Rationale for BRS in Vulnerable Plaque

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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

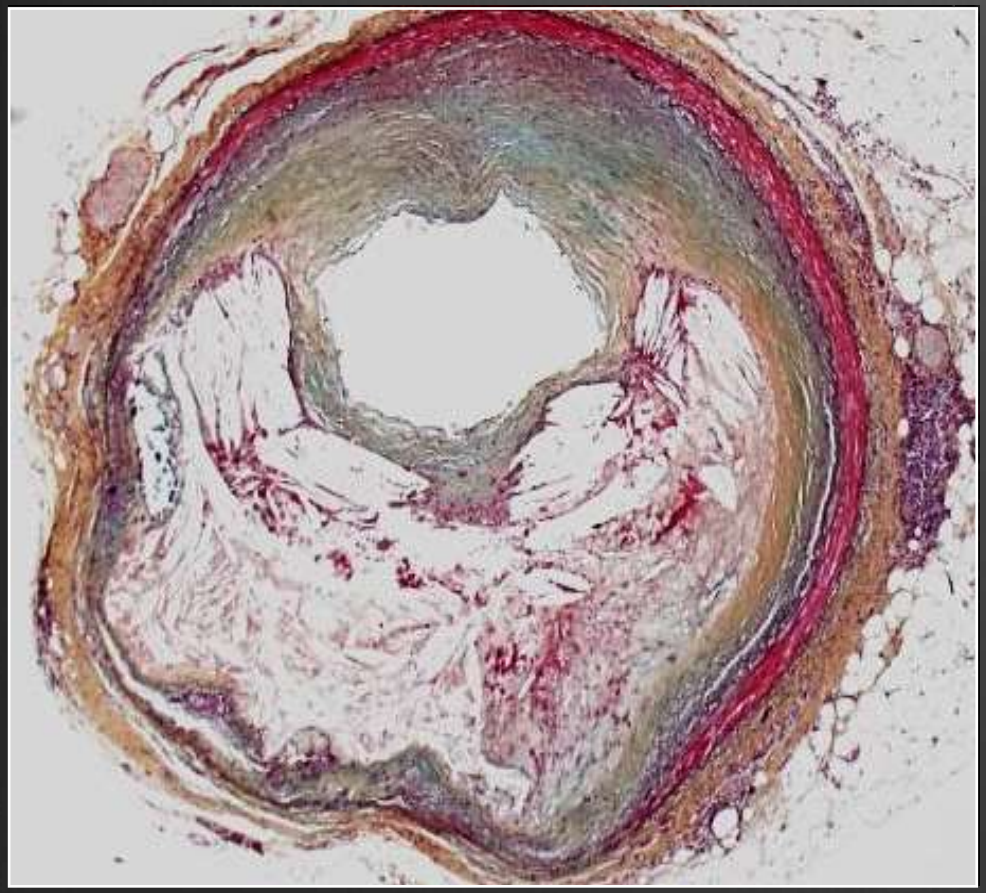
Institutional grant/research support: 480 Biomedical, Abbott Vascular, Atrium, BioSensors International, Biotronik, Boston Scientific, Cordis J&J, GSK, Kona, *CeloNova* Medtronic, MicroPort Medical, OrbusNeich Medical, ReCore, SINO, Stentys Medical Technology, Terumo Corporation, and W.L. Gore.

Owner of a healthcare company: No

Stockholder of a healthcare company: No

Hoping to Achieve Plaque Sealing Using BRS Technology !!!!

Identify patients with VP using non-invasive/invasive imaging

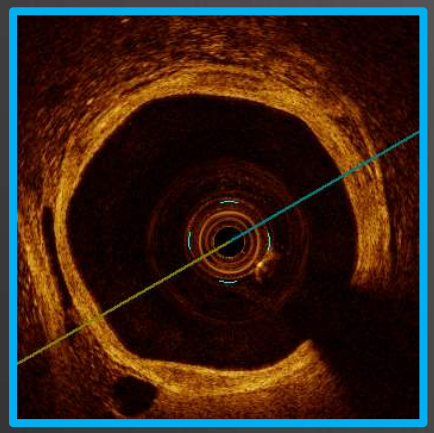


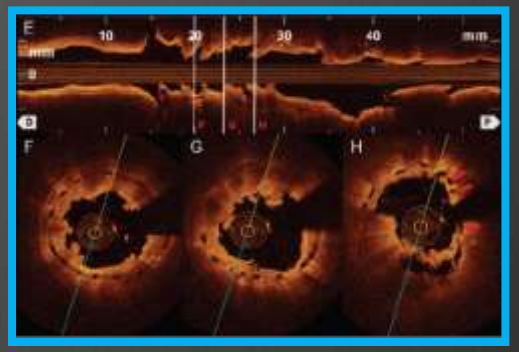
1. VP prior to BRS implantation
   Severe luminal narrowing, large necrotic core with thin fibrous cap

2. After BRS implantation
   Even expansion of obstructive lesion, minimal penetration of struts into NC

3. Healed Plaque after Resorption
   NC is encapsulated by thick fibrous cap with increase in lumen over time

The Reality !





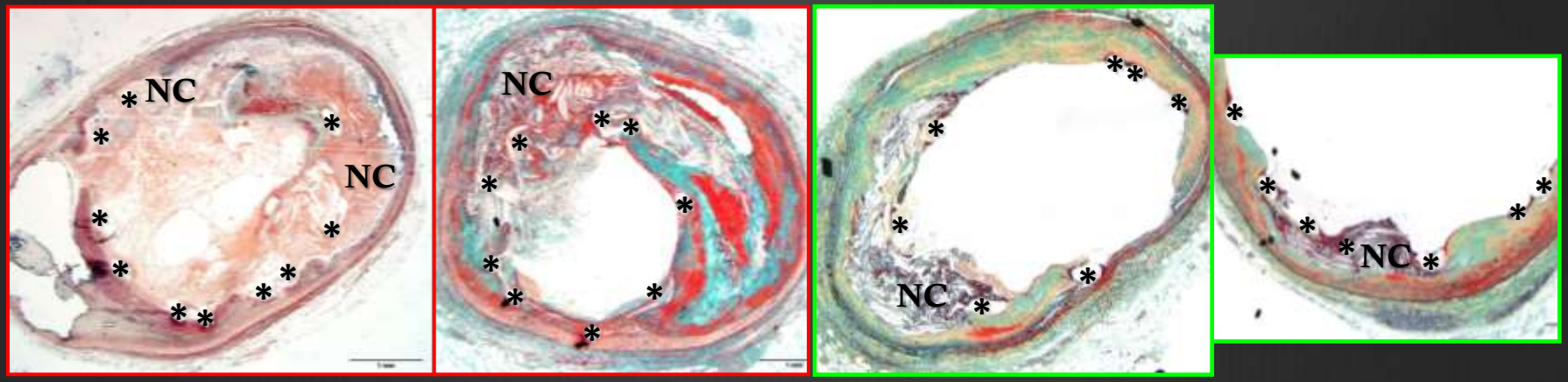
3 Major Issues Identified in Treatment of Vulnerable Lesions with(out) Thrombus

