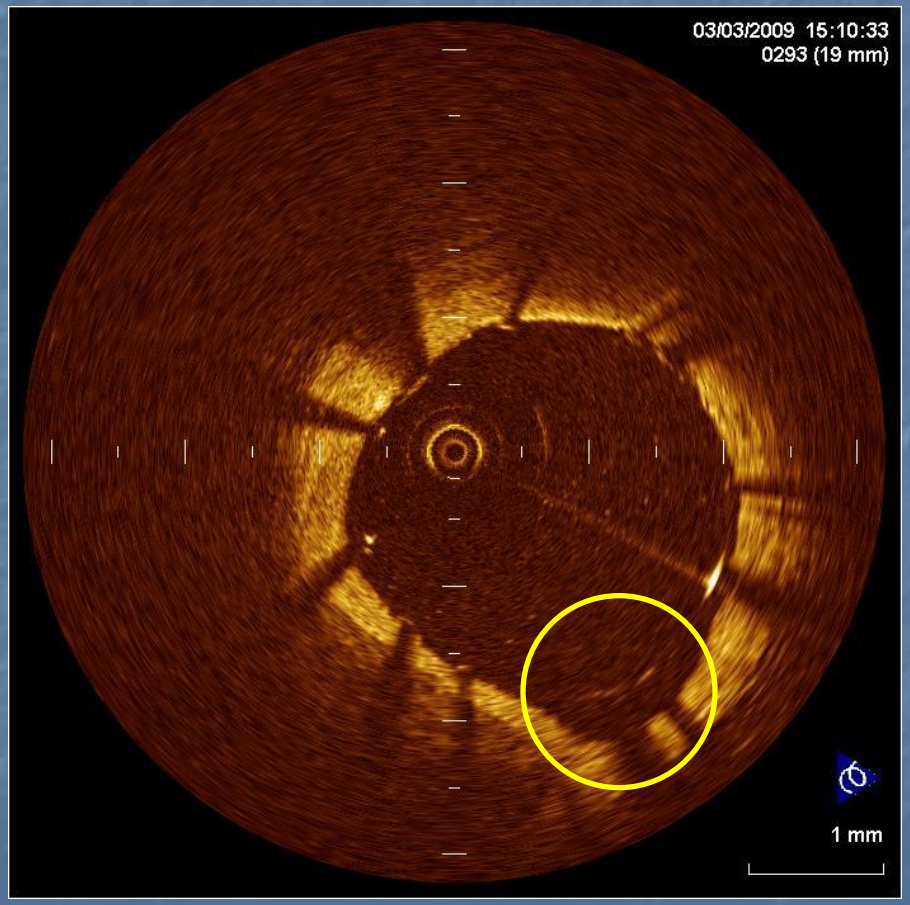
Immediately after PCI

8 month follow-up

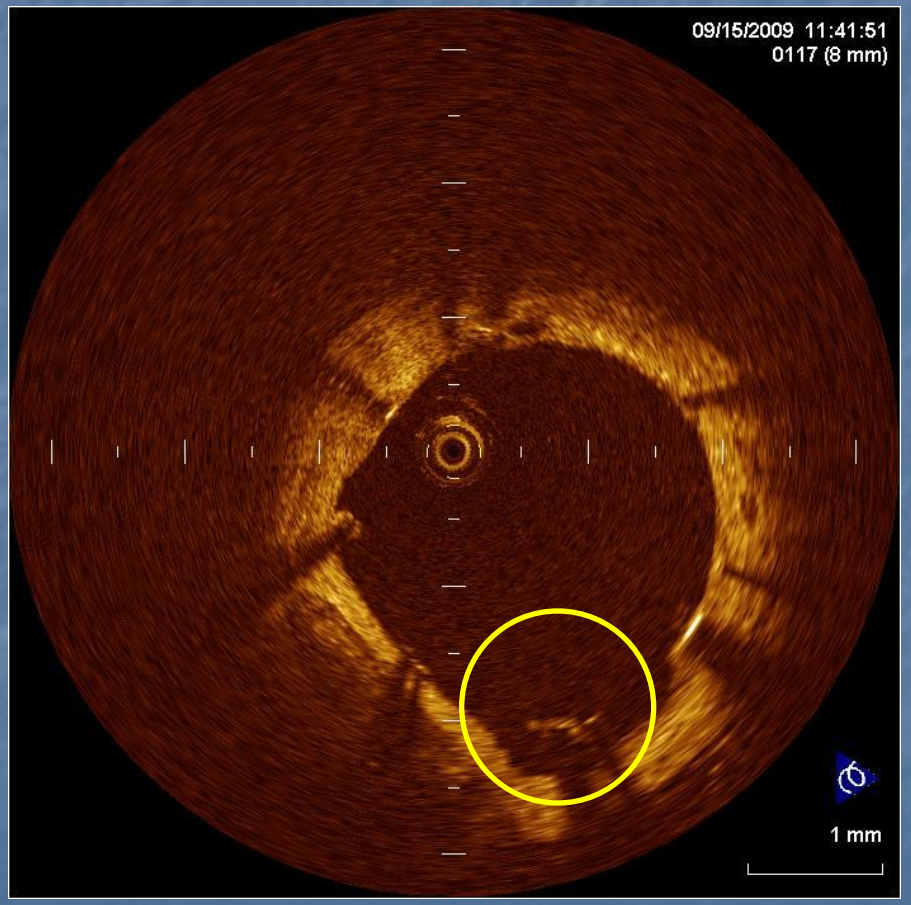
KOBE UNIVERSITY

Persistent stent malapposition

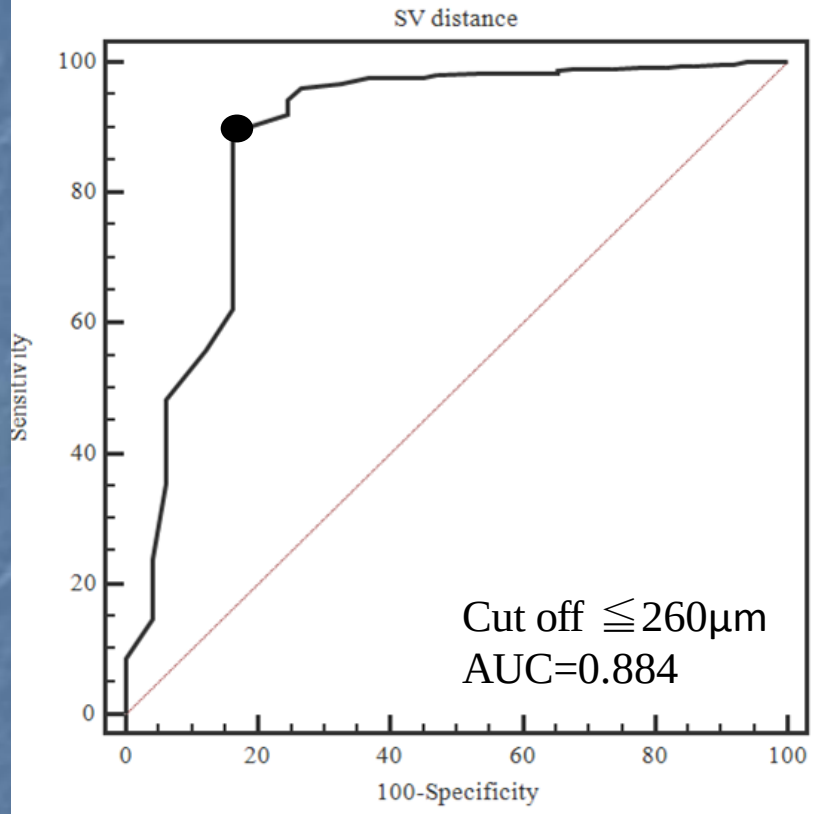
Immediately after PCI



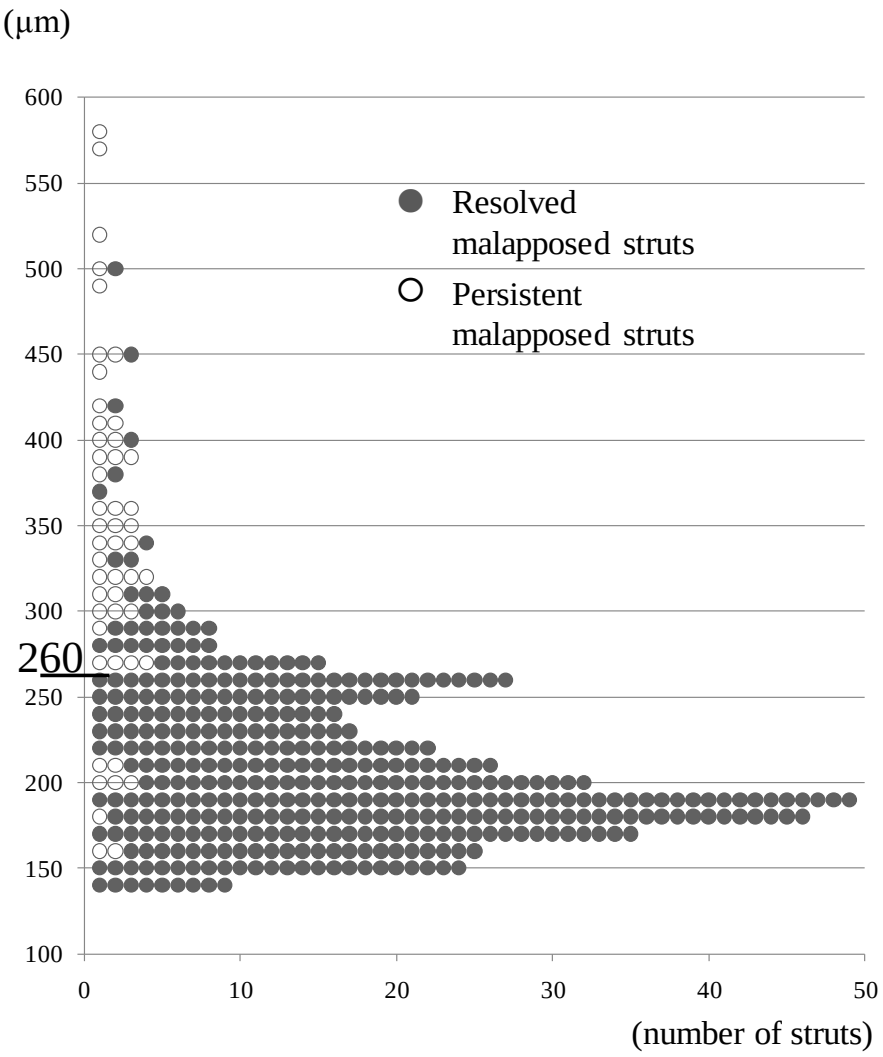
Follow-up



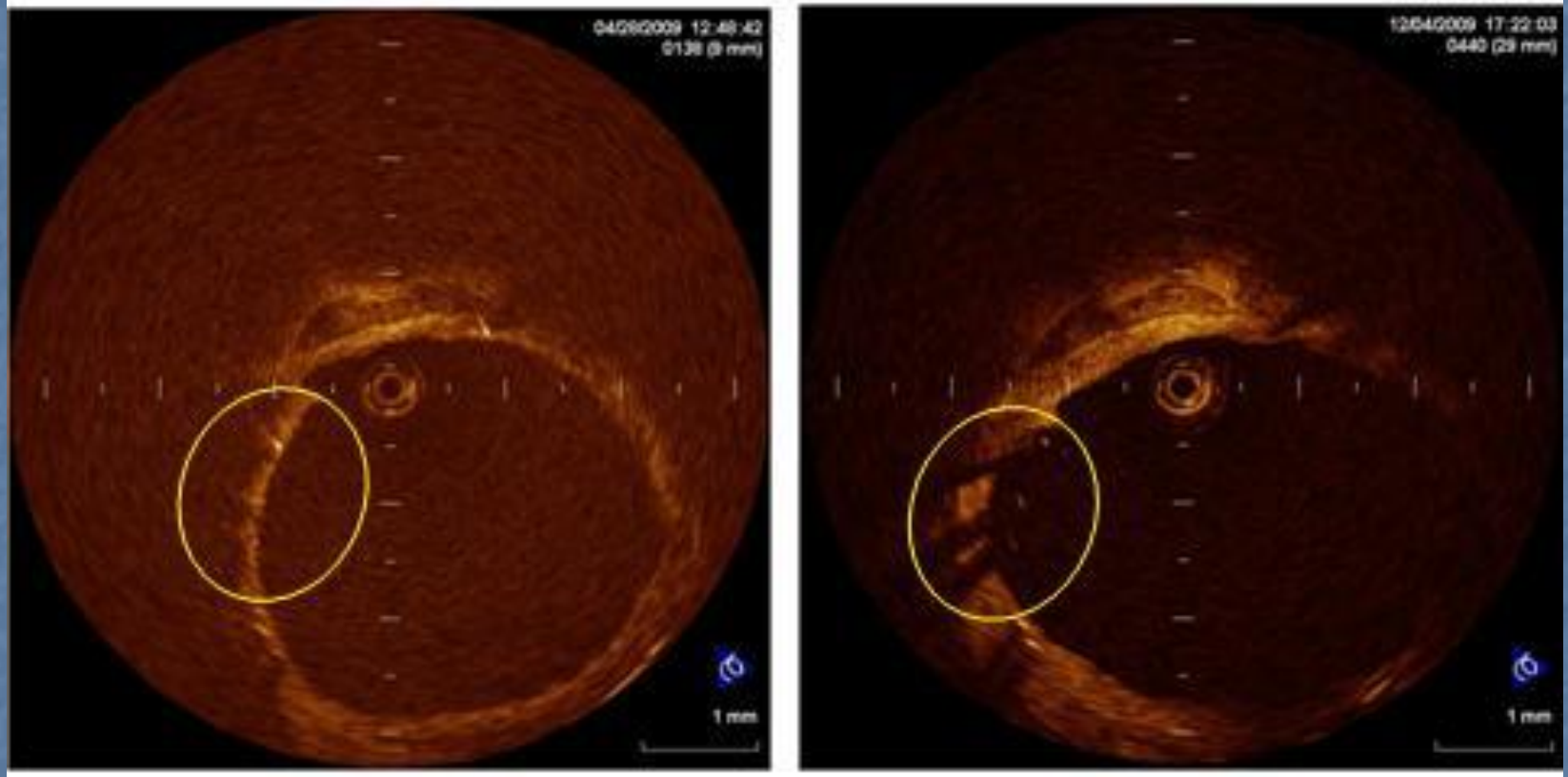
KOBE UNIVERSITY



Sensitivity: 89.3%
Specificity: 83.7%



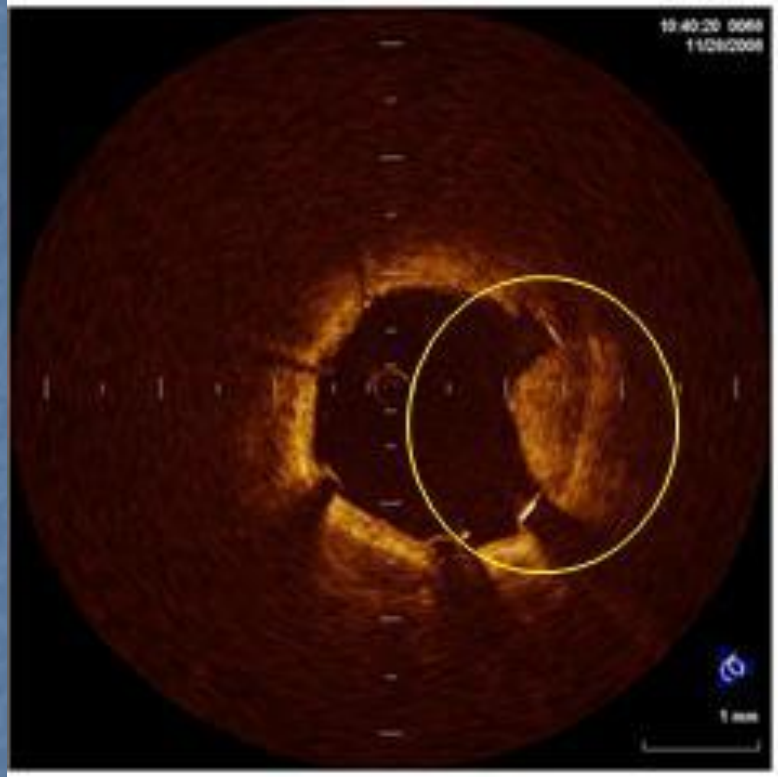
Late-acquired malapposition



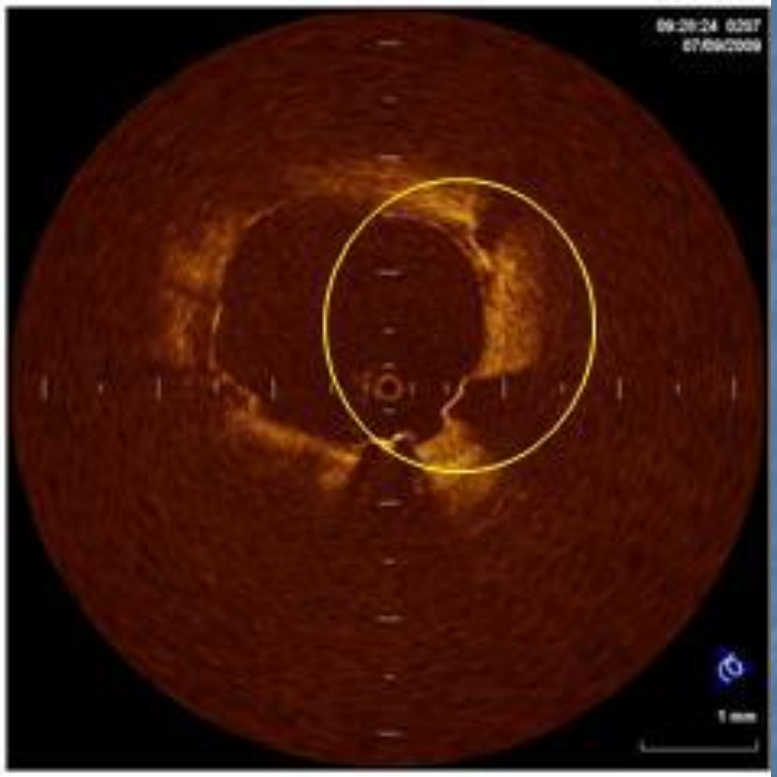
Immediately after PCI

Follow-up

Thrombus resolution



