ABSORB® - ACS

Bernhard Metzler

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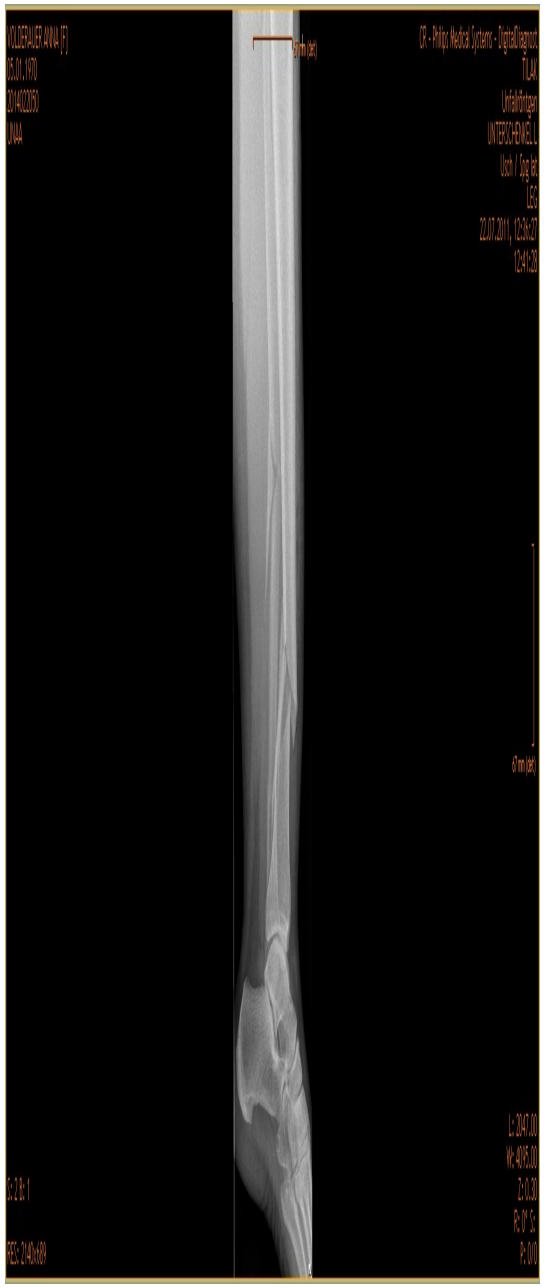
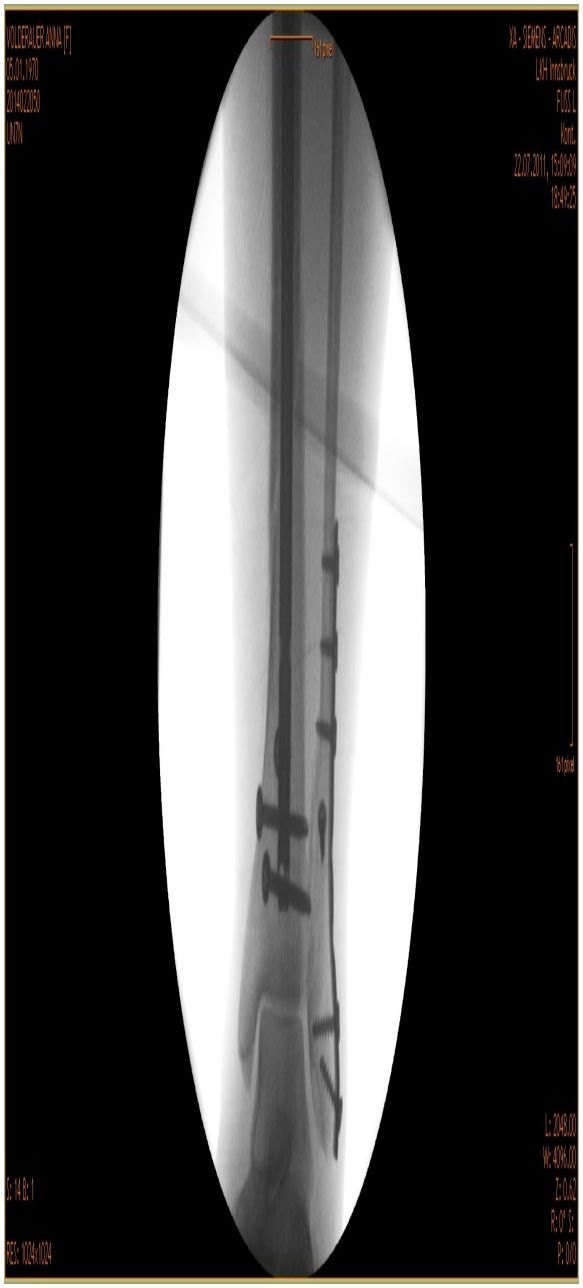
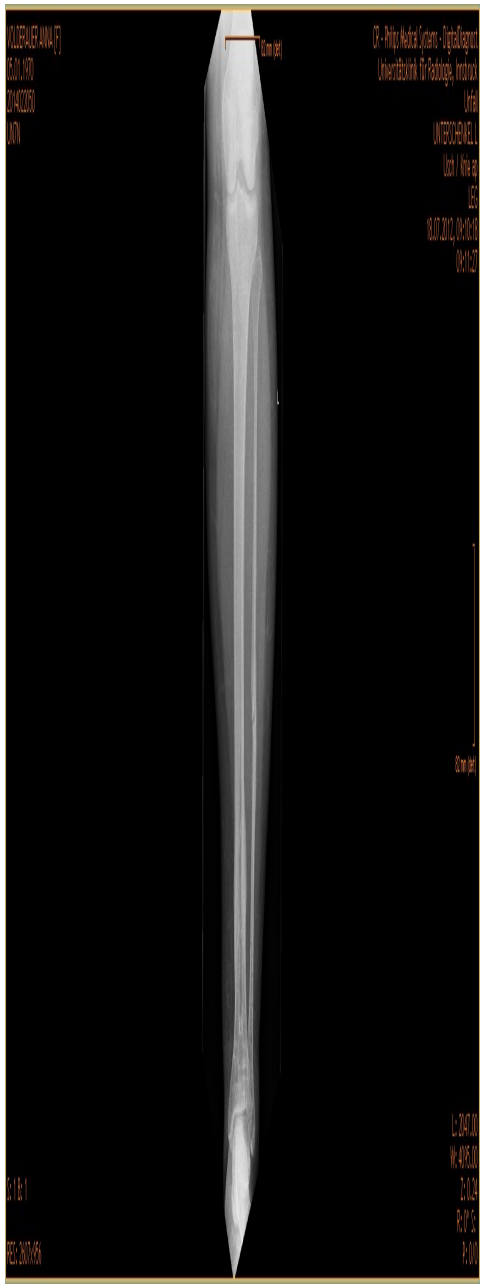
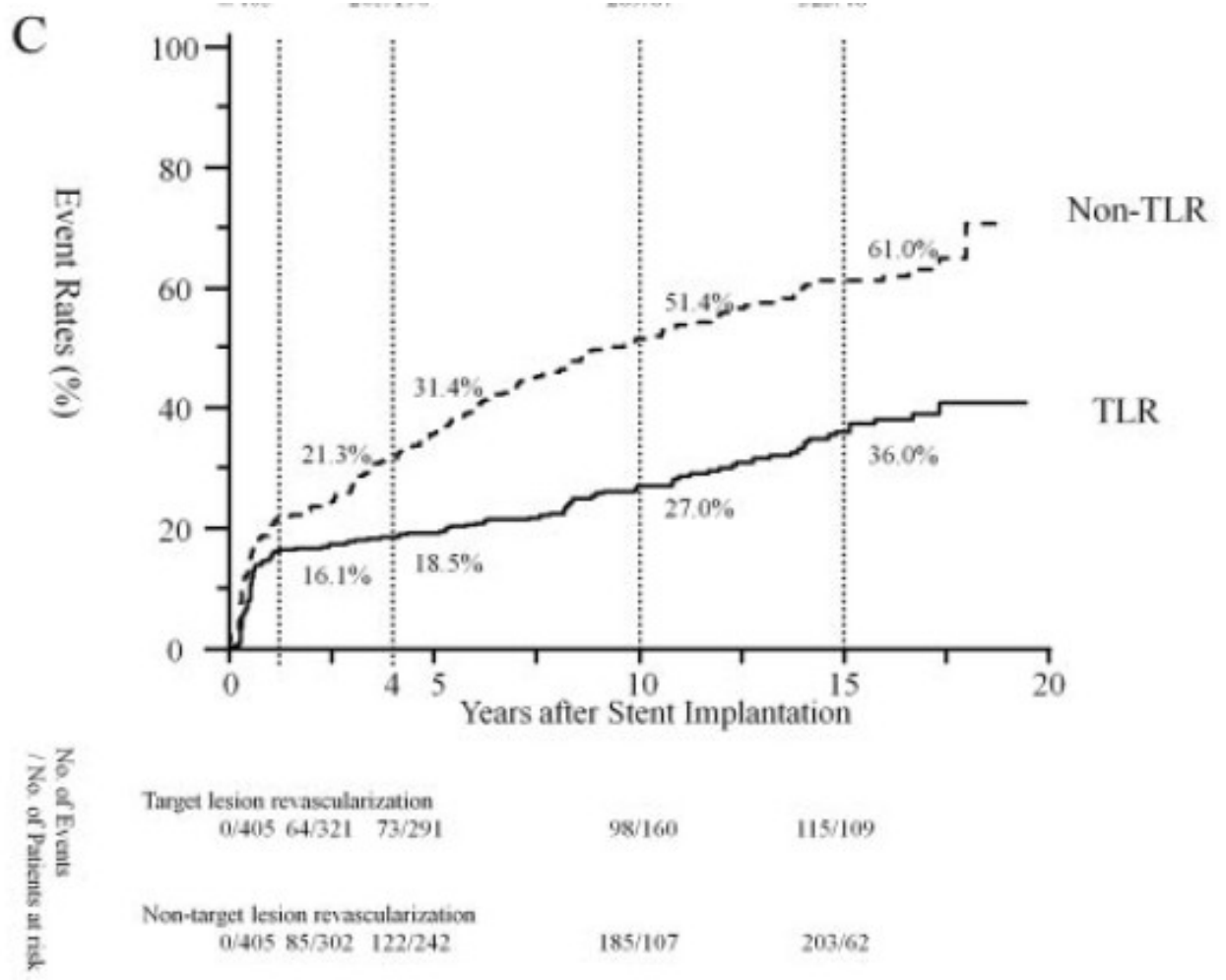




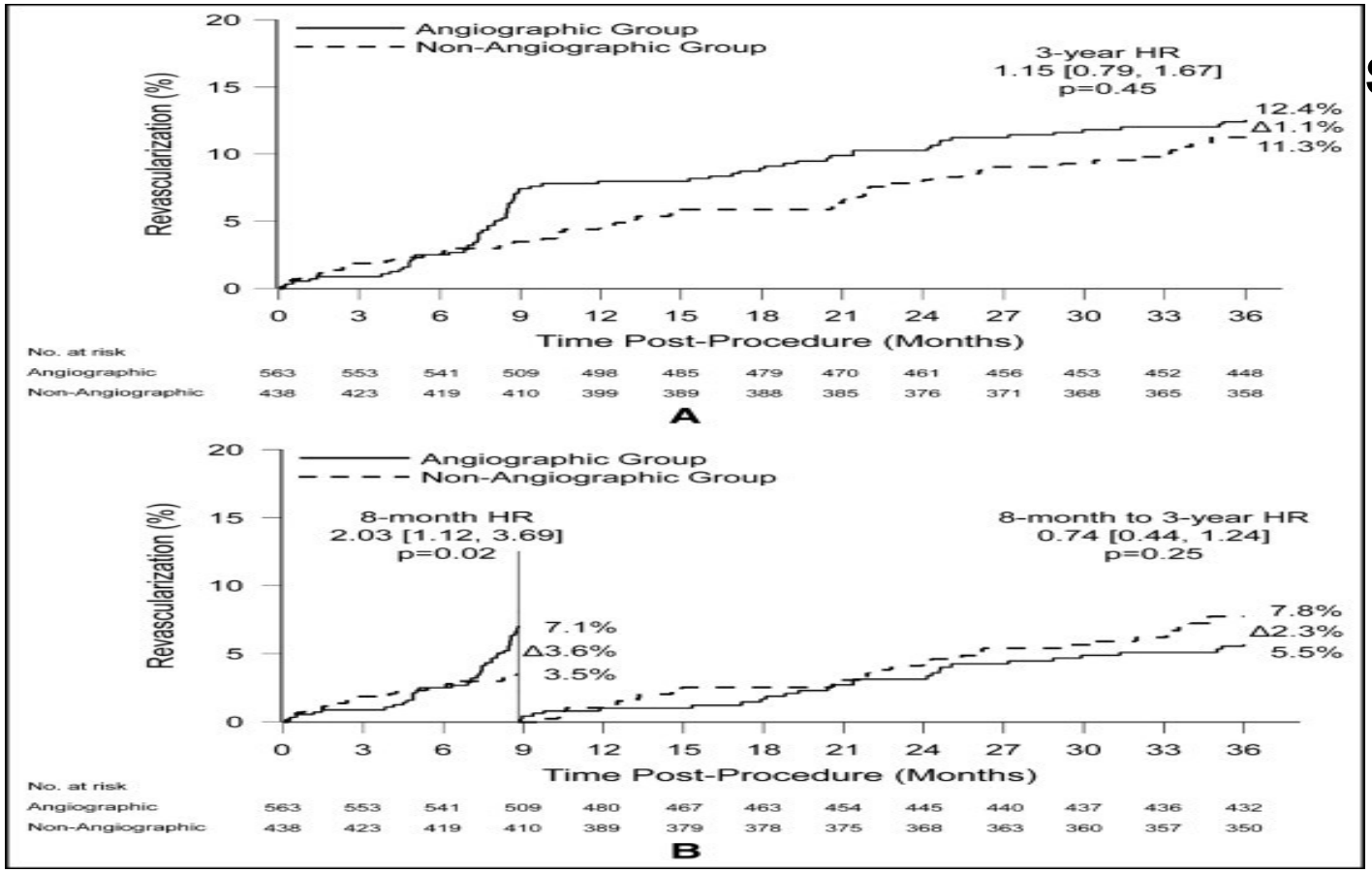


Long-term BMS Event-Rate



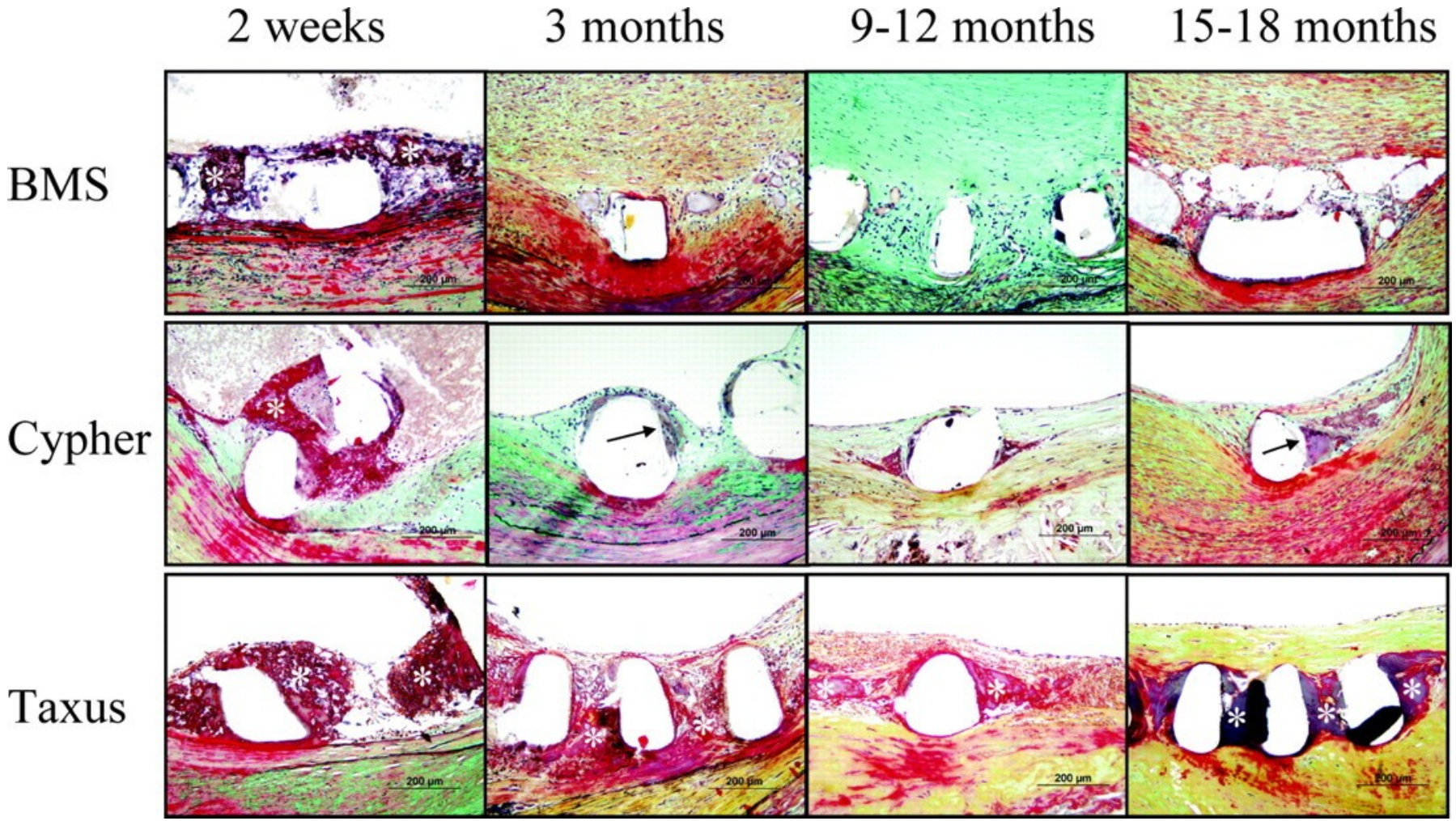
Yamaji Y. et al., Circulation 2010

Long-term DES Event-Rate



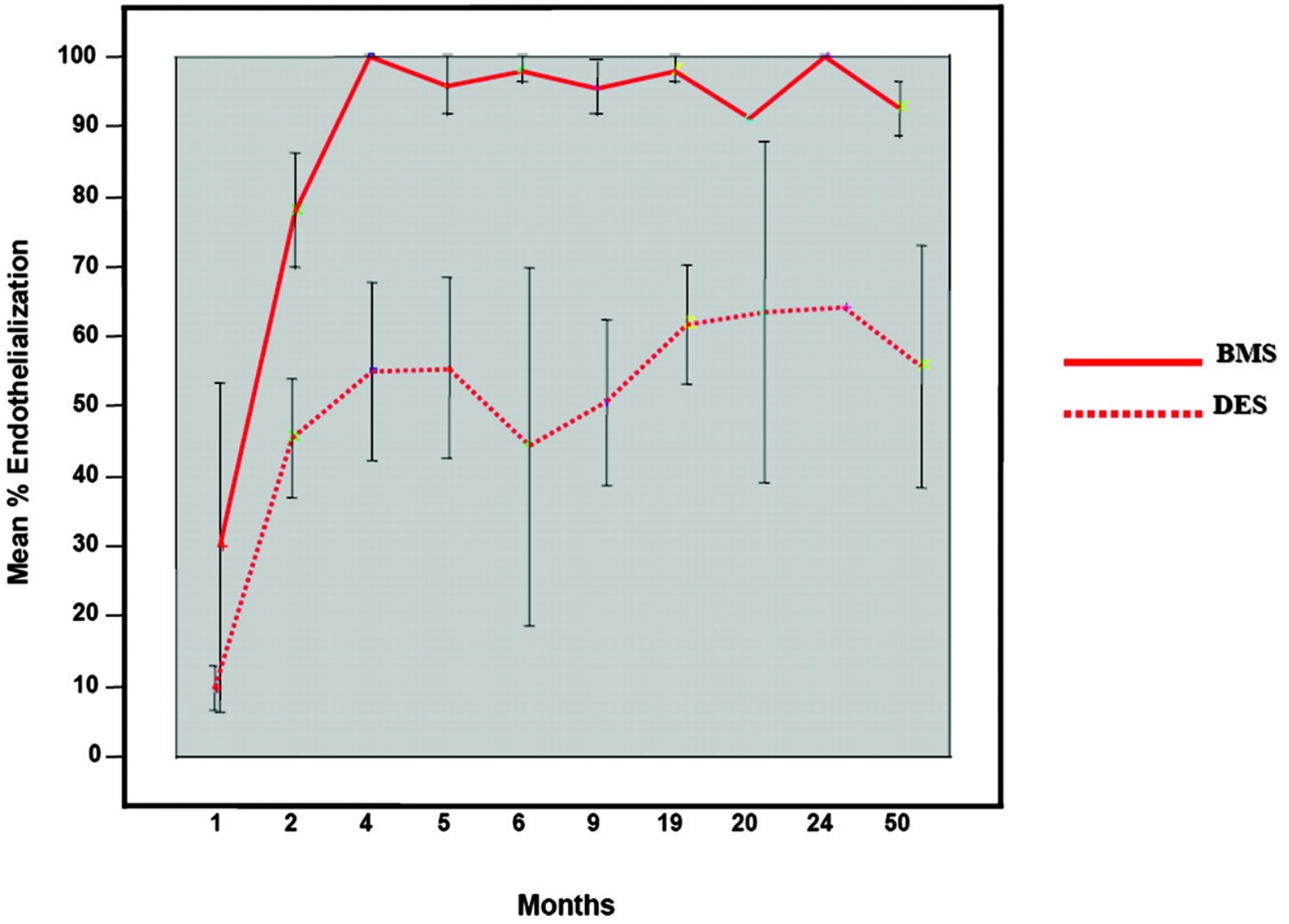
SPIRIT III

Lansky A, et al., Am J Cardiol 2012

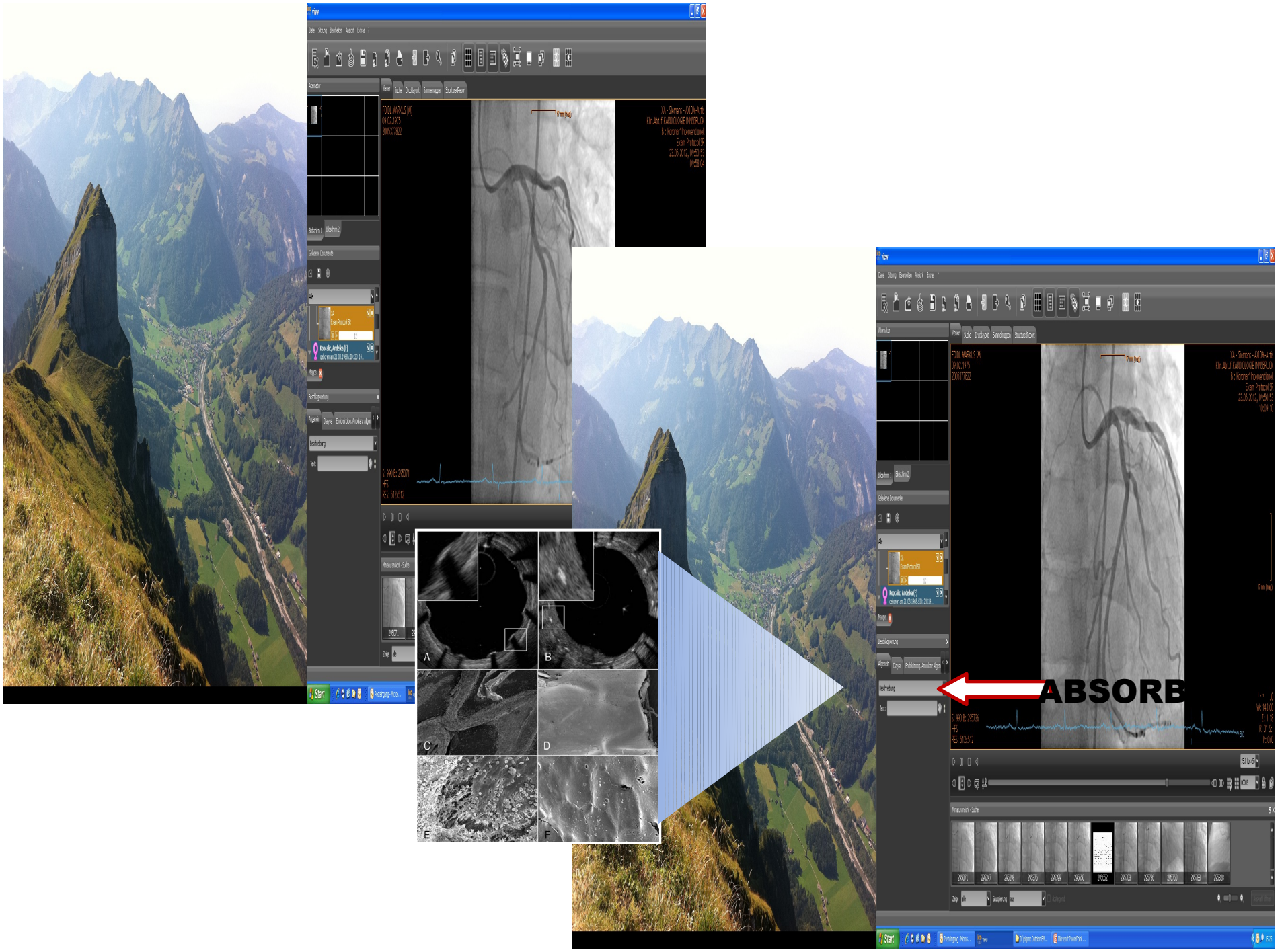


Finn et al., ATVB 2007

Stent-Endothelialization



Finn et al, ATVB 2007
Lüscher et al, Circ 2007


A
B
C
D
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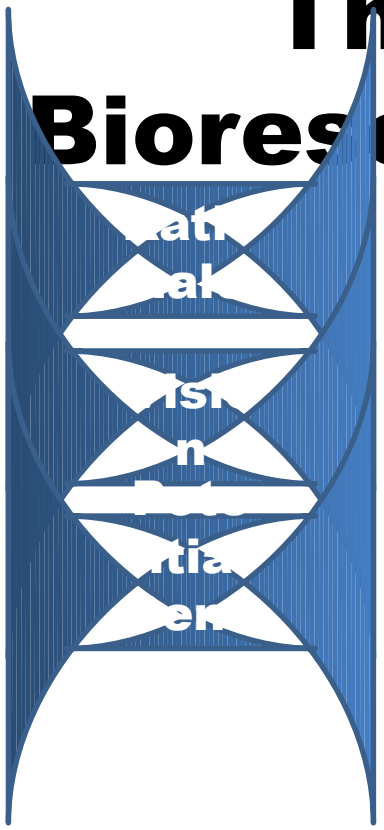
ABSORB

The Clinical Need for a Bioresorbable Vascular Scaffold



Vessel scaffolding is only needed transiently*

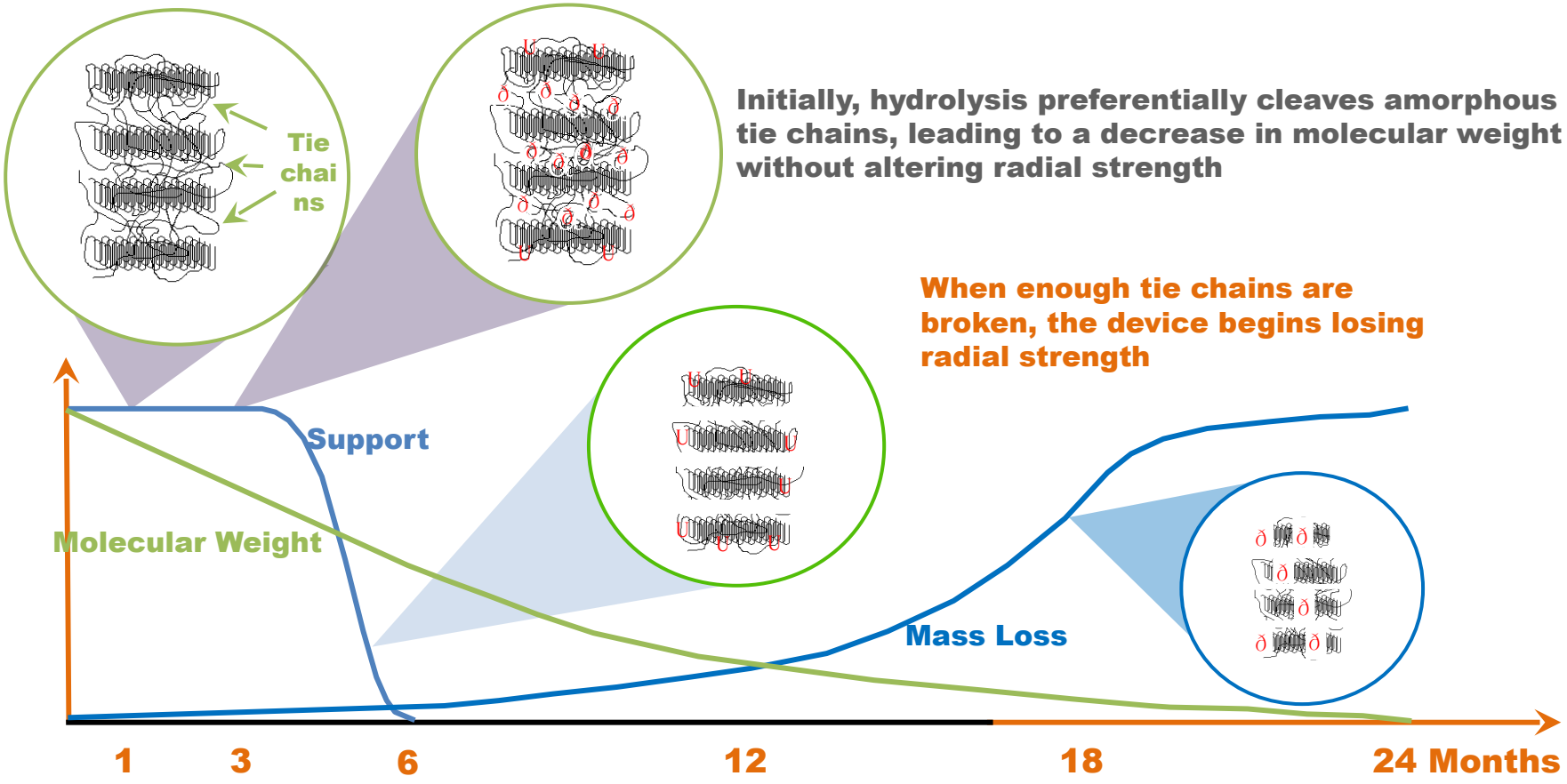
Improve Long Term Outcomes for Patients by Leaving No Scaffold Behind1

- Restore the vessel to a more natural state, capable of natural vascular function
- Eliminate chronic sources of vessel irritation and inflammation
- Vessels remain free for future treatment options
- Reduce the need for prolonged DAPT2
- Allows for use of non-invasive imaging techniques (CCTA)
- Improve patient quality of life

*Serruys PW, et al., Circulation 1988; 77: 361. Serial study suggesting vessels stabilize 3-4 months following PTCA.
1 – Small platinum markers at scaffold edges remain for fluoroscopic landmarking. 2. The Absorb IFU indicates DAPT for a minimum of 6 months.

How Absorb Resorbs

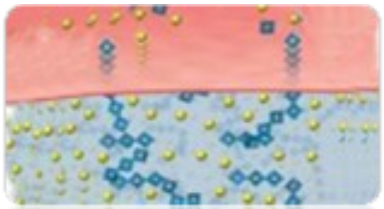
- Blood penetrates polymer matrix
- Long polymer chains become shorter and shorter



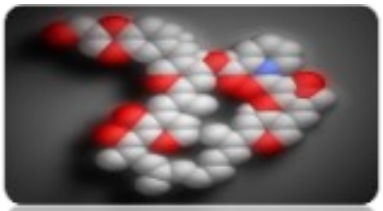
Absorb BVS: Design Components

- Poly (L-lactide) (PLLA)
- Based on proven MULTI-LINK pattern
- Naturally resorbed, fully metabolized*

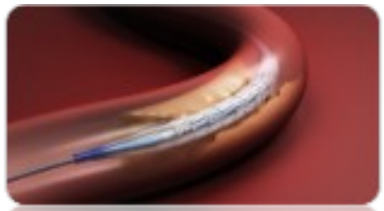
- Poly (D,L-lactide) (PDLLA)
- Naturally resorbed, fully metabolized



- Similar dose density and release rate to XIENCE V

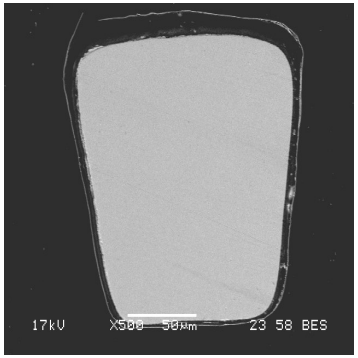
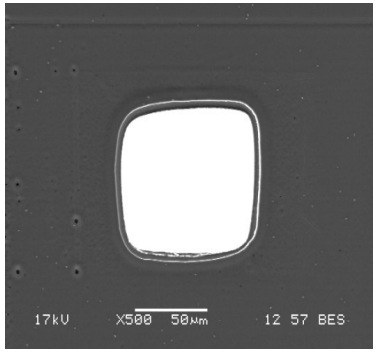
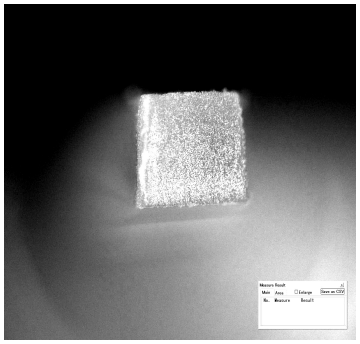


- World-class deliverability

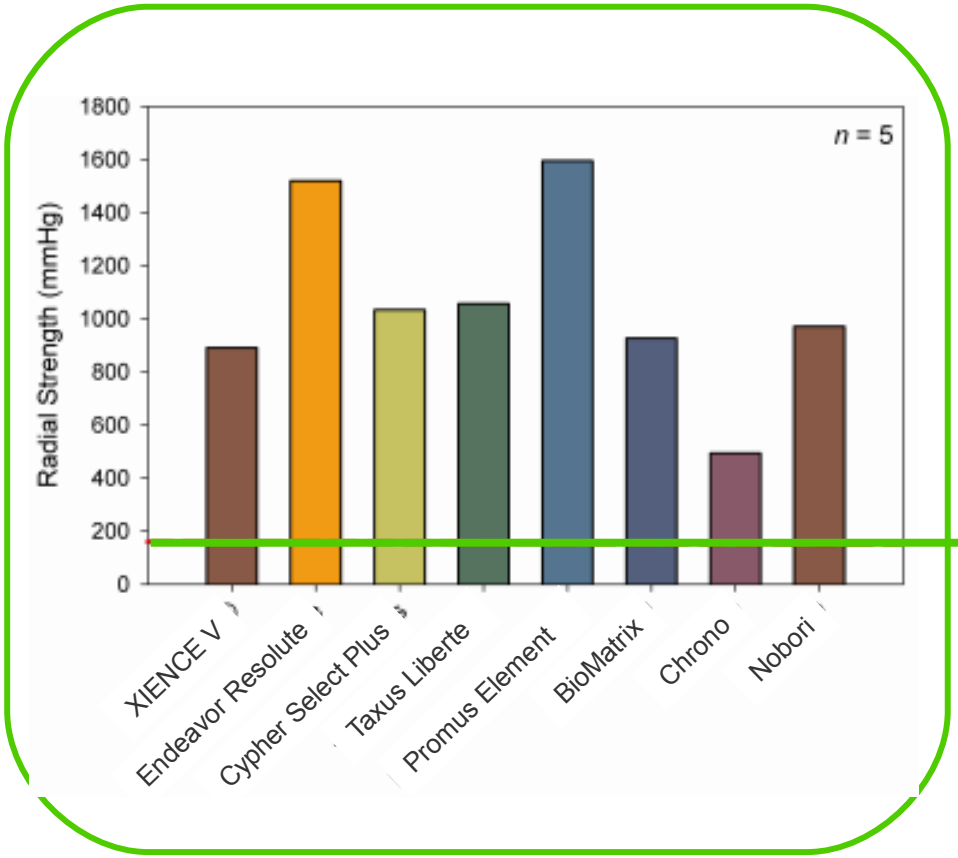


*Except for platinum markers

Strut Thickness Comparison

CYPHER	XIENCE V	BVS
		
Strut Thickness		
140 µm	81 µm	~152 µm \ 0 µm*
Total Thickness		
158 µm	94 µm	~157 µm \ 0 µm*

How Much Radial Strength is Needed?

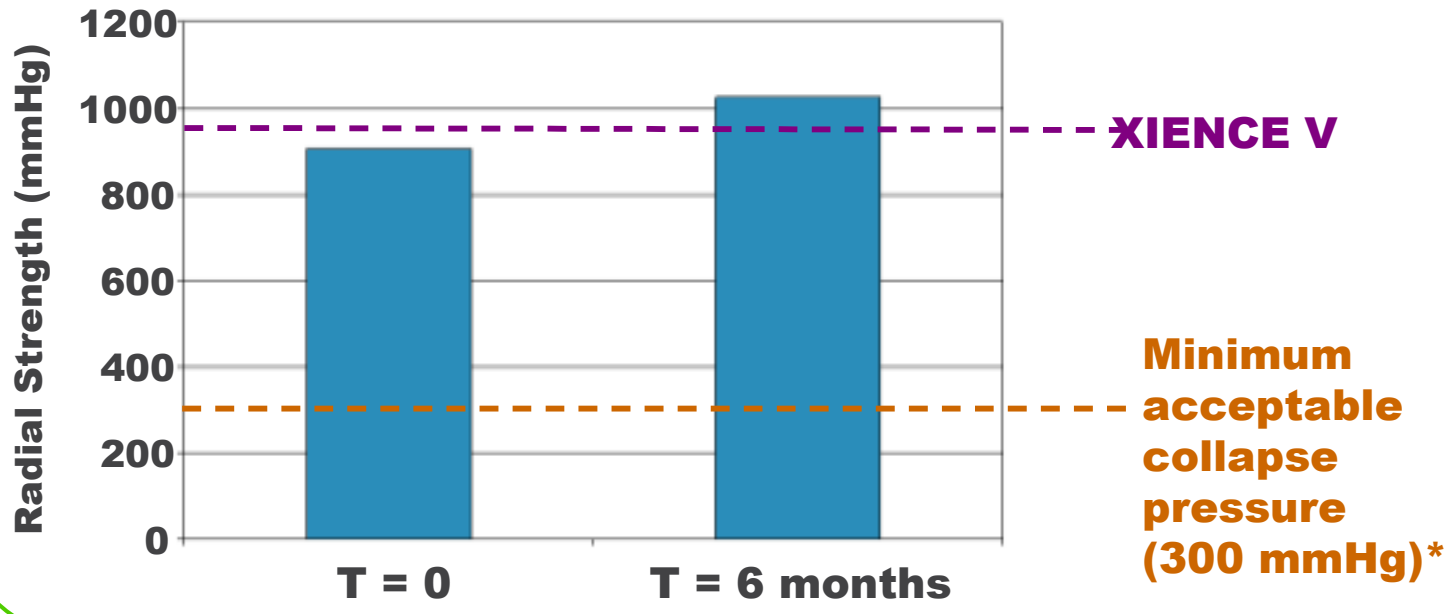


- **Radial strength varies widely across metallic stents**
- **There is no correlation between the magnitude of radial strength and clinical outcomes**
- **Perhaps it is only important to exceed a minimum threshold?**

175 mmHg is the estimated difference between transluminal (canine model1) and extraluminal pressures[2]

1Dobrin P.B., *Am. J .Physiol.* 1973; **225**: 659.
2Agrawal C.M,. *Biomaterials* 1992; **13**: 176.

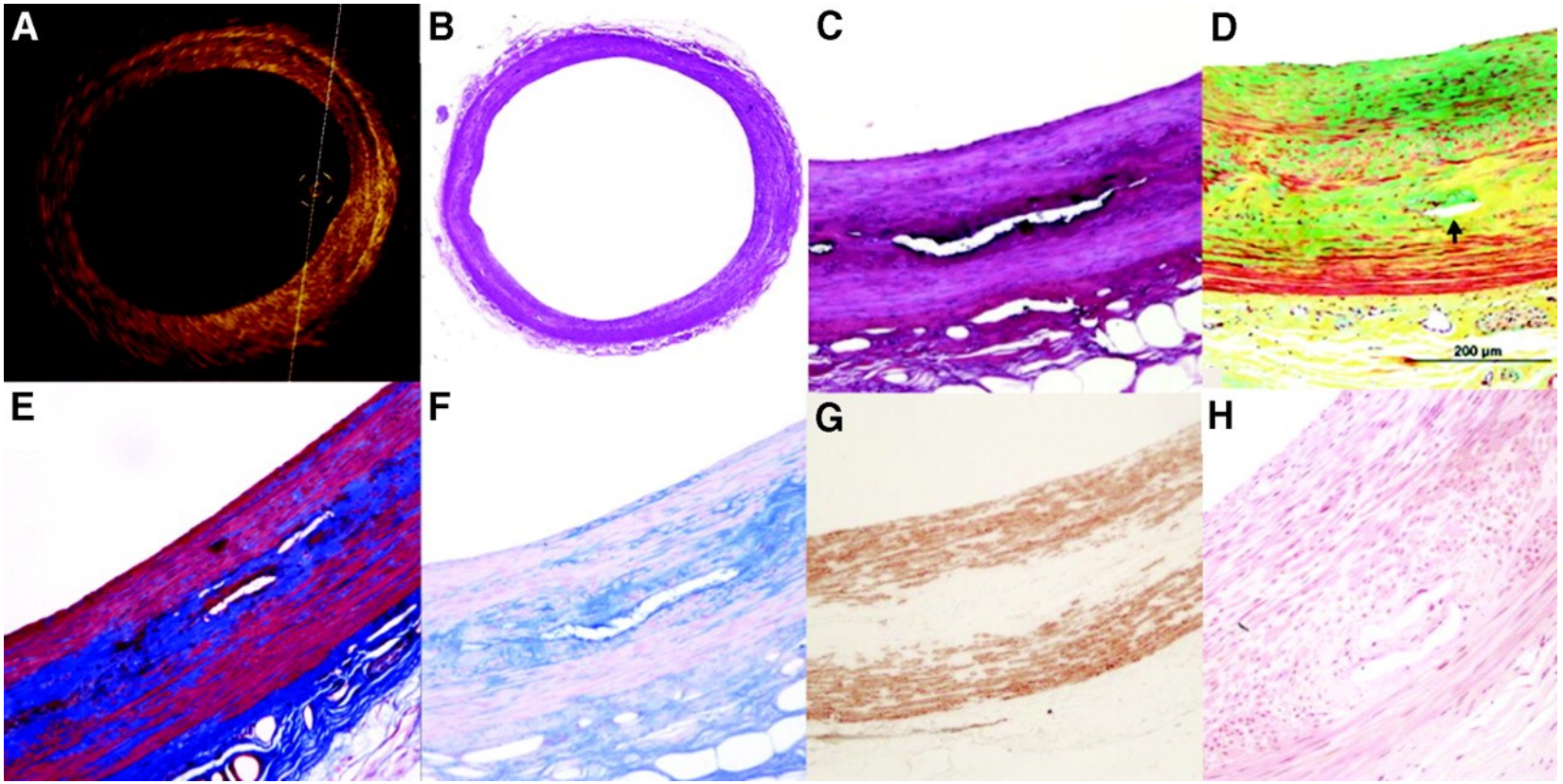
Absorb Radial Strength



ABSORB appears to maintain adequate support for at least as long as is needed

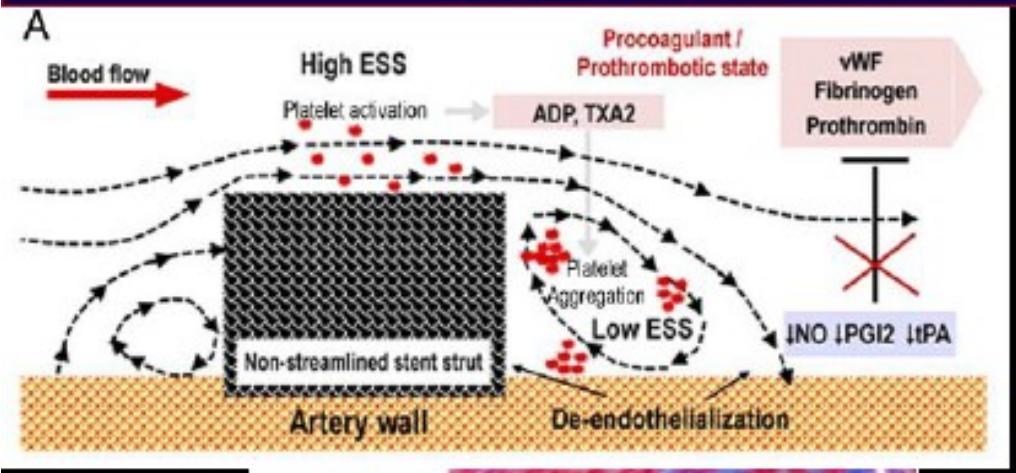
Devices subjected to simulated physiologic environment (fatigue testing). Tests performed at and data on file at Abbott Vascular.
*Agrawal, CM, et.al. *Biomaterials*. 1992; 13: 176-182.

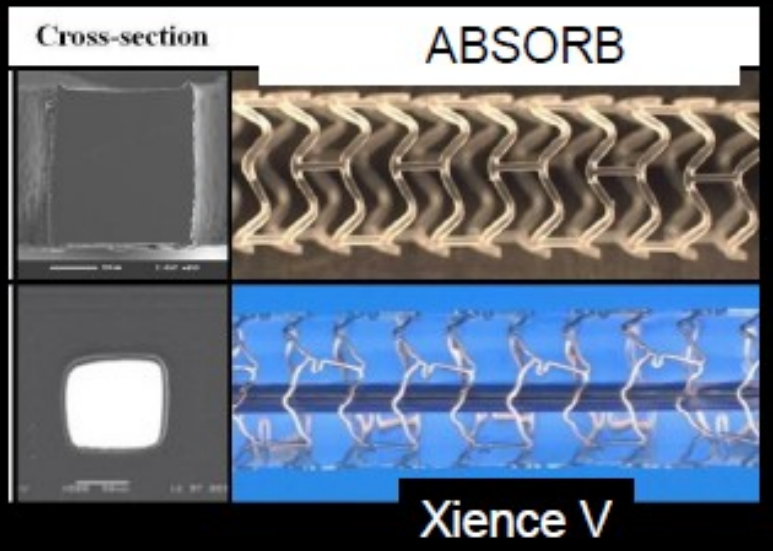
4 Jahres - *follow up*

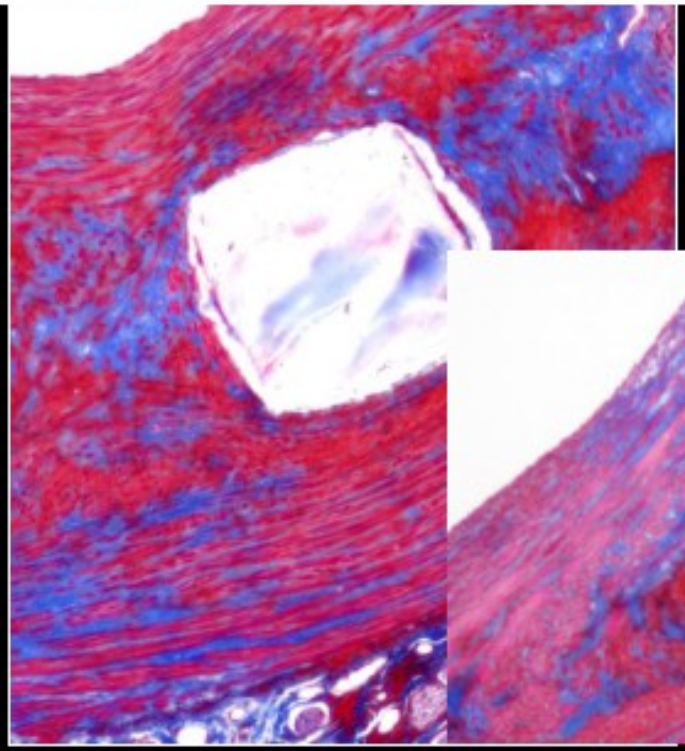


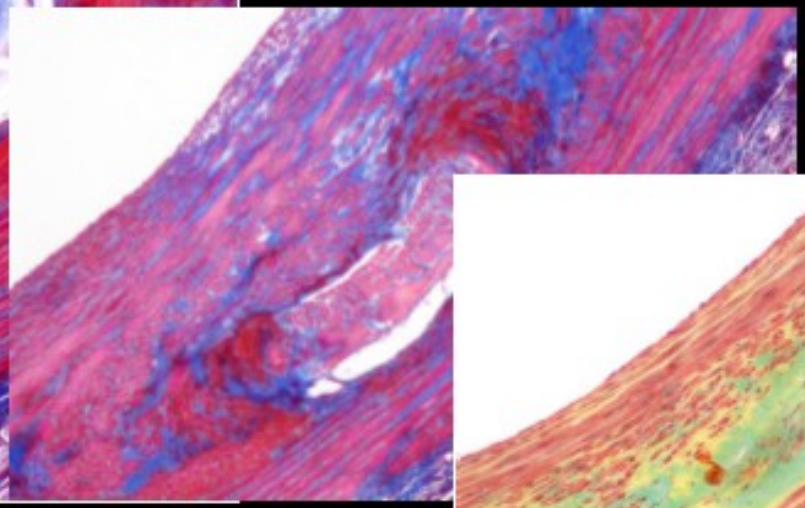
Onuma Y. et al., Circulation 2010

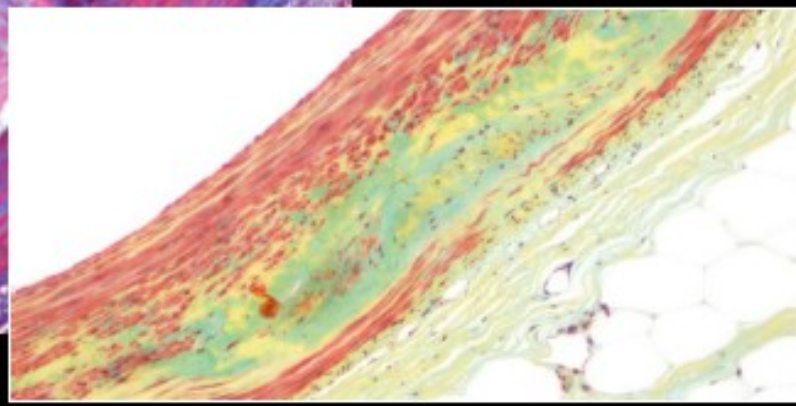
#4. Low shear-stress behind the strut will disappear after neointimal formation and its subsequent thinning





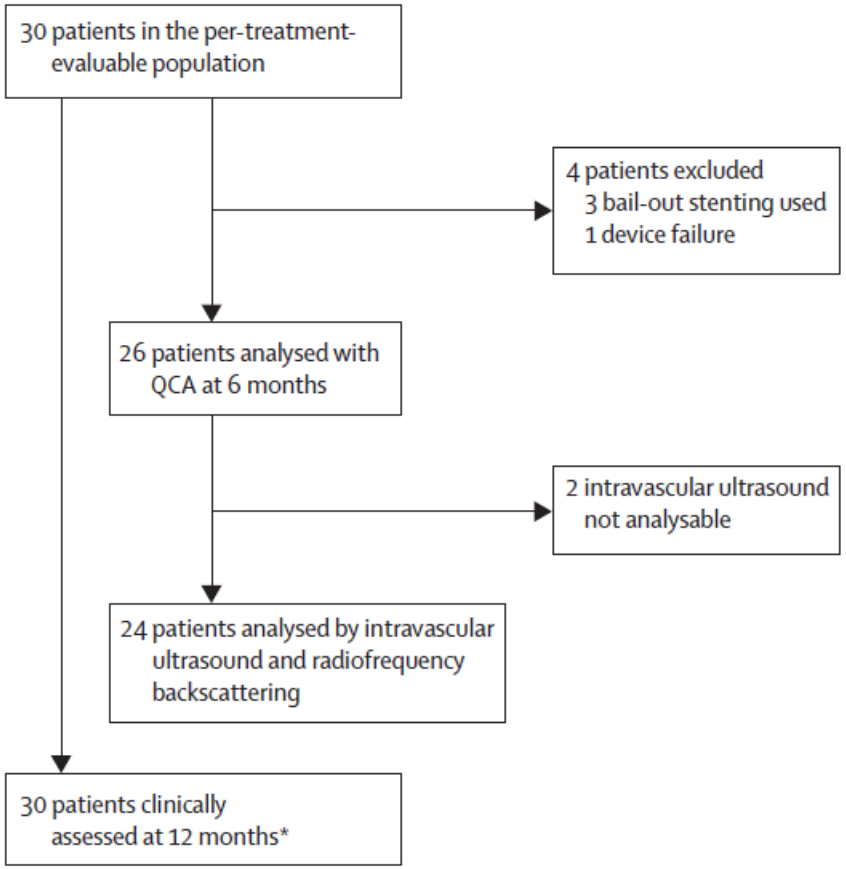






A bioabsorbable everolimus-eluting coronary stent system for patients with single de-novo coronary artery lesions (ABSORB): a prospective open-label trial

John A Ormiston, Patrick W Serruys, Evelyn Regar, Dariusz Dudek, Leif Thuesen, Mark W I Webster, Yoshinobu Onuma, Hector M Garcia-Garcia, Robert McGreevy, Susan Veldhof



6 Monate FU

1 Jahr FU

2 Jahre FU

4 Jahre FU

5 Jahre FU

Ormiston J. et al., Lancet 2008

A bioabsorbable everolimus-eluting coronary stent system (ABSORB): 2-year outcomes and results from multiple imaging methods

Patrick W Serruys, John A Ormiston, Yoshinobu Onuma, Evelyn Regar, Nieves Gonzalo, Hector M Garcia-Garcia, Koen Nieman, Nico Bruining, Cécile Dorange, KarineMiquel-Hébert, Susan Veldhof, Mark Webster, Leif Thuesen, Dariusz Dudek

	6 months (n=30)	12 months (n=29)*	18 months (n=29)*	2 years (n=28)†
Cardiac death	0%	0%	0%	0%
MI	3·3% (1)‡	3·4% (1)‡	3·4% (1)‡	3·6% (1)‡
Q-wave MI	0%	0%	0%	0%
Non-Q-wave MI	3·3% (1)‡	3·4% (1)‡	3·4% (1)‡	3·6% (1)‡
Ischaemia-driven TLR	0%	0%	0%	0%
By PCI	0%	0%	0%	0%
By CABG	0%	0%	0%	0%
Ischaemia-driven MACE (cardiac death, MI, or ischaemia-driven TLR)	3·3% (1)‡	3·4% (1)‡	3·4% (1)‡	3·6% (1)‡
Stent thrombosis	0%	0%	0%	0%

Data are % (number of patients). MI=myocardial infarction. TLR=target lesion revascularisation. PCI=percutaneous intervention. CABG=coronary artery bypass graft. MACE=major adverse cardiac event.*One patient officially withdrew from the study, but his vital status and clinical follow-up are made available through his referring physician. †One patient died from a non–cardiac cause. ‡Same patient. This patient also underwent a target lesion revascularisation, not qualified as ischaemia-driven target lesion revascularisation (diameter stenosis=42%).

