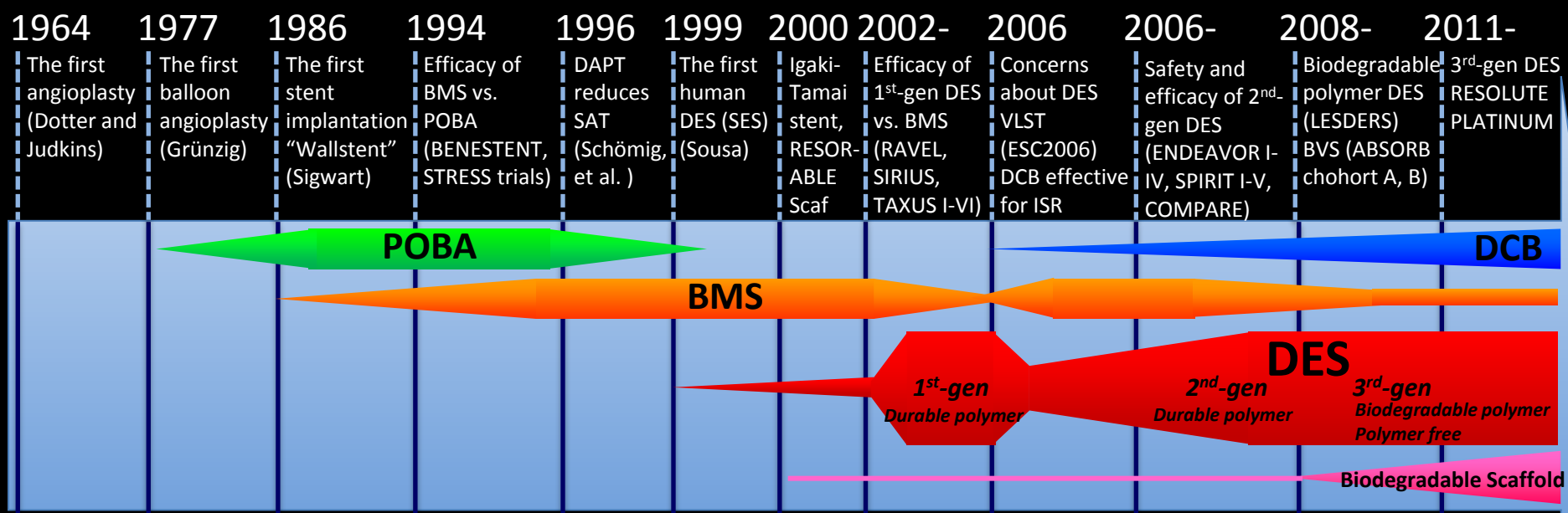


**Bioresorbable Vascular Scaffolds:
No, it is not yet ready**

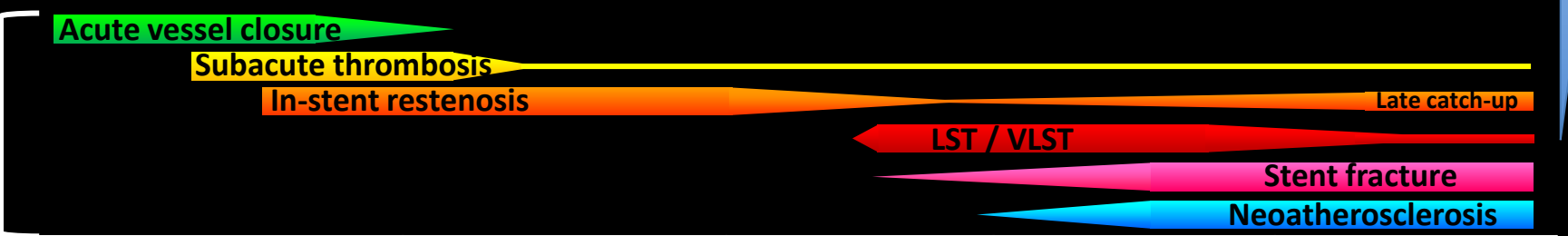
A pathologist's view

**Renu Virmani, MD
CVPath Institute, Inc.
Gaithersburg, MD, USA**

History of Percutaneous Coronary Intervention








Raised Issues



	Balloon Angioplasty	BMS	DES	BRS
Success rate	70-85%	>95%	>95%	>95%
Restenosis	40-45%	20-30%	<10%	<15% ?
Early Thrombosis (≤30 days)	3-5%	1-2%	1-2%	>2% ?
Late Thrombosis (>30 days, ≤1y)	NA	<0.5%	1%	>3% ?
Very Late Thrombosis (>1y)	NA	≈0%	1-2%	Case reports ?

Completely Bioabsorbable Scaffolds



				
Igaki-Tamai	Biotronik	Abbott Vascular	Bioabsorbable Therapeutics, Inc.	REVA Medical
PLLA	Magnesium alloy	PLLA	PAE salicylic acid /	Poly (DTE carbonate)
NA	NA	Everolimus	Sirolimus	Paclitaxel
<ul style="list-style-type: none"> •Zigzag design •Heated balloon deployment 	<ul style="list-style-type: none"> •High collapse pressure •Low elastic recoil 	<ul style="list-style-type: none"> •80% drug release @ 30days 	<ul style="list-style-type: none"> •Anti-inflammatory effect 	<ul style="list-style-type: none"> •Radio-opaque •Ratchet lock design

PLA = poly-L-lactide, PAE = poly (anhydride ester), DTE = desaminotyrosyl-tyrpsine ethyl ester

Arterial Remodeling Technologies



PLDA
No drug

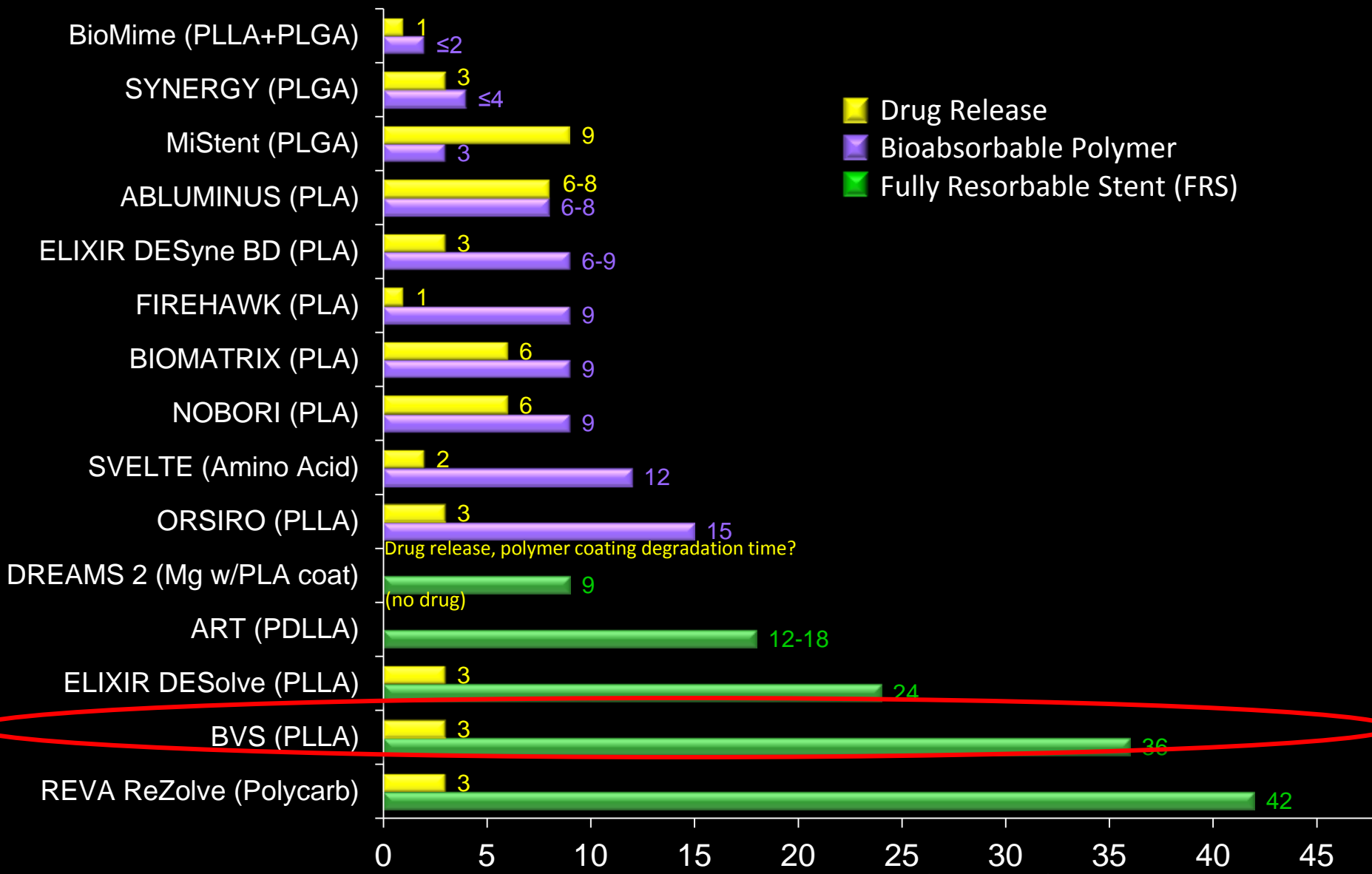
ELIXIR: DESolve Bioabsorbable Coronary Scaffold