1. Acute Thrombogenicity of Stents
2. Procedural Failure Modes
3. Delayed Healing of Stents in Vulnerable Lesions

Effect of Necrotic Core Prolapse

	Thrombosis (n=37 lesions)	Patent (n=30 lesions)	
	Section with thrombus (n=124)	Section without thrombus (n=252)	P value
% strut penetrating into necrotic core	7.8±14.8	1.9±5.7	*<0.001*
NC area, mm^2	0.72±1.66	1.3±0.55	*<0.001*
Strut penetration into NC (%)	88.1±208.3	10.7±38.9	*<0.001*
Penetration depth (Max), μm	114.4±27.6	11.5±41.9	*<0.001*

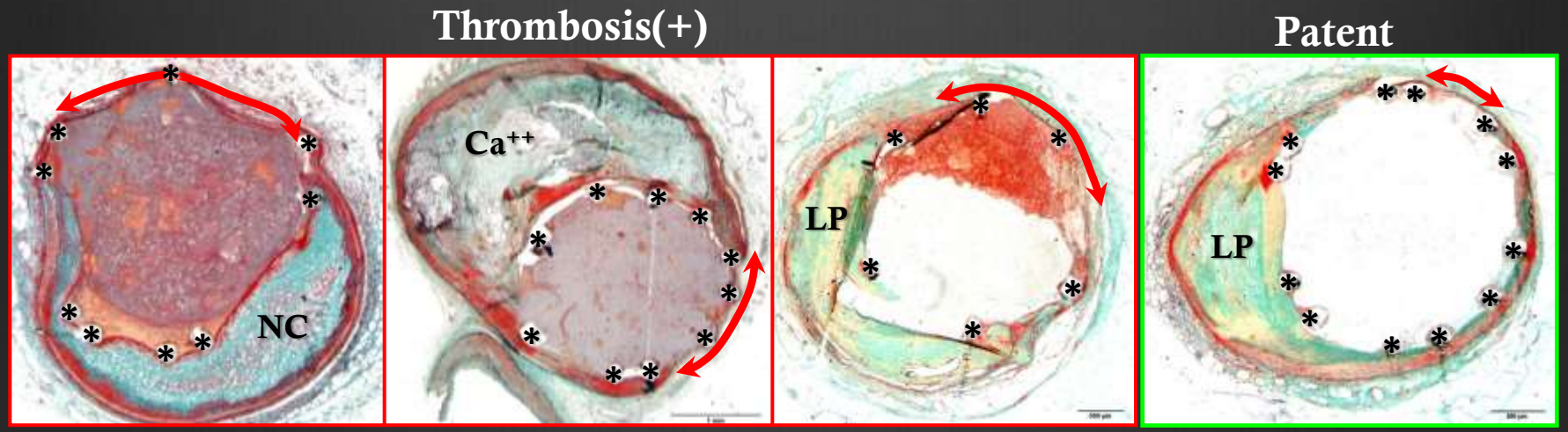
Thrombosis(+) Patent



Deep strut penetration into large necrotic core is likely to cause early stent thrombosis

Effect of Media Tear

	Thrombosis (n=37 lesions)	Patent (n=30 lesions)	
	Section with thrombus (n=124)	Section without thrombus (n=252)	P value
% strut with medial tear	10.2±19.0	3.9±8.7	***0.015***
Medial tear length, mm	0.71±1.42	0.27±0.62	***0.017***
Medial tear arc, °	26.3±52.9	8.3±19.5	***0.020***

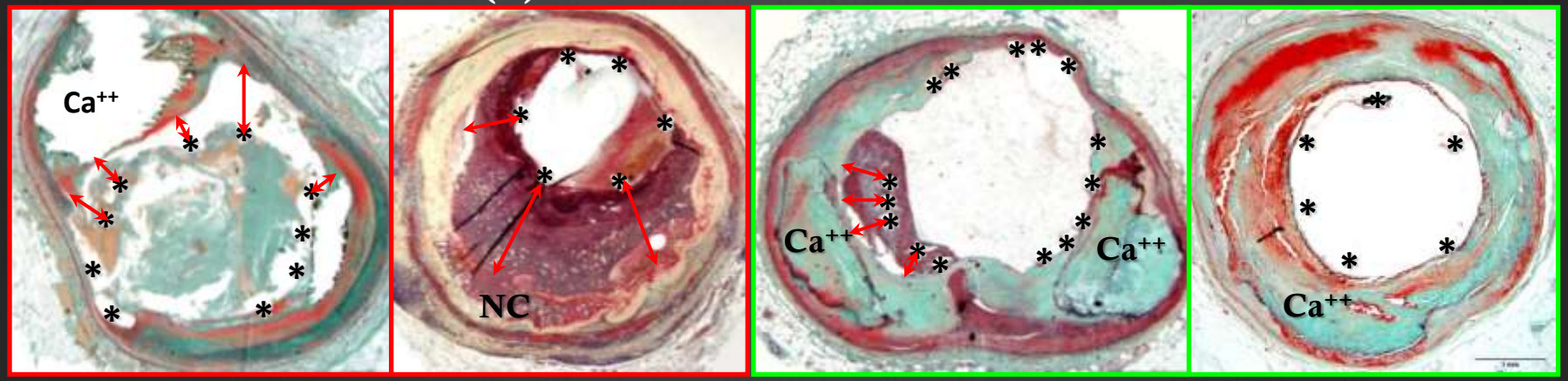


Media disruption tends to occur at the opposite site or shoulder region of eccentric plaque

Effect of Incomplete Apposition

	Thrombosis (n=37 lesions)	Patent (n=30 lesions)	
	Section with thrombus (n=124)	Section without thrombus (n=252)	P value
% strut with incomplete apposition	0.14±0.23	0.05±0.11	*<0.001*
Incomplete apposition area, mm^2	0.52±1.34	0.08±0.27	*0.010*
Incomplete apposition distance (Mean), μm	153.9±34.4	42.5±9.8	*0.001*
Incomplete apposition distance (Max) , μm	20.4±45.7	5.08±11.9	*0.001*

Thrombosis(+) **Patent**



Malapposition in fibrocalcific plaque

Underlying plaque rupture and malapposition

Focal malapposition and minor thrombus (<30% lumen)

