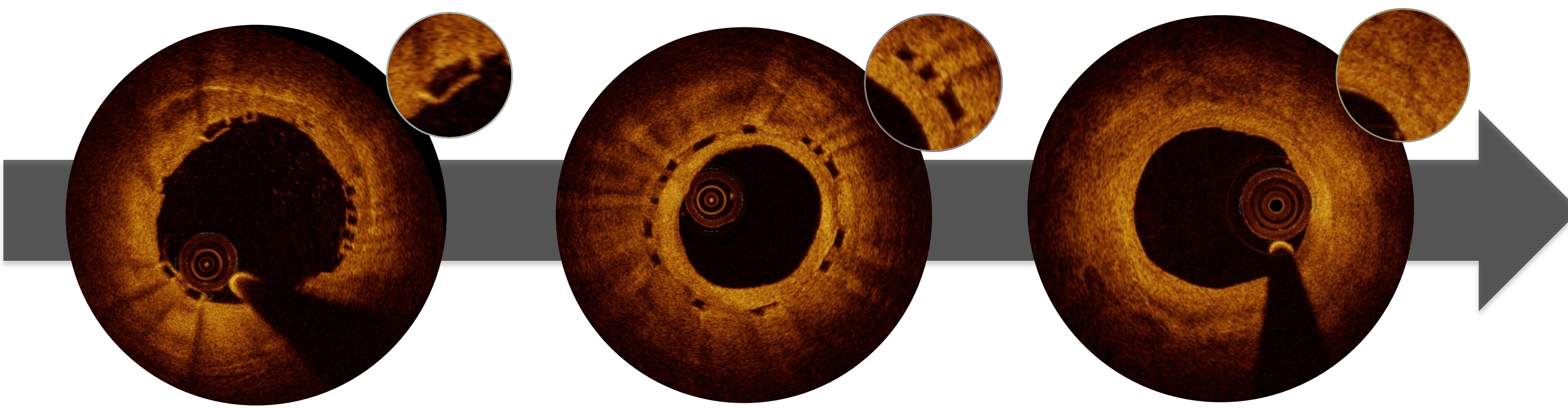
Bioresorbable Scaffolds, MTE Lugano 2016

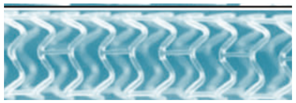
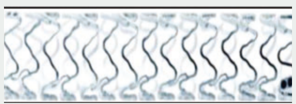
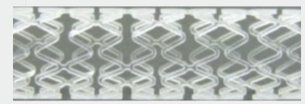
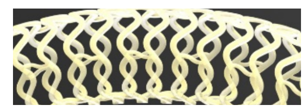
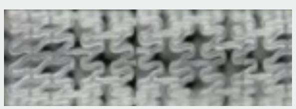
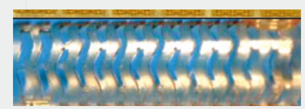
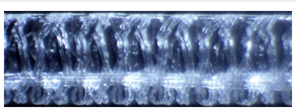
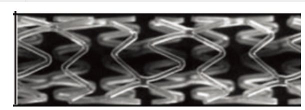
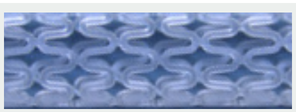
Current limitations
Future perspectives

Lorenz Räber, MD, PhD
Bern University Hospital



Bioresorbable scaffolds

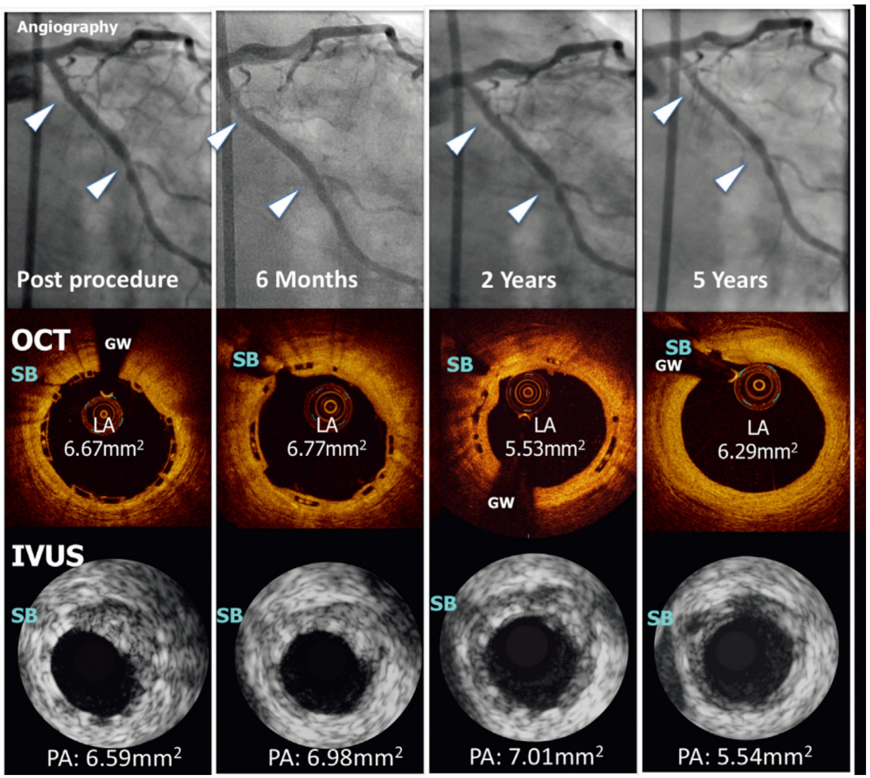
Iqbal J et al. Eur Heart J 2014; 35:765–776, updated

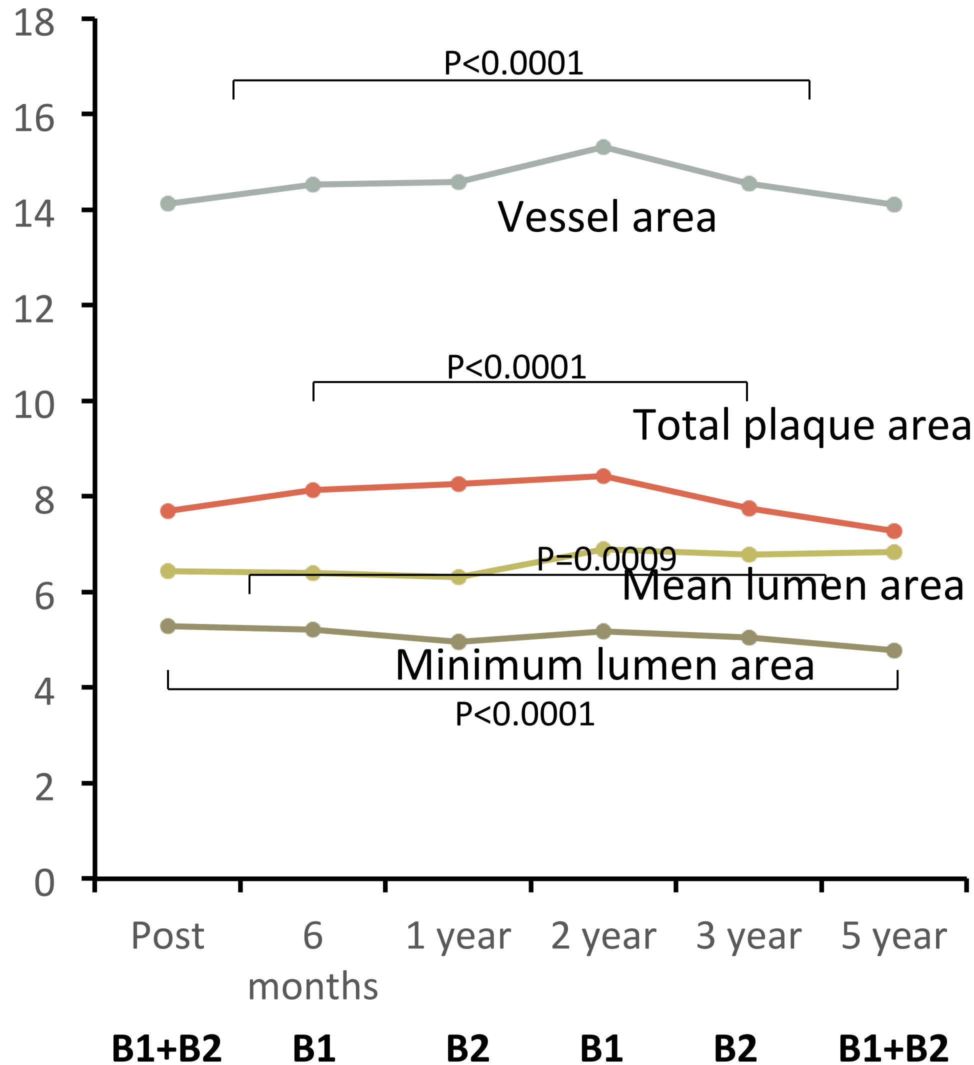
Scaffold		Material	Drug	Scaffold		Material	Drug
Igaki-Tamai (Kyoto Medical)		PLLA	None	**ART18Z (ART)**		PDLLA	None
BVS 1.1 (Abbott Vascular)		PLLA	Everolimus	**DESolve 150/100* (Elixir)**		PLLA	Novolimus
DREAMS 2 (Biotronik)		Mg	Sirolimus	Xinsorb (Huaan)		PLLA+PCL +PLGA	Sirolimus
Fortitude (Amaranth)		PLLA	Sirolimus	Fantom* (REVA)		PTD-PC	Sirolimus
MeRes100 (Meril)		PLLA	Sirolimus	IDEAL biostent (Xenogenics)		Polylactide and salicylates	Sirolimus
Mirage BRMS		PLLA	Sirolimus	ON-AVS (Orbus Neich)		PLLA+PCL +PDLLA	Sirolimus CD34+
ArterioSorb* (Arterius)		PLLA	Sirolimus	FAST (Boston Scientific)	Not available	Not available	Everolimus

Bold: CE approval, Red: clinical study results available, Plain: clinical study ongoing/animal data

* Data will be presented in EuroPCR 2016

Serial IVUS follow-up: ABSORB B1+B2



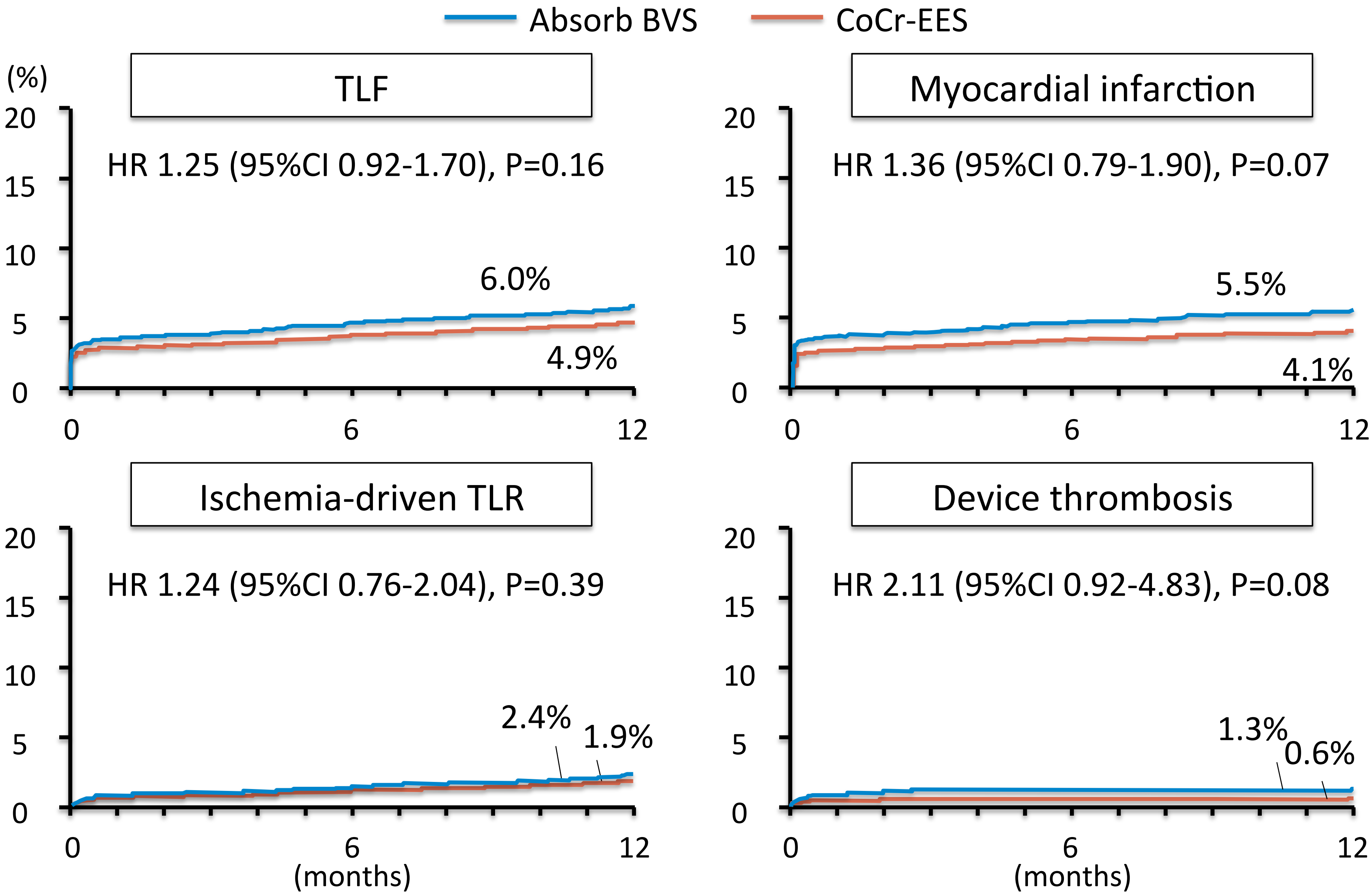


Serruys et al. JACC 2016;7:766-76.

