How Do Stents and Scaffolds Fail: From Hypersensitivity to Neoatherosclerosis

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Potential conflict of interest

Speaker's name: Michael Joner, MD

☑ I have the following potential conflicts of interest to report:

Consultant: Biotronik

Employment in industry: No

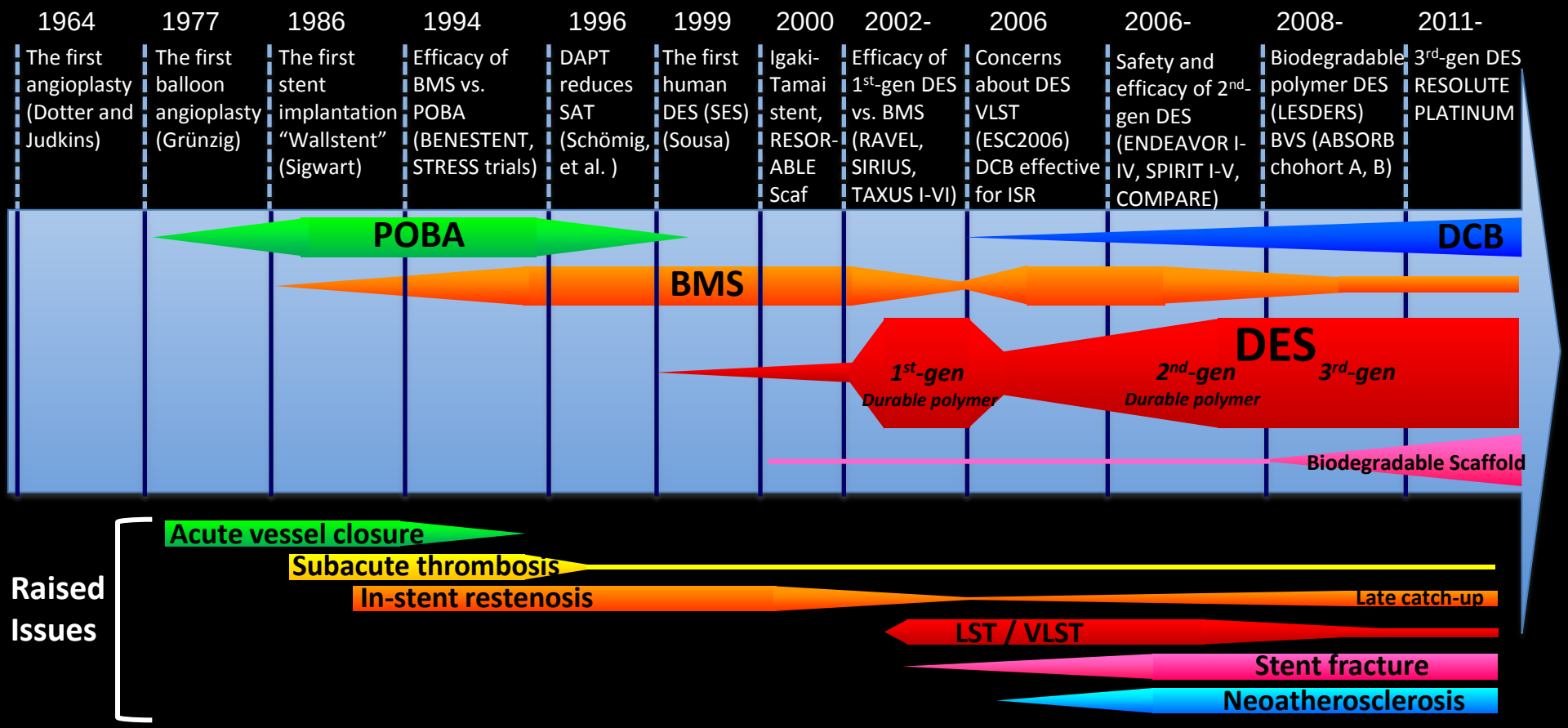
Honorarium: Orbus Neich, Biotronik

Institutional grant/research support: 480 Biomedical, Abbott Vascular, Atrium, BioSensors International, Biotronik, Boston Scientific, Cordis J&J, GSK, Kona, *CeloNova* Medtronic, MicroPort Medical, OrbusNeich Medical, ReCore, SINO, Stentys Medical Technology, Terumo Corporation, and W.L. Gore.

Owner of a healthcare company: No

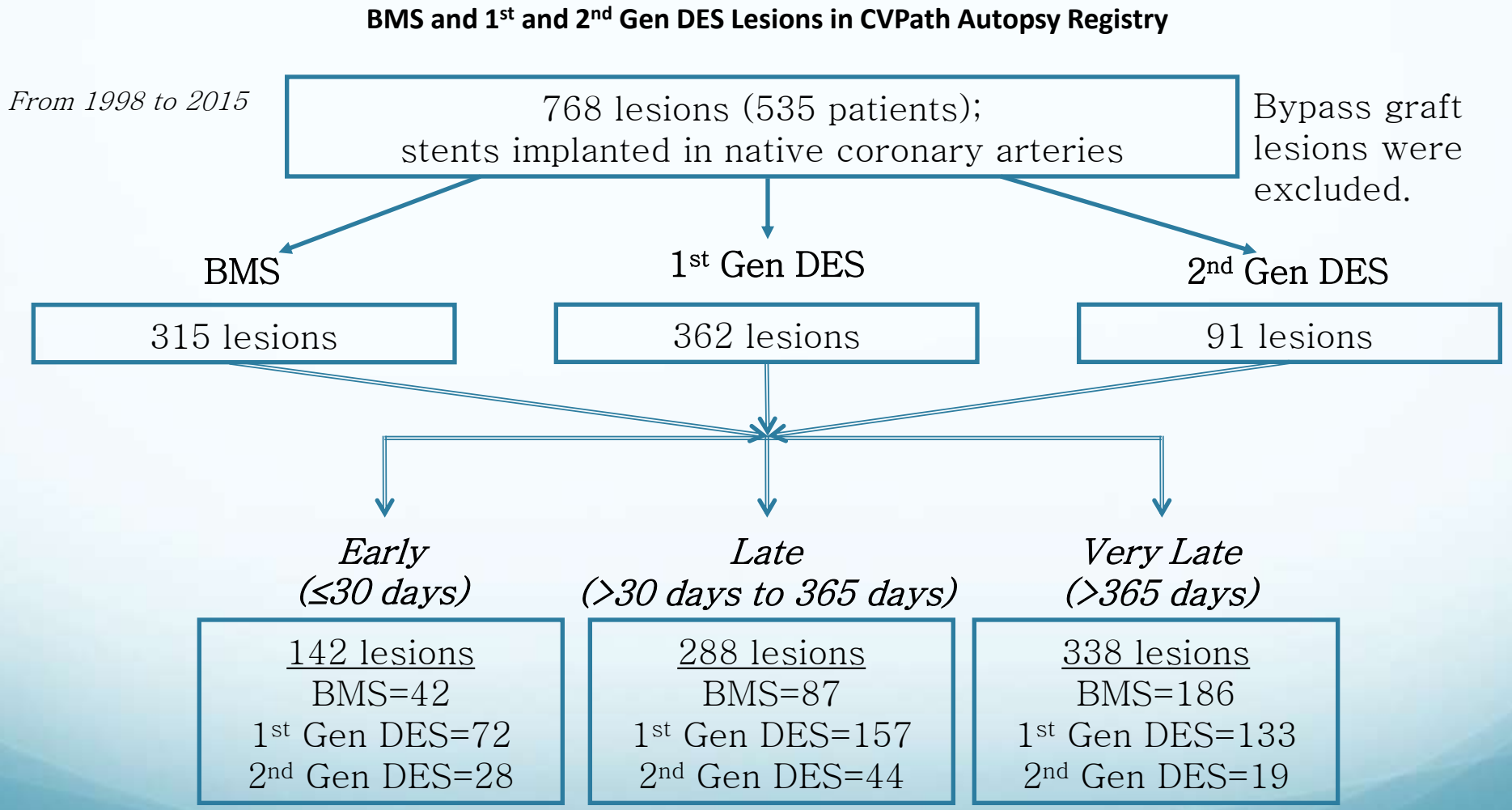
Stockholder of a healthcare company: No

History of Percutaneous Coronary Intervention



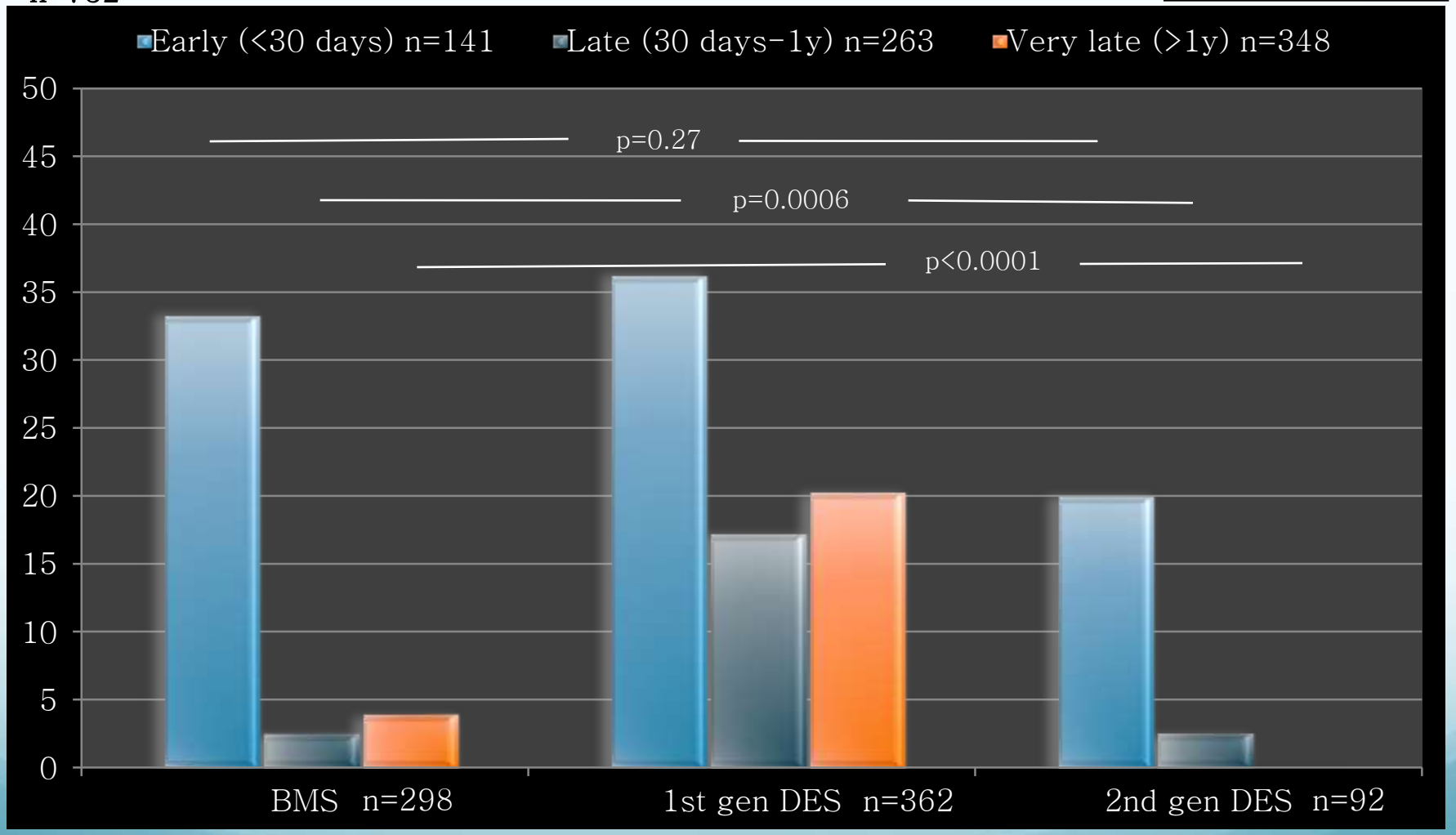
	Balloon Angioplasty	BMS	DES
Success rate	70-85%	>95%	>95%
Restenosis	40-45%	20-30%	<10%
Early Thrombosis (≤30 days)	3-5%	1-2%	1-2%
Late Thrombosis (>30 days, ≤1y)	NA	<0.5%	1%
Very Late Thrombosis (>1y)	NA	≈0%	1-2%