PLLA resorbes in 2 years,
Myolimus Eluting

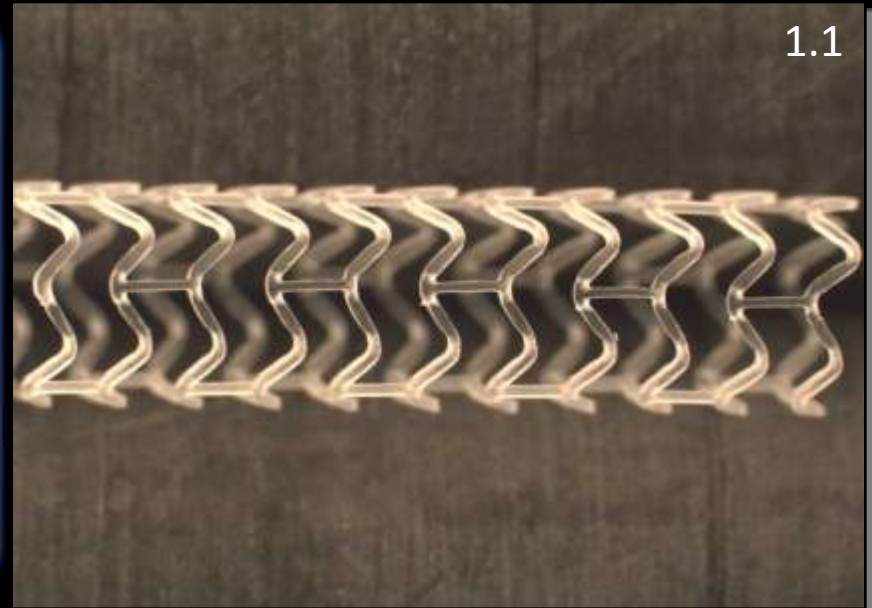
Time Course For Polymer Bioabsorption

Not all bioabsorbable technologies are the same

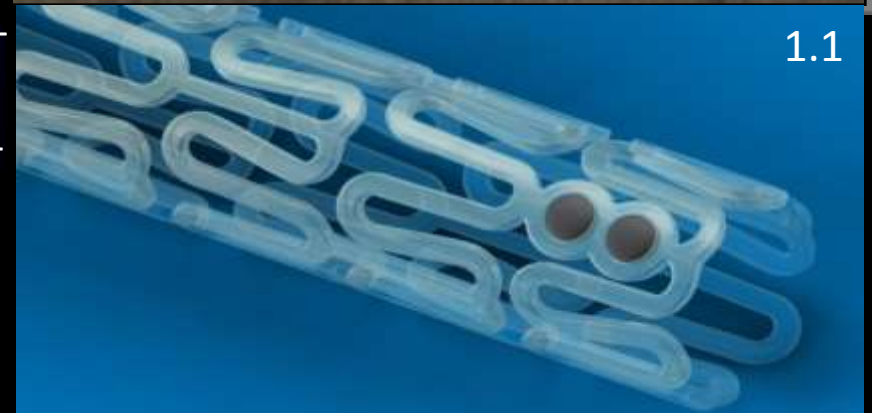


The SYNERGY™ stent is an investigational device and not for sale in the US. CE Mark Approved 2012. Information for SYNERGY is for use in countries with applicable product registrations

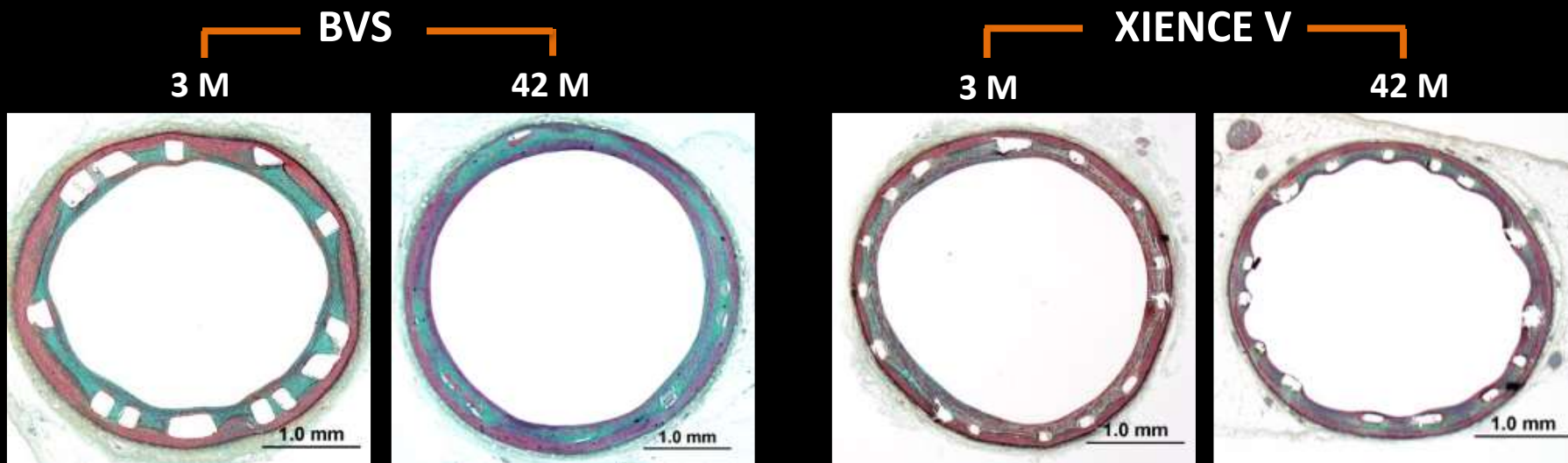
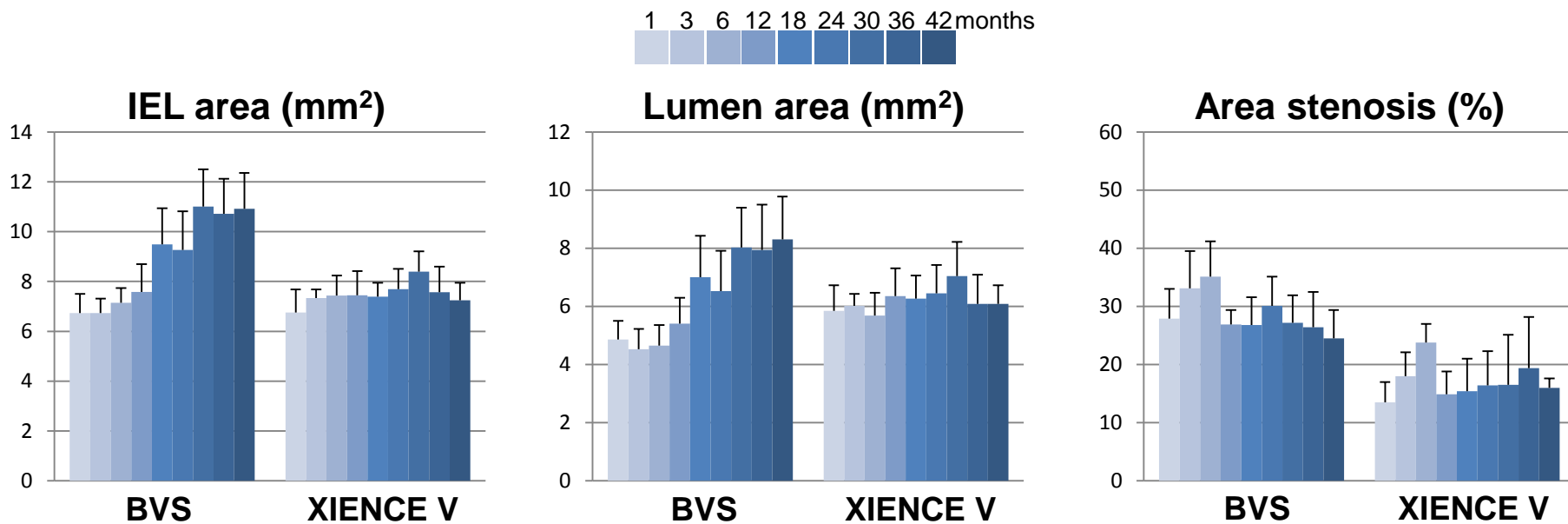
Absorb BVS 1.1