P< 0.004 is regarded as significant (Bonferroni correction).

Patient-level pooled analysis (1-year, N=3389) of ABSORB II, ABSORB Japan, ABSORB China, ABSORB III

Stone et al. Lancet 2016



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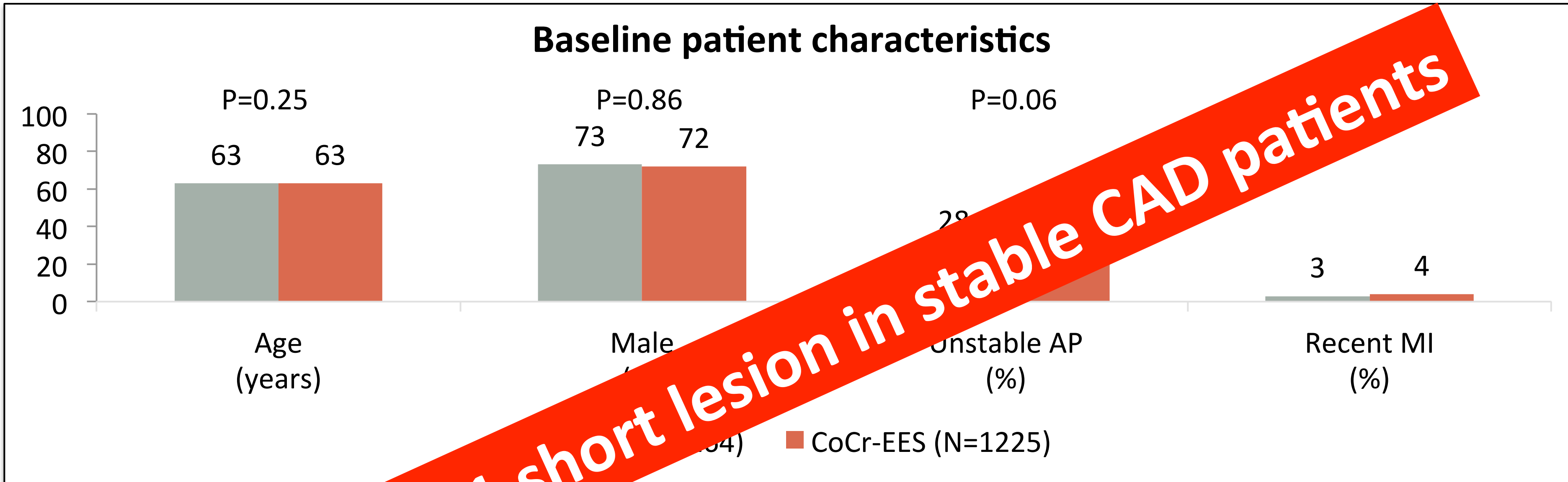
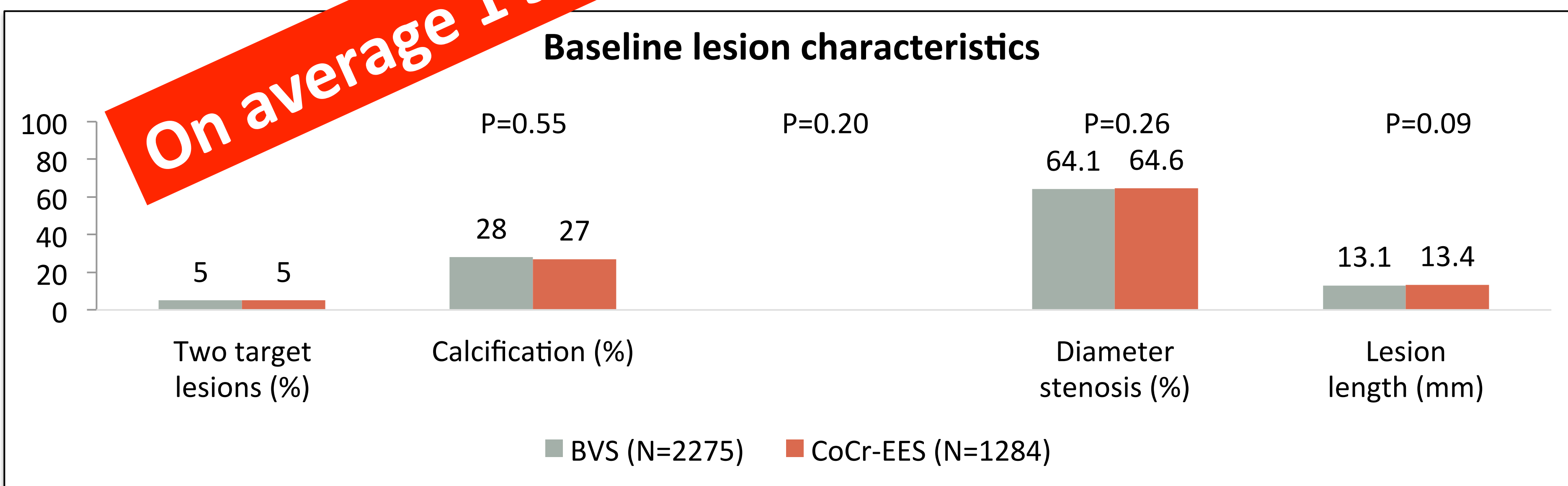
Stone et al. Lancet 2016





On average 1 short lesion in stable CAD patients

First-generation BRS

Resolved*

- Plaque reduction and return of vasomotion in stable CAD low risk lesions
- Equivalent performance in terms of MACE in low risk stable CAD patients
- Similar device efficacy despite angiographic inferiority
- Potential disadvantage in device safety (MI and stent thrombosis)

*applicable for BVS ABSORB 1.1

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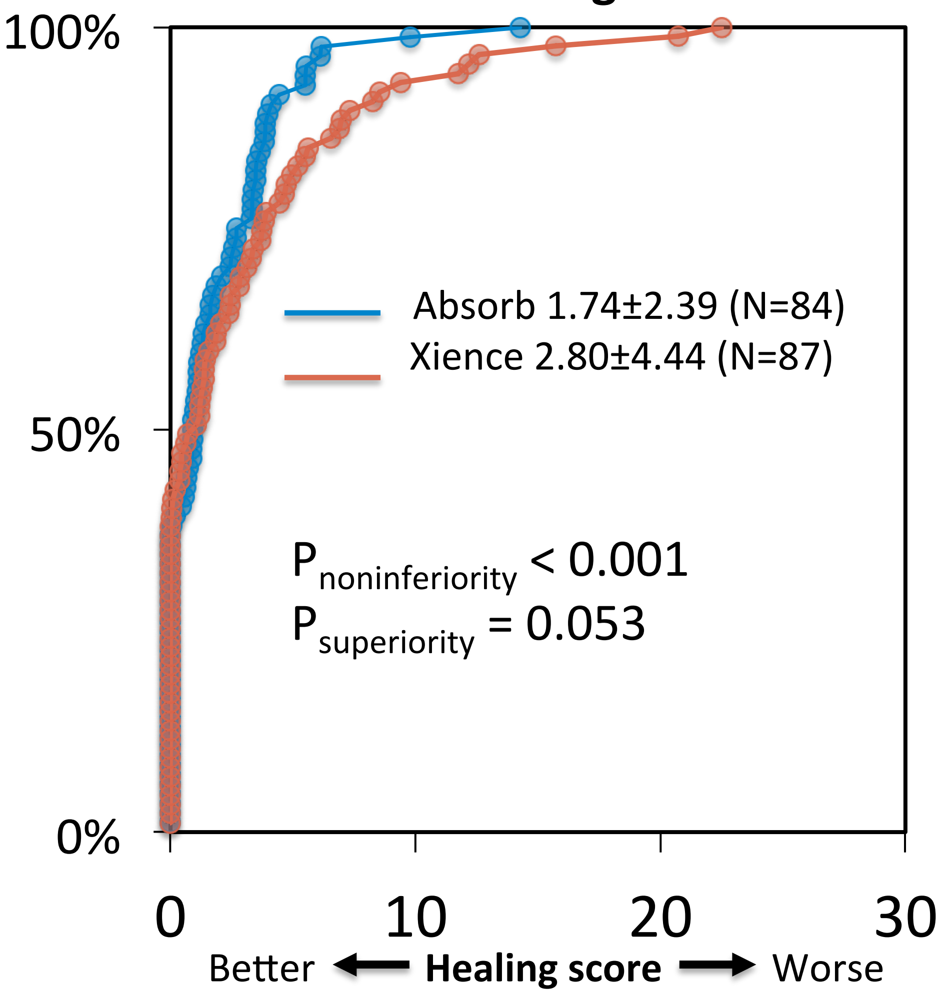
Unresolved

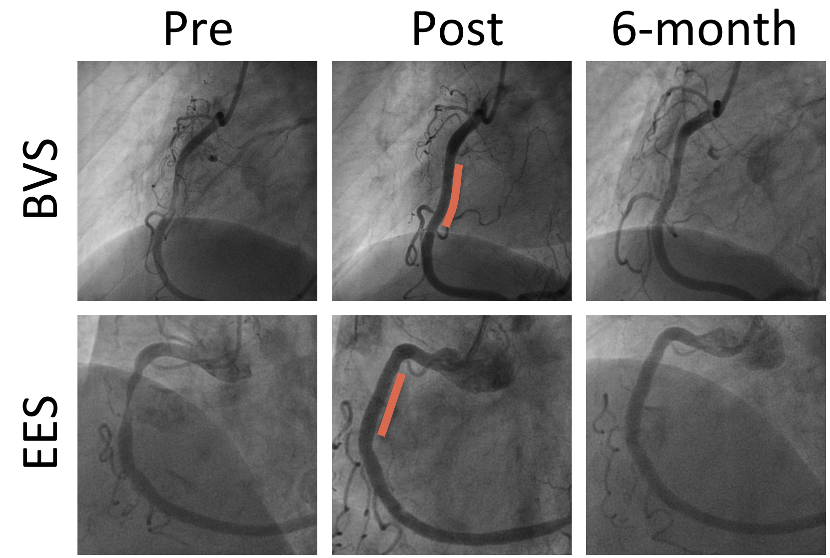
- Efficacy/safety in specific subsets
  - STEMI

