



BRS Thrombosis Is Multifactorial: Do Not Always Blame the Device

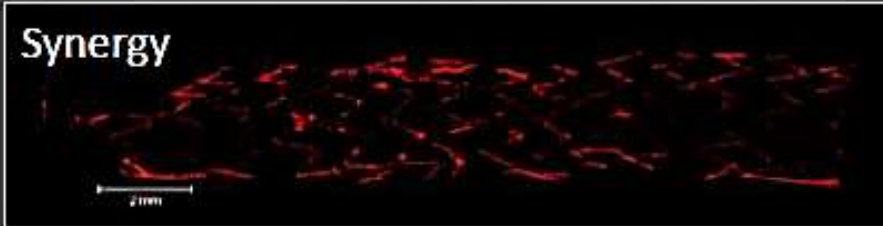
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Platelet Deposition By Confocal Microscopy Of Immunofluorescent Staining (CD61/CD42b)

74 μm

Synergy



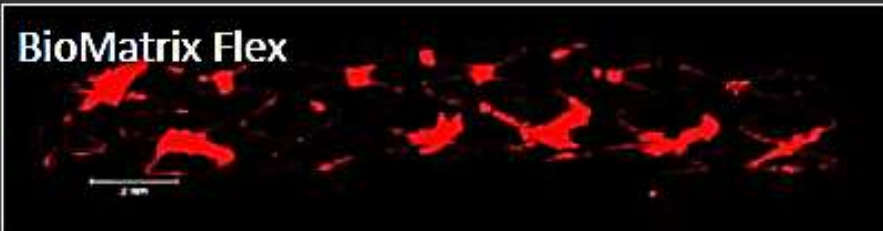
150 μm

Absorb BVS



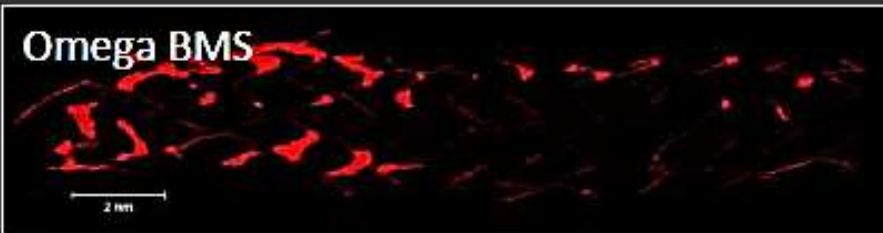
120 μm

BioMatrix Flex



81 μm

Omega BMS

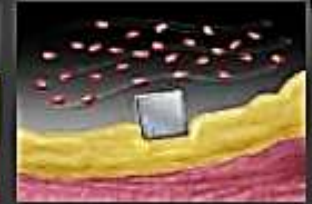


Platelet deposition was assessed by immunofluorescence staining for platelet marker CD61/CD42b as shown in red after 1 hour in ex-vivo pig AV shunt model

Thick Strut DES

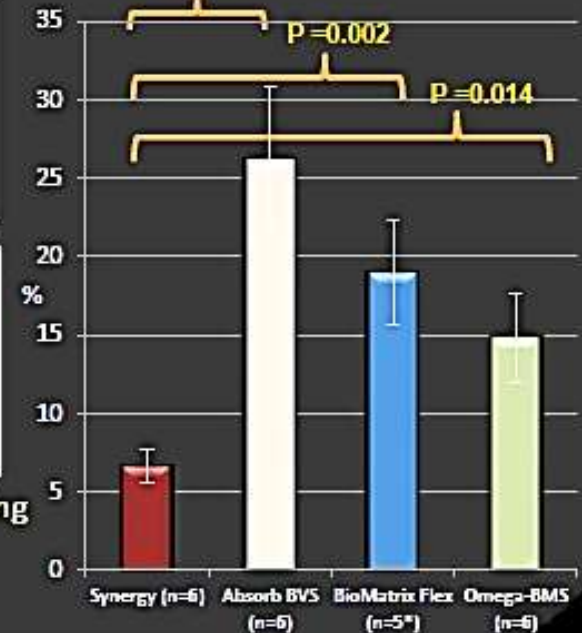


Thin Strut DES



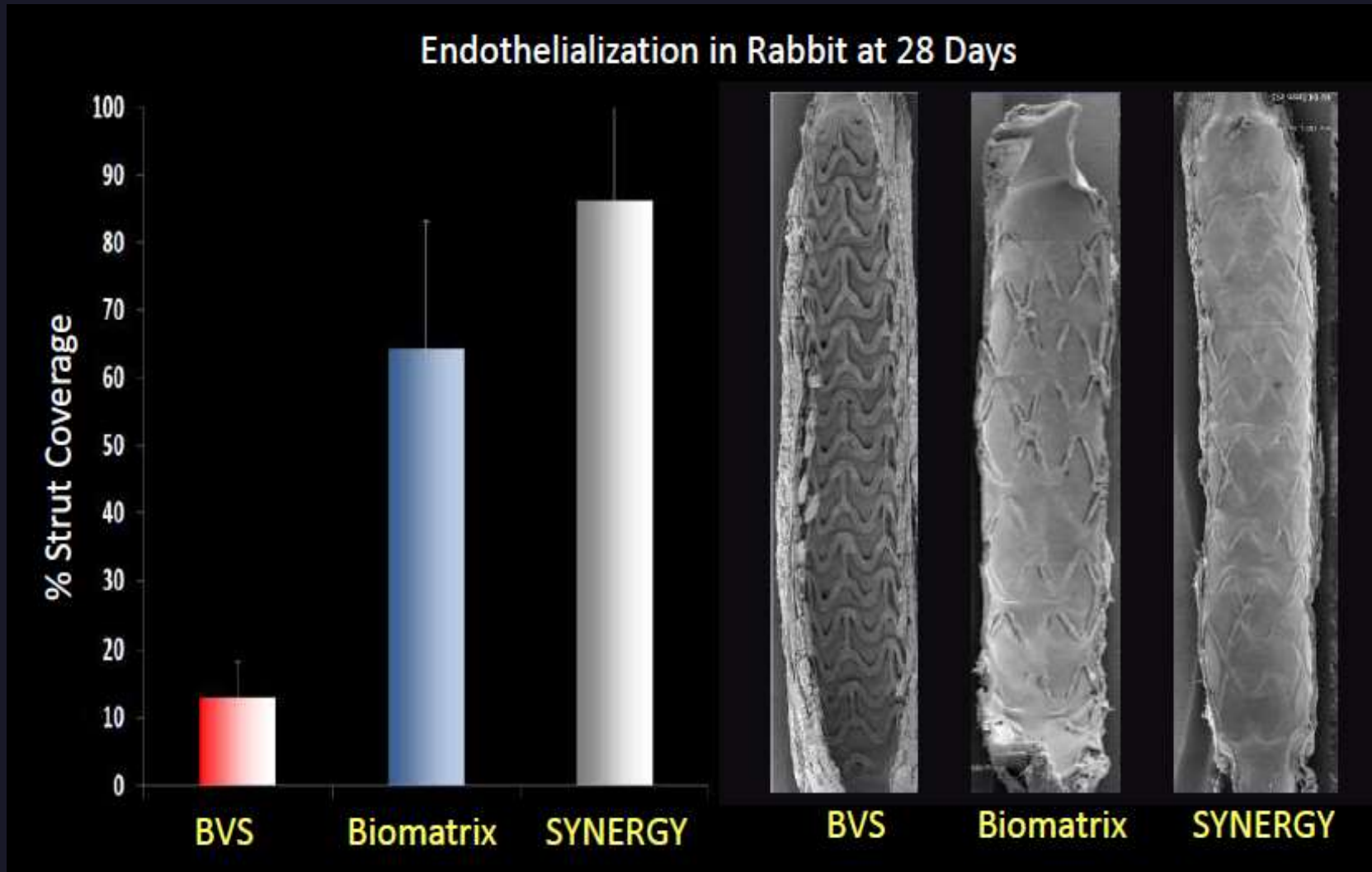
Mean positive area of adherent platelets

$P < 0.001$




Thick vs. Thin Struts DES

Healing & Endothelialization In SYNERGY, Biomatrix & ABSORB BVS



Risk Factors of Scaffold Thrombosis

Device-related factors	Platelet – related factors	Angioplasty-related factors (correctable)	Lesion-related factors	Patient-related factors
<ul style="list-style-type: none"> • Strut thickness • Delayed or incomplete endothelialization • Chronic, late recoil • Late intraluminal dismantling (predisposed by acute malapposition) • Peristrut low intensity area • Neointimal hyperplasia • Restenosis 	<ul style="list-style-type: none"> • High platelet reactivity / APT resistance • Discontinuation of APT 	<ul style="list-style-type: none"> • Underexpansion (small MSA) • Edge issues (dissection, residual disease) • Geographic miss • Acute fracture • ↓ TIMI flow <div style="text-align: center; margin-top: 20px;">  <p>OCT / IVUS !!</p> </div>	<ul style="list-style-type: none"> • Diffuse disease • Bifurcation • Small vessel • Thrombus containing lesion • CTO • SVG • Tandem lesions • Stasis • Multivessel CAD 	<ul style="list-style-type: none"> • Diabetes (insulin-dependent) • Renal failure • Low EF • ACS • Predisposing thrombotic conditions • Cigarette smoking • Malignancy • Genetic traits • Surgery