Absorb BVS is a balloon expandable, drug-eluting device with a backbone of poly-L-lactide coated with poly-D, L-lactide. Poly-D lactide backbone solidifies into a crystalline and amorphous phases with a strut thickness of 150 μm . The coating poly-D, L-lactide on the surface of BVS elutes slowly everolimus

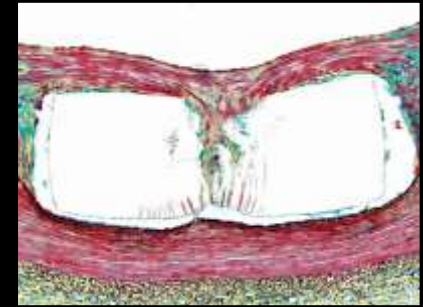
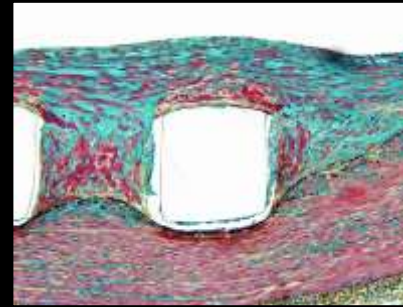
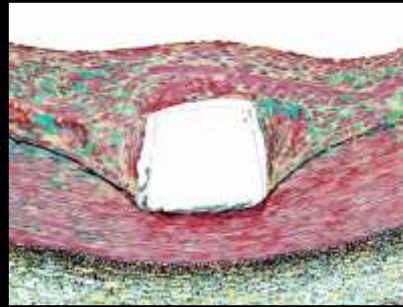
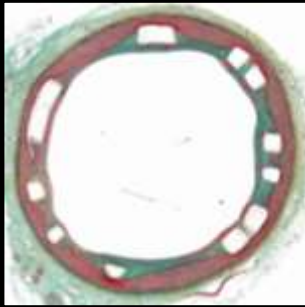


Morphometric Analysis of BVS and XIENCE V in Porcine Coronary Model – Cohort B



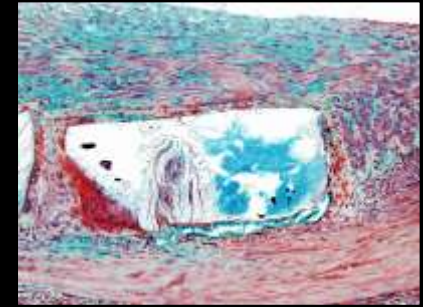
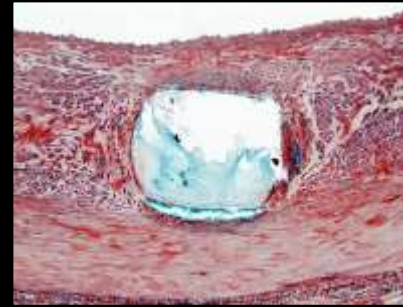
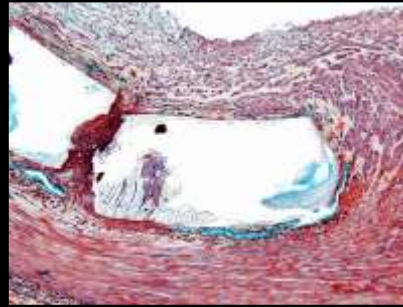
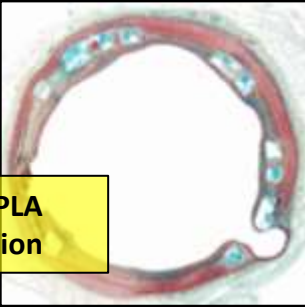
Degradation of BVS (Cohort B) in Porcine Coronary Arteries

3 M



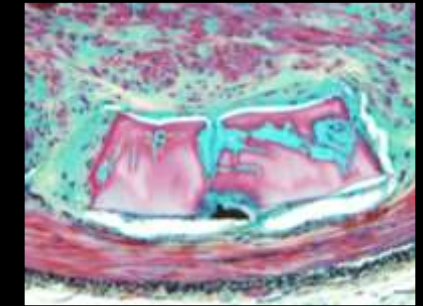
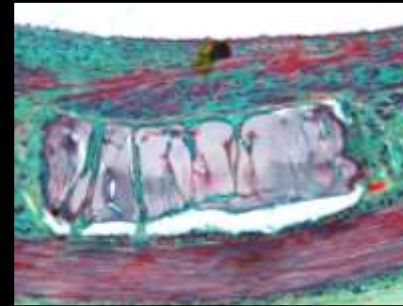
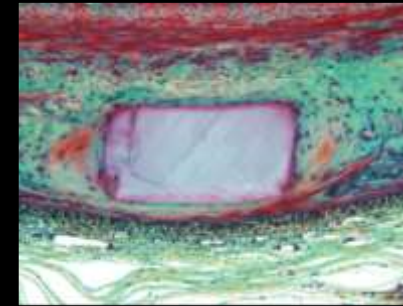
24 M