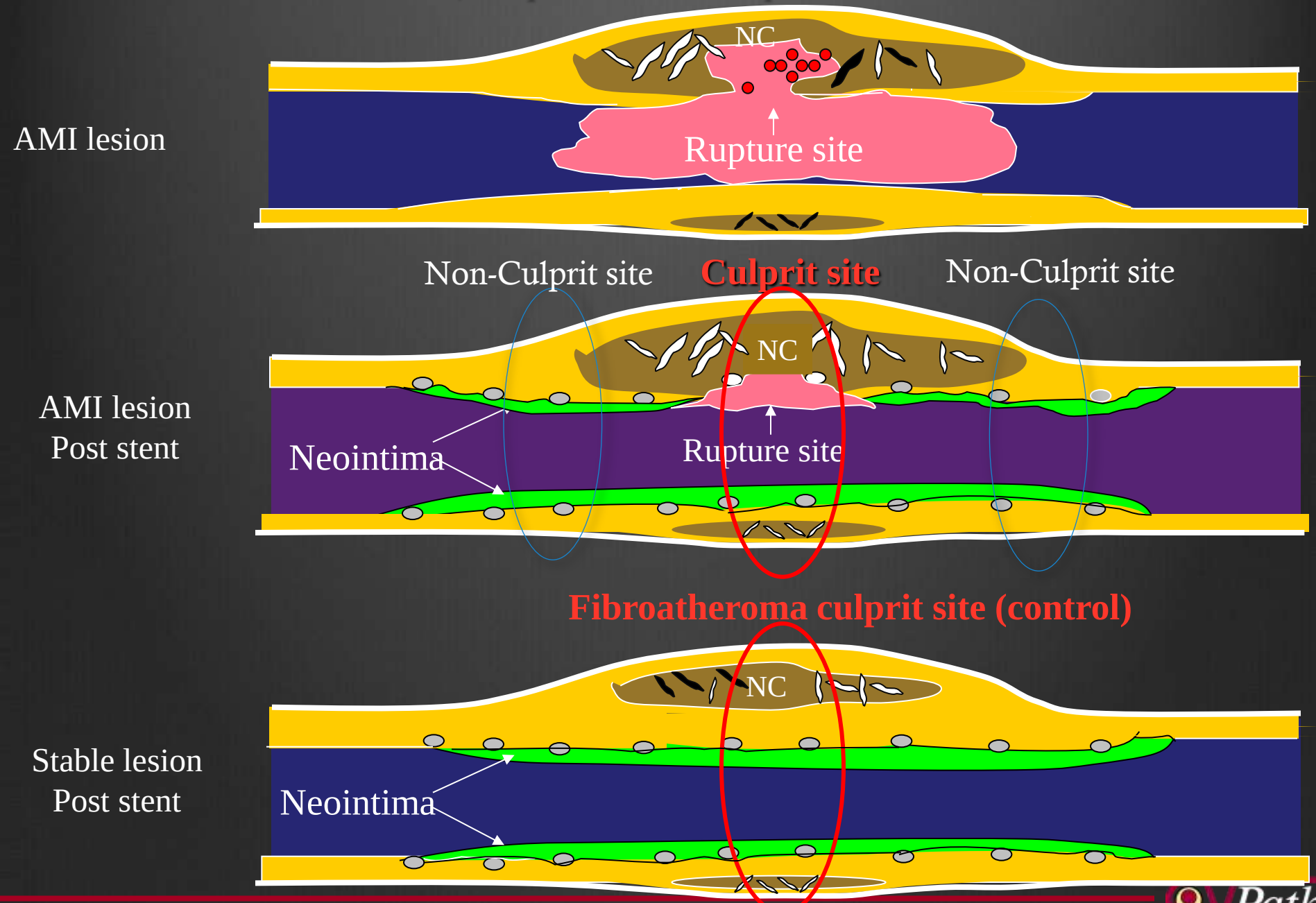
Minor malapposition Without thrombus formation

The Reality !

3 Major Issues Identified in Treatment of Vulnerable Lesions with(out) Thrombus

1. Acute Thrombogenicity of Stents
2. Procedural Failure Modes
3. Delayed Healing of Stents in Vulnerable Lesions

Definition; *Culprit and Non-culprit sites in AMI and stable*



Morphometry and Pathologic Assessment at Culprit Site (AMI vs. stable patients)

	AMI with rupture (n=17)	Stable with FA (n=18)	p value AMI vs. Stable
Neointimal thickness, mm	0.04 (0.02, 0.09)	0.11 (0.07, 0.21)	**0.008**
Strut with fibrin deposition, %	63 ± 28	36 ± 27	**0.008**
Strut with inflammation, %	35 (27, 49)	17 (7, 25)	**0.003**
Uncovered strut, %	49 (16, 96)	9 (0, 39)	**0.01**

Nakazawa, G et al. Circulation 2008

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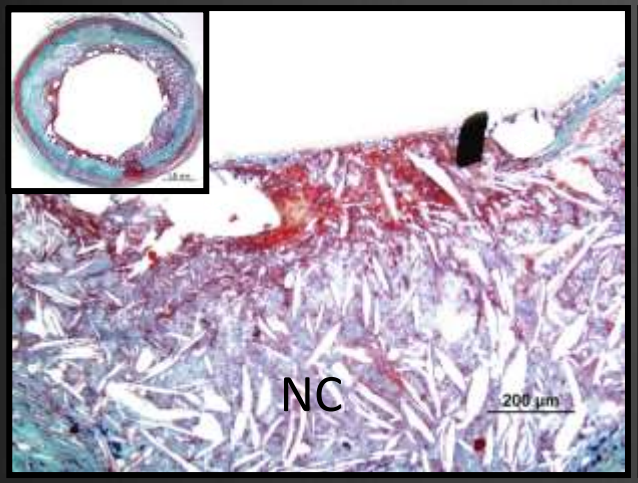
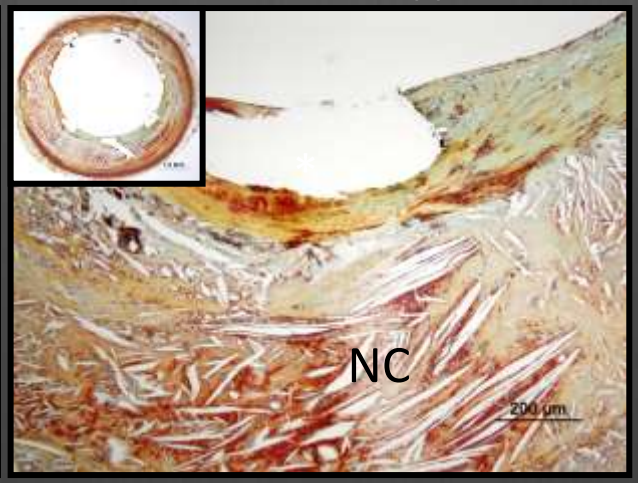
AMI lesions (with Plaque Rupture)

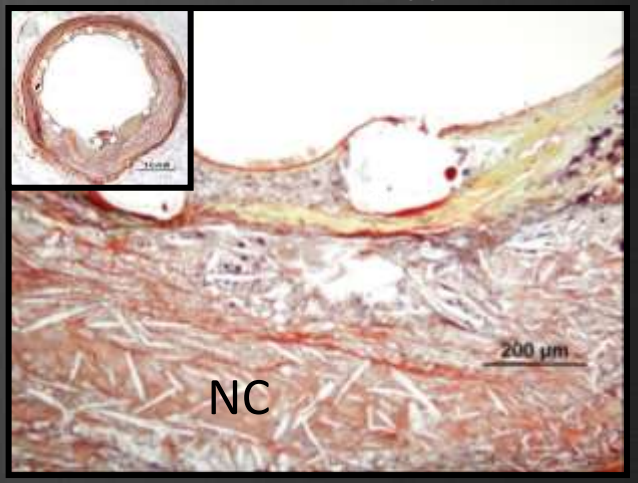
9 months (Taxus)