ABSORB Studies:

PSP Analysis

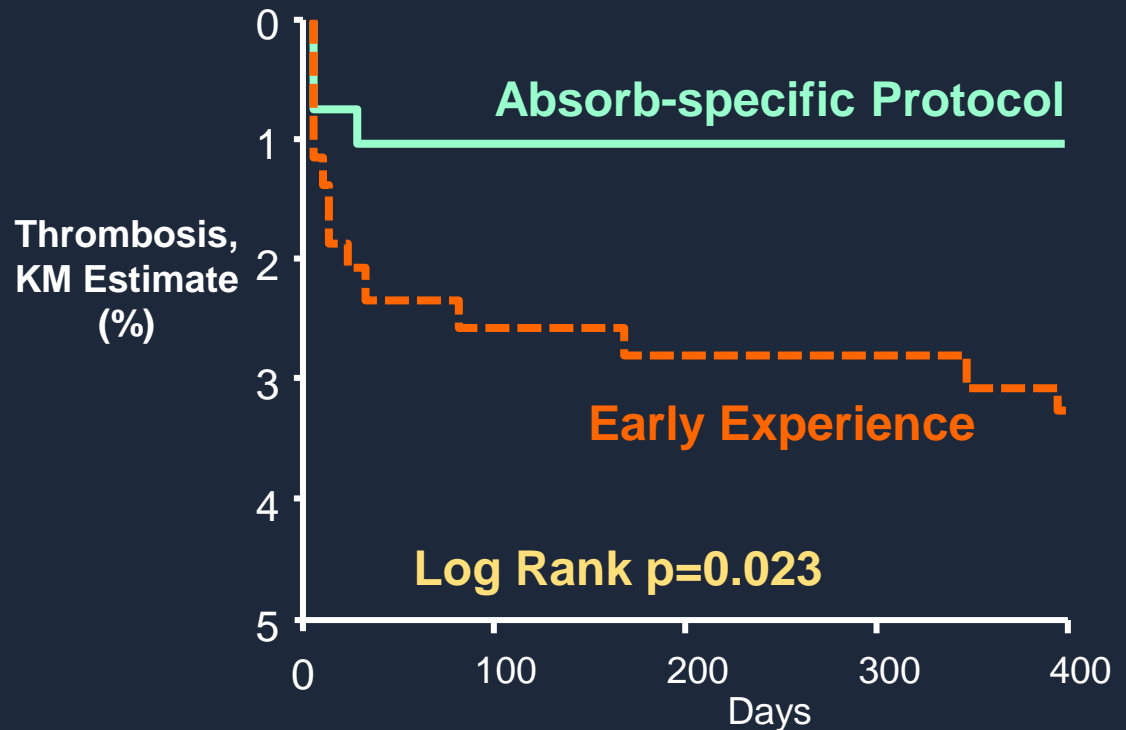
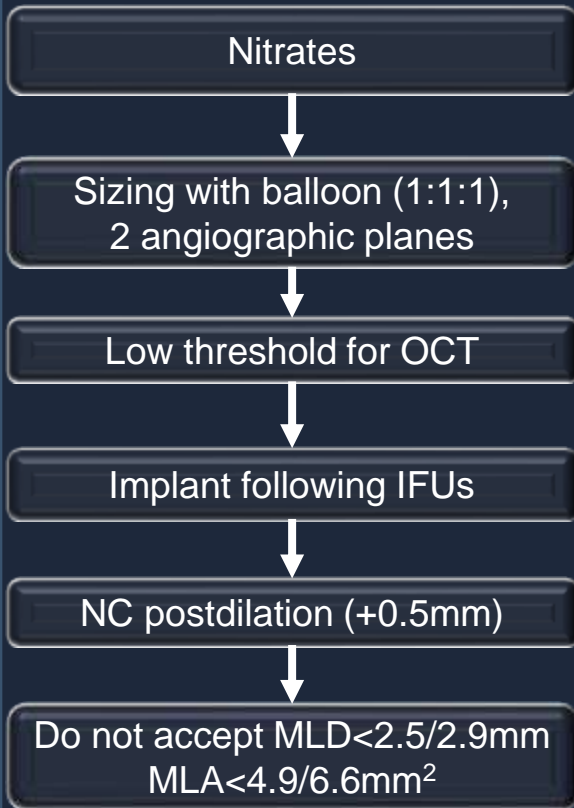
- Definition of PSP (must satisfy all the criteria below)
 - **P**re-dilatation
 - **S**izing (vessel): $2.25\text{mm} \leq \text{QCA RVD} \leq 3.5\text{mm}$
 - **P**ost-dilatation:
 - Pressure >16 atm
 - Balloon diameter: Scaffold diameter $> 1:1$
 - Balloon diameter \leq Scaffold diameter + 0.5mm
- Comparing the clinical outcomes of PSP vs Non-PSP subgroups*

* Based on subjects treated with at least one Absorb BVS. For subjects with multiple target lesions, all lesions have to be treated per PSP



4 Cities Registry: Reduction In Absorb Scaffold Thrombosis With Improved Technique

4 German & Swiss centers BVS specific protocol

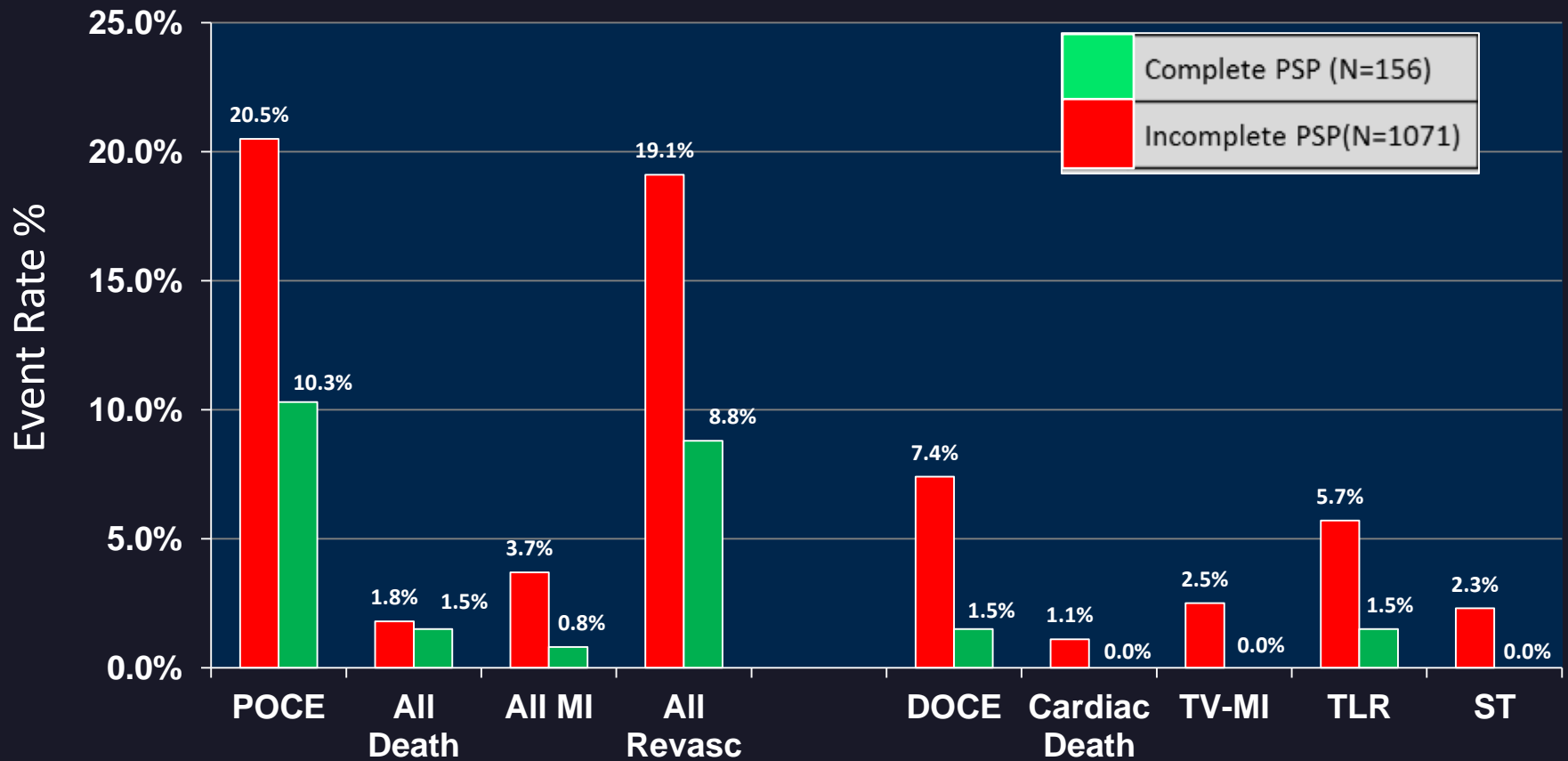


Patients					
Early Experience	369	369	369	369	369
Absorb-specific	292	292	281	217	155