Active PLA
resorption



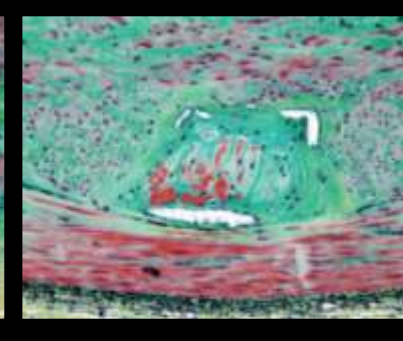
36 M

Replacement with
provisional matrix

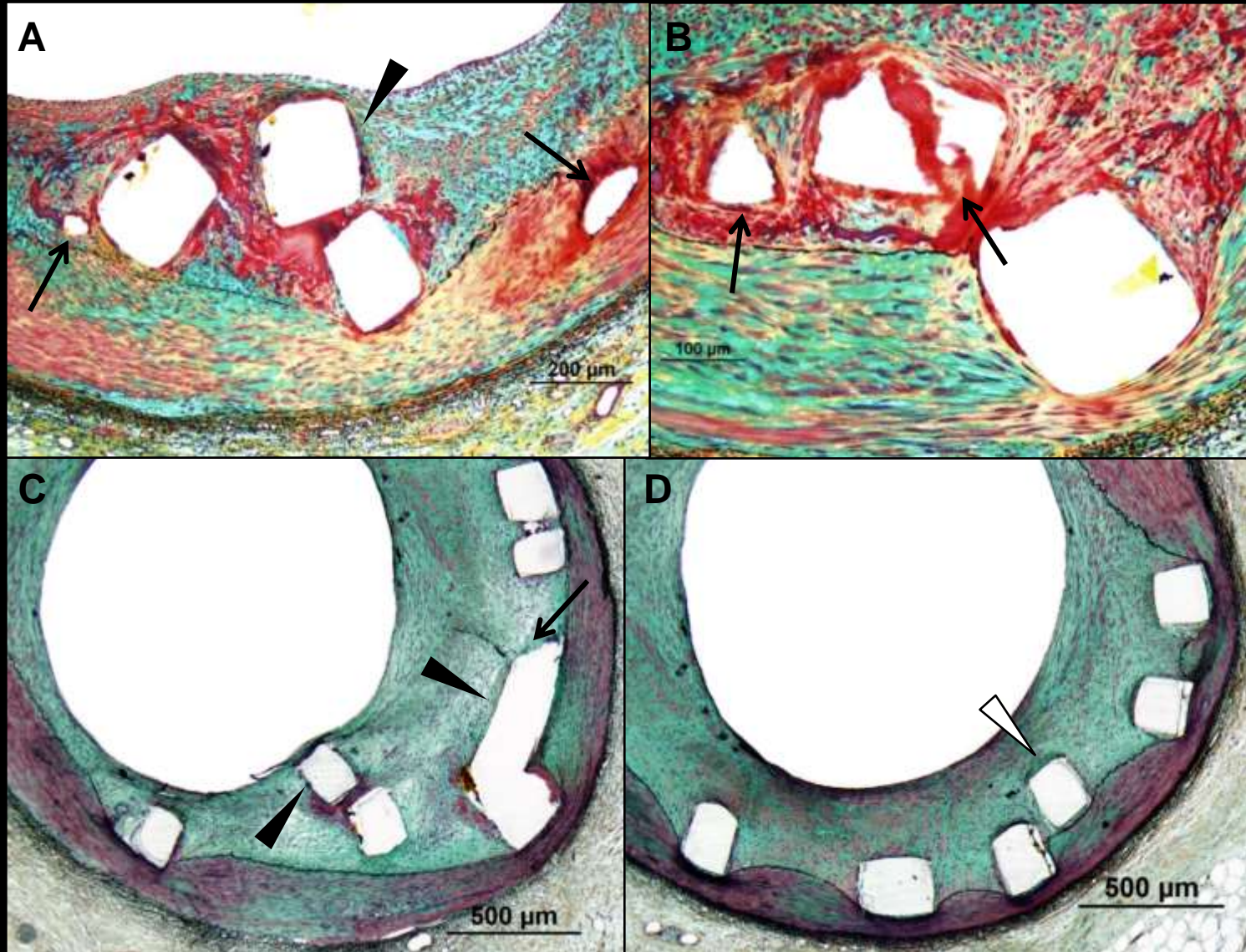


42 M

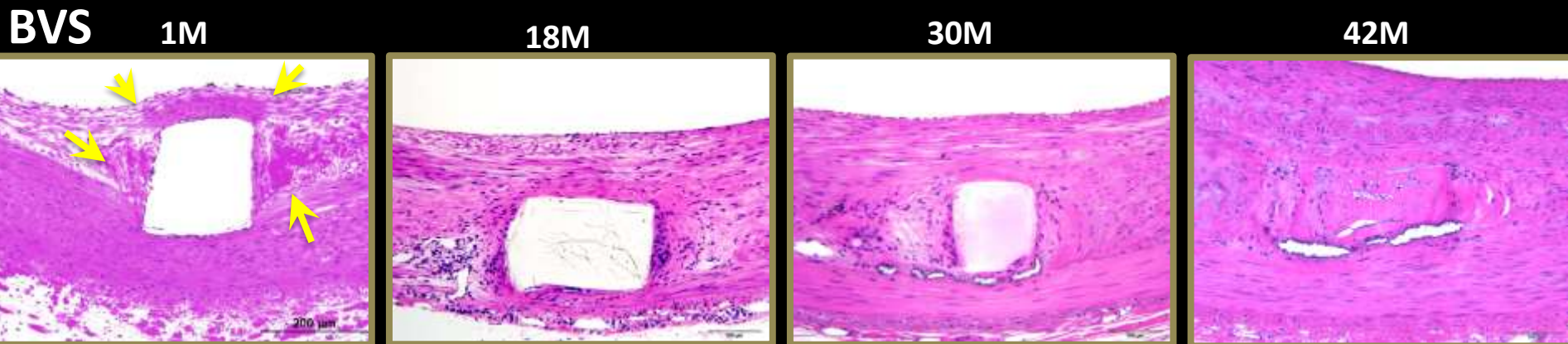
Provisional matrix
maturation &
Connective tissue
replacement



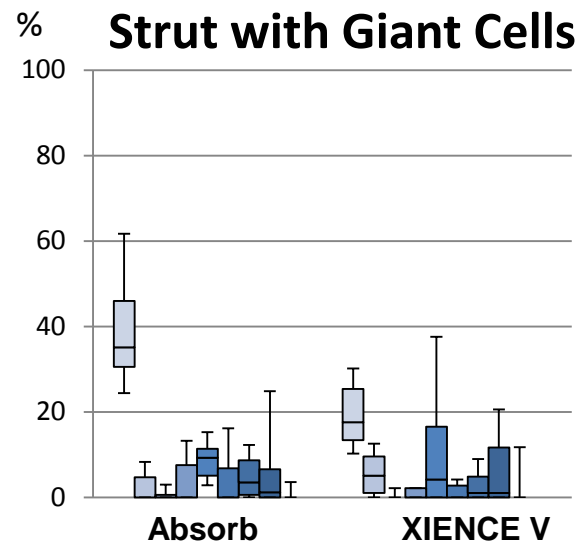
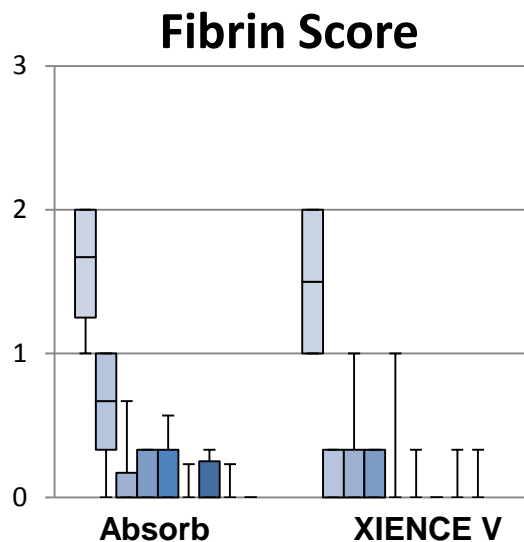
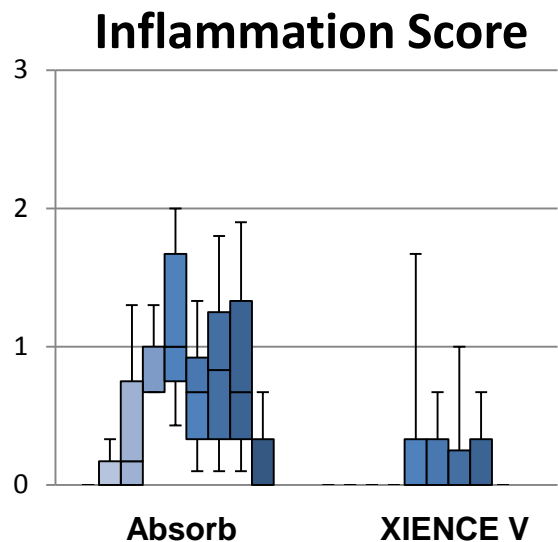
Discontinuities of scaffolds observed in two arteries implanted with Absorb



Inflammatory Reaction to BVS and Xience V – Cohort B



← 1M, 3M, 6M, 12M, 18M, 24M, 30M, 36M, 42M →



Severe granulomas were observed in 3/102 stents (3%) of BVS, and 4/67stents (6%) of Xience V, which were excluded from analysis.