CVPath Stent Registry

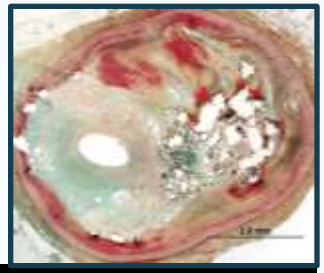


Stent Thrombosis
Lesion-based Analysis

n=752



Restenosis
Lesion-based Analysis



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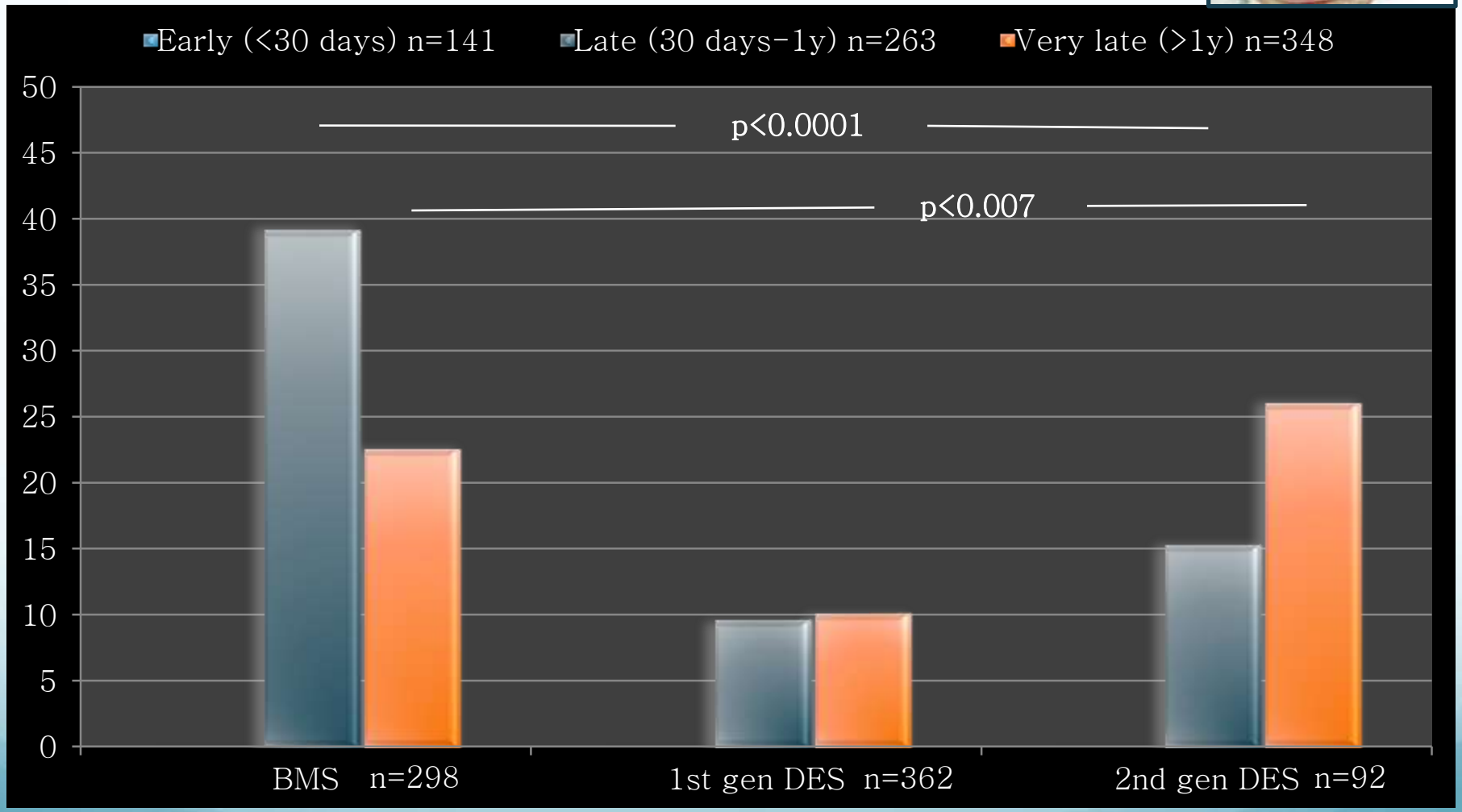
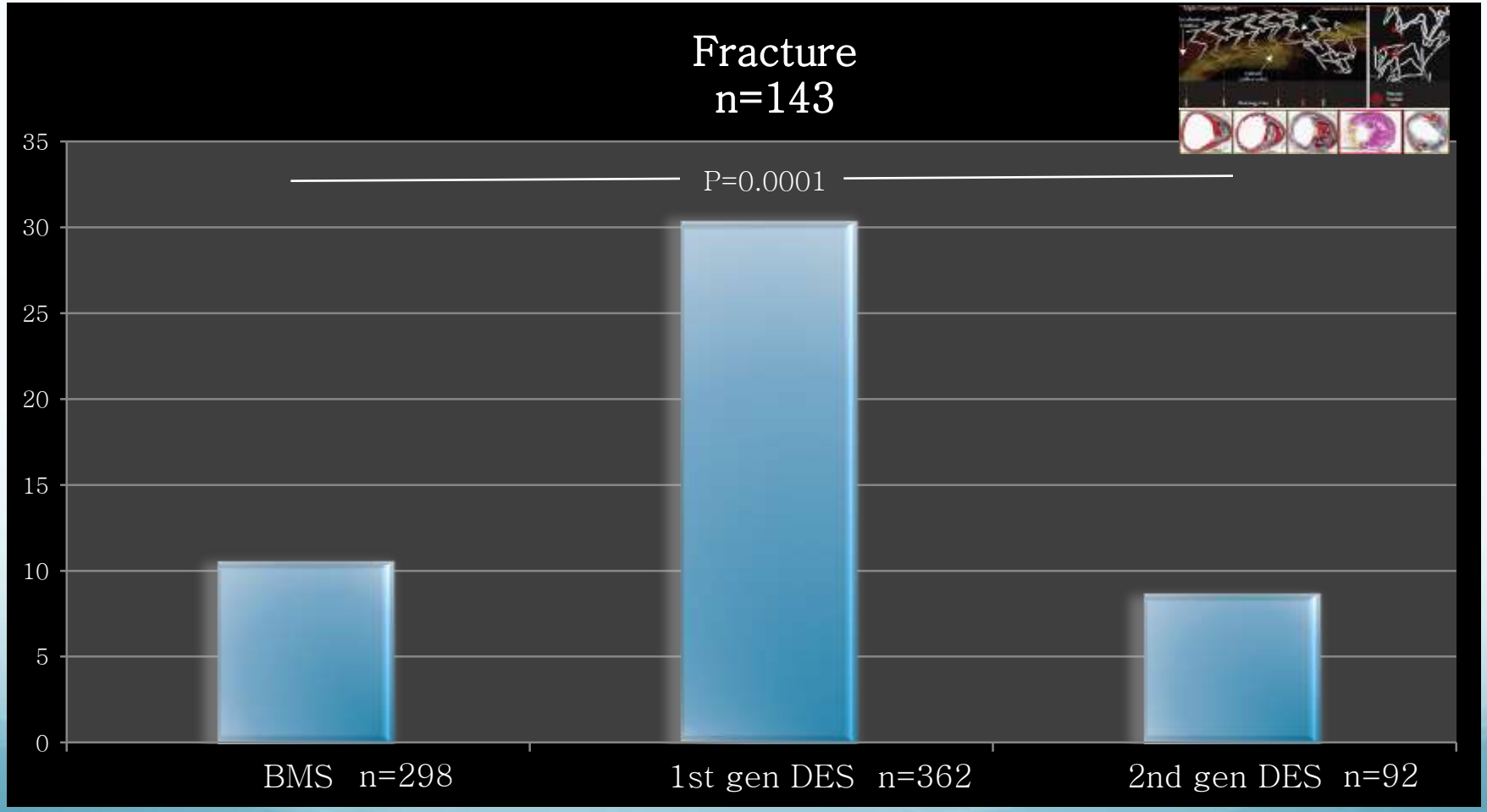