Table 2: **Clinical outcomes at 2 years**

Serruys P. et al., Lancet 2009

Revascularize like a best-in-class DES, XIENCE

Safety: Low scaffold thrombosis rates in ABSORB Cohorts A & B and ABSORB EXTEND

ABSORB Cohort A

0.0% ST throughout 5 years1

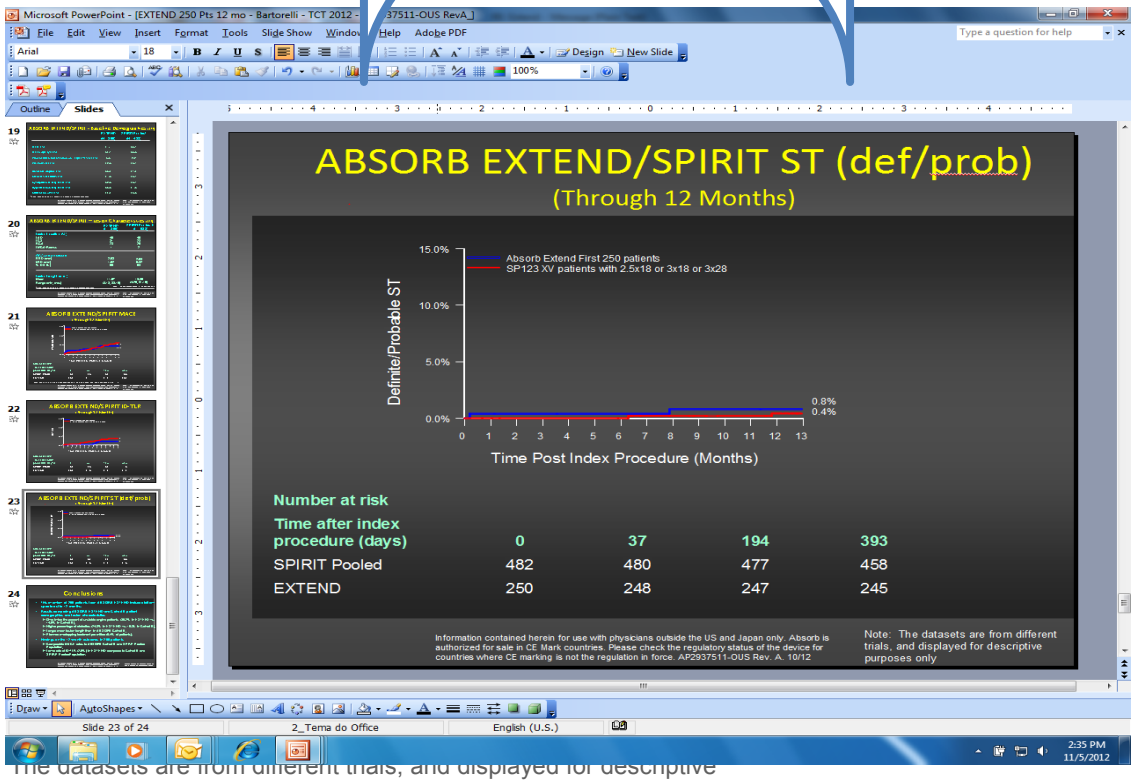
ABSORB Cohort B1

0.0% ST up to 3 years[2]

ABSORB EXTEND

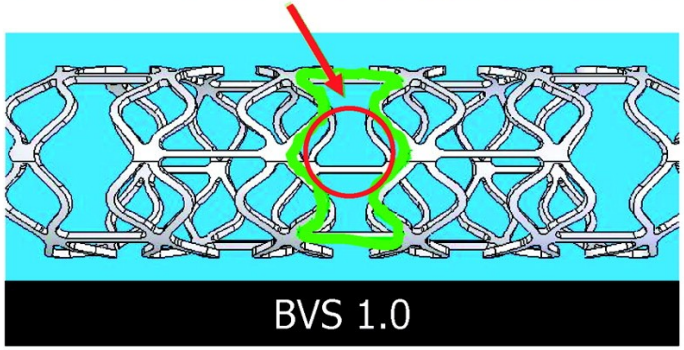
0.8% at 12 months3

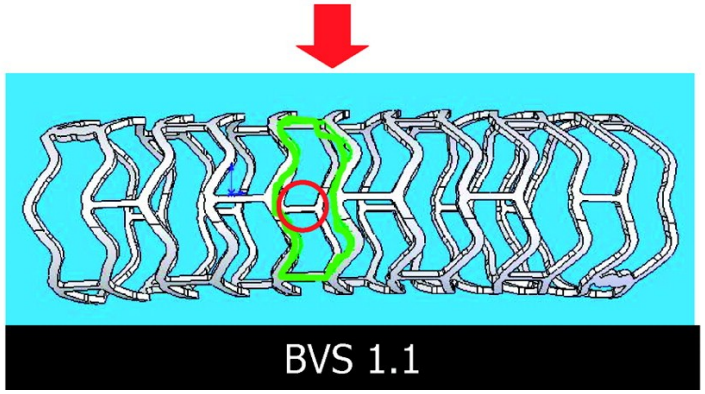
ABSORB EXTEND

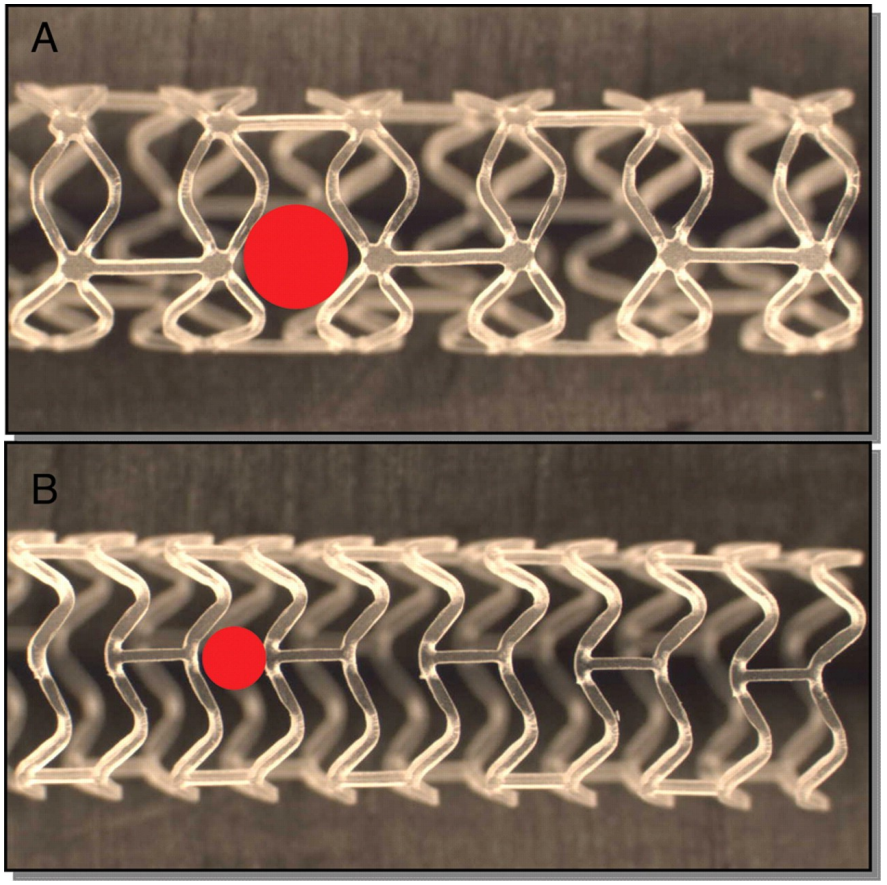


1 Serruys PW, 5-Year Cohort A and 2-Year Cohort B Results: Integrated Insights, TCT2011, 2 Smits P. ABSORB Cohort B 3-year data, TCT 2012; 3Bartorelli, A, ABSORB EXTEND preiliminary 6 months and 1 year data, TCT 2012;

Larger Maximum Circular Unsupported scaffold area (MCUSA)

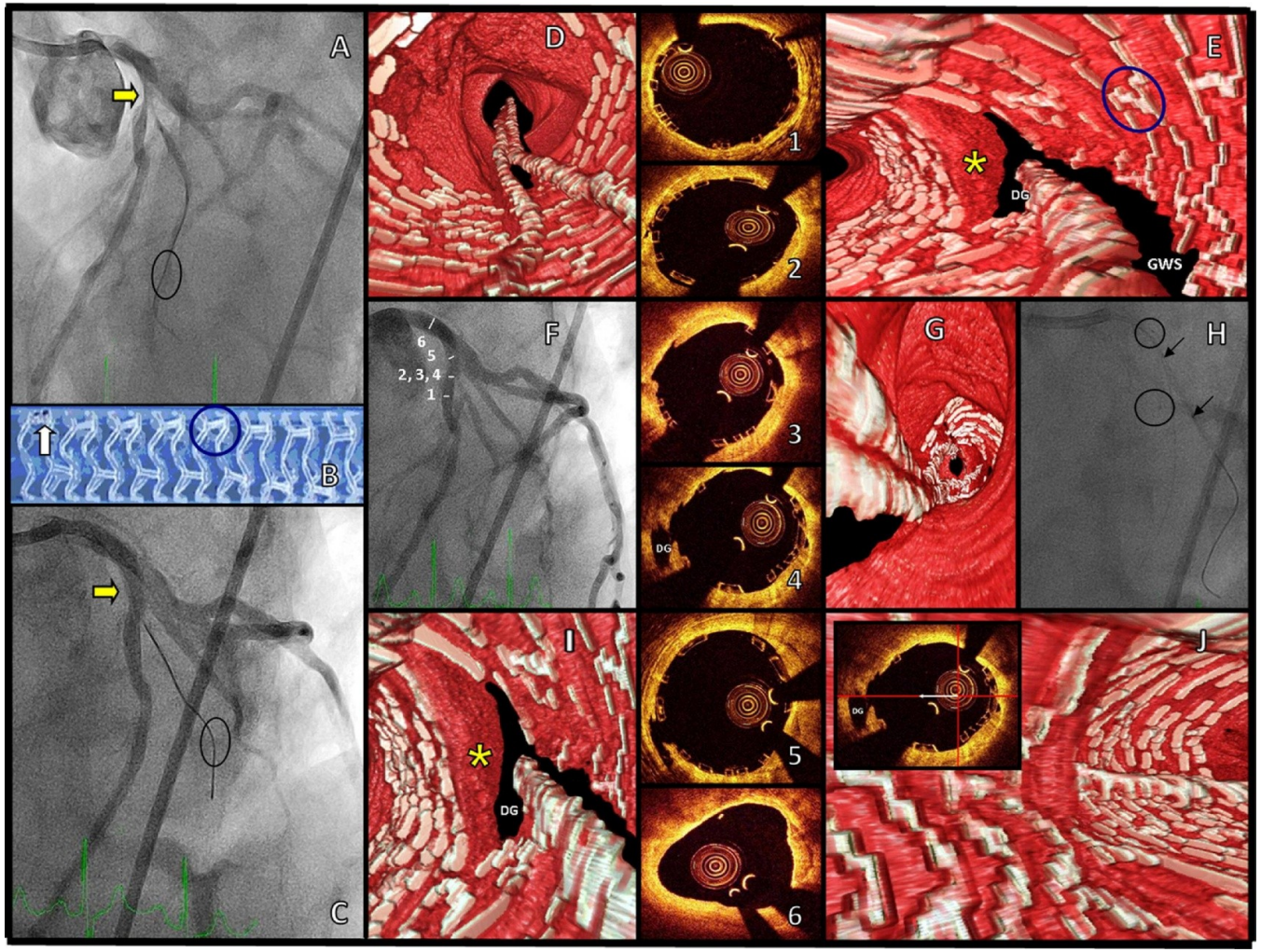






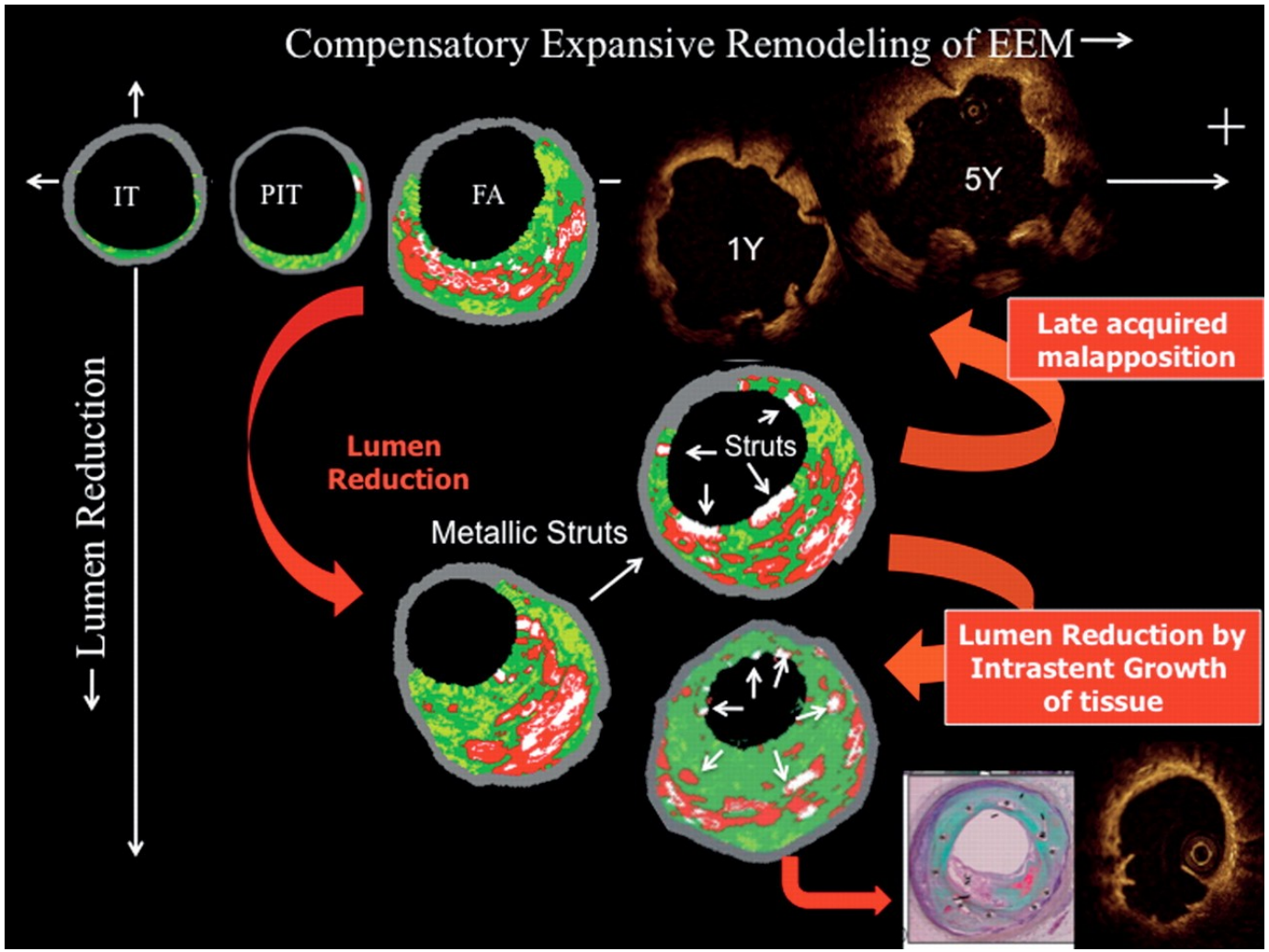
Serruys PW et al., Circulation 2010
Gomez-Lara J. et al., EHJ 2011

3D-virtuel OCT-pictures



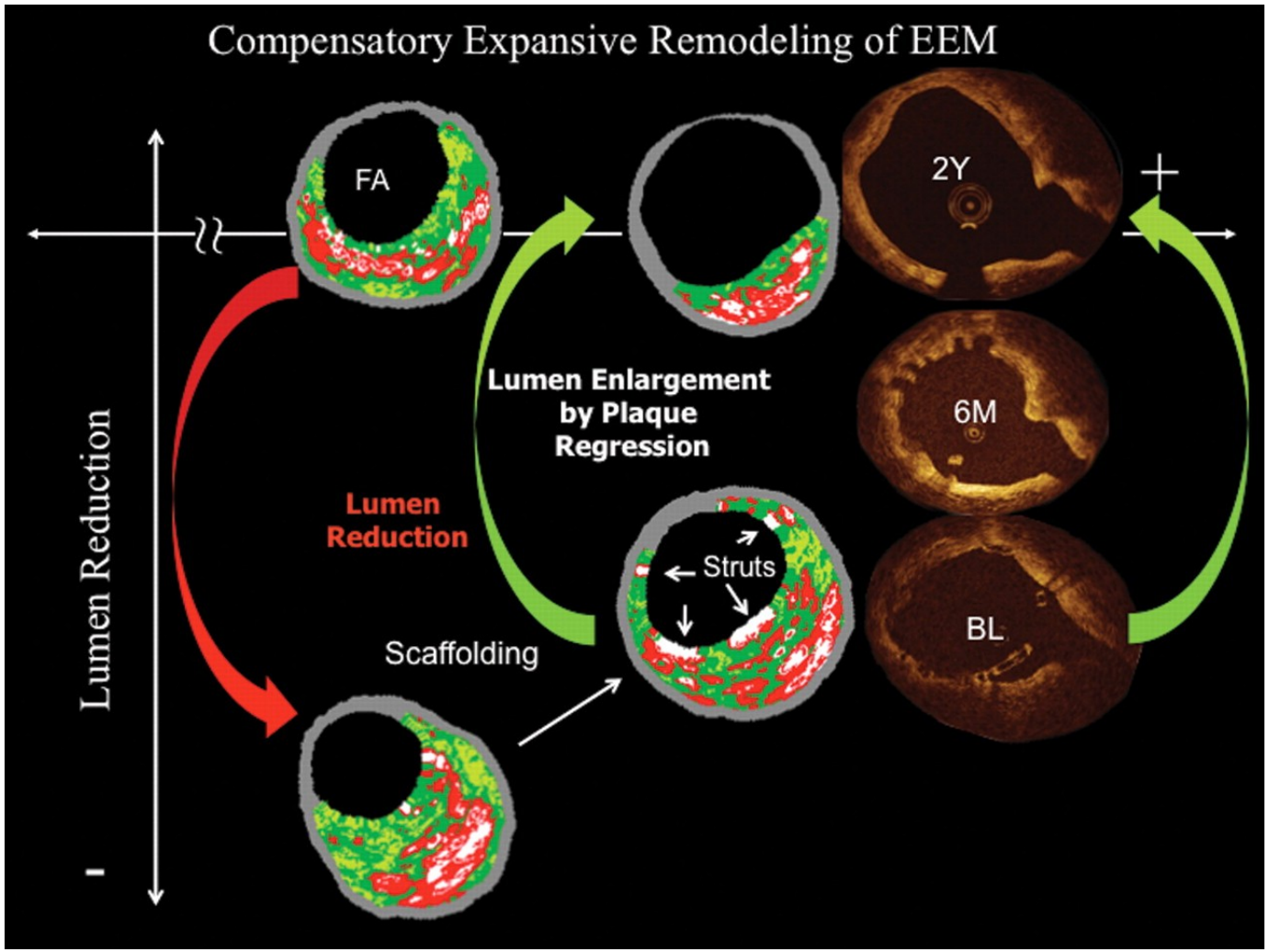
Gogas B. et al., JACC 2011

Atherosclerotic Process after DES-Implantation



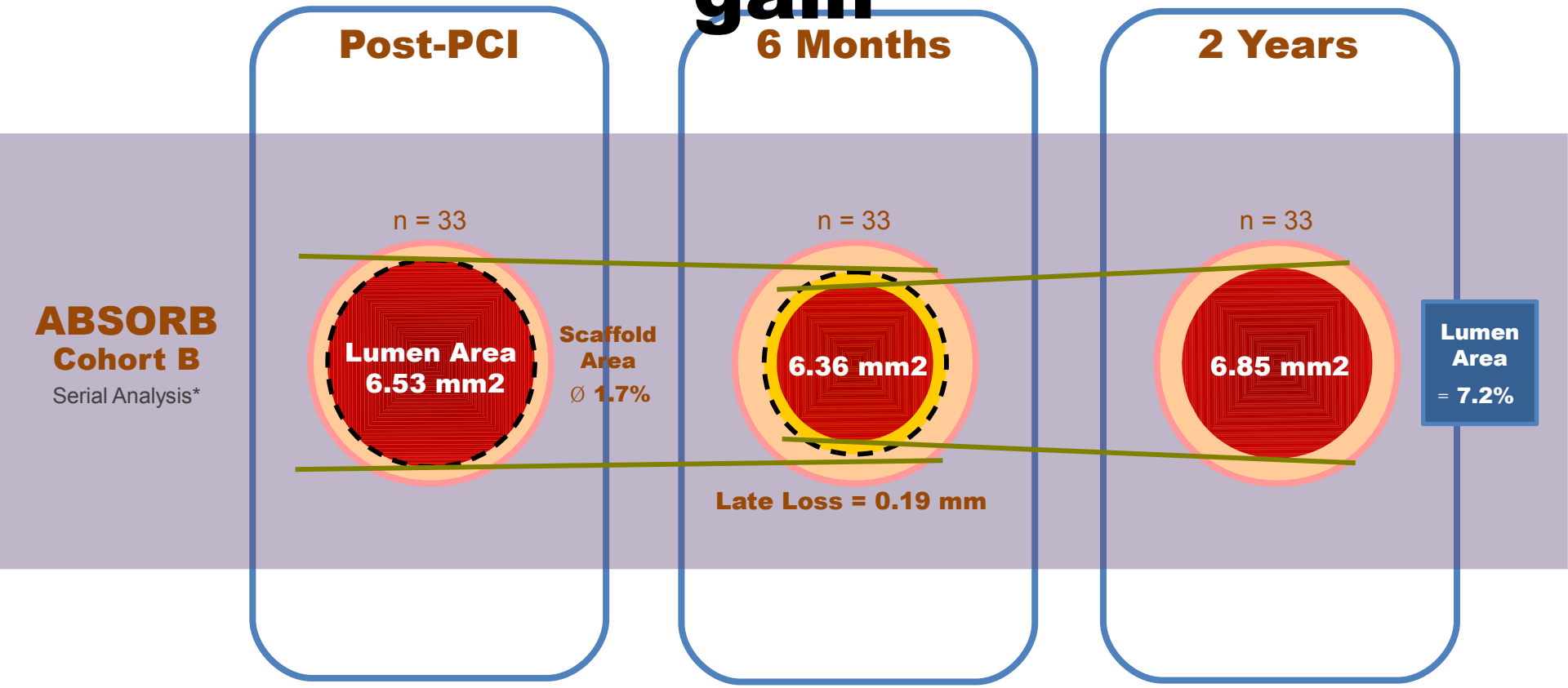
Serruys PW et al., EHJ 2012

Atherosclerotic Process after BVS-Implantation

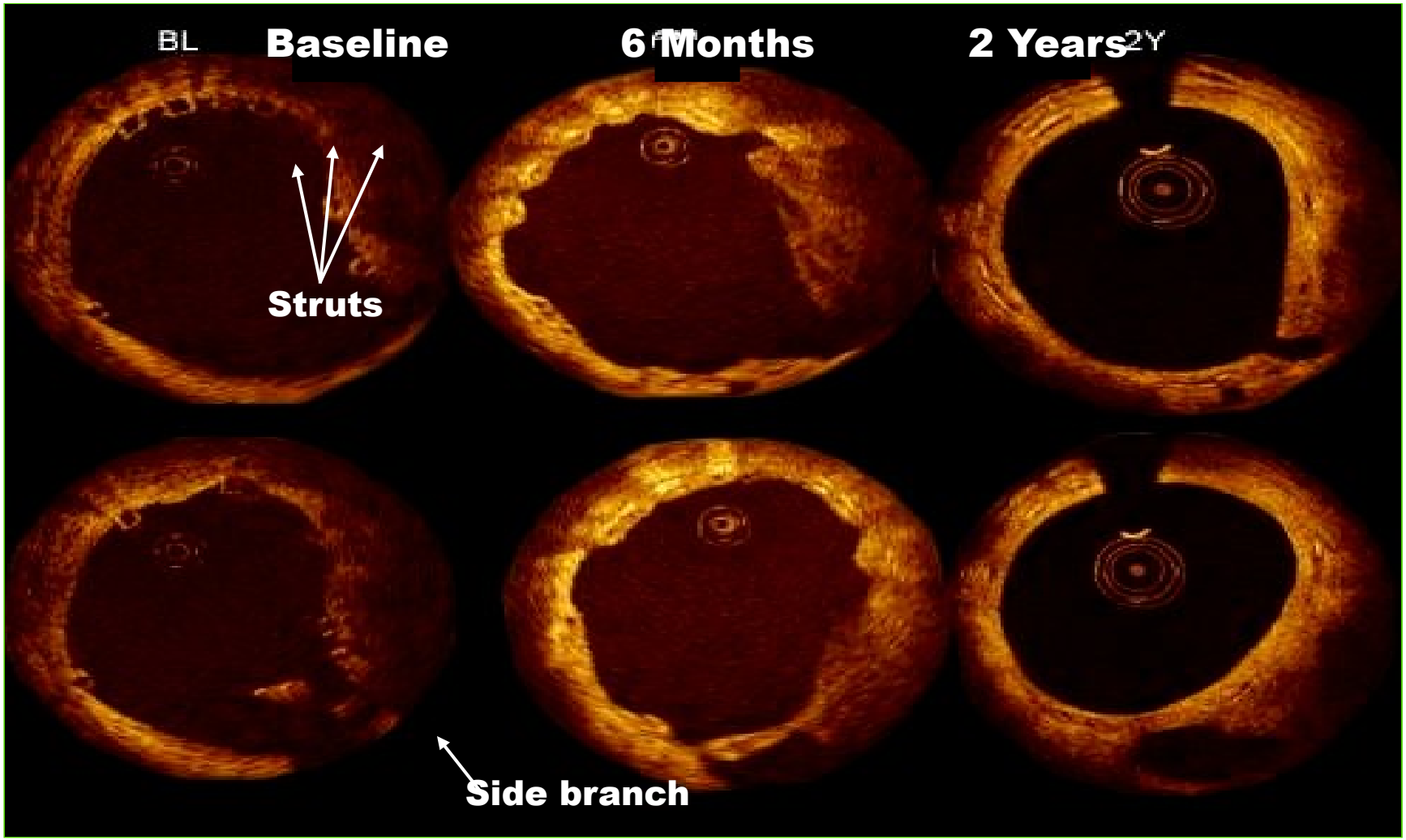


Serruys PW et al., EHJ 2012

Paradigm Shift: Late Lumen Loss to Late Lumen gain



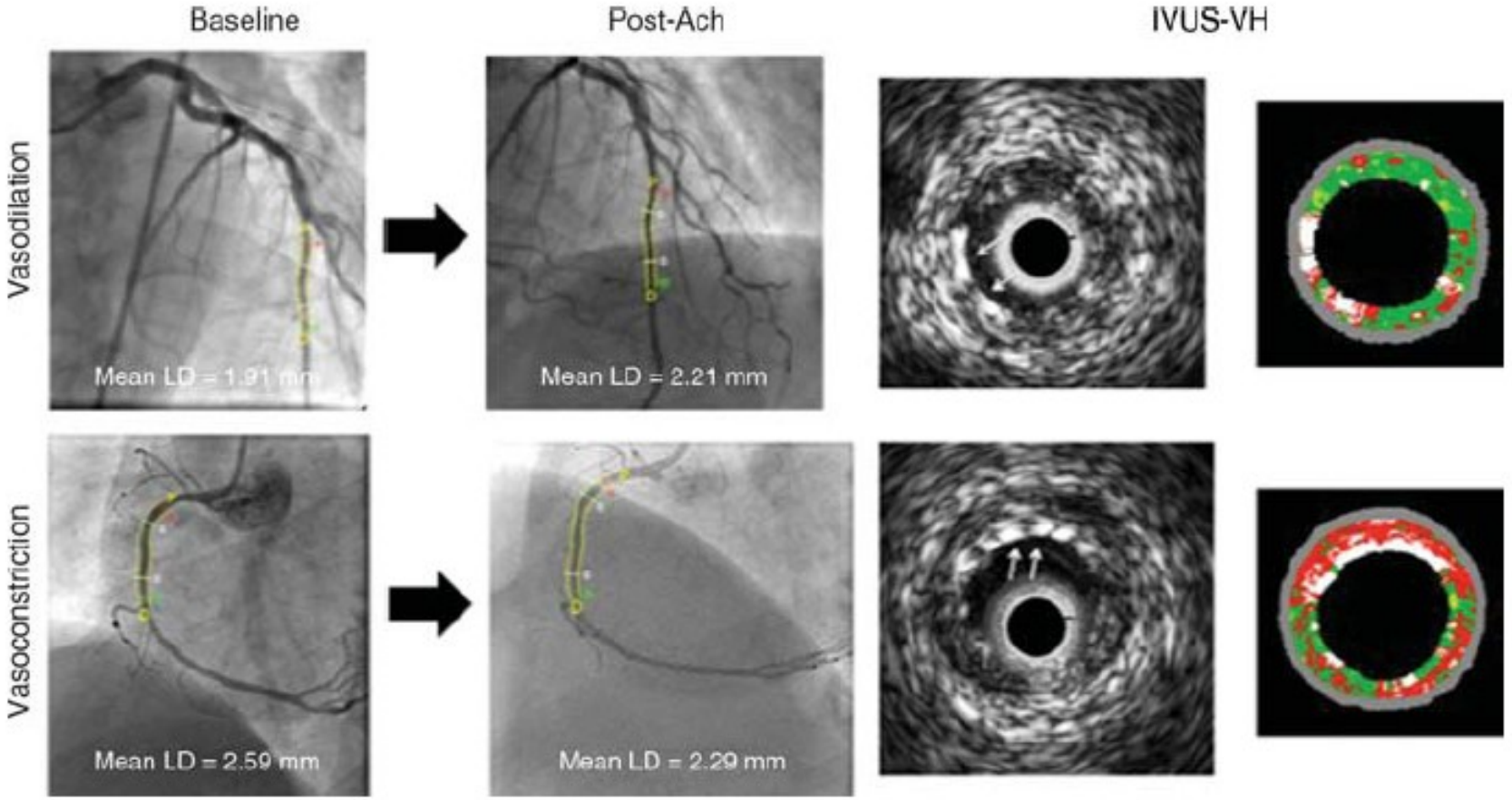
*Serruys, PW., TCT 2011



Serruys, PW., ESC 2008.

European Heart Journal (2012) **33**, 1325–1333
doi:10.1093/eurheartj/ehr466

Endothelial-dependent vasomotion in a coronary segment treated by ABSORB everolimus-eluting bioresorbable vascular scaffold system is related to plaque composition at the time of bioresorption of the polymer: indirect finding

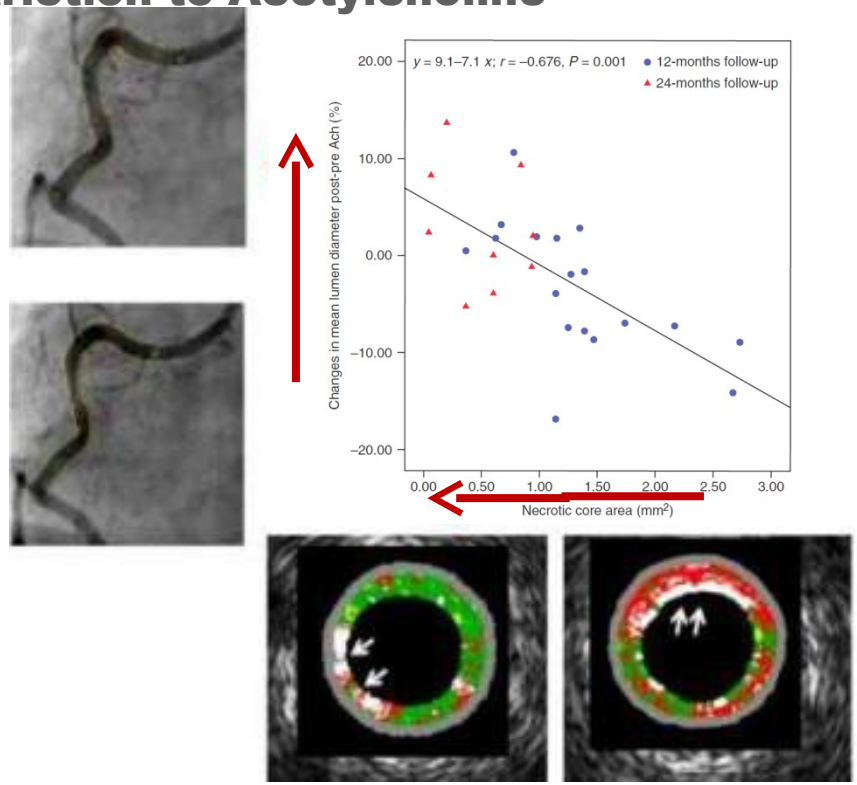


Brugaletta S. et al., EHJ 2012

Restoration and Resorption
Factors influencing Vasomotion

Factors influencing vasomotion: lesion morphology

Large necrotic core area is associated with vasoconstriction to Acetylcholine



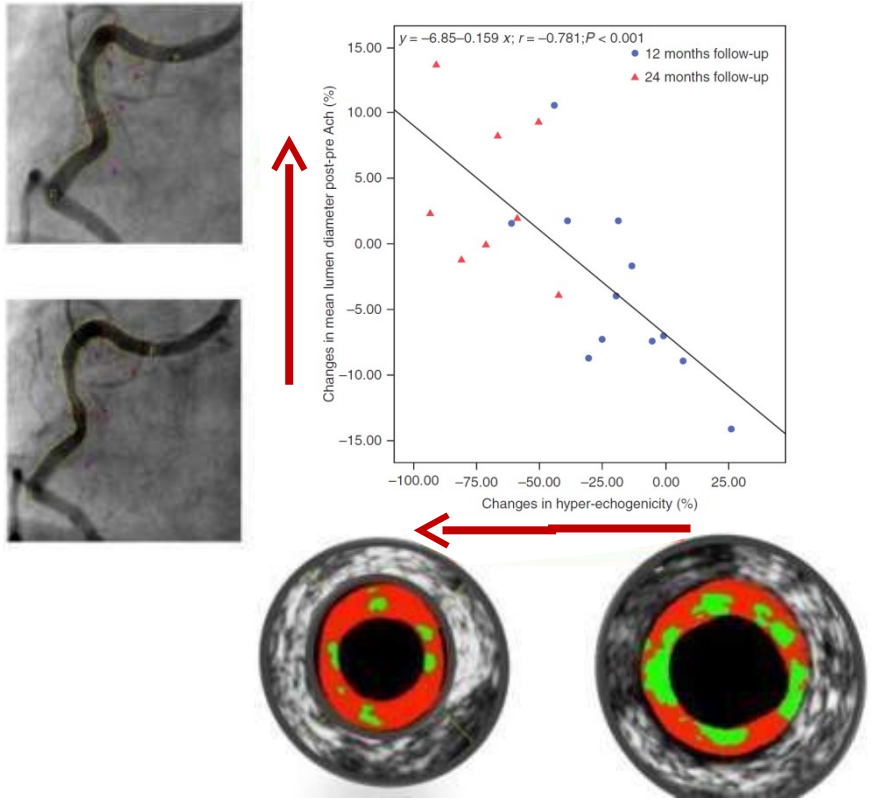
The smaller the *necrotic core*, the higher the vasomotion

Brugaletta S. et al., EHJ 2012

Restoration and Resorption
Factors influencing Vasomotion

Factors influencing vasomotion: changes in hyper-echogenicity

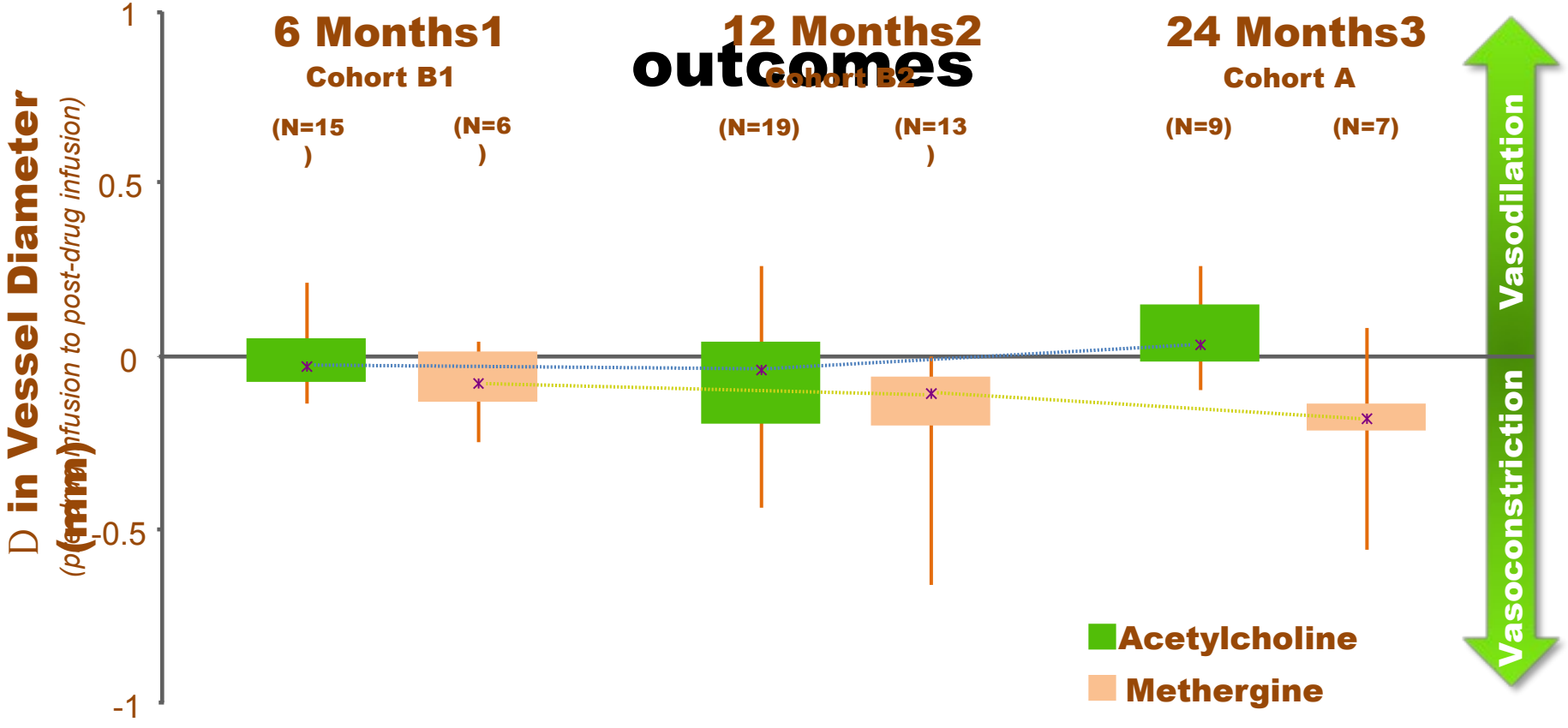
Positive response to Acetylcholine is associated with a reduction in hyper-echogenicity of the polymeric struts



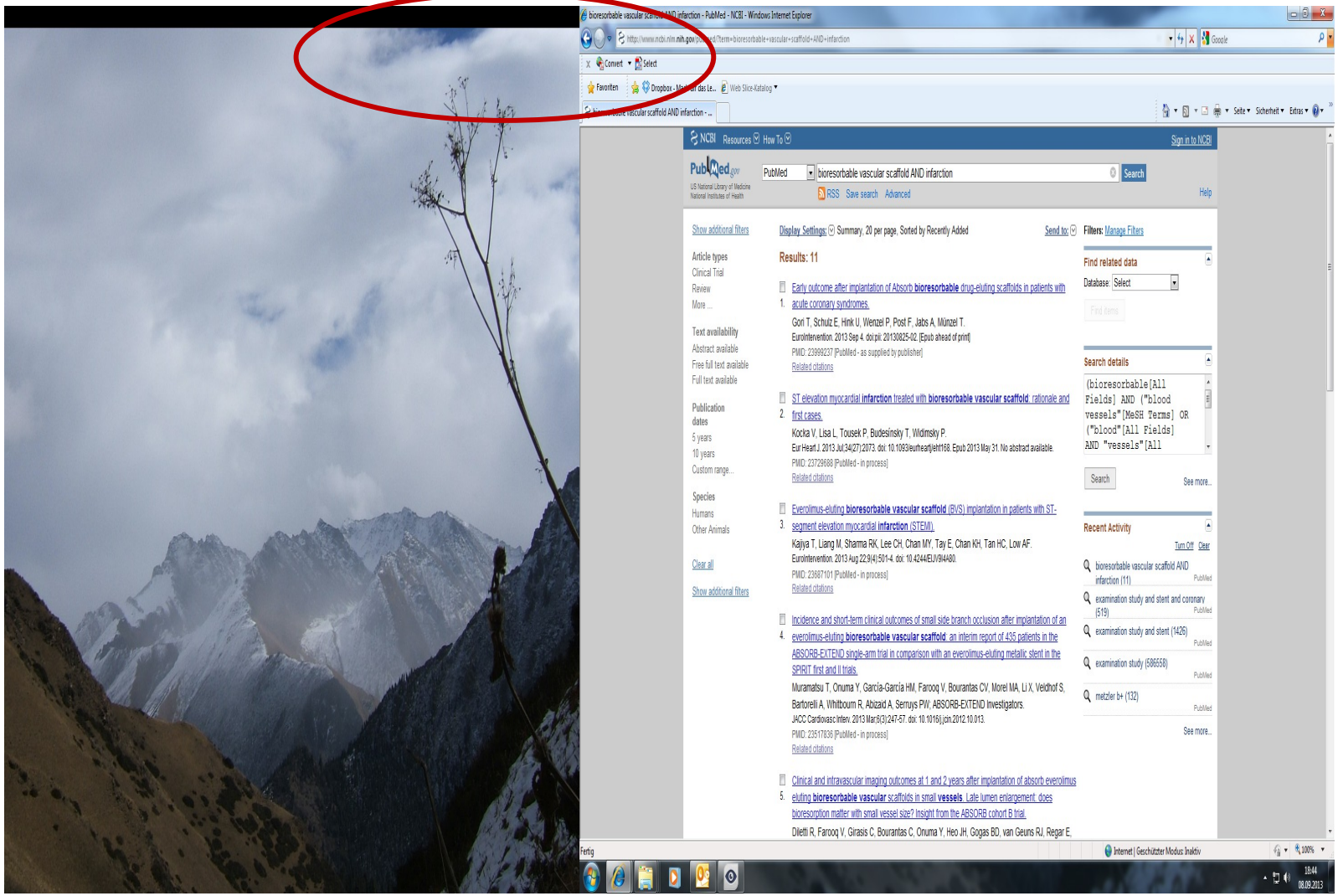
The less *struts*, the higher the vasomotion

Brugaletta S. et al., EHJ 2012

Early evidence of Vasomotion suggest improved long term outcomes



1. Adapted from Serruys, PW. ACC 2011 / 2. Adapted from Serruys, PW. ACC 2011 / 3. Adapted from Serruys, PW, et al. Lancet 2009; 373: 897-910.


bioresorbable vascular scaffold AND infarction - PubMed - NCBI - Windows Internet Explorer
NCBI Resources How To Sign in to NCBI
PubMed.gov
US National Library of Medicine
National Institutes of Health
PubMed
bioresorbable vascular scaffold AND infarction
Search
RSS Save search Advanced
Help
Show additional filters
Display Settings: Summary, 20 per page, Sorted by Recently Added
Send to:
Filters: Manage Filters
Article types
Clinical Trial
Review
More ...
Text availability
Abstract available
Free full text available
Full text available
Publication dates
5 years
10 years
Custom range...
Species
Humans
Other Animals
Clear all
Show additional filters
Results: 11
1. Early outcome after implantation of Absorb bioresorbable drug-eluting scaffolds in patients with acute coronary syndromes.
Gori T, Schulz E, Hink U, Wenzel P, Post F, Jabs A, Münzel T.
EuroIntervention. 2013 Sep 4. doi:pii: 20130825-02. [Epub ahead of print]
PMID: 23899237 [PubMed - as supplied by publisher]
Related citations
2. ST elevation myocardial infarction treated with bioresorbable vascular scaffold, rationale and first cases.
Kocka V, Lisa L, Tousek P, Budesinsky T, Widimsky P.
Eur Heart J. 2013 Jul;34(27):2073. doi: 10.1093/eurheartj/eht168. Epub 2013 May 31. No abstract available.
PMID: 23729688 [PubMed - in process]
Related citations
3. Everolimus-eluting bioresorbable vascular scaffold (BVS) implantation in patients with ST-segment elevation myocardial infarction (STEMI).
Kajiya T, Liang M, Sharma RK, Lee CH, Chan MY, Tay E, Chan KH, Tan HC, Low AF.
EuroIntervention. 2013 Aug 22;9(4):501-4. doi: 10.4244/EIJV9I4A80.
PMID: 23687101 [PubMed - in process]
Related citations
4. Incidence and short-term clinical outcomes of small side branch occlusion after implantation of an everolimus-eluting bioresorbable vascular scaffold: an interim report of 435 patients in the ABSORB-EXTEND single-arm trial in comparison with an everolimus-eluting metallic stent in the SPIRIT first and II trials.
Muramatsu T, Onuma Y, García-García HM, Farooq V, Bourantas CV, Morel MA, Li X, Veldhof S, Bartorelli A, Whitbourn R, Abizaid A, Serruys PW; ABSORB-EXTEND Investigators.
JACC Cardiovasc Interv. 2013 Mar;6(3):247-57. doi: 10.1016/j.jcin.2012.10.013.
PMID: 23517836 [PubMed - in process]
Related citations
5. Clinical and intravascular imaging outcomes at 1 and 2 years after implantation of absorb everolimus eluting bioresorbable vascular scaffolds in small vessels. Late lumen enlargement: does bioresorption matter with small vessel size? Insight from the ABSORB cohort B trial.
Diletti R, Farooq V, Girasis C, Bourantas C, Onuma Y, Heo JH, Gogas BD, van Geuns RJ, Regar E,
Find related data
Database: Select
Find items
Search details
(bioresorbable[All Fields] AND ("blood vessels"[MeSH Terms] OR ("blood"[All Fields] AND "vessels"[All
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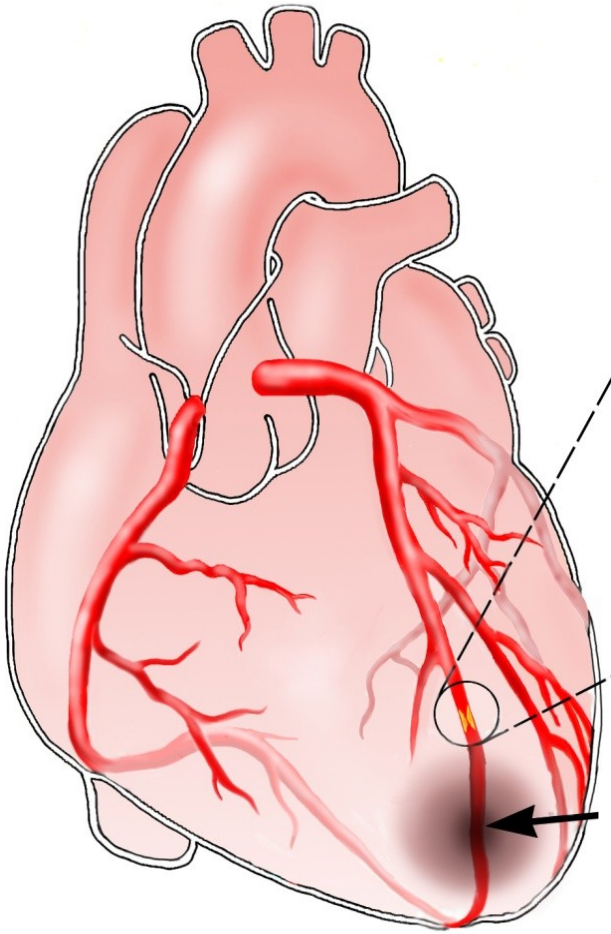
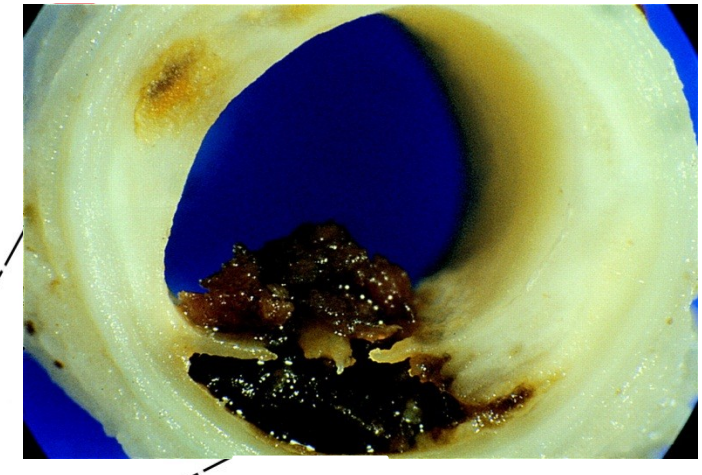
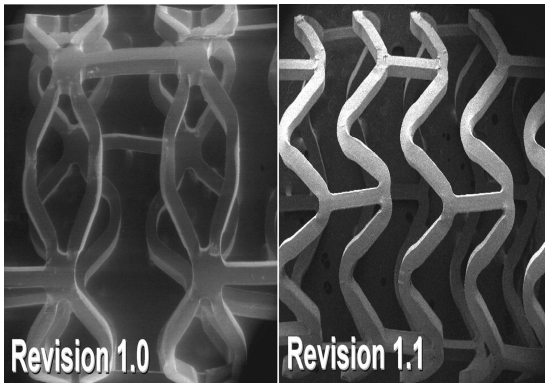





Revision 1.0
Revision 1.1

resorbable vascular scaffolds in acute STEMI (PRAGUE-19 study)

Petr Widimsky

Procedural result and BVS feasibility

- **42 BVS successfully implanted to 35/36 patients**
- **1 BVS could not be delivered to LCX with sharp take-off (bare metal stent was delivered successfully)**
- **32/35 BVS patients had ideal result**

PRAGUE-19 (in-hospital phase) conclusions

- **BVS implantation in acute STEMI is feasible and safe**
- **With the currently available size spectrum and expiration times BVS can be used in 25-33% of STEMI patients. Availability of 4.0 mm size would substantially increase this proportion**

Widimsky P. EuroPCR 2013

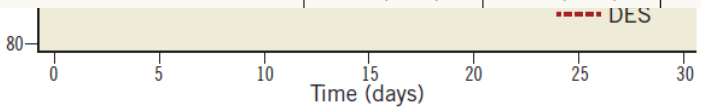
BVS group - safety

- **0% mortality**
- **0% reinfarction during hospital stay**
- **3% reinfarction (1BVS thrombosis 3 days after stopping ticagrelor)**
- **0% stroke**
- **0% clinical restenosis within 5 months**

Widimsky P. EuroPCR 2013

ABSORB BVS in STEMI-patients

	BVS N=150, n=194 scaffolds	DES N=103, n=129 stents	p
Patient characteristics			
Age	61.7±12.5	62.0±10.9	0.81
Male sex	110 (73%)	72 (70%)	0.77
Hypertension	95 (63%)	72 (70%)	0.50
Hypercholesterolaemia	45 (30%)	50 (49%)	0.002
Smoking	85 (57%)	53 (51%)	0.36
Diabetes	23 (15%)	21 (20%)	0.21
Prior revascularisation	25 (17%)	23 (23%)	0.15
Prior myocardial infarction	15 (10%)	15 (15%)	0.23
Clinical presentation			
Unstable angina	24 (16%)	20 (19%)	0.40
NSTEMI	60 (40%)	46 (45%)	0.51
STEMI	66 (44%)	37 (36%)	0.12
Single-vessel disease	64 (43%)	38 (37%)	0.43
Two- or three-vessel disease	86 (57%)	66 (64%)	



	BVS	DES	p
In-hospital outcome			
Death	1 (0.7%)	1 (1%)	1
Non-fatal MI	3 (2.1%)	1 (1%)	0.63
Non-target lesion revascularisation	0	0	1
Definite in-stent/scaffold thrombosis	2 (1.4%)	1 (1%)	0.77
Hospital stay, days	4.9±2.7	4.7±2.6	0.8
One-month outcome			
Death	2 (1.4%)	3 (2.9%)	0.66
Non-fatal MI	6 (4.0%)	4 (3.9%)	1
Non-target lesion revascularisation	10 (6.6%)	7 (6.9%)	1
Definite in-stent/scaffold thrombosis	3 (2.0%)	2 (1.9%)	1
Probable in-stent/scaffold thrombosis	1 (0.7%)	1 (1%)	1