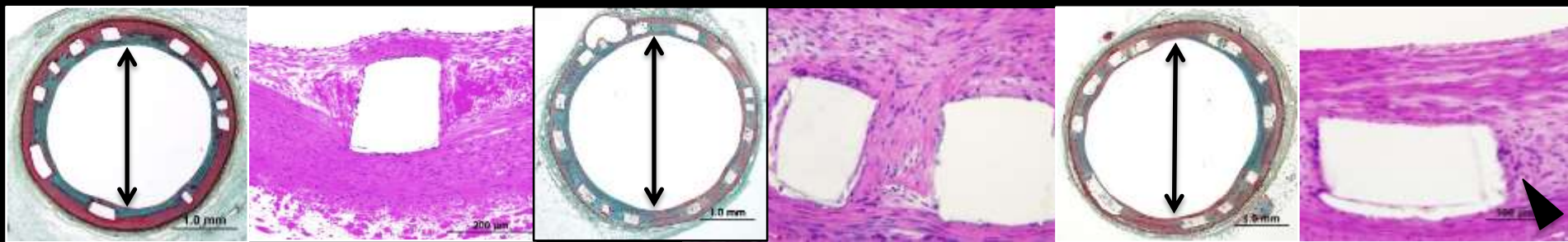
Association Between Inflammation and Lumen Area in BVS

Absorb

1 Mo

6 Mo

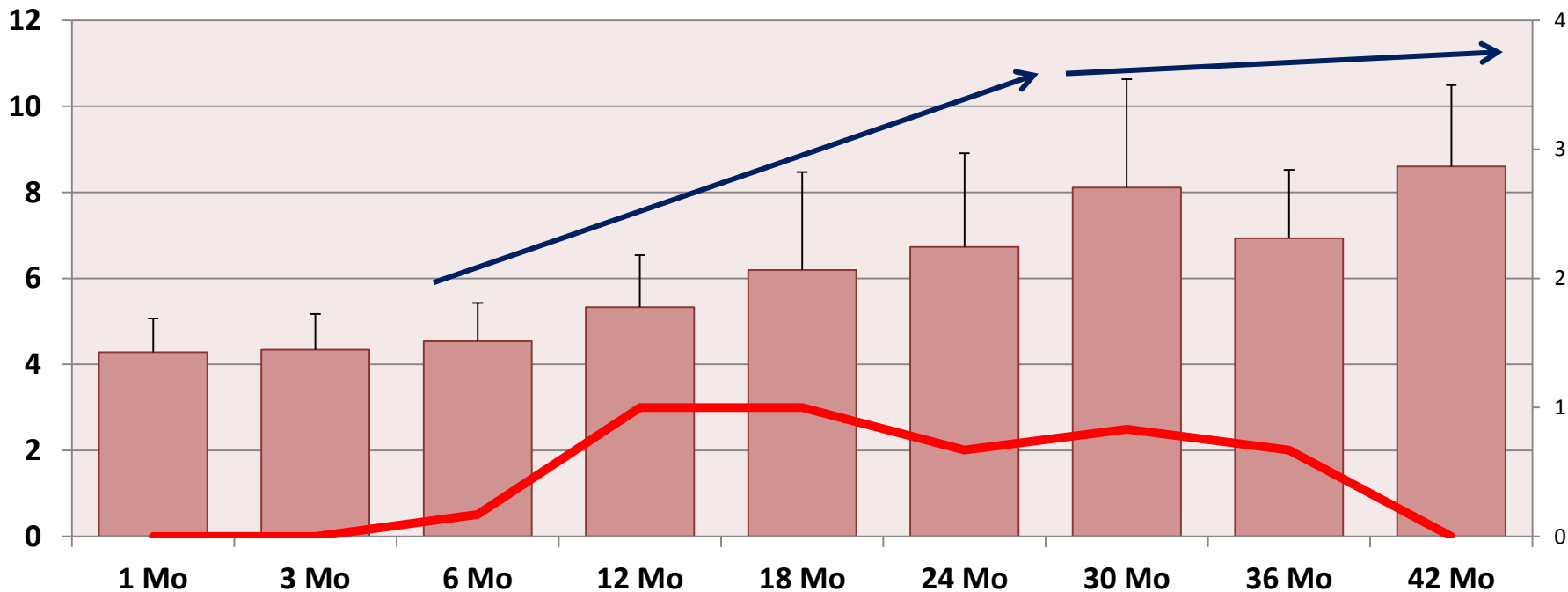
18 Mo



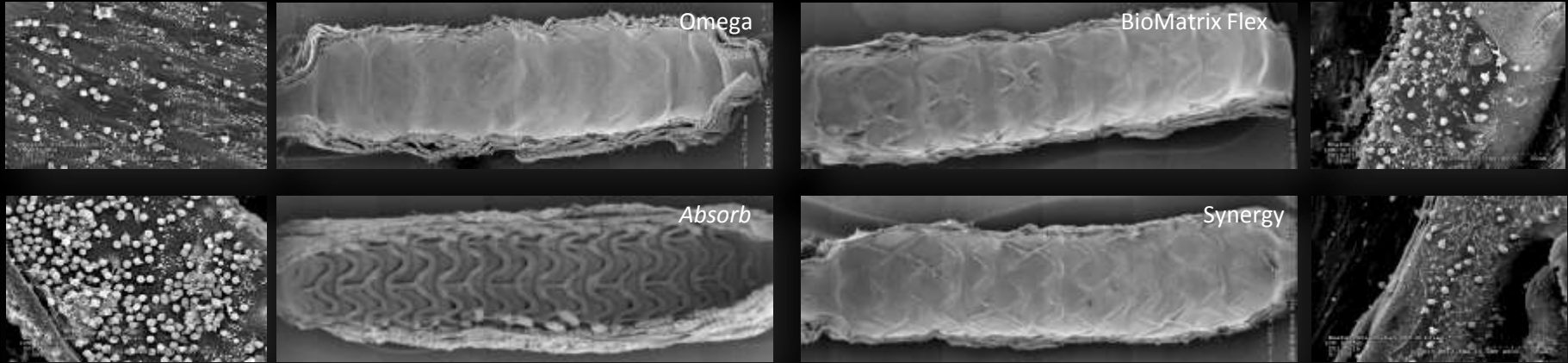
(mm²)