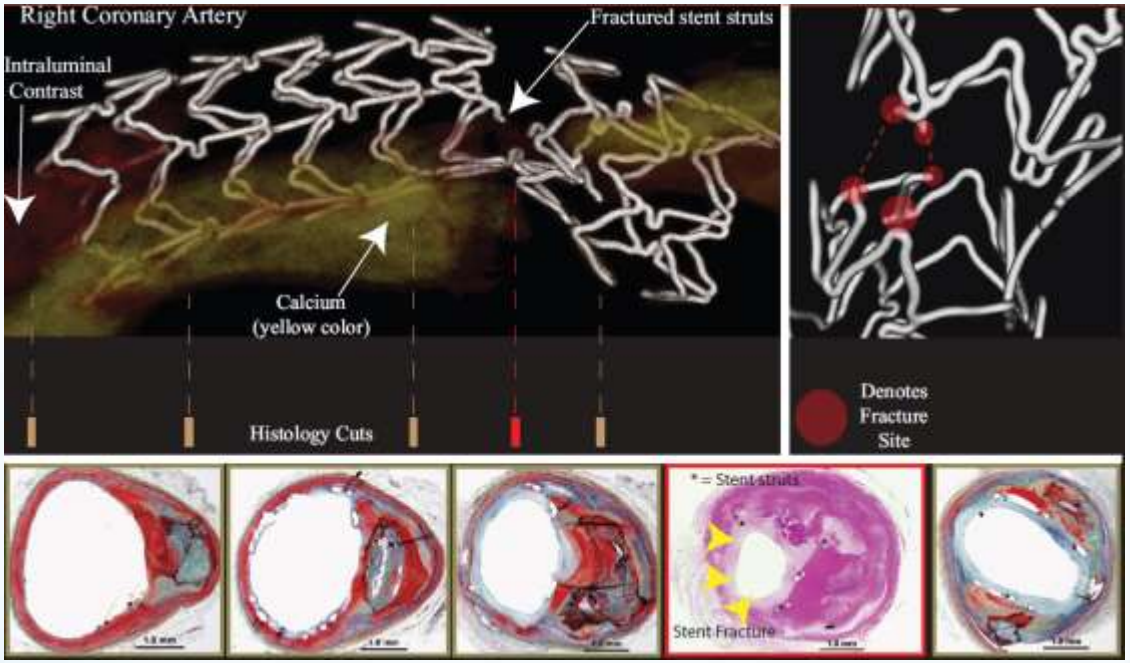
Stent Fracture
Lesion-based Analysis

n=752

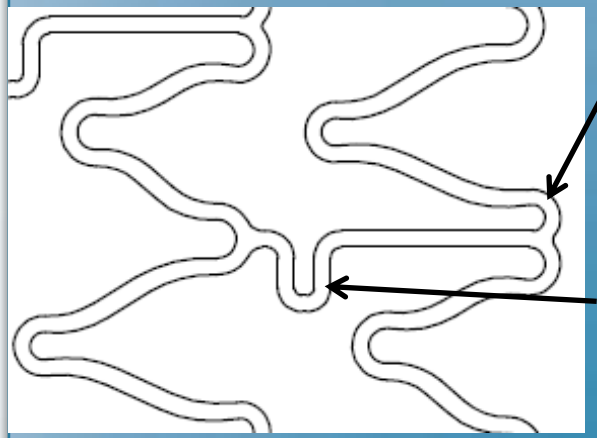


Xience V™ Restenosis Associated with Stent Fracture

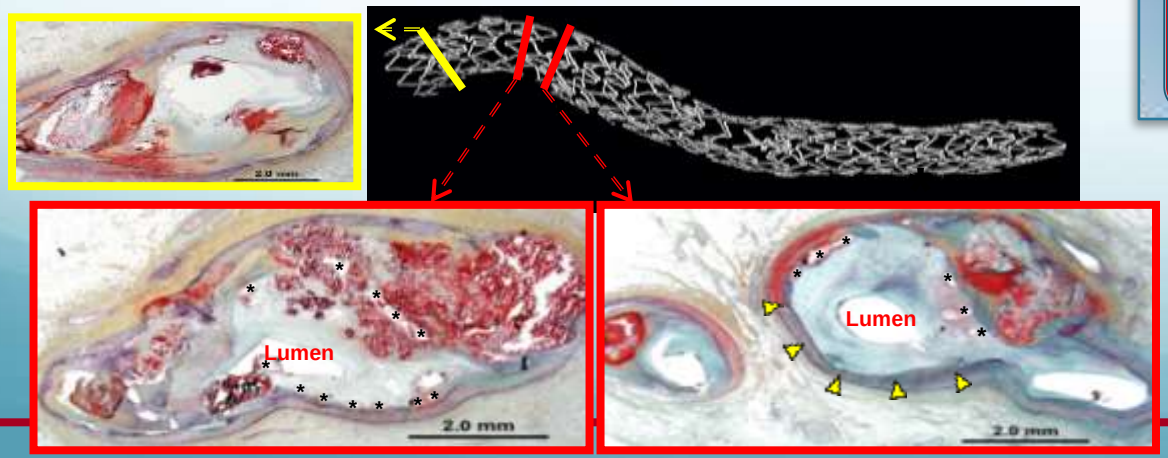
70-year-old woman, CoCr-EES implanted in RCA for 6 months



Cumulative Fracture Map of Clinical Xience V™ Stent Fractures from Autopsy



20 Total Fracture Sites in 6 Lesions (8 Xience V Stents)



Foerst JR, et al. J Am Coll Cardiol Intv 2012;5:239-42.
Otsuka F, et al. Circulation. 2014;129:211-223.

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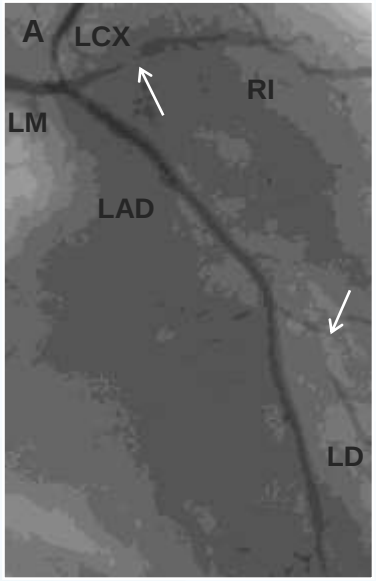
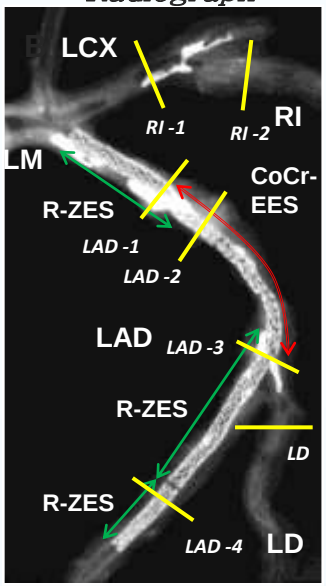
Hypersensitivity Reaction in 2nd Generation DES

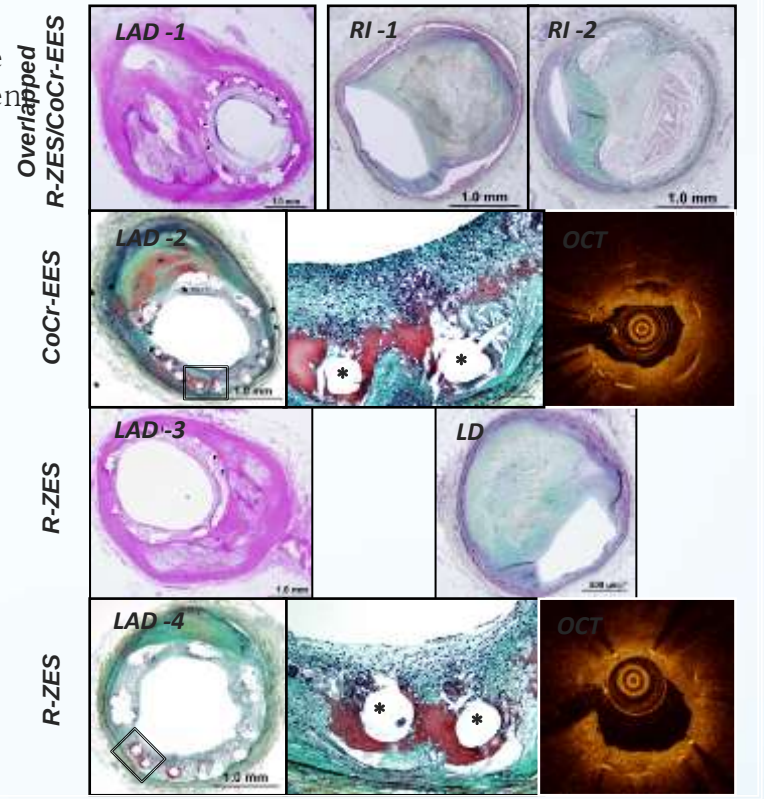
A 55-year old male who presented with unstable angina secondary to diffuse disease in the LAD; four stents implanted (3 R-ZES and a single CoCr-EES. At 238-days following implantation of the 4 stents the patient died suddenly.