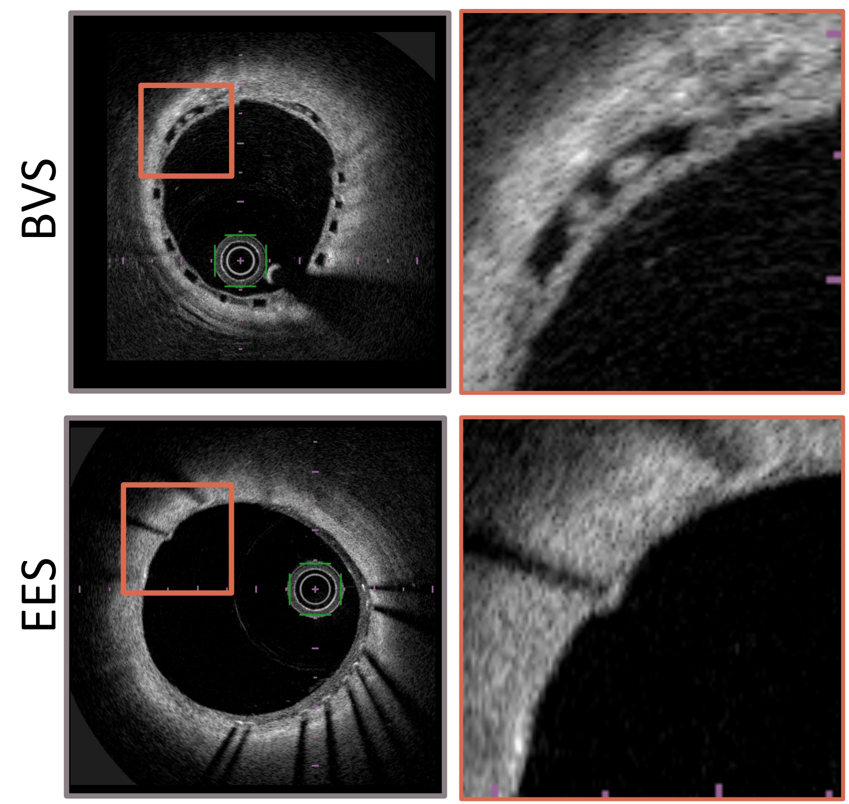
Vascular healing in STEMI patients: BVS versus CoCr-EES

Sabaté M et al. ABSORB STEMI TROFI II EHJ 2015
Räber L et al. EuroIntervention 2015

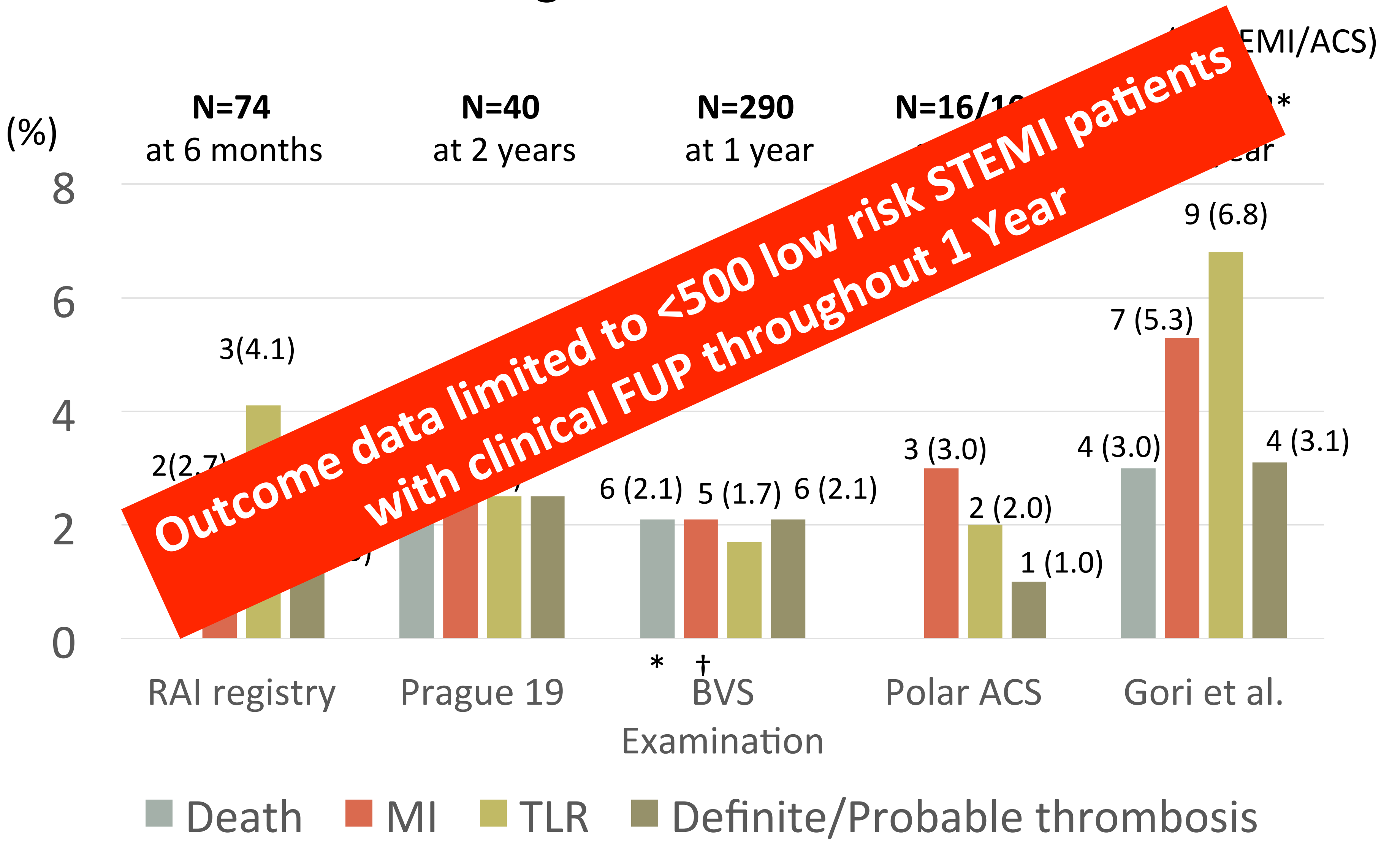
Cumulative distribution curves of 6-month healing score







Clinical outcomes following primary PCI using ABSORB BVS 1.1



* Cardiac death † Target vessel MI

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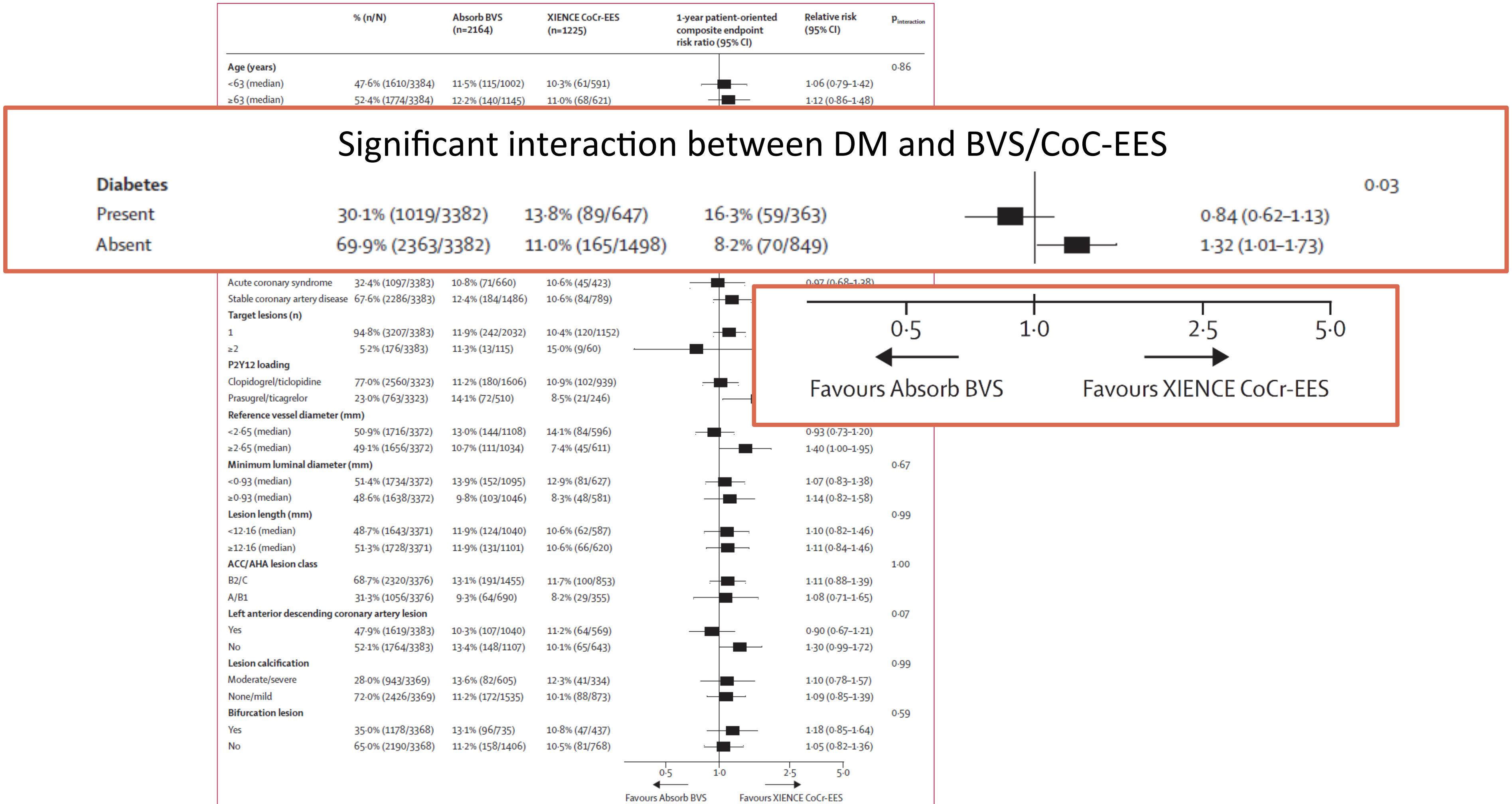
Unresolved

- Efficacy/safety in specific subsets
  - STEMI
  - Diabetes

Hypothetical benefit in diabetic patients: ABSORB BVS versus CoCr-EES



	% (n/N)	Absorb BVS (n=2164)	XIENCE CoCr-EES (n=1225)	Relative risk (95% CI)	$p_{interaction}$
Age (years)					0·86
<63 (median)	47·6% (1610/3384)	11·5% (115/1002)	10·3% (61/591)	1·06 (0·79–1·42)	
≥63 (median)	52·4% (1774/3384)	12·2% (140/1145)	11·0% (68/621)	1·12 (0·86–1·48)	
Acute coronary syndrome	32·4% (1097/3383)	10·8% (71/660)	10·6% (45/423)	0·97 (0·68–1·38)	
Stable coronary artery disease	67·6% (2286/3383)	12·4% (184/1486)	10·6% (84/789)		
Target lesions (n)					
1	94·8% (3207/3383)	11·9% (242/2032)	10·4% (120/1152)		
≥2	5·2% (176/3383)	11·3% (13/115)	15·0% (9/60)		
P2Y12 loading					
Clopidogrel/ticlopidine	77·0% (2560/3323)	11·2% (180/1606)	10·9% (102/939)		
Prasugrel/ticagrelor	23·0% (763/3323)	14·1% (72/510)	8·5% (21/246)		
Reference vessel diameter (mm)					
<2·65 (median)	50·9% (1716/3372)	13·0% (144/1108)	14·1% (84/596)	0·93 (0·73–1·20)	
≥2·65 (median)	49·1% (1656/3372)	10·7% (111/1034)	7·4% (45/611)	1·40 (1·00–1·95)	
Minimum luminal diameter (mm)					0·67
<0·93 (median)	51·4% (1734/3372)	13·9% (152/1095)	12·9% (81/627)	1·07 (0·83–1·38)	
≥0·93 (median)	48·6% (1638/3372)	9·8% (103/1046)	8·3% (48/581)	1·14 (0·82–1·58)	
Lesion length (mm)					0·99
<12·16 (median)	48·7% (1643/3371)	11·9% (124/1040)	10·6% (62/587)	1·10 (0·82–1·46)	
≥12·16 (median)	51·3% (1728/3371)	11·9% (131/1101)	10·6% (66/620)	1·11 (0·84–1·46)	
ACC/AHA lesion class					1·00
B2/C	68·7% (2320/3376)	13·1% (191/1455)	11·7% (100/853)	1·11 (0·88–1·39)	
A/B1	31·3% (1056/3376)	9·3% (64/690)	8·2% (29/355)	1·08 (0·71–1·65)	
Left anterior descending coronary artery lesion					0·07
Yes	47·9% (1619/3383)	10·3% (107/1040)	11·2% (64/569)	0·90 (0·67–1·21)	
No	52·1% (1764/3383)	13·4% (148/1107)	10·1% (65/643)	1·30 (0·99–1·72)	
Lesion calcification					0·99
Moderate/severe	28·0% (943/3369)	13·6% (82/605)	12·3% (41/334)	1·10 (0·78–1·57)	
None/mild	72·0% (2426/3369)	11·2% (172/1535)	10·1% (88/873)	1·09 (0·85–1·39)	
Bifurcation lesion					0·59
Yes	35·0% (1178/3368)	13·1% (96/735)	10·8% (47/437)	1·18 (0·85–1·64)	
No	65·0% (2190/3368)	11·2% (158/1406)	10·5% (81/768)	1·05 (0·82–1·36)	