Lumen area by OCT

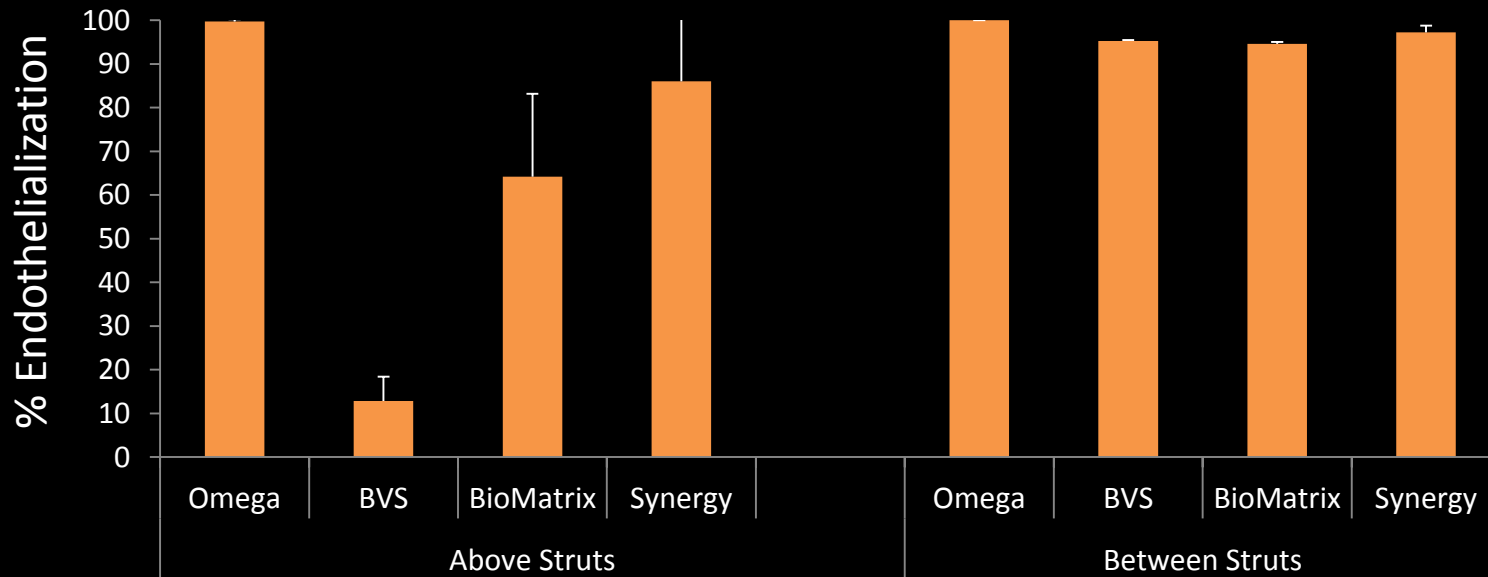
Inflammation score



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



$p < 0.0001$

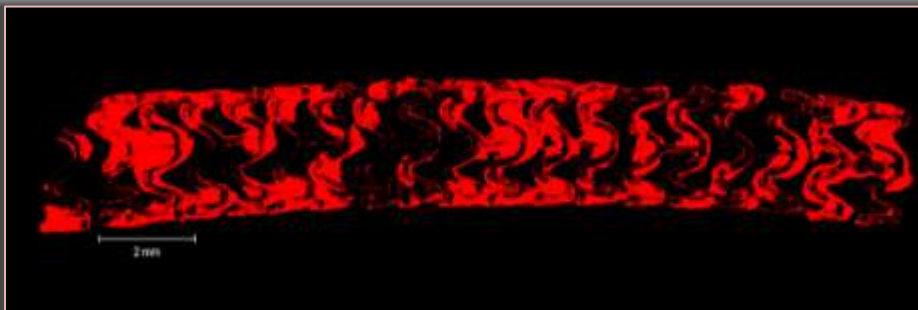


Impact of Strut Thickness on Thrombogenicity

Thicker Struts Associated with Increased Acute Thrombogenicity

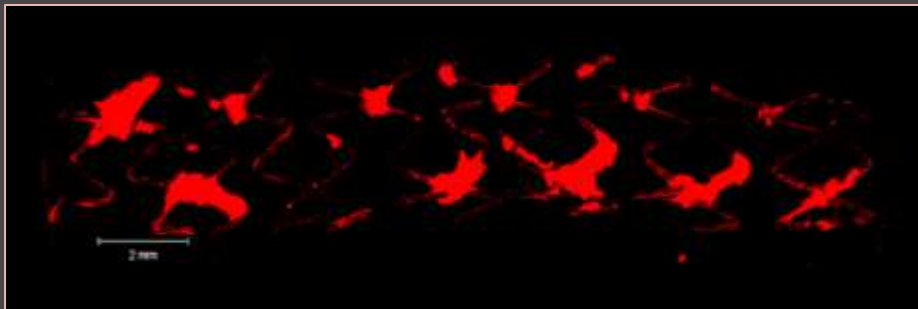
150 μm

Absorb



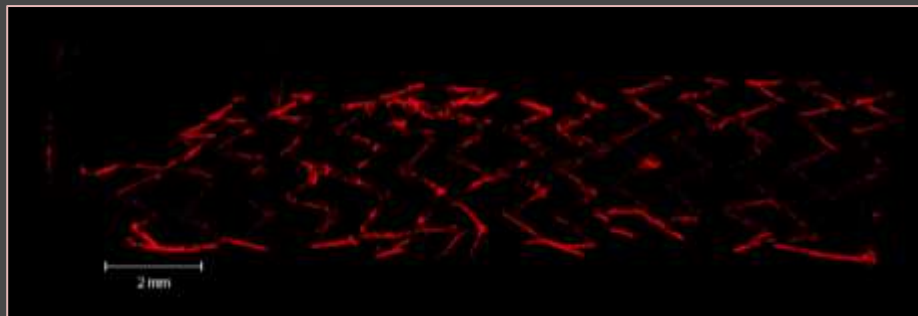
120 μm

BioMatrix Flex

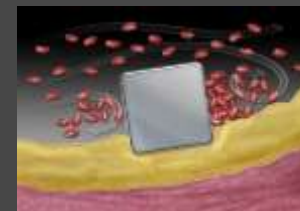


74 μm

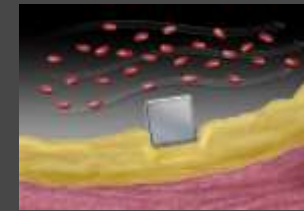
Synergy



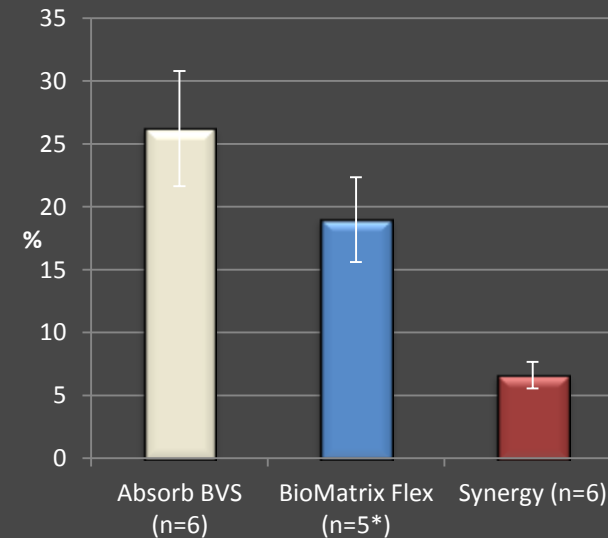
Thick Strut DES



Thin Strut DES



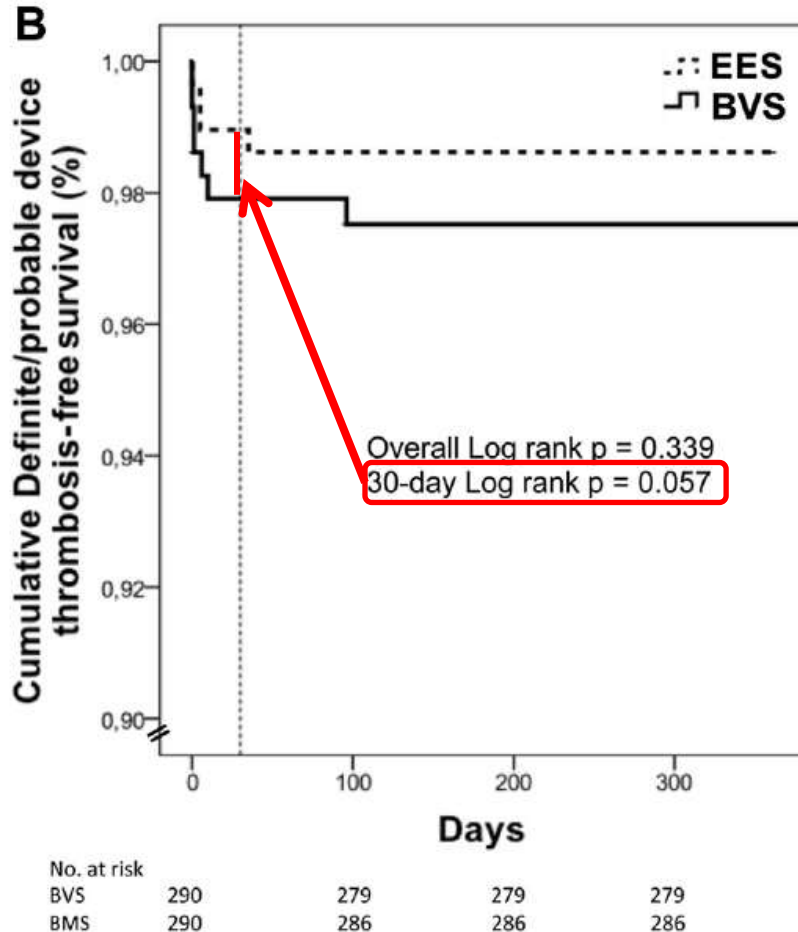
Mean positive area of adherent platelets