Outcome after implantation. MI: myocardial infarction

Gori T. et al, EuroIntervention

ent 1:

ale patient

chest pain

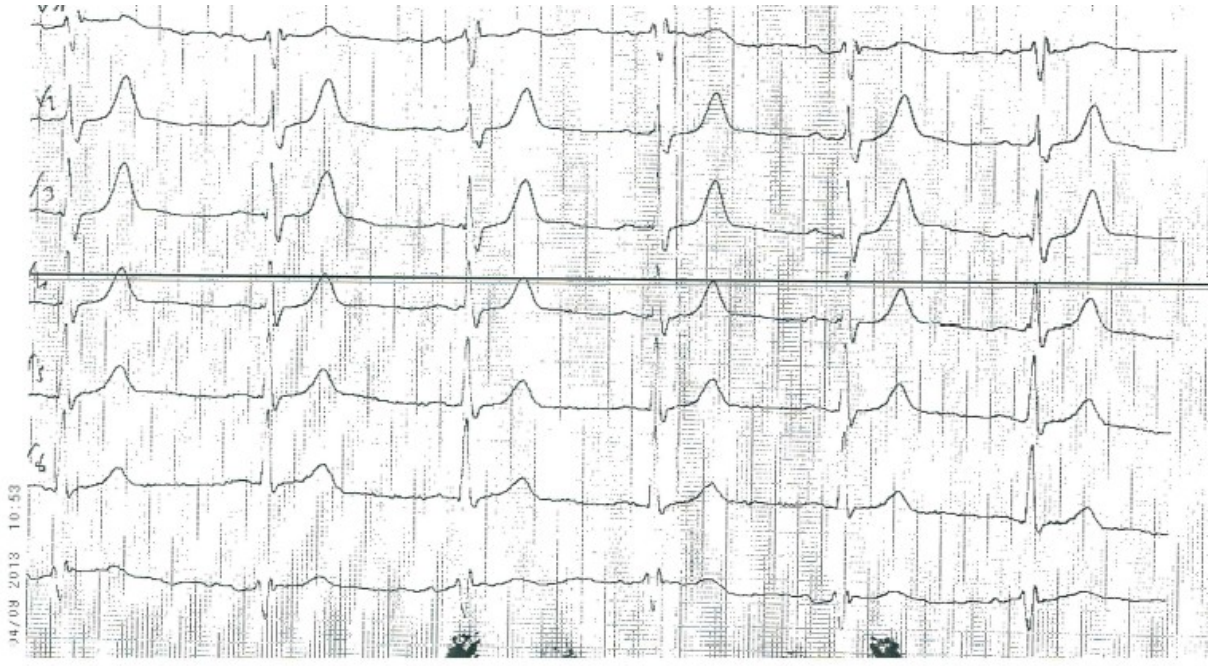
osis: acute ST-elevation myocardial infarction - anterior wall

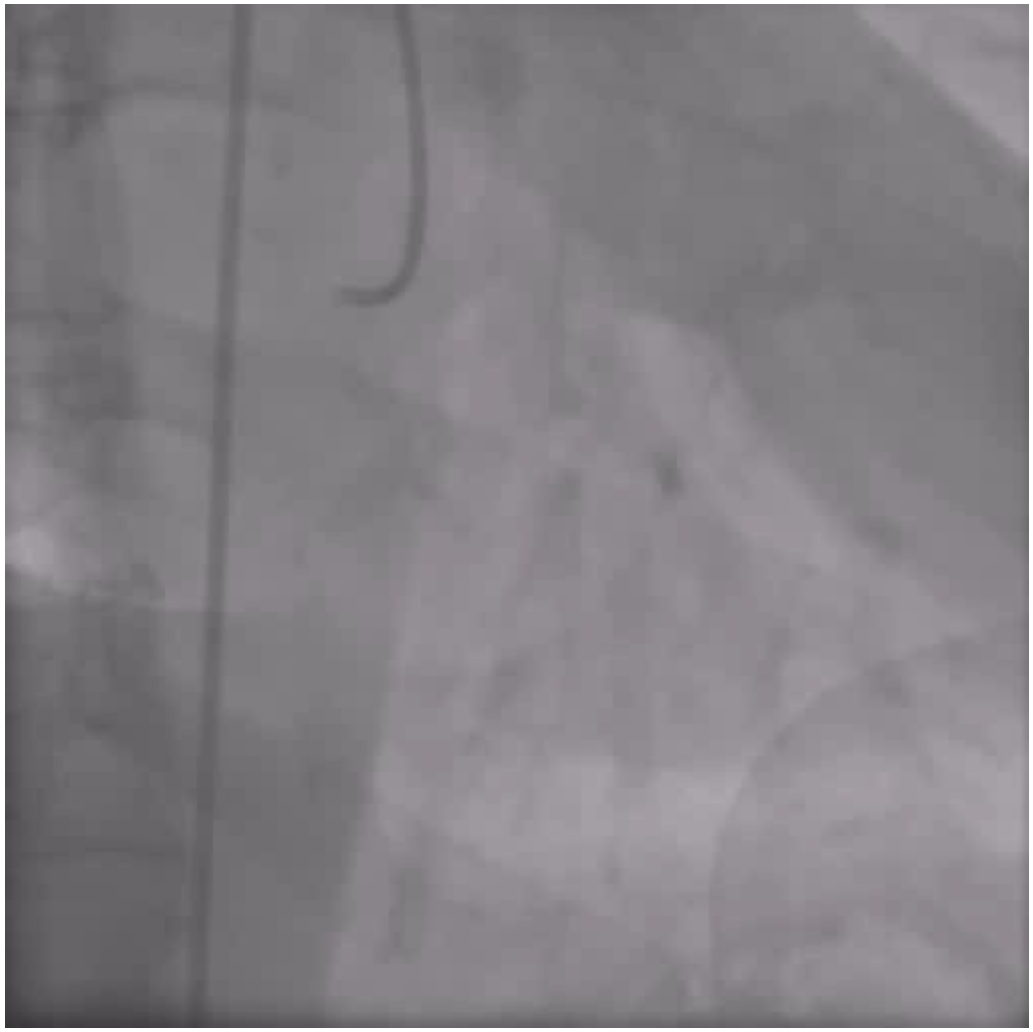
actors: family history, hypercholesterolemia, massive nicotine abu

o ballon time: ca. 2h

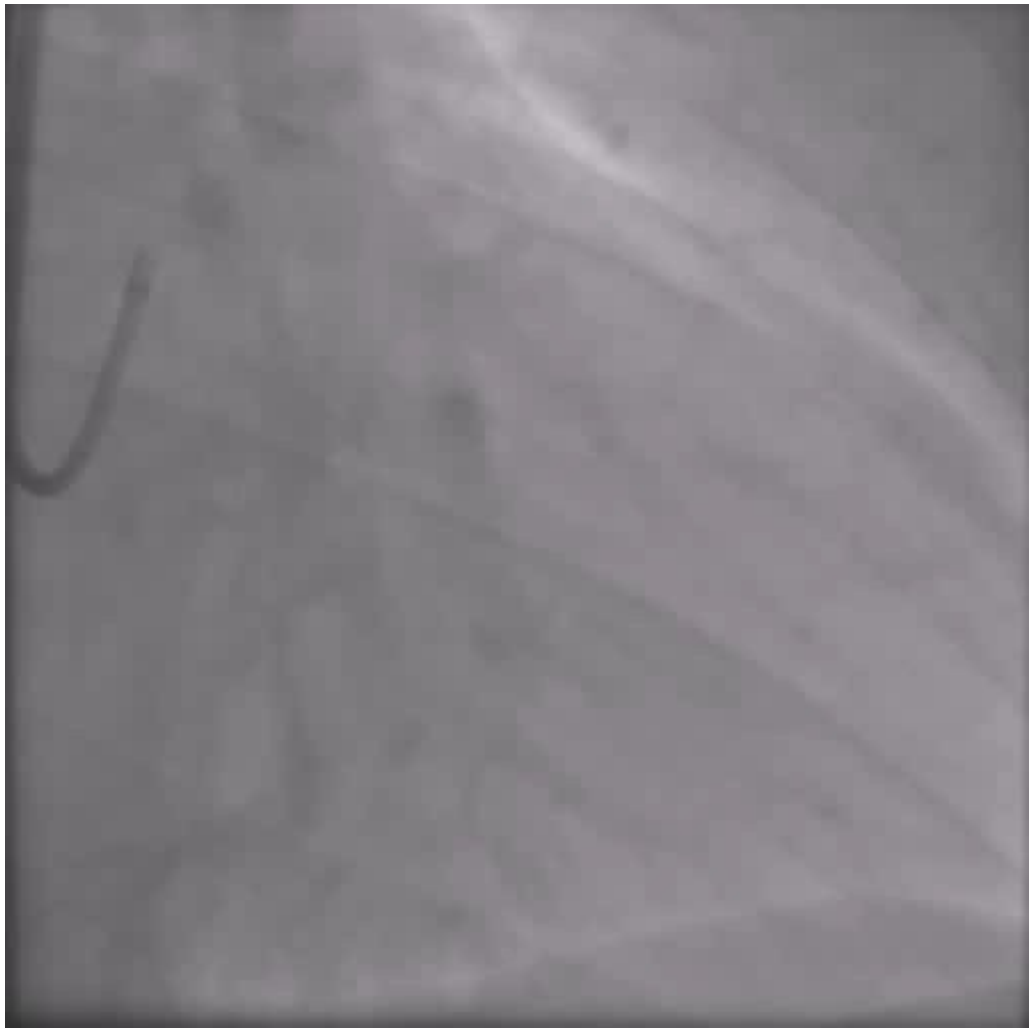
.000 IE Hep., 250 mg Acetyl salicylic acid, Prasugrel 60mg, Abcixi

04.09.2013

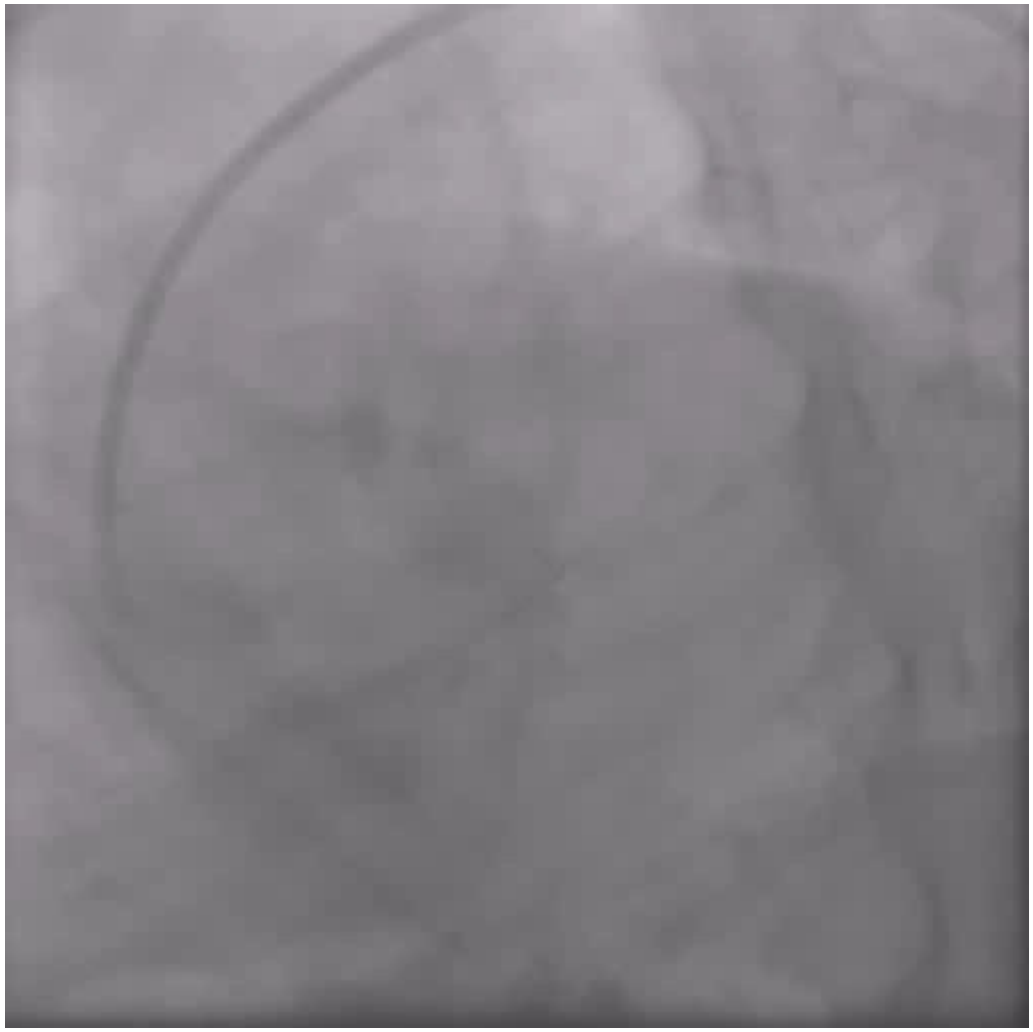


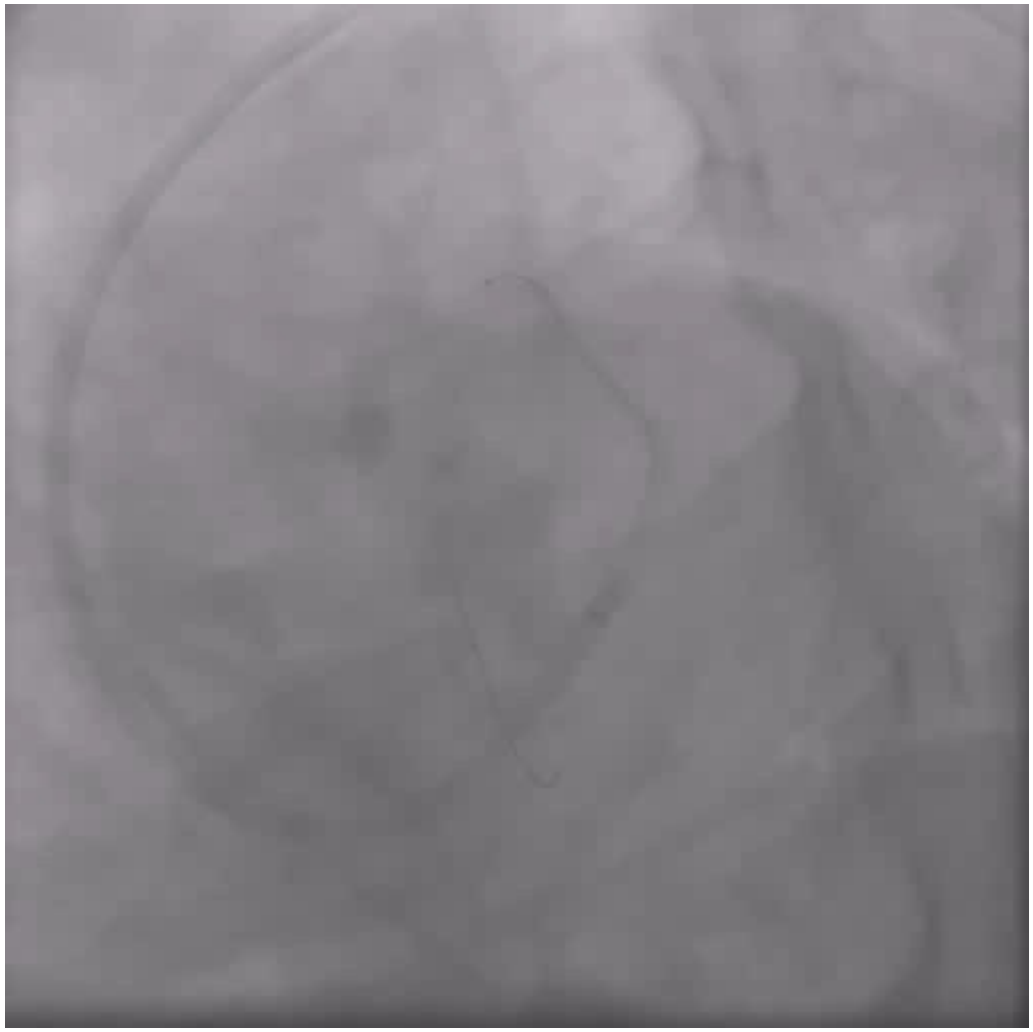


RCA: normal

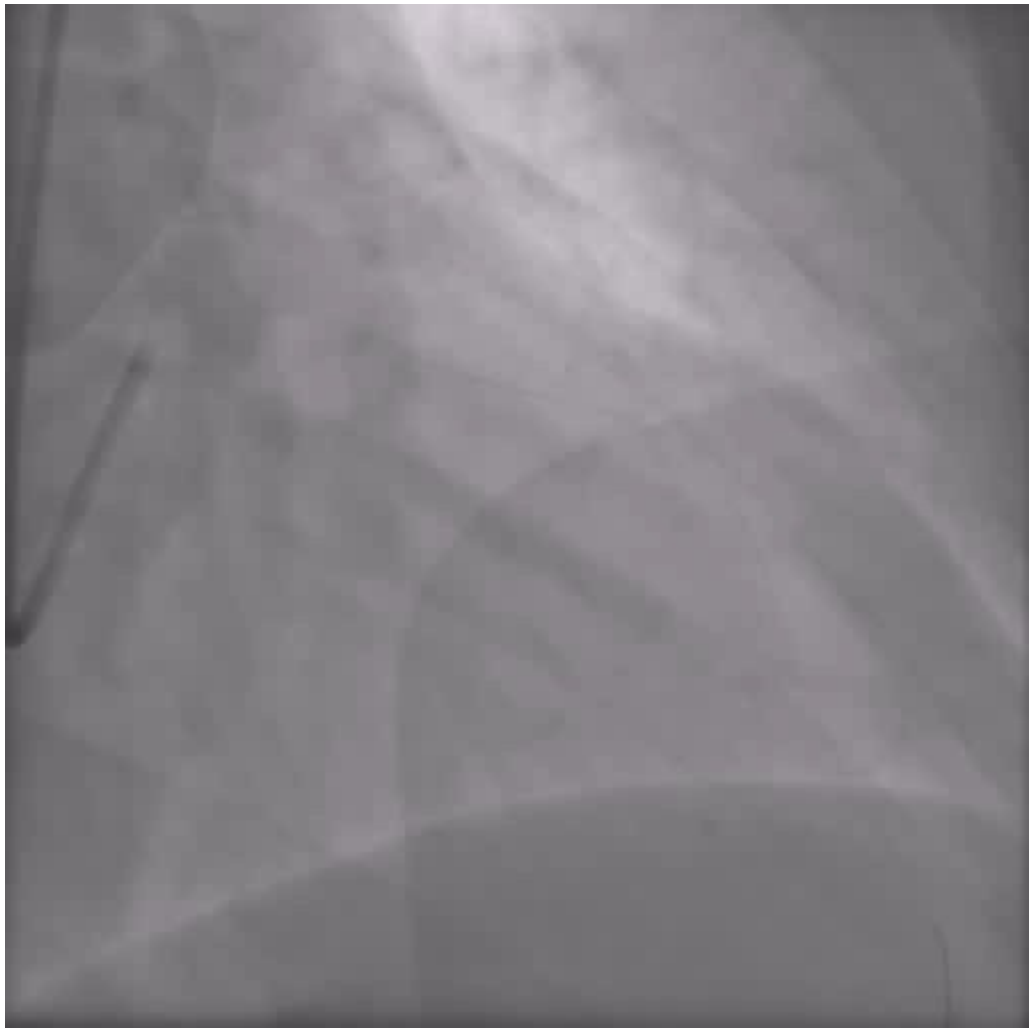


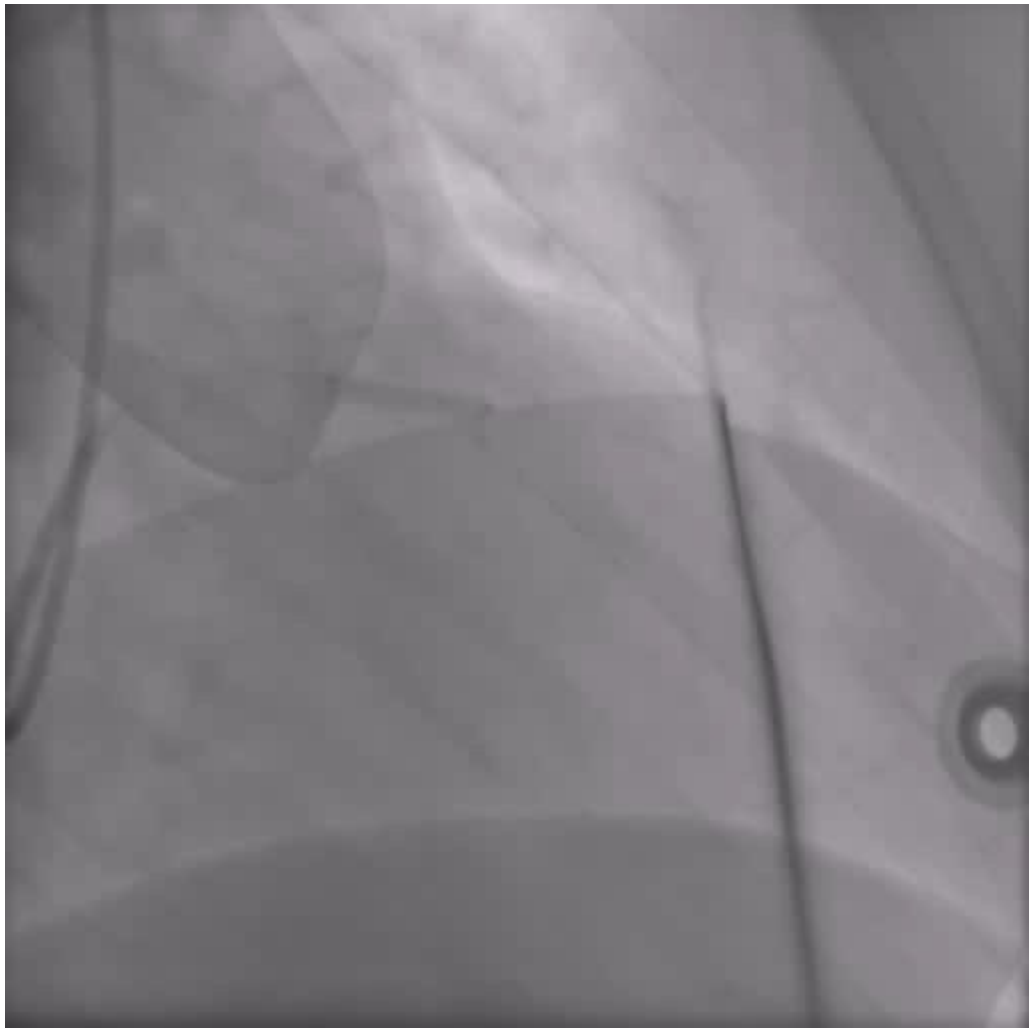
Infarct related, occluded LAD



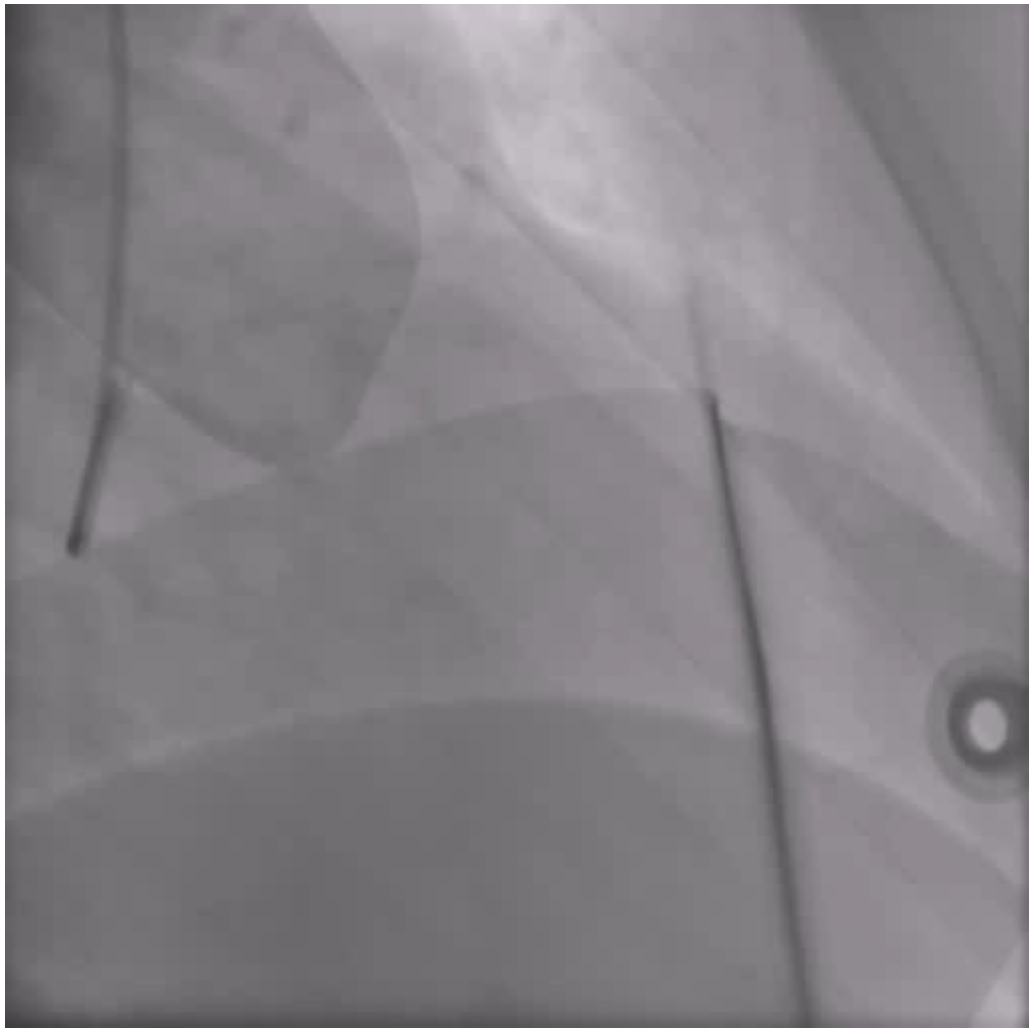


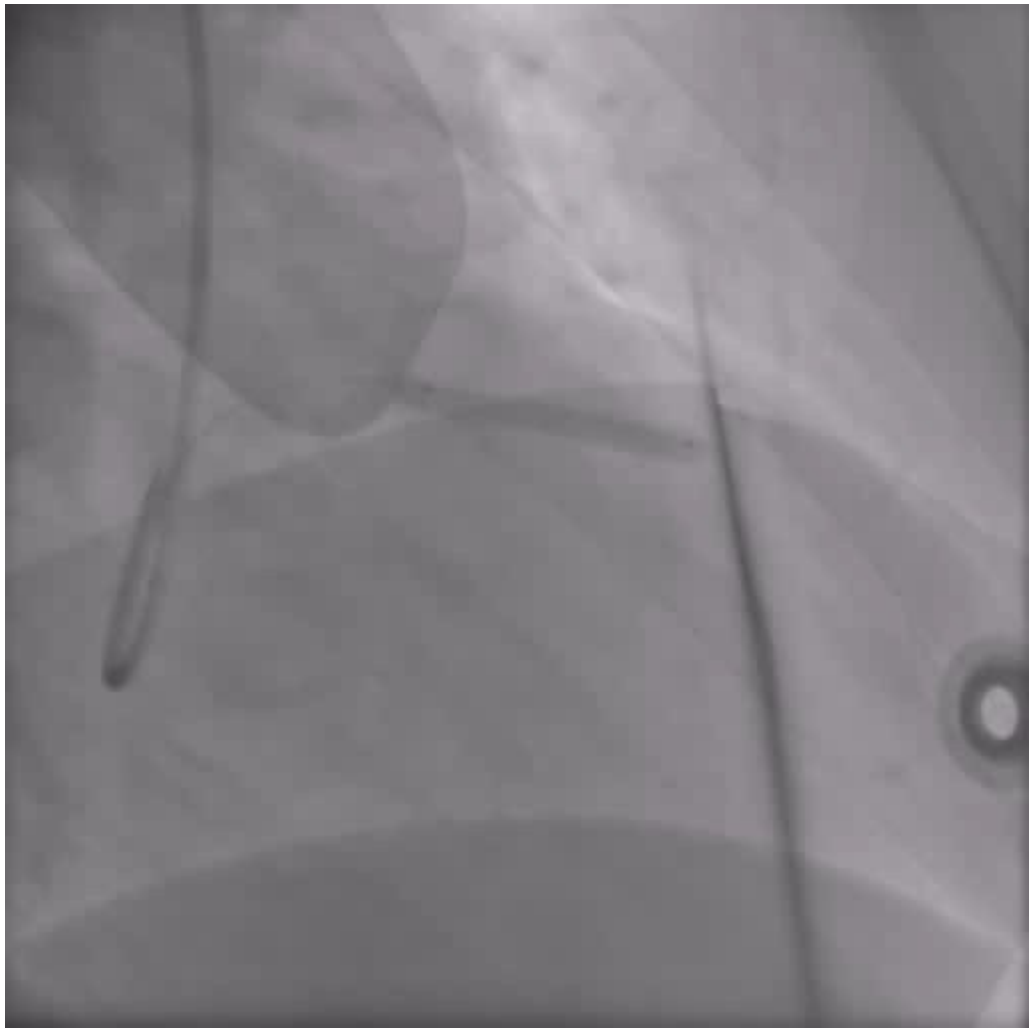
Thrombus aspiration



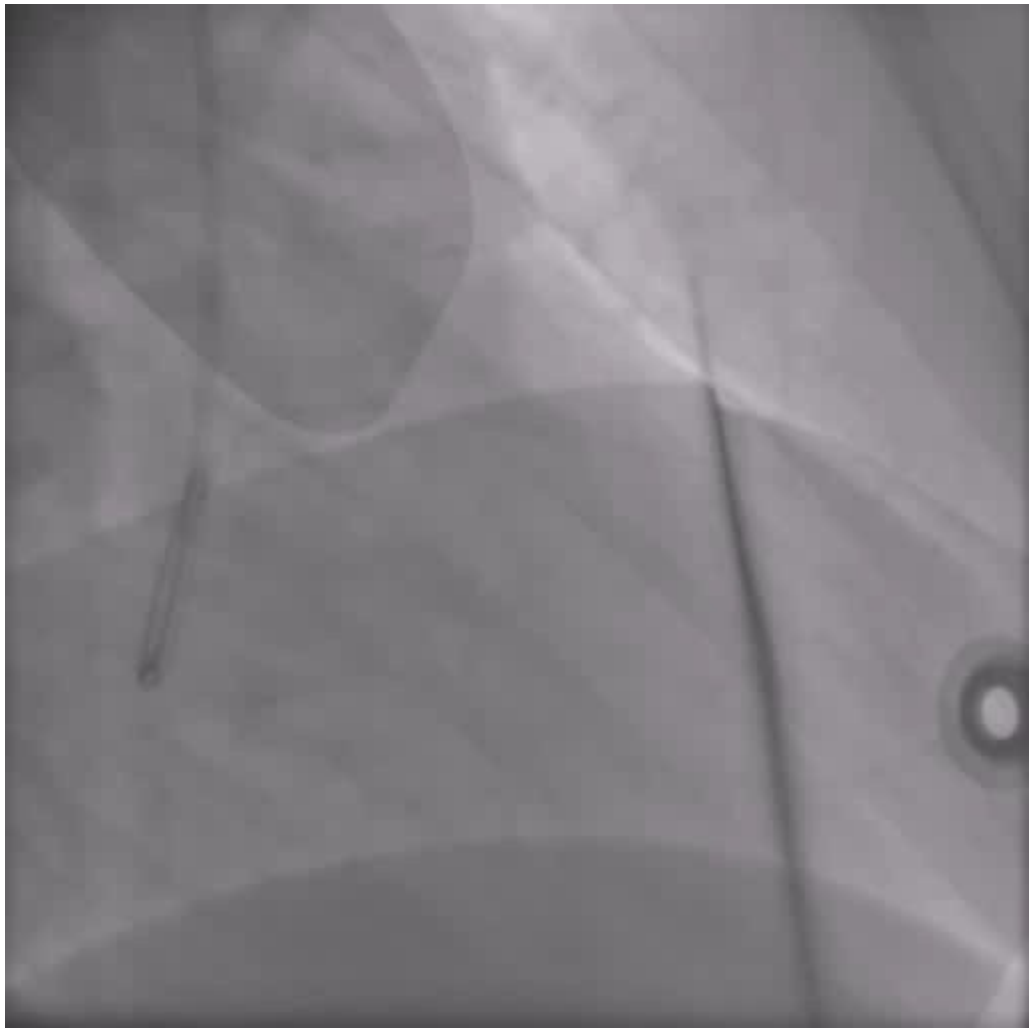


Predilatation with 2,5 x 20 mm ballon

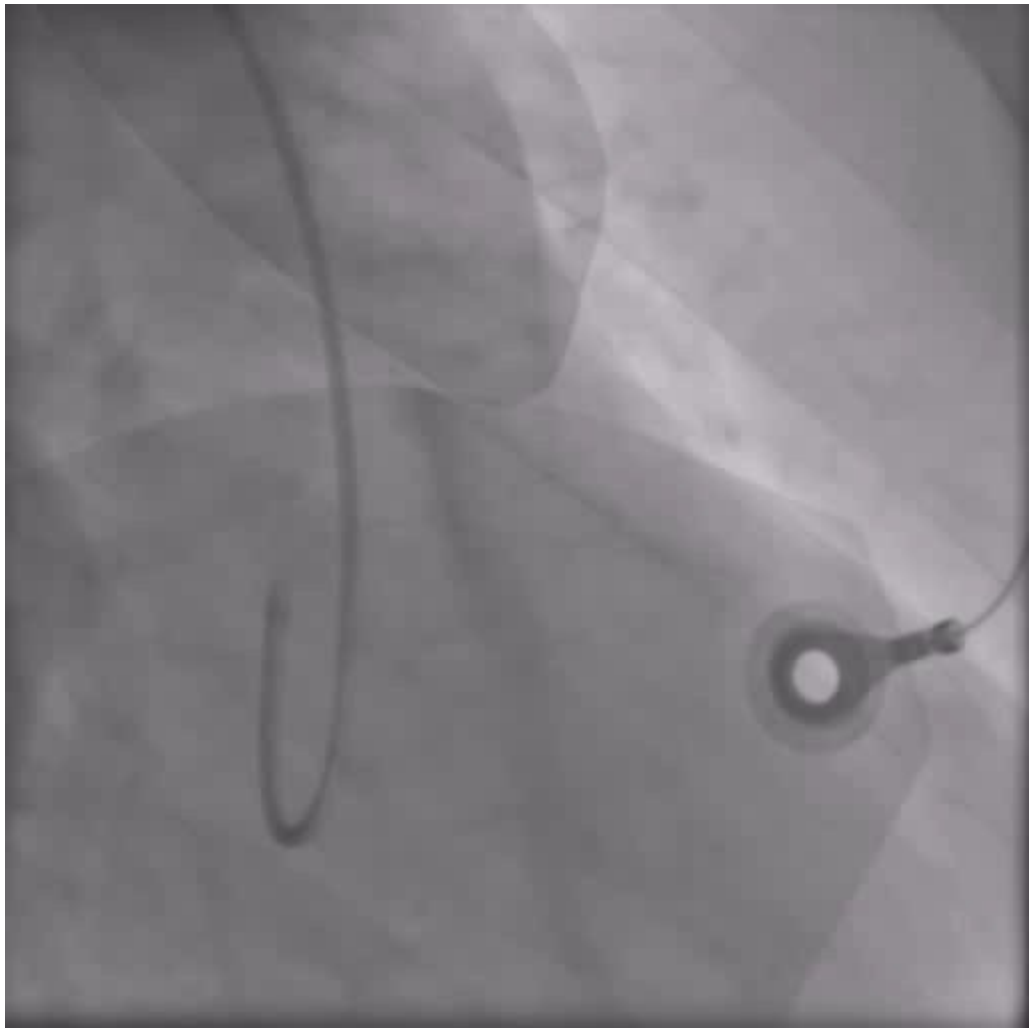




Implantation of ABSORB 3,5 x 28 mm, 12 atm



Final result (after 0,3 mg Nitro i.c.)



ent 2:

ale patient

chest pain while playing soccer

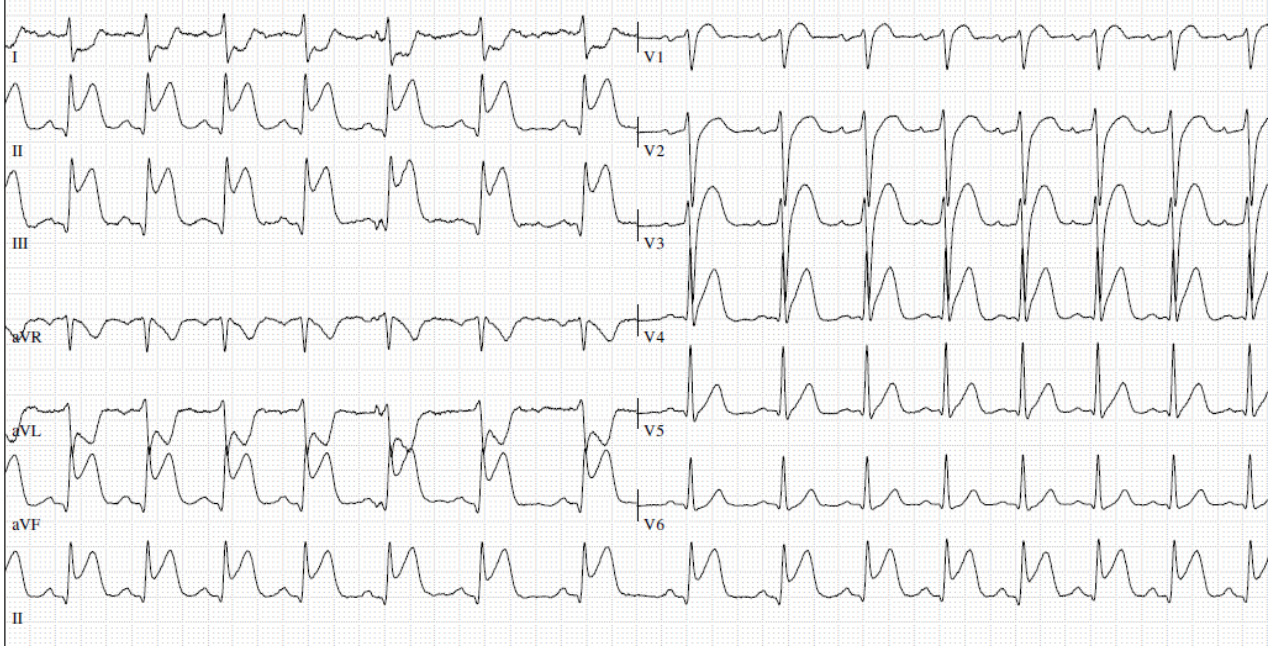
sis: acute ST-elevation myocardial infarction - inferior wall

ctors: arterial hypertension, nicotine abuse

o ballon time: ca. 2h

.000 IE Hep., 250 mg ~~Acetyl salicylic acid, Prasugrel 60mg, Bivalir~~

ximab (bail out)



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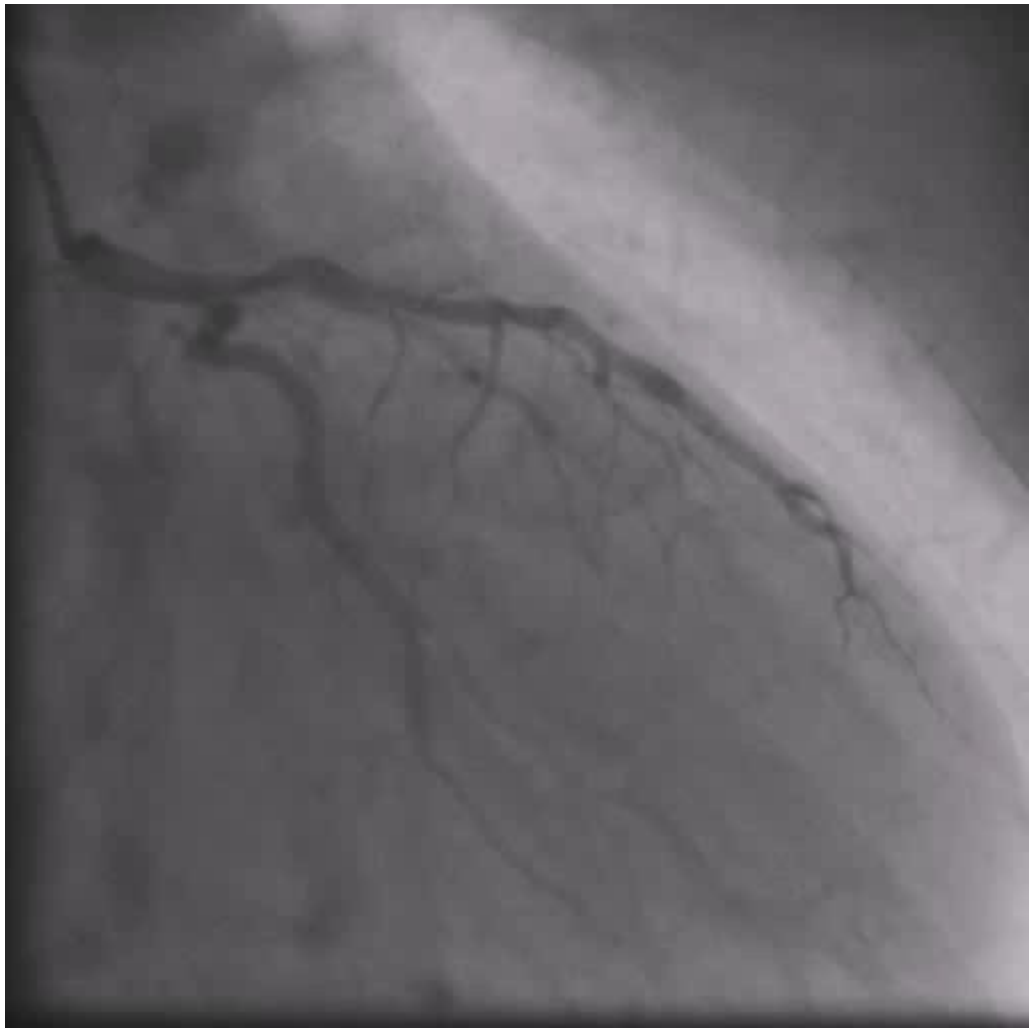
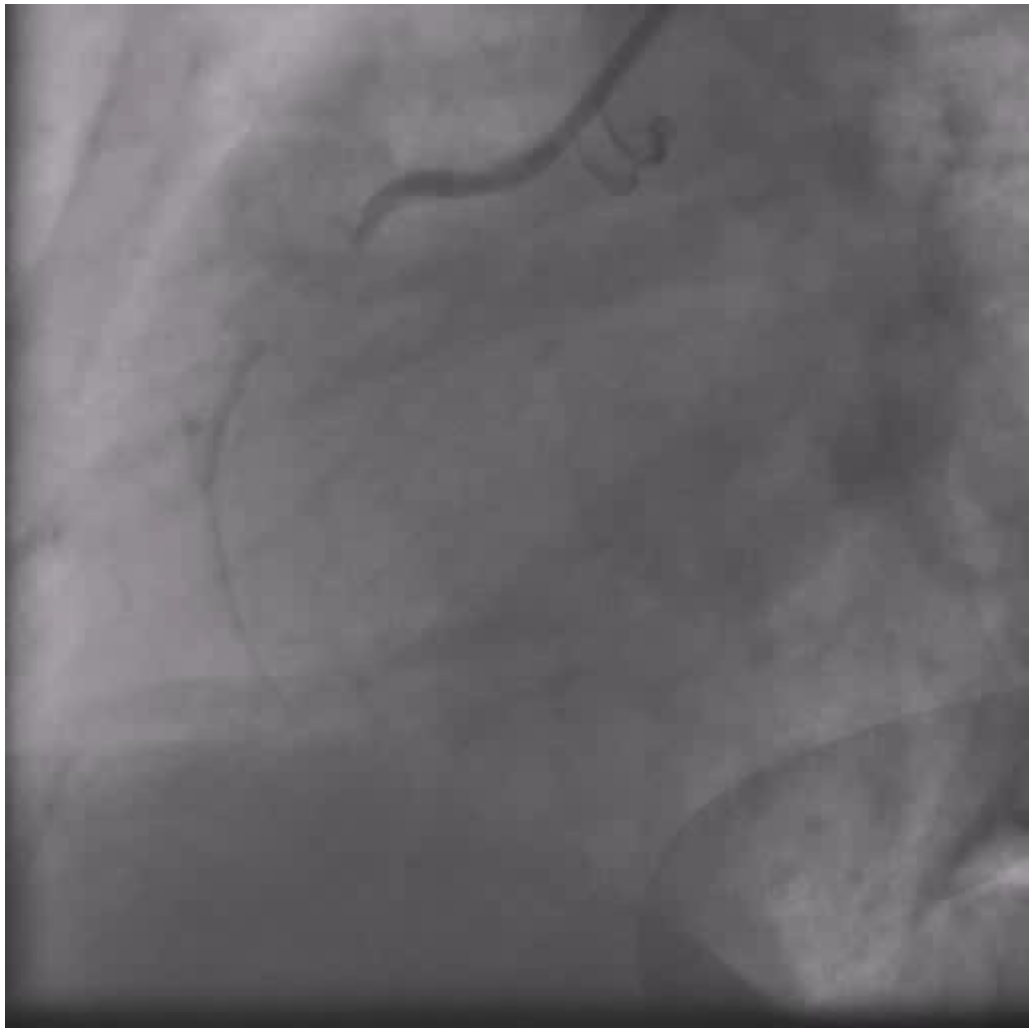
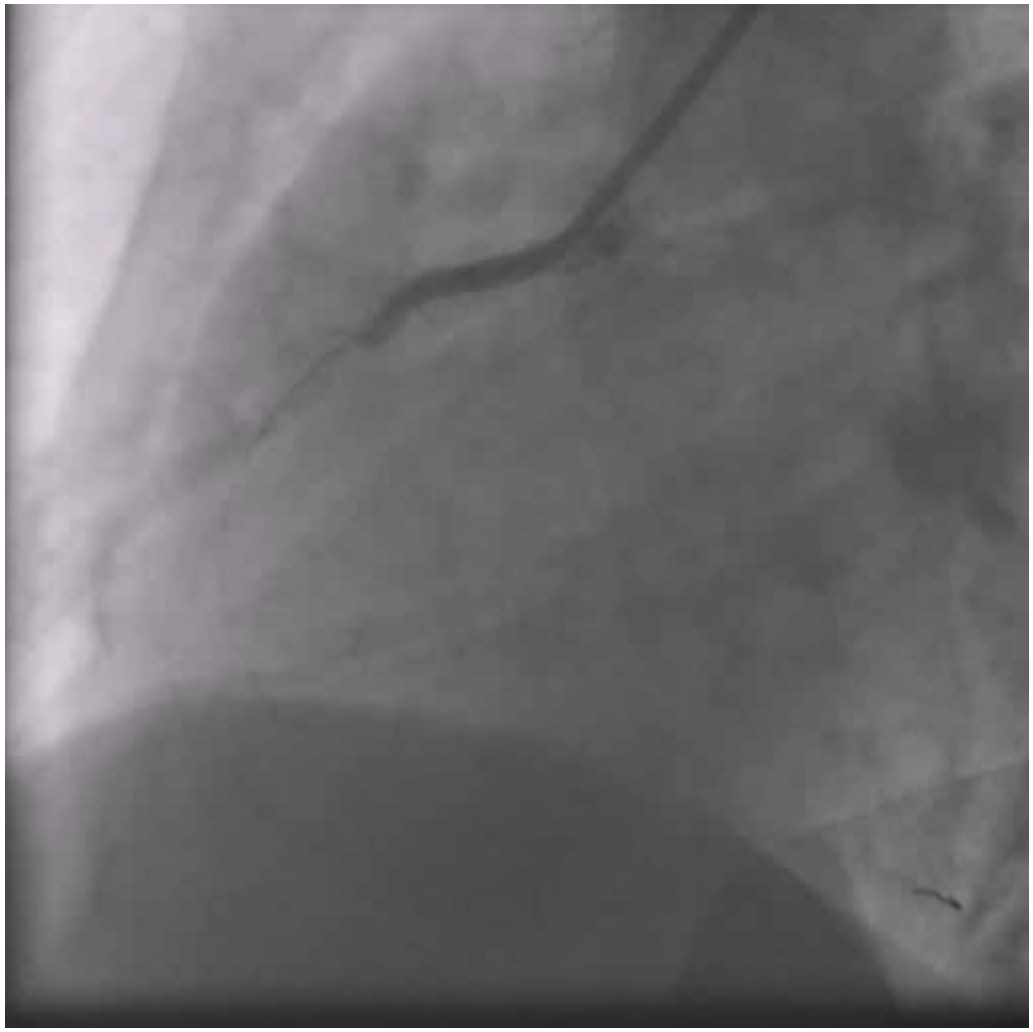
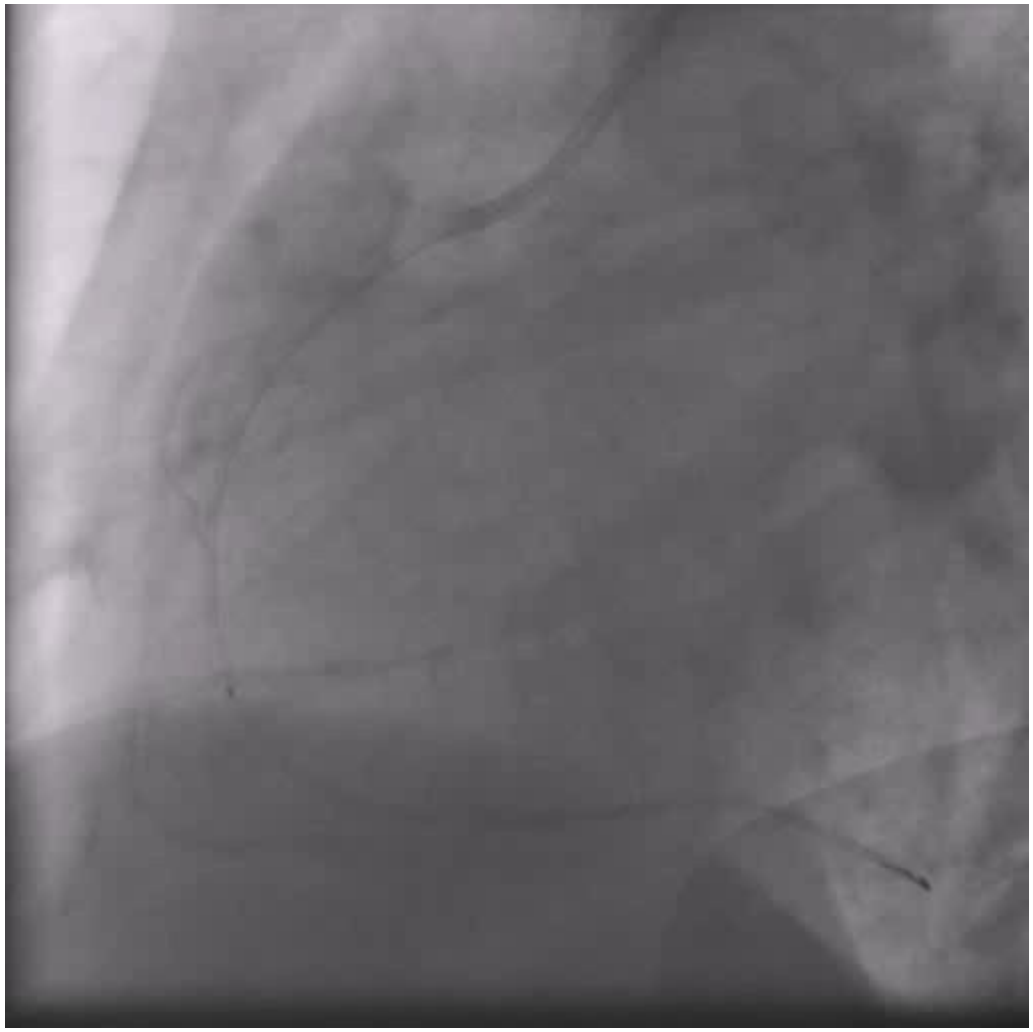