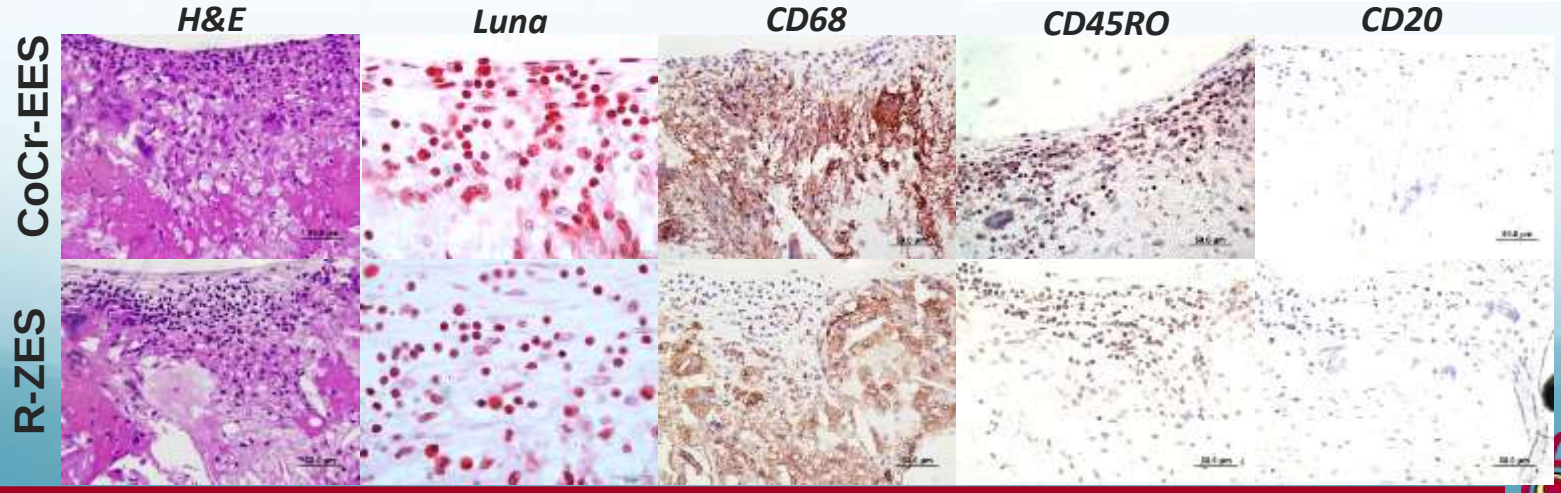
Coronary angiograph



Radiograph







Otsuka et al., Circulation. 2015 Jan 20;131(3):322-4

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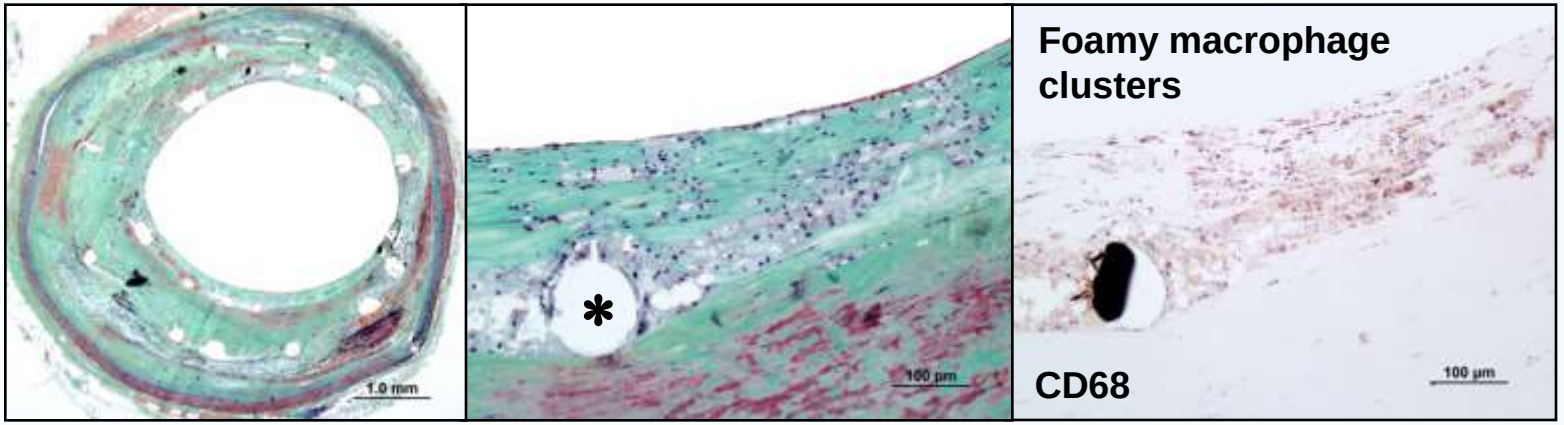
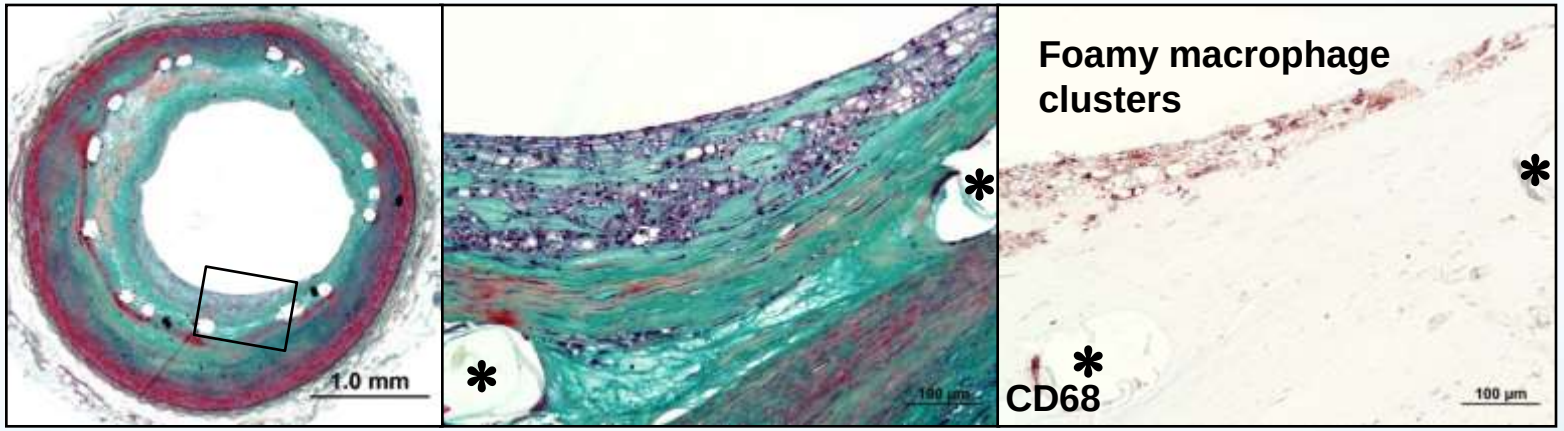
In-Stent Neoatherosclerosis: A New Disease Manifestation with Impact on Stent Failure?

Neoatherosclerosis in the 2nd-generation DES

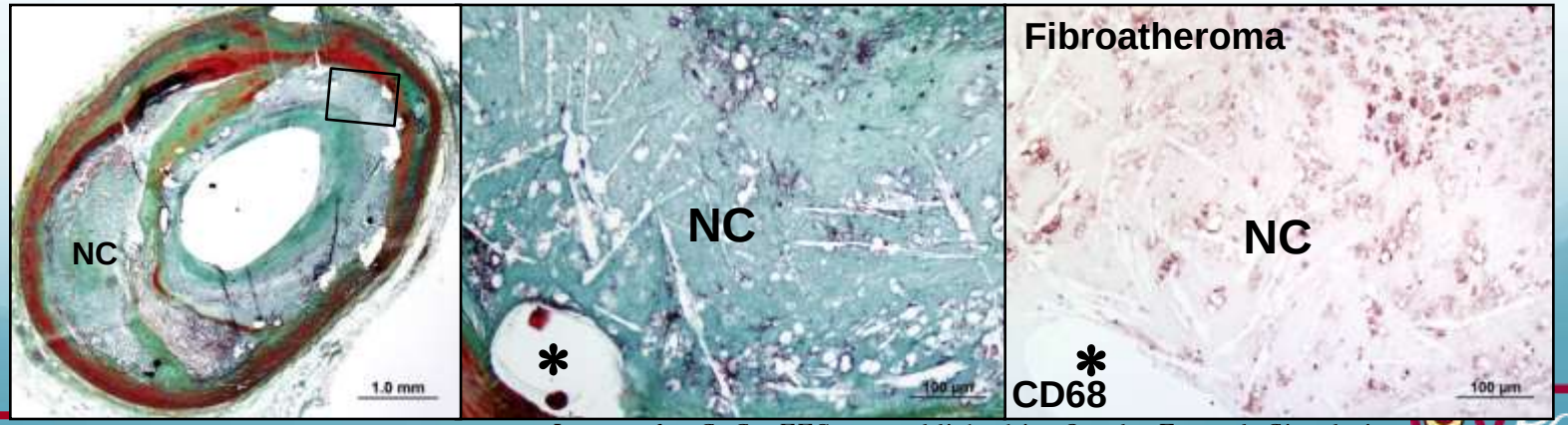
R-ZES 12M



CoCr-EES 24M

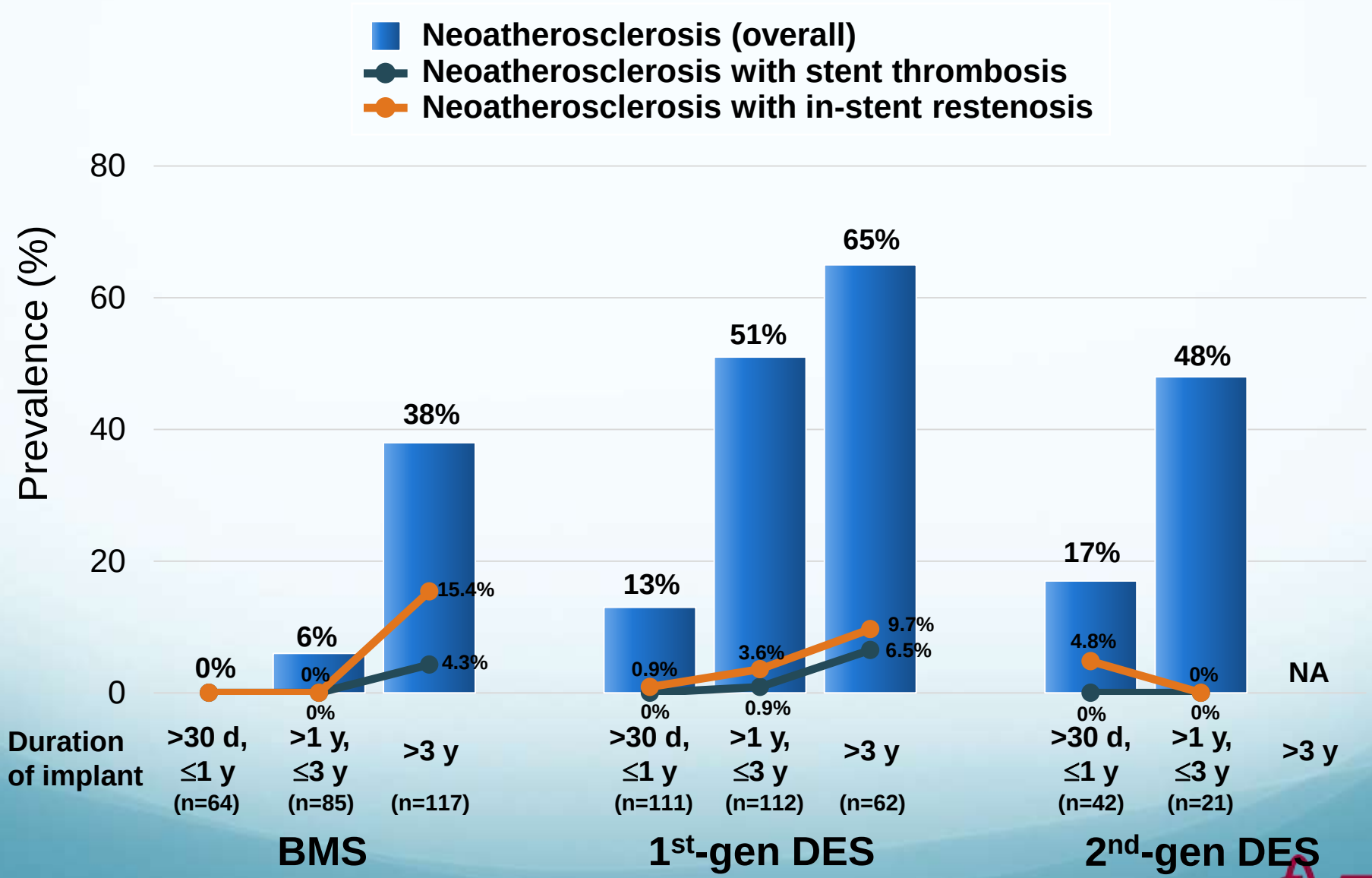


CoCr-EES 36M



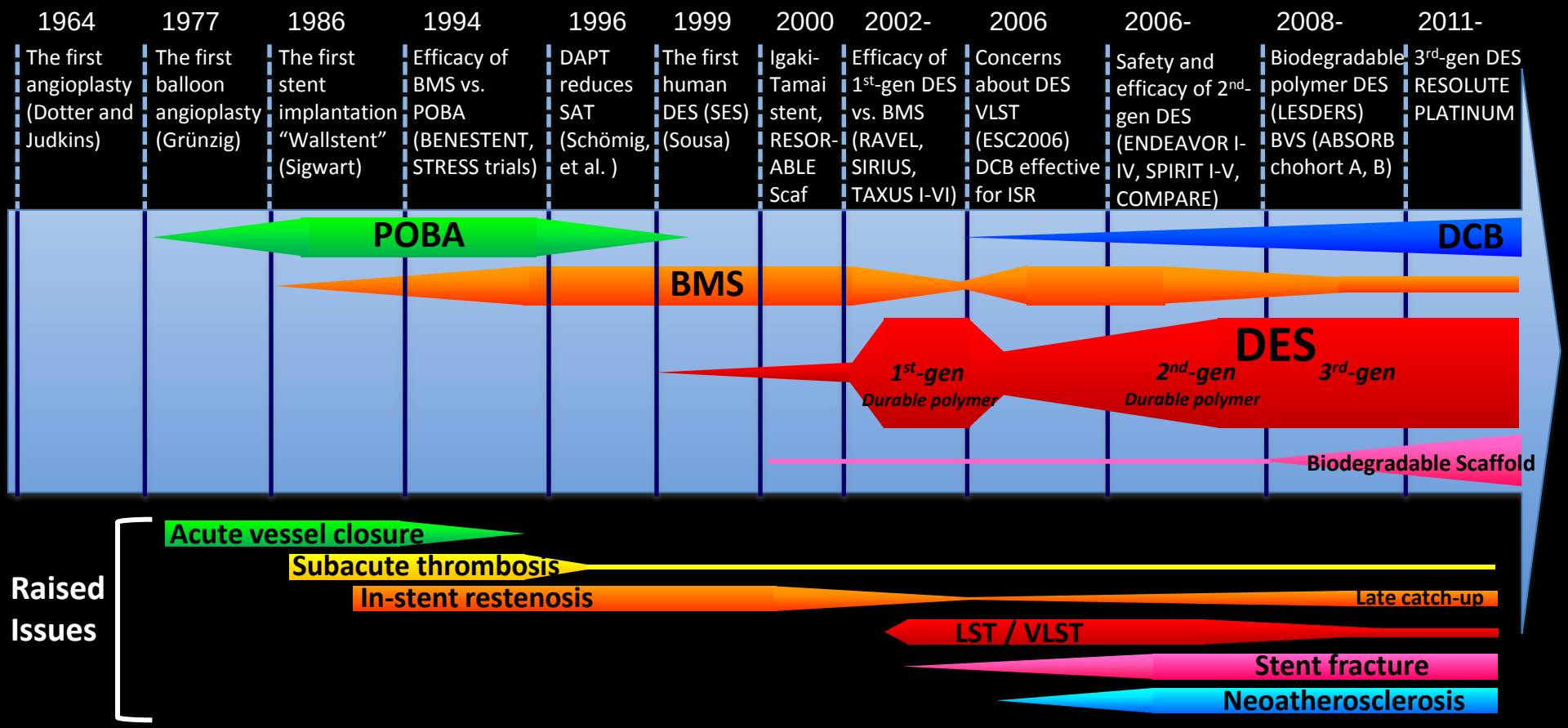
Images for CoCr-EES are published in: Otsuka F, et al. Circulation 2014;129:211-223