*For a 2.5-3.0 mm & 3.5 mm scaffold respectively

Optimal Implantation Technique Is Imperative For Good Clinical Outcomes

Significant Improvement In GHOST-EU Outcomes At 1 Yr With Optimal Implantation





ABSORB Studies

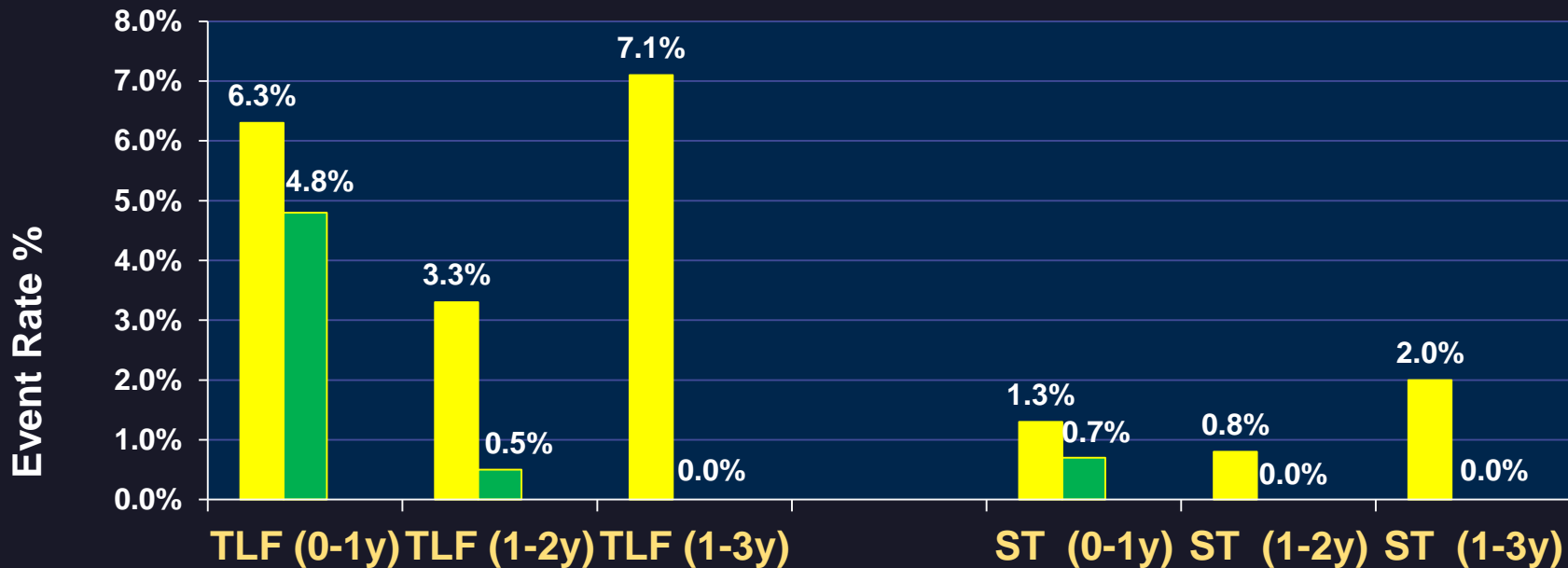
ABSORB (A) EXTEND, A II, A III, A-Japan, A-China: Performance Of Optimal PSP Techniques

	Lesions (n=3,149)	Patients (n=2,973)
Predilatation ¹	60.1 %	58.2%
Sizing²	82.3%	81.6%
Post-dilatation³	12.7%	12.4%
All PSP	5.0%	4.9%

¹Performed in all lesions with a balloon to QCA-RVD ratio $\geq 1:1$; ²QCA-RVD > 2.25 mm- < 3.75 mm for all treated lesions; ³Performed with a non-compliant balloon at > 18 atm.& with a nominal diameter larger than the nominal scaffold diameter, but not > 0.5 mm larger

Optimal Implantation Technique Is Imperative for Good Clinical Outcomes

Pooled Absorb Outcome With PSP Analysis*



		Non-PSP	PSP
0-1y	A-EXTEND, A-II, A-Japan, A-China, A-III	N=2540	N=294
1-2y	A-EXTEND, A-II, A-Japan, A-China	N=1381	N=194
1-3y	A-II	N=297	N=21

**This is even more critical if we are dealing with complex cases
Different lesion subset may need different & specific technique**

Outcomes of BVS Implantation in Real World Cohort Utilizing Optimized Implantation Strategy

1. Aggressive lesion preparation (97.3%); (2). High pressure post-dilatation (99.8%); (3). IV imaging (85.8%)(IVUS 82.0%/OCT 14.0%)

N=264 pts, 400 lesions	1 year	2 years
TLF	17 (7.9%)	22 (11.6%)
Cardiac death	3 (1.3%)	4 (2.0%)
Target vessel MI	4 (1.8%)	4 (1.8%)
All cause death	14 (6.6%)	19 (10.4%)
Any myocardial infarction	6 (2.8%)	7 (3.5%)
TVR	17 (8.0%)	25 (13.8%)
Definite/probable ST	3 (1.2%)	3 (1.2%)

IRIS-BVS Registry (in Korea)

Design: multicenter, all comer, prospective, observational study (aim n=1000)

Objective: to compare the ourcomes of BVS with other DES in “real world practice”

Primary end-points: target vessel failure (TVF)

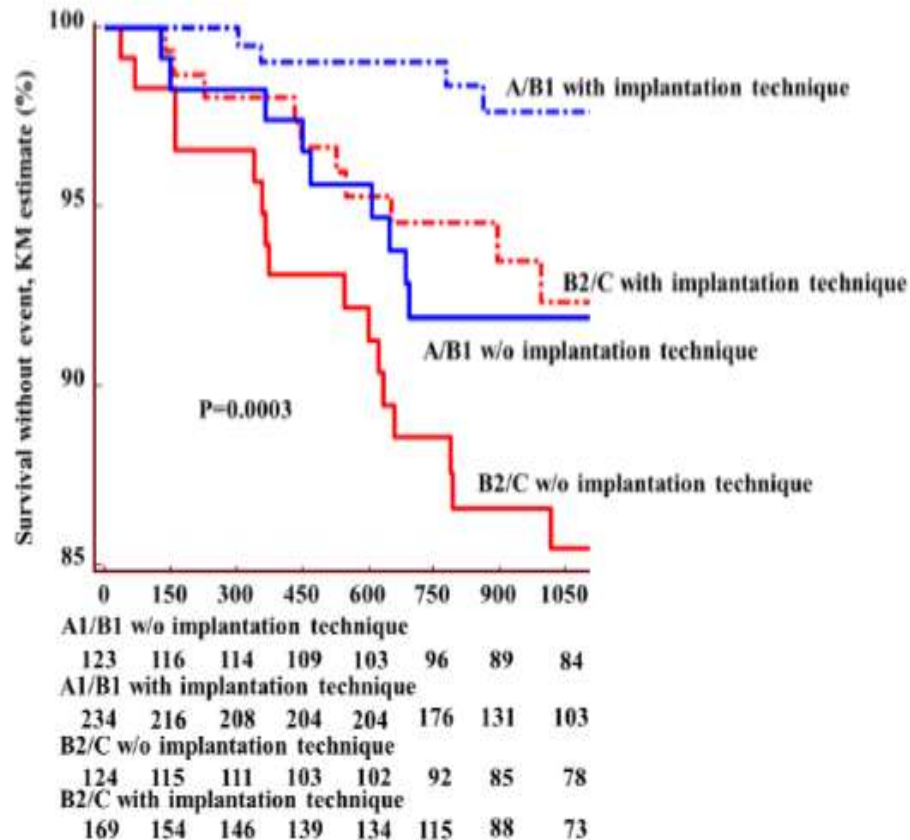
- Composite outcomes of (1) Cardiac death, (2) Myocardial infarction (Periprocedural MI = CK-MB > 10 x UNL; Spontaneous M = any cardiac enzyme elevation); (3) Target vessel repeat revascularization