LAD and CX: normal

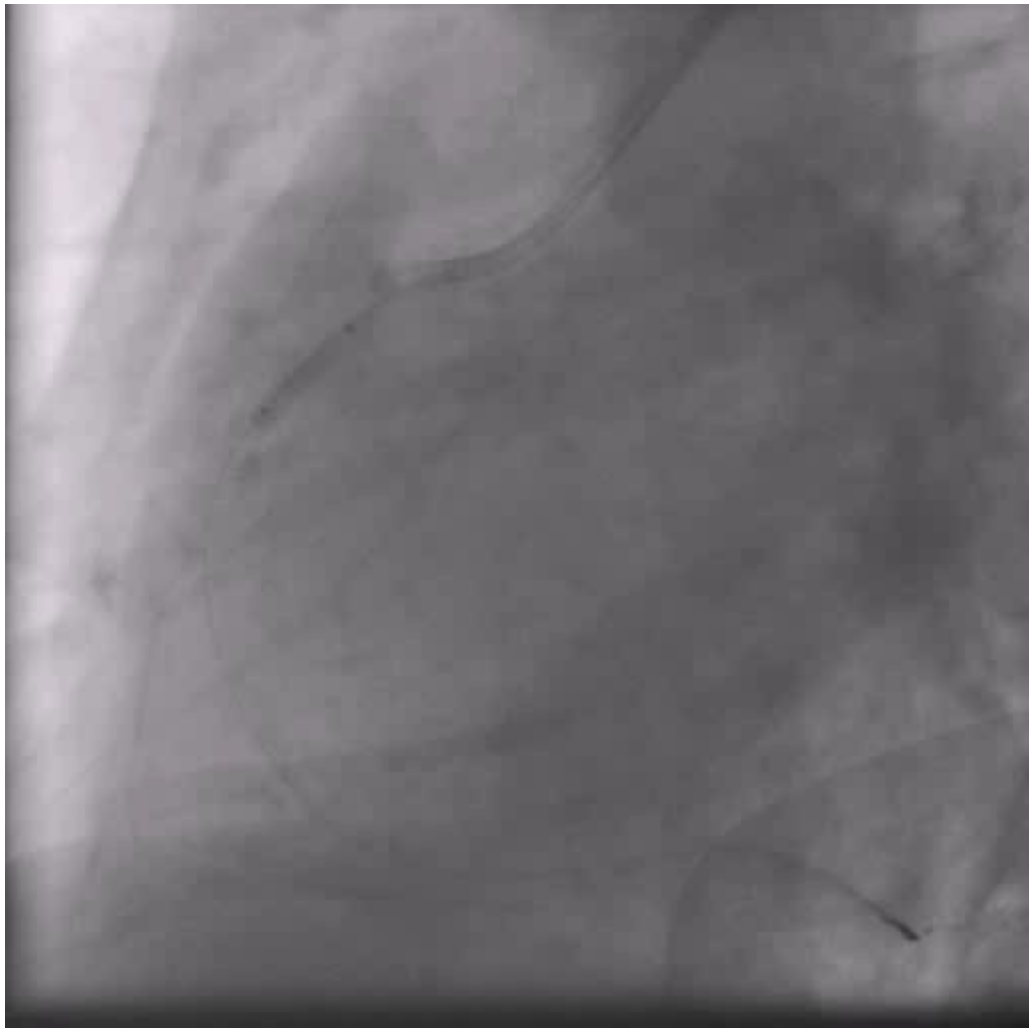


Infarct related, occluded RCA

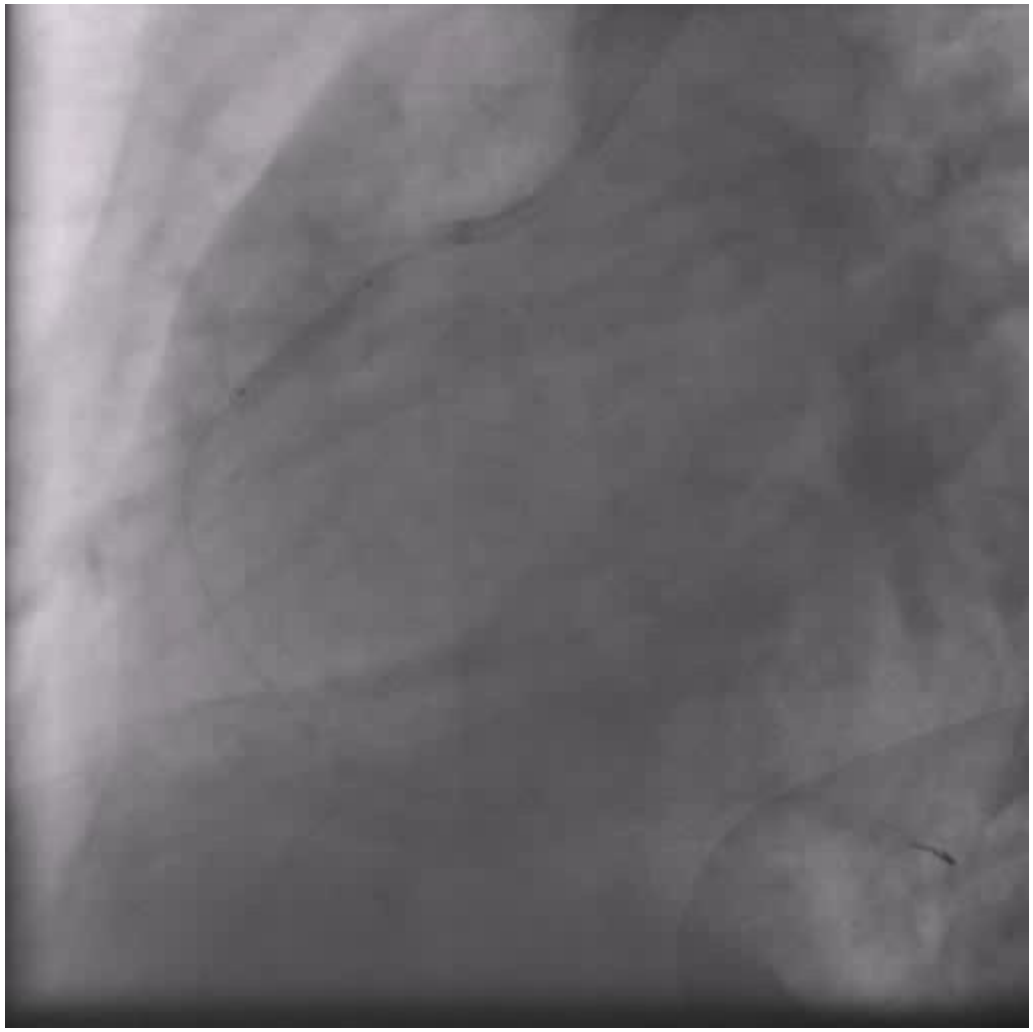




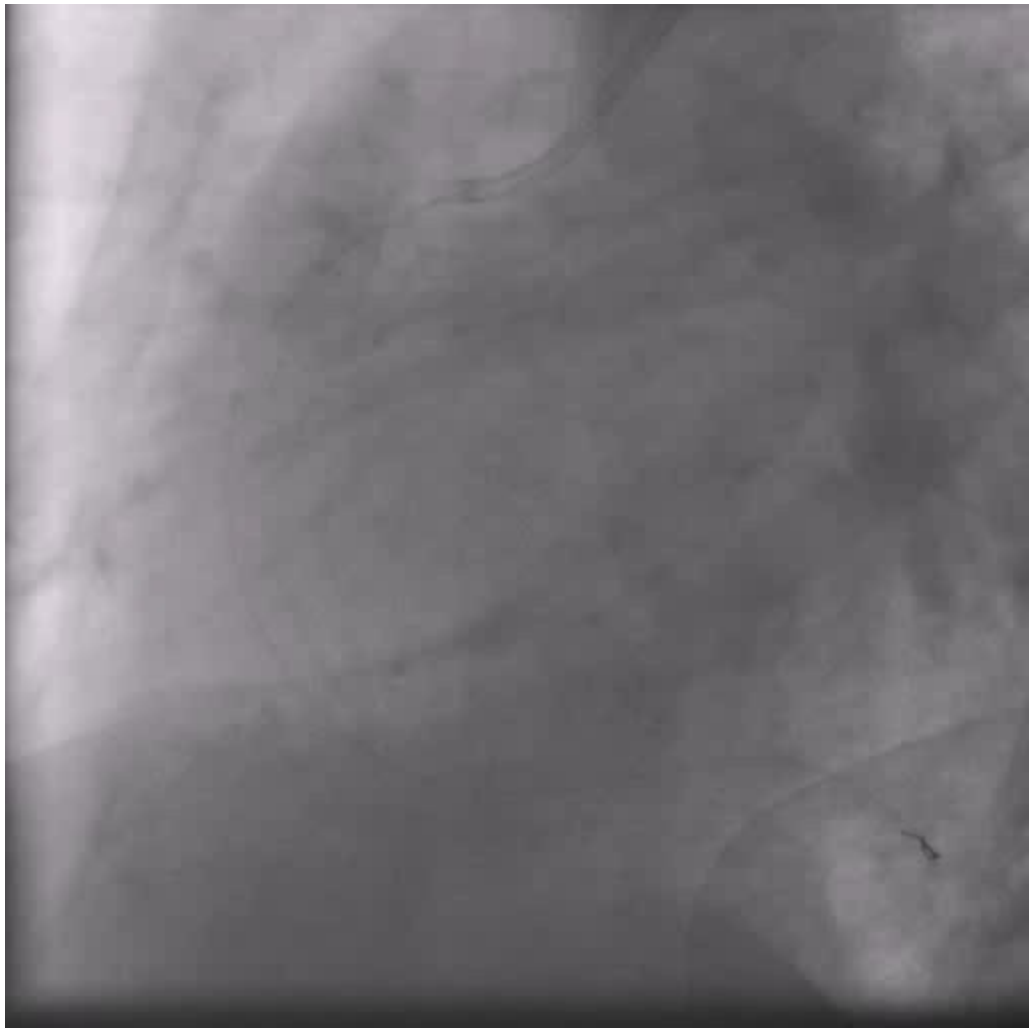
Thrombus aspiration

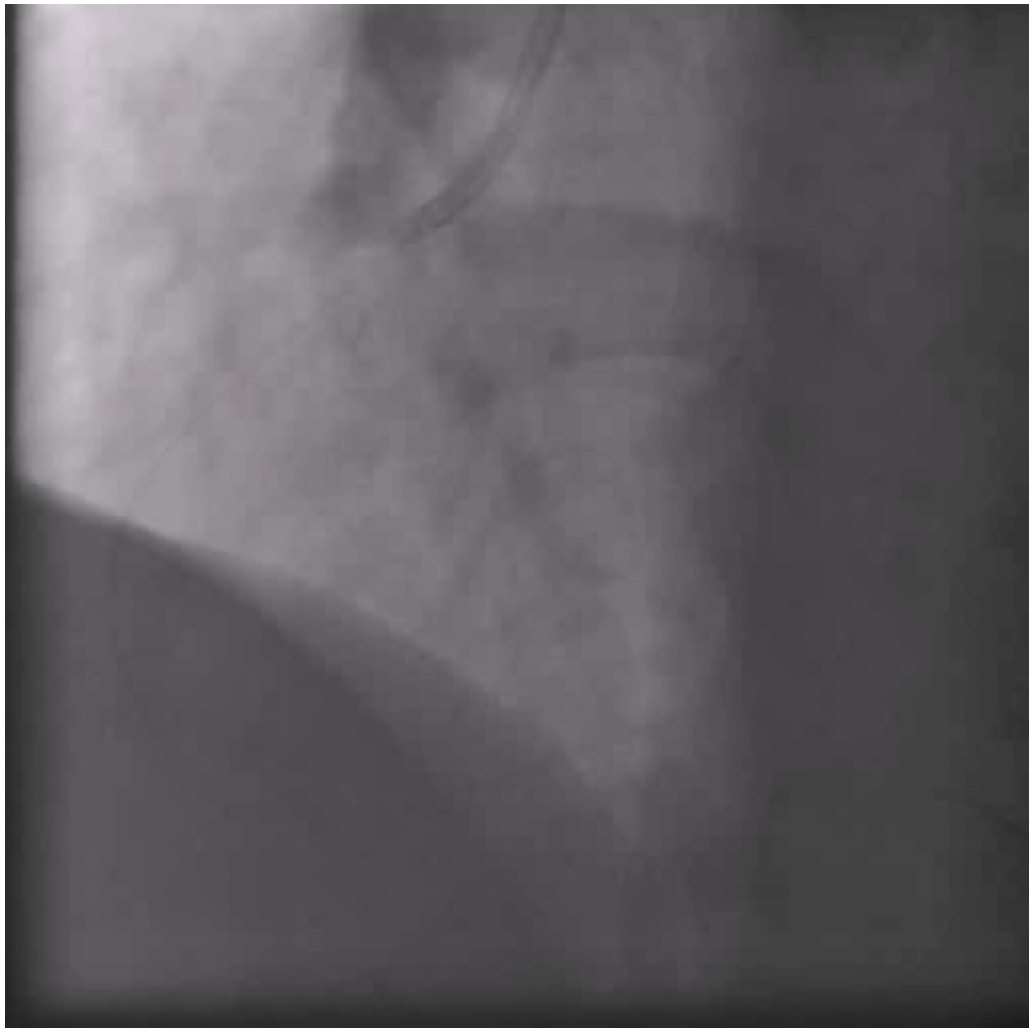


Predilatation with 2,5 x 15 mm ballon



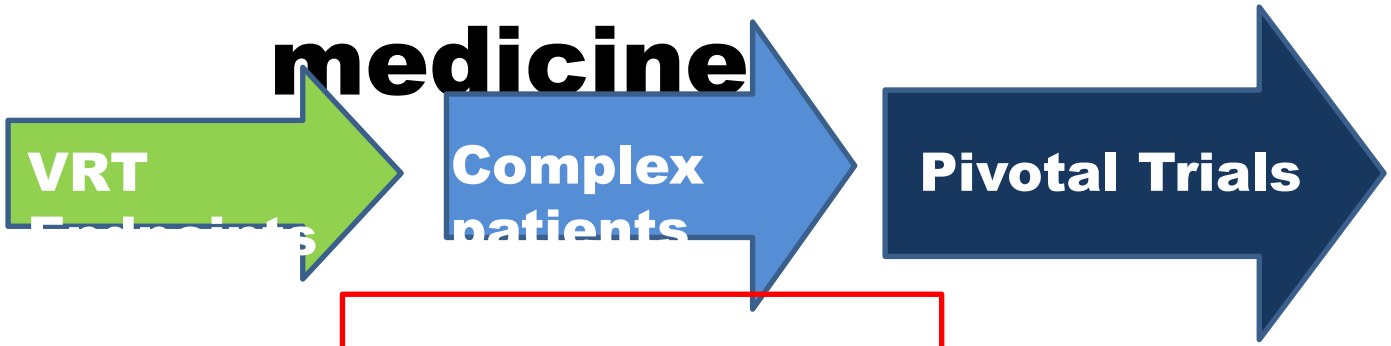
Implantation of ABSORB 3,0 x 18 mm, 20 atm





Final result (after 0,3 mg Nitro i.c.)

Building evidence based medicine

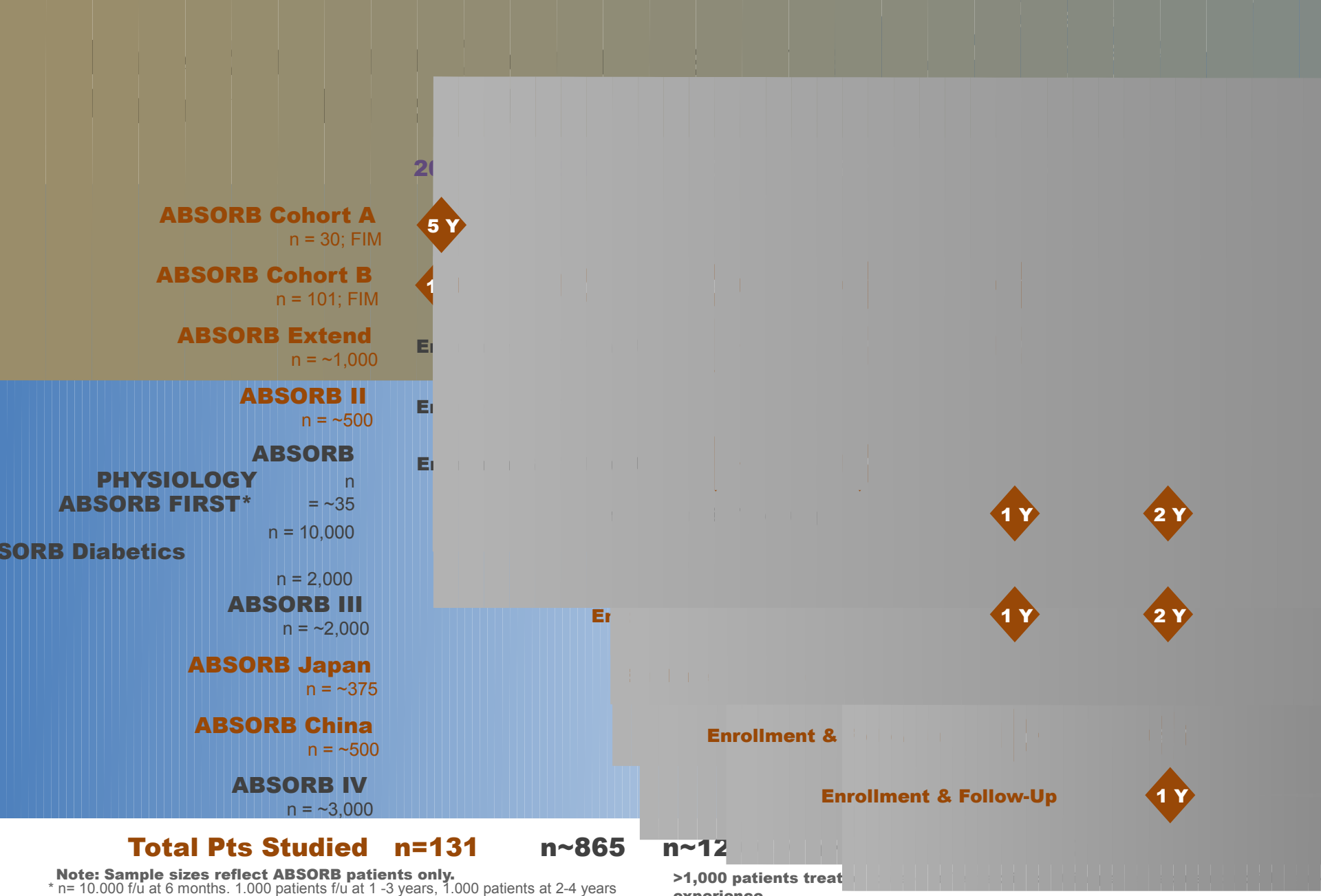


- Cohort A
- Cohort B

- ABSORB II

- ABSORB Extend
- **ABSORB First**
- AIDA
- BVS Expand
- ASSURE
- PRAGUE 19
- ABSORB STEMI-TROFI II

- ABSORB III/IV
- ABSORB Japan
- ABSORB China



Note: Sample sizes reflect ABSORB patients only.

* n= 10.000 f/u at 6 months. 1.000 patients f/u at 1 -3 years, 1.000 patients at 2-4 years

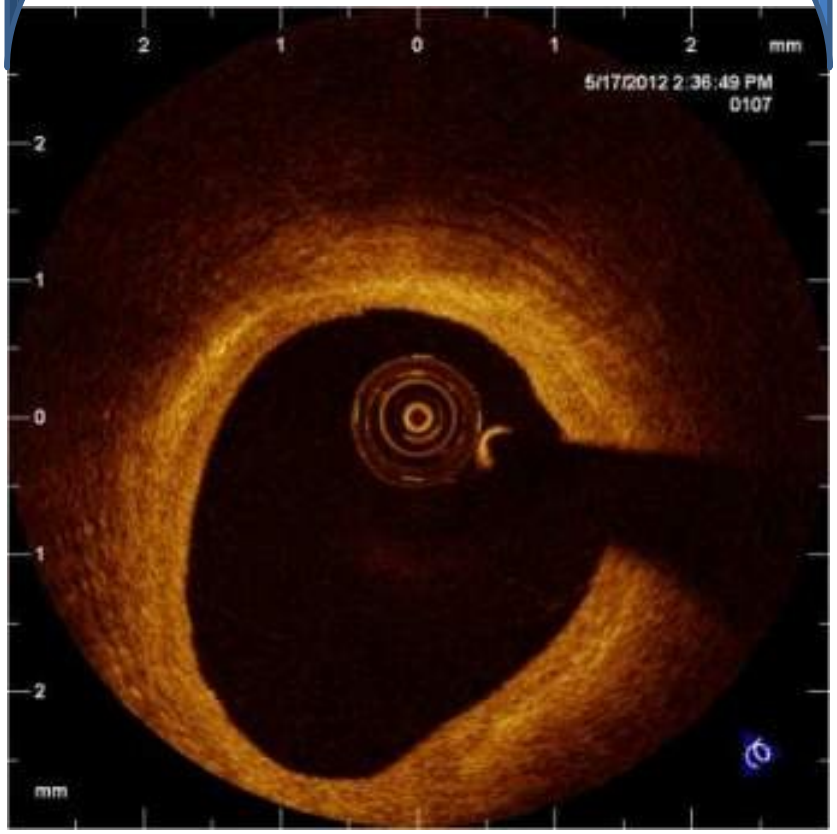
>1,000 patients treat
experience.

How the theoretical advantages will translate into clinical benefit of the patients?

- No interference with and CT
- No „full metal jacket“ arteries (to enable future coronary surgery)
- Restoration of coronary vasomotion
- Potential to enter bifurcations during future PCI
- Eliminate the long-term DAPT without a subsequent risk of stent thrombosis

The long-term benefit of Absorb BVS

The 'final golden tube' at 5 years



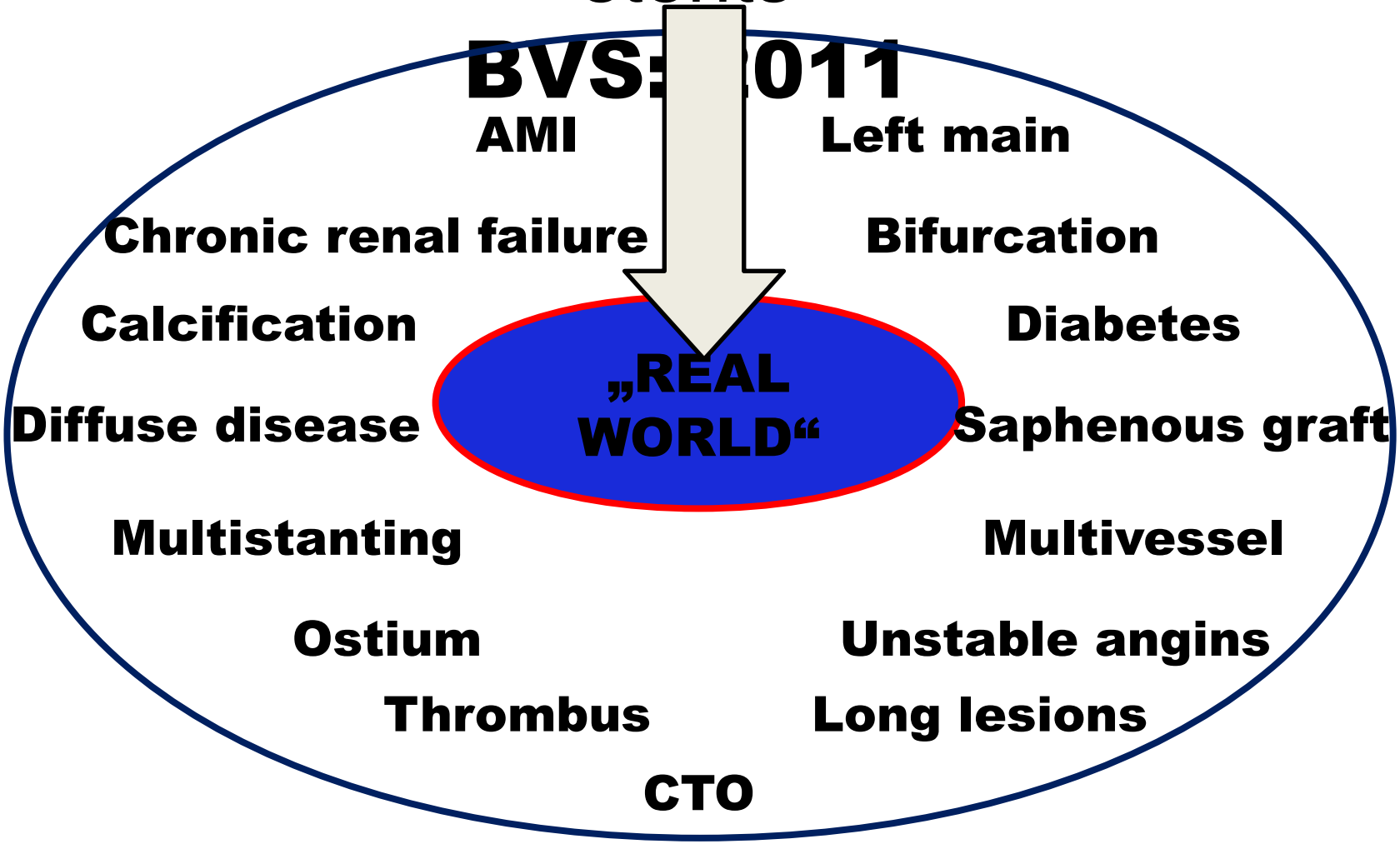
Images courtesy of Thoraxcenter, Erasmus MC, Rotterdam, The Netherlands, ABSORB A 5 yr

Thank you

Conclusion

- **The five-year follow-up of the cohort A showed**
  - Late lumen enlargement (OTC, IVUS, QCA)
  - Plaque reduction with adaptive remodeling (IVUS)
  - Non-invasive imaging at follow-up was feasible and reliable
- **3-year follow-up of the Cohort B showed**
  - Stable late loss
  - Return of vasomotion
  - Enlargement of scaffold area as well as mean lumen area despite persisting increase of neointima

CE mark approval for drug-eluting stents



… We do not yet have any randomized pivotal trial

Ideal patient for BVS

- **Diffuse disease of LAD requiring long stents**
- **Diffuse disease of any vessel 2.5 mm or larger requiring long stents**
- **Any lesion in a young patient**

Clinical Endpoint Considerations

Potential Clinical Benefits of BRS

- Reduction in ischemic adverse events → *Endpoints*
  - Improved live expectancy → Death, MI
- Enhanced vascular healing and vasomotion → Death, MI
- Protection against future vascular events → Death, MI, TVR
  - Vascular protective effects
  - Plaque sealing
- Elimination of (late) stent thrombosis

Endpoint Considerations

Potential Clinical Risks of BRS

	Endpoints	
· Rapid drug release	→ Insufficient effect	TVR
· Inhomogenous drug release	→ Focal restenosis	TVR
	→ Late restenosis	TVR
· Duration of drug effect	→ Stent thrombosis	Death, MI
· Platelet adhesion	→ Cavity formation	Death, MI
· Tissue necrosis	→ Vasomotor tone	Death, MI
· Endothelial damage	→ Vessel aneurysm	Death, MI
· Vascular remodeling	→ Chronic inflammation	Death, MI
· Hypersensitivity reaction		

Summary

What Needs to Be Demonstrated?

- **Asymptomatic Coronary Artery Disease**

  - BRS versus medical treatment (i.e., plaque sealing)

- **Stable Coronary Artery Disease**

  - BRS versus newer generation DES

    - Demonstrate at least equivalent efficacy and safety in simple lesions/patients

    - Extension of results to more complex lesion/patients

Only 25% of STEMI pts fullfilled the prespecified inclusion/exclusion criteria for

Inclusion criteria	Exclusion criteria - clinical	Exclusion criteria - angiographic
STEMI <24 hours from symptom onset	**Killip III-IV class (i.e. high likelihood of death within BVS absorbtion time)**	**Infarct artery reference diameter <2.3 mm or >3.7 mm (i.e. not suitable for currently available BVS sizes)**
Signed written informed consent	**Any other disease with probable prognosis <3 years**	**Lesion length >24 mm (i.e. precluding single BVS implanation)**
	Indication for oral anticoagulation (e.g. atrial fibrillation)	**Extensive infarct artery calcifications or severe tortuosity**
	Contraindication to prolonged DAPT or high likelihood of non-compliance to DAPT	**STEMI caused by in-stent restenosis or stent thrombosis**

Procedural result and BVS feasibility

- **42 BVS successfully implanted to 35/36 patients**
- **1 BVS could not be delivered to LCX with sharp take-off (bare metal stent was delivered successfully)**
- **32/35 BVS patients had ideal result (TIMI-3 flow, 0% residual stenosis, no**

Zusammenfassung

er über 1.000 Patienten mit ABSORB-Stent behandelt

hre FU Daten vorliegend

vergleichbar mit dem eines neuen Generations-DES

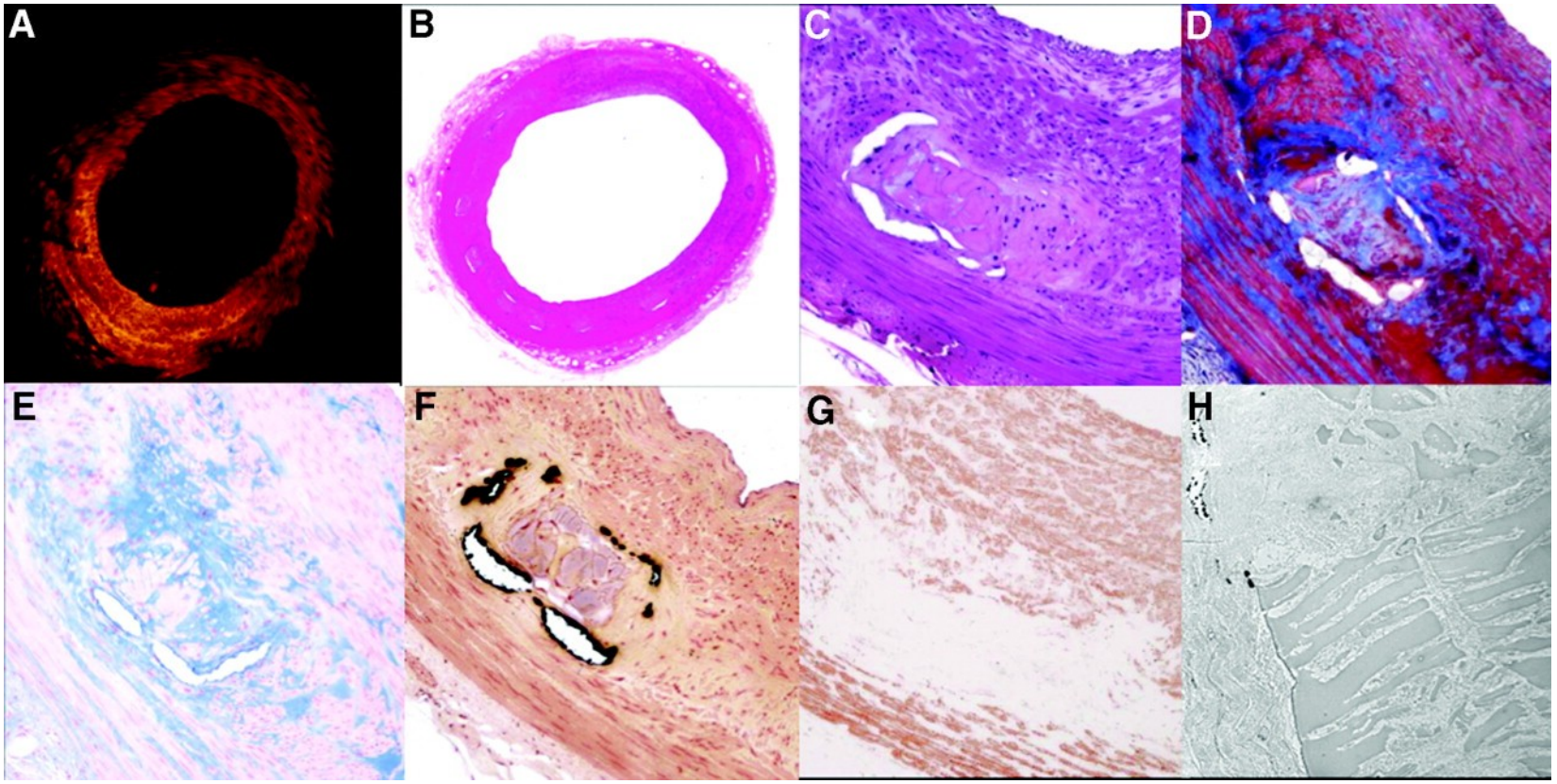
verability vergleichbar mit der eines neuen Generations

kuläre Reagibilität bleibt erhalten

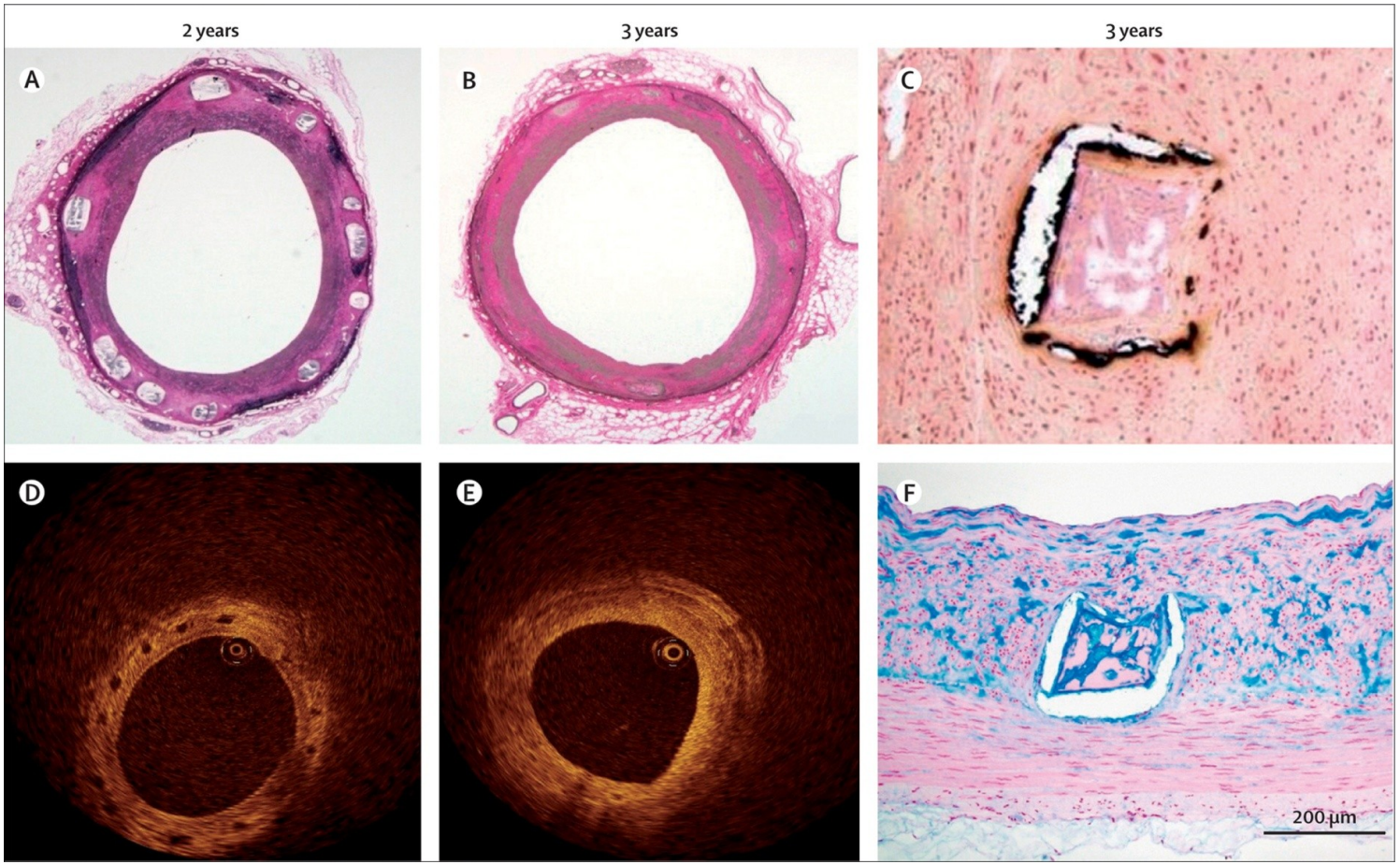
äß bleibt frei (für zukünftige Behandlungen)

DANKE

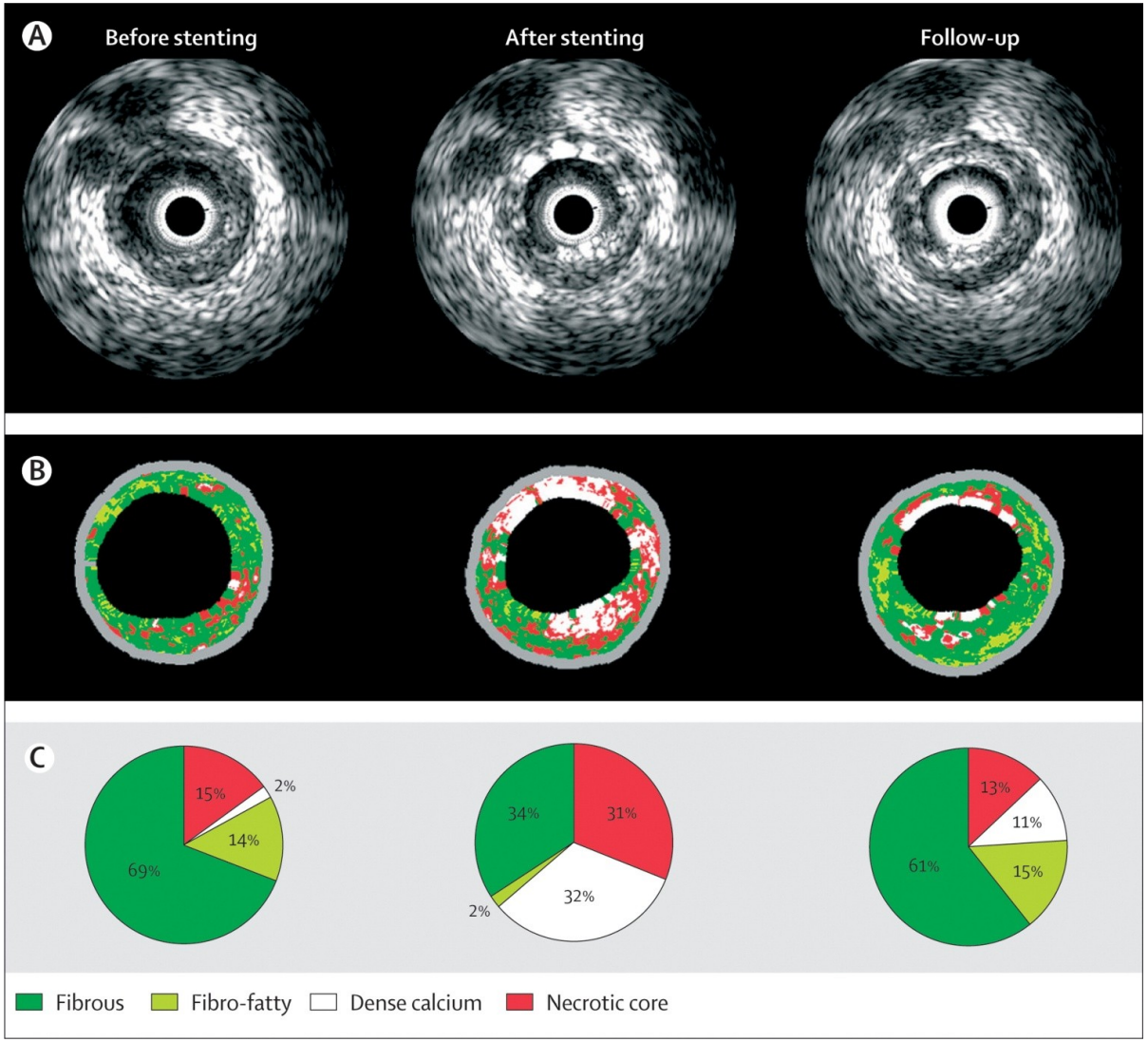
3 Jahres - *follow up*



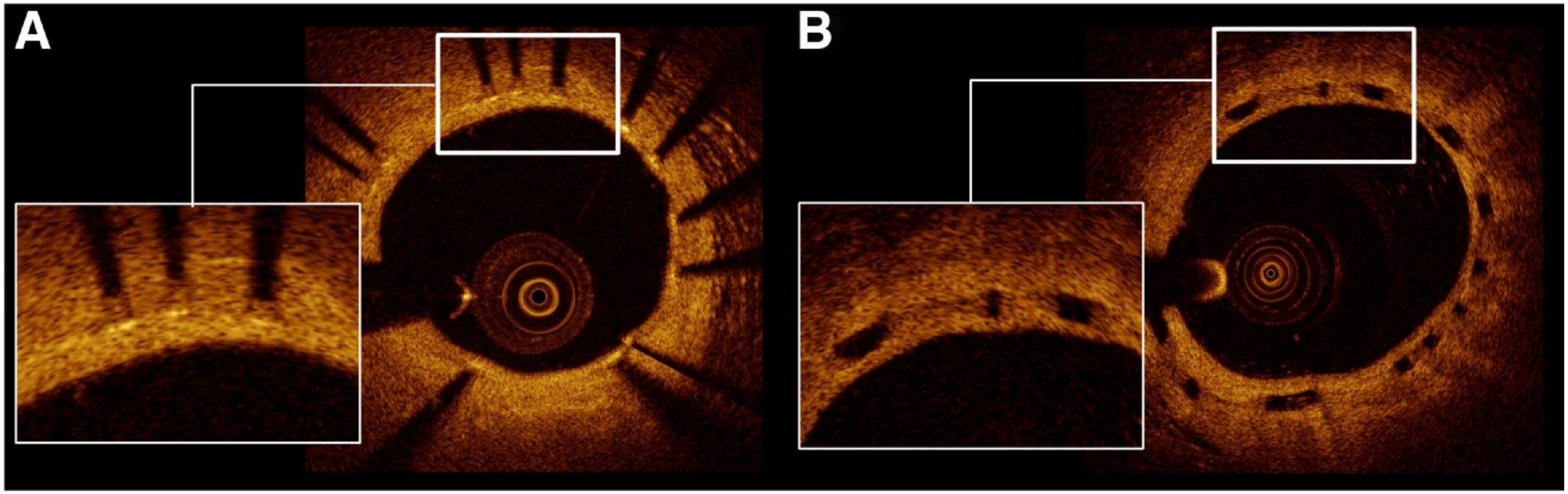
Onuma Y. et al., Circulation 2010



Serruys PW et al. Lancet 2009



Ormiston JA et al. Lancet 2008



Gomez-Lara J et al.JACC 2011

Table 1. Baseline Clinical Parameters

Patient Level (n = 44)	Everolimus DES (n = 14)	Everolimus BVS (n = 30)	p Value
Age, yrs	60.9 ± 8.6	60.0 ± 8.4	0.82
Male	12 (85.7)	22 (73.3)	0.36
Hypertension	8 (57.1)	21 (70.0)	0.40
Hypercholesterolemia	11 (78.6)	23 (76.7)	0.89
Diabetes mellitus	3 (21.4)	2 (6.7)	0.15
Smoking history	6 (42.9)	7 (23.3)	0.19
Prior myocardial infarction	8 (57.1)	3 (10.0)	<0.01
Prior PCI	4 (28.6)	4 (13.3)	0.22
Prior CABG	1 (7.1)	0 (0)	0.20
Clinical indication			0.26
Stable or silent angina	9 (64.3)	24 (80.0)	
Unstable angina*	5 (35.7)	6 (20.0)	
Number of vessel disease			0.01
1	7 (50.0)	27 (90.0)	
2	5 (35.7)	3 (10.0)	
3	2 (14.3)	0 (0)	

Values are mean ± SD or n (%). *ST-segment elevation myocardial infarctions were excluded from the analysis.

BVS = bioresorbable vascular scaffold(s); CABG = coronary artery bypass graft; DES = drug-eluting stent(s); PCI = percutaneous coronary intervention.

Gomez-Lara J et al. JACC 2011

Table 3. Quantitative OCT Findings at 1-Year Follow-Up (Lesion Level)

Lesion Level (n = 50)	Everolimus DES (n = 19)	Everolimus BVS (n = 31)	p Value
Reference lumen area, mm^2	6.99 ± 2.28	7.40 ± 2.53	0.80
Mean lumen area, mm^2	6.16 ± 2.02	5.90 ± 1.68	0.44
Minimal lumen area, mm^2	4.98 ± 1.87	4.31 ± 1.41	0.18
Mean scaffold area, mm^2	6.91 ± 1.97	6.50 ± 1.13	0.33
Minimal scaffold area, mm^2	5.82 ± 1.89	5.23 ± 1.04	0.16
Mean nonapposition area, mm^2	0.02 ± 0.07	0.11 ± 0.29	0.54
Mean neointimal area, mm^2	0.78 ± 0.32	0.84 ± 0.51	0.99
In-stent/scaffold area obstruction, %	12.5 ± 7.1	13.6 ± 9.7	0.91
Maximal in-stent/scaffold area obstruction, %	23.9 ± 11.3	25.1 ± 15.8	0.73
Neointimal thickness, μm	120.6 ± 46.0	136.1 ± 71.4	0.82
Maximal neointimal thickness, μm	354.7 ± 95.8	407.7 ± 164.6	0.54
Area stenosis, %	28.7 ± 15.6	40.5 ± 15.9	0.03

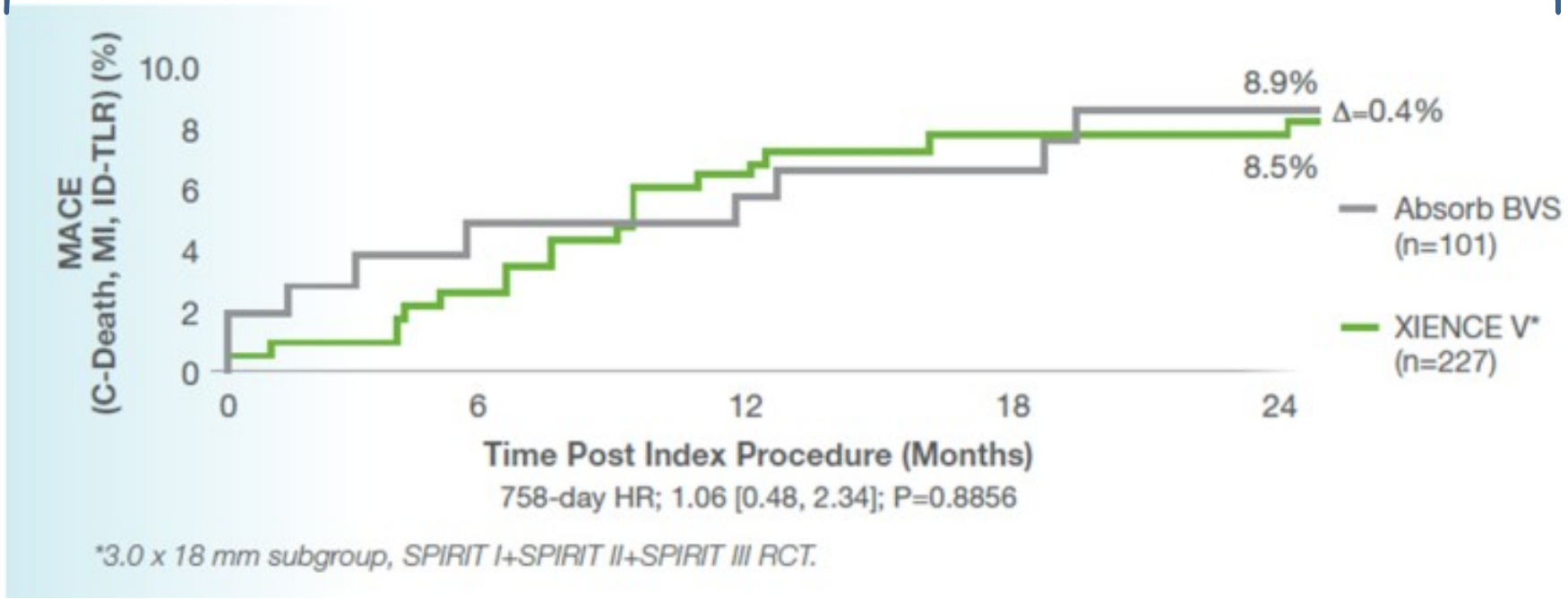
Values are mean ± SD.

OCT = optical coherence tomography; other abbreviations as in Table 1.

Gomez-Lara J et al. JACC 2011

Absorb BVS clinical outcomes are comparable to best-in-class DES, XIENCE

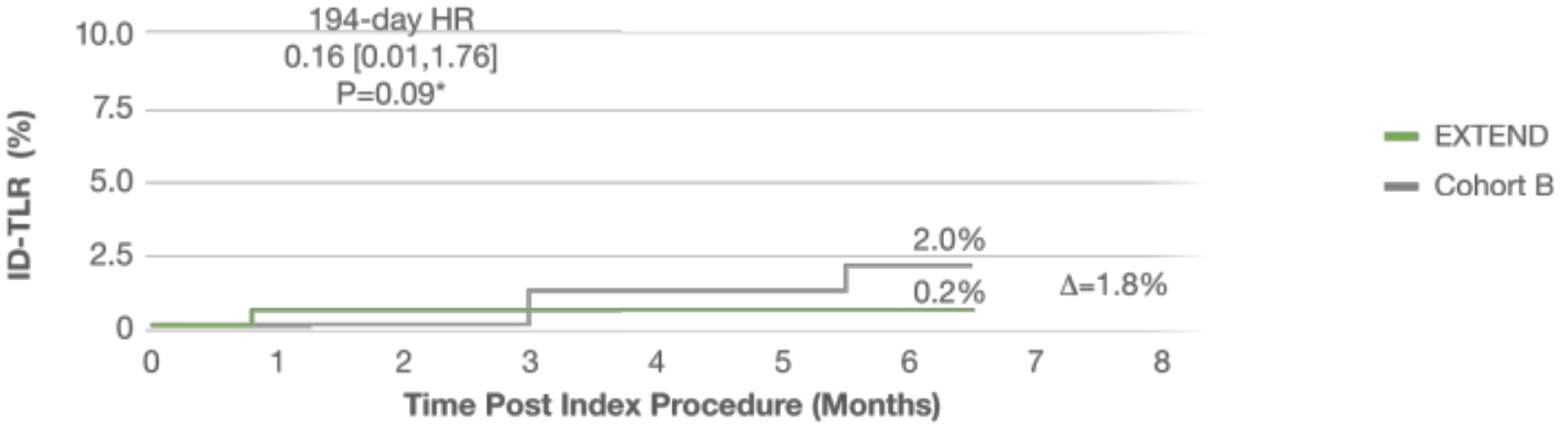
Similar Rates of MACE Compared to Historical XIENCE Data



Dudek, D., ACC 2012.

Absorb BVS clinical performance remains consistent across complex patient

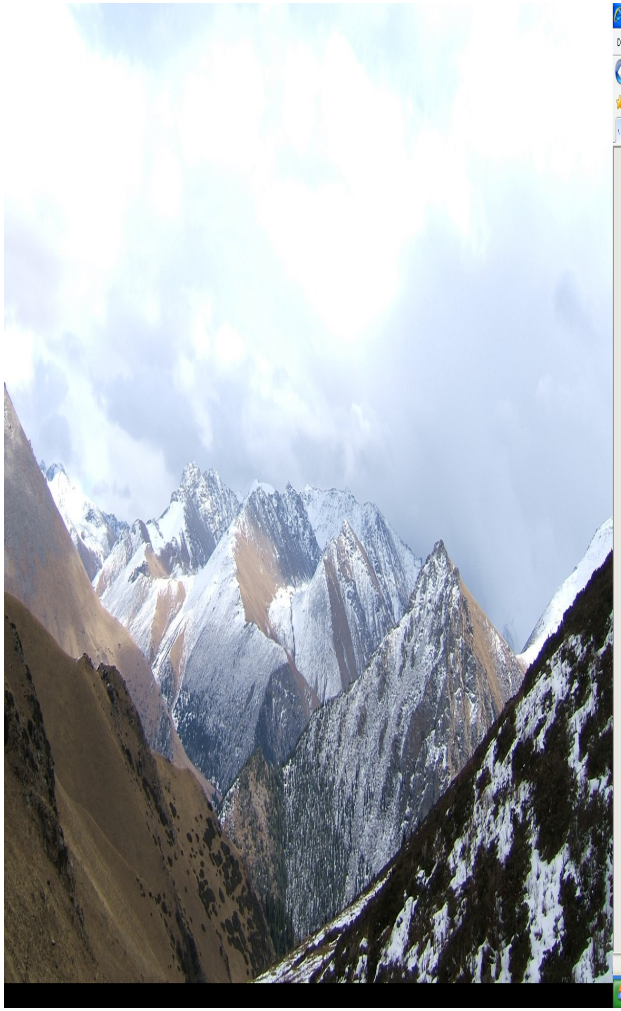
Low Rates of ID-TLR in More Complex EXTEND Trial



- **Longer lesions treated in Extend as overlapping scaffolds (max 2) allowed**

Van Geuns RJ PCR Rotterdam, 2013

*P-value is not from formal hypothesis testing and is displayed for descriptive purpose only.



Search of: "absorb" and "BVS" - List Results - ClinicalTrials.gov - Windows Internet Explorer

ClinicalTrials.gov

A service of the U.S. National Institutes of Health

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9 studies found for: "absorb" and "BVS"

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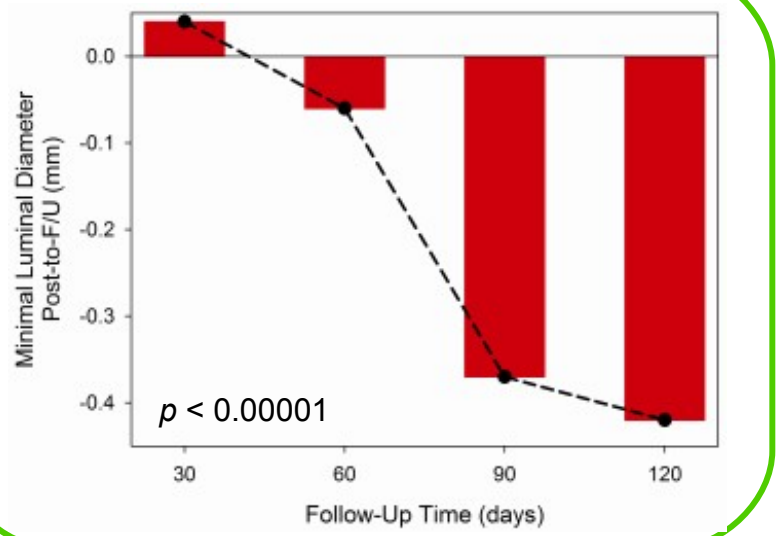
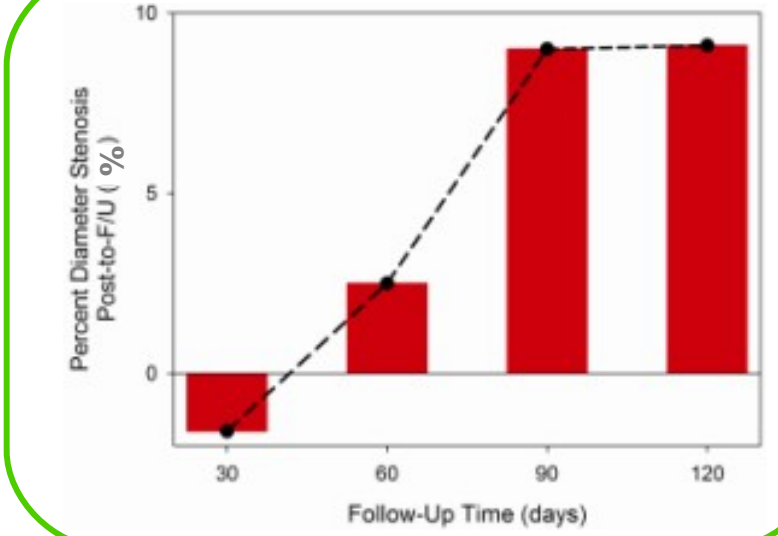
Rank	Status	Study
1	Recruiting	A Clinical Evaluation of Absorb™ Bioresorbable Vascular Scaffold (Absorb™ BVS) System **Conditions:** Coronary Artery Disease; Coronary Artery Stenosis; Coronary Disease; Coronary Stenosis **Interventions:** Device: Absorb BVS; Device: XIENCE V or XIENCE PRIME
2	Recruiting	ABSORB EXTEND Clinical Investigation **Conditions:** Myocardial Ischemia; Coronary Artery Stenosis; Coronary Disease; Coronary Artery Disease; Coronary Restenosis; Cardiovascular Disease **Intervention:** Device: ABSORB BVS
3	Completed	ABSORB Clinical Investigation, Cohort A (ABSORB A) Everolimus Eluting Coronary Stent System Clinical Investigation **Conditions:** Coronary Disease; Coronary Artery Disease; Coronary Restenosis **Intervention:** Device: Bioabsorbable Everolimus Eluting Coronary Stent
4	Recruiting	ABSORB FIRST Registry **Conditions:** Chronic Total Occlusion of Coronary Artery; Coronary Occlusion; Coronary Artery Disease; Coronary Artery Restenosis; Coronary Artery Stenosis;

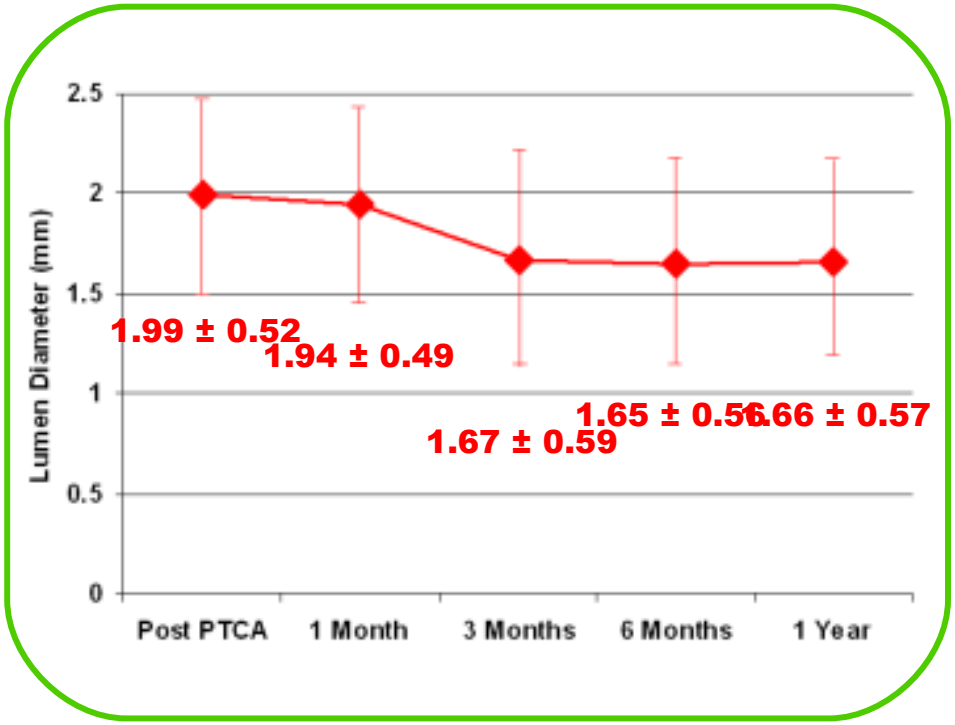
Quantitative angiographic study in 342 consecutive patients at 1, 2, 3, and 4 months





The lumen appears to stabilize **approximately three months** after PTCA

Serruys PW, et al., *Circulation* 1988; **77:** 361.