13 months (Cypher)

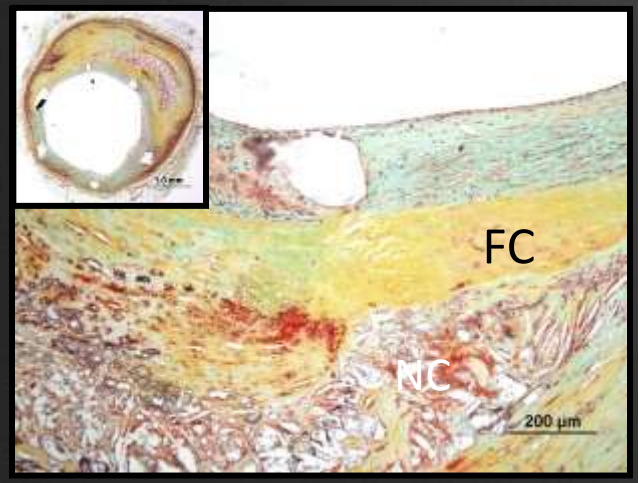


24 months (Cypher)

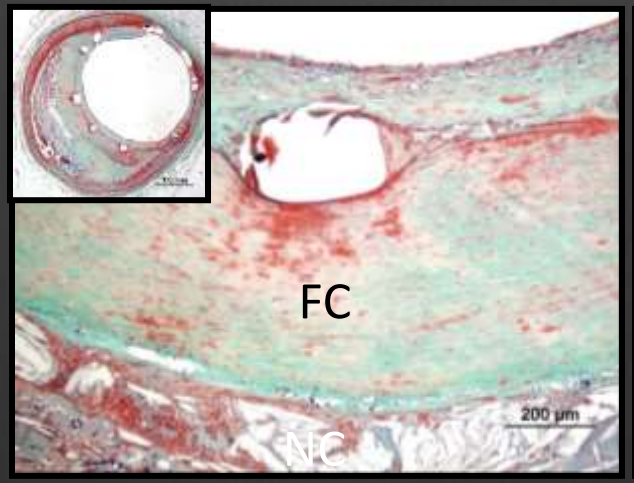


Stable Lesions (with Fibroatheroma and thick cap)

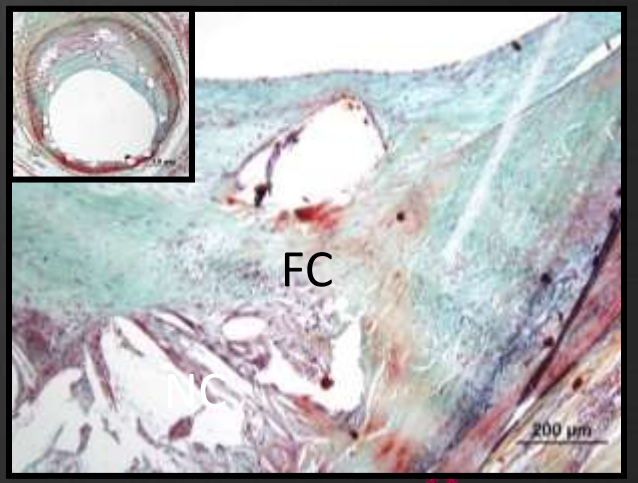
7 months (Cypher)



18 months (Taxus)



19 months (Cypher)



Nakazawa, G et al. Circulation 2008

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The Reality !

How will BRS Technology Impact on These Failure Modes?

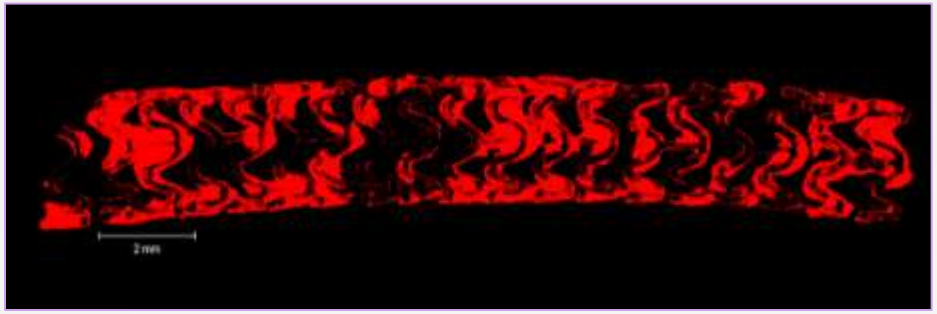
1. Acute Thrombogenicity of Stents
2. Procedural Failure Modes
3. Delayed Healing of Stents in Vulnerable Lesions