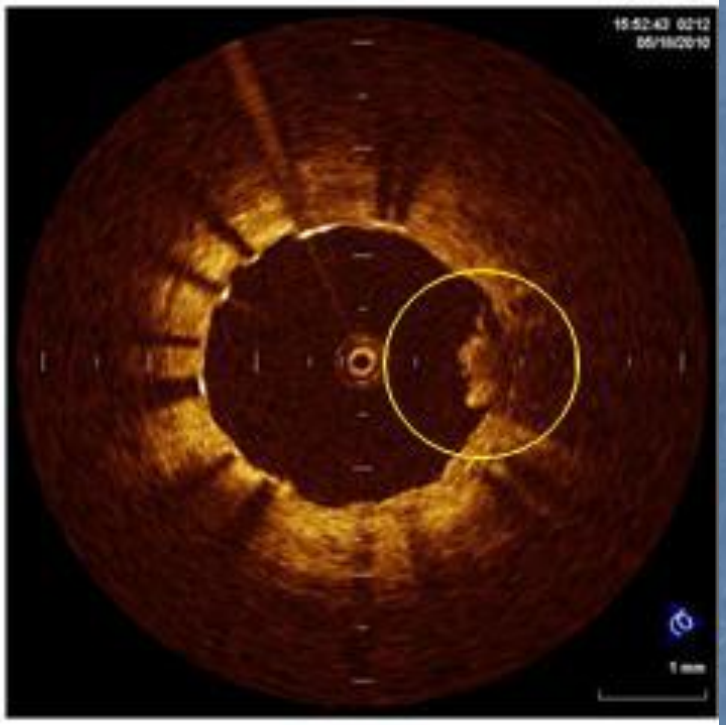
Immediately after PCI



Follow-up

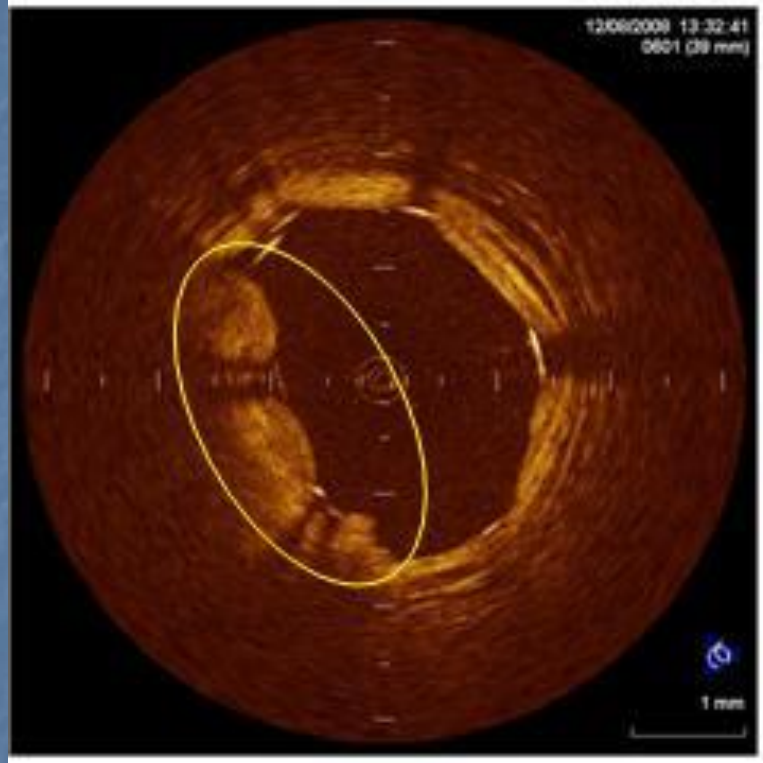
Late-acquired thrombus

Immediately after PCI

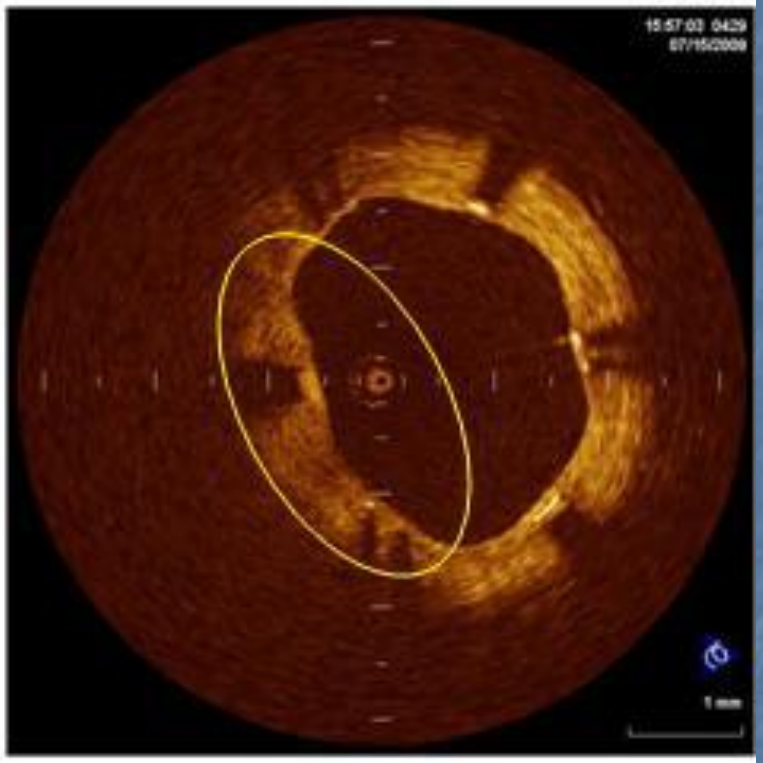


Follow-up

Tissue prolapse

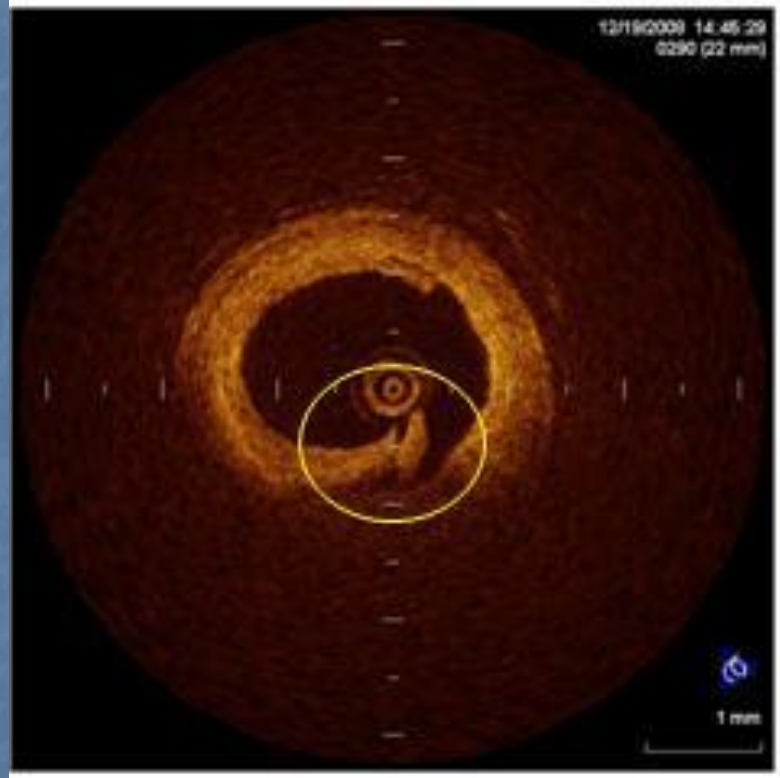


Immediately after PCI

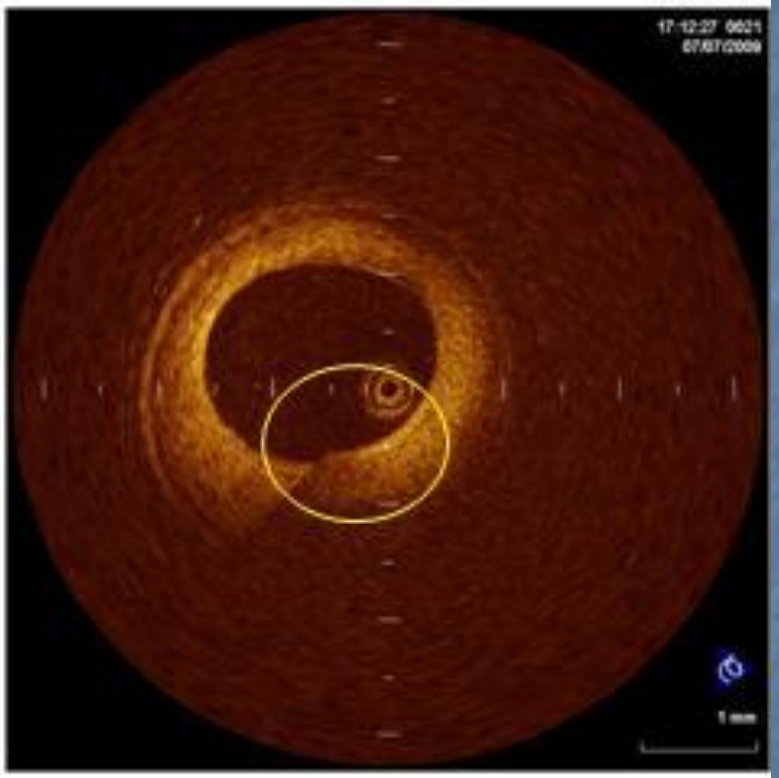


Follow-up

Edge dissection



Immediately after PCI



Follow-up

To get enough expansion and well apposition to the vessel may be important to prevent thrombosis. OCT may guide optimal stenting and show serial changes of DES findings.