PS matched	IRIS BVS N=352	IRIS EES N=352	P value
Device-Oriented Endpoint			
Target vessel failure	2 (0.06%)	16 (1.8%)	0.88
Cardiac death	0 (0.0%)	3 (0.9%)	0.41
Myocardial infarction	2 (0.06%)	11 (3.1%)	0.019
- Peri-procedural MI	2 (0.06%)	9 (2.6%)	0.033
- Spontaneous MI	0 (0.0%)	2 (0.06%)	0.30
Target vessel revascularization	0 (0.0%)	3 (0.09%)	0.68
Patient oriented end point			
Death from any cause	0 (0.0%)	5 (1.5%)	0.35
- Cardiac death	0 (0.0%)	3 (0.9%)	0.063
- Non-cardiac death	0 (0.0%)	2 (0.06%)	0.64
Stroke	0 (0.0%)	1 (0.03%)	0.47

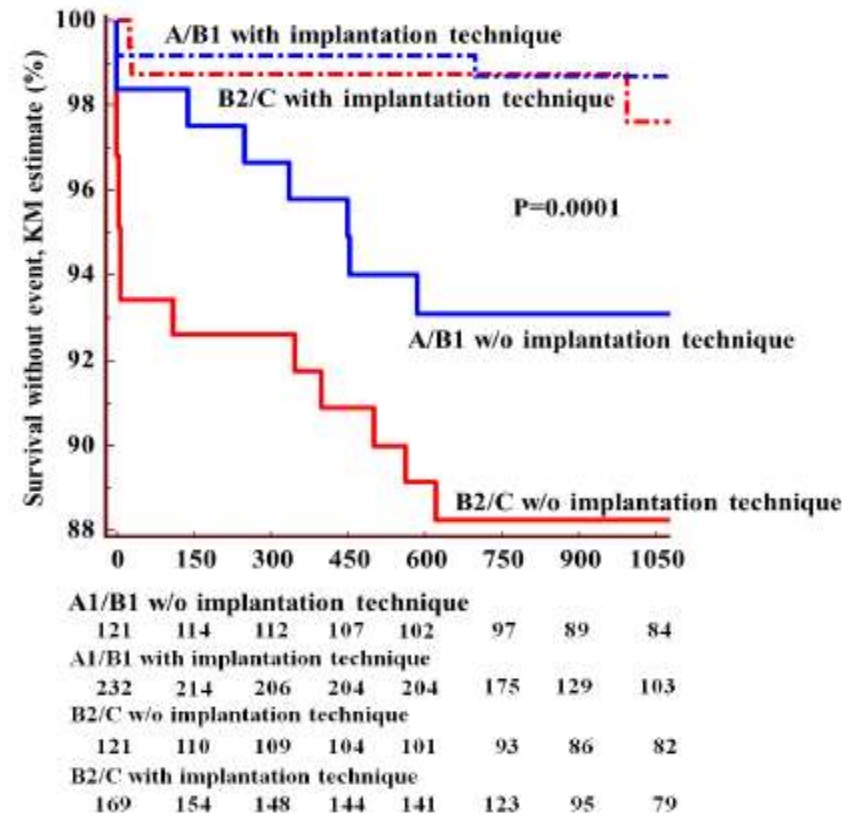
PS matched	IRIS BVS N=352	IRIS EES N=352
Definite		
Acute (0-1 day)	0 (0.0%)	0 (0.0%)
Subacute (2-30 days)	0 (0.0%)	0 (0.0%)
Late (31-265 days)	0 (0.0%)	0 (0.0%)
Very late (> 365 days)	0 (0.0%)	0 (0.0%)
Definite or probable		
Acute (0-1 day)	0 (0.0%)	0 (0.0%)
Subacute (2-30 days)	0 (0.0%)	0 (0.0%)
Late (31-265 days)	0 (0.0%)	0 (0.0%)
Very late (> 365 days)	0 (0.0%)	0 (0.0%)

Impact Of Implantation Technique In Simple & More Complex Lesions

Scaffold Restenosis

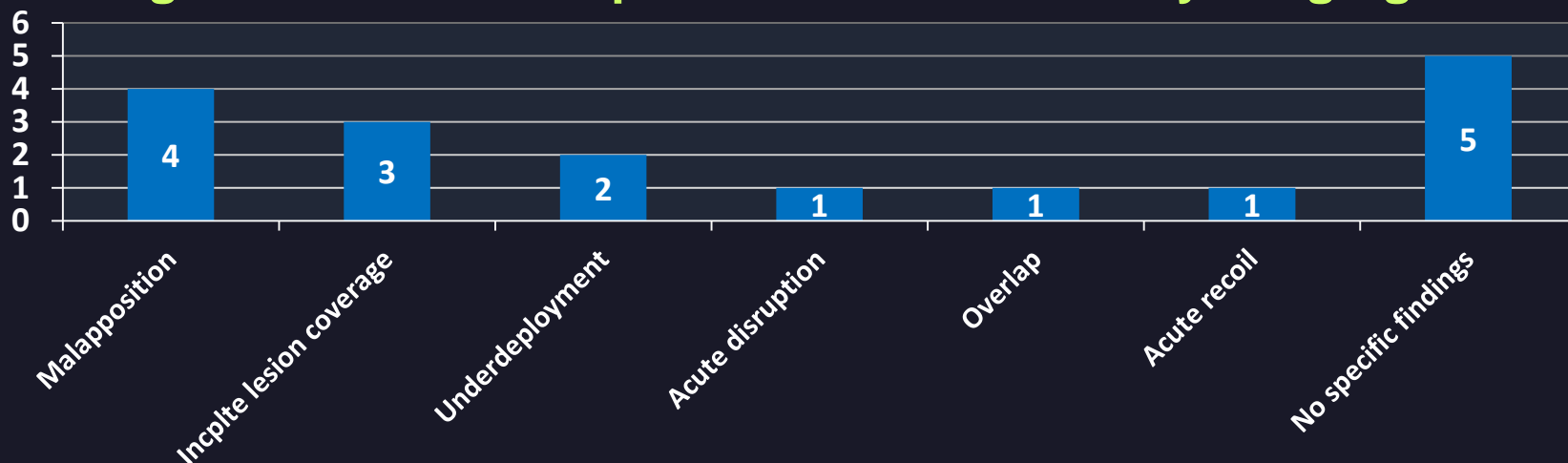


Scaffold Thrombosis

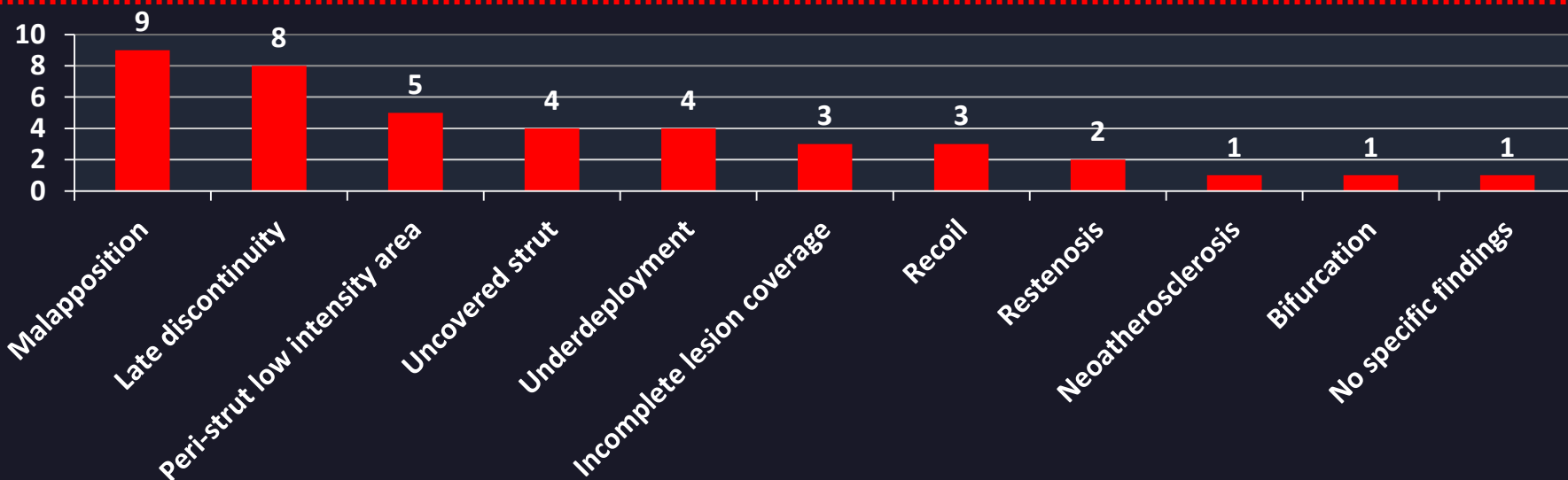


* N = 657

Possible Mechanical Causes Of Scaffold Thrombosis: Insights From Case Reports With Intracoronary Imaging