Impact of Strut Thickness on Thrombogenicity

Thicker Struts Associated with Increased Acute Thrombogenicity

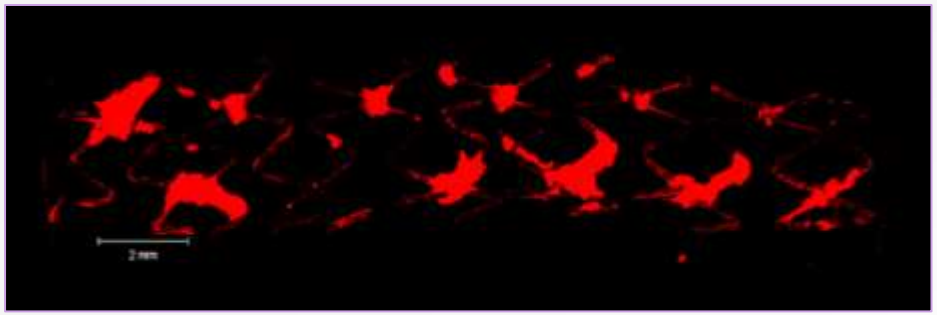
150 µm

Absorb



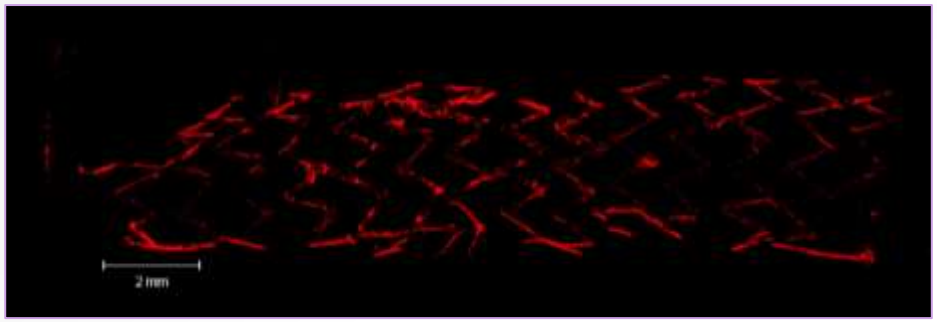
120 µm

BioMatrix Flex

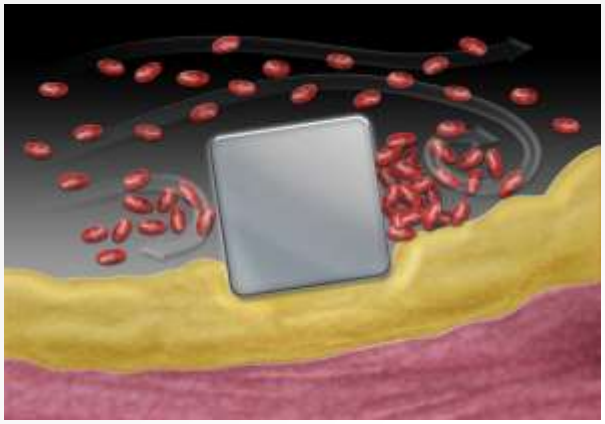


74 µm

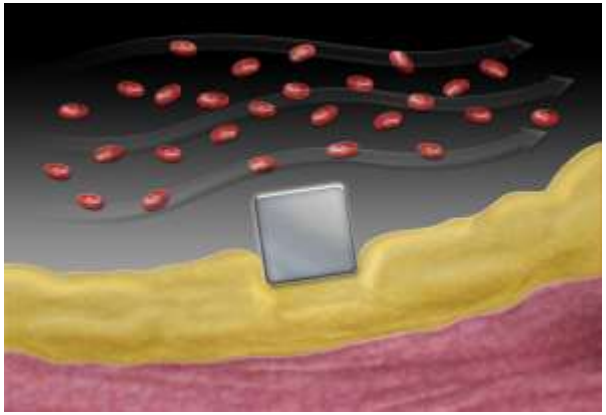
Synergy



Thick Strut DES



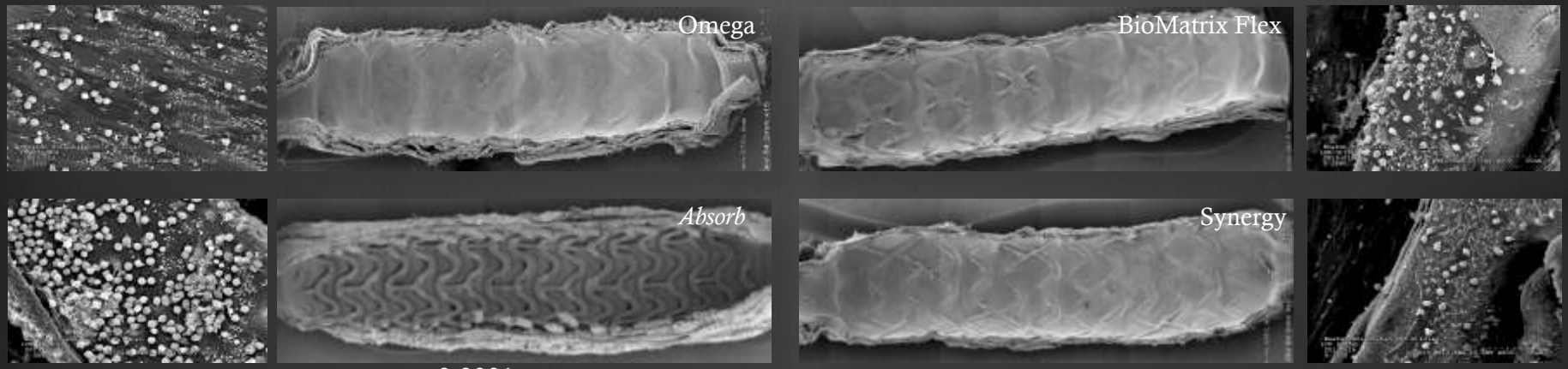
Thin Strut DES

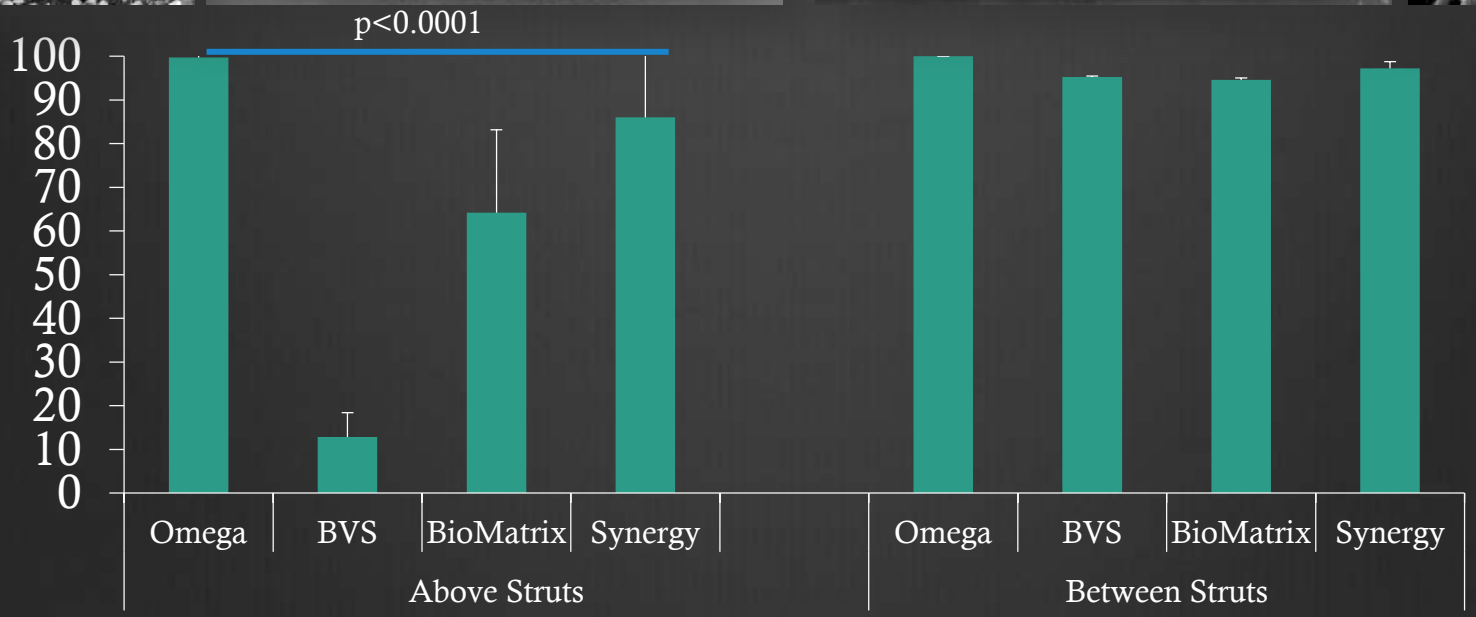


Thrombus formation assessed by immunofluorescence staining for platelet marker CD61 after 1 hour in ex-vivo pig AV shunt model

Sanchez, Joner, Virmani, et al. , TCT 2014; Modified from Koskinas et al. *J Am Coll Cardiol* 2012;59:1337–49