KOBE UNIVERSITY

Major factors for stent thrombosis

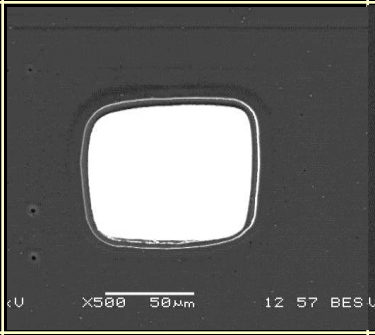
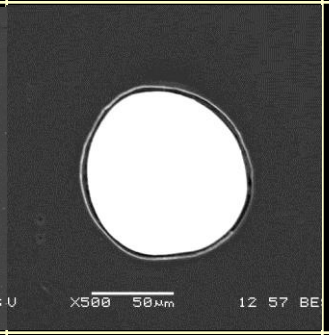
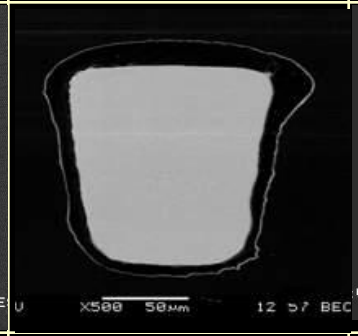
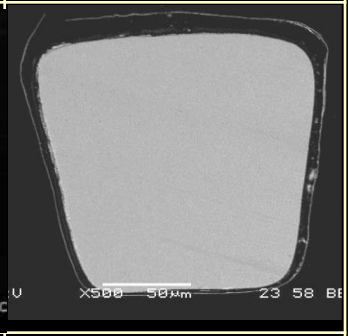
Incomplete neointimal Coverage.
Atypical neoitimal tissue
Endothelial dysfunction
Late acquired malapposition

Stent under-expansion
Stent malapposition
Stent edge dissection
etc.

DES

Is there any difference between 1st and 2nd generation DES?

Difference of Strut & Polymer Thickness* in DES

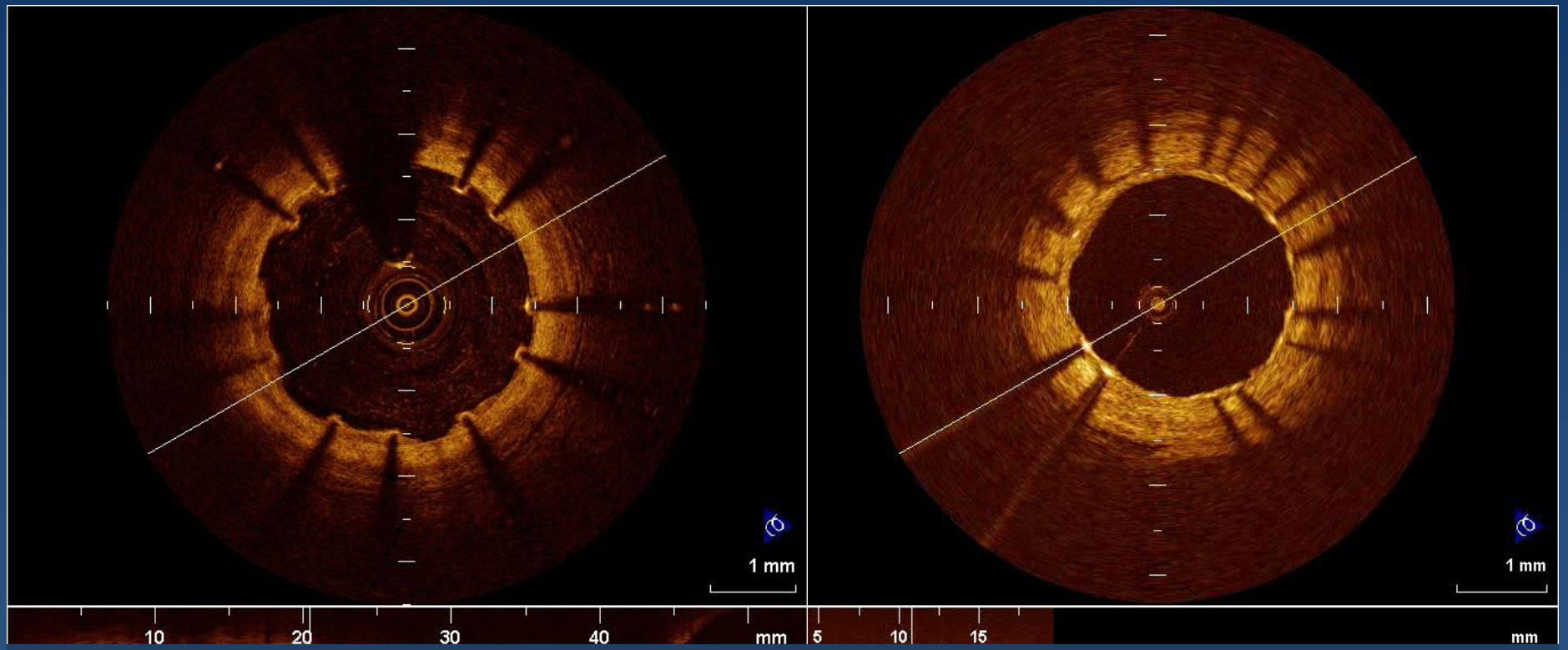
	PROMUS /Xience	ENDEAVOR	TAXUS Liberté	CYPHER
				
Stent Material	Cobalt Chromium	Cobalt Chromium	Stainless Steel	Stainless Steel
Strut Thickness	0.0032” 81µm	0.0036” 91µm	0.0038” 97µm	0.0052” 140µm
Polymer Thickness	7 x 2µm	6 x 2µm	14 x 2µm	14 x 2µm
Total	95µm	103µm	125µm	168µm

*3.0 mm diameter stents, 500x magnification

8M F/U of Cypher and Promus/Xience

Cypher

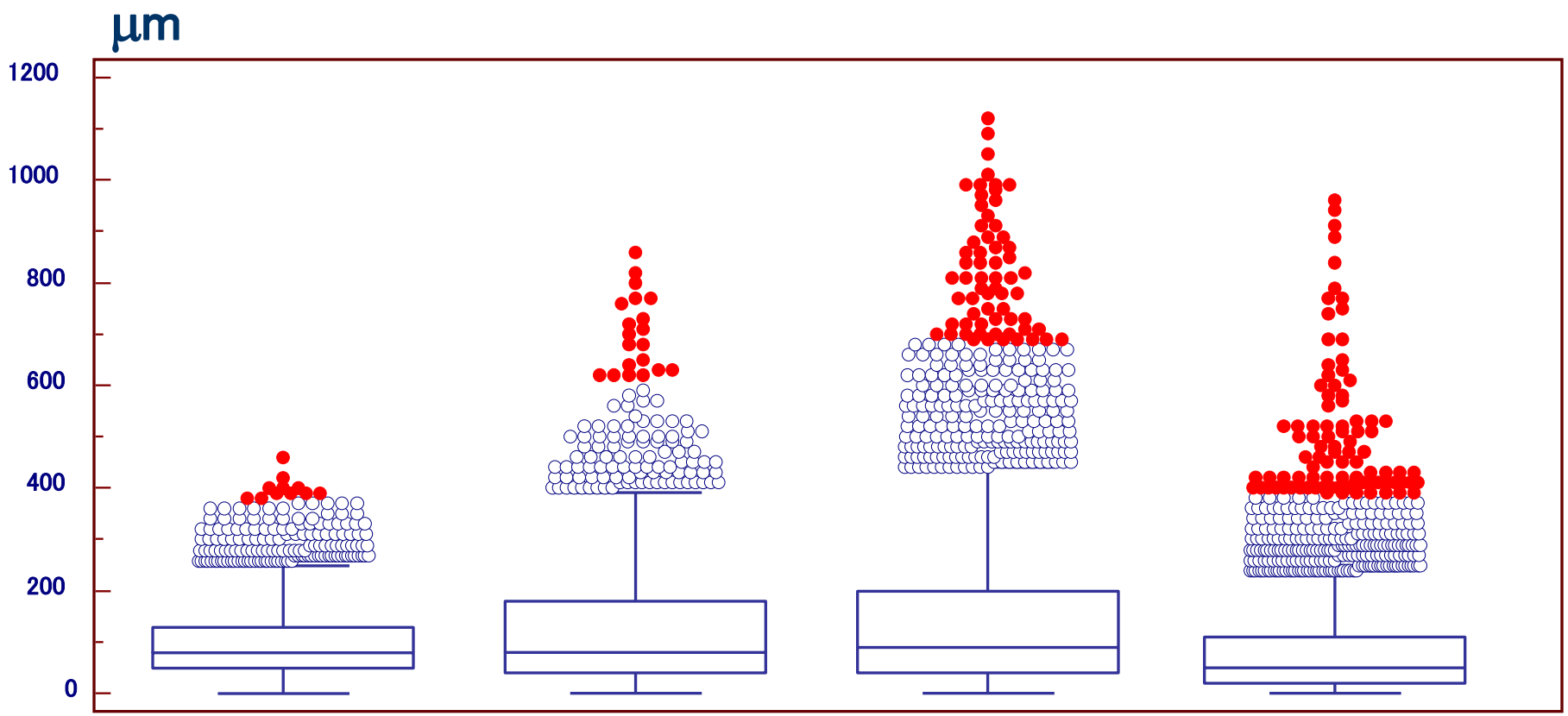
Promus/Xience



Thinner strut has an advantage for neointimal coverage if the neointima is thin.

KOBE UNIVERSITY

Distributions of Neointimal Thickness (median value)



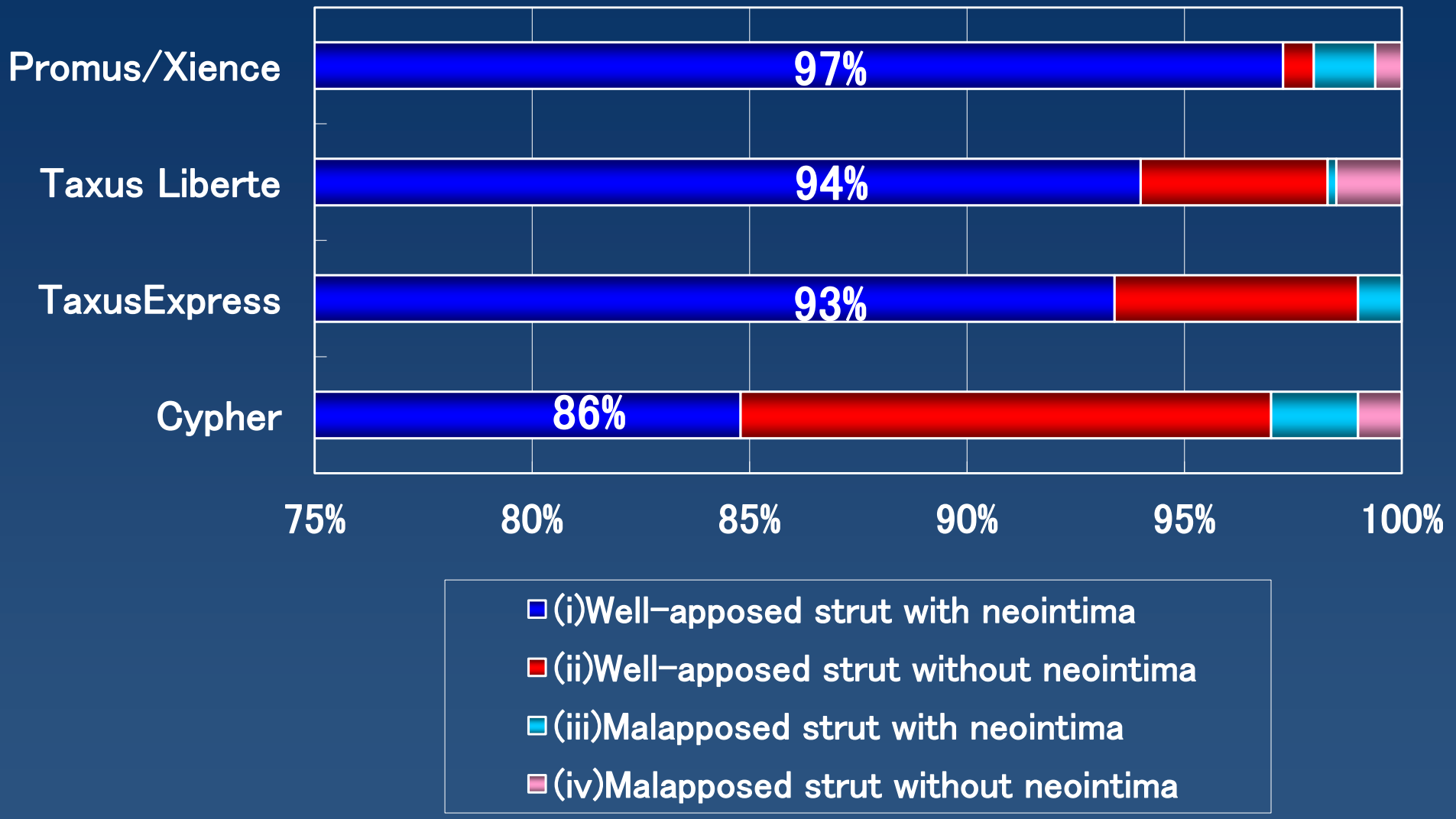
Promus/Xience | Taxus Liberte | Taxus Express | Cypher

Miyoshi N, Shite J et al.Circulation Journal 2010 ;74: 903-908.