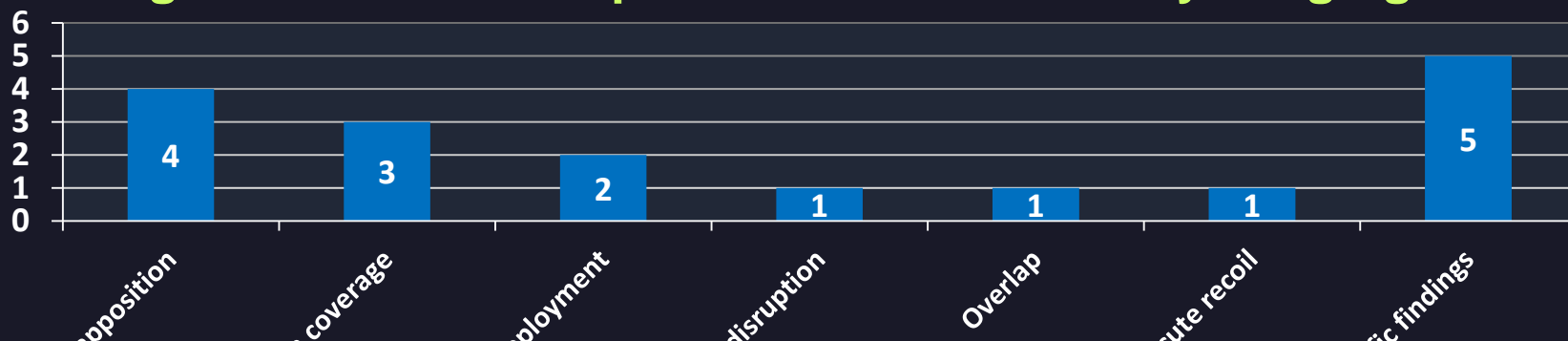


Early ScT (n=17): Malapposition (24%), incomplete lesion coverage (18%) & underdeployment (12%)

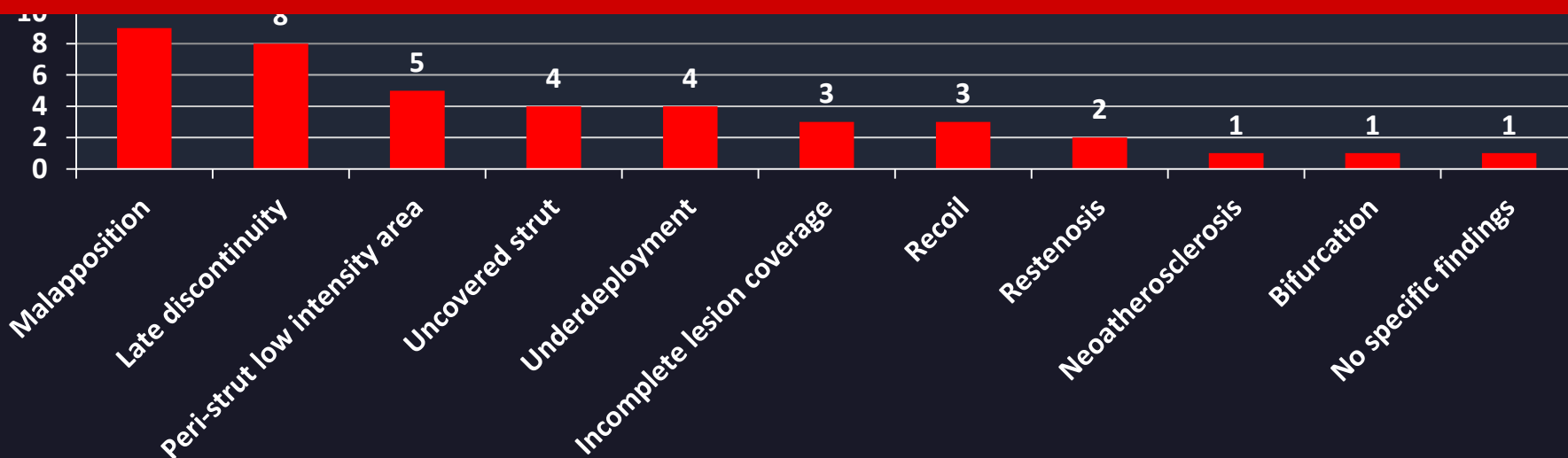


Late/VLScT (n=26): Malapposition (33%), late discontinuity (31%), & peristrut low intensity area (19%)

Possible Mechanical Causes Of Scaffold Thrombosis: Insights From Case Reports With Intracoronary Imaging



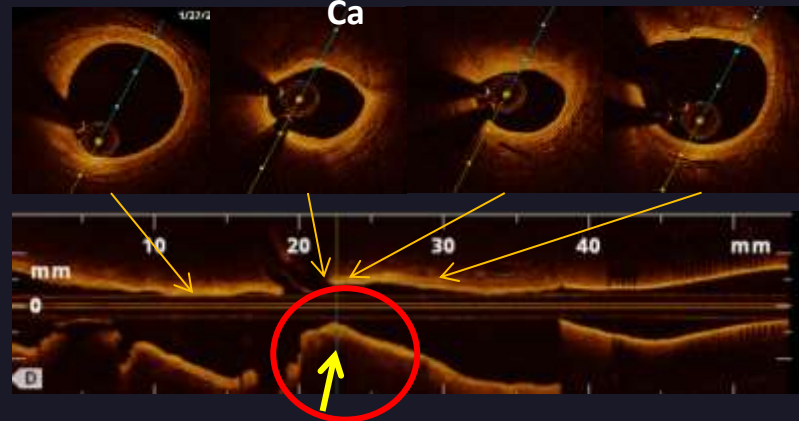
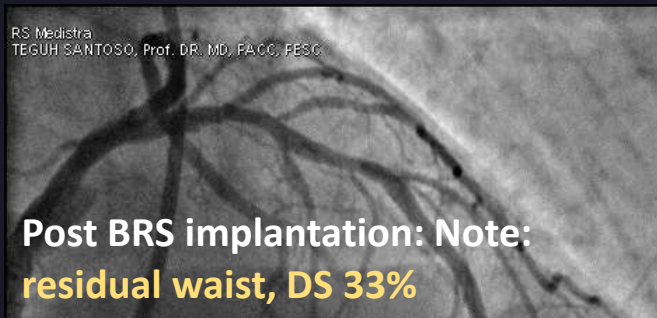
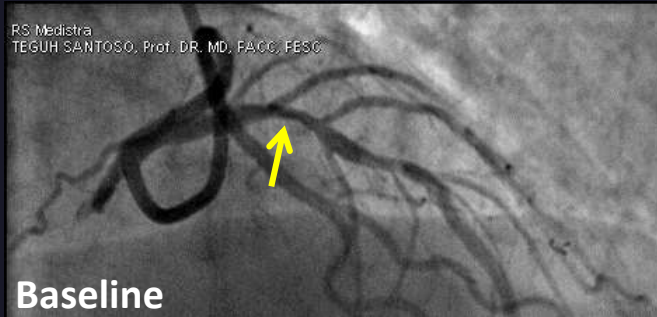
**Main factors for BRS failure:
MECHANICAL FACTORS !!!**



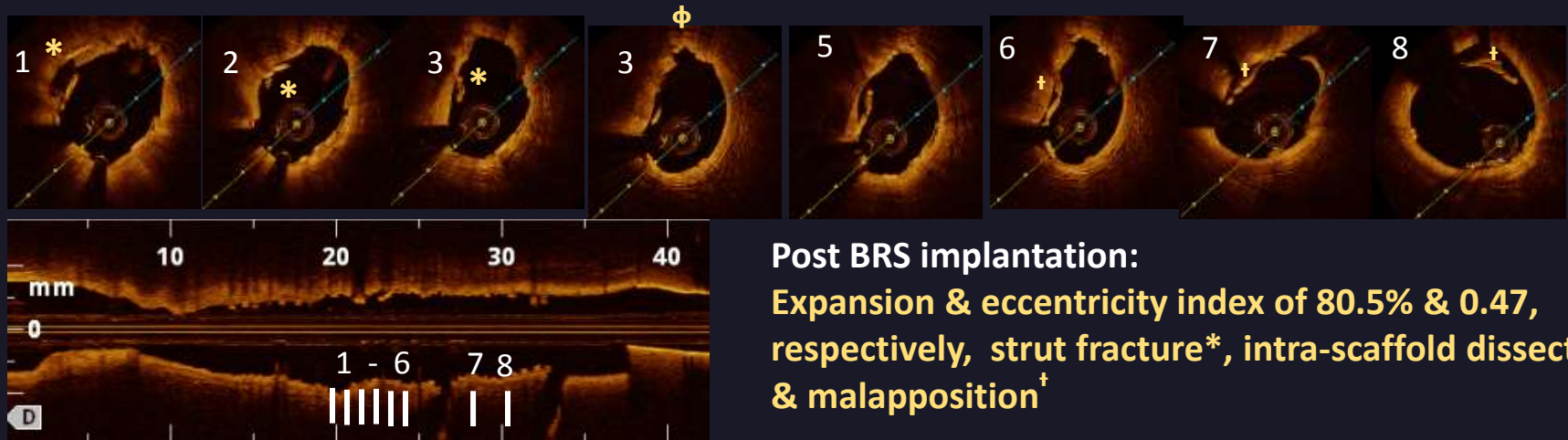
Late/VLScT (n=26): Malapposition (33%), late discontinuity (31%), & peristrut low intensity area (19%)

Case 1: BRS Thrombosis

Mr. AW, 72 yrs old, male, **silent ischemia (TMT)**, **MSCT: 80% proximal LAD**.
 Risk factor: dyslipidemia, ↓ HDL, hypertension.