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



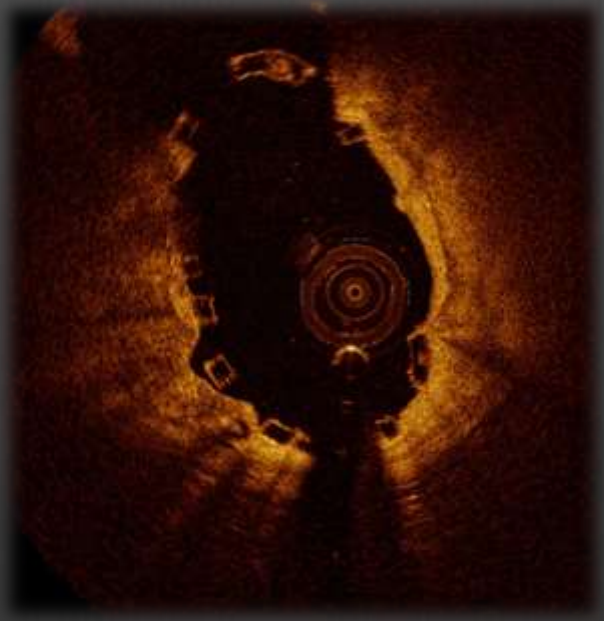


Incomplete Apposition in Calcified VP Results in Subacute ST

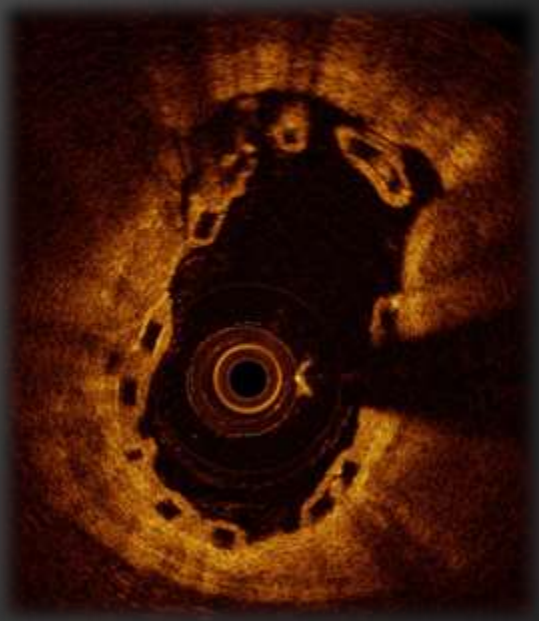
63-year old woman presenting with ACS

Presentation with ST 3 weeks later

TCFA with calcification prior to BRS implantation

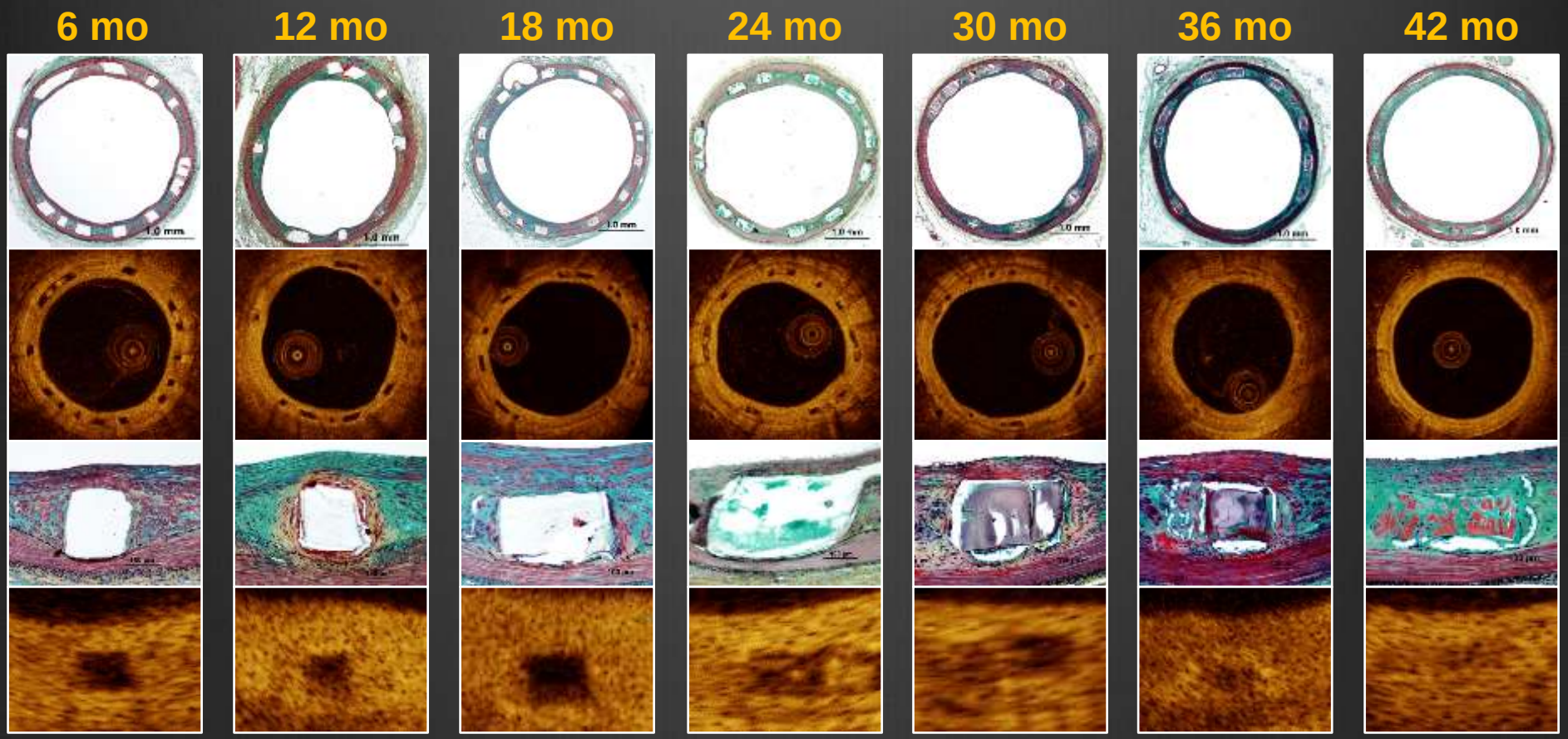


Incomplete expansion after post-dilatation with non-compliant balloon in calcified areas with minimal incomplete apposition



Subacute ST with moderate to severe malapposition

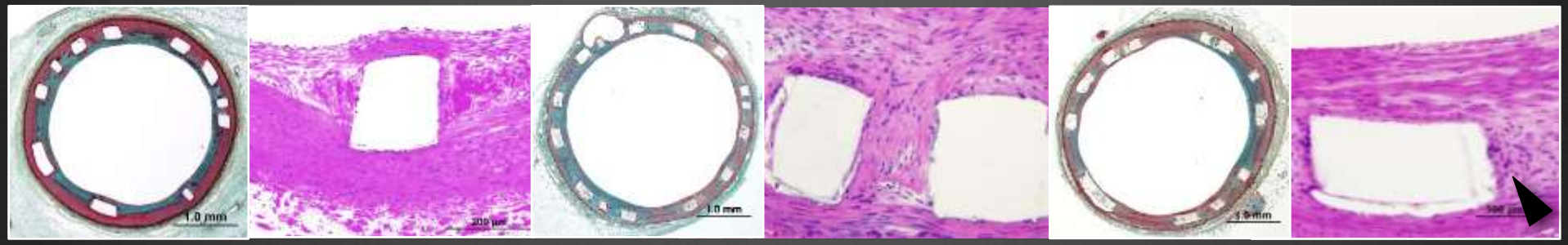
Representative OCT and Histologic Images Following BVS Placement in a Porcine Coronary Artery Model – *Cohort B*