Inoue T, Shite J., Yoon J. et al Heart 2011, 97; 1379-1384

KOBE UNIVERSITY

Region of neointimal coverage

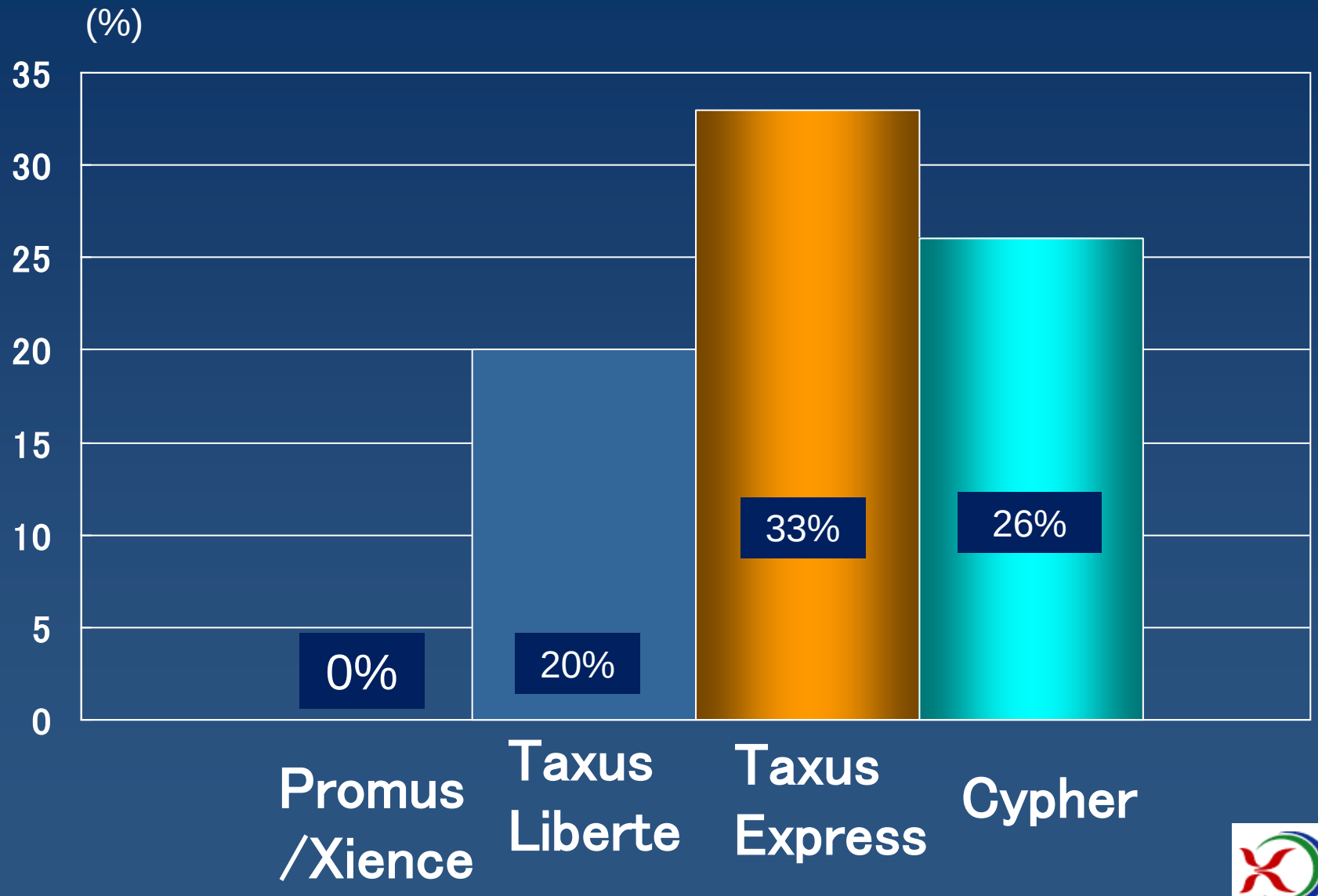


Miyoshi N, Shite J et al.Circulation Journal 2010 ;74: 903-908.

Inoue T, Shite J., Yoon J. et al Heart 2011, 97; 1379-1384

KOBE UNIVERSITY

Frequency of Mural Thrombus



KOBE UNIVERSITY

Thinner struts and lipophilic everolimus may promote thin and uniform neointimal coverage in Promus/Xience Stent.

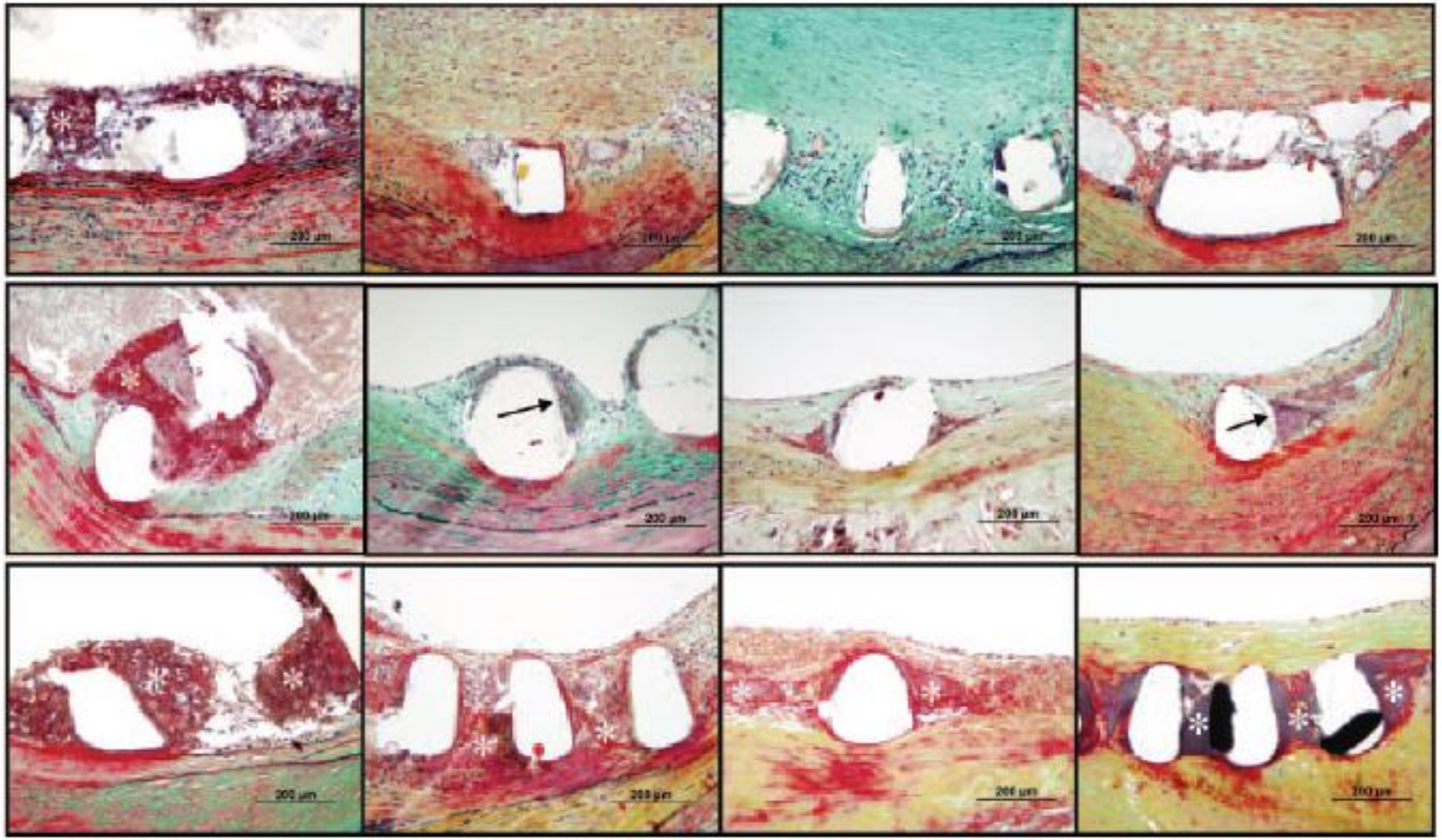
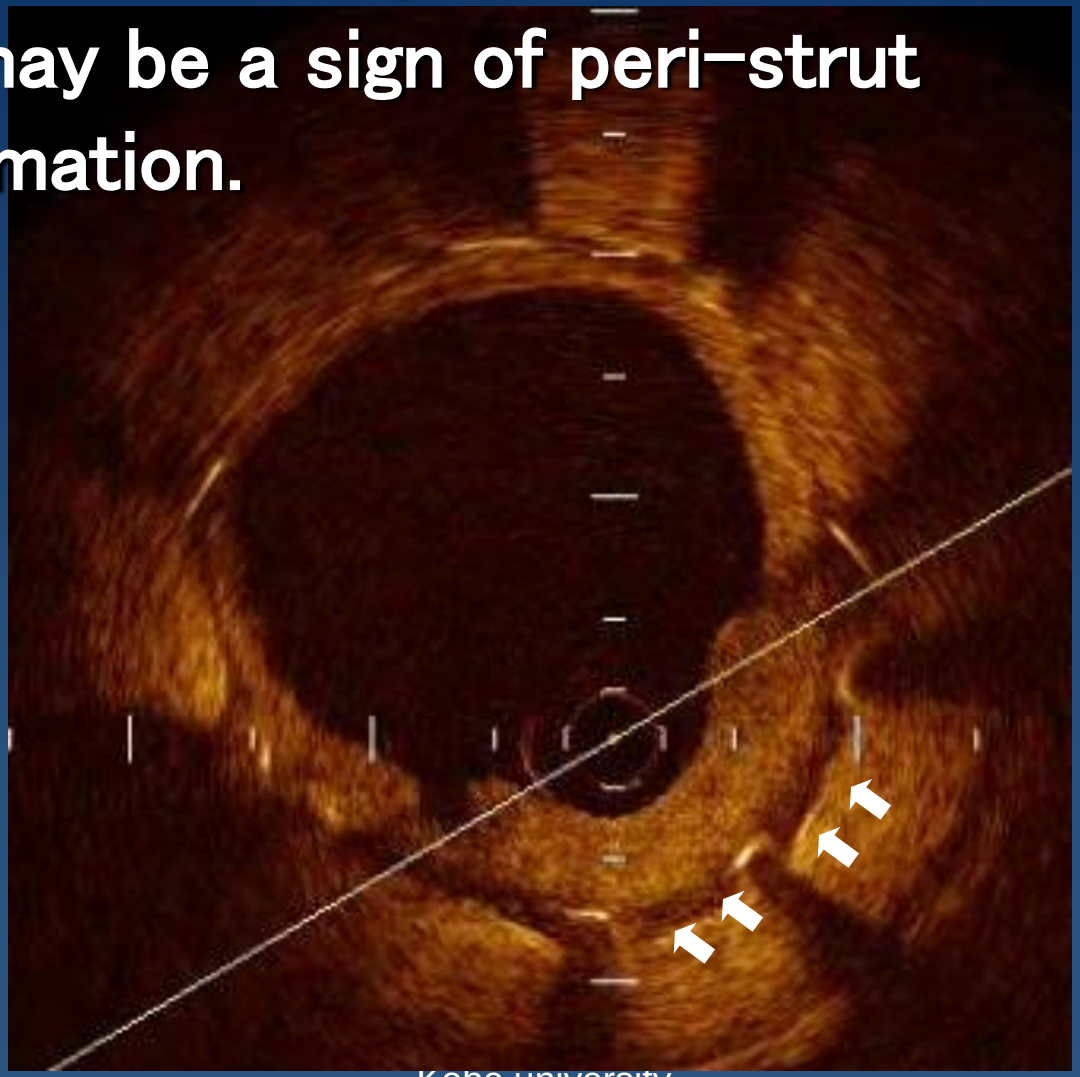