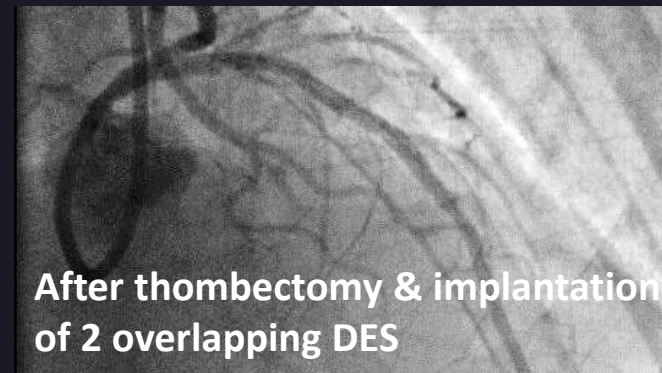
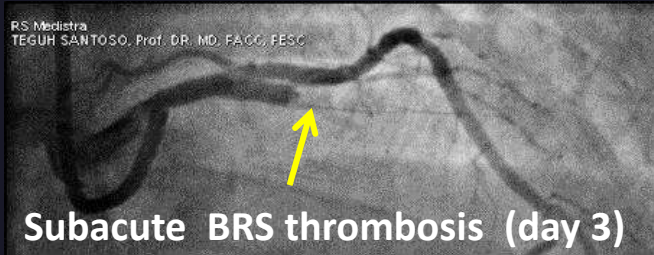
Baseline: **calcific nodules** (arrow)



Post BRS implantation:
 Expansion & eccentricity index of 80.5% & 0.47,
 respectively, strut fracture*, intra-scaffold dissection^φ
 & malapposition[†]

Case 1: BRS Thrombosis

In day 3: acute anterior wall infarction caused by subacute BRS thrombosis, complicated with cardiogenic shock . Put on IABP & underwent successful PCI.

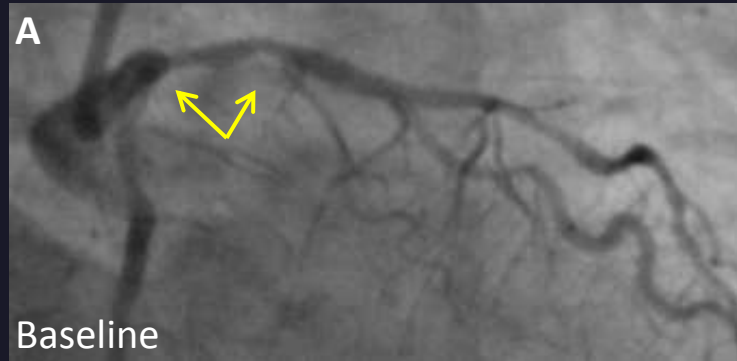


- Patient showed **antiplatelet resistance both to clopidogrel & aspirin** (576 ARU) & genotype analysis indicated a decreased CYP2C19 activity & a poor metabolizer phenotype.
- The patient received 2 DES & was further treated with ticagrelor & higher dose of aspirin
- **Risk factors for BRS thrombosis: suboptimal implantation & DAPT resistance**

Both the **doctor** & the **patient**
are **MORE THROMBOGENIC** than the device

Case 2: BVS Thrombosis

CY. F, 62 yr old, stable angina, **DM**.



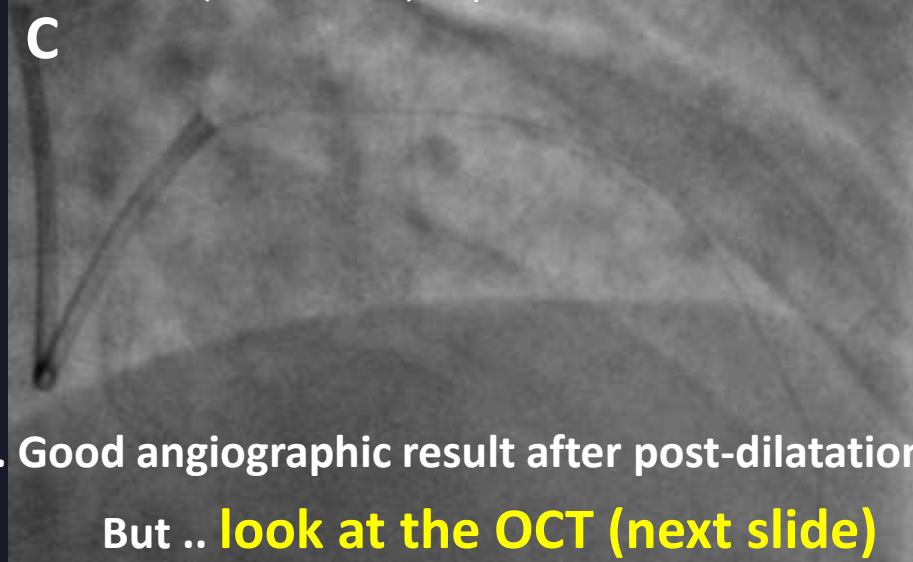
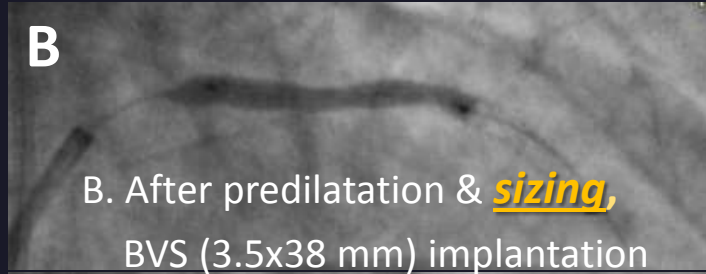
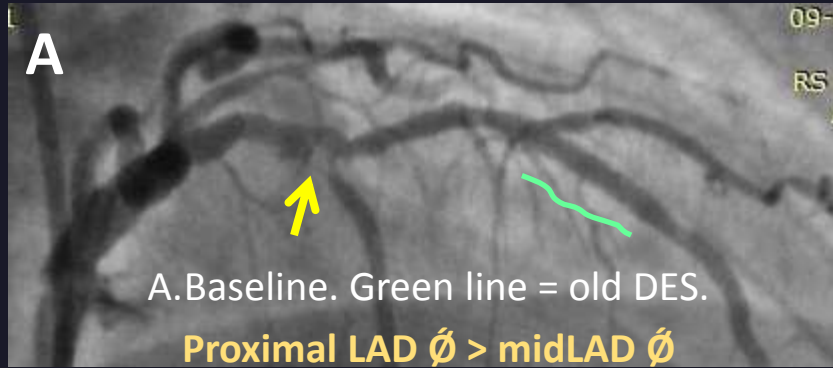
At day 15, upon her own initiative, patient **discontinued her antiplatelet medications** for 5 days as she needed to undergo dental surgery. She developed STEMI caused by subacute BVS thrombosis. Treated with thrombectomy & IC/IV GP2b/2a inhibitor. **Risk factors for ScT: DM & premature DAPT discontinuation**