1-year patient-oriented composite endpoint risk ratio (95% CI): 0·5, 1·0, 2·5, 5·0 — Favours Absorb BVS / Favours XIENCE CoCr-EES

Stone et al. Lancet 2016

First-generation BRS

Resolved*

- Plaque reduction and return of vasomotion in stable CAD low risk lesions
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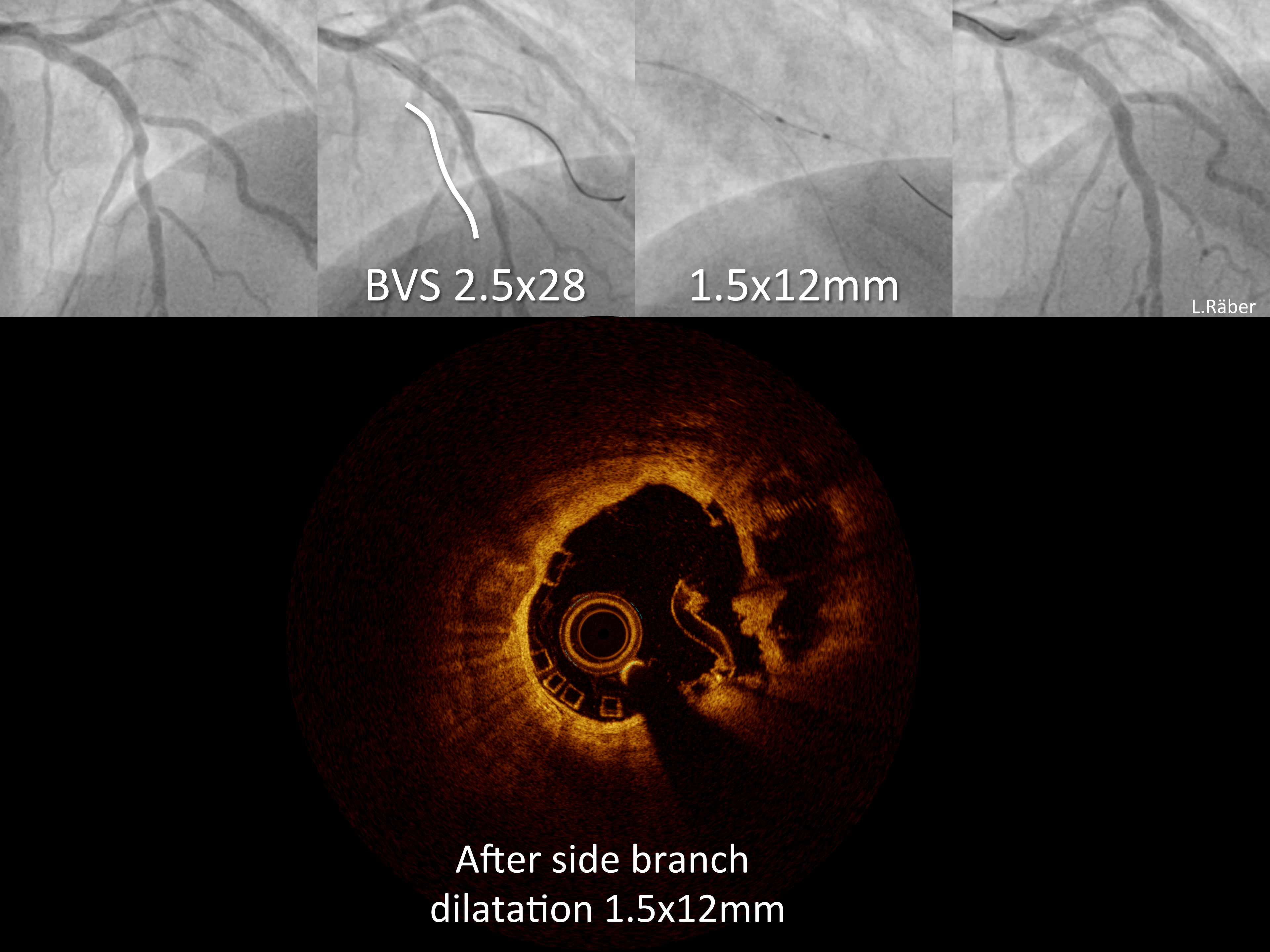
*applicable for BVS ABSORB 1.1

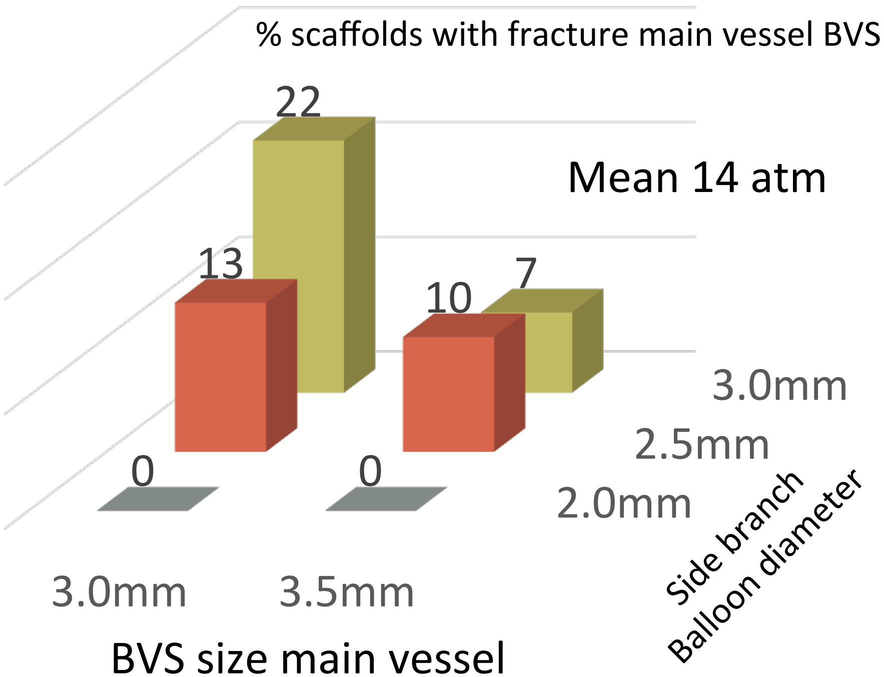
Unresolved

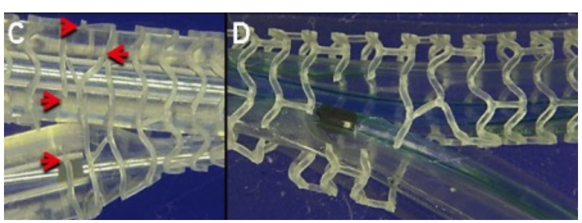
- Efficacy/safety in specific subsets
  – STEMI
  – Diabetes
  – Bifurcations


BVS 2.5x28
1.5x12mm
L.Räber
After side branch
dilatation 1.5x12mm

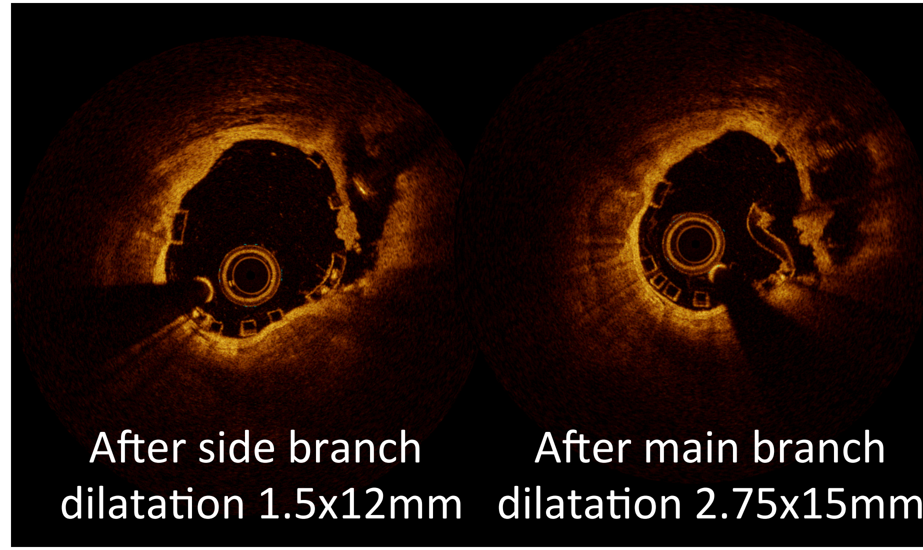
Larger side branch dilatation may cause scaffold fracture

Bench study





Ormiston et al. EuroIntervention 2015



BRS + sidebranch dilatation (N=49)

- Fracture 3 (6%)
  - Restored after prolonged inflation
    - TLR at 1 year 0 (0%)
- No fracture 43 (94%)
  - TLR at 1 year 2 (4%)

Pan et al. EuroPCR 2016

Clinical outcomes after bifurcation scaffolding

ABSORB BVS

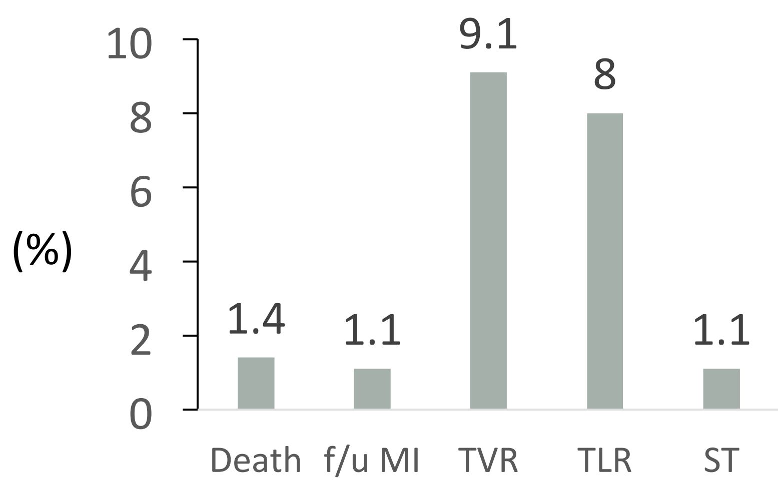
119 patients
132 bifurcations
(SB diameter ≥2.25mm)

→ Provisional scaffolding (N=99)

→ Double scaffolding (N=23)

→ Ostium scaffolding (N=10)

Clinical outcomes @ 1 years



Kawamoto et al. CCI 2015;86:644-52.