Thrombus formation assessed by immunofluorescence staining for platelet marker CD61 after 1 hour in ex-vivo pig AV shunt model
Modified from Koskinas et al. *J Am Coll Cardiol* 2012;59:1337-49

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)

Stent thrombosis in perspective from “all comer” clinical studies?

First generation sirolimus and paclitaxel eluting DES :
Windecker S. et al.
SIRTAX

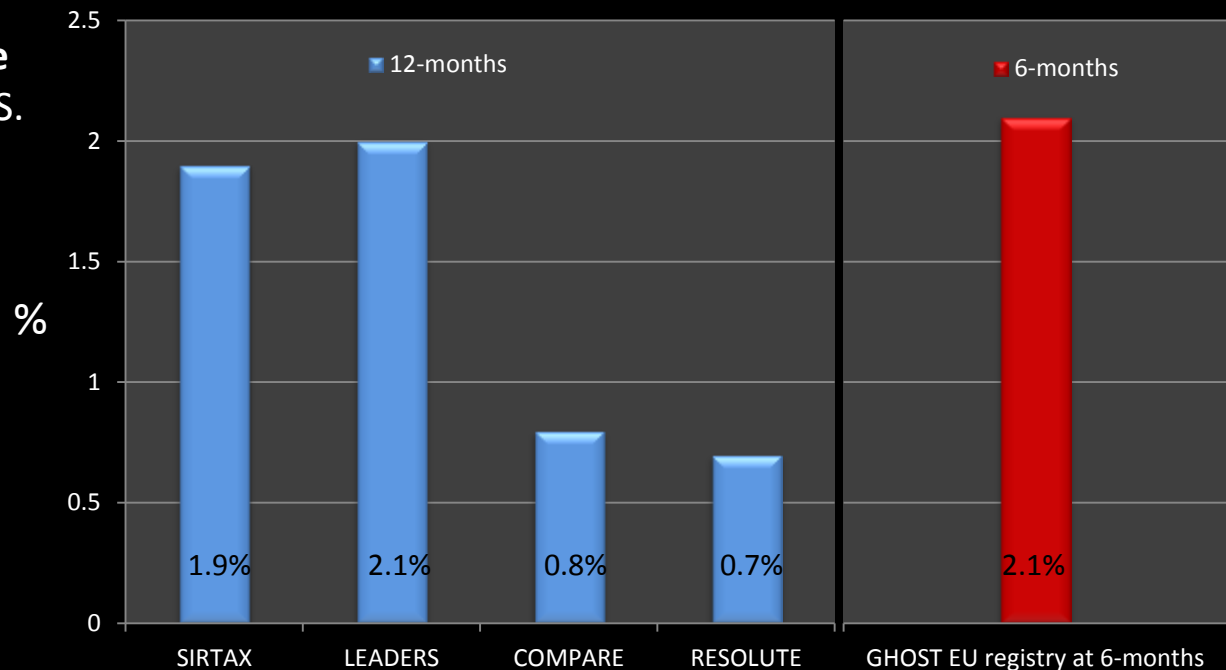
Second generation biodegradable biolimus eluting DES: Windecker S. et al. LEADERS

Second-generation everolimus-eluting DES:
Kedhi E. et al. COMPARE

Second generation zotarolimus-eluting DES:
Serruys PW et al. RESOLUTE

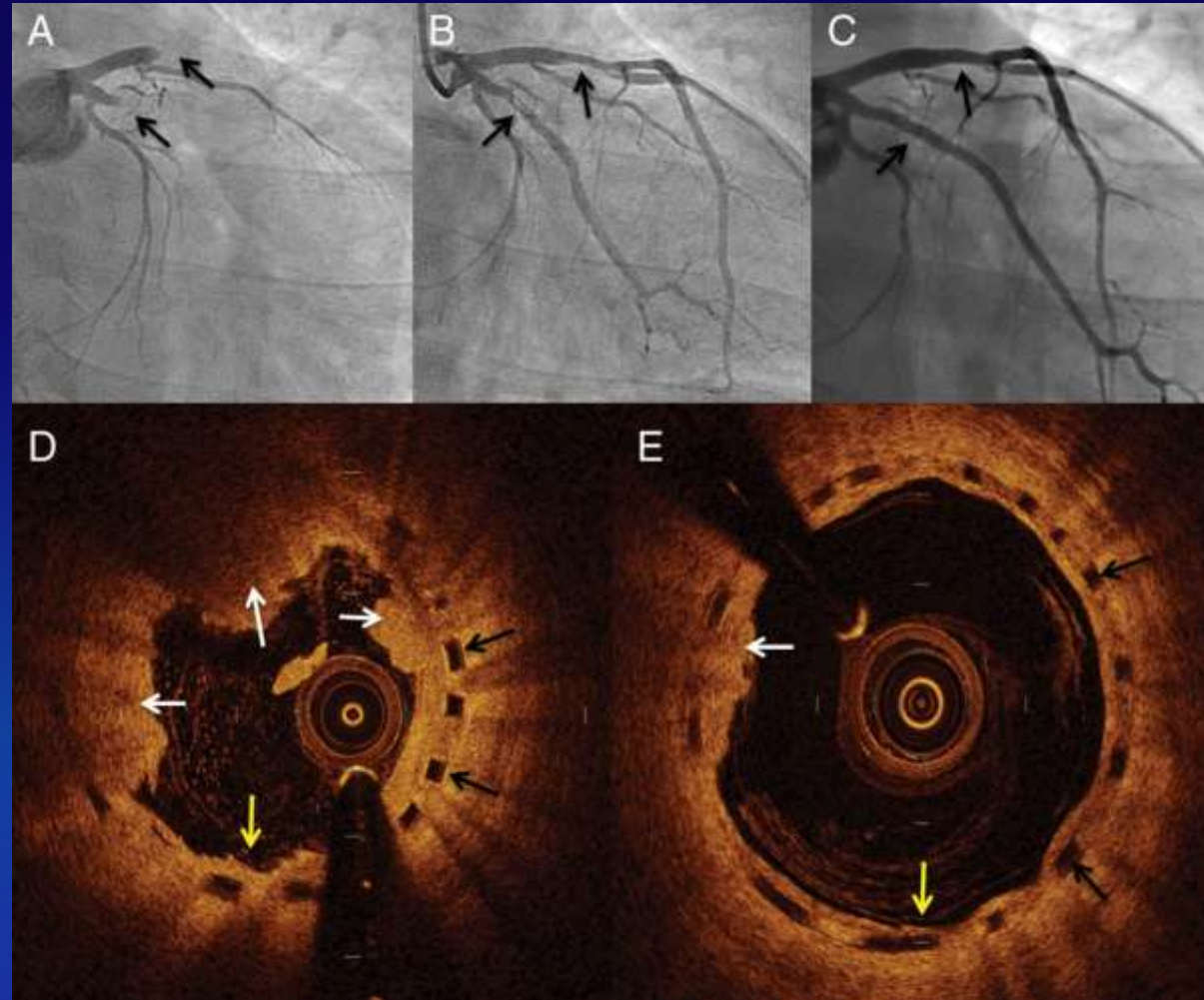
Everolimus-eluting bioresorbable scaffolds (BVS): Capodanno et al. GHOST-EU registry