Serial changes in MLD in treated vessel segments following PTCA.

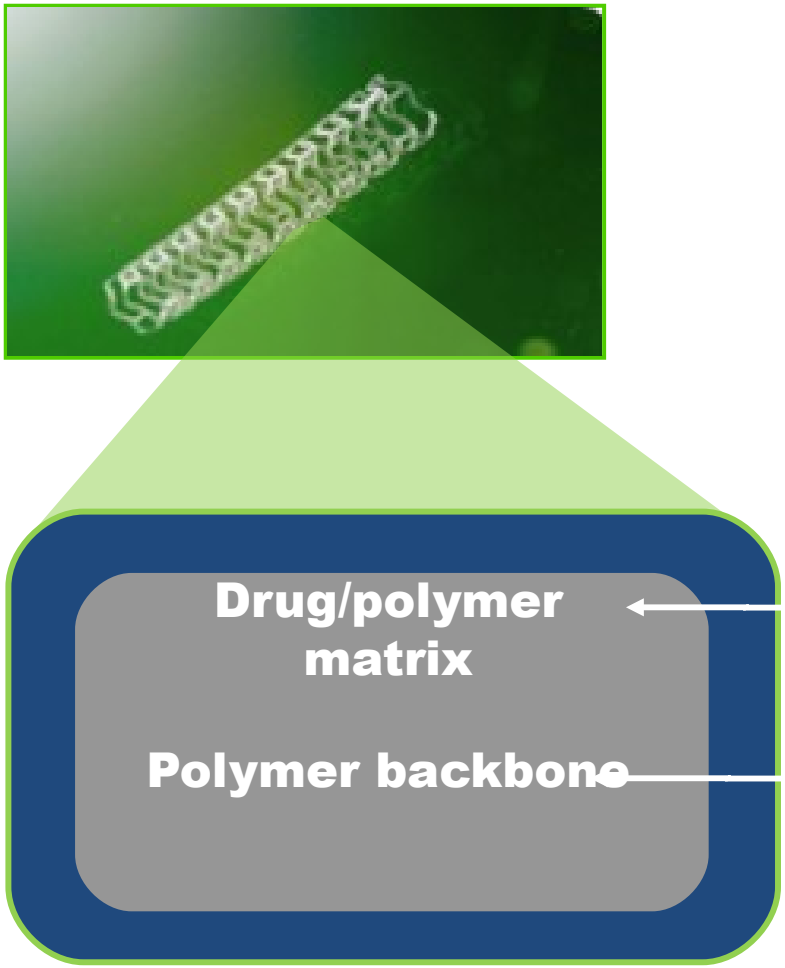
Restenosis is most prevalent between 1 and 3 months and rarely occurs beyond 3 months after coronary angioplasty.

Changes in MLD following PTCA stabilize at **3 months**

Nobuyoshi M, et al., *J Am Coll Cardiol.* 1988; **12:** 616-623.

- Degradation
  - Breaking down of the scaffold structure is inevitable and desired, by design
  - Structural discontinuities must not occur until after struts are fully covered by tissue; i.e., the scaffold is encapsulated within the vessel wall
- Benign resorption
  - Material selection is important: materials that degrade to substances naturally metabolized by the body will enable assimilation of degradation by products1

1. Vert, M. *EuroIntervent Suppl*. 2009; 5: F58-F64.
2. Soares, J. *Minerva Biotech*. 2009; 21: 217-220.
3. Waksman, R. *Cathet Cardiovasc Intervent*. 2007; 70: 407-414.

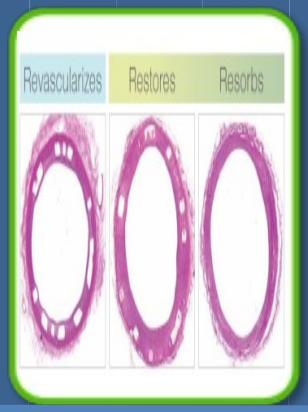


Everolimus/PDLLA Matrix Coating

- Thin layer
- Amorphous (non-crystalline)
- 1:1 ratio of Everolimus/PDLLA matrix
- Conformal coating, 2-4 mm thick
- Controlled drug release

PLLA Scaffold

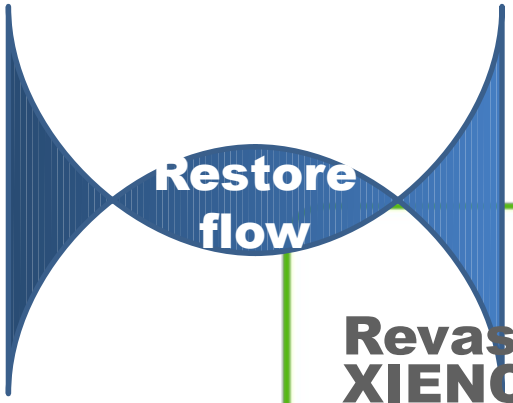
- Semi-crystalline
- Provides device structure
- Processed for required radial strength



Early evidence of vasomotion indicates natural vessel function is

Vascular Reparative Therapy

*Small platinum markers at scaffold edges remain for fluoroscopic landmarking.

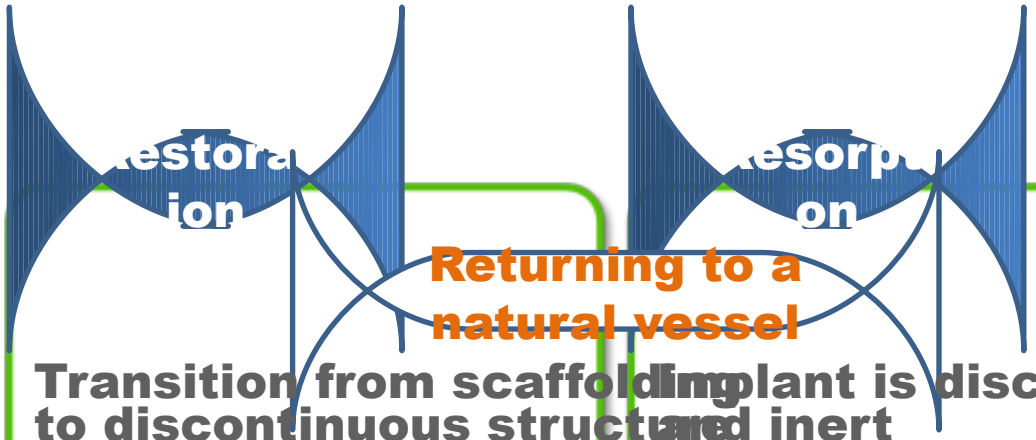


Revascularize like a best-in-class DES, XIENCE

- Controlled drug release to inhibit NIH
- Provide support to the vessel for at least 3 months
- Excellent conformability
- Safety and efficacy seem comparable to best-in-class DES, XIENCE

Post-dilatation expansion limits per CE labeling (IFU):

Scaffold Size	Maximum Noncompliant Balloon Diameter	Post-Dilatation Limit
2.5 mm	2.75 mm	3.0 mm
3.0 mm	3.25 mm	3.5 mm
3.5 mm	3.75 mm	4.0 mm



Returning to a natural vessel

Transition from scaffolding to discontinuous structure

- Gradually lose radial strength
- Struts must be incorporated into the vessel wall (strut coverage)
- Become structurally discontinuous

Implant is discontinuous and inert

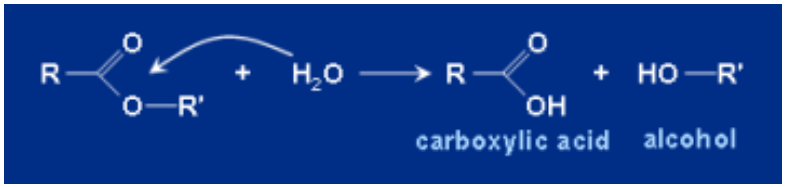
- Resorb in a benign fashion
- Allow the vessel to respond naturally to physiological stimuli

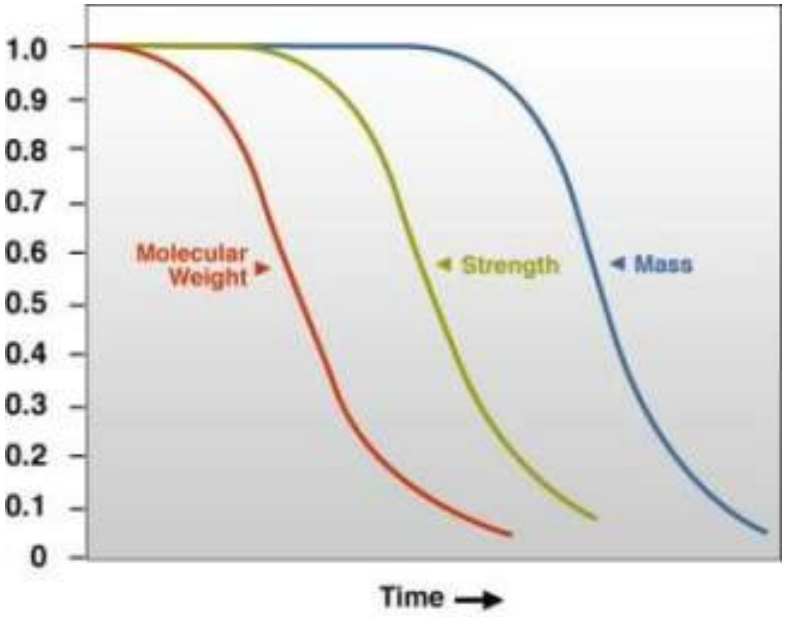
- Restoration of vasomotion
- Lumen preservation
- Late lumen enlargement
- Complete resorption of the scaffold*

Potential for improved long-term outcomes

*Small platinum markers at scaffold edges remain for fluoroscopic landmarking.

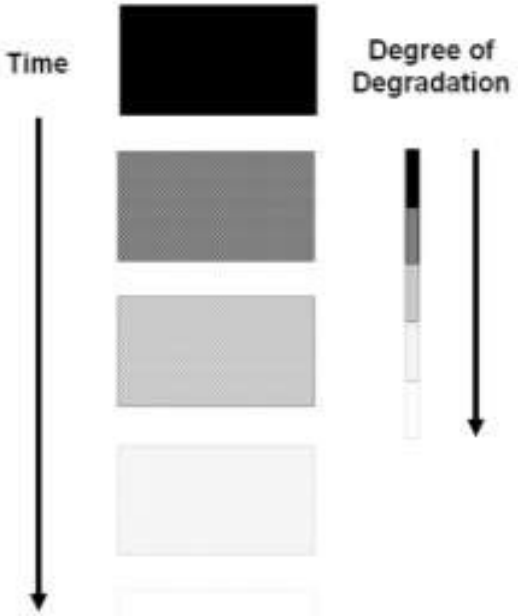
- Primary mode of degradation is by hydrolysis of ester bonds
- Water preferentially penetrates amorphous regions of the polymer matrix
- Hydrolysis initially results in a loss of molecular weight, but not radial strength, as the strength comes from crystalline domains
- Once polymer chains are sufficiently short to diffuse from struts or become soluble, mass loss occurs





Middleton JC, Tipton AJ, Biomaterials, 21 (2000) 2335-2346.

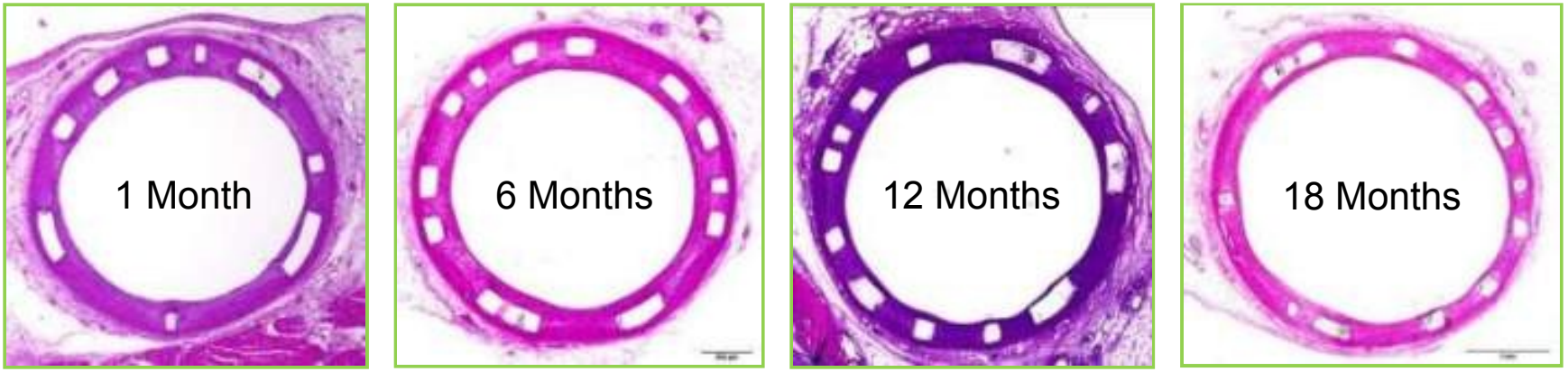
Bulk Erosion



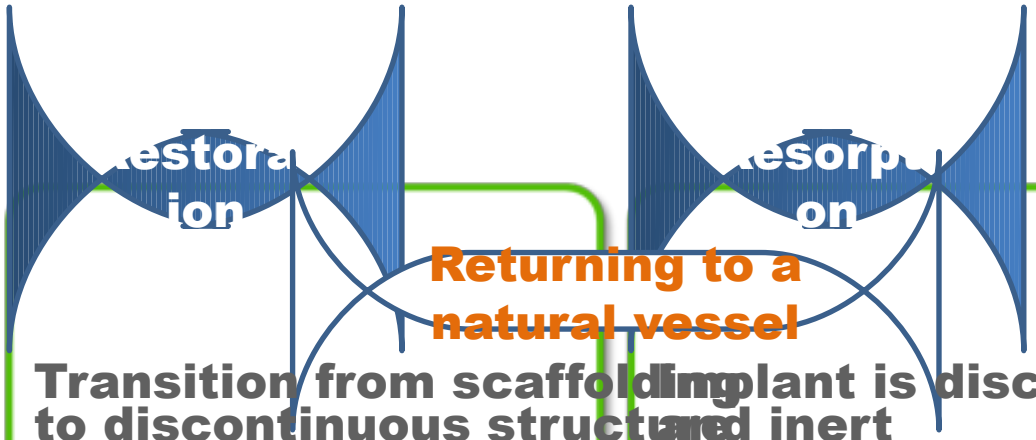
Von Burkersroda, F.,
et al. *Biomaterials* 2002; **23**: 4221

Strut degradation occurs via bulk erosion

BVS Cohort B



Tests performed by and data on file at Abbott Vascular.



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- Allow the vessel to respond naturally to physiological stimuli

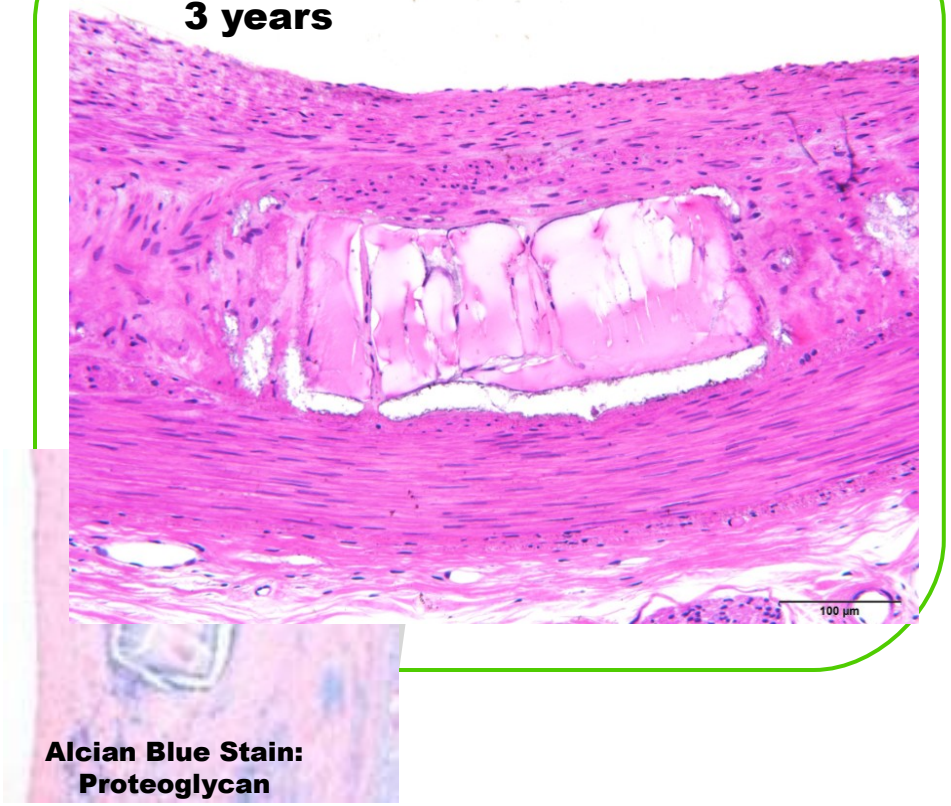
- Restoration of vasomotion
- Lumen preservation
- Late lumen enlargement
- Complete resorption of the scaffold*

Potential for improved long-term outcomes

*Small platinum markers at scaffold edges remain for fluoroscopic landmarking.

- While the sites of the pre-existing struts are still apparent after 2 years, the constitution of that shape has been predominantly replaced with provisional matrix
- No inflammation around the site
- 3 years: struts fully replaced by tissue

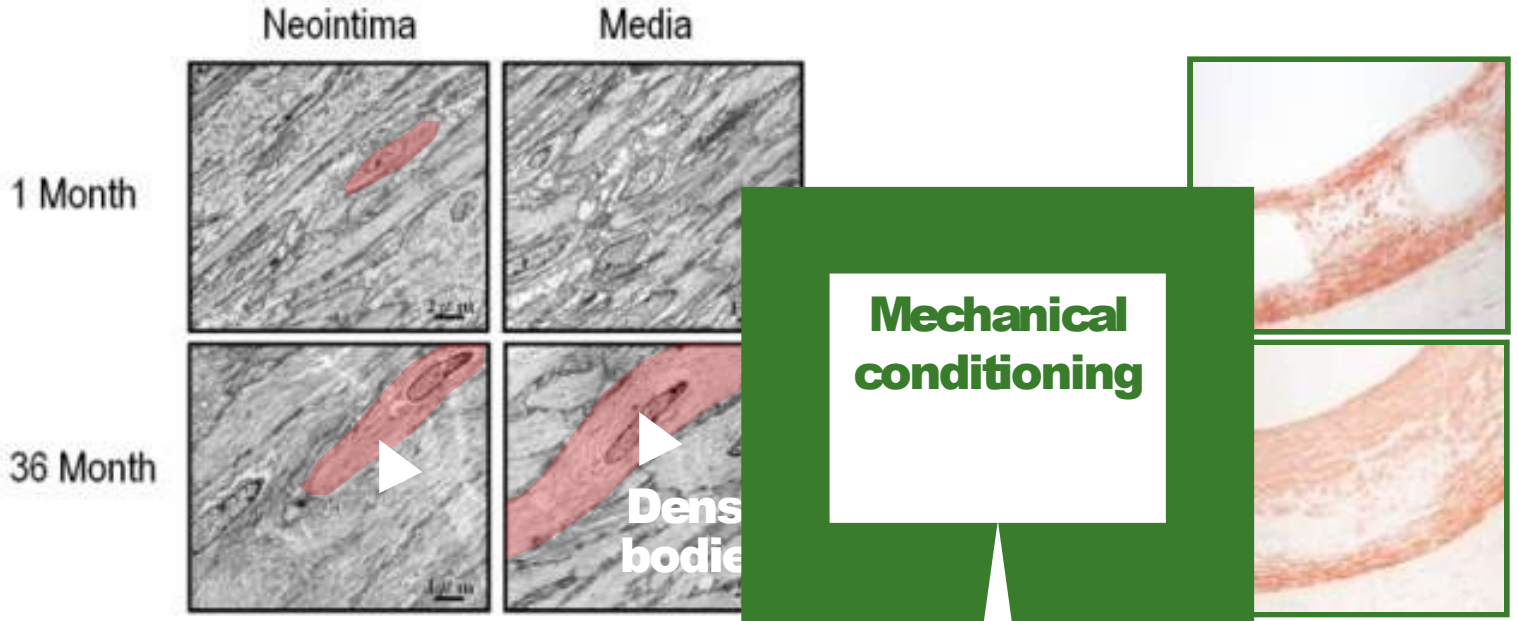
Representative porcine coronary arteries, 2x objective



Photos taken by and on file at Abbott Vascular.
Tests performed by and data on file at Abbott Vascular.

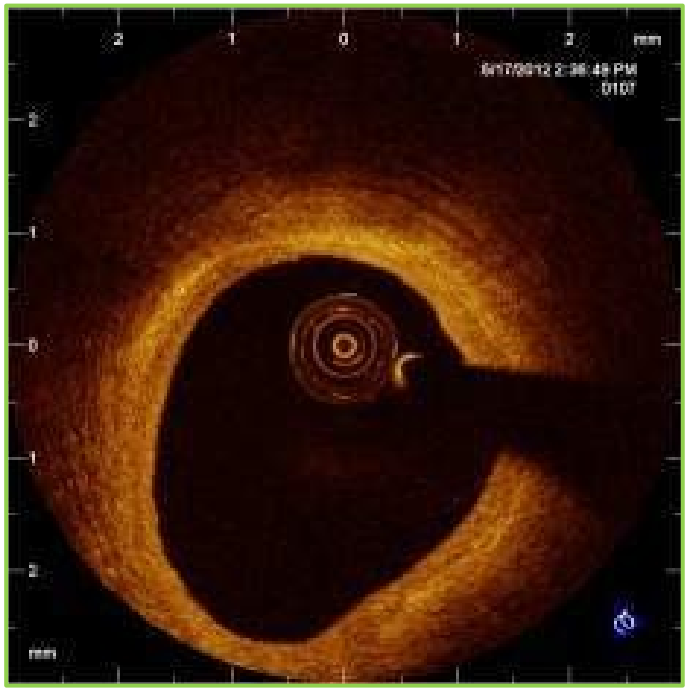
Transmission Electron Microscopy (TEM)

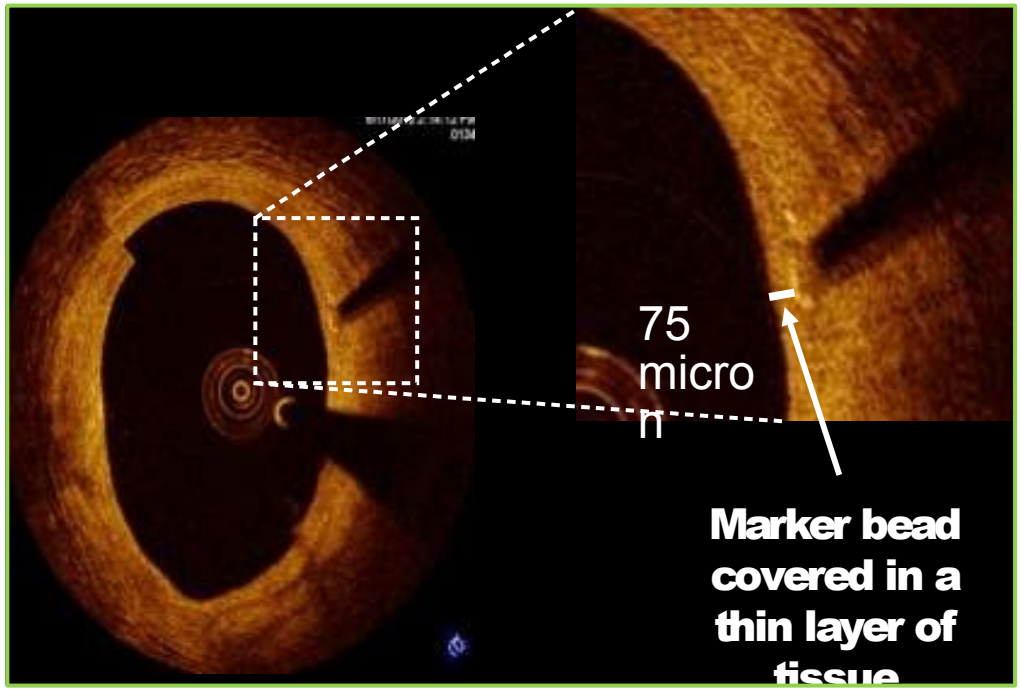
Smooth Muscle a-Actin



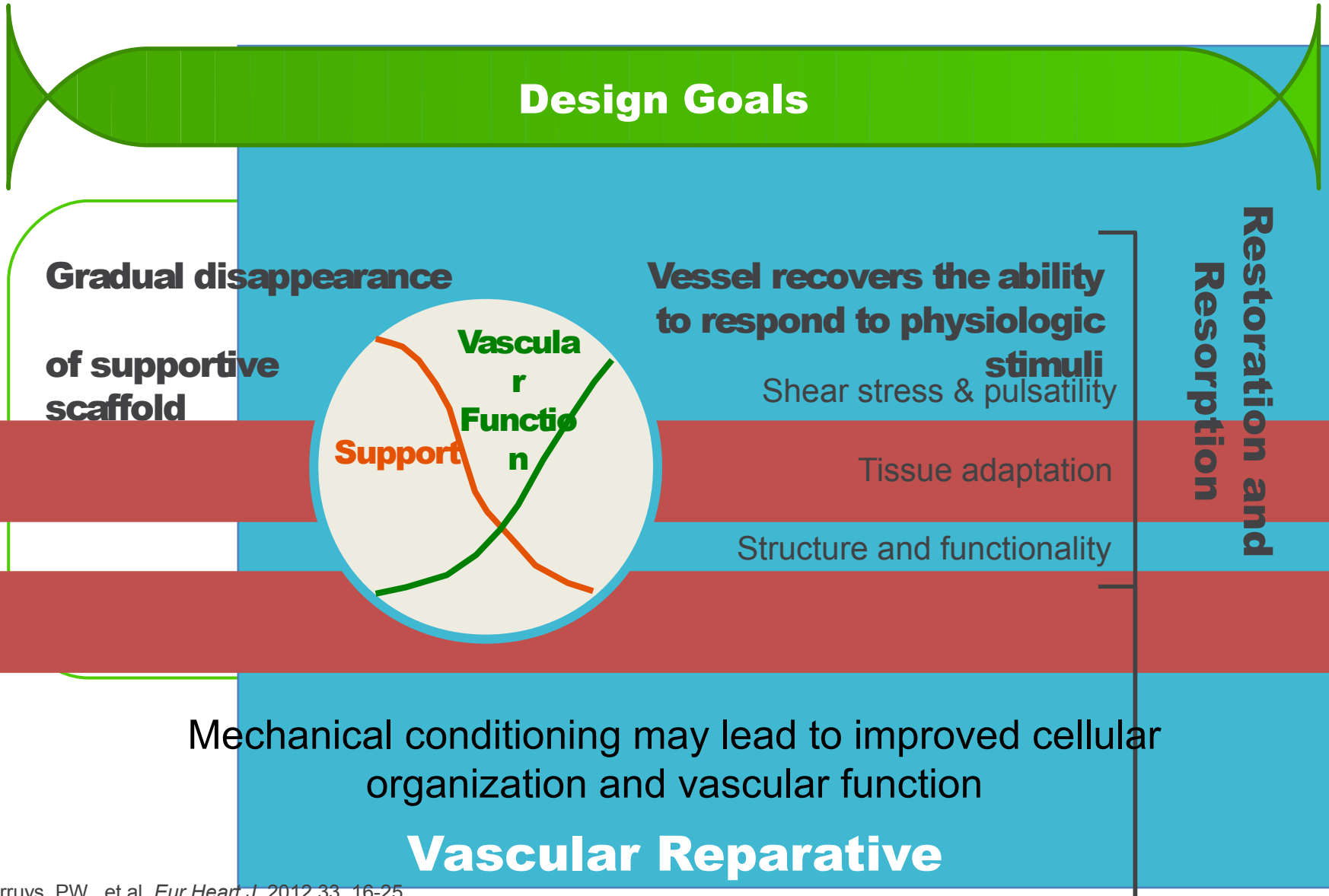
At 36 months, SMCs are well organized and have undergone transformation to a functional, contractile phenotype

Tests were performed by and data are on file at Abbott Vascular.





Images courtesy of Thoraxcenter, Erasmus MC, Rotterdam, The Netherlands, ABSORB A 5 yr

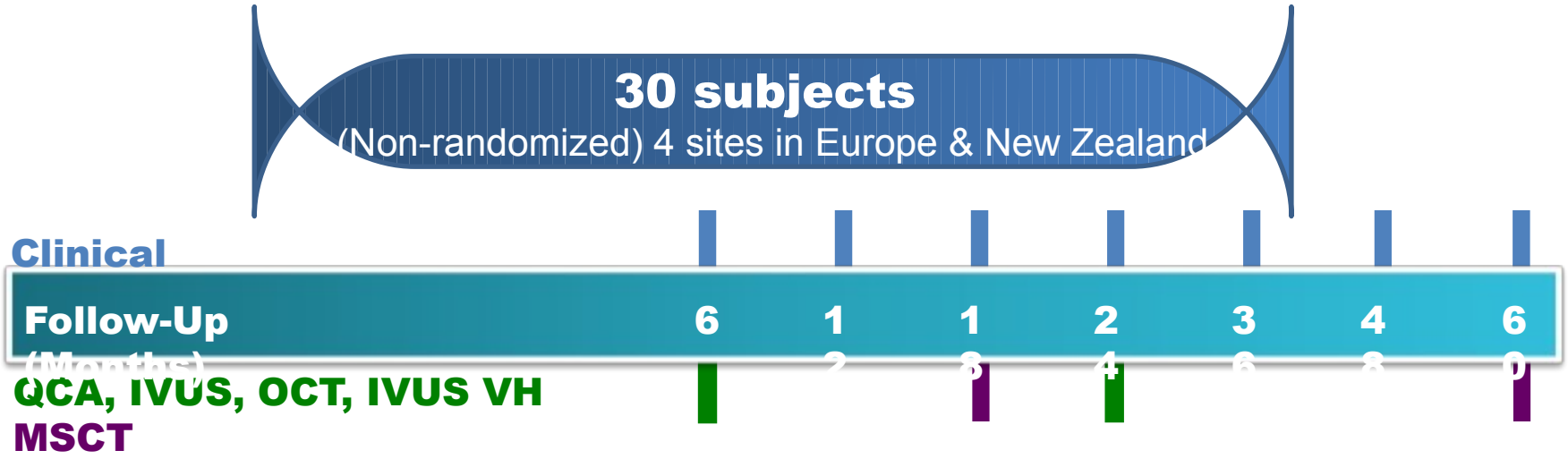


Serruys, PW., et al. *Eur Heart J*. 2012 33, 16-25

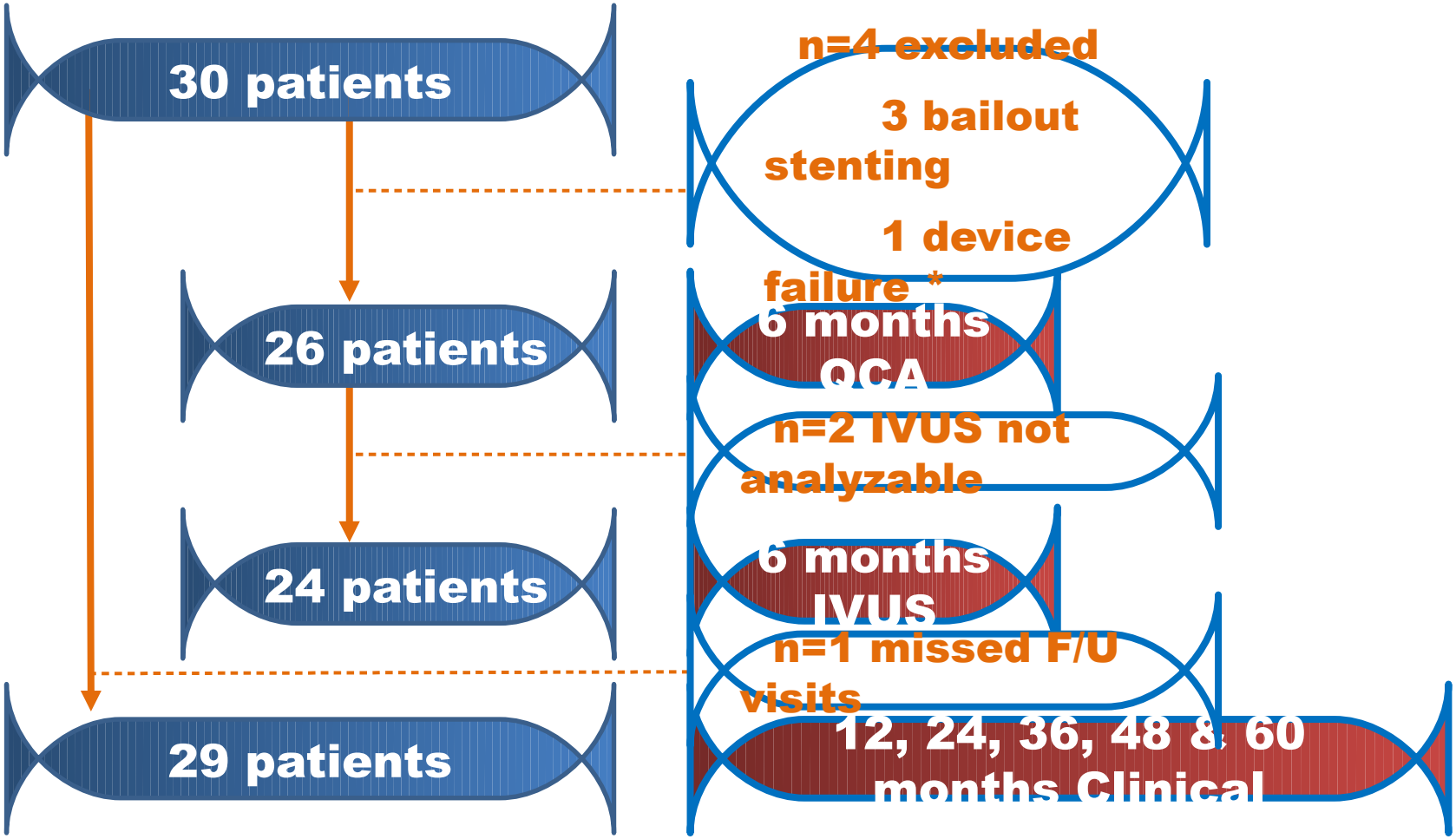
ABSORB
First In Man Clinical Trial

ABSORB Cohort A: 30 patients enrolled March – July 2006

ABSORB Cohort B: 101 patients enrolled March – Nov. 2009



Study Objective	First In Man, Single Arm – safety/performance
Endpoints	Typical PCI clinical and imaging endpoints
Treatment	Single, de novo native coronary lesion in a vessel with a reference vessel diameter of 3.0 mm
Device Sizes	3.0 x 12mm scaffolds (3.0 x 18mm scaffolds available after enrolment start and used in 2 pts)



* Per treatment evaluable population. Four patients were excluded who received a non-BVS bailout stent, including one patient who did not receive a BVS stent at the target lesion.

Baseline Demographics

Male	58%
Diabetes Mellitus	4%
Location of Lesions	
LAD	50%
LCX	23%
RCA	27%
Lesion Classification	
Type B1	65%
Type B2	35%
Pre-Procedure	
Lesion length (mm)	8.66 ± 3.97
RVD (mm)	2.78 ± 0.47
MLD (mm)	1.10 ± 0.26
DS (%)	59 ± 12

Onuma, AHA 2009

ABSORB Cohort A Clinical Results at Each Phase: Intent to Treat

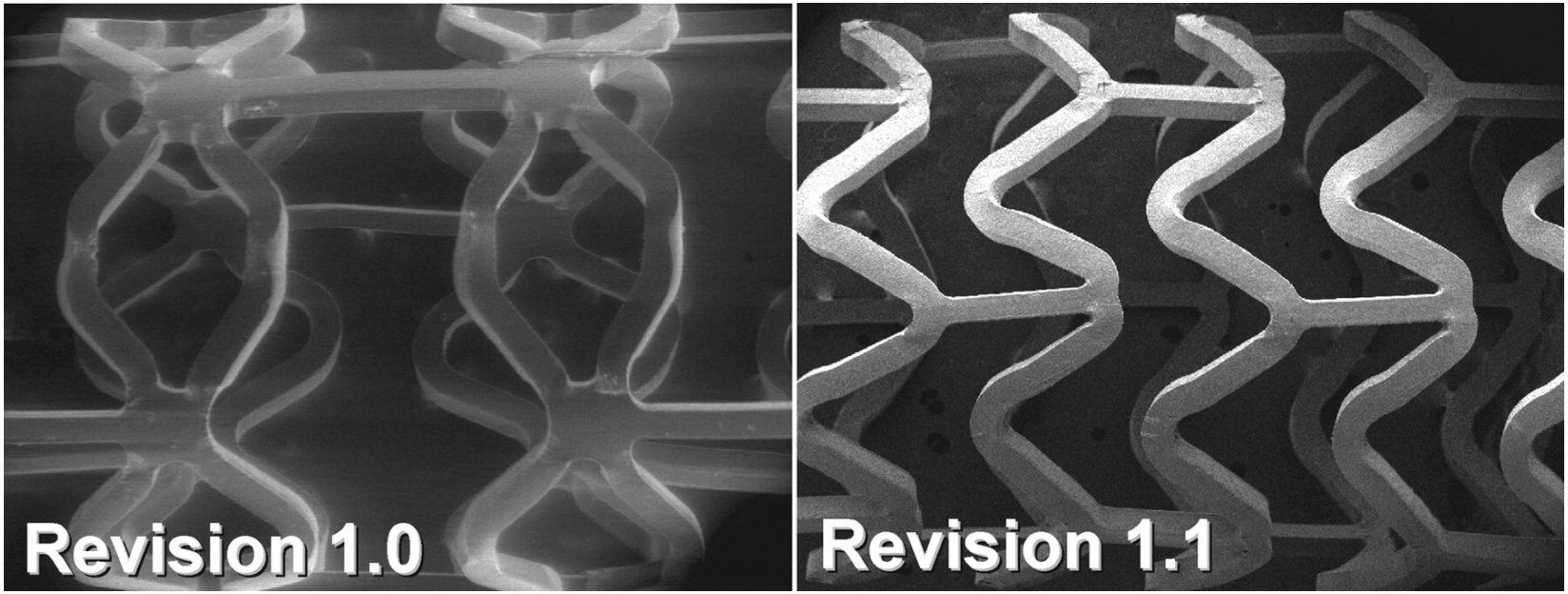
	RESTORATION		RESORPTION	
Hierarchical	6 Months 30 Patients	1 year 29 Patients**	2 Year 29 Patients**	5 Year 29 Patients**
Ischemia Driven MACE***	1 (3.3%)*	1 (3.4%)*	1 (3.4%)*	1 (3.4%)*
Cardiac Death	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MI	1 (3.3%)*	1 (3.4%)*	1 (3.4%)*	1 (3.4%)*
Q-Wave MI	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Non Q-Wave MI	1 (3.3%)*	1 (3.4%)*	1 (3.4%)*	1 (3.4%)*
Ischemia Driven TLR	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
by PCI	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.%)
by CABG	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.%)

No scaffold thrombosis by ARC or Protocol

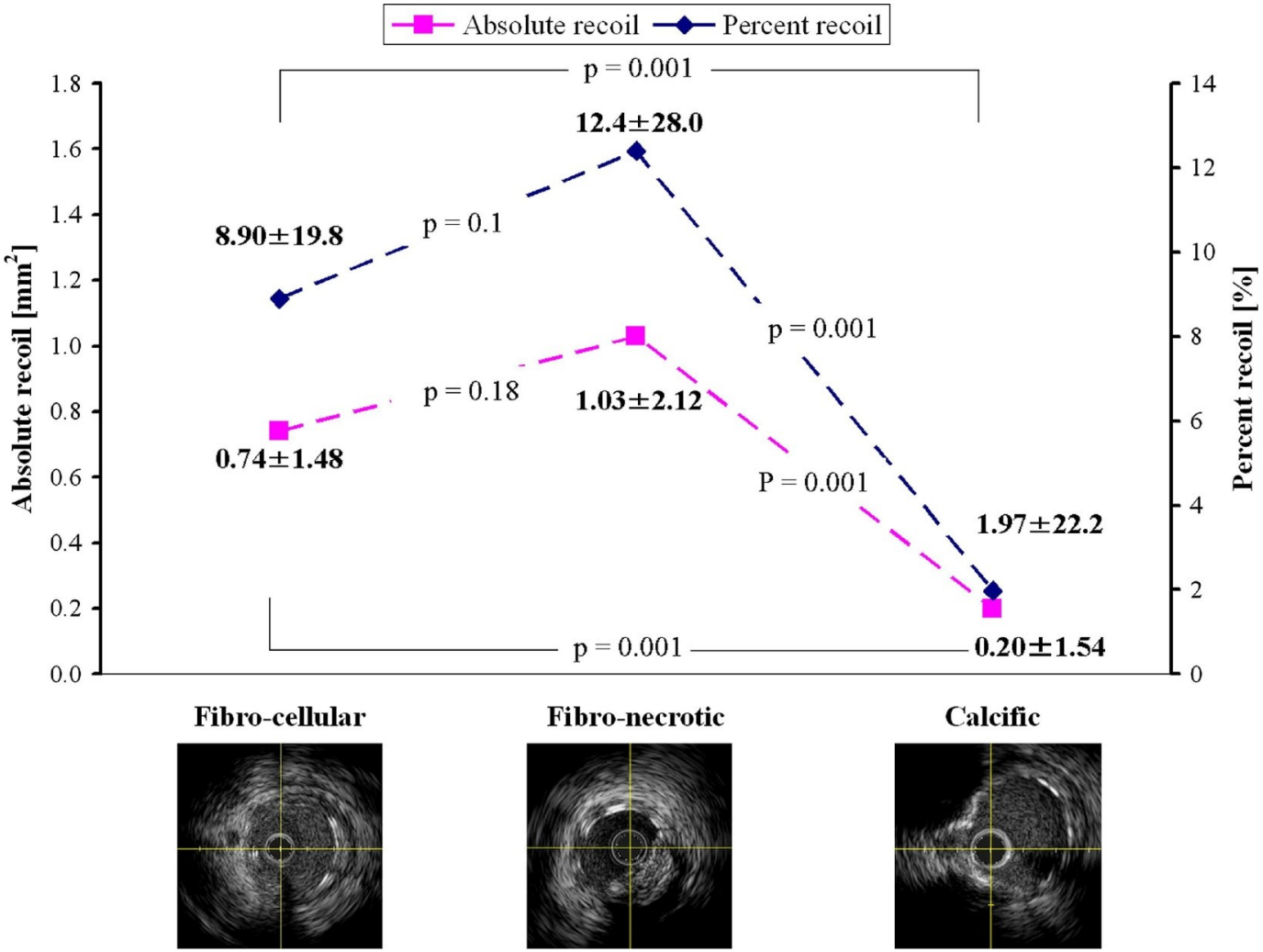
* Same patient – this patient also underwent a TLR, not qualified as ID-TLR (DS = 42%)
** One patient missed the 9, 12, 18 month and 2, 3, and 4 year visits; one patient died from a non-cardiac cause 706 days post procedure
*** MACE – Composite endpoint comprised of cardiac death, myocardial infarction (MI) and ischemia-driven target lesion revascularization (TLR) by PCI or CABG

Serruys, TCT, 2011

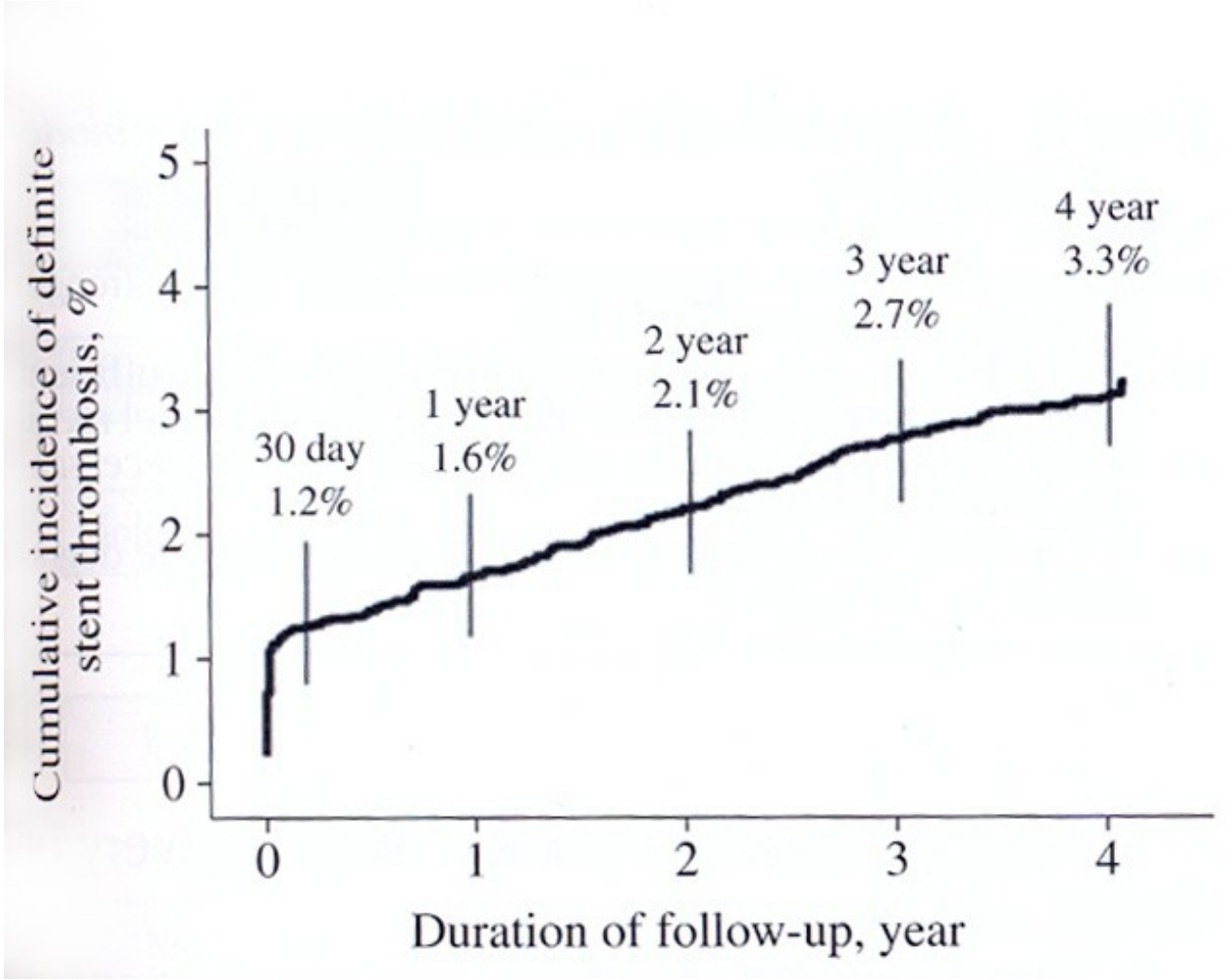
Danke



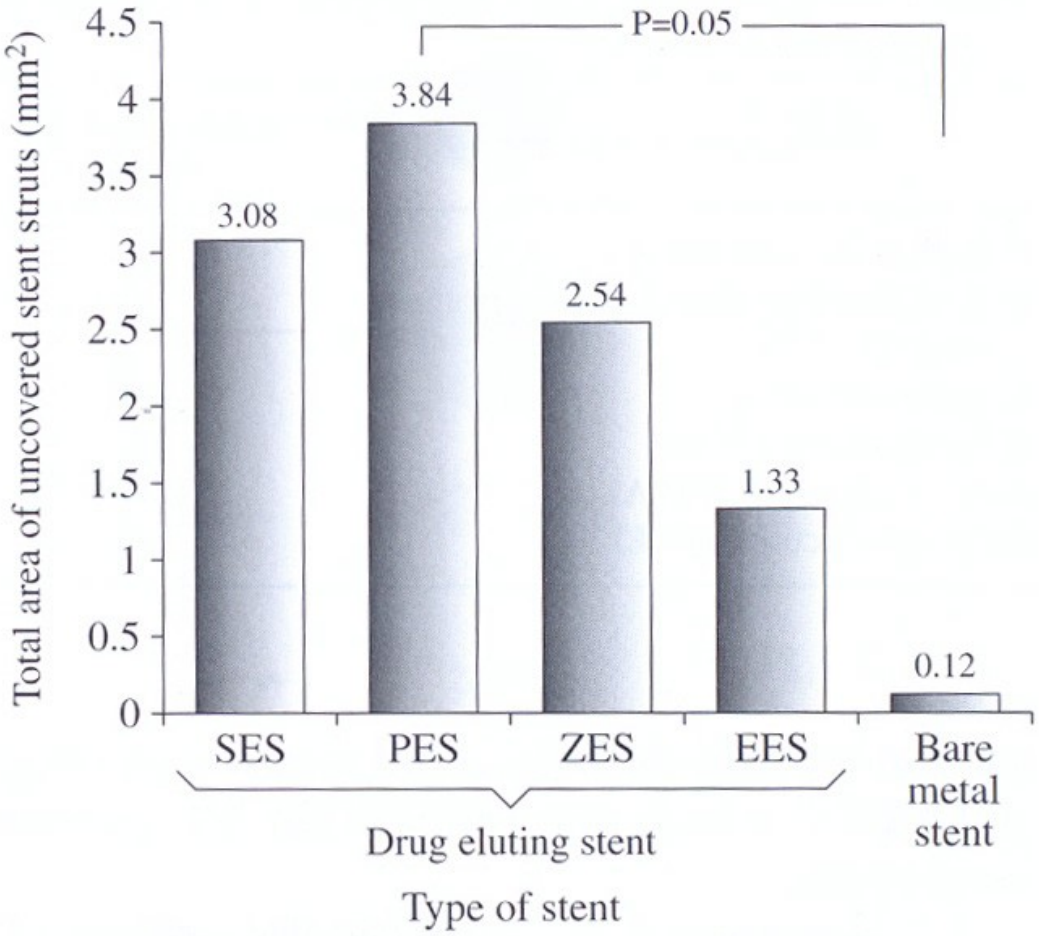
Ormiston JA & Serruys PW CCI 2009



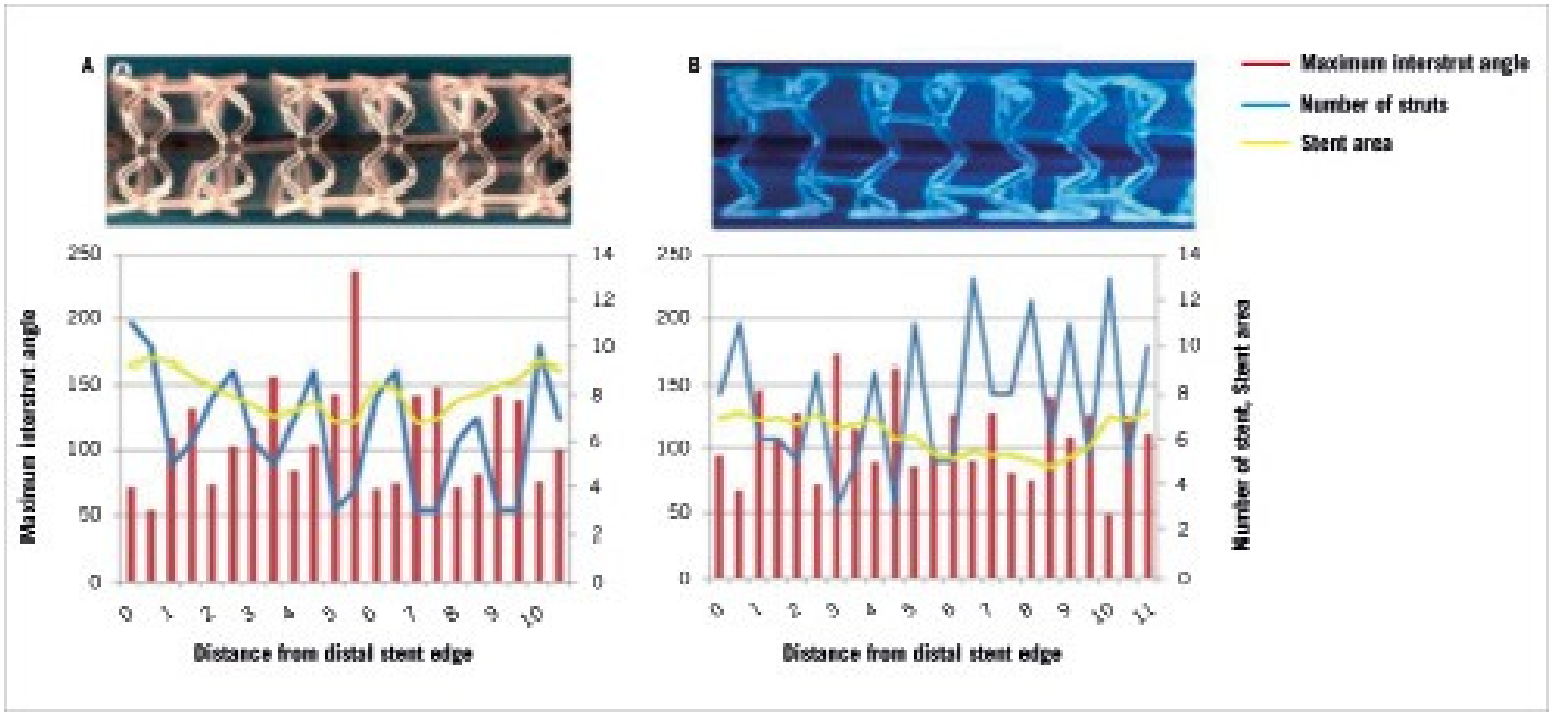
Tanimoto S et al. JACC 2007



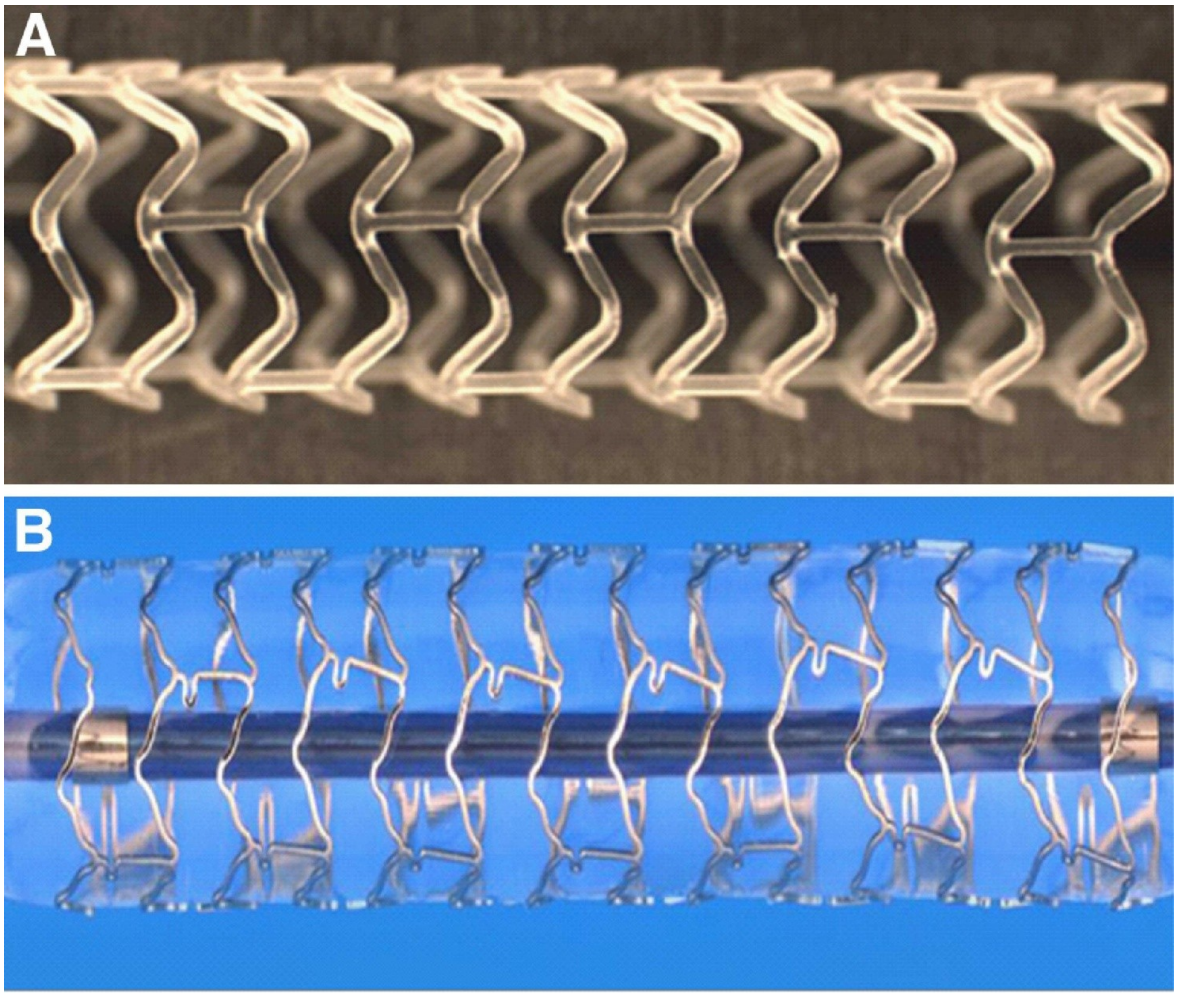
Garg S & Serruys PW Minerva Cardioangiol. 2009