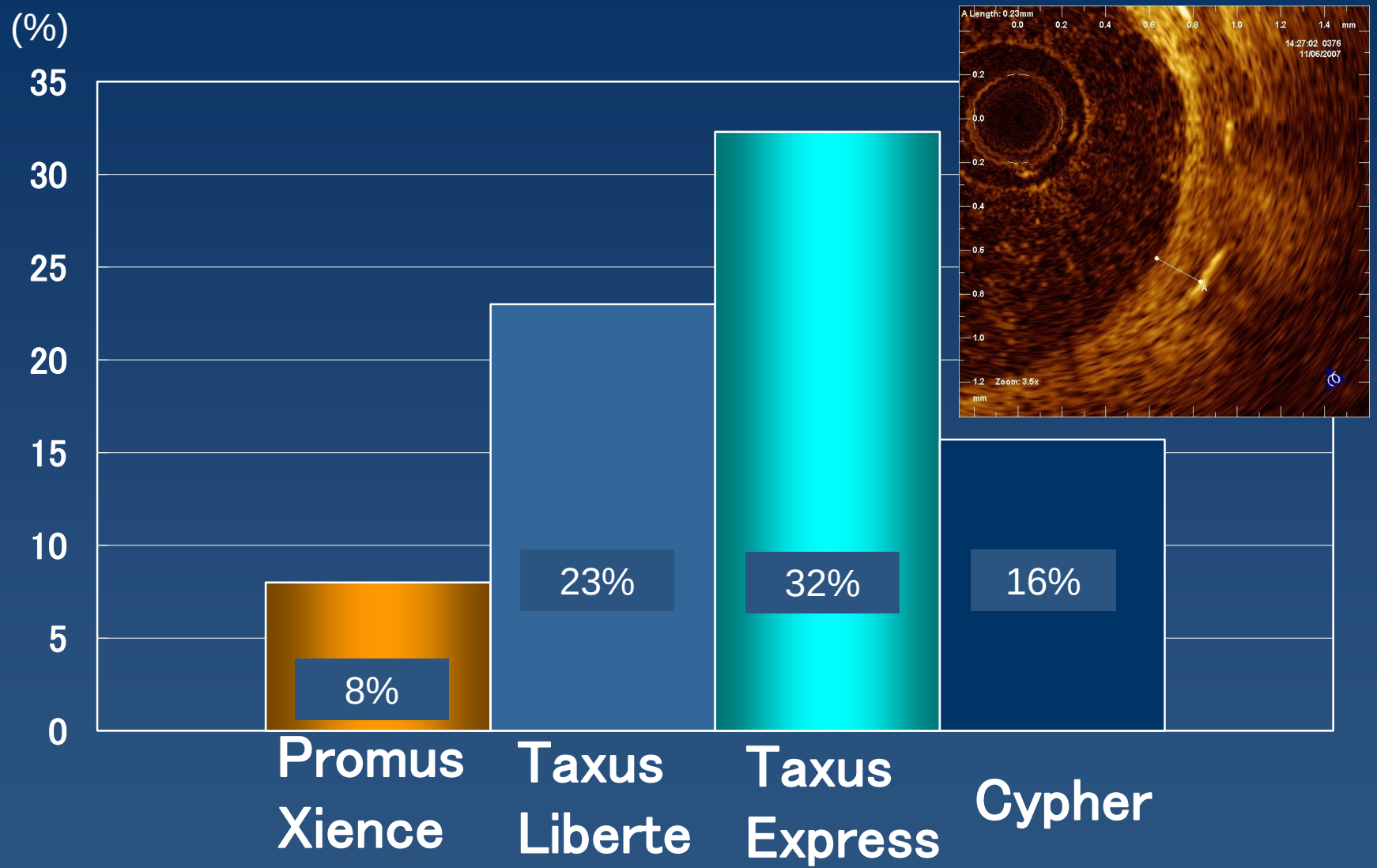
Figure 4. Time course of morphological changes after DES (Cypher and Taxus) and BMS implantation in human pathologic specimens from 2 weeks to 18 months after stenting. Peristrut fibrin thrombus is most prominent at 2 weeks but is no different in BMS and DES. At 3 months, complete arterial healing, including a well-established neointimal layer, with neointimal thickness peaking around 9 to 12 months and regression is seen thereafter in BMS. Cypher stents show an inflammatory infiltrate, fibrin deposition, and only rare smooth muscle and endothelial cells at 3 months with minimal to no significant increase in neointima at 15 to 18 months. In contrast, Taxus stents show more fibrin deposition surrounding stent struts (*), which persists up to 18 months. In contrast, Cypher DES shows predominance of inflammatory cells, including giant cell formation (black arrowheads), at early and late time points with less fibrin deposition than in Taxus stents.

Finn AV et al. ATVB 2007

By OCT findings of DES, localized peri-strut low intensity neointima was observed . This may be a sign of peri-strut inflammation.



Frequency of peri-strut low intensity

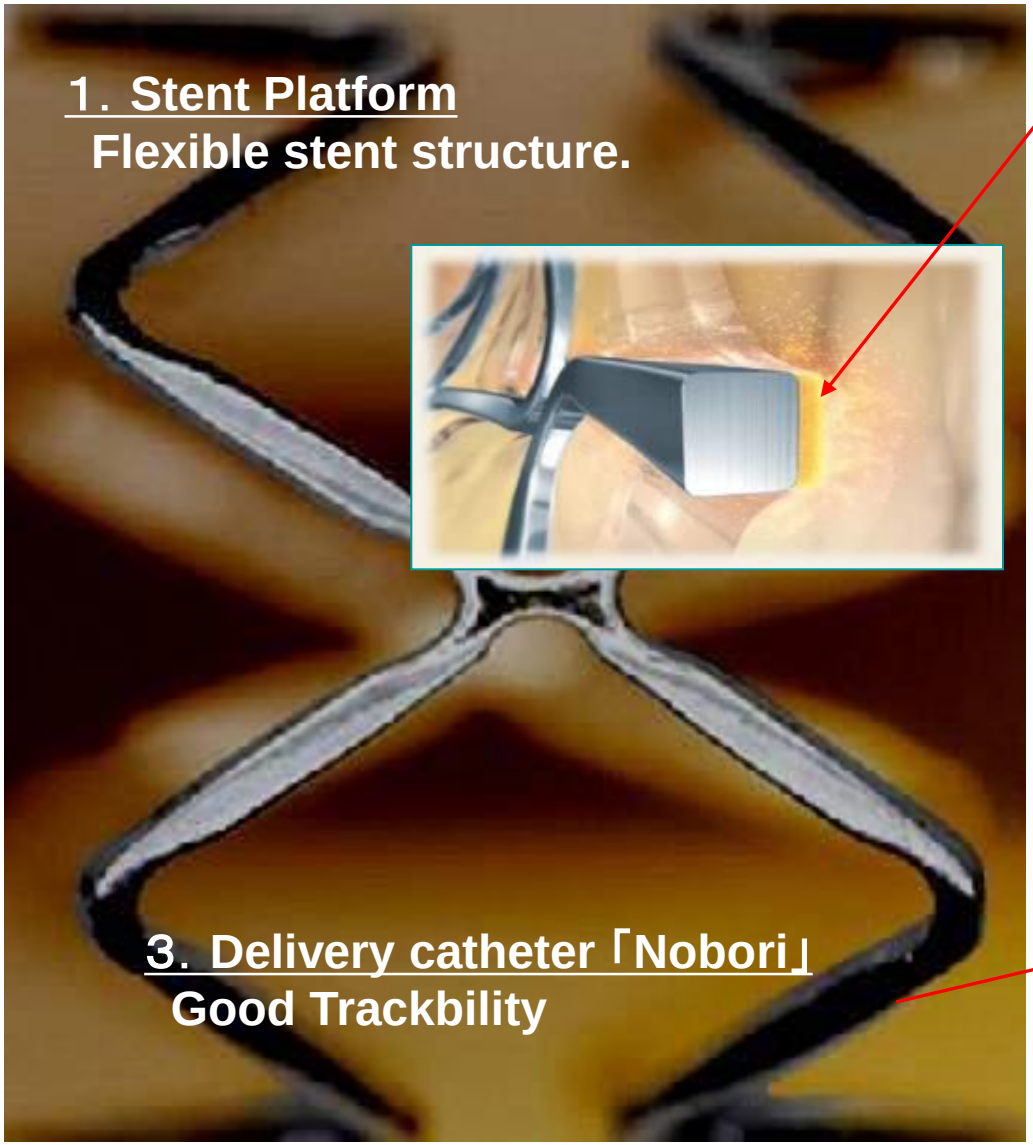


Miyoshi N, Shite J et al.Circulation Journal 2010 ;74: 903-908.

Inoue T, Shite J., Yoon J. et al Heart 2010 in press

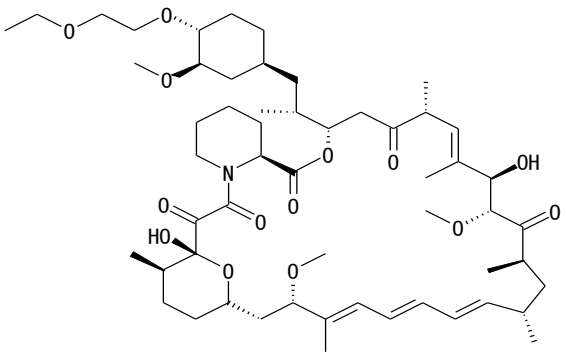
KOBE UNIVERSITY

Nobori Components

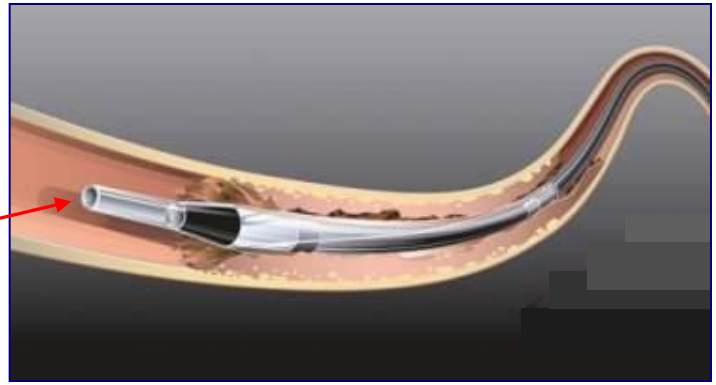


1. Stent Platform
Flexible stent structure.

2. Drug and polymer
Biolimus A9™ and
Biodegradable Polymer (PLA)
coated only abluminal side.

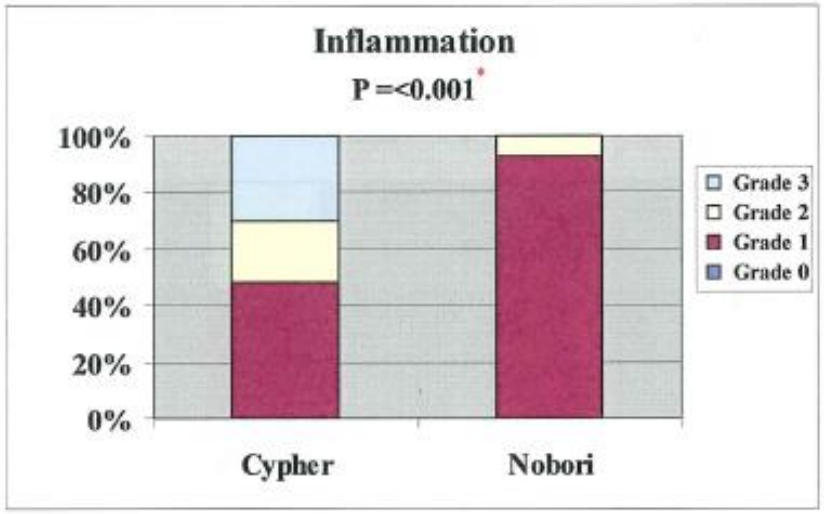


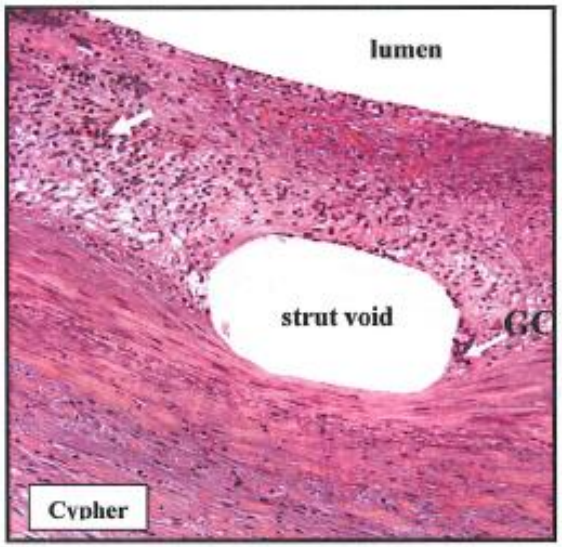
3. Delivery catheter「Nobori」
Good Trackbility