ARC definitive/probable stent thrombosis



Very late bioresorbable vascular scaffold thrombosis following discontinuation of antiplatelet therapy

A 39-year-old man was referred to catheterization laboratory with an acute anterolateral myocardial infarction. 18 months before, he received bioresorbable vascular scaffolds (BVS) in the left anterior descending coronary artery (LAD) and obtuse marginal (OM) branch. After 12 months of treatment with aspirin and clopidogrel, both medications were discontinued as advised by the treating cardiologist.



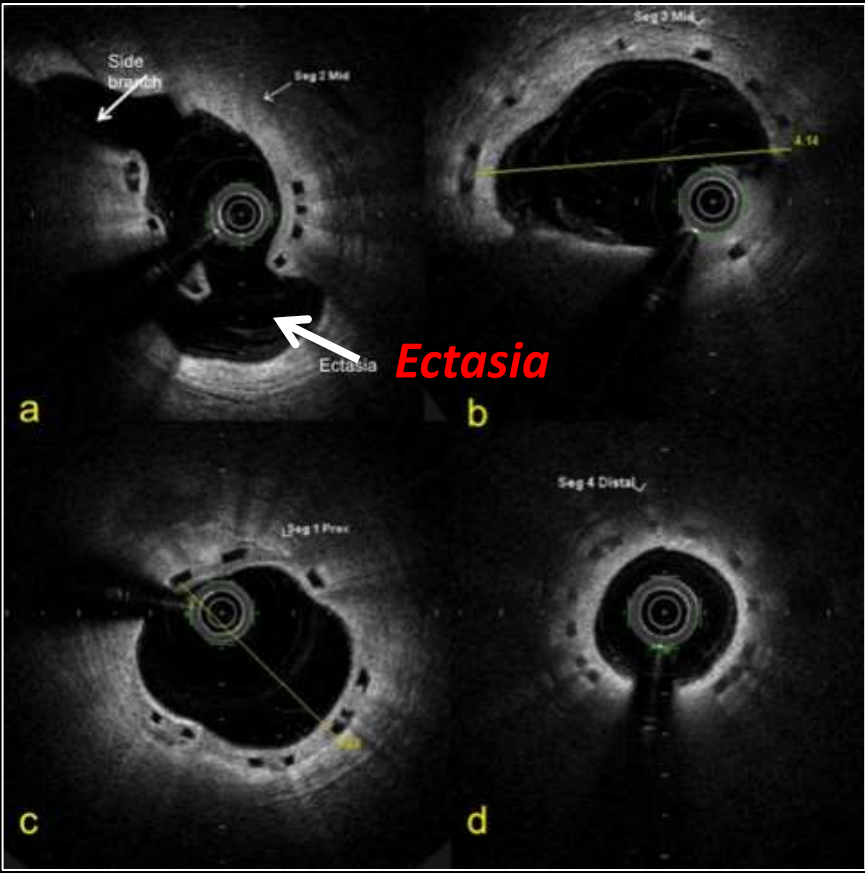
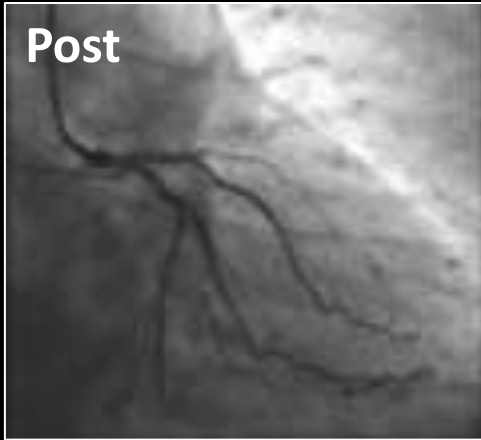
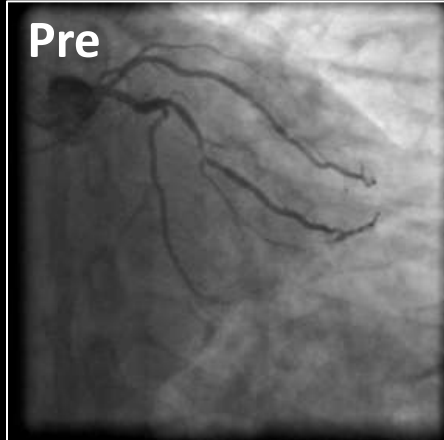
3 days following Rx with aspirin, ticagrelor, and tirofiban, see E

Late coronary BVS malapposition and aneurysm

A 54-year-old man with unstable angina underwent percutaneous-coronary-intervention (PCI) for a tight stenosis of a marginal branch.

Treatment: Absorb 2.5 x 18mm (Abbott Vascular, CA)

OFDI images



Case reports of late BRS failure

➤ Very Late Scaffold Thrombosis (VLST)

	Author	Age	Sex	Treatment	Duration	Symptom	DAPT
1	Karanasos A, et al.	57	Male	Absorb	24 months	Unstable angina	DAPT were discontinued 4 days prior to ST
2	Timmers L, et al.	39	Male	Absorb	18 months	Acute myocardial infarction	DAPT were discontinued after 12 months of implantation
3	Sato T, et al.	47	Male	Absorb	22 months	Atypical symptoms	Treated with antiplatelets and oral anticoagulation due to atrial fibrillation Antiplatelet therapy was discontinued after 6 months of implantation.
4	Kesavamoorthy B, et al.	42	Male	Absorb (3.0x28 mm)	15 months	Acute coronary syndrome	DAPT were discontinued 1 months prior to ST

Karanasos A. et al. Eur Heart J. 2014;35:1781
Timmers L. et al. Eur Heart J. 2015;36(6):393
Sato T. et al. Eur Heart J. 2015 [Epub ahead of print]

➤ Malapposition / Aneurysm

	Author	Age	Sex	Treatment	Duration	Symptom
1	Cortese B, et al.	54	Male	Absorb (2.5x18 mm)	11 months	atypical effort angina
2	Cortese B, et al.	56	Female	Absorb (3.5 x12 mm)	2 months	None (scheduled PCI)
3	Nakatani S, et al.	83	Male	Absorb (3.0x18mm)	6 months	None (follow-up angiography)

Cortese B. et al. Catheter Cardiovasc Interv. 2014 [Epub ahead of print]
Nakatani S. et al. Circulation 2015;131:764-7

All publications by Dr. Surreys
regarding Absorb BVS Studies are
Positive only those by other authors
do seem to suggest CAUTION



**“He is the Guru
of Absorb BVS”**

“ ”



Summary

Bioresorbable Vascular Scaffolds:

No, it is not yet ready

➤ Major issues were identified by histopathological evaluation of BRS on a preclinical level:

- Degradation of stent struts is associated with dismantling of the structural integrity and loss of radial strength.
- Bioresorption of polymeric BRS is associated with increased inflammatory reaction.
- Acute Thrombogenicity is increased with current BRS technology
- Re-endothelialization of stent struts is delayed with current bioresorbable EES technology when compared to contemporary metallic EES.

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