Garg S & Serruys PW Minerva Cardioangiol. 2009



Okamura T et al. EuroIntervention 2010



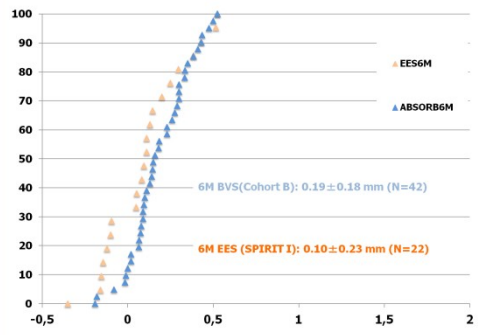
Gomez-Lara J et al. JACC 2010

No change in late lumen loss from 12 to 24 months*

The Evolution of Cumulative Frequency Distribution Curves for Late Loss Over Time:

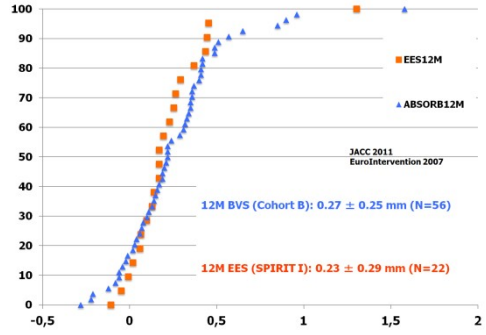
BVS Cohort B and XIENCE V (Non-Matched Population)

6 Months



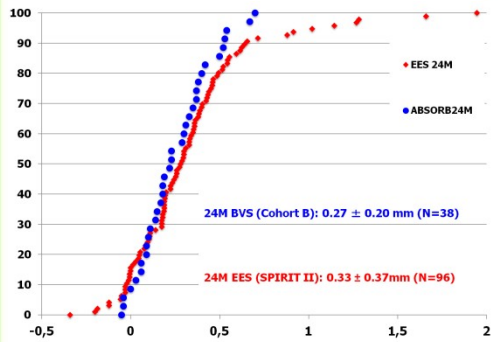
BVS: 0.19 + 0.18 mm (n = 42)

12 Months



BVS: 0.27 + 0.32 mm (n = 56)

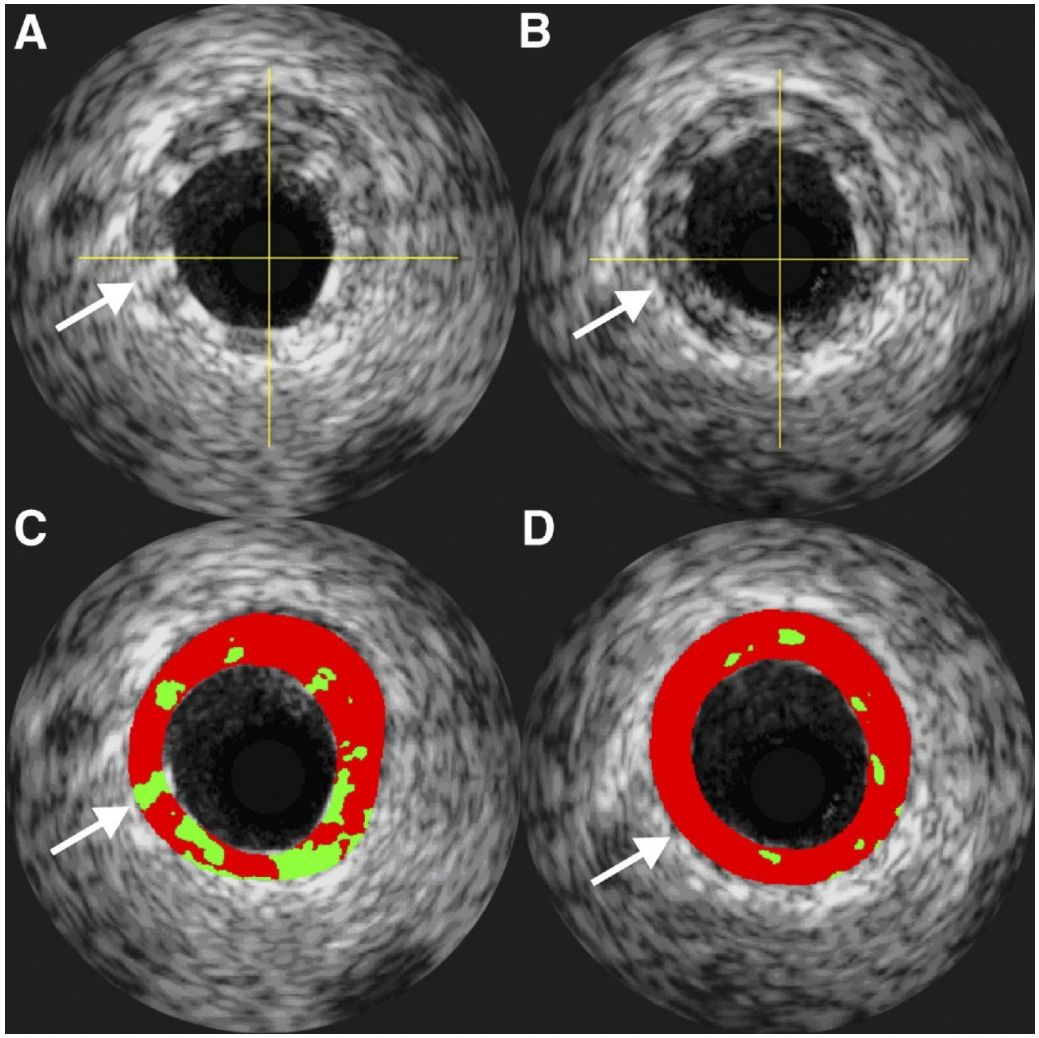
24 Months



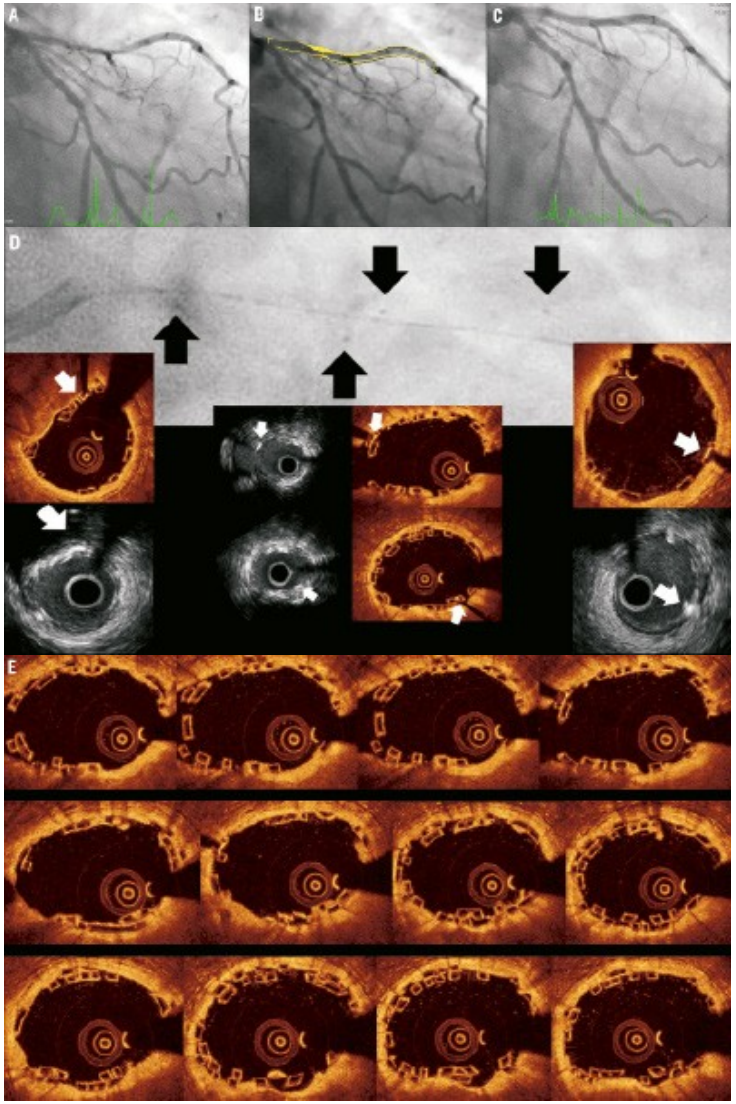
BVS: 0.27 + 0.19 mm (n = 38)

Serruys, PW., TCT 2011.

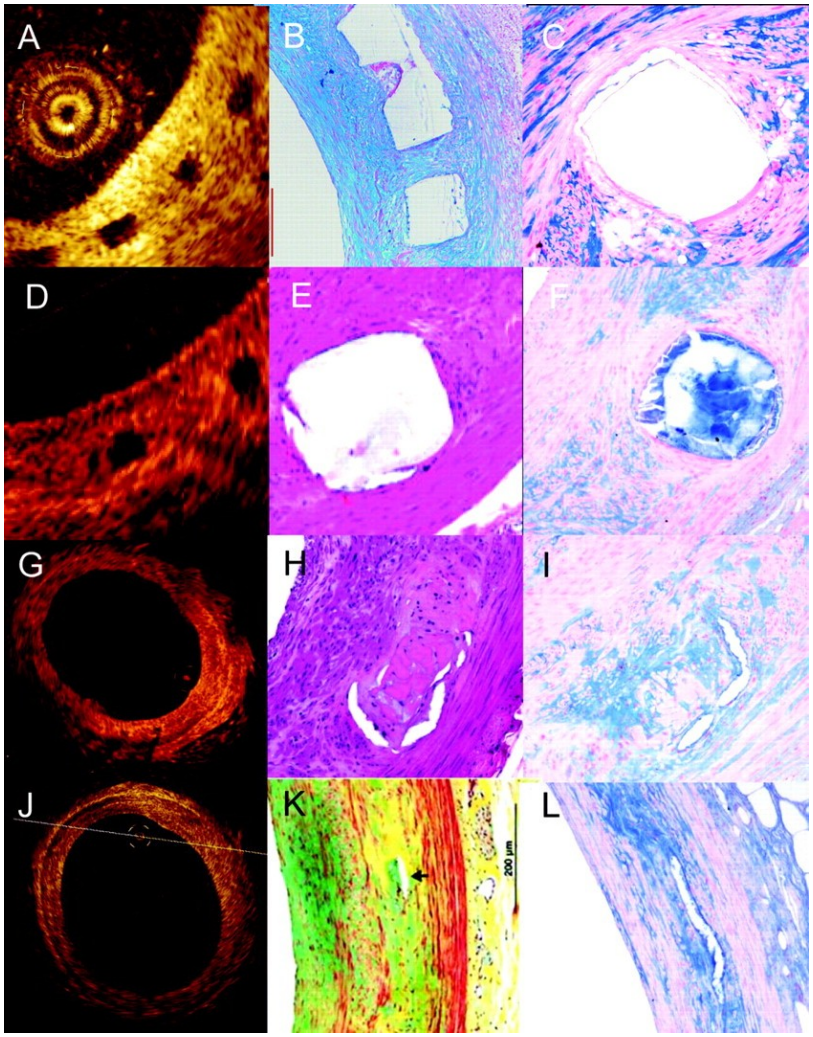
*12-month data is from ABSORB Cohort B Group 2 (n=56), 24-month data is from Cohort B Group 1 (n=45)



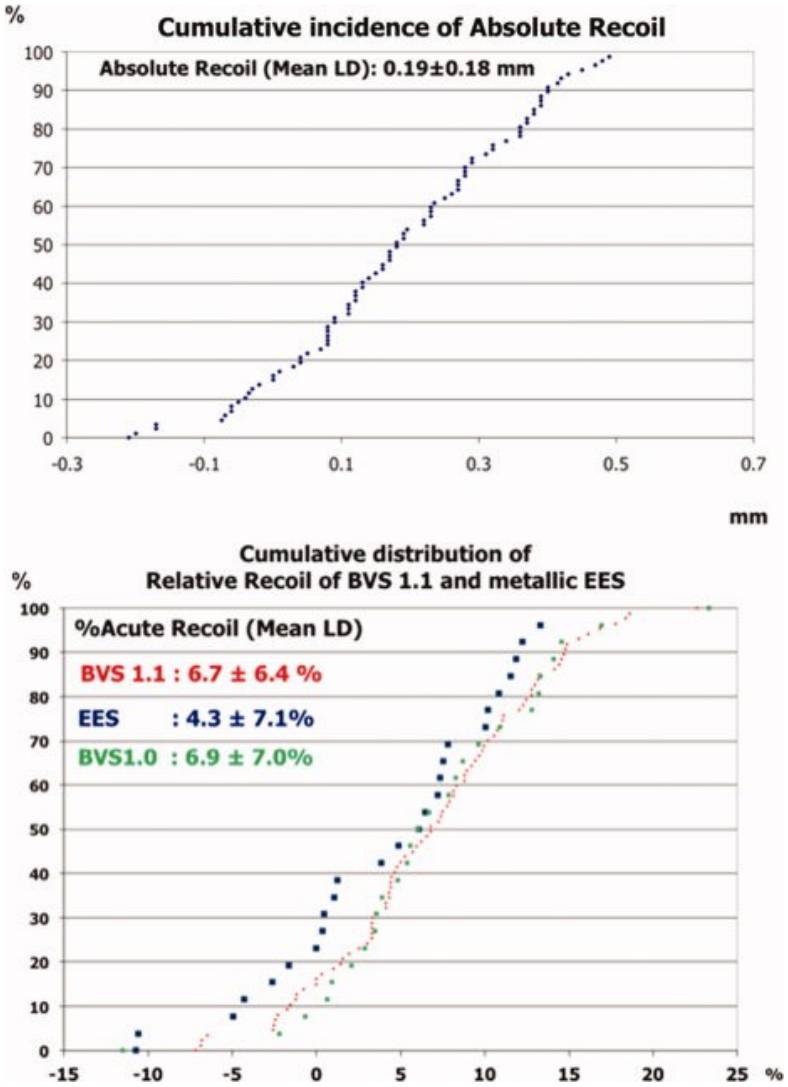
Bruining N et al. JACC 2010



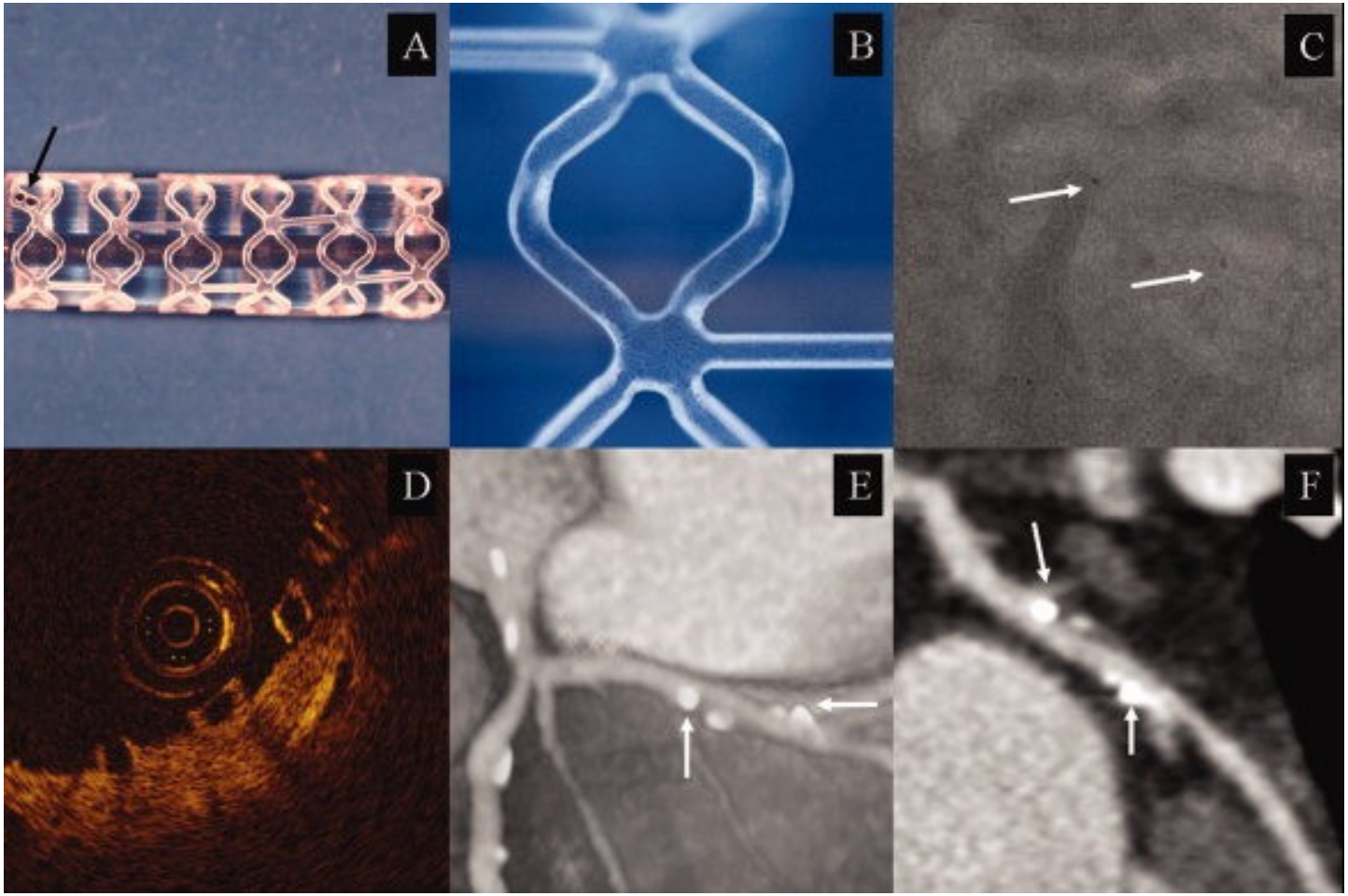
Farooq V et al. EuroIntervention 2011



Onuma Y & Serruys PW Circulation 2011



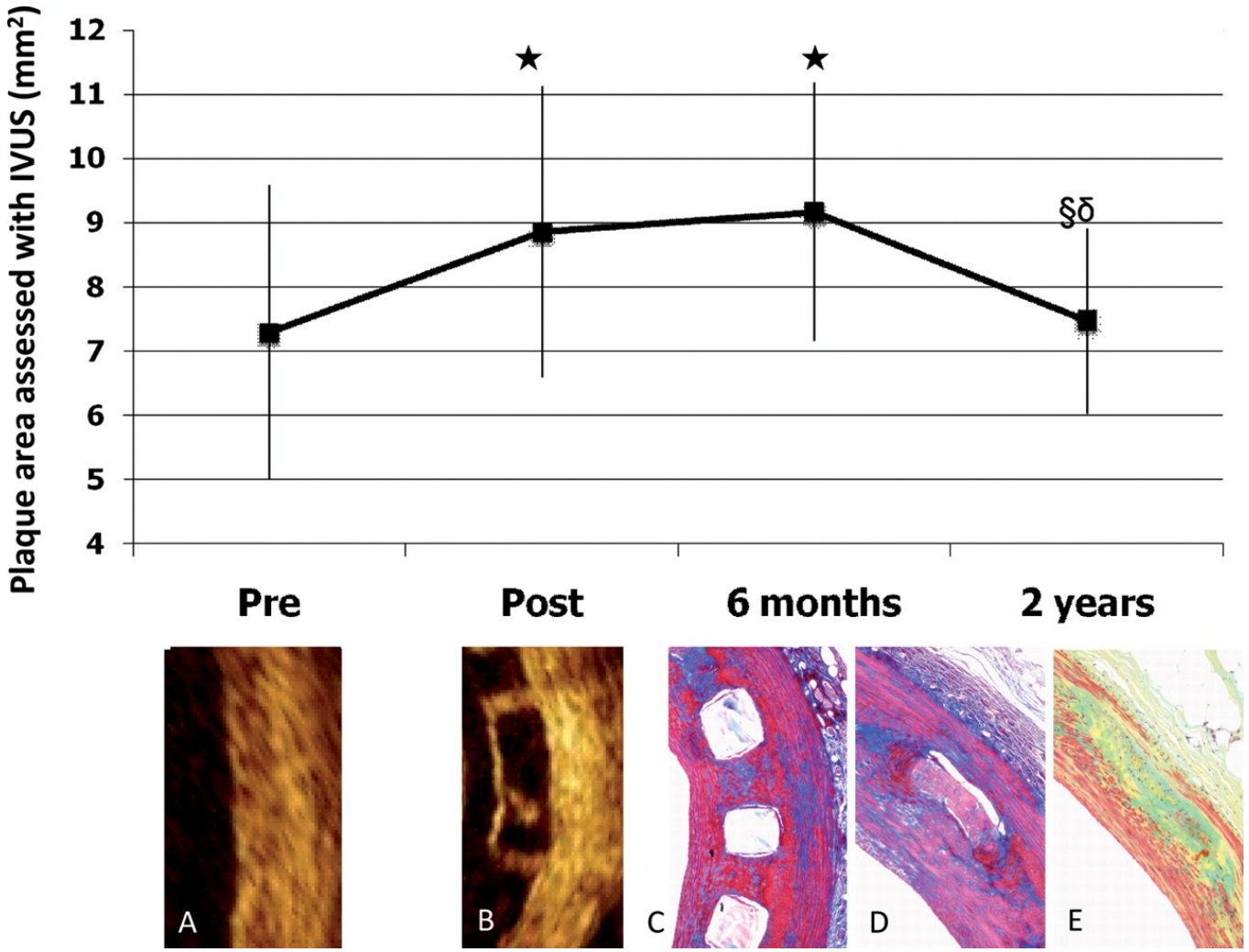
Onuma Y et al. CCI 2011



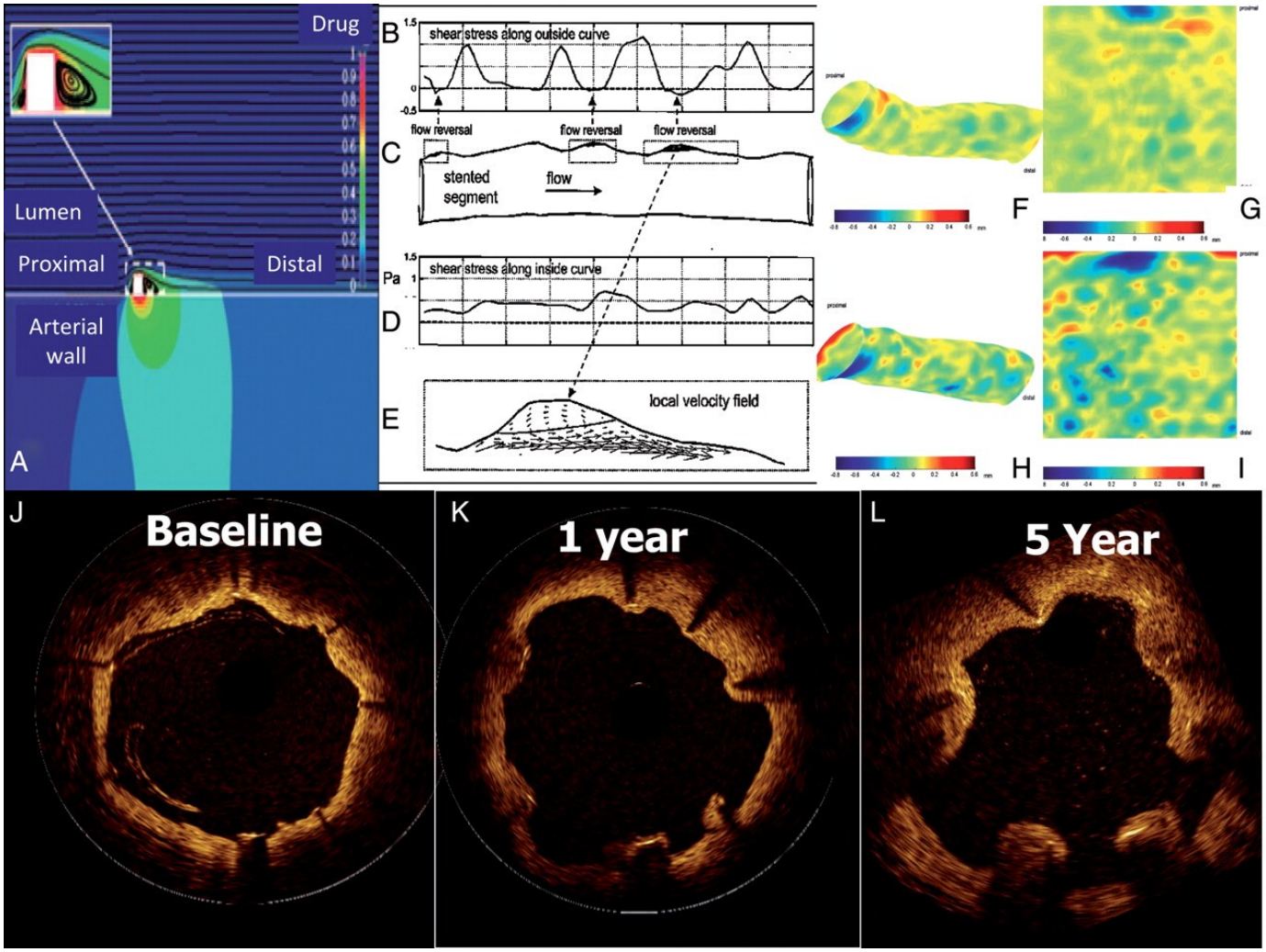
Tanimoto S et al. CCI 2007

Head-to-Head Comparison of the Neointimal Response Between Metallic and Bioresorbable Everolimus-Eluting Scaffolds Using Optical Coherence Tomography

Gomez-Lara J et al.JACC 2011

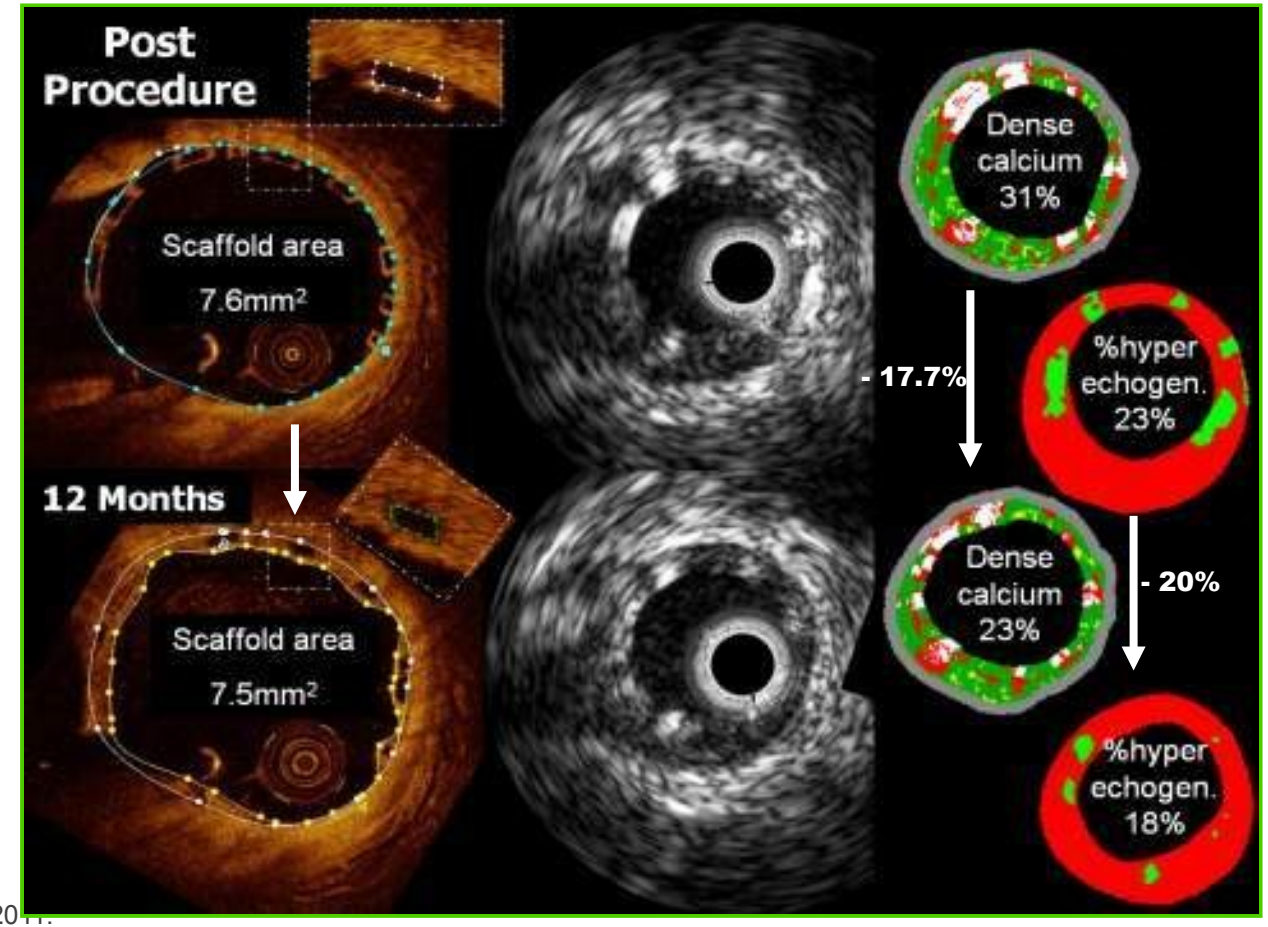


Serruys PW et al.EHJ 2012

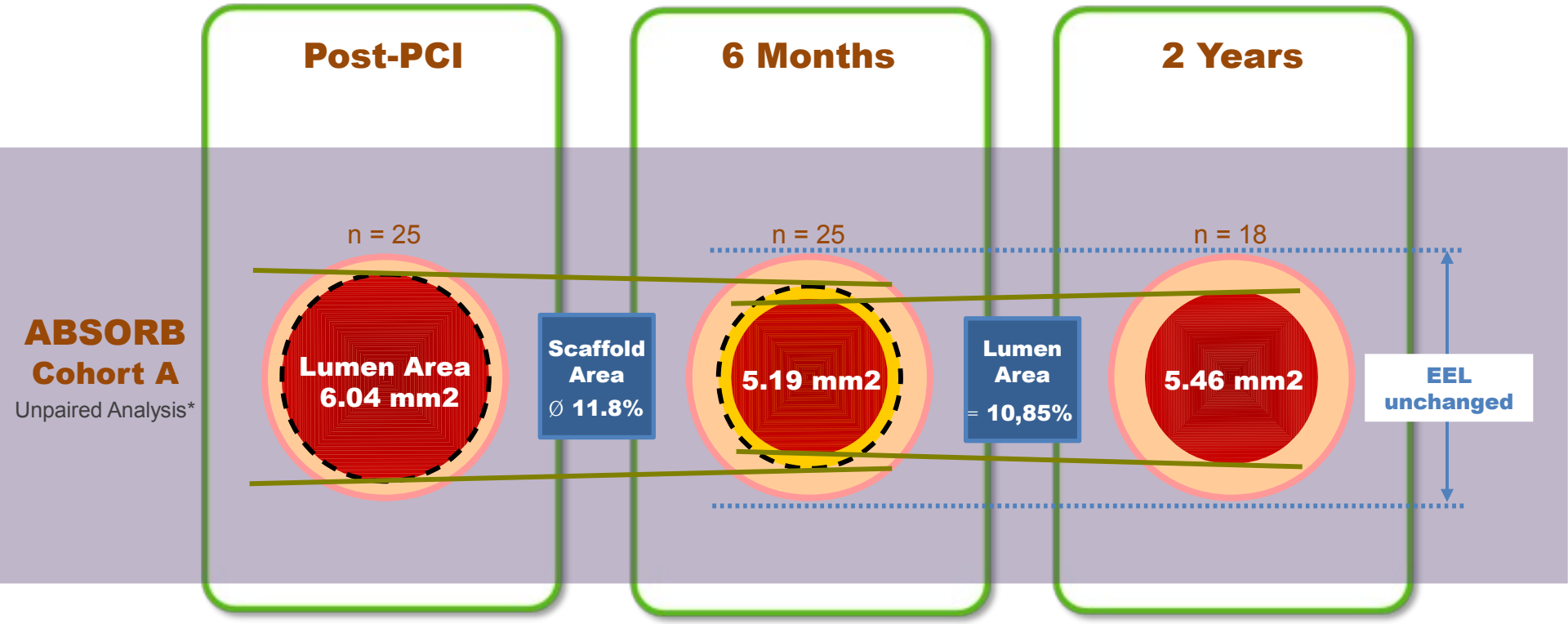


Serruys PW et al.EHJ 2012

The scaffold area remained unchanged, despite early signs of biodegradation observed on OCT, IVUS-VH, and IVUS echogenicity

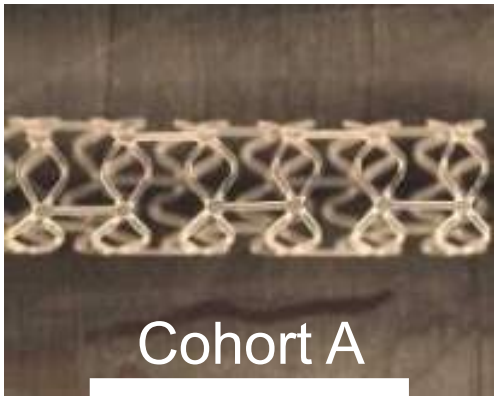


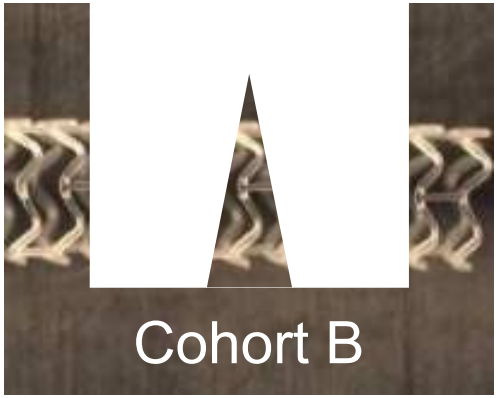
Serruys, PW., ACC 20[illegible].



- Late lumen loss at 6 months mainly due to reduction in scaffold area
- Very late lumen enlargement noted from 6 months to 2 years

*Adapted from Serruys, PW, ACC 2009.





More uniform strut distribution

More even support of arterial wall

Lower late scaffold area loss

- Maintain radial strength for at least 3 months

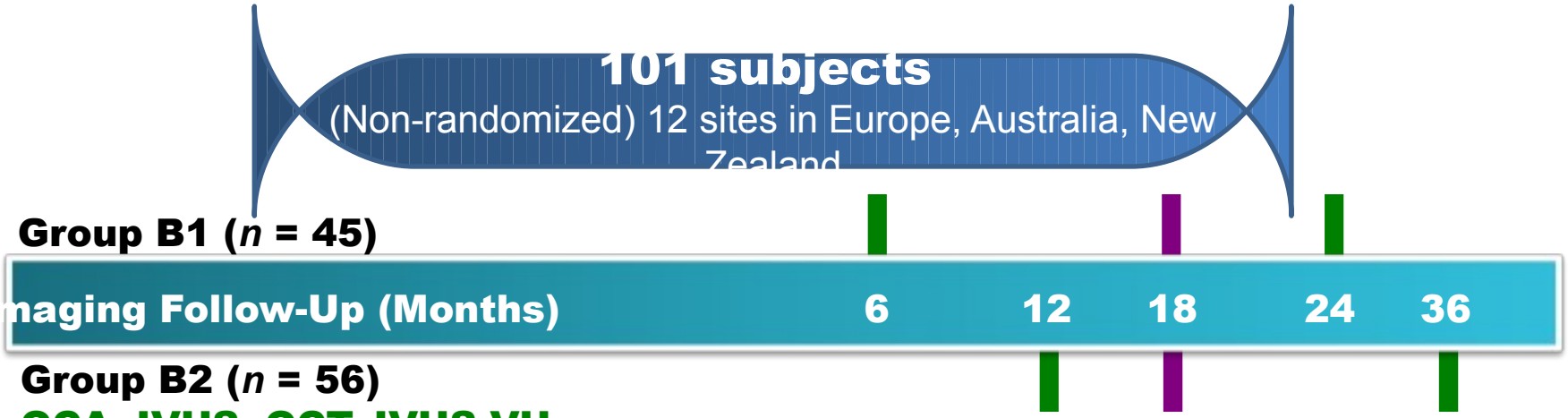
Storage at room temperature

Improved device retention

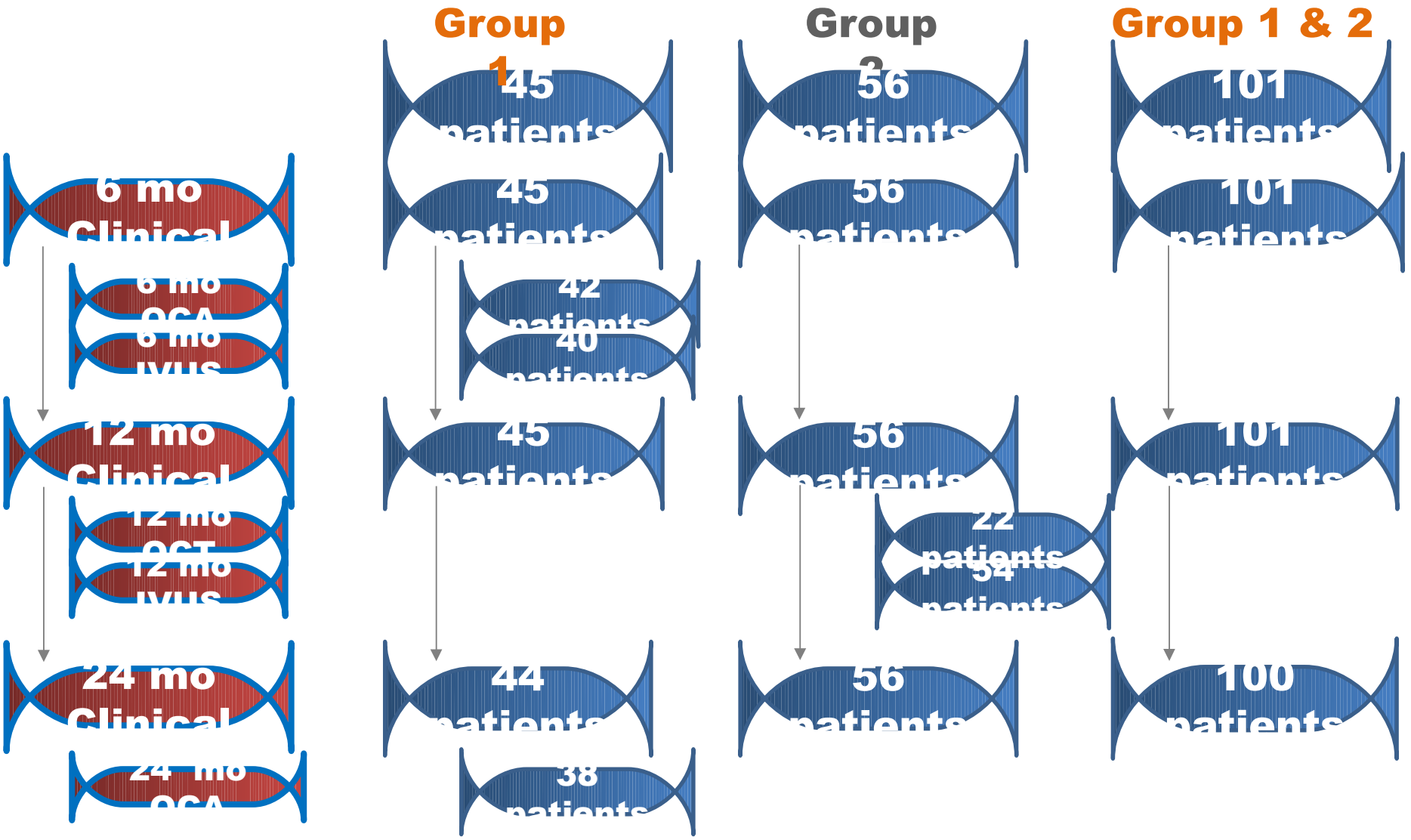
Unchanged:

- Material, coating and backbone
- Strut thickness
- Drug release profile

Photos taken by and on file at Abbott Vascular.



Study Objective	First In Man, Single Arm – safety/performance
Endpoints	Typical PCI clinical and imaging endpoints
Treatment	Up to 2 *de novo* lesions in different epicardial vessels Reference vessel diameter of 3.0 mm, lesions ≤ 14 mm in length
Device Sizes	3.0 x 18mm devices



Serruys, PW., PCR 2010, Serruys PW ACC2011, Serruys PW Circulation 2010

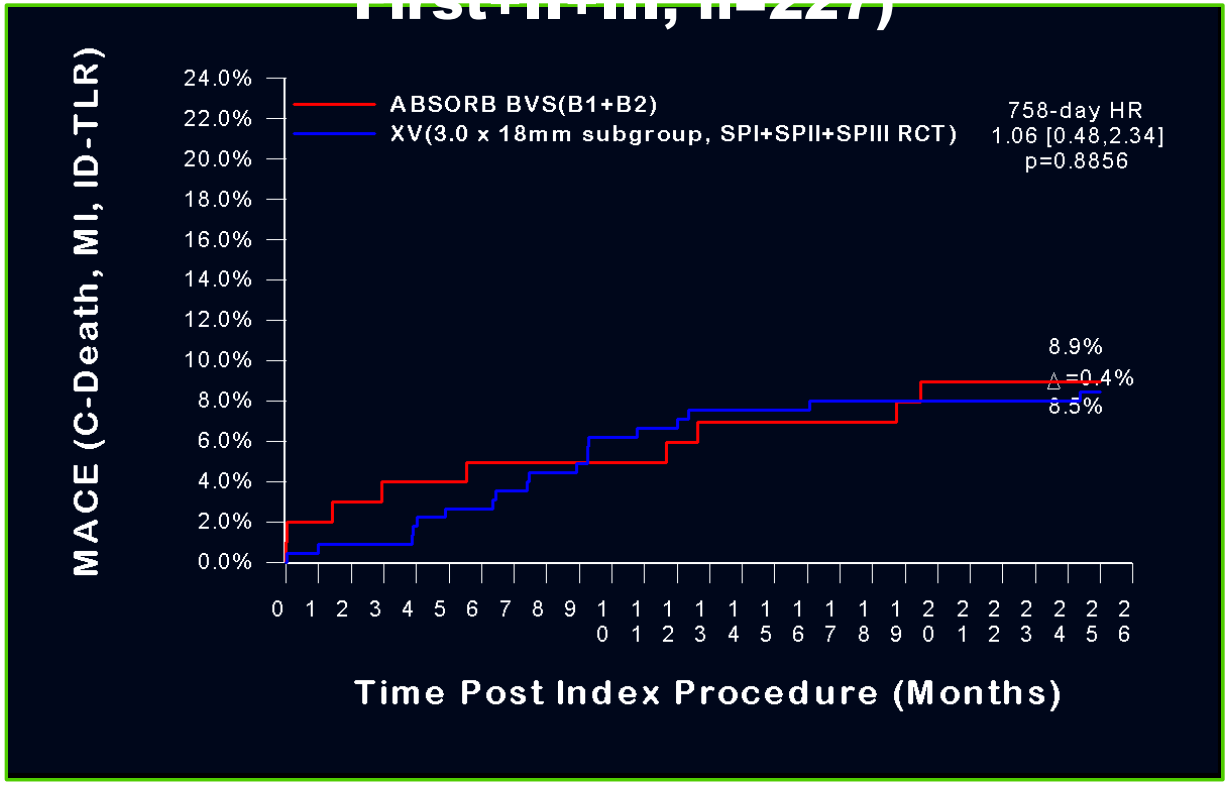
No Hierarchical	30 Days N = 101	6 Months N = 101	1 Year N = 101	2 Years N = 100*
Cardiac Death %	0	0	0	0
Myocardial Infarction % (n)	2.0 (2)	3.0 (3)	3.0 (3)	3.0 (3)
Q-wave MI	0	0	0	0
Non Q-wave MI	2.0 (2)	3.0 (3)	3.0 (3)	3.0 (3)
Ischemia driven TLR % (n)	0	2.0 (2)	4.0 (4)	6.0 (6)
CABG	0	0	0	0
PCI	0	2.0 (2)	4.0 (4)	6.0 (6)
Hierarchical MACE % (n)	2.0 (2)	5.0 (5)	6.9 (7)	9.0 (9)

No scaffold thrombosis by ARC or Protocol out to 2 – Year only 2 additional TLR events between 1 year and 2 year

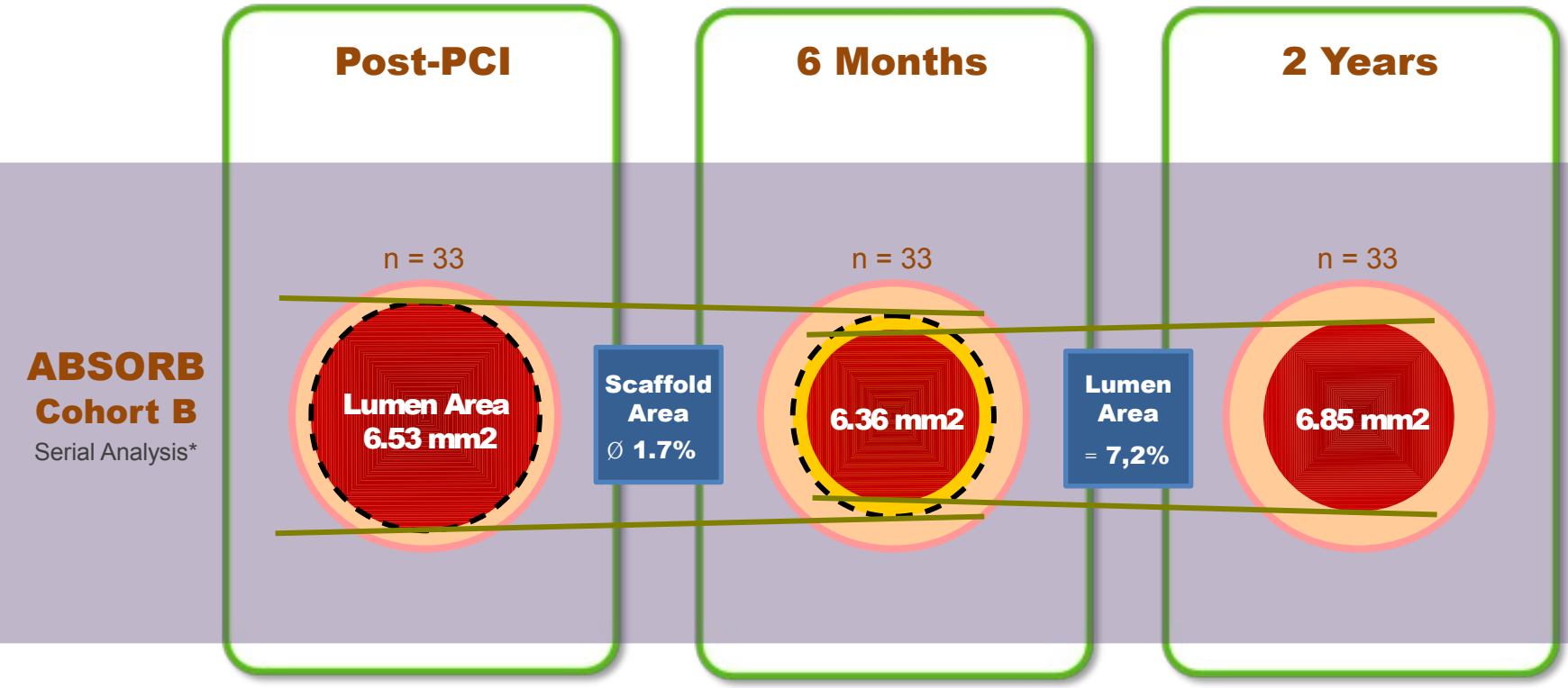
D. Dudek, ACC 2012 / *One patient missed the 2 year FUP

MACE: Cardiac death, MI, ischemia-driven TLR
TVF: Cardiac death, MI, ischemia-driven TLR, ischemia-driven TVR

Estimate of MACE rate in patients treated with Absorb BVS (ABSORB Cohort B, n=101) versus patients treated with a single 3 x 18 mm XIENCE V (SPIRIT First+II+III, n=227)

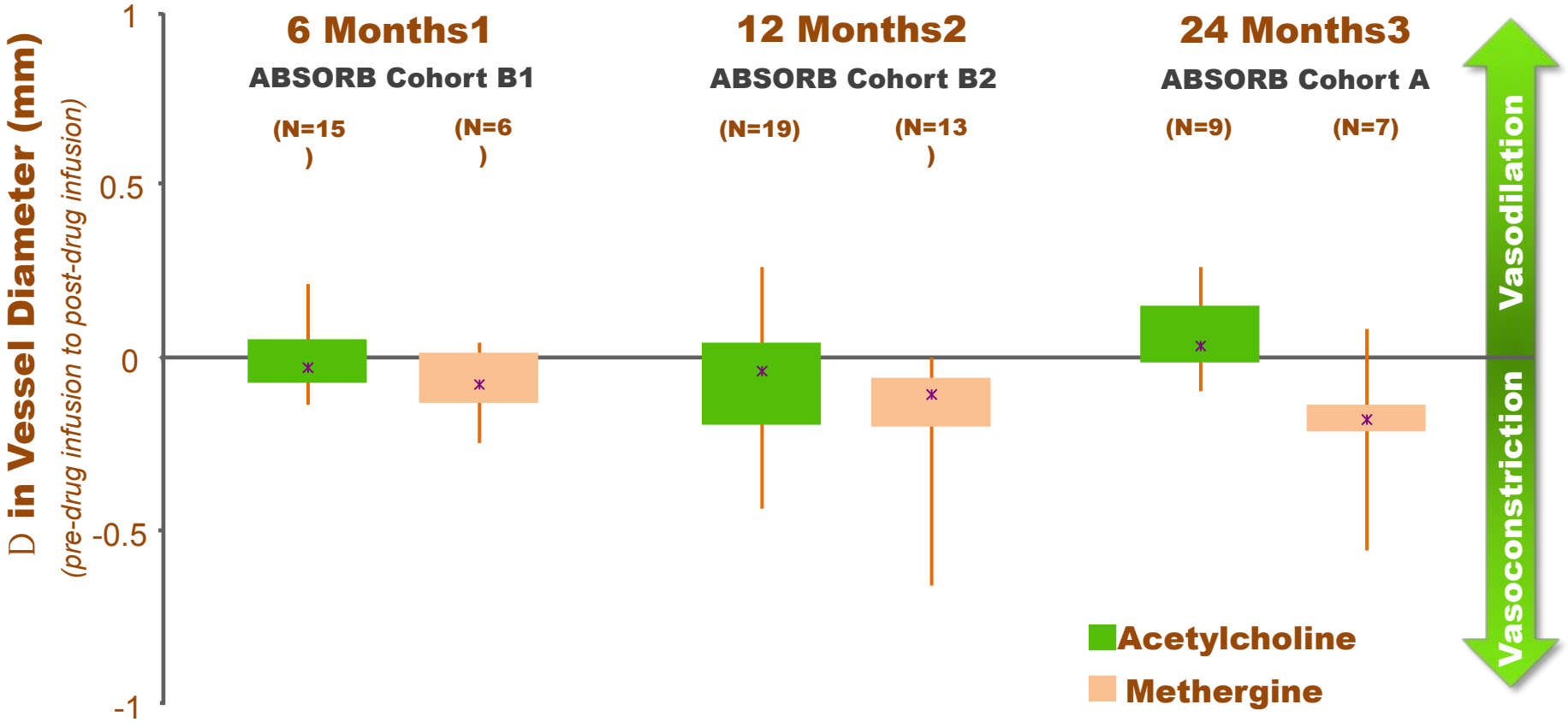


Dudek, D., ACC 2012.