2 BRS strategy for bifurcation lesion

2 BRS bifurcation stenting (N=19)
- TAP (N=1)
- Mini-crush/Crush (N=1)
- T-stenting (N=16)
- V-stenting (N=1)

↓

TLR at 1 years
2 (12.9%)

↓

TLR at 2 years
3 (19.6%)

Tanaka et al. EuroPCR 2016

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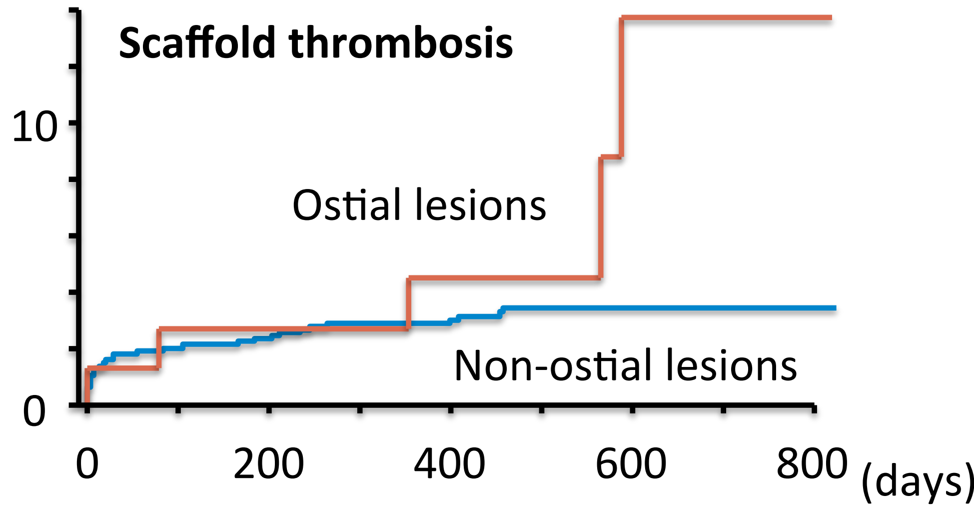
Unresolved

- Efficacy/safety in specific subsets
  - STEMI
  - Diabetes
  - Bifurcation
  - Ostial lesions

Ostial lesion versus non-ostial lesion

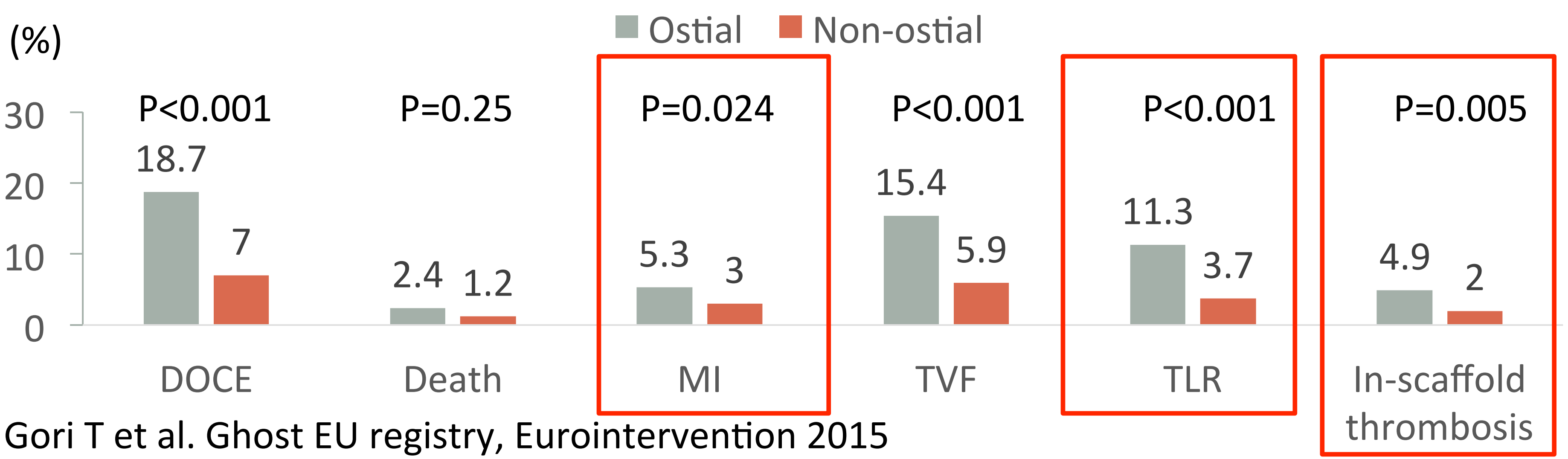


Puricel S et al. J Am Coll Cardiol 2016;67:921-31

Predictors of scaffold thrombosis

	HR (95% CI)	P value
Diabetes	0.46 (0.16-1.30)	0.147
LVEF per 5%	0.82 (0.70-0.97)	0.019
Number of vessels	1.23 (0.45-3.39)	0.692
Total BVS surface	1.10 (0.93-1.29)	0.304
Ticagrelor use	1.37 (0.66-2.86)	0.400
Ostial lesion	2.59 (1.01-6.64)	0.049

Clinical outcomes at 12 months



Gori T et al. Ghost EU registry, Eurointervention 2015

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  - STEMI
  - Diabetes
  - Bifurcations
  - Ostial lesion
- Device specific issues
  - Implantation strategy

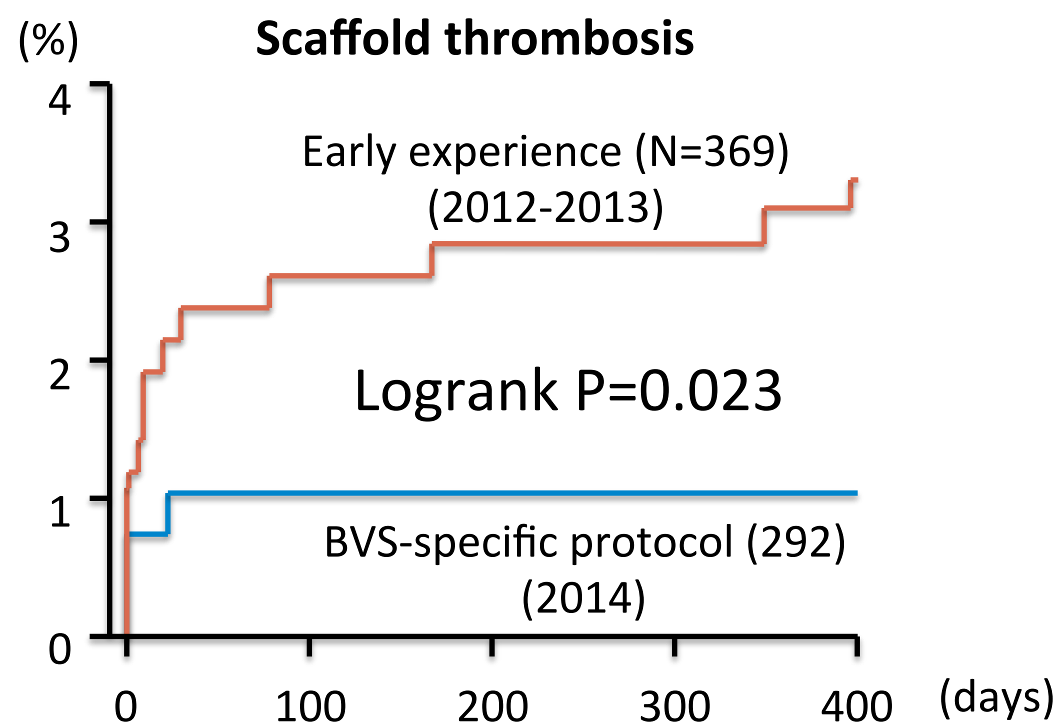
Optimized implantation strategy reduced scaffold thrombosis

Puricel S et al. J Am Coll Cardiol 2016;67:921-31

1305 patients
1870 BVS

42 ScT
10 (24%) acute
11 (26%) subacute
11 (26%) late
10 (24%) very late

1. Predilatation with NC balloon, up to reference
2. Only in case of full expansion
3. Same size as RVD at 10-12atm
4. Post dilatation at 14-16atm (maximum 0.5mm larger)



Expert‘s view on implantation strategy

...ral technique with BVS (more

...scular ultrasound and optical
...apposition need to be studied

***Ron Waksman** JACC Interv 2016*

...scaffold dimensions) might further
...ates. ...

***Gregg Stone** Lancet 2016*

Given the importance of accurate size estimation and the limitations in terms of aggressive post-dilation techniques (due to the risk of polymeric stent disruption in case of excessive overexpansion), intracoronary imaging—in particular optical coherence tomography—to guide and optimize BVS implantation may assume a prominent role for improving post-procedural and presumably longer-term angiographic outcomes, although this requires confirmation in appropriately designed studies.

***Stephan Windecker** JACC 2015*

...m this
...his can be
...timal
...uncertainty in the tunnel of ST. We are in control and we can shed the light!

...more favorable results h...
of the implantation techni...
imaging tools.

***Carlo Di Mario** Internati...*

...The use of intra-coronary (IC) imaging modalities is becoming an essential tool for optimizing BVS implantation.

***Manel Sabate** Circulation Journal 2015*

...Thus, in complex lesions, intravascular imaging should support BRS implantation.

***Holger M. Nef** JACC 2014*

International RCT
Optico BVS

PCI using **ABSORB BVS 1.1** for stable AP, NSTE-ACS and STEMI (N=270)

Randomization 1:1

PI: L. Räber

OCT-guided PCI	**Angiography-guided PCI**
OCT lesion assessment	OCT assessment at end of procedure, blinded intervening physician
OCT based PCI optimization according to prespecified criteria	

Primary endpoint (@ 6 months)

Minimal in-scaffold lumen area (mm^2) assessed by OCT

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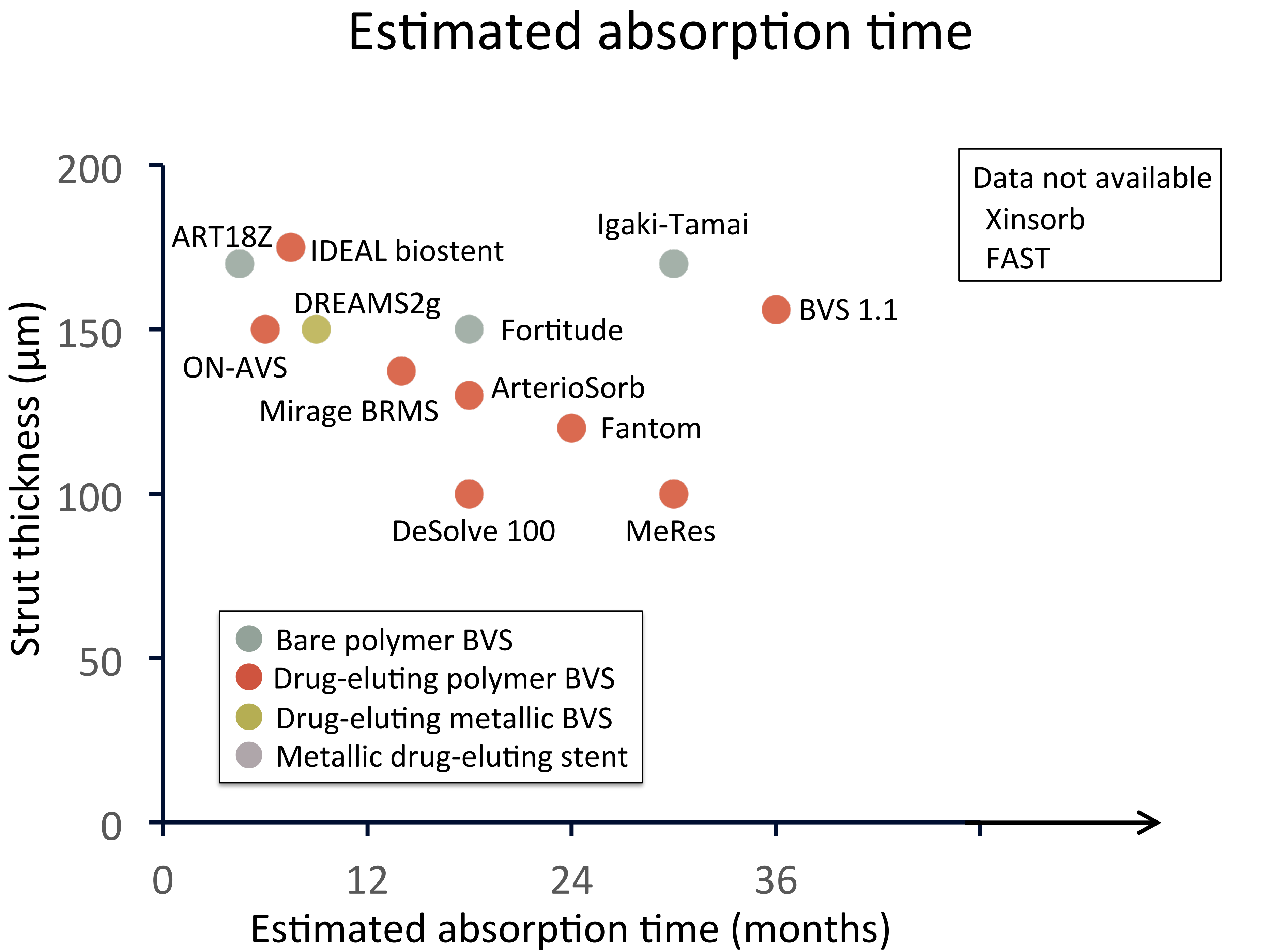
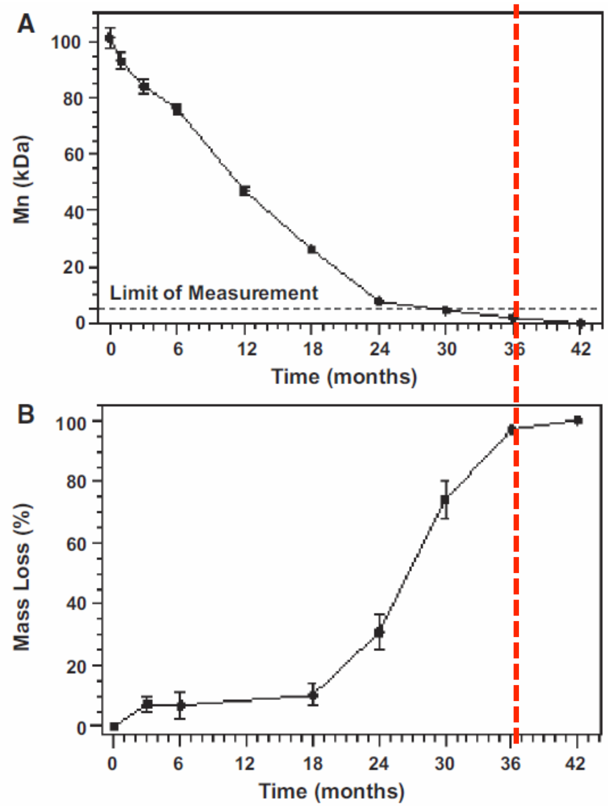
- Efficacy/safety in specific subsets
  - STEMI
  - Diabetes
  - Bifurcations
  - CTO/long lesion
  - Ostial lesion
- Device specific issues
  - Implantation strategy
  - Optimal BRS property
    - Absorption time
    - Strut thickness