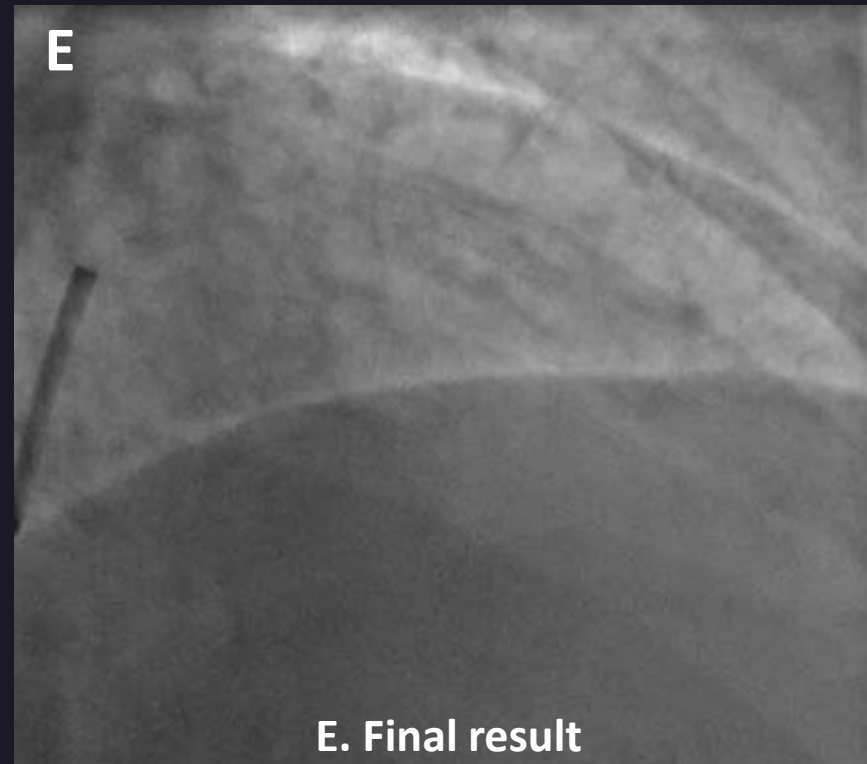
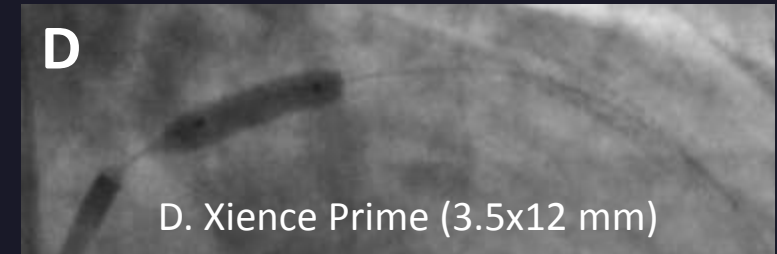
On OCT after thrombectomy, the BVS was concentric, well expanded & well opposed / no malapposition & there were no edge dissection, no fracture. Residual thrombus was present.

The **patient** is **MORE THROMBOGENIC** than the device

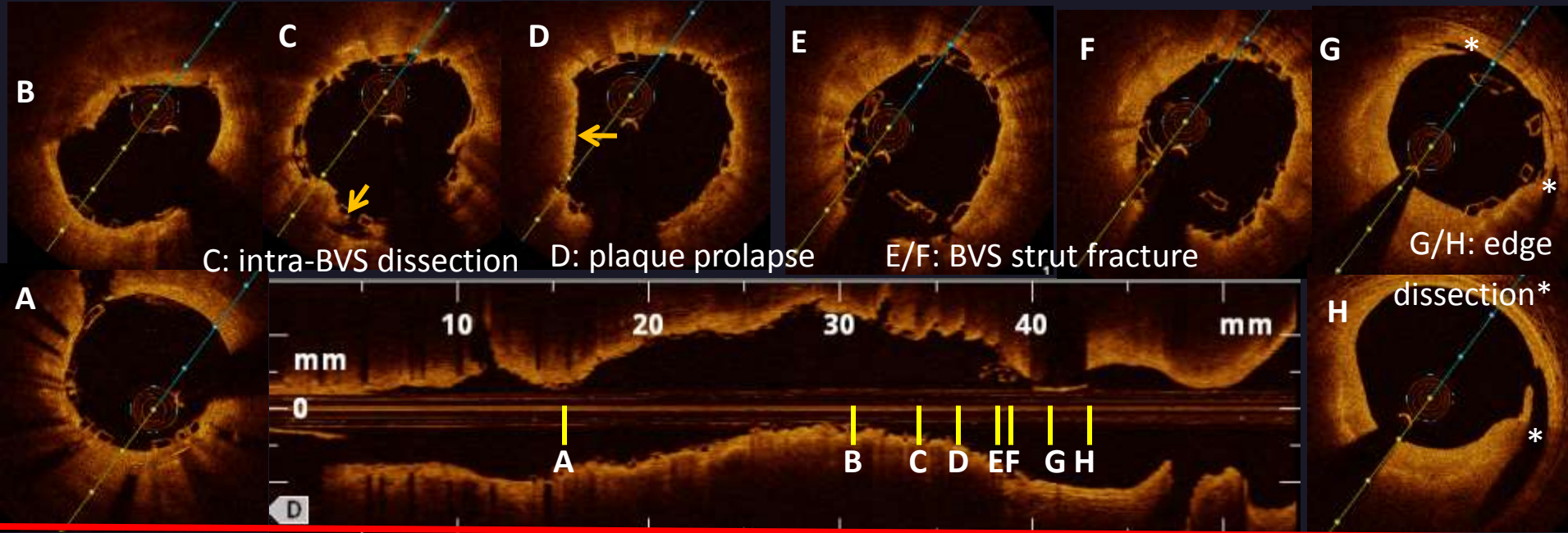
Case 3: Good Angio Result May Not Be Sufficient



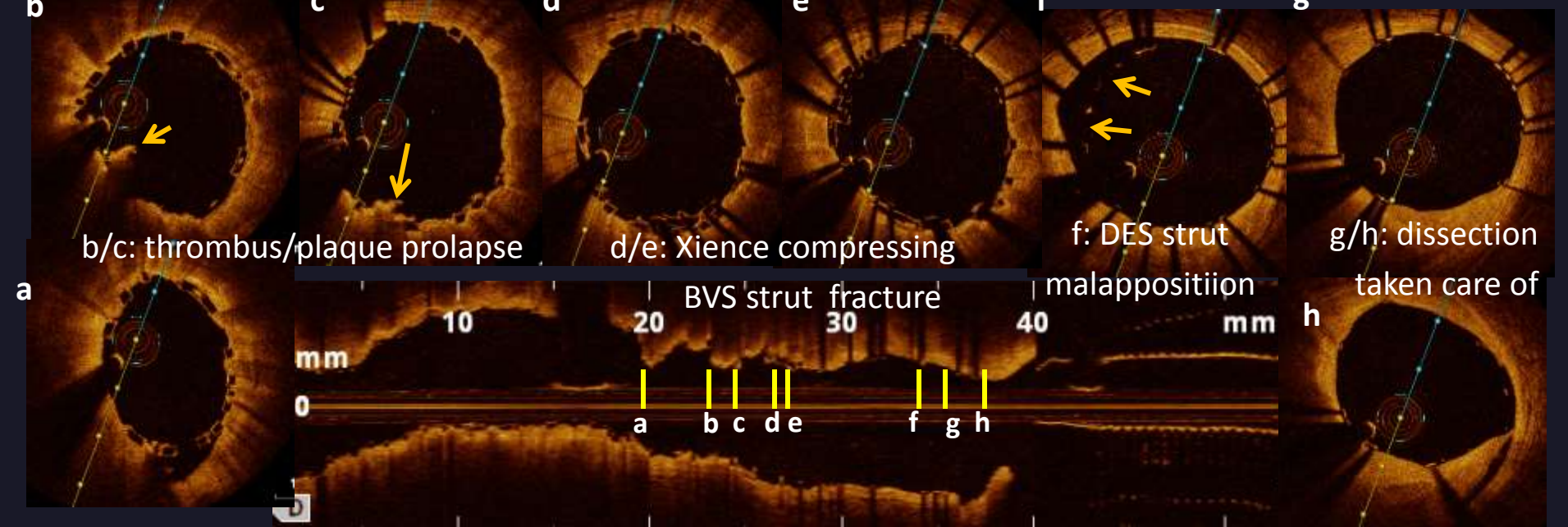
A “Simple Case” With pLAD Stenosis.
PSP strategy was applied



Overdilatation in pLAD led to BVS strut fracture & deep proximal edge dissection



After bail-out with DES (Xience): strut fracture & edge dissection already taken care of