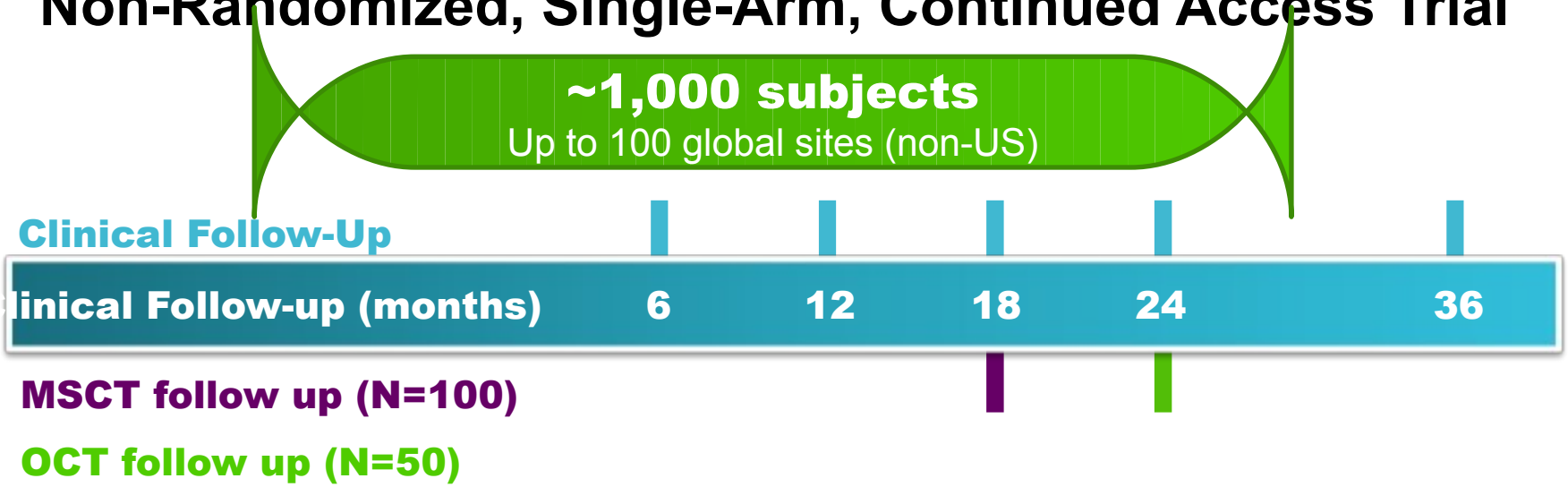
- **Very late lumen enlargement noted from 6 months to 2 years**

*Serruys, PW., TCT 2011



1. Adapted from Serruys, PW. ACC 2011 / 2. Adapted from Serruys, PW. ACC 2011 / 3. Adapted from Serruys, PW, et al. Lancet 2009; 373: 897-910.

ABSORB EXTEND
Non-Randomized, Single-Arm, Continued Access Trial



Study Objective	Continued Access trial. FPI: Jan 11, 2011
Endpoints	Typical PCI clinical endpoints
Treatment	Up to 2 *de novo* lesions in different epicardial vessels Planned overlapping allowed in lesions >22 and ≤ 28 mm
Device Sizes	Scaffold diameters: 2.5, 3.0 mm Scaffold lengths: 18, 28 mm

	N=469
Male (%)	64.6
Mean age (yrs)	61.6
Previous MI (%)	29.3
Prior Cardiac Intervention on Target Vessel (%)	4.9
Diabetes mellitus (%)	26.2
Hypercholesterolemia req. med (%)	62.0
Hypertension req. med (%)	65.9
Current smoker (%)	22.0

	NL= 502; S = 540
Location of lesion (%)	
LAD	44
RCA	26
LCX	30
Ramus	0.6
Lesion classification (%)	
A	2
B1	59
B2	35
C	4
Lesion Length (mm)	11.61
Number of Target lesions per subject (%)	
1 lesion per subject	93.0
2 lesions per subject	7.0
Planned overlap per patient (%)	7.7

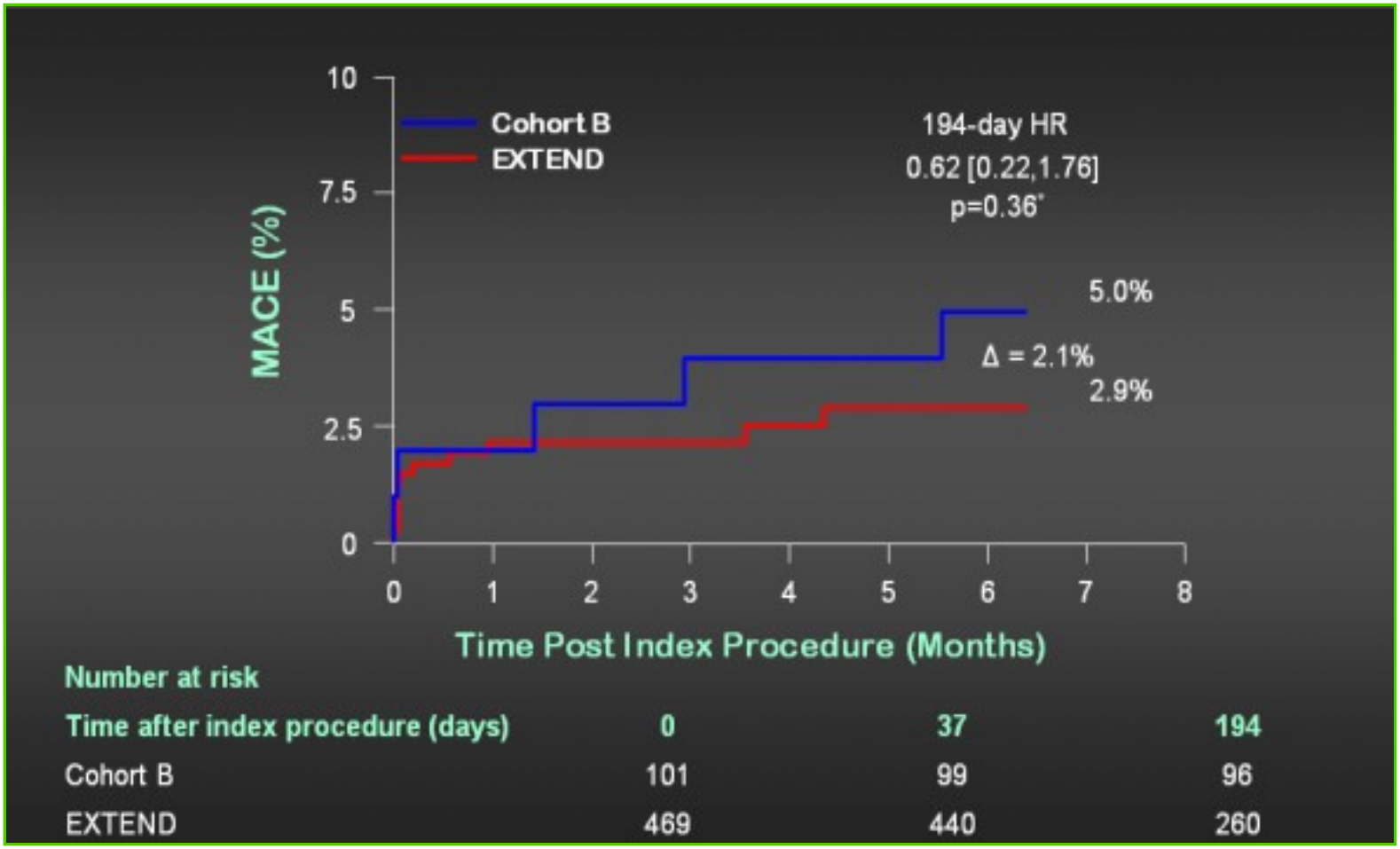
Non-Hierarchical	30 Days* n = 451	6 Months* n = 269
Cardiac Death (%)	**0 (0.0)**	**1 (0.4)****
Myocardial Infarction n (%)	**10 (2.2)**	**7(2.6)**
Q-wave MI	**3 (0.7)**	**3 (1.1)**
Non Q-wave MI	**7(1.6)**	**4 (1.5)**
Ischemia Driven TLR n (%)	**1(0.2)**	**1 (0.4)**
PCI	**1(0.2)**	**1 (0.4)**
CABG	**0**	**0**
Hierarchical MACE n (%)	**10 (2.2)**	**8 (3.0)**

*Reflects an interim snapshot with only cleaned data as of the cut-off date of Jan. 11, **A non-BVS was implanted in the target lesion 2012

MACE: cardiac death, MI, ischemia-driven TLR

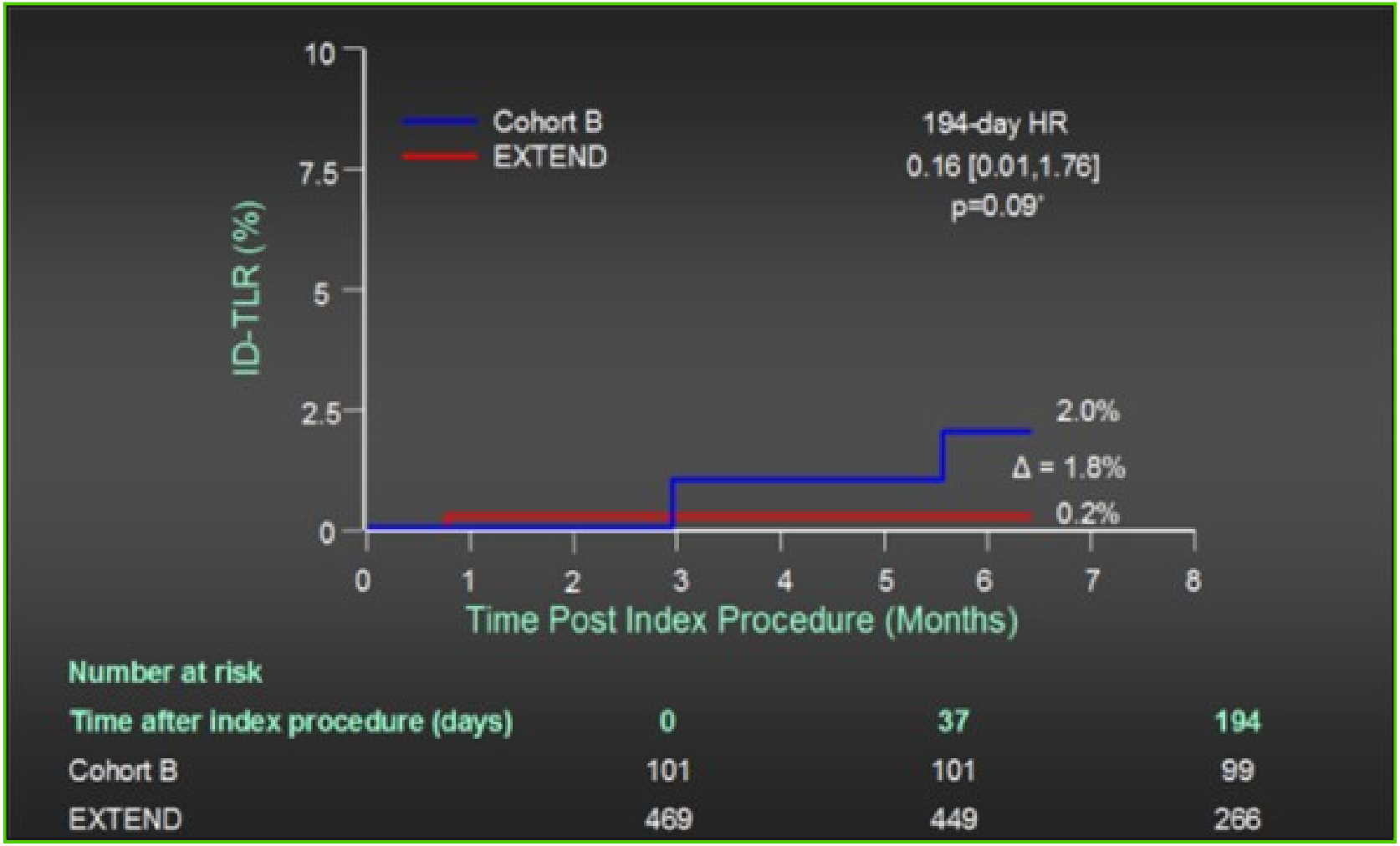
RJ van Geuns, PCR Rotterdam 2012

ABSORB Extend
Clinical Results - Intent to treat; Interim Snapshot



Note: MACE is defined as the composite of cardiac death, MI, and ischemia-driven TLR
*P-value is not from formal hypothesis testing and is displayed for descriptive purpose only.
RJ van Geuns, PCR Rotterdam 2012

ABSORB Extend
Clinical Results - Intent to treat; Interim Snapshot



*P-value is not from formal hypothesis testing and is displayed for descriptive purpose only.

RJ Van Guens, PCR Rotterdam 2012

36 subjects

(6-85sites)

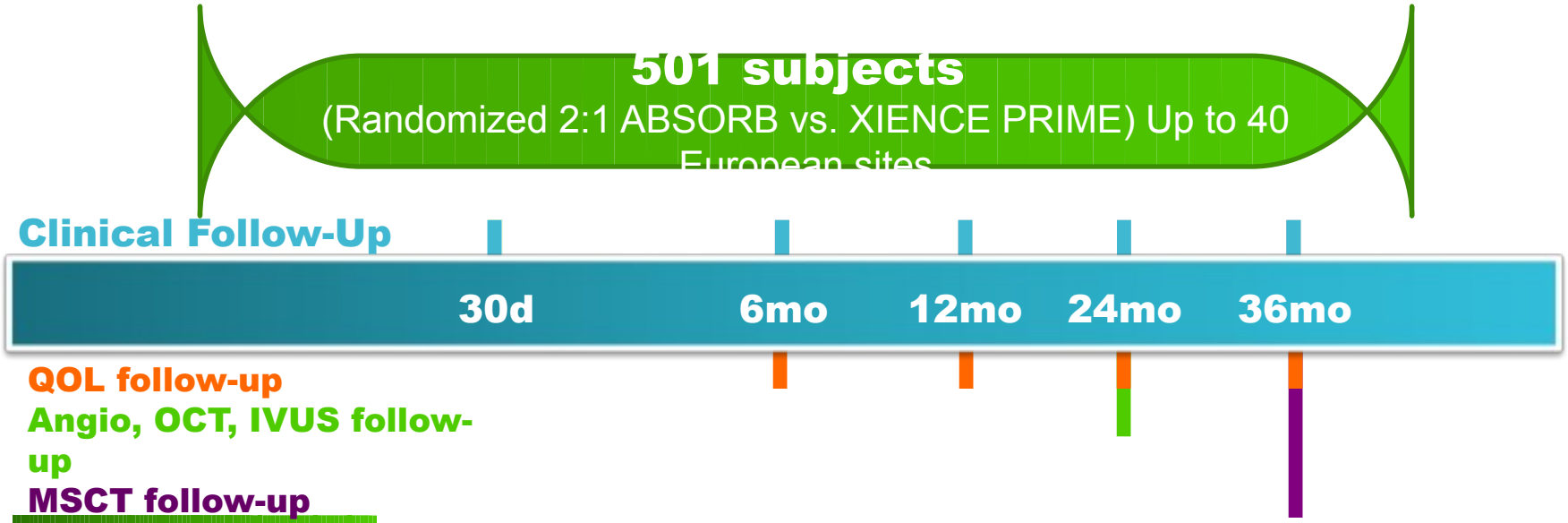
Compare target and non-intervened artery within and between individuals undergoing BVS deployment vs XIENCE V/ XIENCE PRIME deployment

ABSORB Physiology

N = 36 2:1 randomization

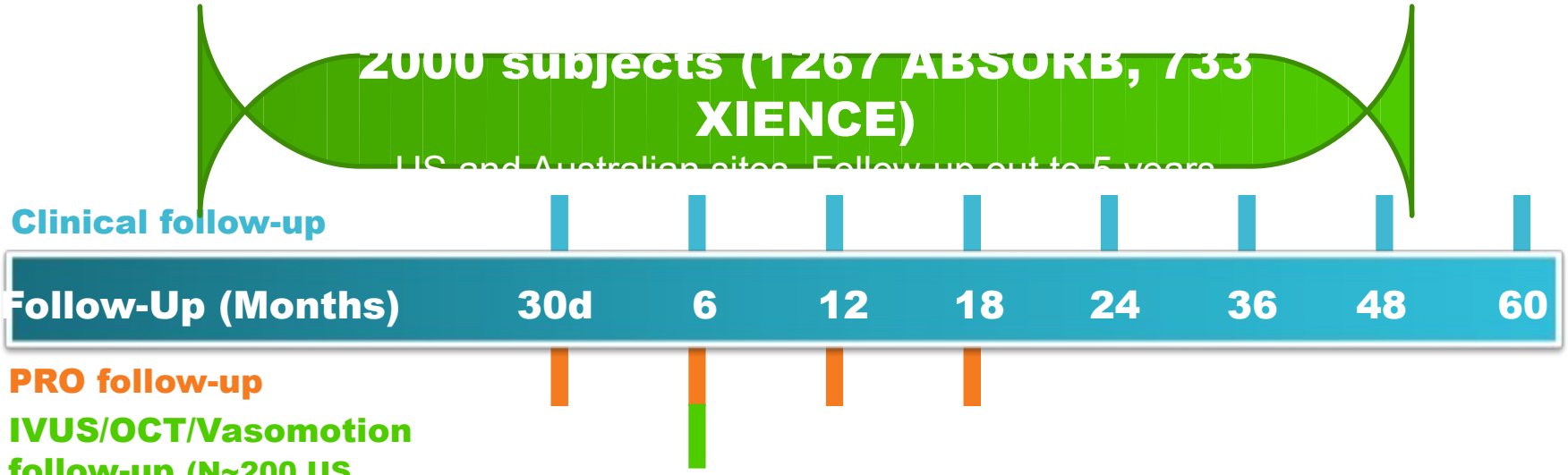
QCA, IVUS, OCT, IVUS VH

Study Objective	To appropriately design and power a randomized clinical trial which will be used to design and determine the appropriate endpoints for the larger US IDE trial
Primary Outcome	FMD induced by physiological stimuli, intracoronary infusion of acetylcholine
Secondary Outcomes	Coronary artery cross-sectional compliance and distensability Fractional Flow Reserve (FFR)/ Coronary Flow Reserve (CFR)



Study Objective	Randomized against XIENCE PRIME control. FPI 28-Nov-2011
Co-primary Endpoints	• Vasomotion assessed by change in Mean Lumen Diameter between pre- and post-nitrate at 2 years (superiority) • Minimum Lumen Diameter (MLD) at 2 years post nitrate minus MLD post procedure post nitrate (non-inferiority, reflex to superiority
Treatment	Up to 2 *de novo* lesions in different epicardial vessels Planned overlapping allowed in lesions ≤ 48 mm
Device Sizes	Scaffold diameters: 2.5, 3.0 mm Scaffold lengths: 18, 28 mm

Number of patients on Aug 6th, 2012.



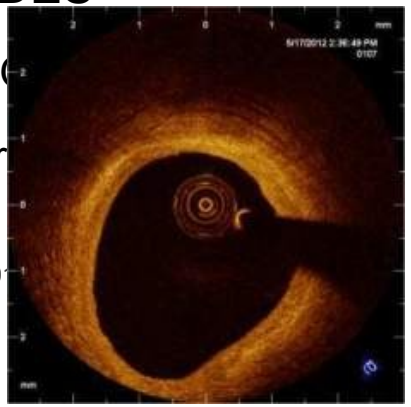
Study Objective	Seek US approval of ABSORB BVS
Primary Endpoint	Clinically indicated target lesion failure at 1-year (composite of cardiac death, target vessel MI or clinically indicated TLR)
Treatment	Up to two *de novo* lesions in different epicardial vessels. No planned overlap allowed
Device Sizes	Scaffold diameters: 2.5, 3.0, 3.5 mm Scaffold lengths: 12, 18, 28 mm

ABSORB
Summary

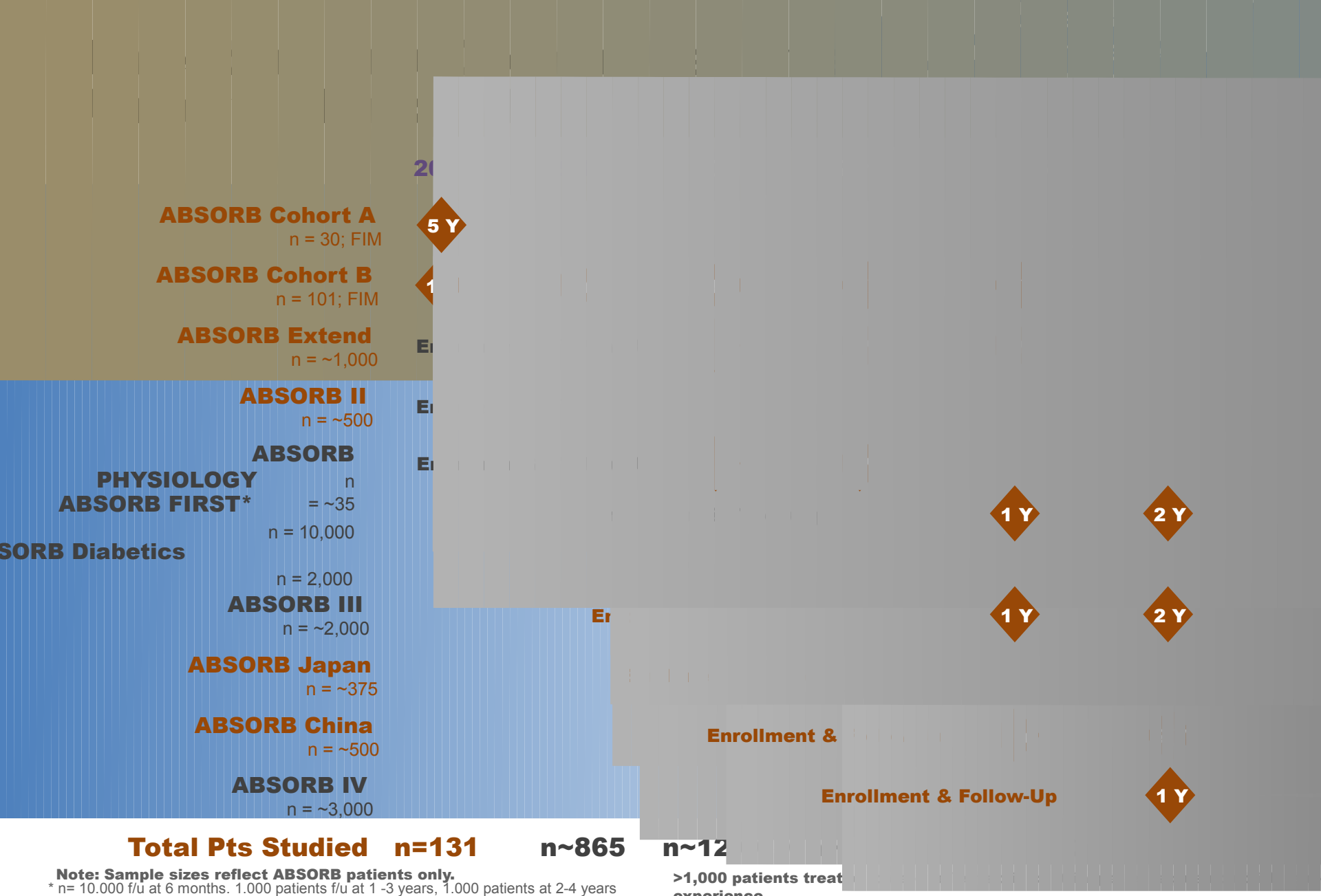
ABSORB
Summary

- Current clinical Absorb data have shown:
  - Revascularization comparable to best in class DES, with late loss of 0.19mm and 0.27mm at 6 and 24 months respectively (ABSORB cohort B)1
  - First signs of restoration by showing
    - Possible restoration of vasomotion function

      (19/33 pts had increasing MLD post Ach – cohort B)2
    - Possible late lumen gain (0.49mm increase in MLD between 6 and 24 months – cohort B)1
  - Comparable safety and efficacy outcomes to best in class DES
    - No ST in ABSORB A (5yr fu)1 and B (2yr fu)3; 0.4% ST in ABS
    - Comparable MACE rates (3.4% at 5 yr (cohort A)1, 9.0% at 2yr 2.9% at 6 mo – Extend4)
- Resorption of Absorb has been shown on OCT, the final golden tube at 5 years*



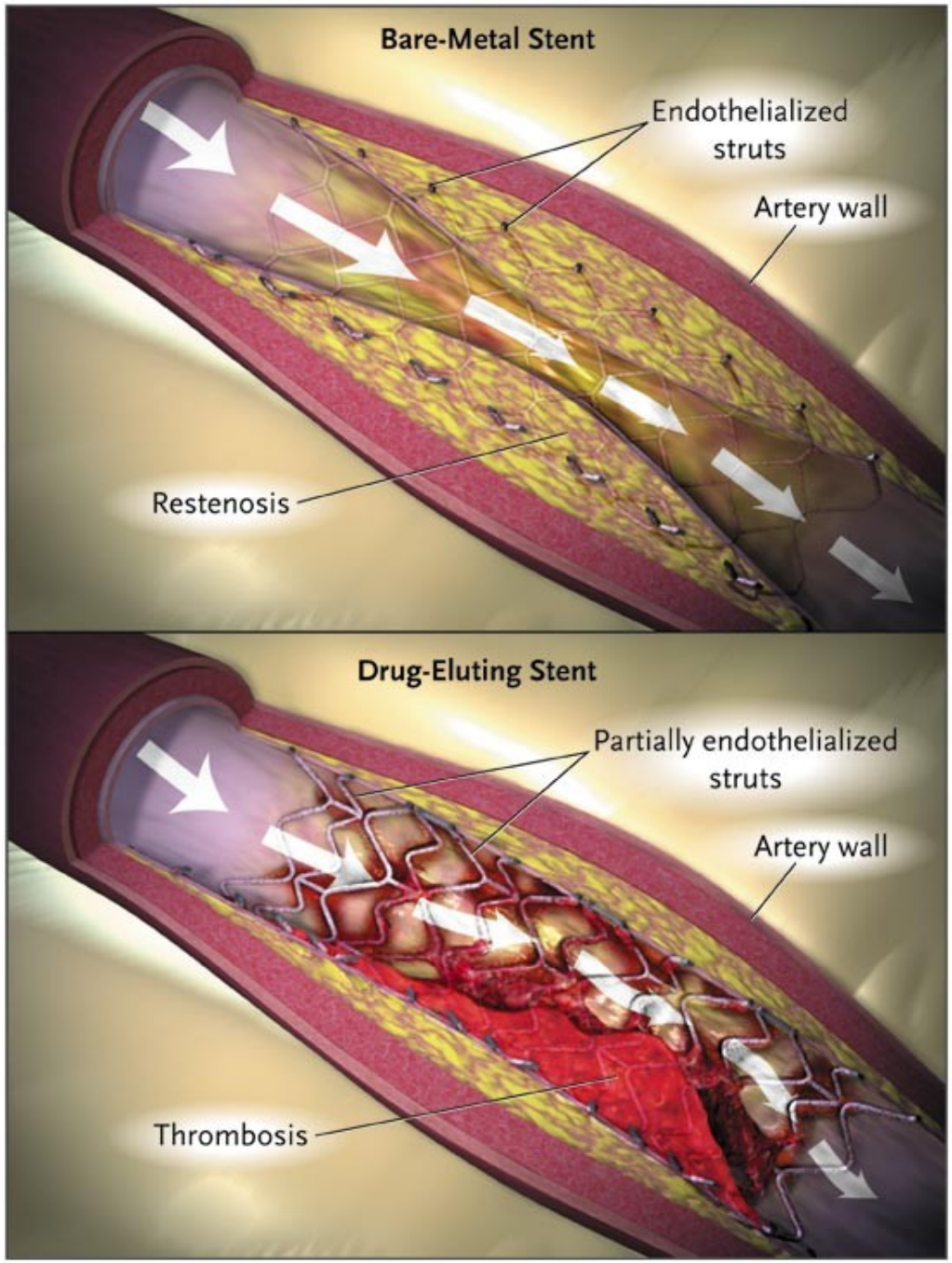
1Serruys, PW., TCT 2011; 2 J. Ormiston, TCT 2011; 3 D. Dudek, ACC 2012; 4 RJ van Geuns, EuroPCR BVS focus Rotterdam 201
* Images courtesy of Thoraxcenter, Erasmus MC, Rotterdam, The Netherlands, ABSORB A 5 yr



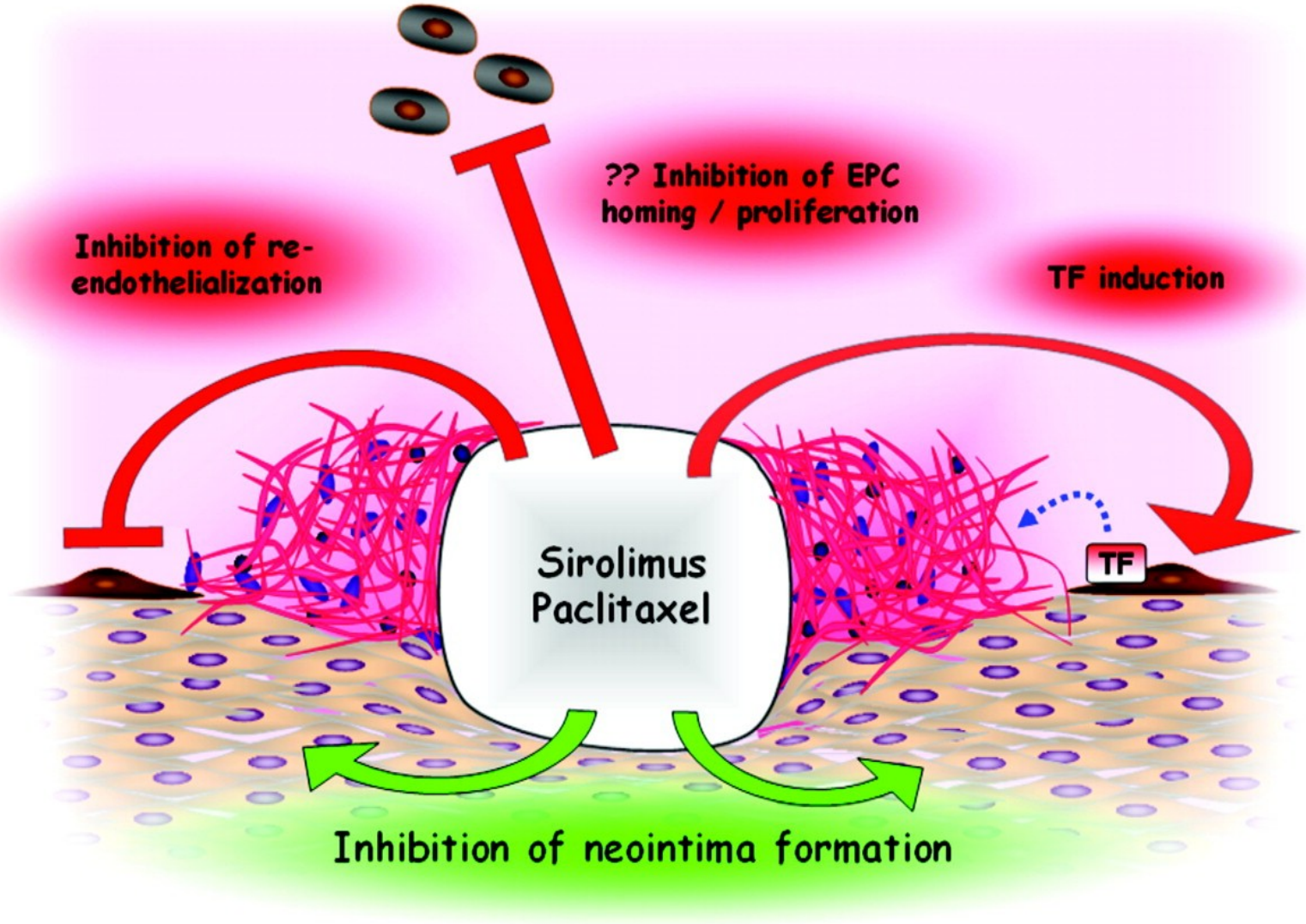
Note: Sample sizes reflect ABSORB patients only.

* n= 10.000 f/u at 6 months. 1.000 patients f/u at 1 -3 years, 1.000 patients at 2-4 years

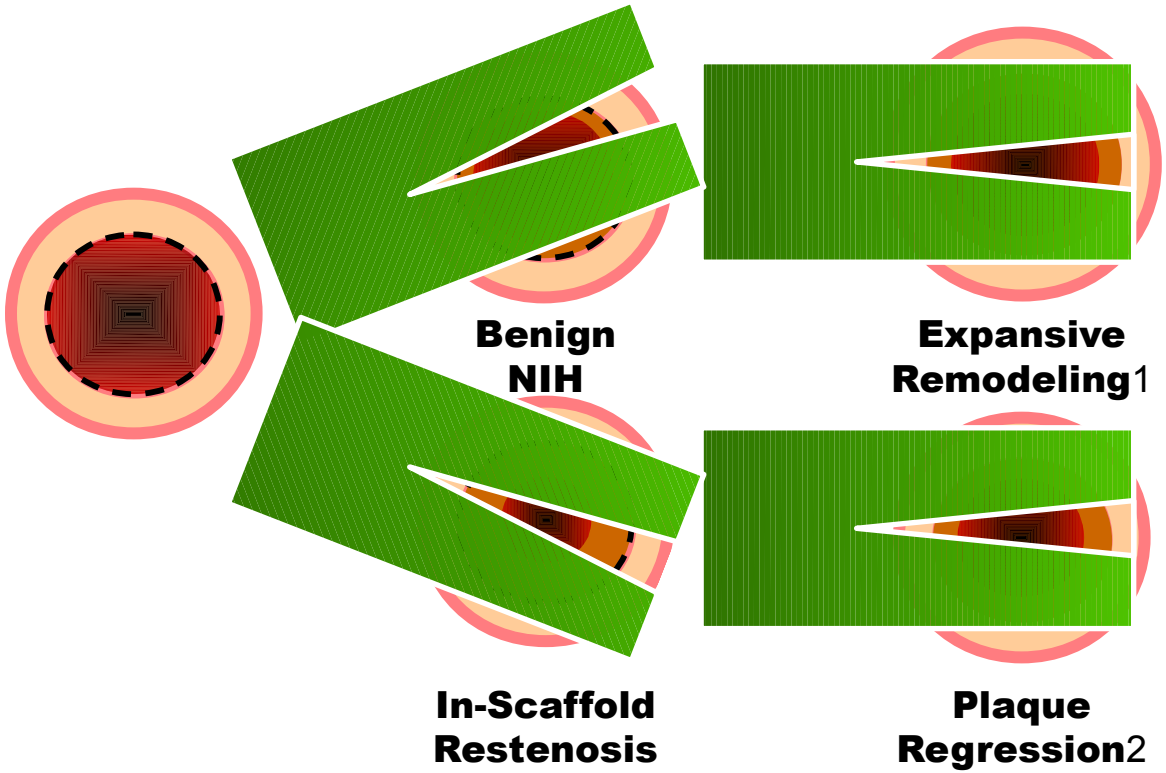
>1,000 patients treat
experience.



Curfman et al., NEJM 2007



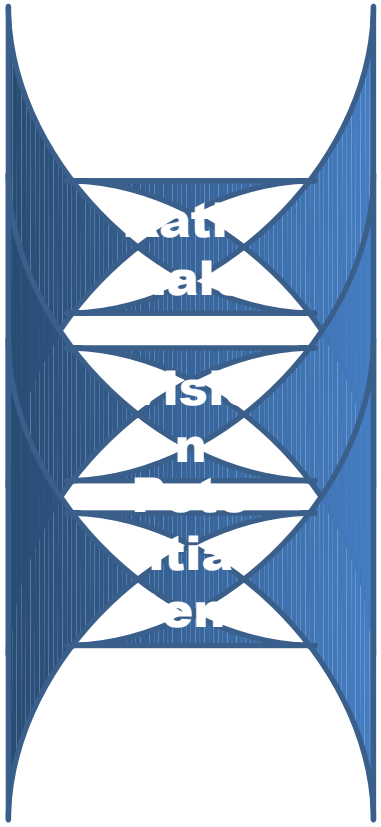
Lüscher et al, Circulation 2007



Late Lumen Enlargement

Since struts disappear, issues related to very late persistent strut malapposition and chronically uncovered struts become irrelevant

1Serruys, PW, ACC 2011 / 2Serruys, PW, et al. *Lancet*. 2009; 373: 897-910.
*Small platinum markers at scaffold edges remain for fluoroscopic landmarking.
NIH: NeoIntimal Hyperplasia



Vessel scaffolding is only needed transiently*

Improve Long Term Outcomes for Patients by Leaving No Scaffold Behind1

- **Restore the vessel to a more natural state, capable of natural vascular function**
- **Eliminate chronic sources of vessel irritation and inflammation**
- **Vessels remain free for future treatment options**
- **Reduce the need for prolonged DAPT**2
- **Allows for use of non-invasive imaging techniques (CCTA)**
- **Improve patient quality of life**

*Serruys PW, et al., Circulation 1988; 77: 361. Serial study suggesting vessels stabilize 3-4 months following PTCA.
1 – Small platinum markers at scaffold edges remain for fluoroscopic landmarking. 2. The Absorb IFU indicates DAPT for a minimum of 6 months.

Design Goals for a Bioresorbable Vascular Scaffold

Absorb BVS: 4th Revolution in PCI

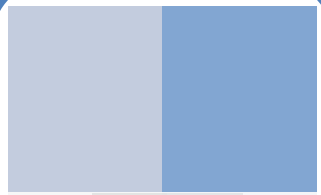
1977

Balloon Angioplasty (PTCA)

1988

Bare Metal Stents (BMS)

2001



Coronary Drug Eluting Stents (DES)

Today

Absorb Bioresorbable Vascular Scaffold (BVS)

Acute *Post*

Histology images are from porcine animal models.

PCI Historical Perspective

197 7 Andreas Gruntzig performs the first PTCA in Zurich, Switzerland

198 8 Julio Palmaz and Richard Schatz develop a stainless steel stent for coronary applications

2001 - 2003 Drug eluting stents are introduced to the European and U.S. markets

Balloon Angioplasty (PTCA)

Bare Metal Stents (BMS)

Coronary Drug Eluting Stents (DES)

Researche… early c… bic… device… funct… temporary… the coron…

J… i…

Abbott Vascul… establishes t… BVS developme… tea…

…scular …patients in …he first …n clinical …g a fully …ble drug …affold

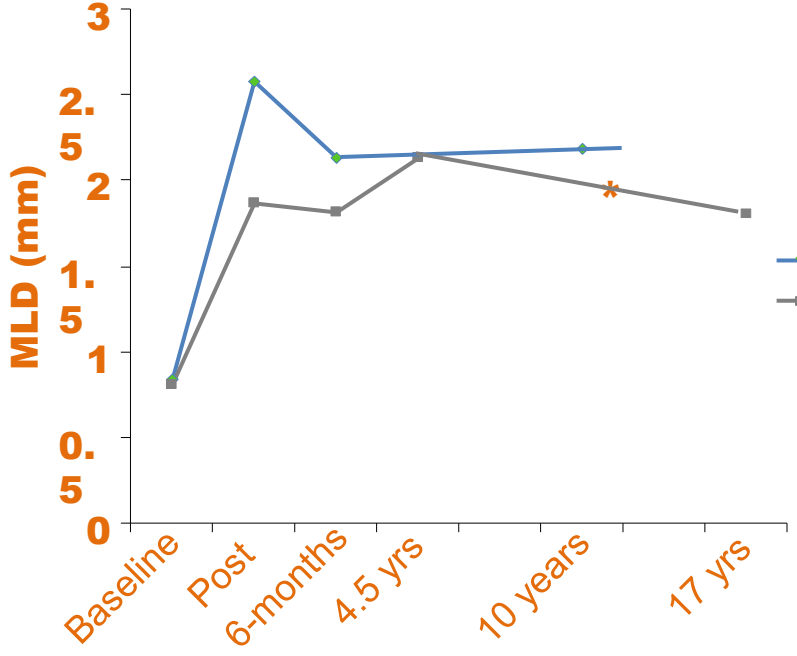
3 9 3 6

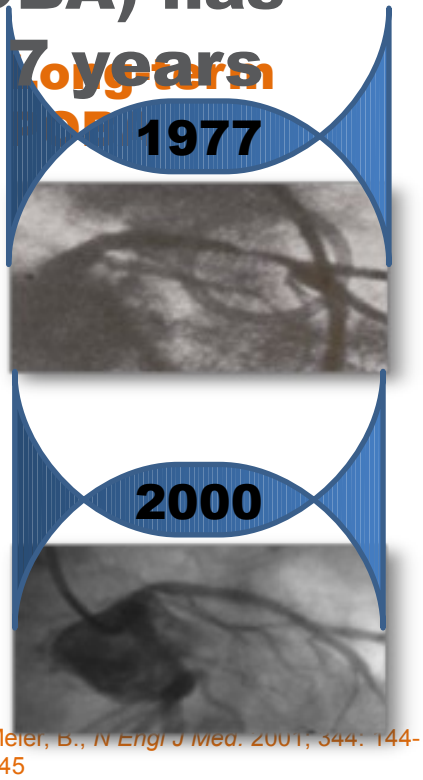
- The idea for developing a temporary coronary scaffold began in the 1980s

Interventional cardiology treatment: a historical unmet need

- **Success of early PCI treatment (POBA) has been demonstrated for as long as 17 years**

Serial Angiography Studies



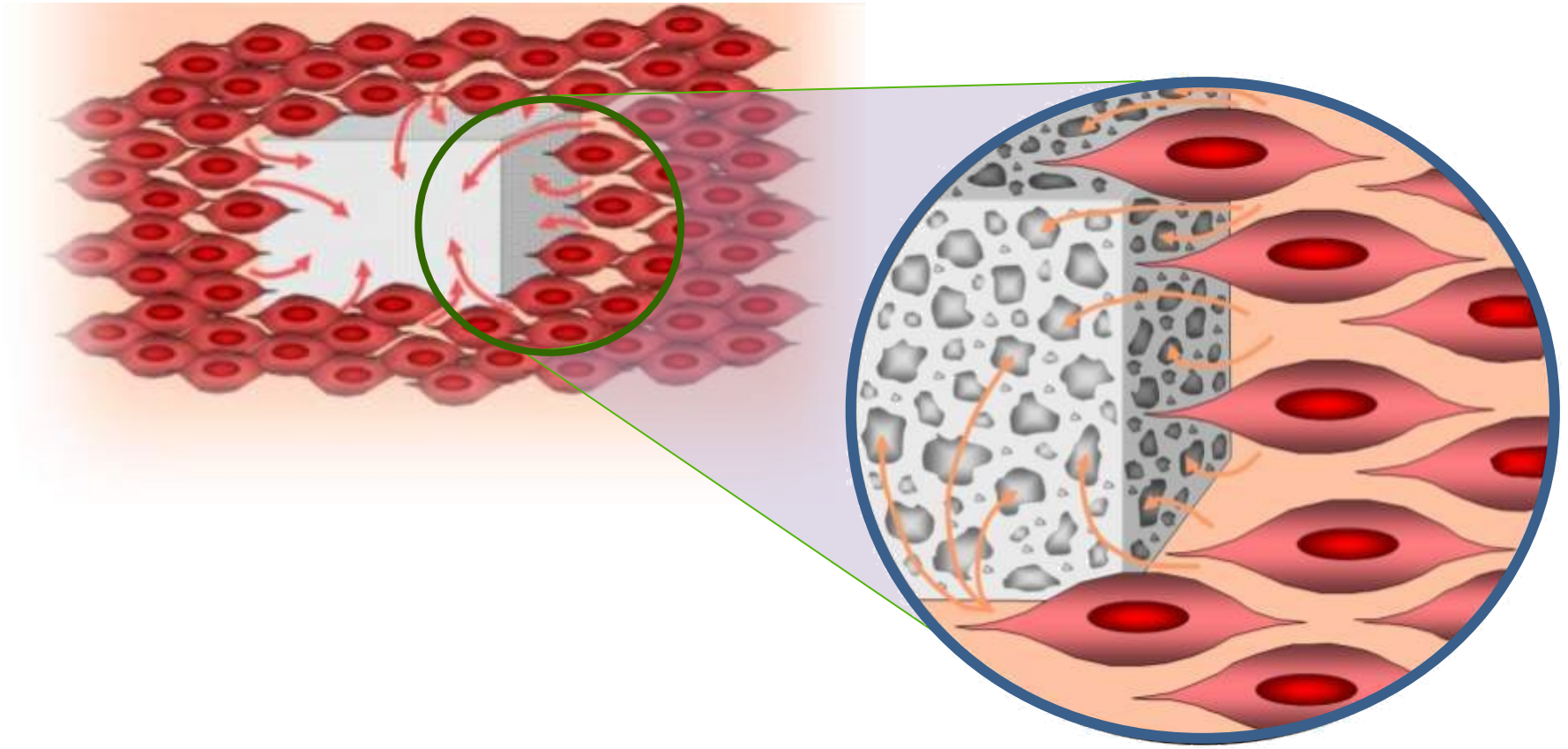


Meier, B., *N Engl J Med*. 2001; 344: 144-145

- **POBA is limited by acute recoil, sub-acute closure, and dissections**

Guiteras-Val, P., et al. *Am J Cardiol*. 1999;83:868-874. / Hatrick, R., et al. *EuroIntervention*. 2009;5:121-126.

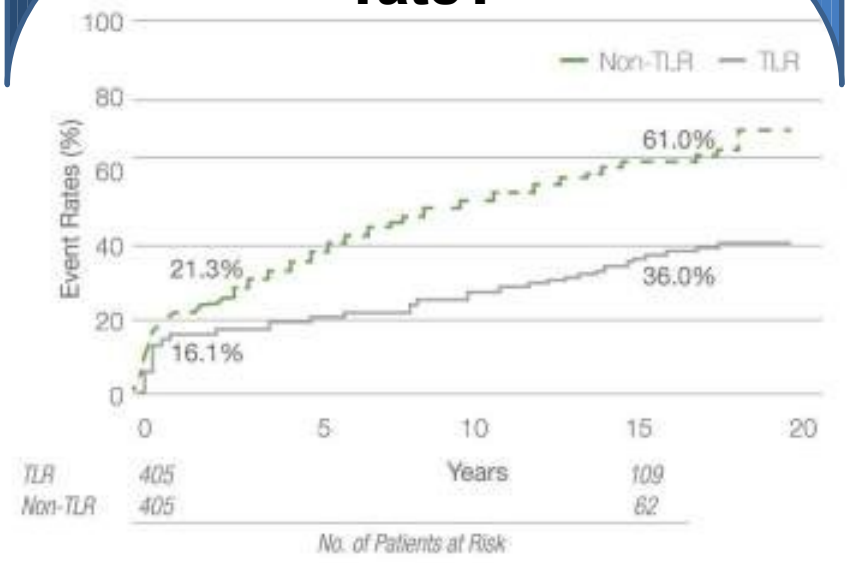
The Absorb BVS scaffold is replaced by functional cellular Matrix



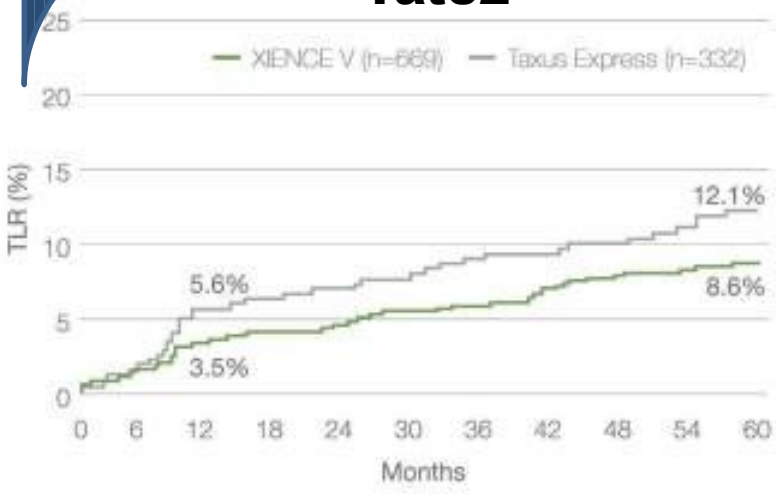
Interventional cardiology treatment: a historical unmet need

- Current treatment options have failed to halt the progressive nature of CAD

Long-term BMS event rate1



Long-term DES event rate2

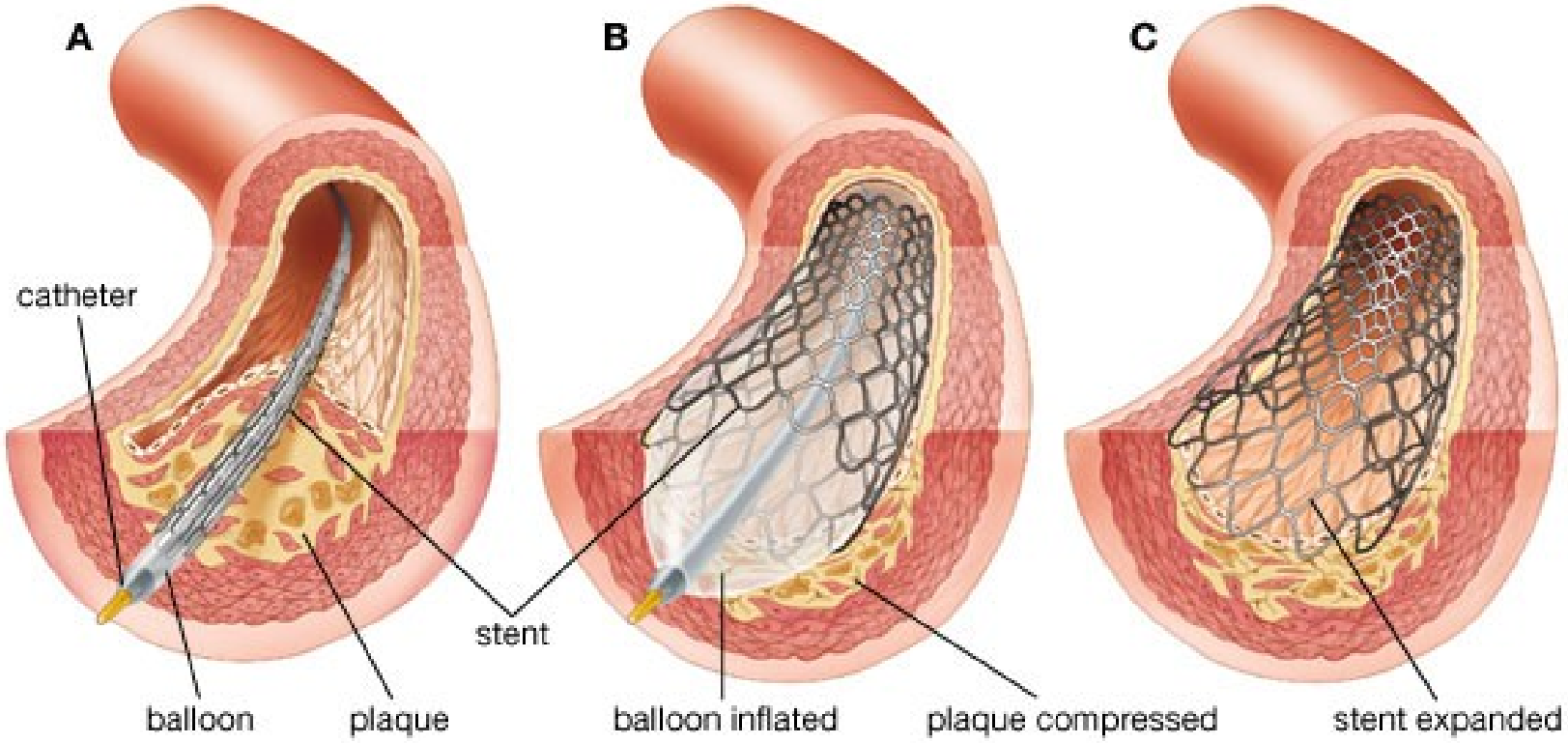


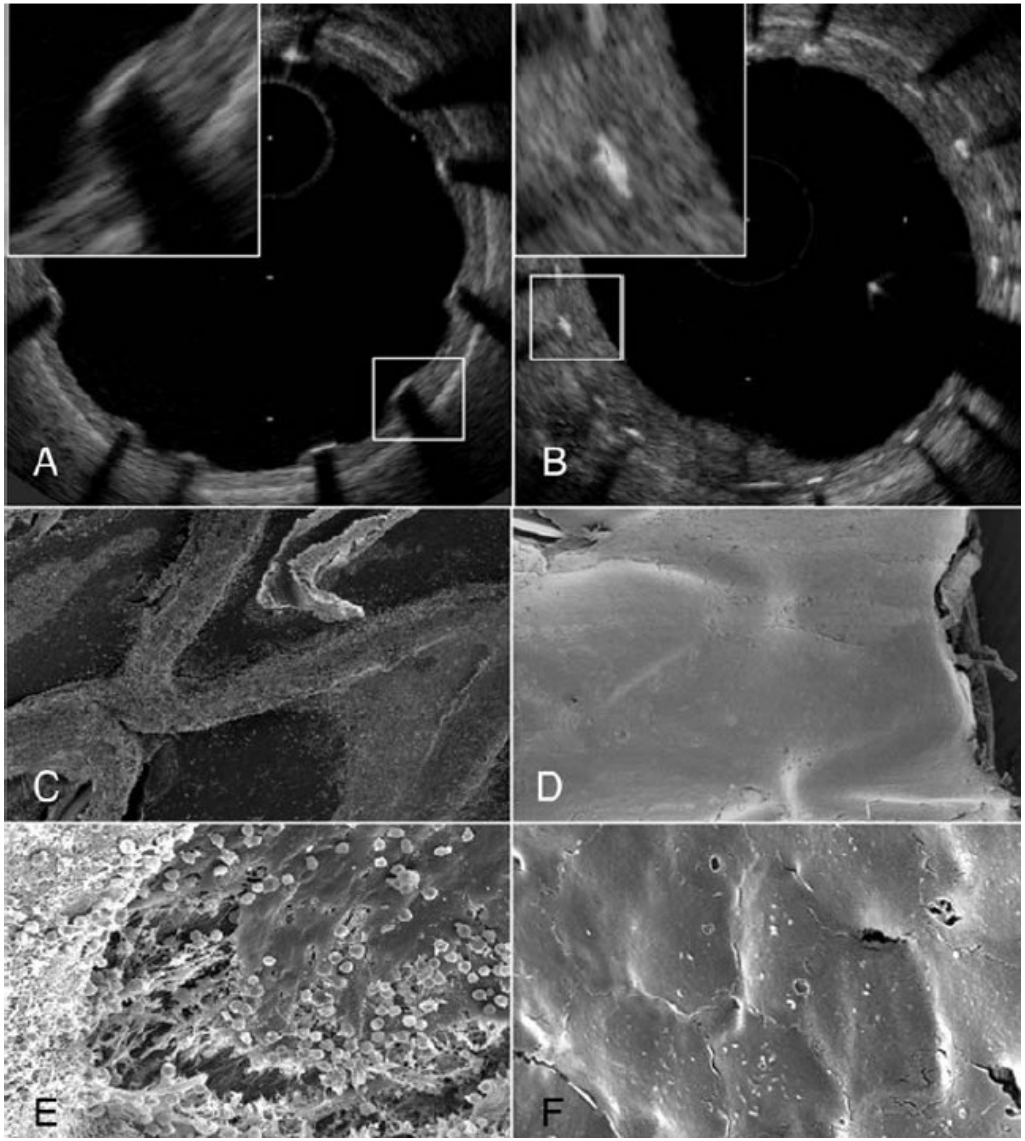
1. Yamaji K, et al. Very long-term (15 to 20 years) clinical and angiographic outcome after coronary bare metal stent implantation. Circ Cardiovasc Interv 2010;3(5):468-75.
2. SPIRIT III: Ischemia-driven TLR through 5 years. Stone GW, TCT 2011.