Estimated absorption time
Data not available
Xinsorb
FAST
200
150
100
50
0
Strut thickness (μm)
ART18Z
IDEAL biostent
Igaki-Tamai
DREAMS2g
Fortitude
BVS 1.1
ON-AVS
Mirage BRMS
ArterioSorb
Fantom
DeSolve 100
MeRes
Bare polymer BVS
Drug-eluting polymer BVS
Drug-eluting metallic BVS
Metallic drug-eluting stent
0
12
24
36
Estimated absorption time (months)

Scaffold resorption: Animal vs. human data ?

Non-atherosclerotic swine model
ABSORB BVS 1.1

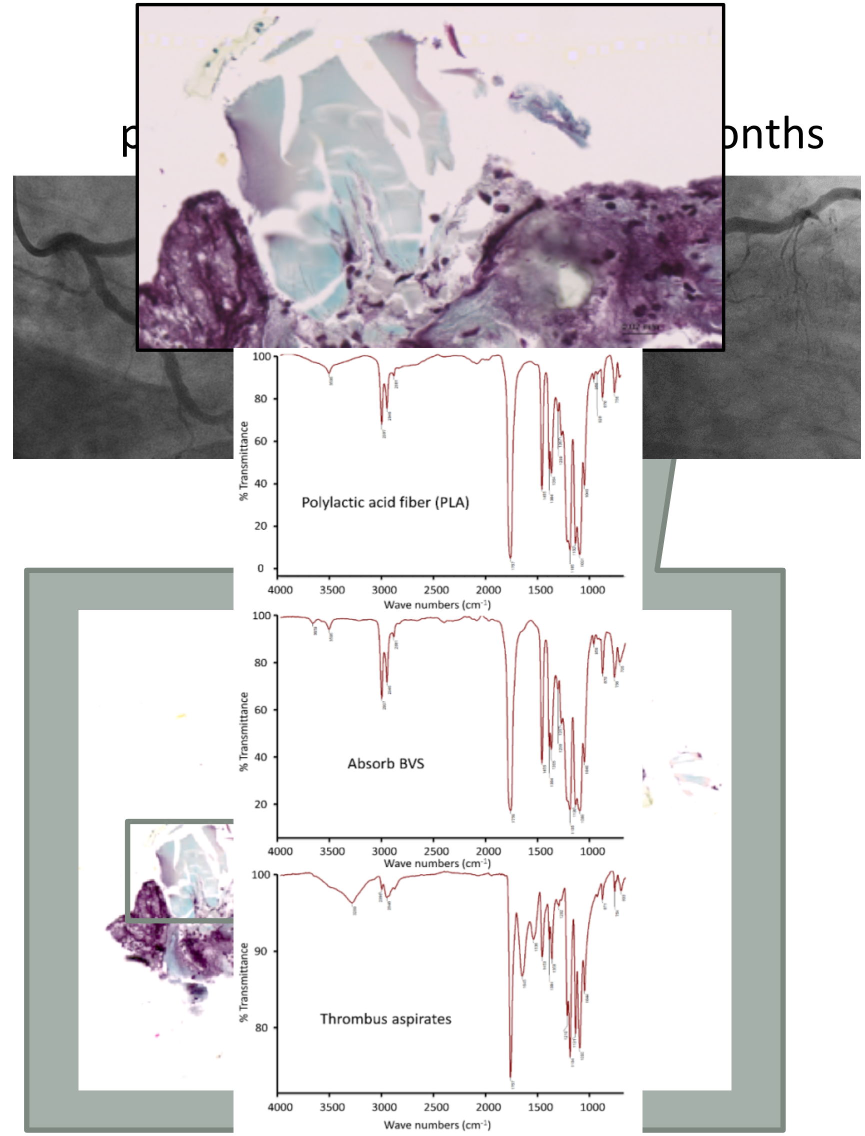


Complete absorption @36 mo

Gel permeation chromatography

N= 20 @36 months
N=21 @42 months

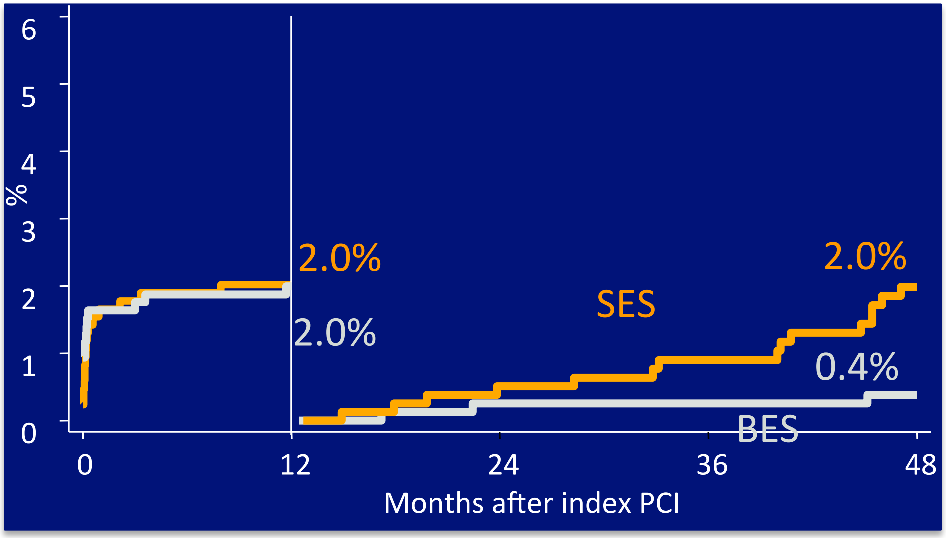
Otsuka F et al. Circulation 2014



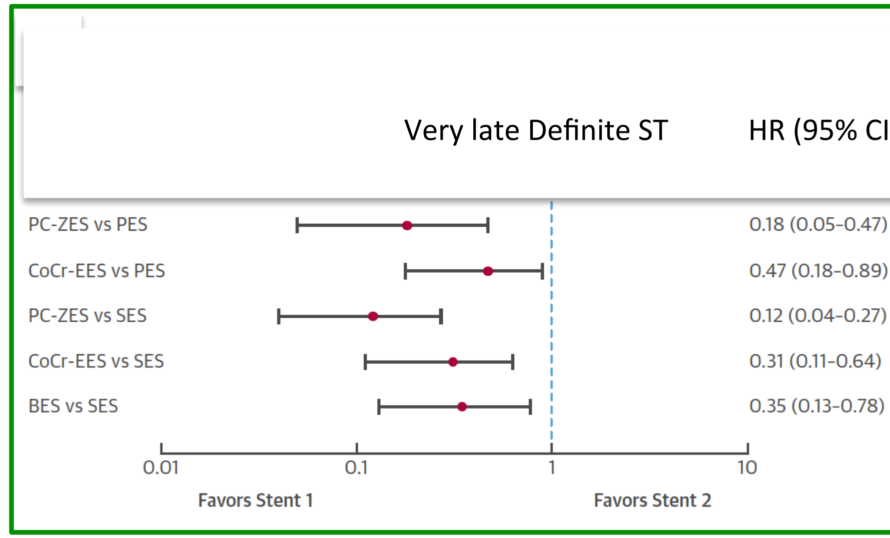
Räber L et al. JACC 2015

Very Late Stent Thrombosis Following New vs. Early Generation DES

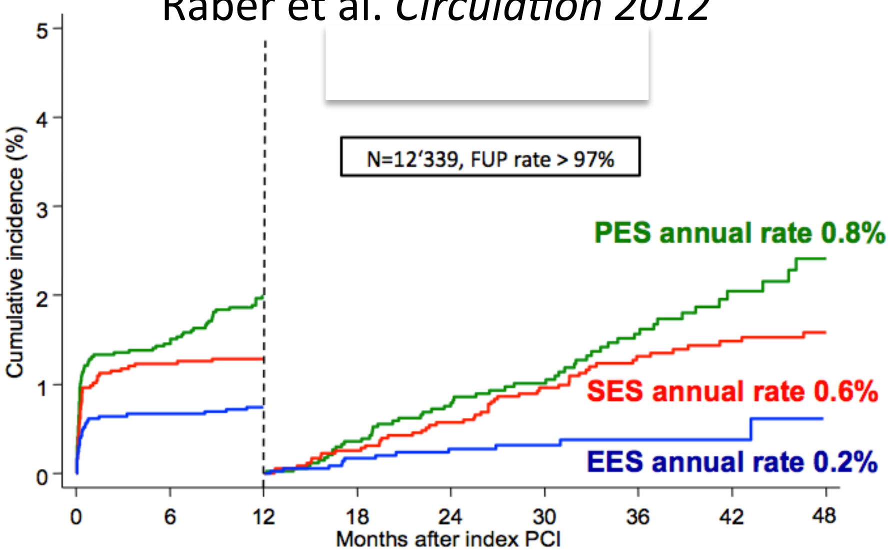
Stefanini et al. *Lancet 2011*



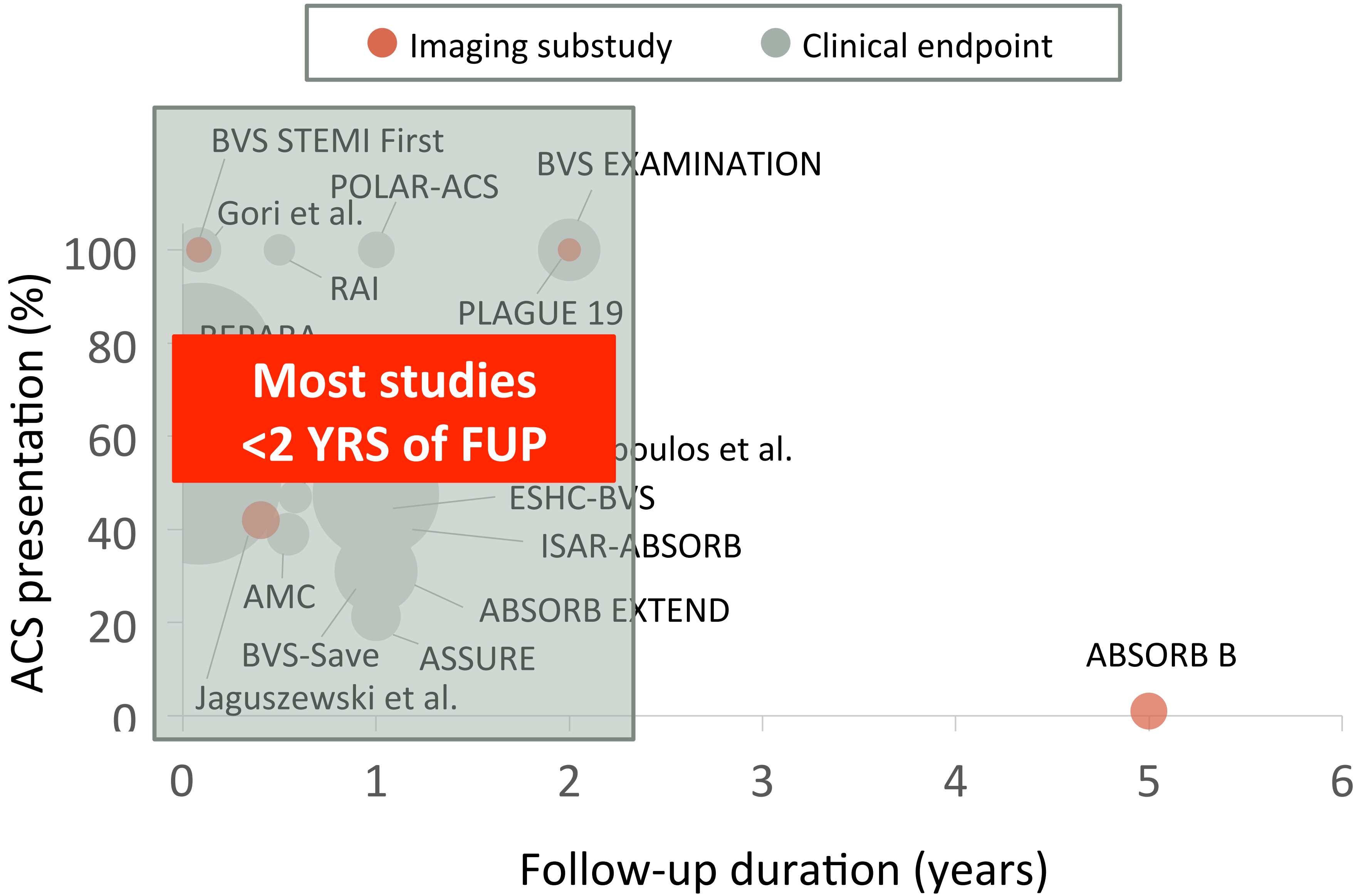
Palmerini et al. *JACC 2015*



Räber et al. *Circulation 2012*



Current registry evidence ABSORB BVS



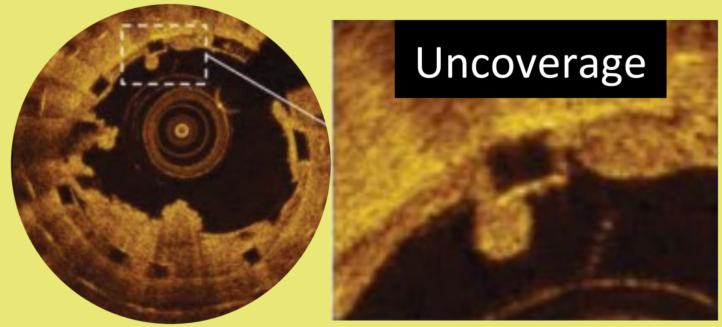
VLST does occur: Case level evidence

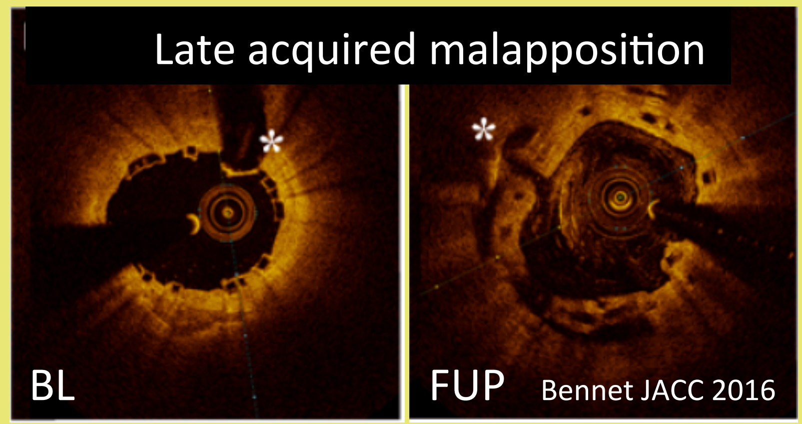
VLScT cases (BVS ABSORB)	Age	Sex	Indication at index	Vessel	N. of BVS	Total length	Post dilatation	Duration (months)	ASA	P2Y12
Azzalini et al.	81	F	NSTEMI	LAD	1	28	Y	14	-	N
Cortese et al.	71	M	stable AP	RCA	2	56	Y	16	N	N