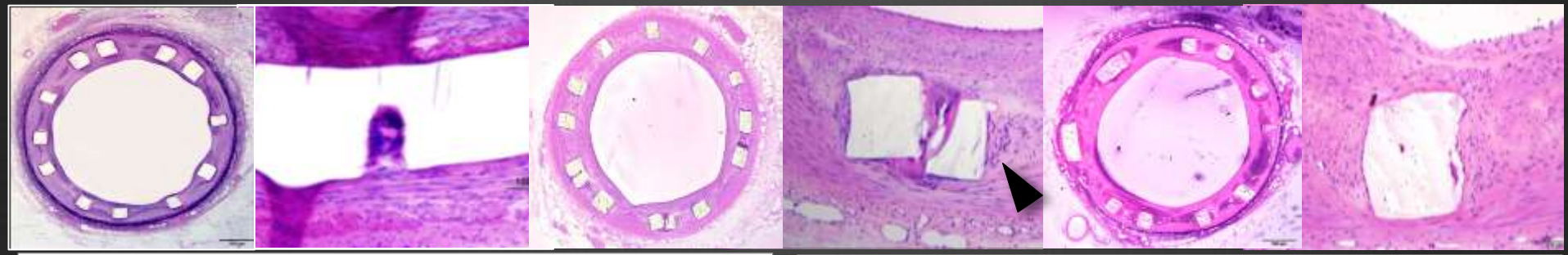
Late luminal gain may have tremendous benefit in the treatment of VP!

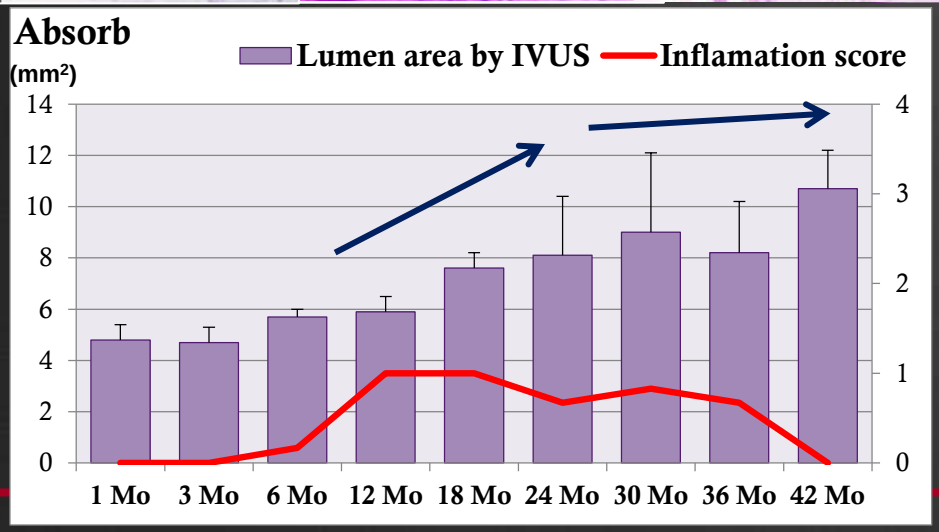
Association Between Inflammation and Lumen Area

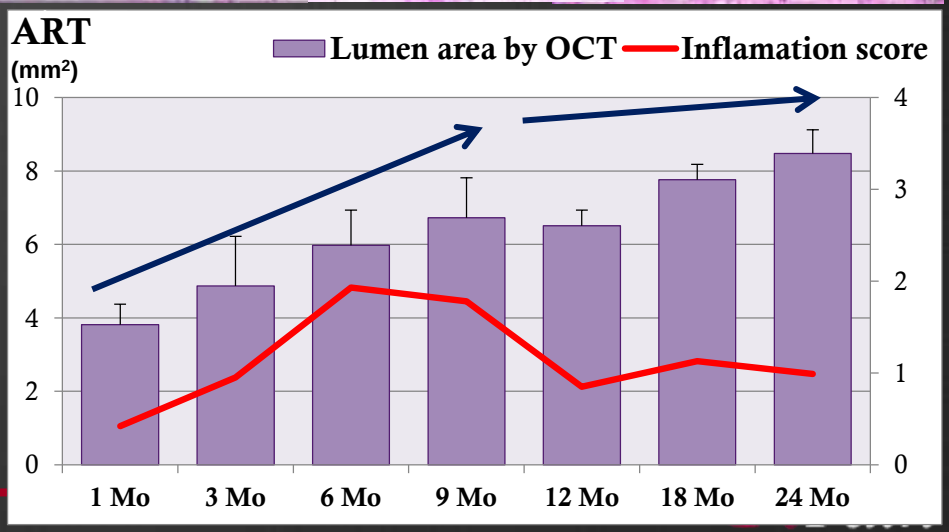
Absorb 1 Mo 6 Mo 18 Mo



ART 1 Mo 6 Mo 18 Mo

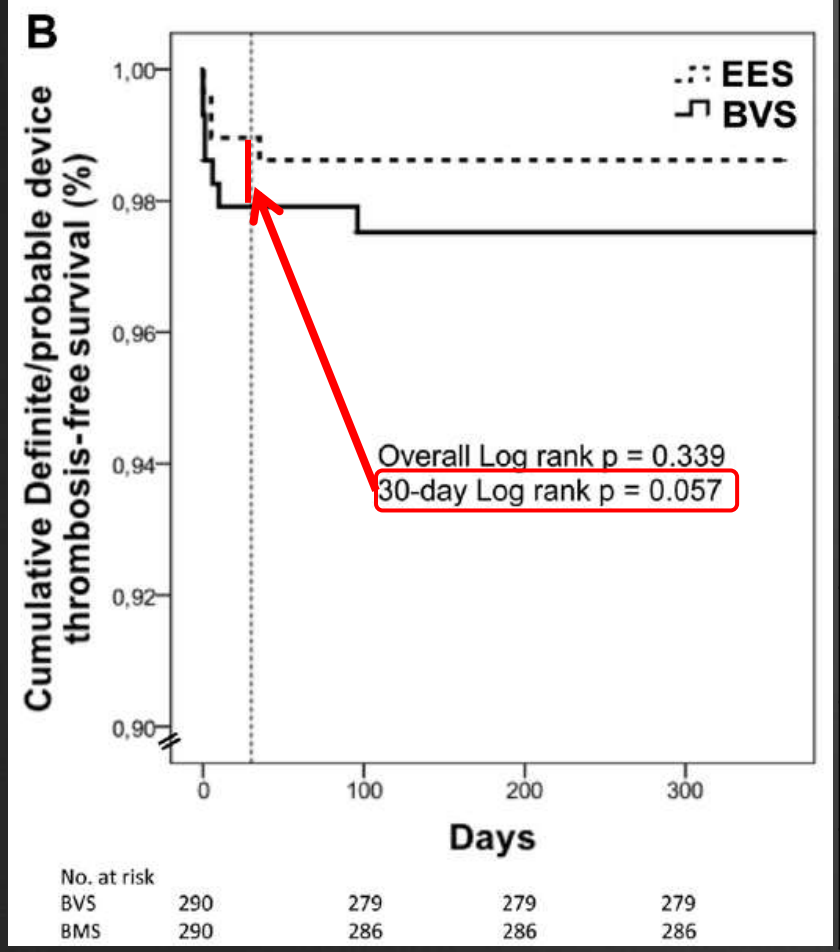






BVS vs EES in STEMI Stent Thrombosis

Absorb Bioresorbable Vascular Scaffold Versus Everolimus-Eluting Metallic Stent in ST-Segment Elevation Myocardial Infarction: 1-Year Results of a Propensity Score Matching Comparison