Prevalence of Neoatherosclerosis: Overall, with Stent Thrombosis, and with Restenosis



Otsuka et al., European Heart Journal May 2015, ahead of print

History of Percutaneous Coronary Intervention



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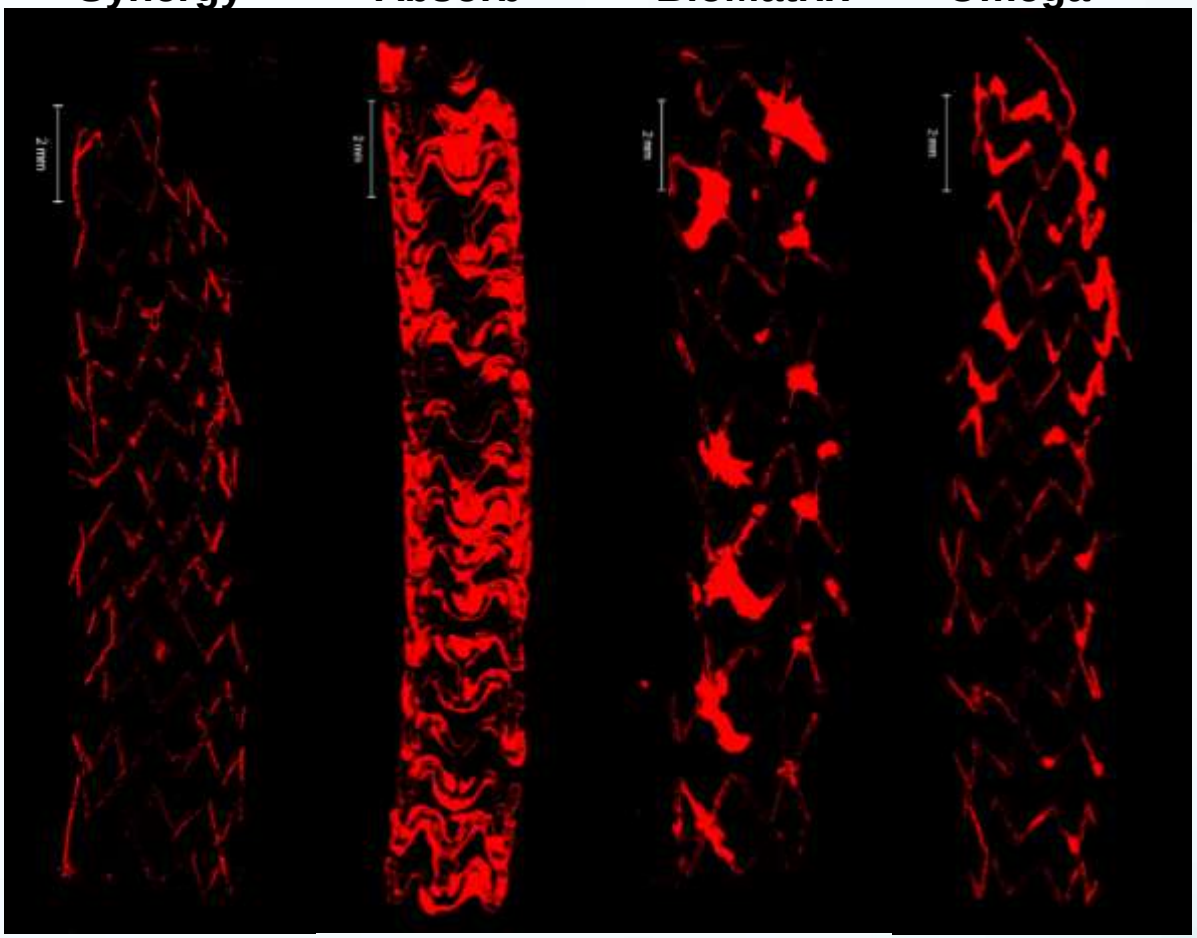
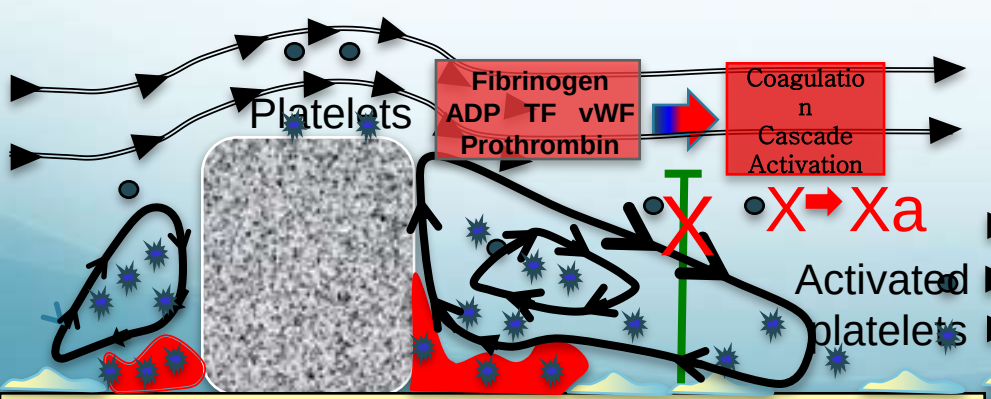
Putative Failure Modes of BRS

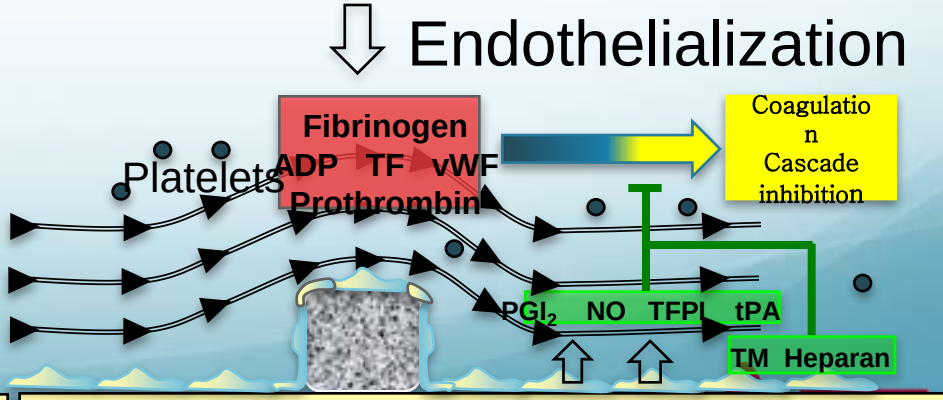
The **two** clinical manifestations of stent failure are:
in-stent restenosis (resulting in angina, ACS) **and stent thrombosis** (sudden cardiac death or ACS)

- Increased thrombogenicity in the acute phase of implantation
- Delayed endothelialization of stent struts
- Loss of radial strength and recoil resulting in collapse and luminal compromise
- Late acquired malapposition and/or evaginations secondary to dismantling/fracture
- Inflammatory responses (acute and chronic) with potential for aneurysm formation

Platelet Deposition in one half of stent following immuno-fluoroscent staining (CD61/CD42b) viewed by Confocal Microscopy in Porcine ex-vivo Arterio-Venous Shunt Model.