Cuculi et al.	55	M	STEMI	RCA	1	12	-	18	-	-
Cuculi et al.	-	-	NSTEMI	LAD	1	12	-	19	-	-
González et al.	39	M	STEMI	RCA	3	74	-	17	Y	Y
Ielasi et al.	49	M	STEMI	RCA	2	40	Y	19	Y	N
Karanasos et al.	55	M	Non-ACS	LCX	1	18	N	22	Y	N
Karanasos et al.	62	-	ACS	RCA	1	28	N	15	Y	N
Karanasos et al.	86	-	ACS	LCX	1	28	N	12	N	N
Meincke et al.	46	-	Stable CAD	RCA	1	28	-	18	-	-
Räber et al.	68	M	stable AP	LCX	1	18	Y	44	Y	N
Räber et al.	53	M	stable AP	RCA	1	18	N	19	Y	N
Räber et al.	55	M	NSTE-ACS	LCX	1	28	N	21	Y	Y
Räber et al.	55	M	stable AP	LCX	1	12	N	19	Y	Y
Sato et al.	47	M	ACS	RCA	1	-	-	22	N	N
Timmers et al.	39	M	-	LAD	-	-	-	12	N	N

Late scaffold failure mechanisms?

Related to <u>prolonged</u> absorption time

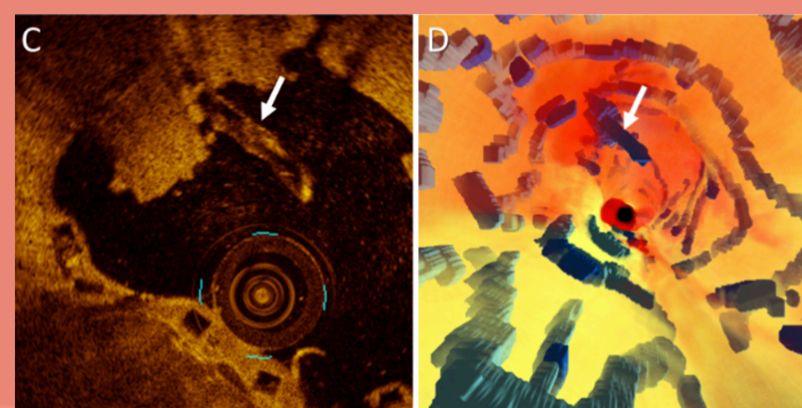
Patho-mechanisms similar to metallic DES





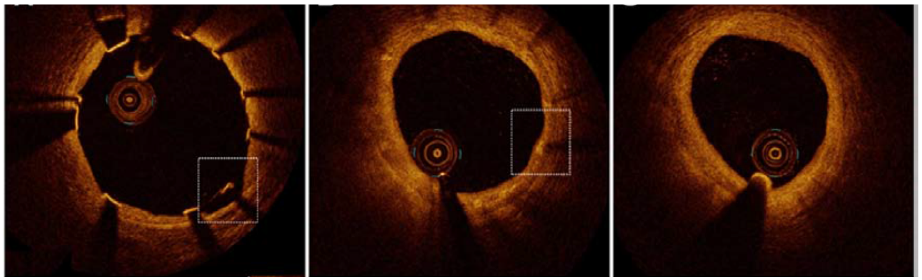
Related to absorption

-> Late scaffold discontinuity
Late acquired malapposition



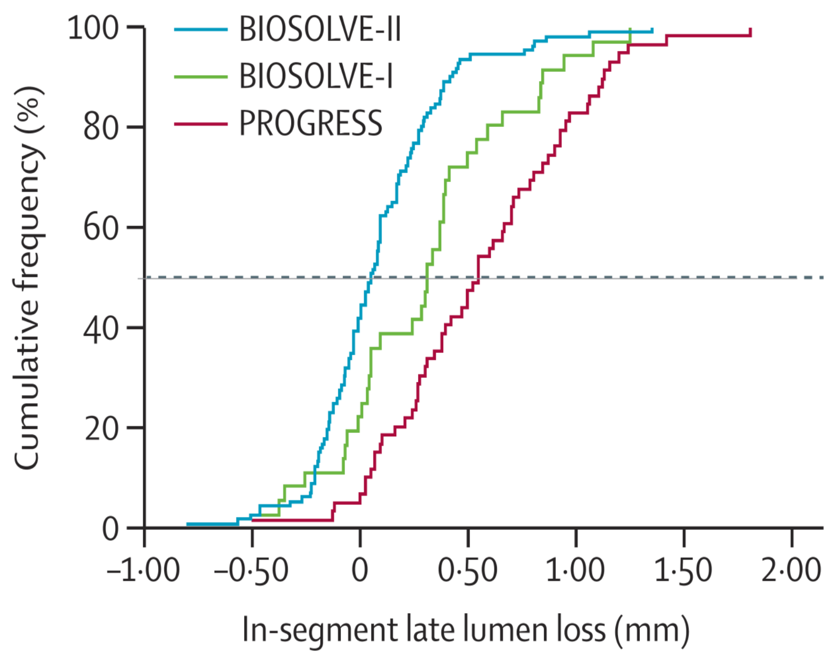
Metallic Bioresorbable Scaffolds (Magmaris)

Haude et al. *Lancet* 2016;387:31-39



- 2nd generation limus eluting magnesium device
- 150 m strut thickness
- Absorbable PLLA coating
- Approximately 95% of Mg absorbed @ 1 YR

Antirestenotic efficacy (Late lumen loss)

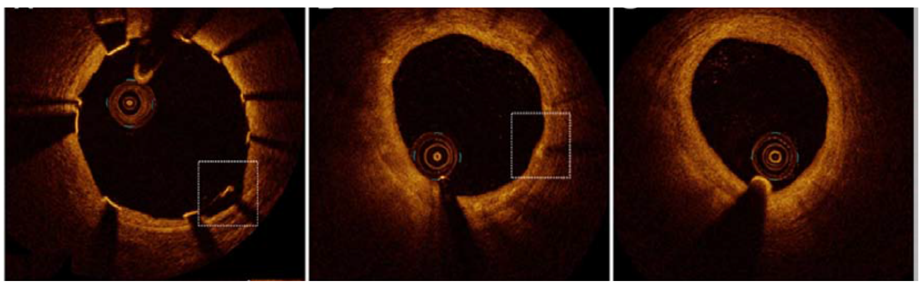


PROGRESS AMS	***1.08±0.49***
DREAMS 1G Biosolve I	***0.52±0.39***
DREAMS 2G Biosolve II	***0.27±0.37***