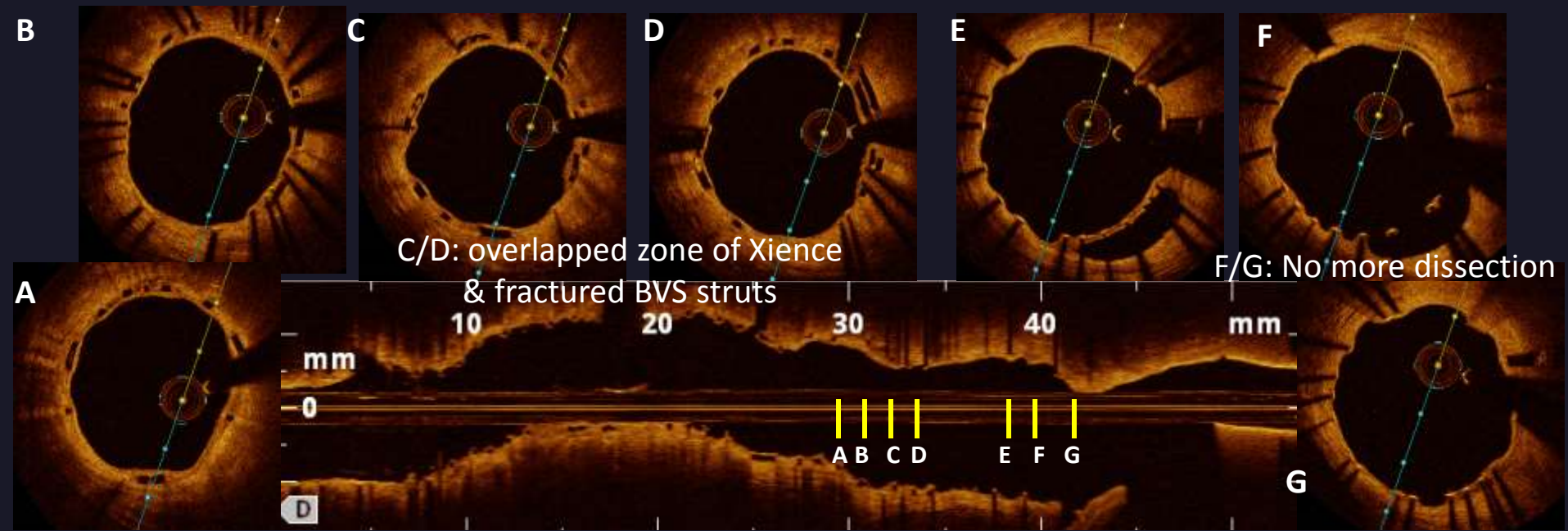


6 Month Follow Up:
No restenosis; No more dissection; & ... No Thrombosis
Patient was doing fine at 2.5 yrs FU

The *doctor* can be **MORE THROMBOGENIC** than the device

No restenosis

E/F: **Nonapposed struts** surrounded by neointimal tissue above the endoluminal border



None Is Perfect And BRS May Also Fail:

But ... We Still Have Gaps In Our Understanding

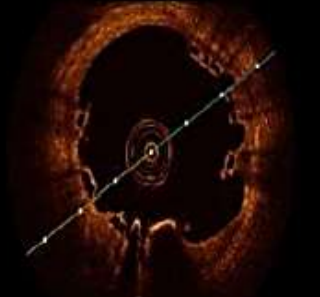
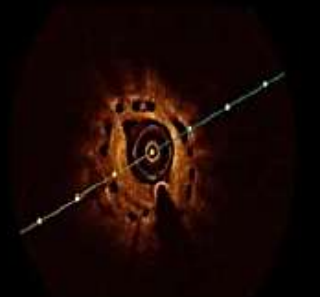
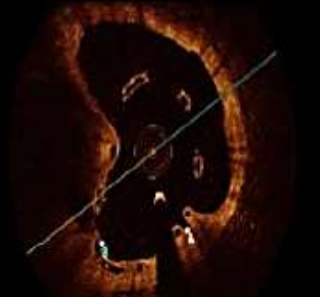
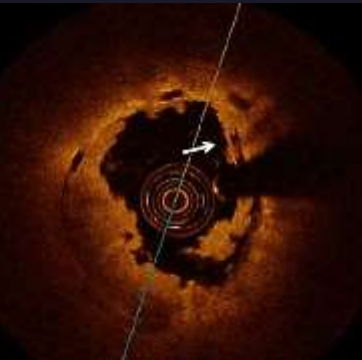
BRS thrombosis:
(most disastrous)

Disruption
Dismantling

Acute or acquired
malapposition

Restenosis
Neoatherosclerosis

Evaginations
Hollows



Is it preventable?
How to treat ?
(arrow: incomplete
strut apposition
[ISA])

To what extent can
be tolerated?. What
is the fate of floating
or embolized struts ?

What is the
incidence & effect of
acute, persistent &
late acquired ISA?

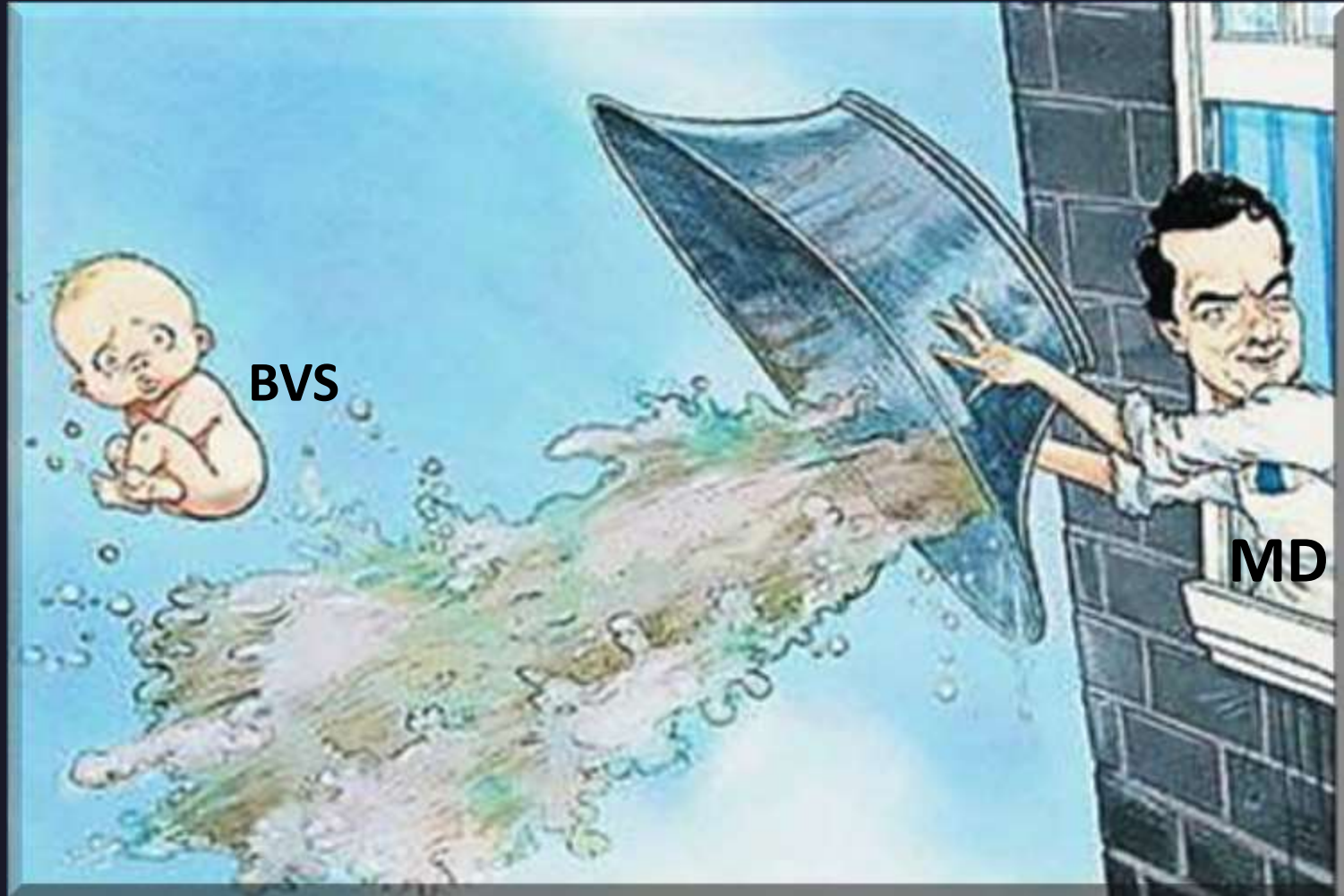
Can we identify
predictors?. Which
treatment strategy?

Cavities & peristurt
contrast staining:
are they innocent
bystander ?

Conclusions

- *BRS thrombosis* is the most dreadful complication of BRS implantation.
- Though strut thickness is one culprit, BRS thrombosis is *multifactorial & all predisposing factors* should also be taken into account
- *Appropriate technique (PSP)* is important, but use of imaging devices (IVUS, OCT, etc) may show that *good angiographic result may not be necessarily acceptable*
- Future of BRS, especially for its application in *complex lesions*, is very dependent on *next generation designs* and availability *long-term clinical data*

Conclusion



Do not throw the baby out with the bath water