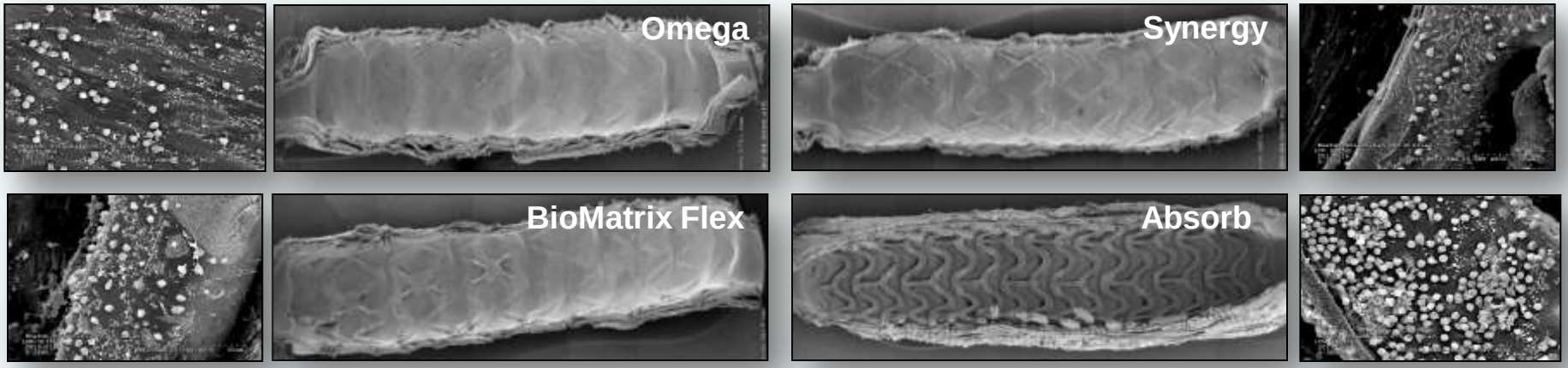


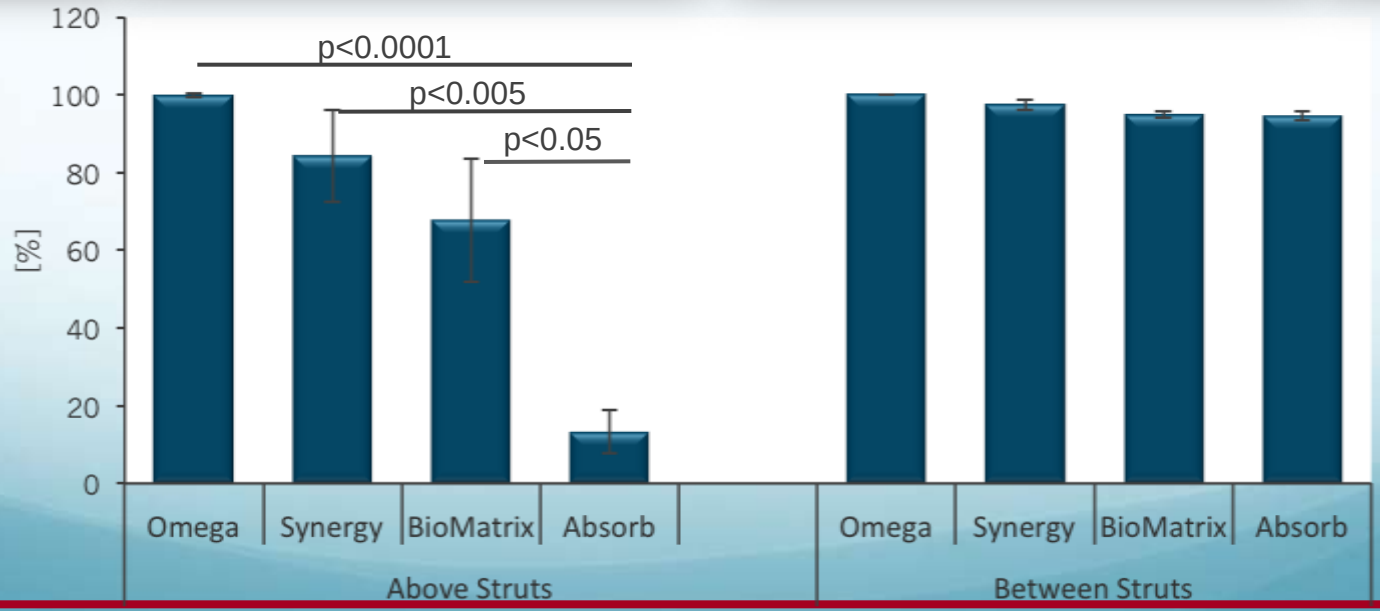


Nonstreamline strut Atherosclerotic lesion

Streamline strut Healed" atherosclerotic les

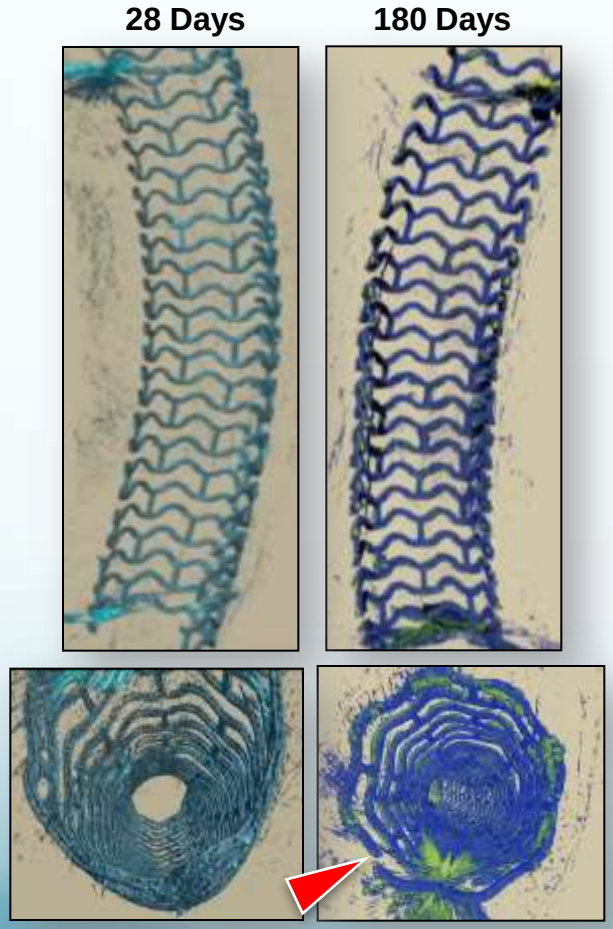
Endothelialization Among Contemporary DES and BRS in Rabbits at 28 Days by SEM





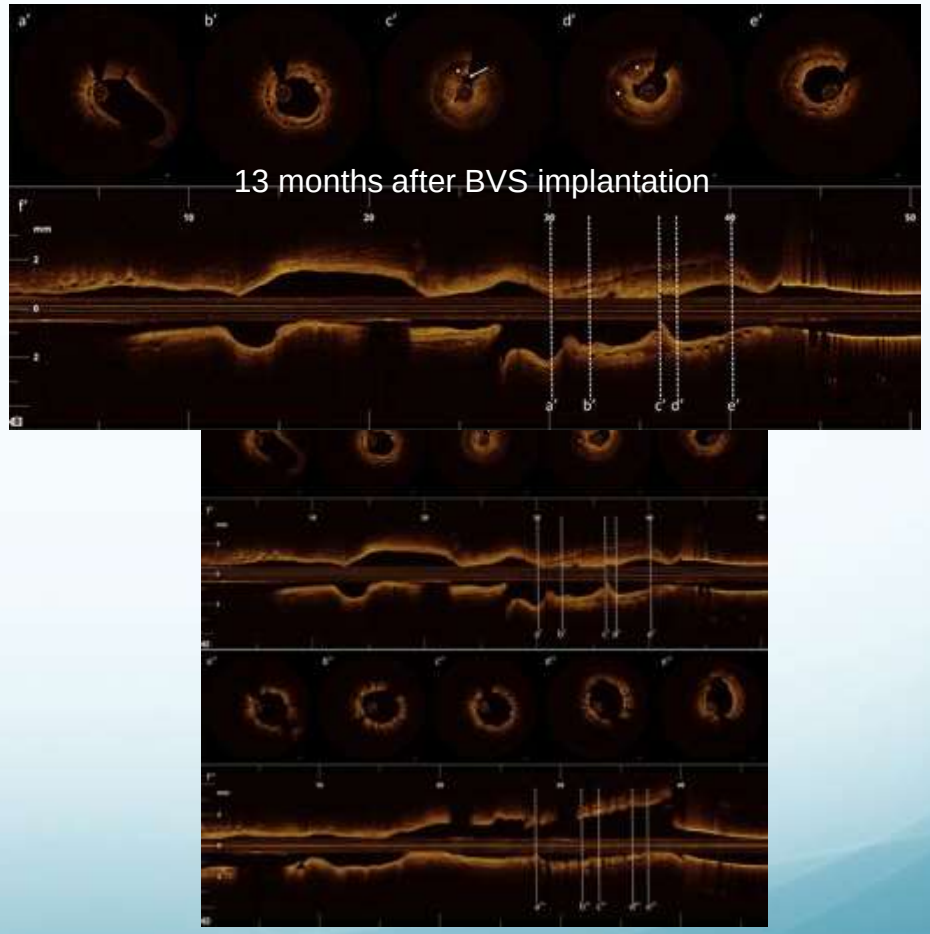
Micro-CT and OCT: Detect Strut Fractures and Signs of Dismantling in Preclinical and Clinical Application of BRS Technology

Preclinical



Beginning dismantling of stent struts at 180 days

Clinical



Focal strut fracture after implantation resulting in focal restenosis

Gargiulo et al., *Am Coll Cardiol Intv*. 2015;8(6):e95-e97. doi:10.1016/j.jcin.2014.12.236

OCT Findings of BRS Thrombosis

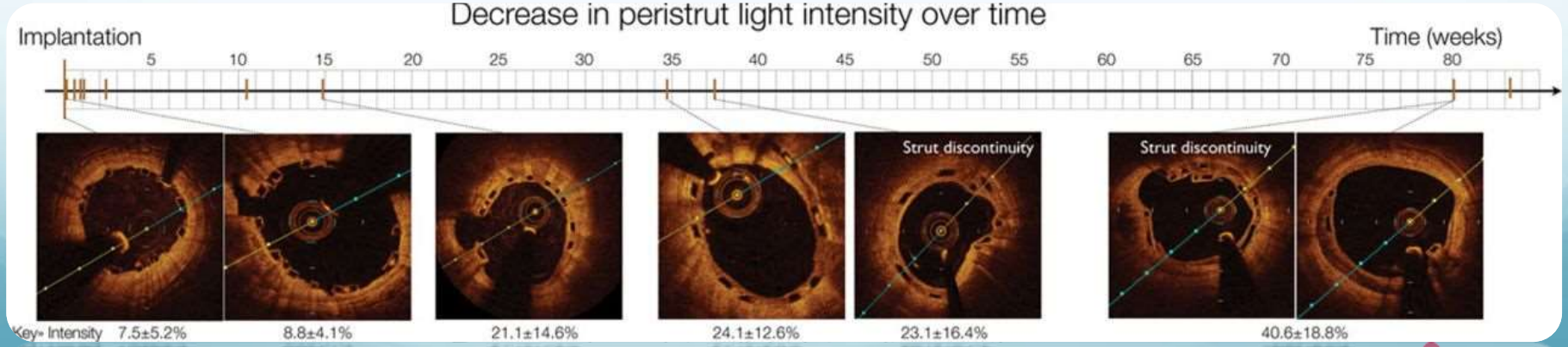
Qualitative OCT Findings in 15 Clinical Cases:

Acute: **8** cases (3 acute, 5 subacute)
- Procedural factors (underexpansion, undersizing, geographical miss) in **27%**
- Insufficient anti-platelet treatment in **13%**
- No obvious cause in **13%**

Late/Very Late: **7** cases (5 late, 2 very late)
- Neovascularization/PSLIA in **33%**
- Scaffold fracture in **13%**
- Scaffold collapse in **7%**
- Extensive malapposition in **7%**
- No obvious cause in **7%**

ID No.	OCT Runs	Failed or Very Poor Quality OCT Runs (Reasons)	Percentage of Good Quality on Analyzed OCT Runs(s)	Reason for Poor Quality	OCT at End of Procedure	Percentage of Good Quality OCT After Treatment	Residual Thrombus Burden, mm²	Final Treatment
1	2	1 (poor flushing)	73%	Backscattering/ attenuation because of thrombus	No			Thrombus aspiration, PTCA with NC 3.0
2	1	0	100%	None	No			PTCA with NC 3.0, implantation of another BVS proximal to the first one
3	2	0	81%	Backscattering/ attenuation because of thrombus	Yes	100%	14.13	PTCA with NC 3.0, implantation of a Xience 3.0
4	3	1 (poor flushing and occlusive thrombus)	71%	Backscattering/ attenuation because of thrombus	No			PTCA with Maverick 1.5 ≤2.5, NC 3.0,
5	3	1 (occlusive thrombus)	66%	Backscattering/ attenuation because of thrombus	Yes	100%	4.93	Thrombectomy, direct stenting with DES
6	2	0	75%	Poor flushing in proximal part of BMS	Yes	100%	2.24	PTCA, DES
7	2	1 (poor flushing)	83%	Backscattering/ attenuation because of thrombus	No			PTCA with 2.75 SC, OCT, 2× implantation Xience 2.75
8	1	0	75%	Backscattering/ attenuation because of thrombus in distal scaffold	No			PTCA, DES
9	4	1 (poor flushing)	100%	None	Yes	90% (poor flushing	3.51	PTCA, DES
10	2	0	93%	Backscattering/ attenuation because of thrombus	No			PTCA without stent
11	4	0	73%	Backscattering/ attenuation because of thrombus	Yes	95% (poor flushing	15.53	PTCA, DES
12	3	0	82%	Backscattering/ attenuation because of thrombus	No			Thrombectomy, DES (XIENCE) implantation with pre- and postdilation
13	1	0	98%	Poor flushing and catheter partly in false lumen	No			Thrombus aspiration, PTCA with NC 3.5 and implantation of a BVS 3.5 mm directly proximal to the BMS
14	1	1 (occlusive thrombus)	83%	Backscattering/ attenuation because of thrombus	Yes	90% (poor flushing)	2.57	Thrombus aspiration, PTCA with NC 3.5, Xience 3.5
15	1	0	92%	Backscattering/ attenuation because of thrombus	No			No intervention