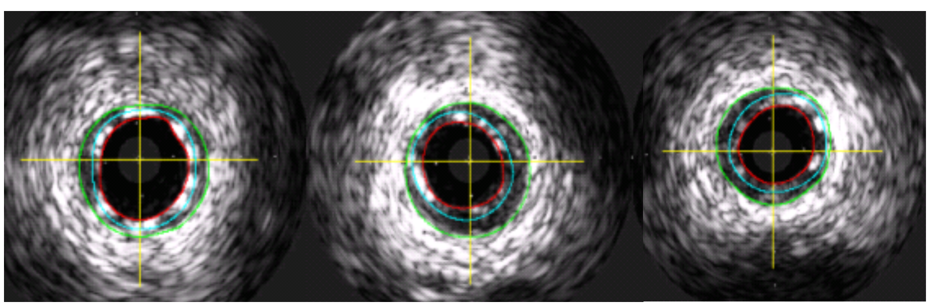
BIOSOLVE-II
123 patients
123 lesions

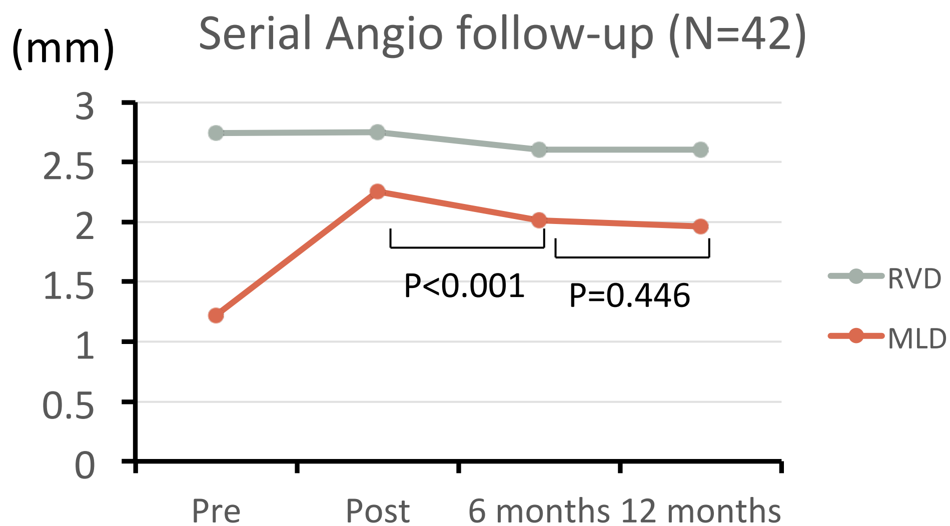
12 months follow-up
Cardiac death 1 (0.8%)
TV-MI, no-reflow 1 (0.8%)
Clinically driven TLR 2 (1.7%)

Post procedure | 6 months | 12 months

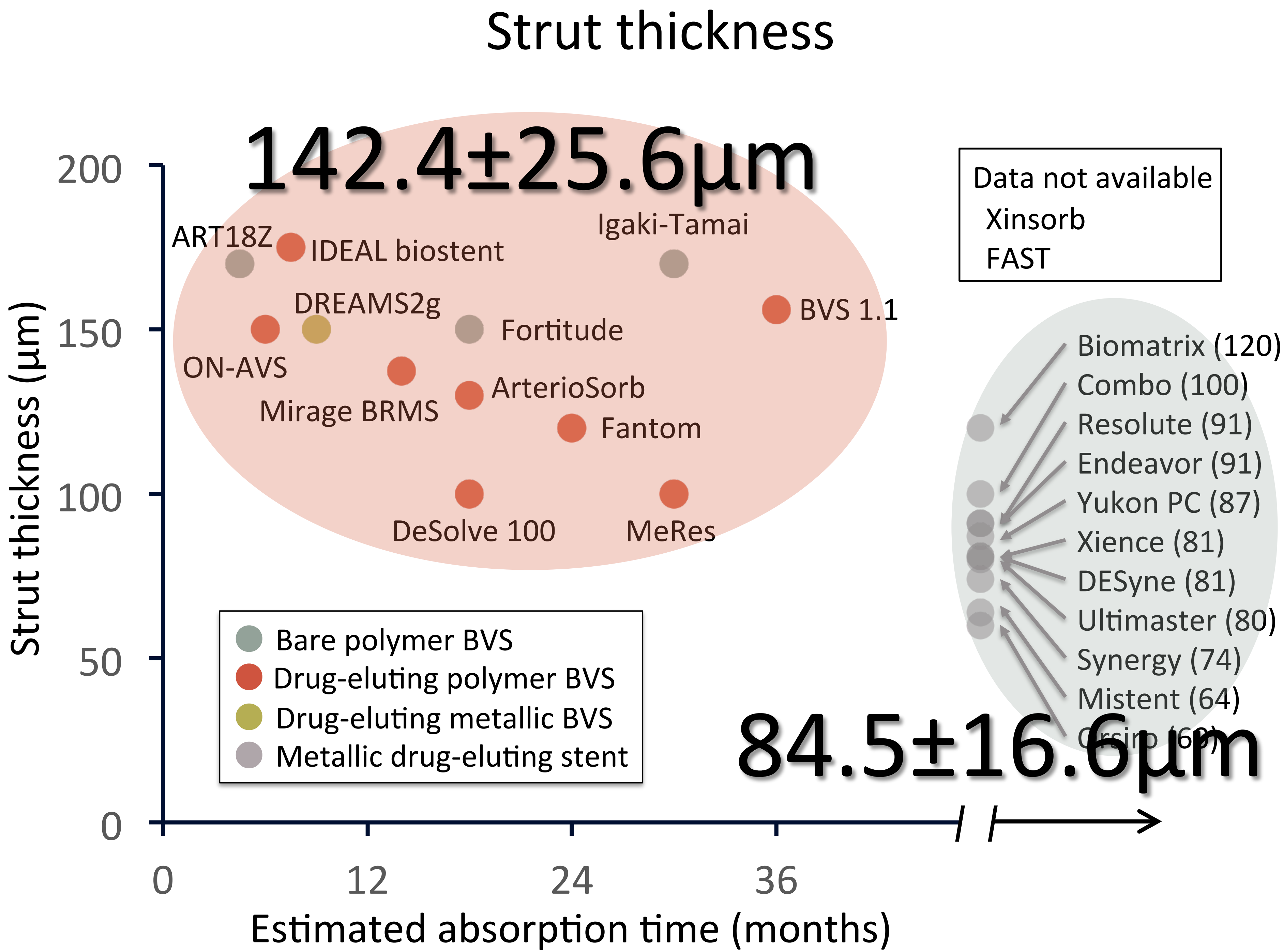


Post procedure | 6 months | 12 months





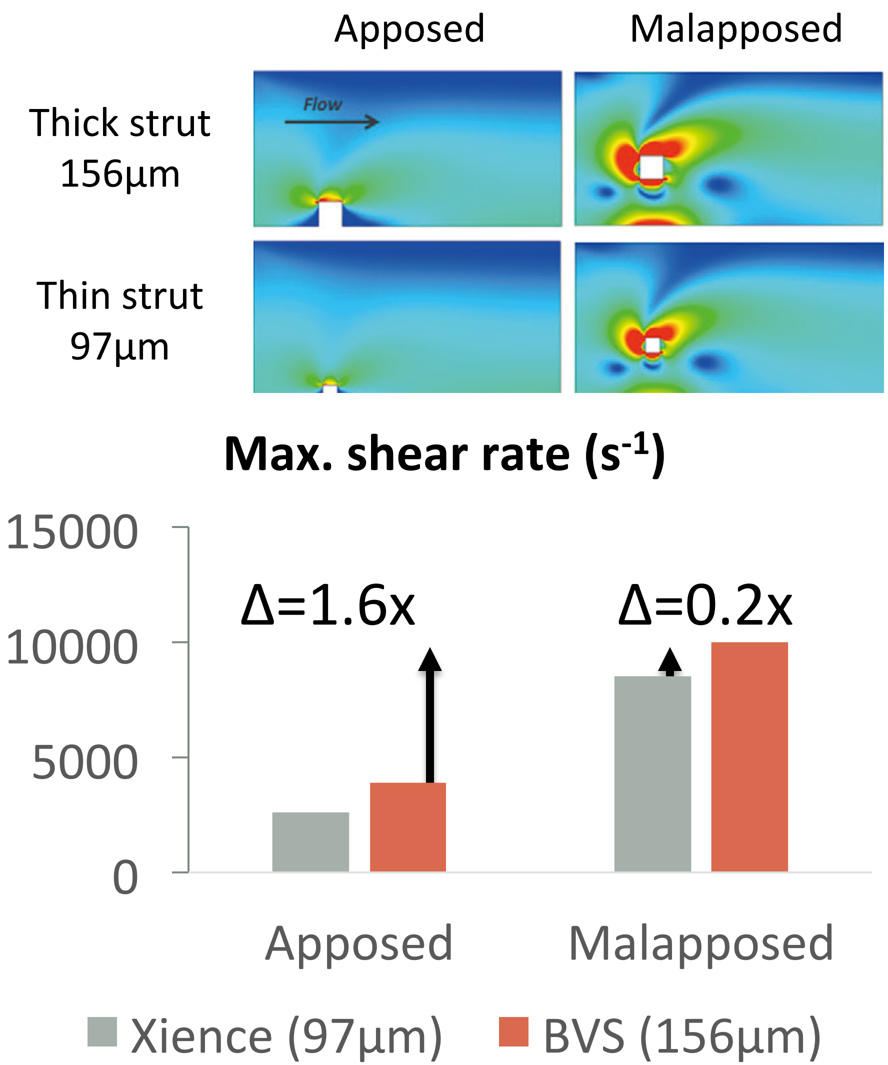
Haude M. et al. BIOSOLVE II Lancet 2015, EHJ 2016



Strut thickness
142.4±25.6μm
200
150
100
50
0
Strut thickness (μm)
ART18Z
IDEAL biostent
Igaki-Tamai
DREAMS2g
Fortitude
BVS 1.1
ON-AVS
Mirage BRMS
ArterioSorb
Fantom
DeSolve 100
MeRes
Data not available
Xinsorb
FAST
Biomatrix (120)
Combo (100)
Resolute (91)
Endeavor (91)
Yukon PC (87)
Xience (81)
DESyne (81)
Ultimaster (80)
Synergy (74)
Mistent (64)
84.5±16.6μm
Bare polymer BVS
Drug-eluting polymer BVS
Drug-eluting metallic BVS
Metallic drug-eluting stent
0
12
24
36
Estimated absorption time (months)

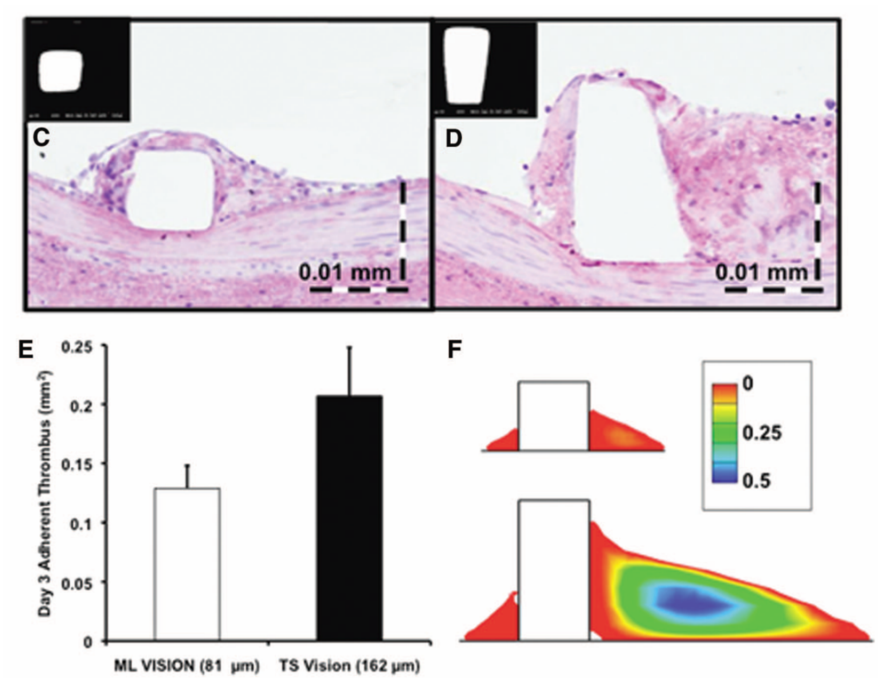
Strut thickness

Thick struts and **flow disturbances**



Foin N et al. EuroIntervention 2015

Thick struts and **thrombogenicity**



Thin (MULTI-LINK VISION [MLV]) vs thick (thick-strut VISION [TSV]) bare metal stents in porcine coronary arteries (n=6 each)

Kolandaivelu K et al. Circulation 2011

Conclusions

Resolved*

- Plaque reduction and return of vasomotion in stable CAD low risk lesions
- Equivalent performance in terms of MACE in lower risk stable CAD patients
- Equivalence in device efficacy despite angiographic inferiority
- Potential disadvantage in safety outcomes (MI and stent thrombosis)

Unresolved issues

- Use of BRS in specific patient and lesion subsets and the associated efficacy and safety

-> as a new technology, BRS should provide superiority in specific clinical settings that do not respond adequately to current interventional approaches

- Validation of proposed BRS specific implantation strategies (e.g. IC imaging guidance)
- Although the optimal absorption time remains unclear in the absence of comparative outcome studies among various BRS, a short absorption time appears superior to mitigate long-term adverse events
- Strut thickness

*applicable for BVS ABSORB 1.1

Thank you for your attention

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