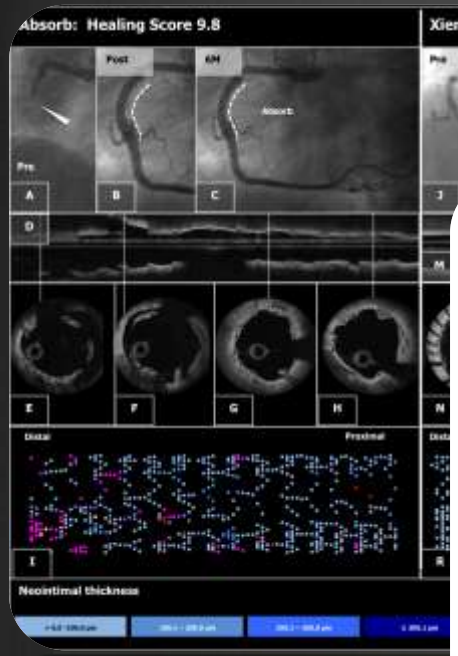
1.9% Thrombosis

(10/529, 9 acute/subacute,1 late)

Journal	Period (months)	Thrombosis(n) /Total(n)	Stop antiplatelet therapy
JACC Cardiovasc Interv. 2015 Jan;8(1 Pt B):189-97	12	7/290	yes(1/7)
Cardiol J. 2014 Nov 27 [Epub ahead of print]	6	1/23	yes(1/1)
EuroIntervention. 2014 Oct 30. [Epub ahead of print]	6	1/74	no
Eur Heart J. 2014 Mar;35(12):787-94	9	1/142	yes(1/1)

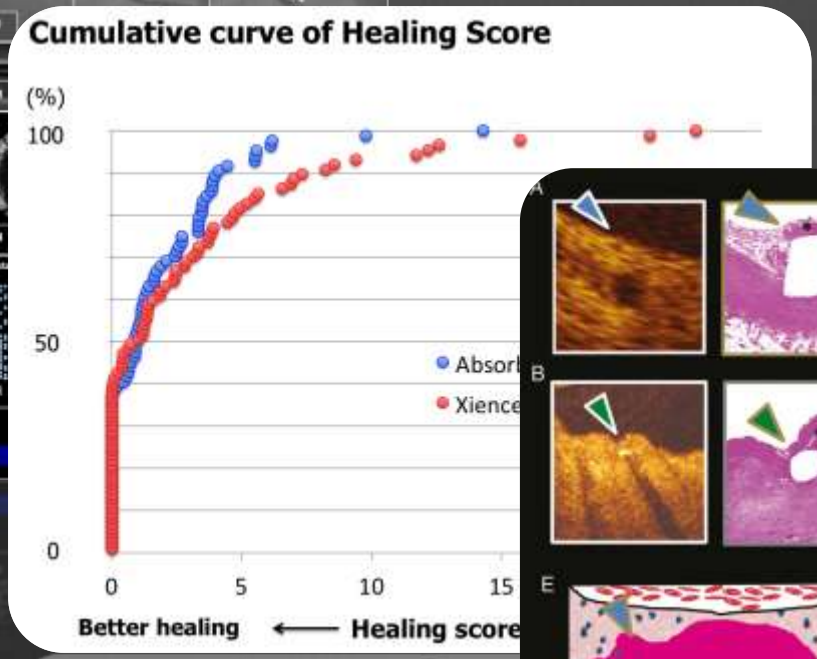
JACC Cardiovascular intervention(2015)1,189-97

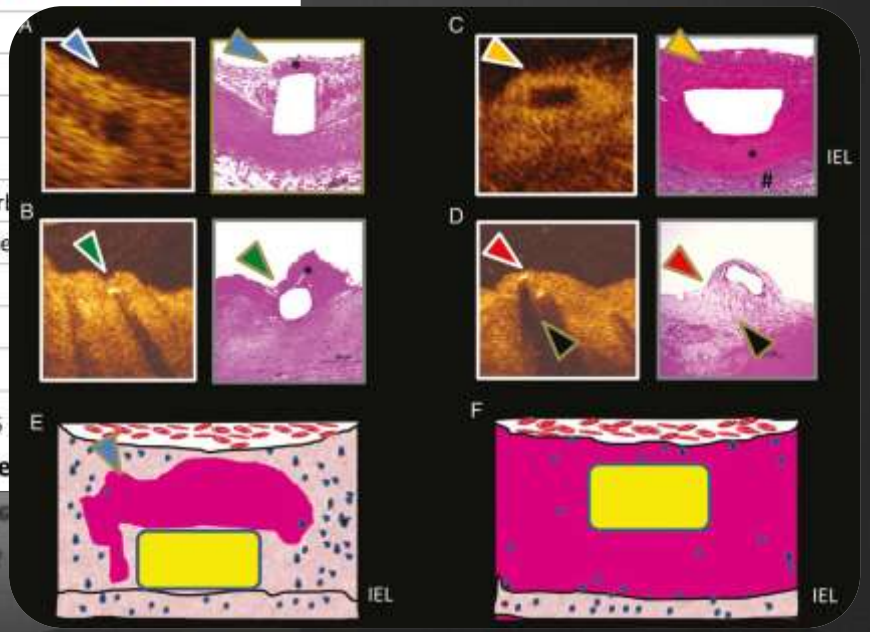
ABSORB STEMI-TROFI II Trial



191 patients in 8 clinical sites randomized 1:1 to Absorb vs. Xience

Primary EP: Healing Score (intraluminal mass, malapposition, uncoverage)





Lack of validation makes healing score unreliable
Diagnosis of malapposition by OCT is different among BRS and DES

Summary

- The concept of plaque passivation has been introduced in the late 90s but could never be achieved with conventional stent technology
- BRS may have potential to seal vulnerable atherosclerotic lesions due to their temporary presence and facilitated neointimal cap formation
- Clinical trials show mostly promising results of BRS in the setting of STEMI, where the clinical issue of malapposition and remodeling may be especially relevant
- While BRS remain an attractive option to achieve this goal, more knowledge is needed to understand vascular remodeling in the setting of diseased atherosclerotic arteries

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