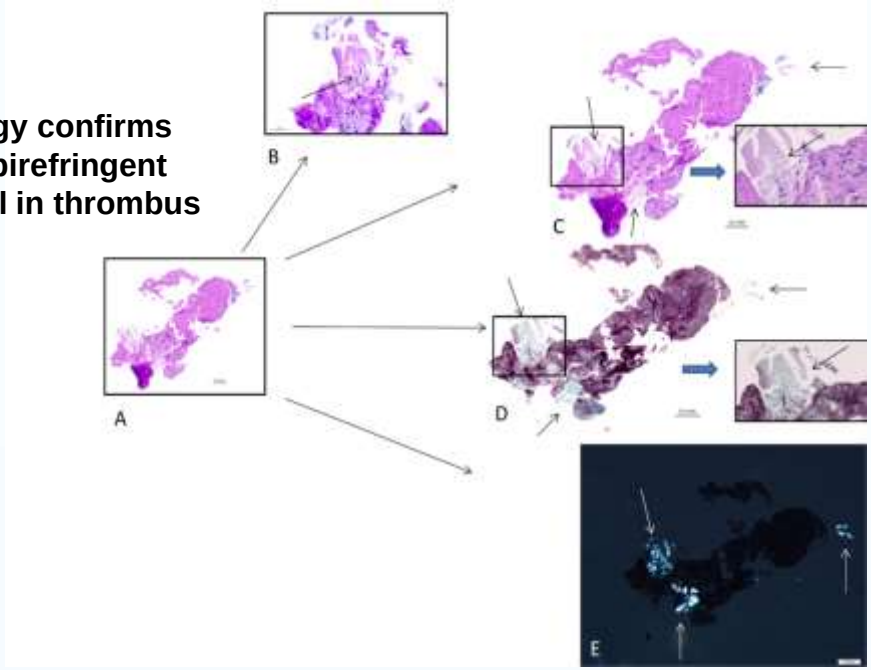
BVS indicates bioresorbable vascular scaffold; DES, drug-eluting stent; NC, noncompliant; OCT, optical coherence tomography; and PTCA, percutaneous transluminal coronary angioplasty.



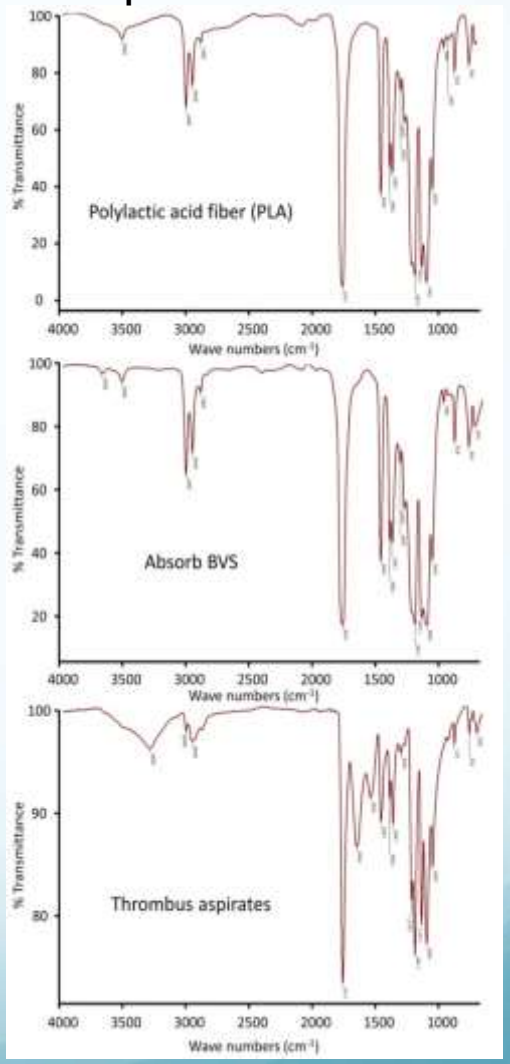
Florim Cuculi et al. Circ Cardiovasc Interv. 2015;8:e002518

Presence of Residual Absorb Scaffold Fragments after 44 months of Implantation

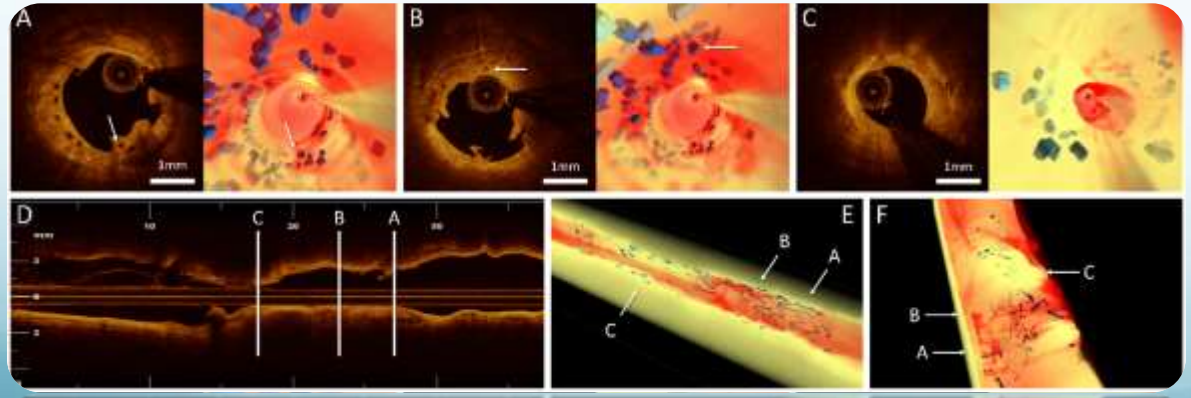
Histopathology confirms presence of birefringent foreign material in thrombus



Spectroscopic analysis confirms presence of PLLA



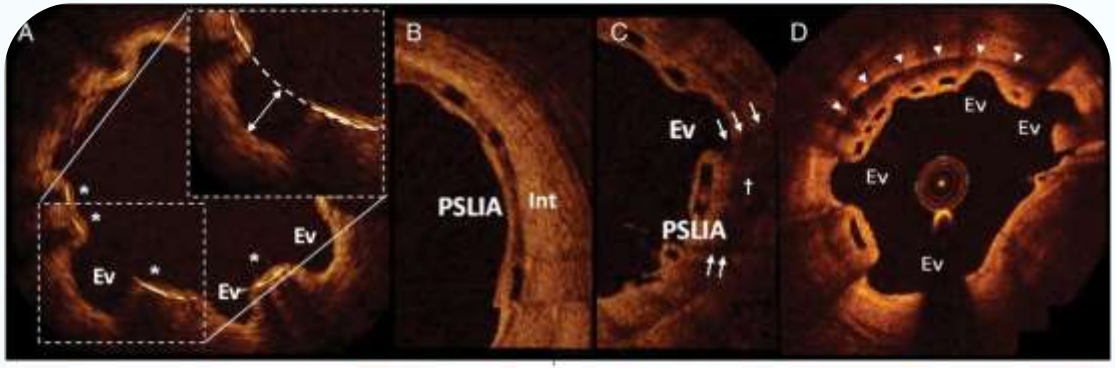
OCT shows signs of strut malapposition, likely a result of strut degradation

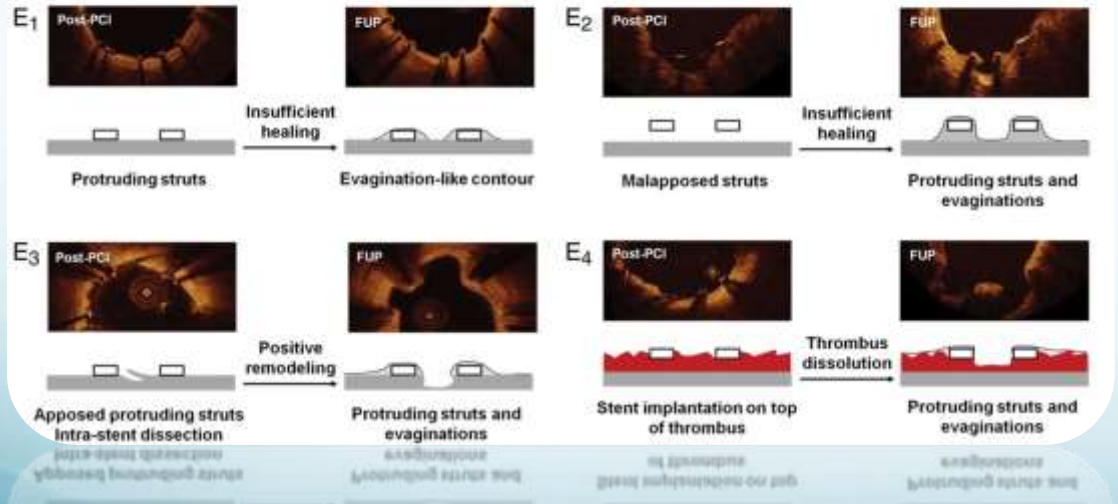


Räber et al., J Am Coll Cardiol. 2015 Oct 27;66(17):1901-14. doi: 10.1016/j.jacc.2015.08.853

Peri-strut Evaginations –

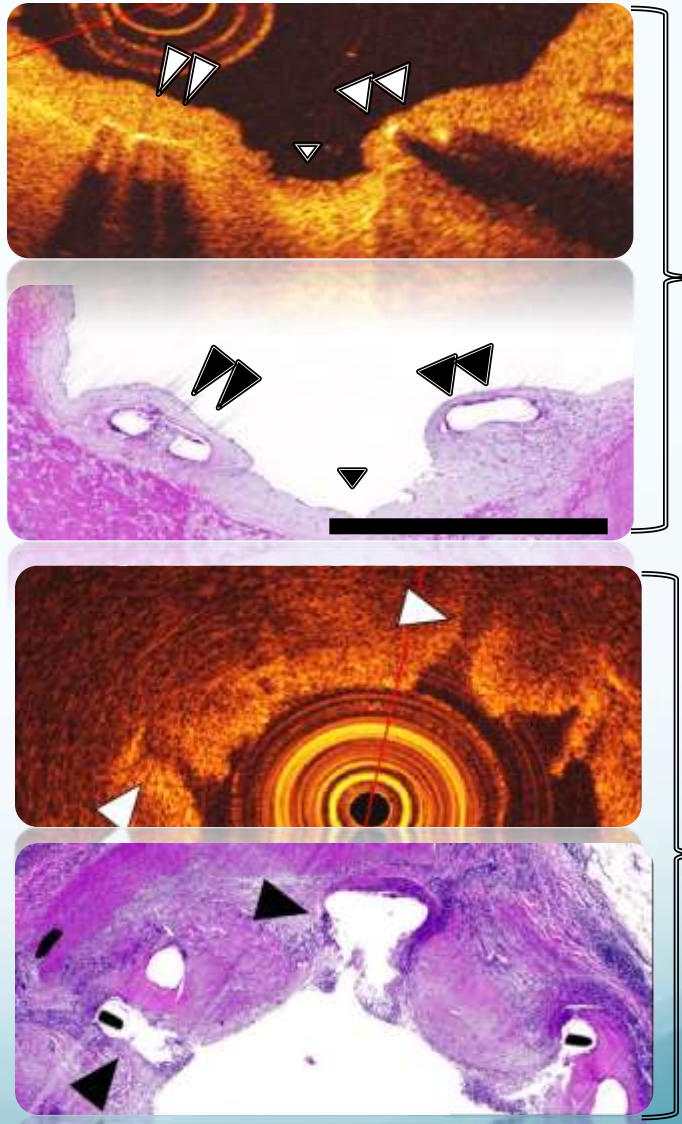
a Potential Failure Mechanism of BRS ?
Or
Artificial Dilatation of the Arterial Wall During Image Acquisition