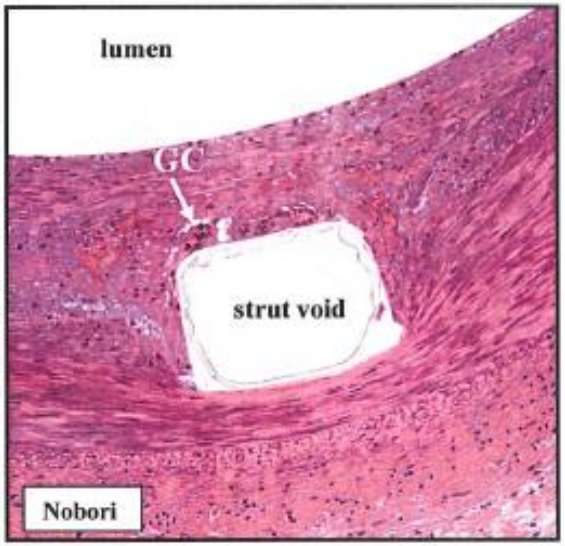


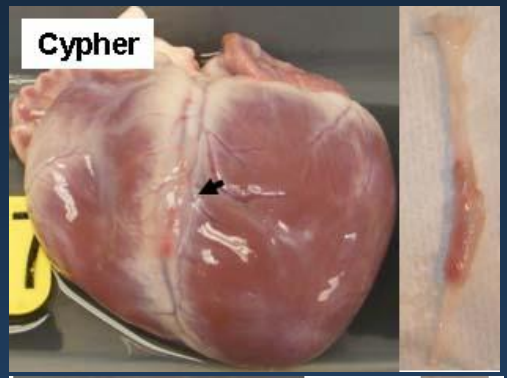
TERUMO

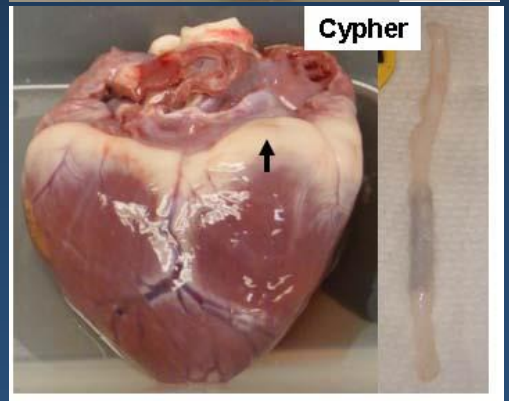
Glossy view / H&E staining and scoring of inflammatory cells infiltration

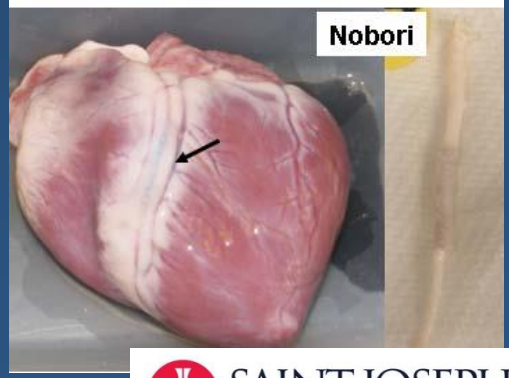








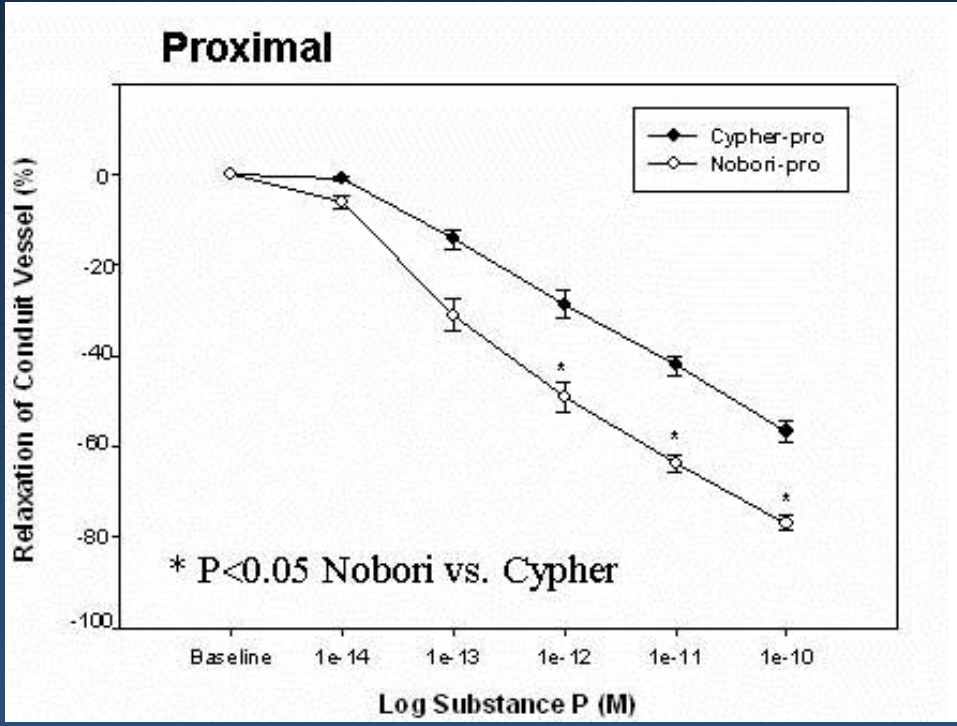


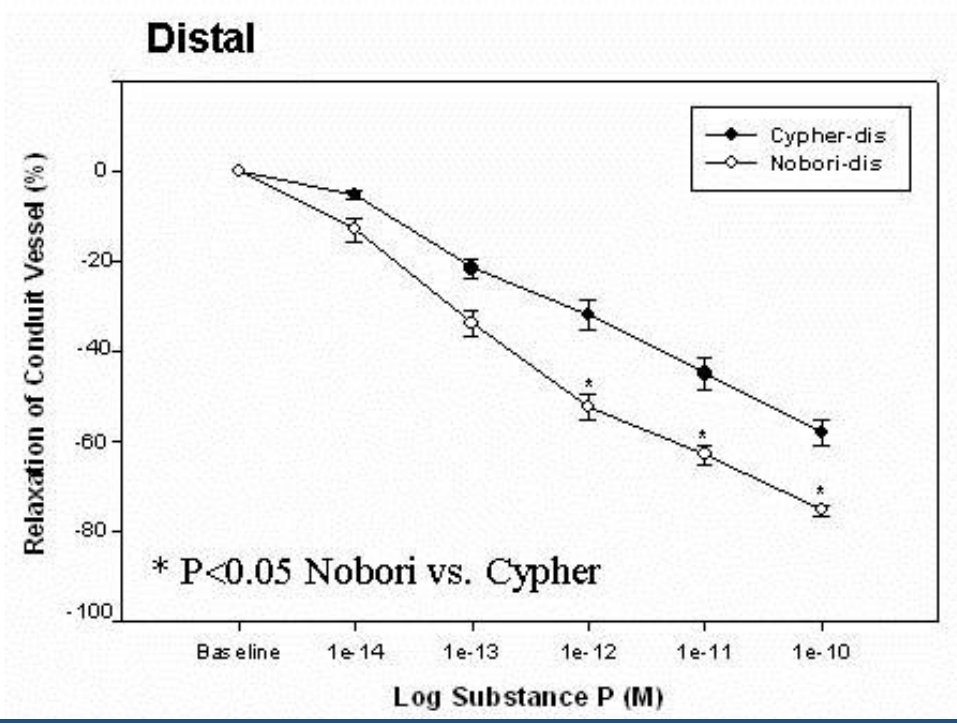


Shinke T et al.

SAINT JOSEPH'S
Translational Research Institute

Endothelial function of the Vessel segments proximal and distal to Nobori and Cypher stent

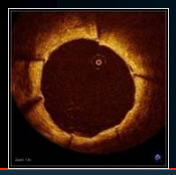




Vessel segments proximal and distal to Nobori stent showed relaxation response to Substance P, endothelium-dependent vasodilator, in a concentration-dependent manner. However, the segment proximal and distal to Cypher stent showed decreasing relaxation at higher concentrations of Substance P.

SAINT JOSEPH'S
Translational Research Institute

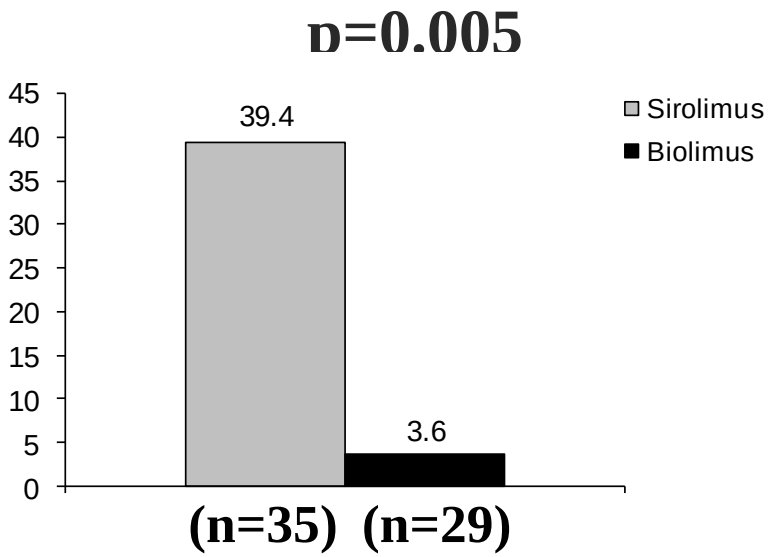
Li J, Pendyala L, Matsumoto D, Shinke T, et al. ACC2010



LEADERS OCT Substudy

BioMatrix™ Stent

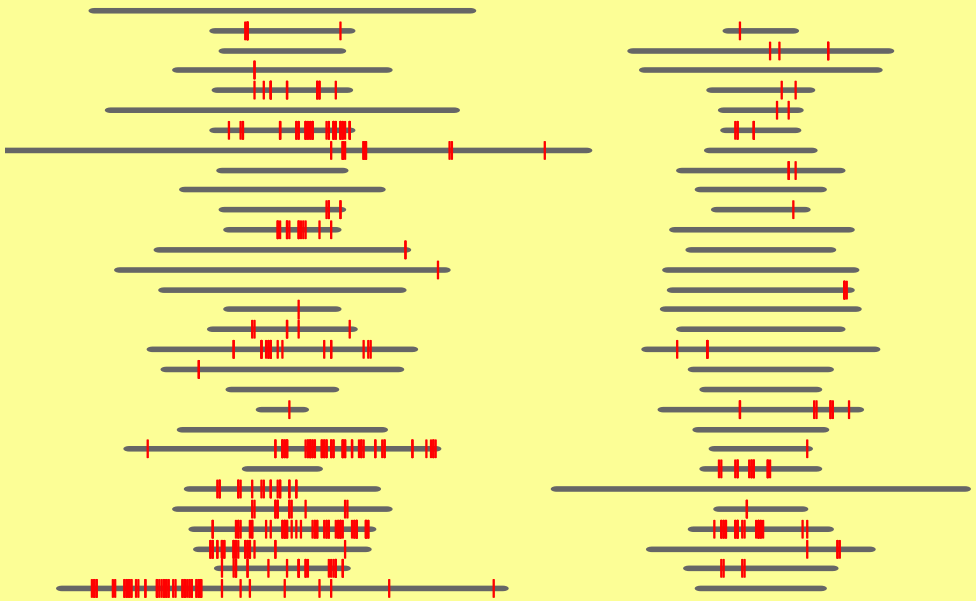
Percentage of lesions with >5% uncovered struts



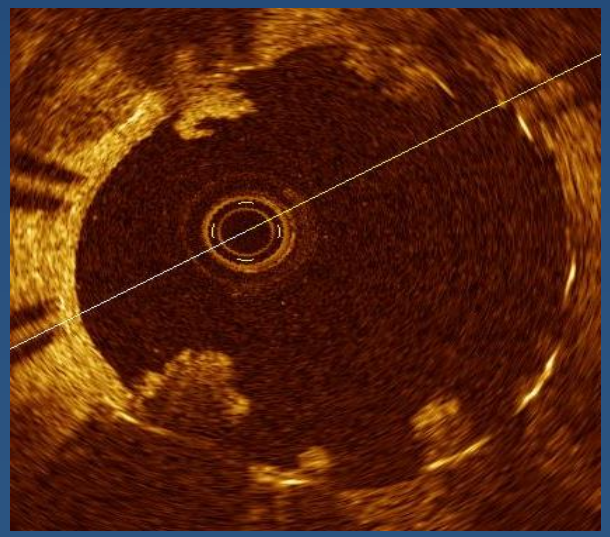
(EHJ 2010;31:165–176)

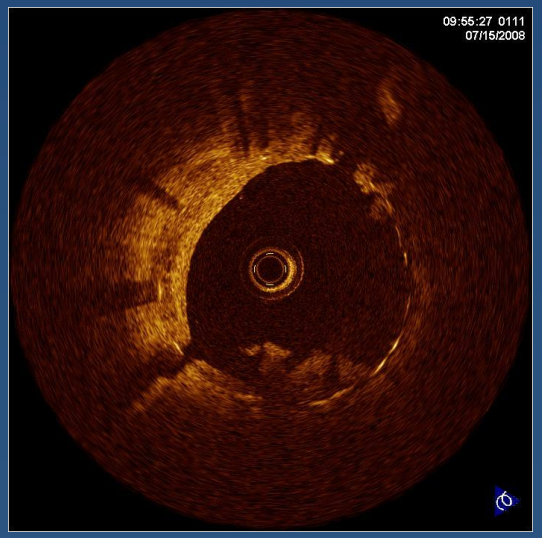
Distribution of Uncovered Struts within Lesions

Sirolimus Biolimus



DES peri-strut inflammation or partial uncovered strut may persist for some lesions. These may have thrombo-genesity. 2nd generation DES may have less peri-strut inflammation and good neointimal coverage and may have less thrombogenesity.