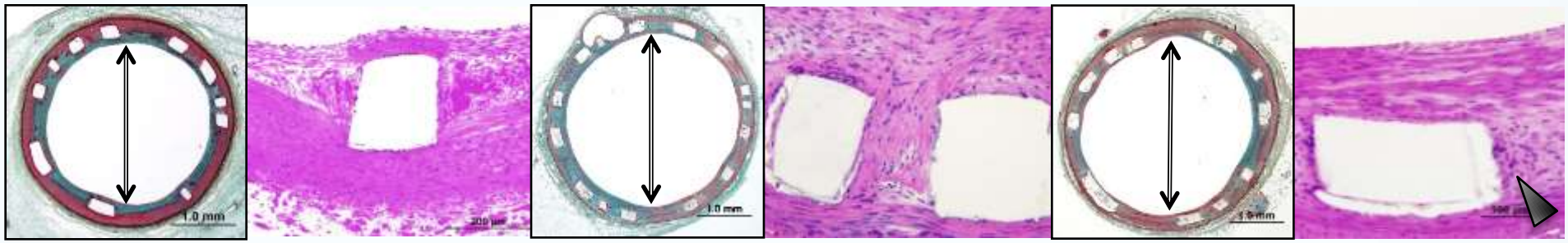
Malapposition may be substantially overrated secondary to artificial arterial wall dilatation

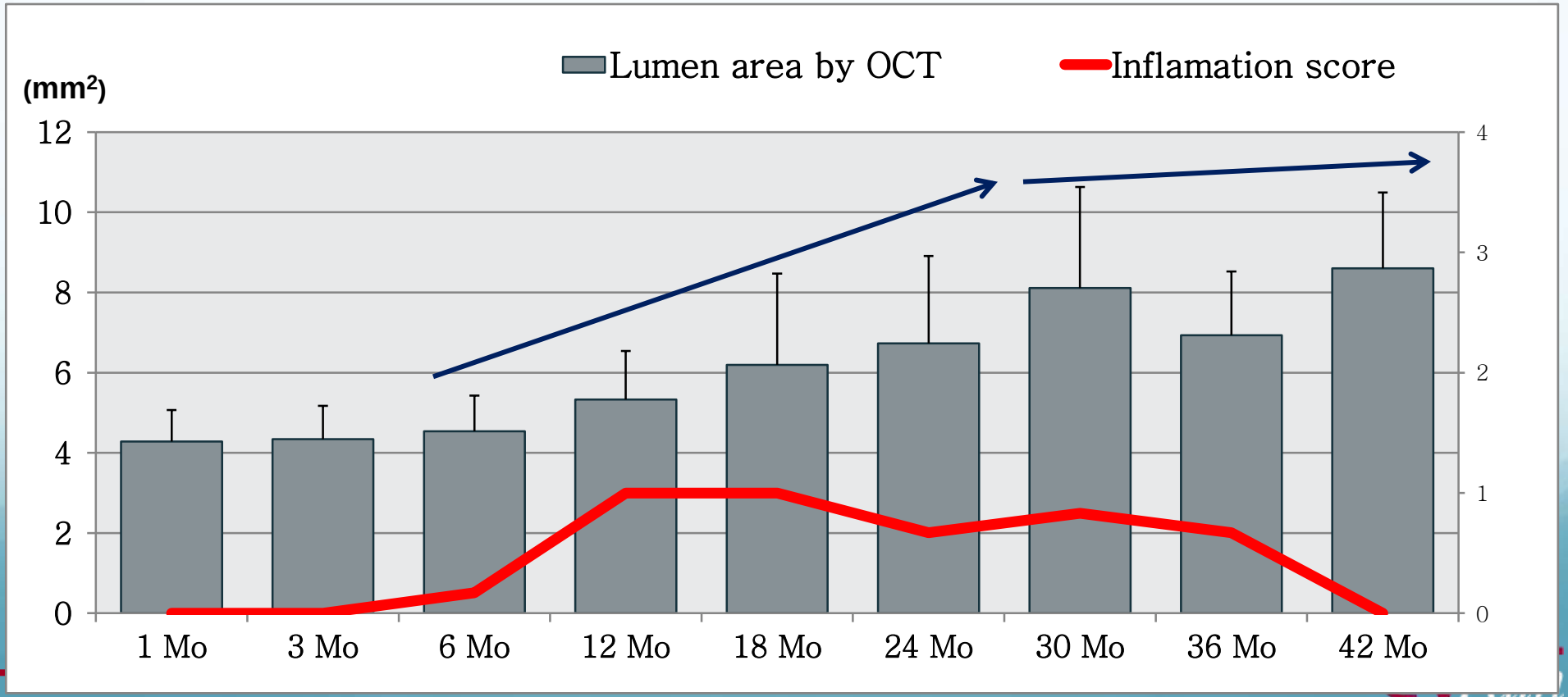
Differential Diagnosis of Evaginations



Association Between Inflammation and Lumen Area in BVS

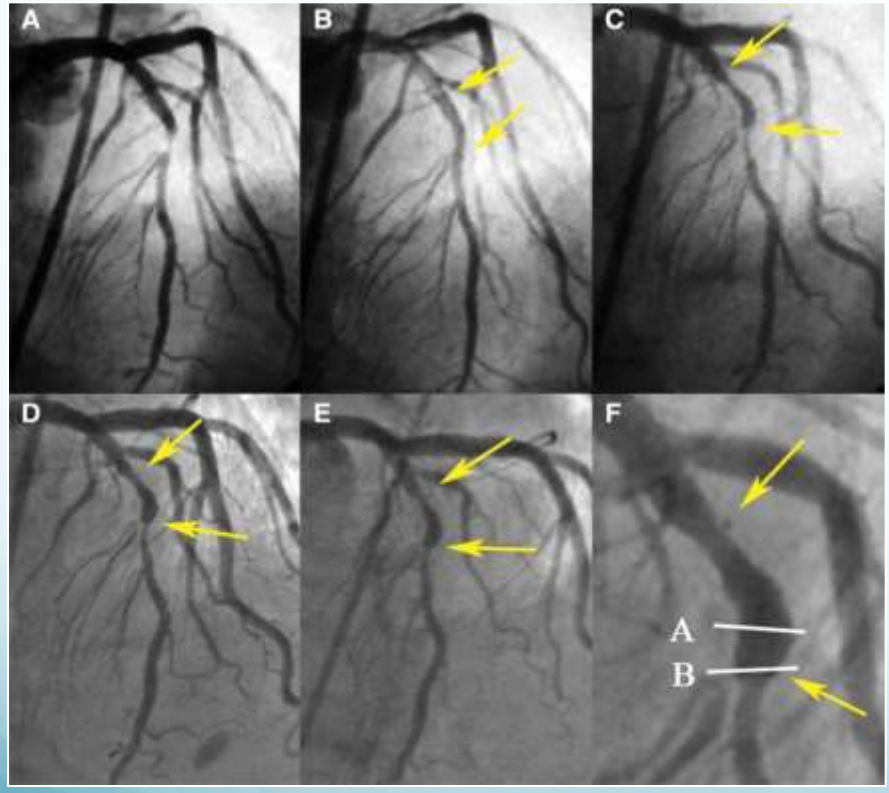
Absorb



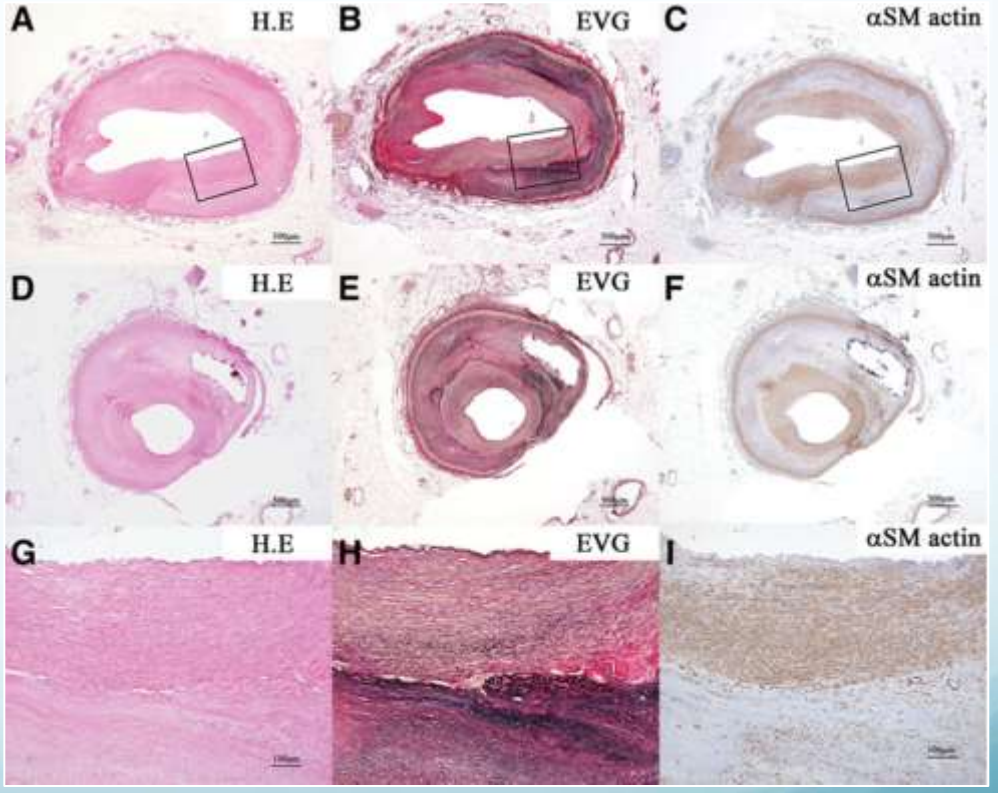


Igaki-Tamai Stent in Proximal LAD after 12 Years

Coronary angiography of the left anterior descending coronary artery (LAD)



Cross-sectional histology of the left anterior descending coronary artery (LAD) at the site where an Igaki-Tamai stent had been implanted



Soji Nishio et al. Circulation. 2014;129:534-535

Summary

Stent failure modes of first generation DES are:

- Early (acute/subacute): **incomplete apposition**, **medial tear** and **penetration of struts into necrotic core**
- Late/very late: **delayed arterial healing resulting in thrombosis, strut fracture, inflammation and hypersensitivity**
- Second generation DES substantially improved this balance with more biocompatible polymers and reduced drug load; however, **inflammation** remains a concern in second generation DES
- **Neoatherosclerosis** is a new disease manifestation of atherosclerosis and plays an important role in late stent failure
- Bioresorbable scaffolds represent a disruptive technology with great potential for vascular restoration

Scaffold failure modes have been identified:

- Early: **underexpansion, undersizing, geographical miss**
- Late/very late: **Neovascularization/inflammation (PSLIA), fracture (collapse), while the impact of evaginations (malapposition) remains to be determined**