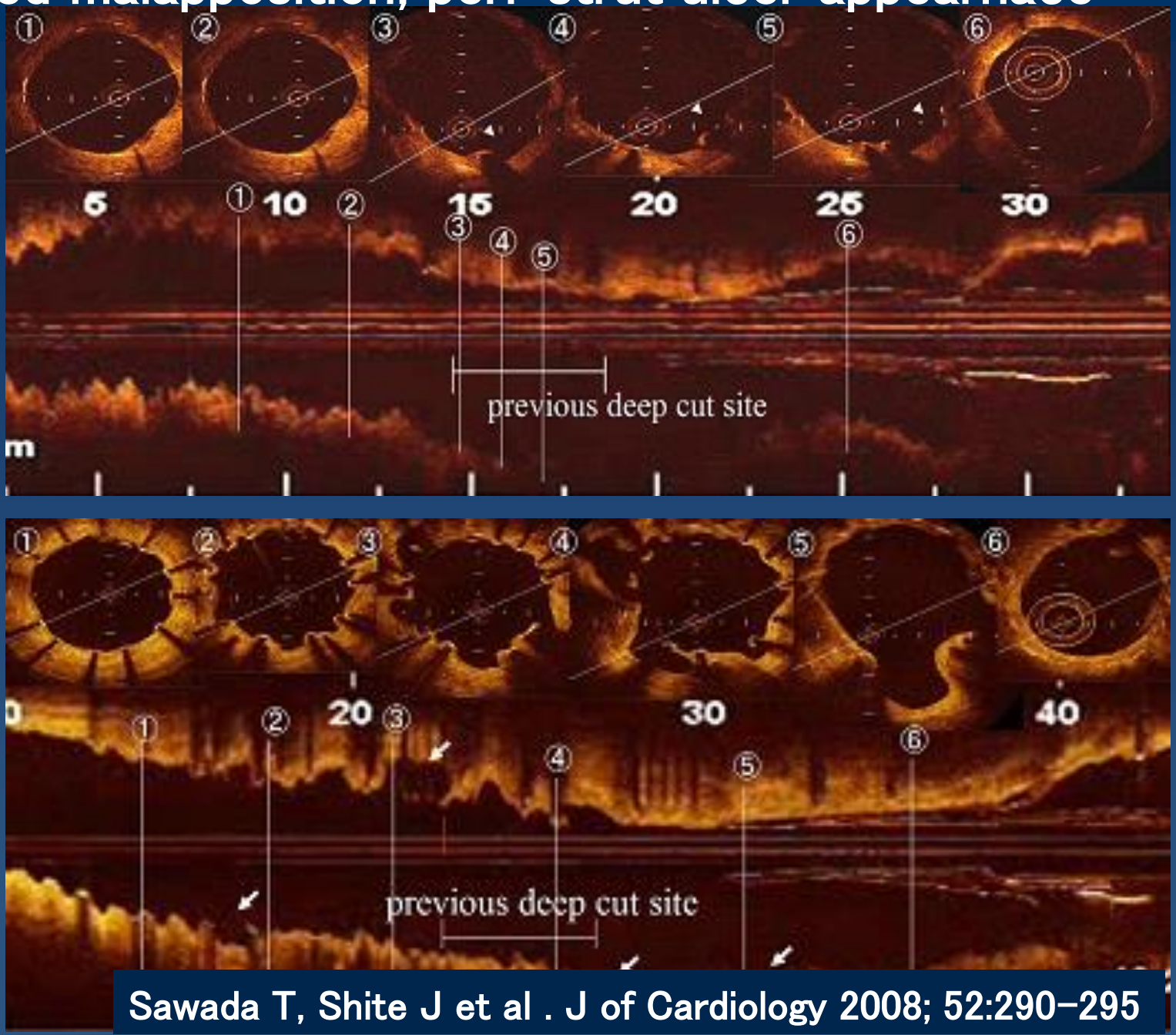


KOBE UNIVERSITY

Late acquired malapposition, peri-strut ulcer appearnace

6 M

29 M



Sawada T, Shite J et al . J of Cardiology 2008; 52:290-295

Major factors for stent thrombosis

Incomplete neointimal Coverage.
Atypical neoitimal tissue
Endothelial dysfunction
Late acquired malapposition

Stent under-expansion
Stent malapposition
Stent edge dissection
etc.

Drug resistance
Discontinuation of antiplatelet therapy

Association of cytochrome P450 2C19*2 polymorphism with clopidogrel response variability and cardiovascular events in Koreans treated with drug-eluting stents

Il-Young Oh, Kyung Woo Park, Si-Hyuk Kang, Jin Joo Park, Sang-Hoon Na, Hyun-Jae Kang, Bon-Kwon Koo, Young-Hoon Jeong, Jin-Yong Hwang, Choong Hwan Kwak, Yongwhi Park, Seok-Jae Hwang, Young-Guk Ko,
Dong Jik Shin, Yangsoo Jang, Hyo-Soo Kim.

Heart 2011

Table 2 Clinical outcome up to 1 year according to *CYP2C19*2* allele

	***CYP2C19*2* allele**			
	Non-carrier (n=1135)	**Carrier (n=1011)**	**RR (95% CI)**	**p Value**
Repeat revascularisation	94 (8.3%)	99 (9.8%)	1.20 (0.89 to 1.62)	0.222
Non-fatal MI	5 (0.4%)	12 (1.2%)	2.71 (0.95 to 7.73)	0.052
Cardiac death	5 (0.4%)	10 (1.0%)	2.26 (0.77 to 6.63)	0.128
Stent thrombosis	2 (0.2%)	15 (1.5%)	8.53 (1.95 to 37.4)	<0.001
MACE	100 (8.8%)	108 (10.7%)	1.24 (0.93 to 1.65)	0.143
Composite hard outcome	10 (0.9%)	23 (2.3%)	2.62 (1.24 to 5.53)	0.009

MI, myocardial infarction; MACE, major adverse cardiac events (=composite of cardiac death, MI, repeat revascularisation). Composite hard outcome (=composite of cardiac death, MI, stent thrombosis).

Il-Young Oh, Hyo-Soo Kim. Et al Heart 2011.

Impact of cytochrome P450 2C19 polymorphism on target lesion outcome after drug-eluting stent implantation in Japanese patients receiving clopidogrel

Ryo Nishio, Toshiro Shinke Junya Shite et al.

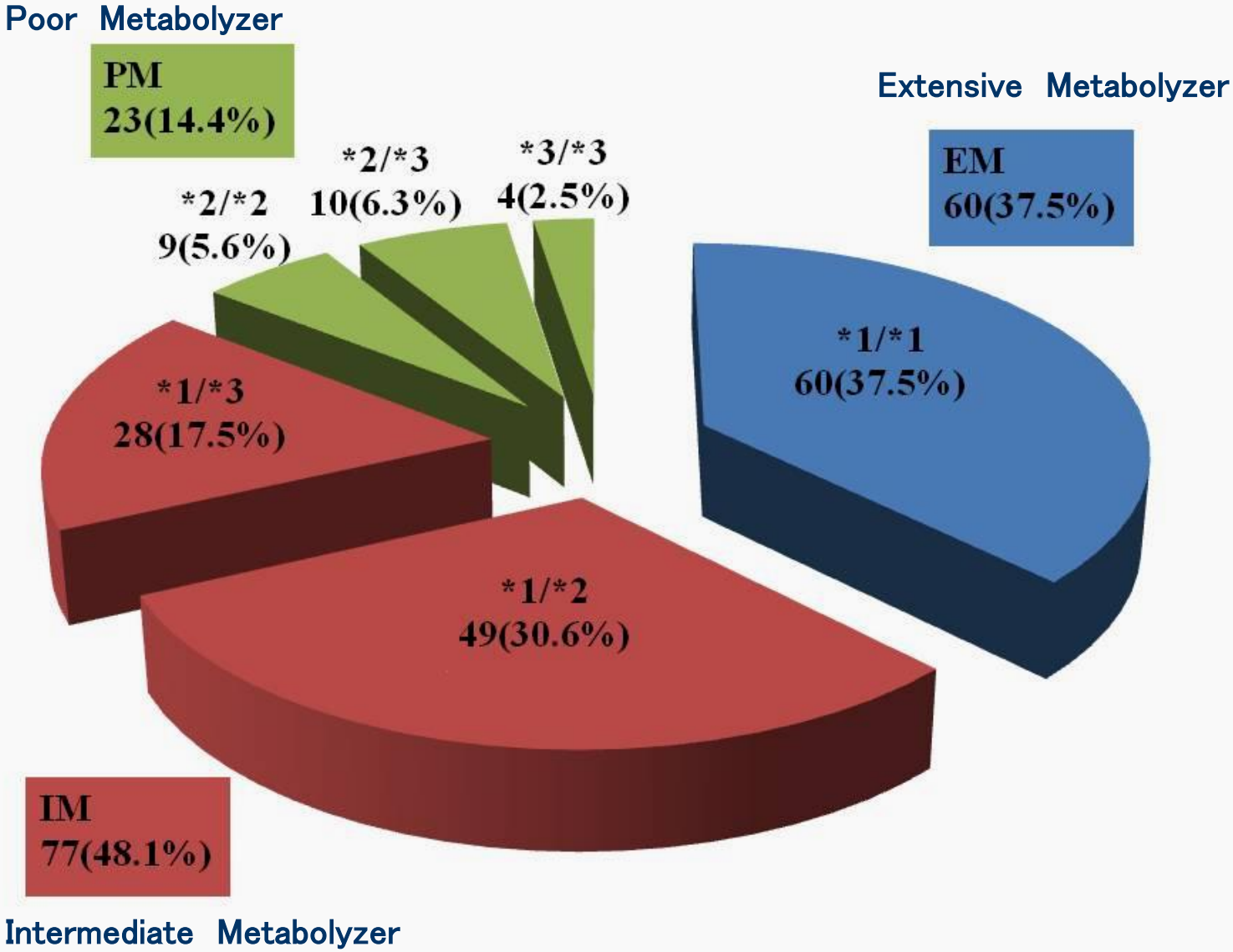
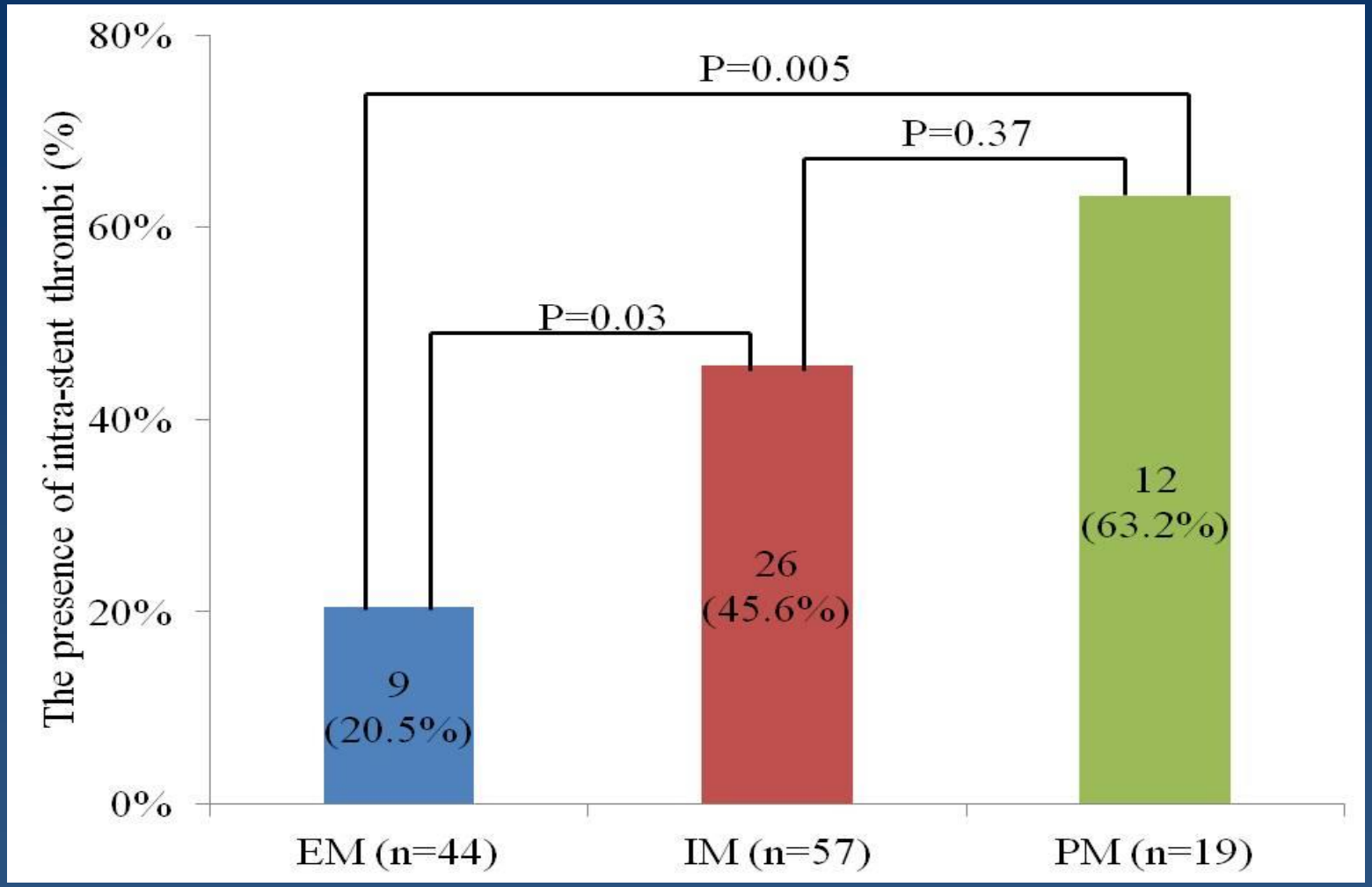
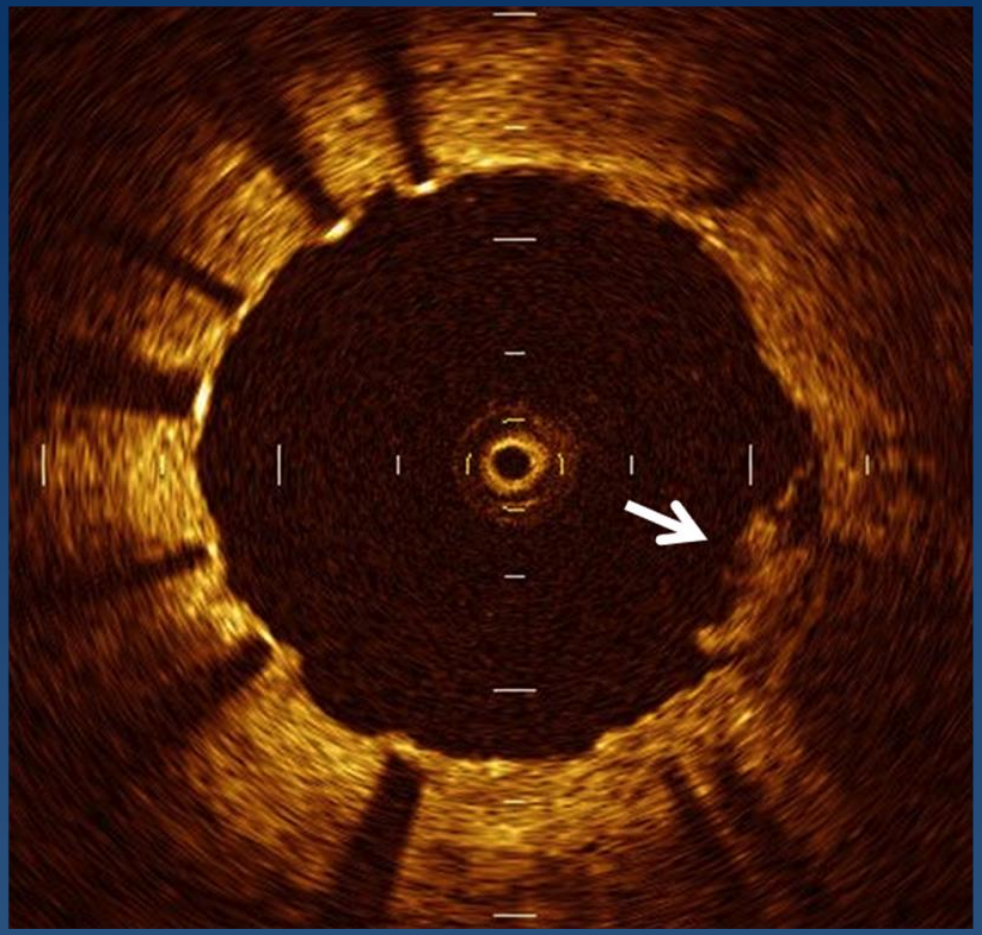

Poor Metabolyzer
PM
23(14.4%)
*2/*2
9(5.6%)
*2/*3
10(6.3%)
*3/*3
4(2.5%)
Extensive Metabolyzer
EM
60(37.5%)
*1/*1
60(37.5%)
*1/*3
28(17.5%)
*1/*2
49(30.6%)
IM
77(48.1%)
Intermediate Metabolyzer

Table 3. Major adverse cardiac event (MACE)

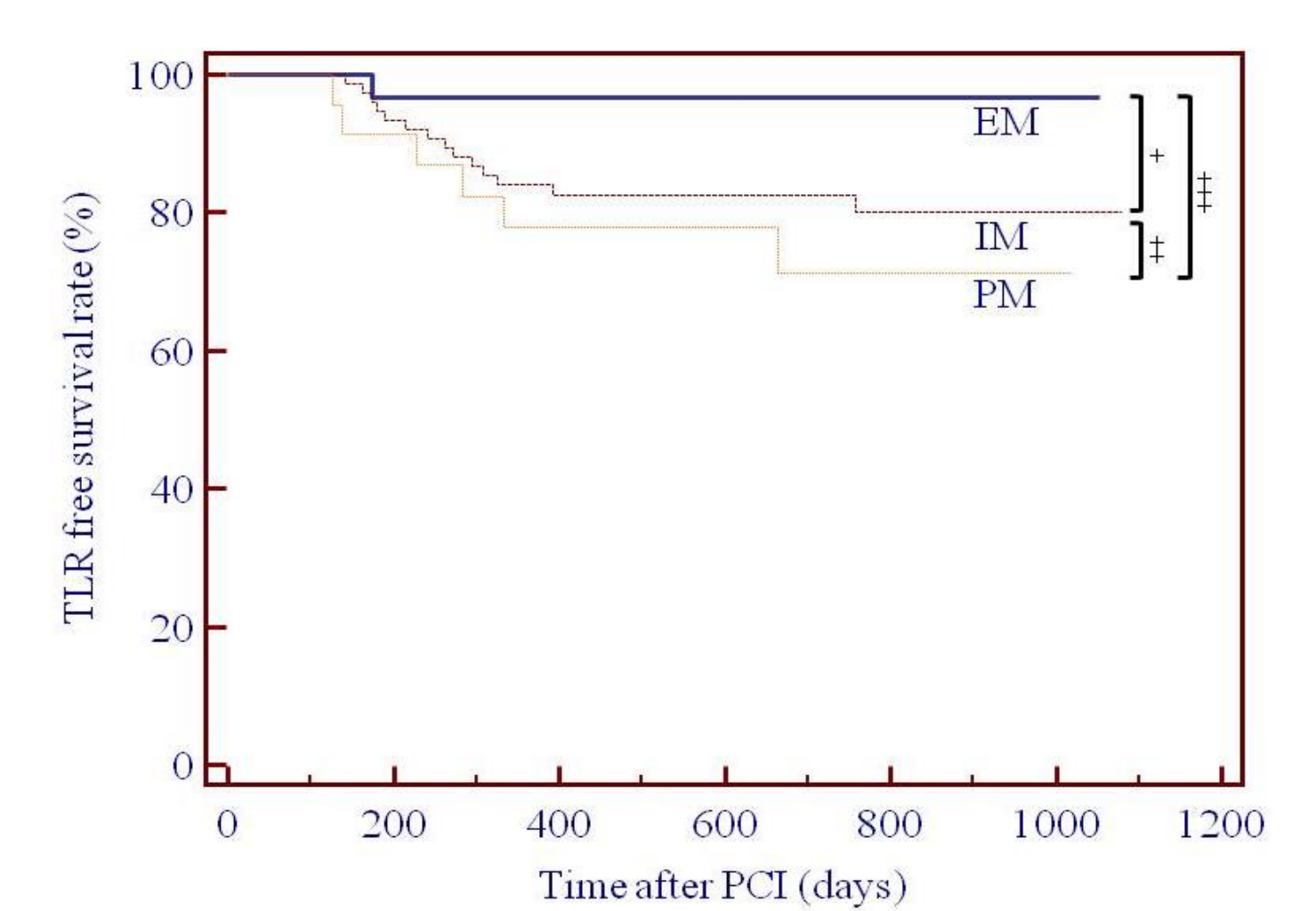
	EM (n=60)	IM (n=77)	PM (n=23)	P value
Death n(%)	1 (1.7)	2 (2.6)	2 (8.7)	0.34
Cardiac death (n)	0	2 (2.6)	0	
Myocardial infarction (n)	1 (1.7)	1 (1.3)	1 (4.3)	0.69
Target lesion revascularization (n)	2 (3.3)	14 (18.2)*	6 (26.1)**	0.008
Stent thrombosis	1 (1.7)	2 (2.6)	1 (4.3)	0.79
MACE	3 (5.0)	17 (22.1) +	7 (30.4) ++	0.005



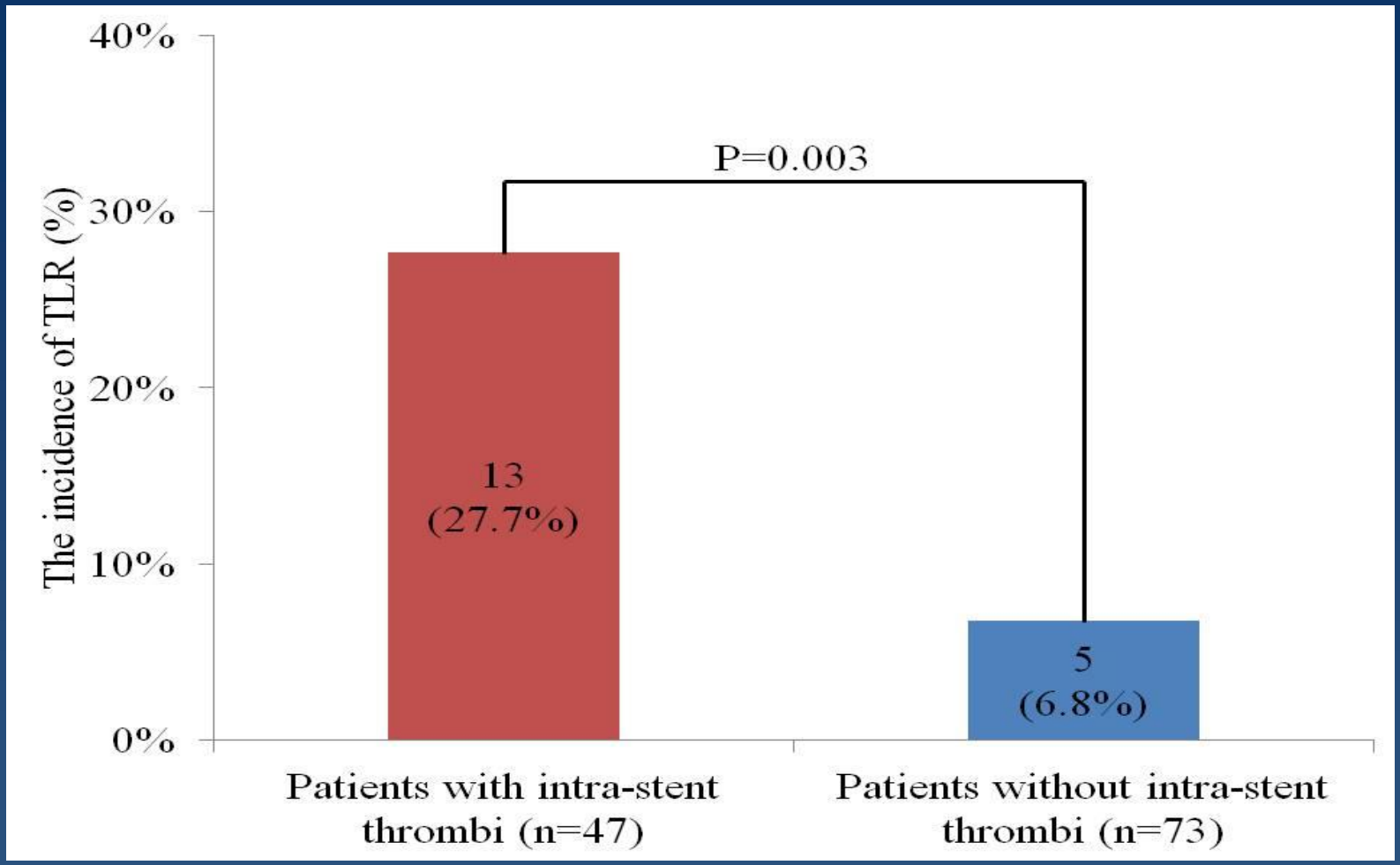
Intra-stent thrombi detecteed by OCT



Representative case of an intra-stent thrombus.



TLR free survival curve



The incidence of TLR in the patients with or without intra-stent thrombi

CYP2C19 loss of function polymorphism might be associated with intra-DES thrombus and restenosis.

Major factors for stent thrombosis

Incomplete neointimal Coverage.
Atypical neoitimal tissue
Endothelial dysfunction
Late acquired malapposition

Stent under-expansion
Stent malapposition
Stent edge dissection
etc.

Drug resistance
Discontinuation of antiplatelet therapy

We may be able to reduce DES thrombosis by IVUS or OCT guided optimal stenting, indication of New DES and effective antiplatelet therapy.


Thank you !
2010.11.02