Table 3. Efficacy and Safety of Drug-Eluting Stents, Bare-Metal Stents, and Coronary-Artery Bypass Grafting (CABG), According to Clinical Indication.*

Outcome and Intervention	Stable Coronary Artery Disease	Acute Myocardial Infarction	Diabetes	Multivessel Disease	Left Main Coronary Artery Disease
Restenosis					
Implantation of bare-metal stent	+	+	+	+	+
Implantation of drug-eluting stent					
Early-generation	++	++	++	++	++
New-generation	+++	+++	++	++ [+]	++ [+]
CABG	+++	–	+++	+++	+++
Cardiac death, myocardial infarction, or stent thrombosis					
Implantation of bare-metal stent	+	+	+	+	+
Implantation of drug-eluting stent					
Early-generation	+	+/–	+	+	+
New-generation	+ [+]	+ [+]	+	+ [+]	++ [+]
CABG	+	–	++	++	++

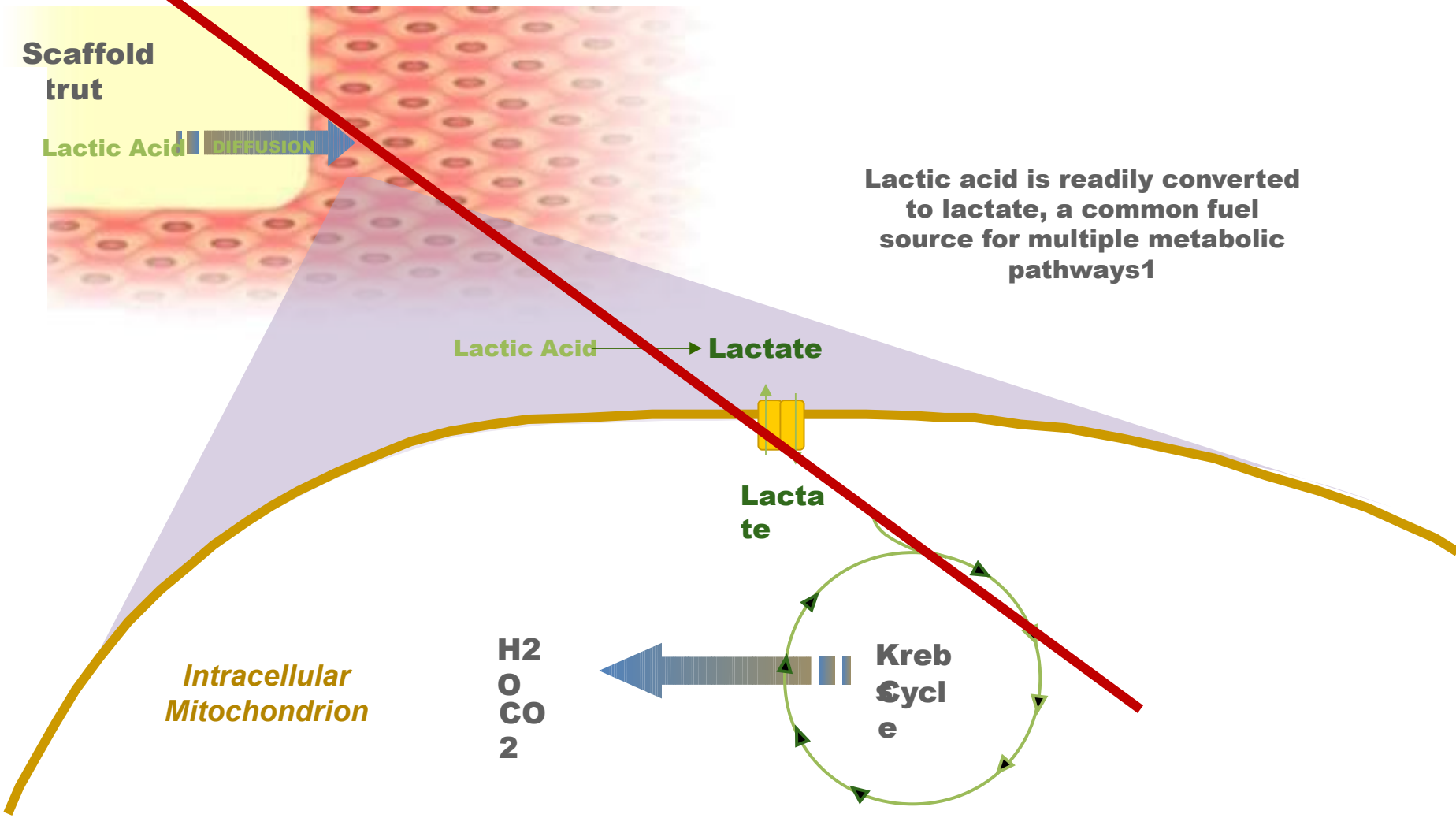
Stefanini G. et al., NEJM 2013


A
B
C
catheter
stent
balloon
plaque
balloon inflated
plaque compressed
stent expanded



Corti R. et al., EHJ 2012

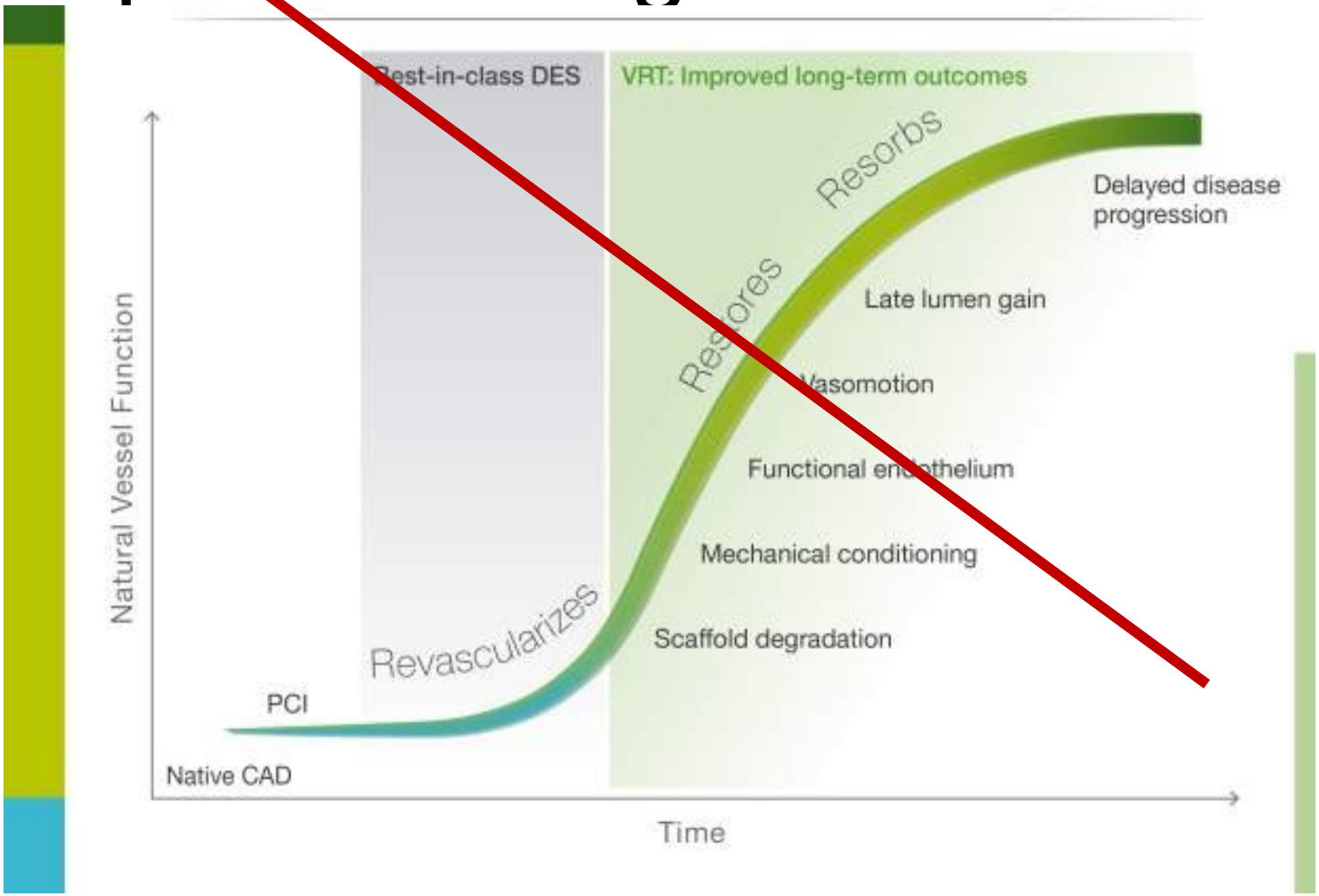
Absorb is Resorbed by a Natural Process



1Philp A., et al., J. Exp. Biol. 2005; 208: 4561

ev weglassen

Goal of VRT: Improved Long-term Outcomes



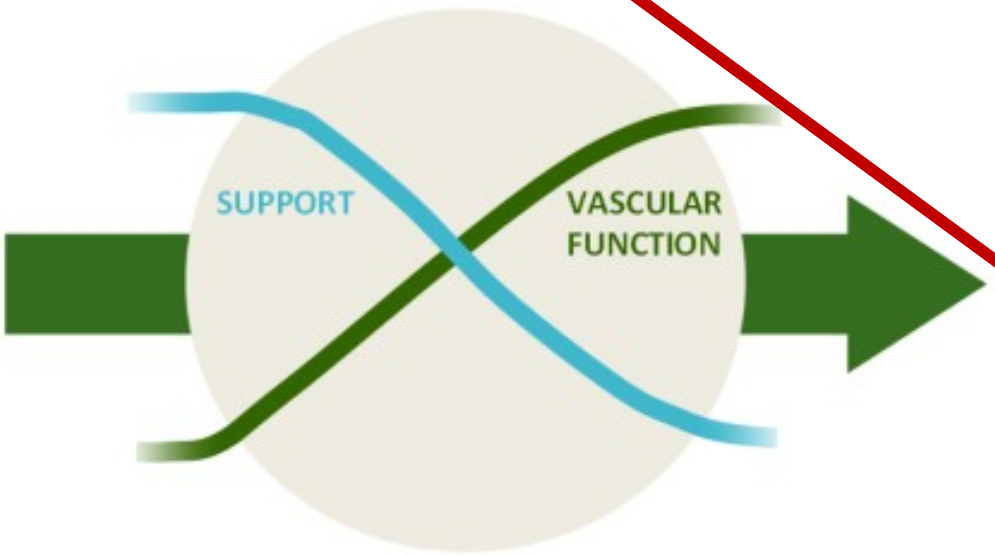
Serruys PW. et al. Eur Heart J. 2012;331(1):16-25

Absorb BVS Defines a New Paradigm: Vascular Reparative Therapy (VRT)

ev weglassen

- **Mechanical Conditioning**

Gradual disappearance of supportive structure



over ability respond to

Shear stress, pulsatility & cyclic str

Tissue adaptation*

Structure and functionality*

- **Tissues in the body require physiologic stress to maintain normal structure and function**

Serruys PW, et al. Eur Heart J. 2012;33(1):16-25. Data and images on file at Abbott Vascular. Histology images are from porcine animal models.

VRT represents a paradigm shift in interventional cardiology

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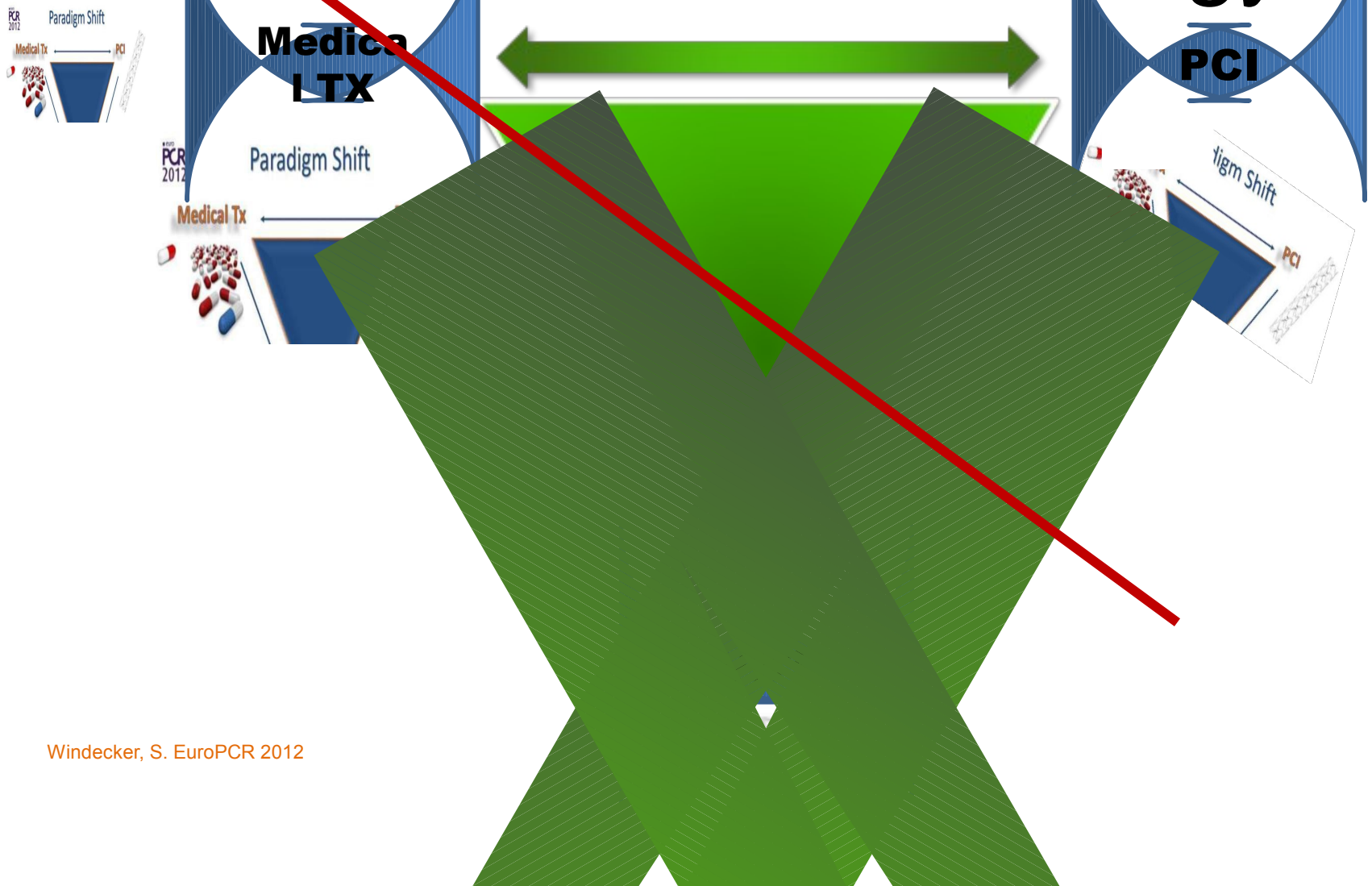
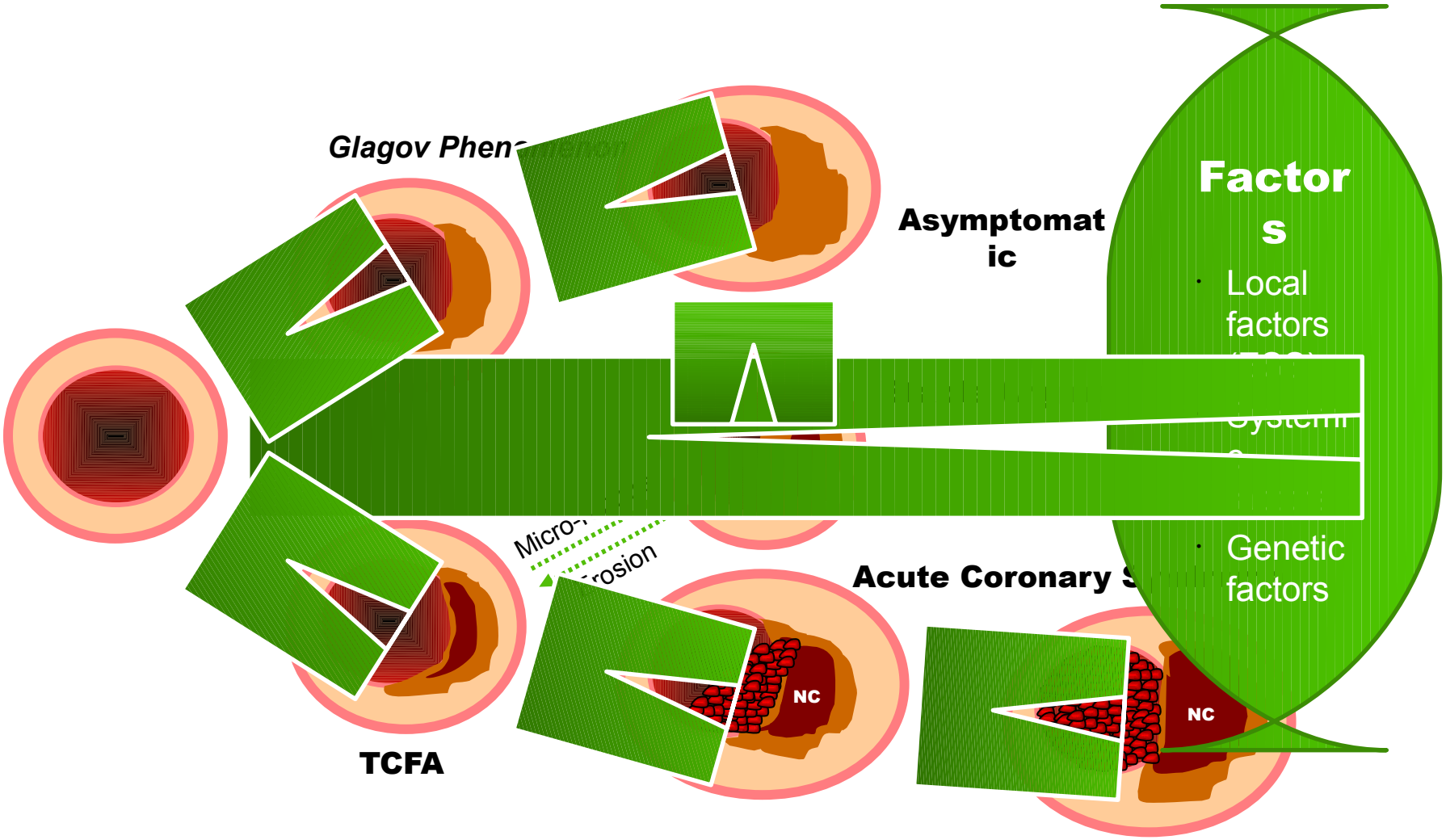
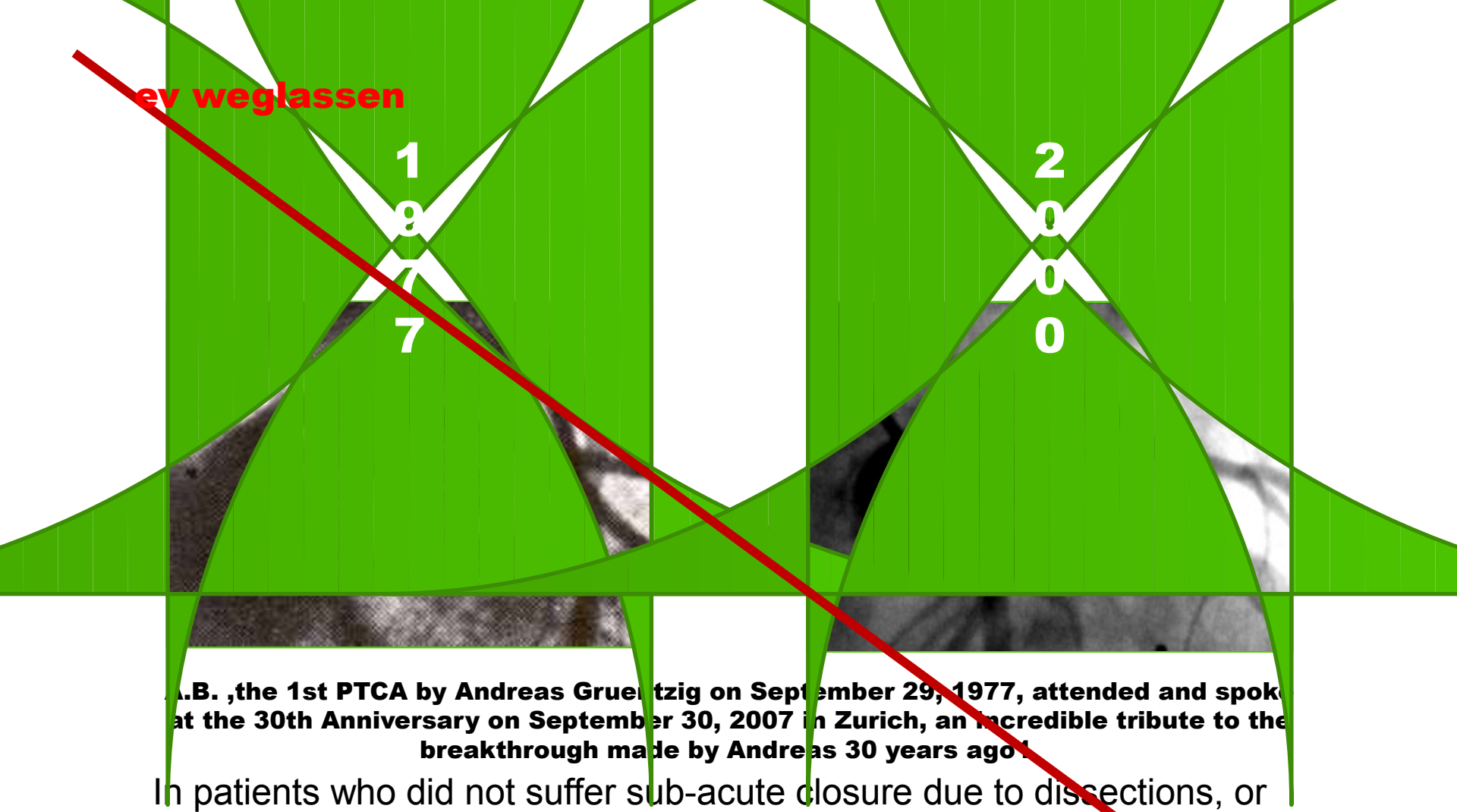


Windecker, S. EuroPCR 2012



Chatzizisis, Y. et.al. *J Am Coll Cardiol*. 2007; 49:2379-2393.
TCFA: Thin-Cap FibroAtheroma; ESS: Endothelial Shear Stress
NC: Necrotic Core



A.B. ,the 1st PTCA by Andreas Gruentzig on September 29, 1977, attended and spoke at the 30th Anniversary on September 30, 2007 in Zurich, an incredible tribute to the breakthrough made by Andreas 30 years ago[1]

In patients who did not suffer sub-acute closure due to dissections, or restenosis due to negative remodeling in the first few months, long term results following balloon angioplasty were very encouraging and durable, with loss in MLD not seen until
17 years post procedure2

1. Meier, B., *N Engl J Med.* 2001; 344: 144-145.
2. Hatrick, R., et al. *EuroIntervention*. 2009;5:121-126.

ev weglassen

* uncovered struts1

layed Healing Stent Thrombosis?

NIH

Atheroma

Ste t

ombosis?

Reste sis

e Acquired Malapposition Stent Thrombosis?

1. Virmani, R. CIT 2010
NIH: NeoIntimal Hyperplasia

Absorb BVS: 4th Revolution in PCI

1977

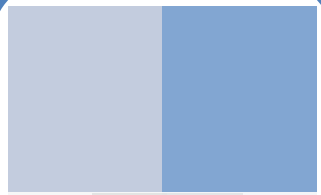
1

Balloon Angioplasty (PTCA)

1988

Bare Metal Stents (BMS)

2001



Coronary Drug Eluting Stents (DES)

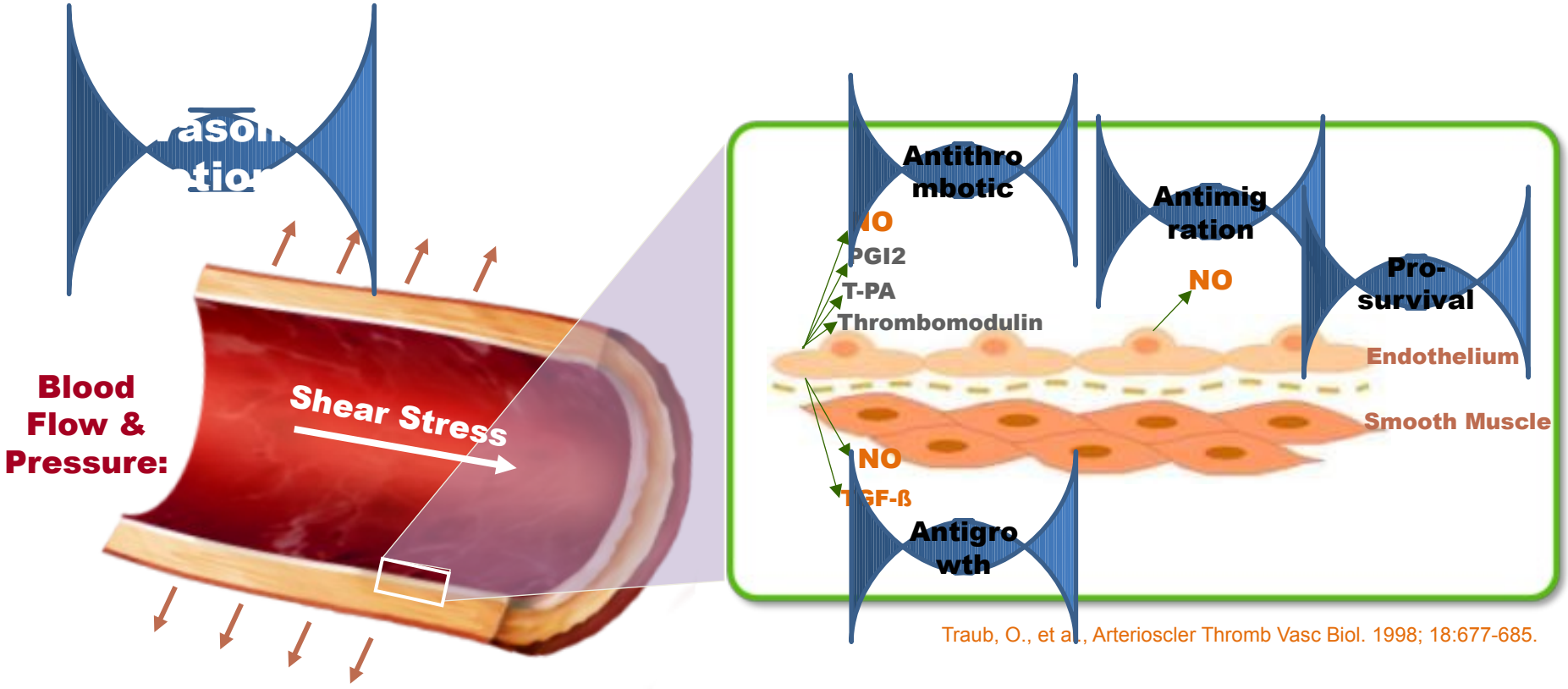
Today

Absorb Bioresorbable Vascular Scaffold (BVS)

Acute *Post*

Histology images are from porcine animal models.

Functional Endothelial Cells Protect Against Thrombosis and Disease Progression



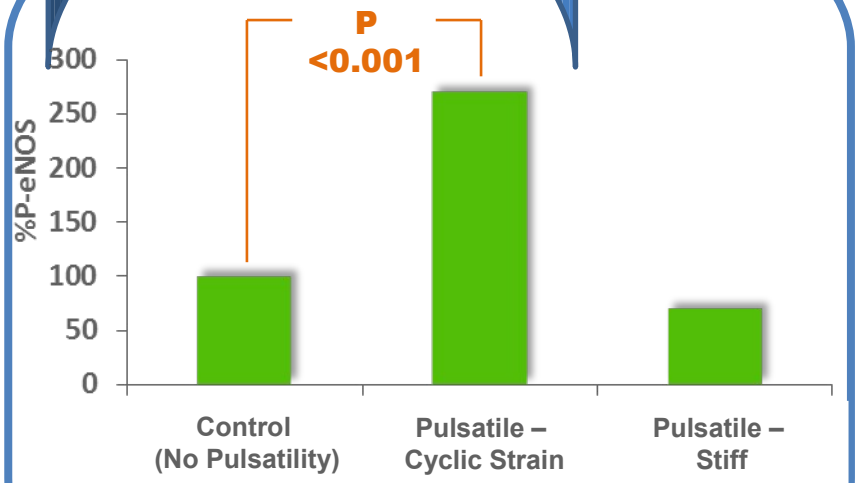
Traub, O., et al., Arterioscler Thromb Vasc Biol. 1998; 18:677-685.

Stretching of the vessel (cyclic strain) due to pulsatile flow

Chien, S. Am J Physiol Heart Circ Physiol. 2007; 292: H1209-H1224.

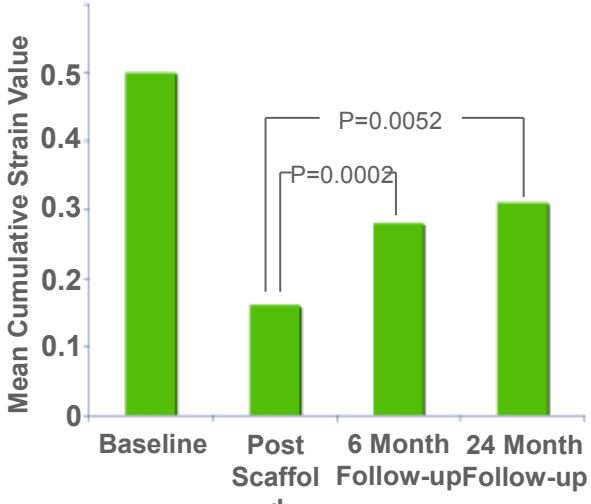
Pulsatility and Cyclic Strain Provide Pr[illegible]

Importance of Pulsatility



Nitric oxide production is significantly increased in compliant vessels exposed to pulsatile flow due to cyclic strain[1,2]

ABSORB Cohort A Palpography



Restored cyclic strain in vessels treated with Absorb as the scaffold degrades and no longer constrains the vessel[4,5]

[illegible]cyclic stra[illegible]
[illegible]n and the protection

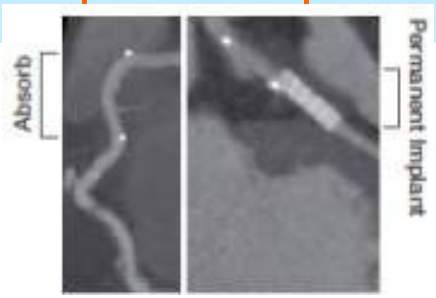
1Awolesi, M. et al. *J Clin Invest.* 1995;96:1449-1454. / 2Peng, X. et al. *Hypertension.* 2003;41:378-381.
3Balligand, J-L. et al. *Physiol Rev.* 2009; 89:481-534. / 4Garcia-Garcia H.M., *et.al*., *EuroInterv.* 2008; **4**: 443. / 5 Serruys, PW et al. Lancet. 2009; 373: 897-910.

Value of Non-Invasive Imaging Cost & Time to Diagnosis from a Health Economic Perspective

Study	n	SOC (based on charges)	CCTA (MSCT) (based on charges)	Difference	P-value
May et al. AJR 2009	**53**	**$7,597**	**$6,153**	**$1,444**	**P<0.001**
	Time to discharge	**25.4 hours**	**14.3 hours**	**11.1 hours**	**P<0.001**
Chinnaiyan et al. AHA 2009	**749**	**$3,458**	**$2,137**	**$1,321**	**P<0.001**
	Time to diagnosis	**6.2 hours**	**2.9 hours**	**3.3 hours**	**P<0.0001**
Goldstein et al. JACC 2007	**197**	**$1,872**	**$1,586**	**$286**	**P<0.001**
	Time to diagnosis	**15.0 hours**	**3.4 hours**	**11.6 hours**	**P<0.001**

For these studies, standard of care defined as serial ECGs, cardiac biomarkers, same day nuclear stress test (does not include PCI)

- Overall cost lowered for MSCT primarily due to decreased length of stay

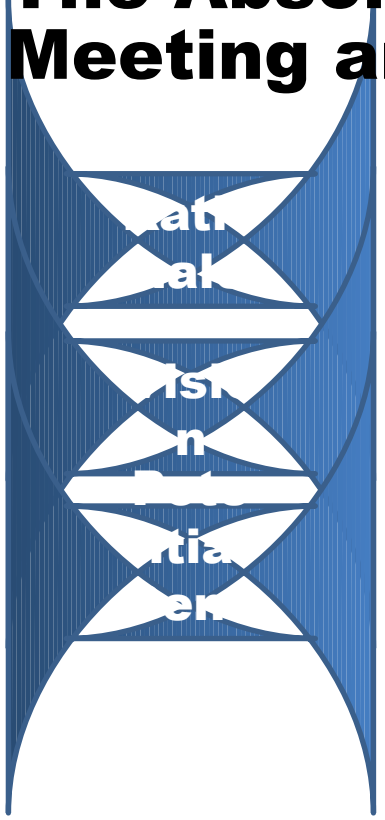


CCTA: Absorb vs. Permanent Implant

Chinnaiyan KM, et al. Cardiol Clin. 2009 Nov;27(4):587-96.
Goldstein et al. J Am Coll Cardiol 2007;49:863–71.
May et al. AJR 2009; 193:150–154.
CMS 2012 Payment Rates – www.cms.gov

CCTA images courtesy of K Nieman, Erasmus Medical Center, Rotterdam, Netherlands.

The Absorb BVS System
Meeting an unmet clinical need?



Vessel scaffolding is only needed transiently*

Improve Long Term Outcomes for Patients by Leaving No Scaffold Behind1

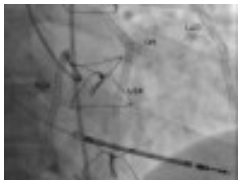
- **Restore the vessel to a more natural state, capable of natural vascular function**
- **Eliminate chronic sources of vessel irritation and inflammation**
- **Vessels remain free for future treatment options**
- **Reduce the need for prolonged DAPT**2
- **Allows for use of non-invasive imaging techniques (CCTA)**
- **Improve patient quality of life**

*Serruys PW, et al., Circulation 1988; 77: 361. Serial study suggesting vessels stabilize 3-4 months following PTCA.
1 – Small platinum markers at scaffold edges remain for fluoroscopic landmarking. 2. The Absorb IFU indicates DAPT for a minimum of 6 months.

Absorb May be Especially Beneficial for Certain Patient Types

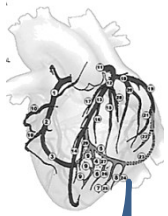
First time, young patients*

- Young patients may need future interventions that can be complicated or compromised by a permanent implant



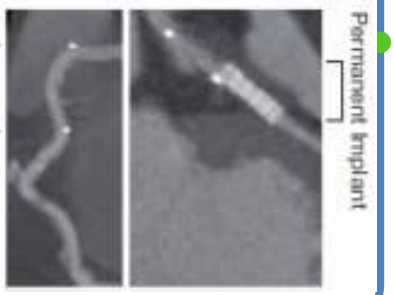
Patients at risk for future intervention

- Bioresorbable vascular scaffolds will preserve more treatment options for future interventions



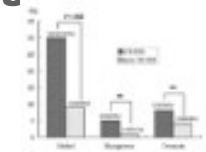
Non-invasive assessment of patients by

- Non-invasive imaging for and late follow up is feasible with BVS

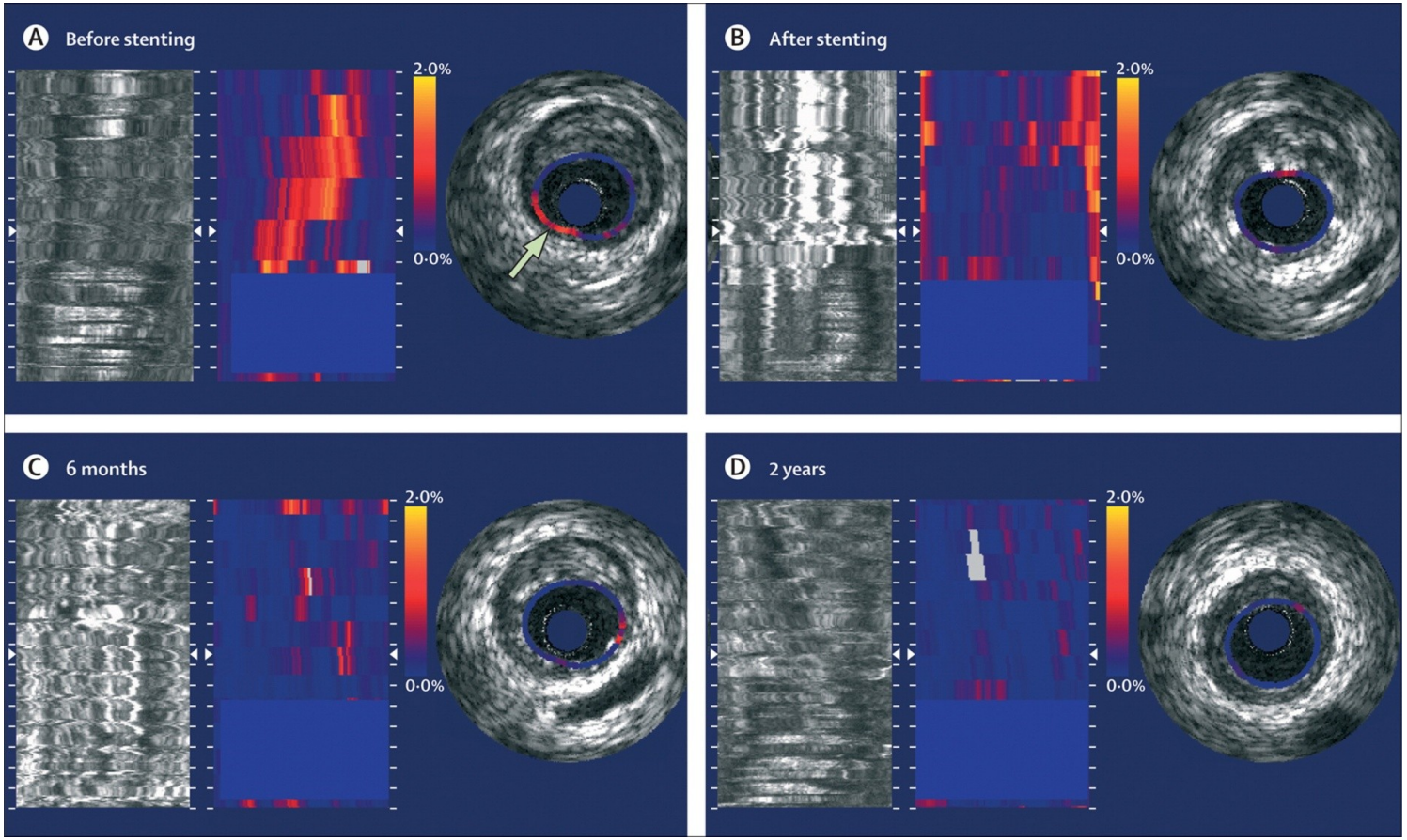


Patients with metal allergy

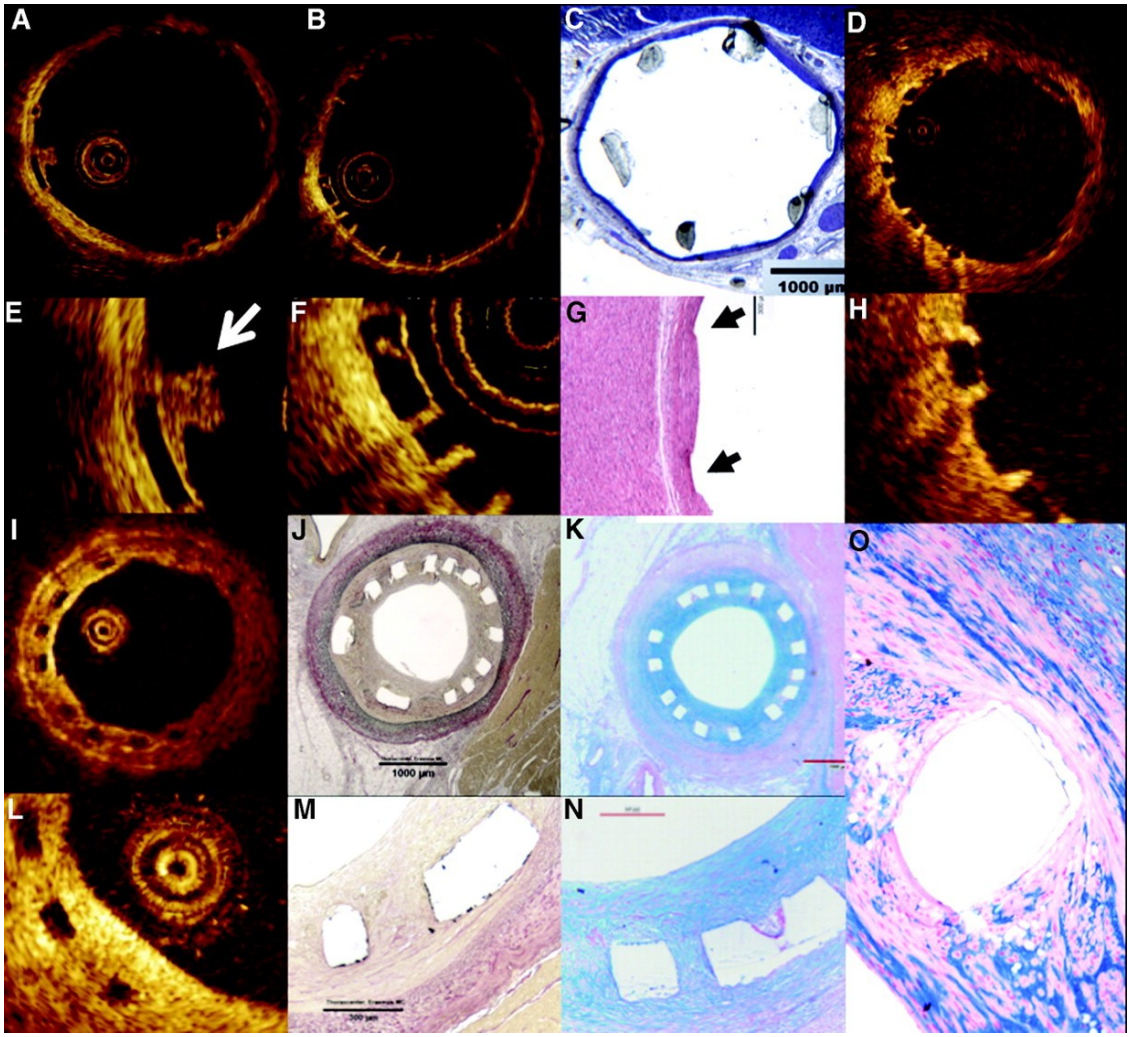
- Population with nickel allergy is estimated to be 8.6% of the general population1
- Allergic reactions to nickel and molybdenum released from stents may be one of the triggering mechanisms for in-stent restenosis2



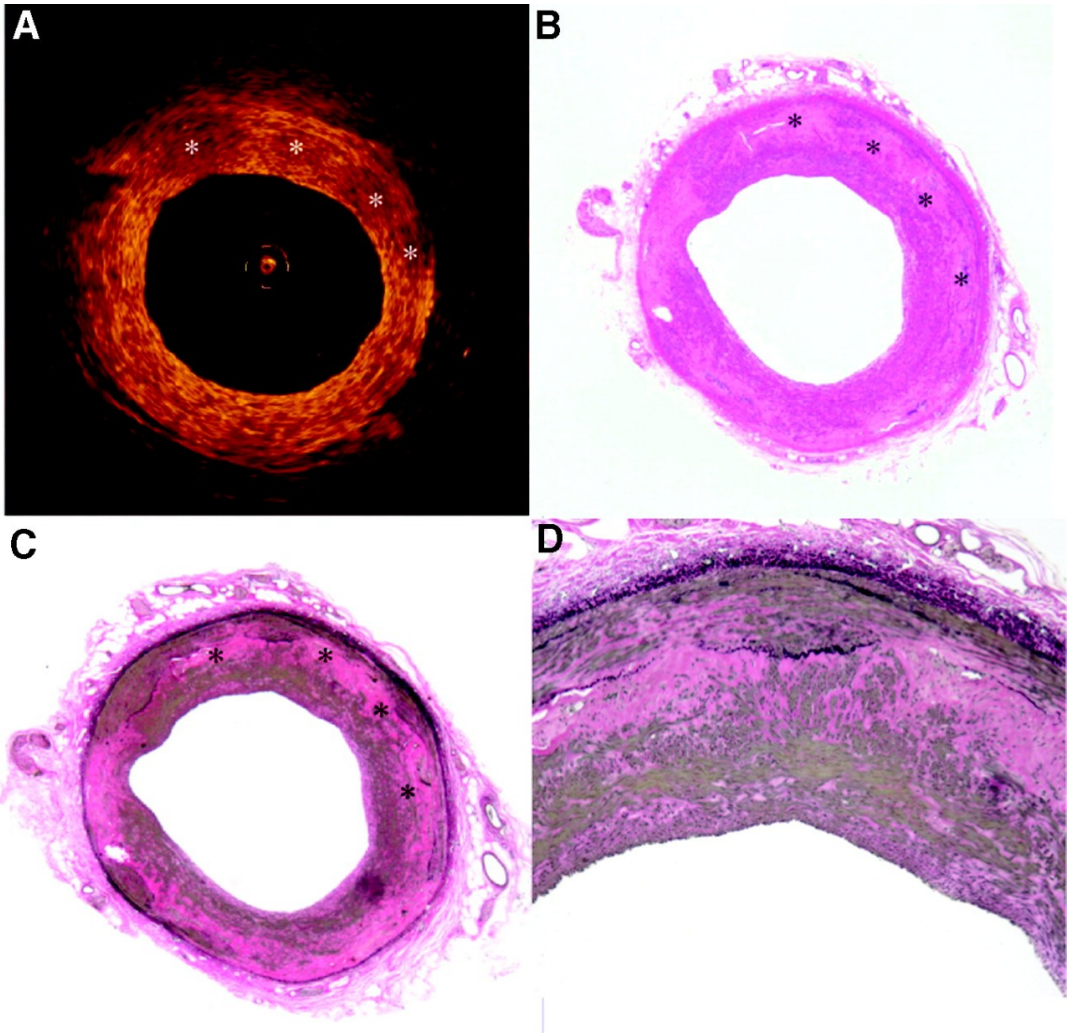
*Young patient defined as <65 years of age / 1. Thyssen et al. Contact Dermatitis 2007 / 2. Koster, Lancet, Vol 356, 12/2/00



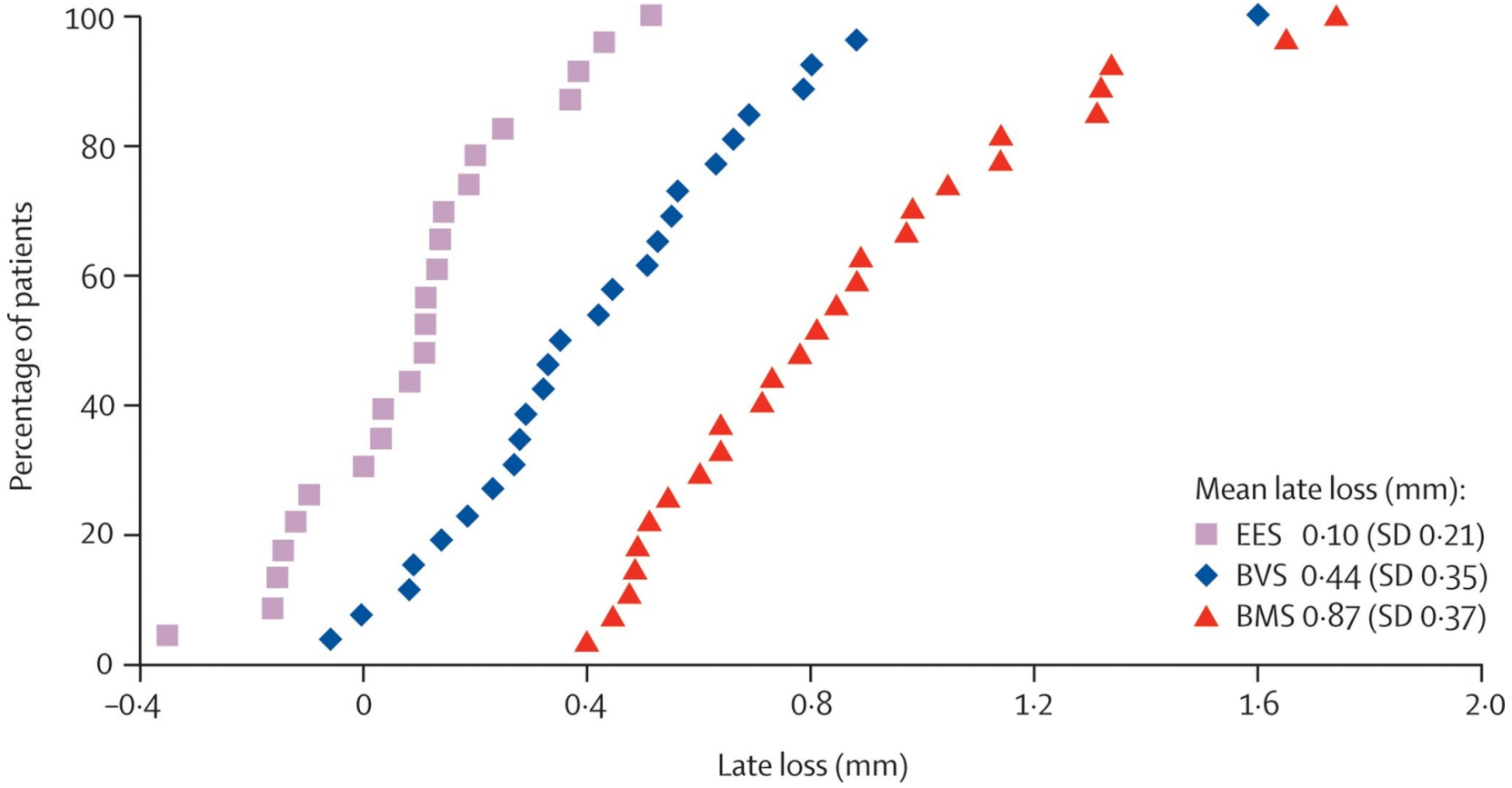
Serruys PW et al. Lancet 2009



Onuma Y et al. Circulation 2010



Onuma Y et al. Circulation 2010

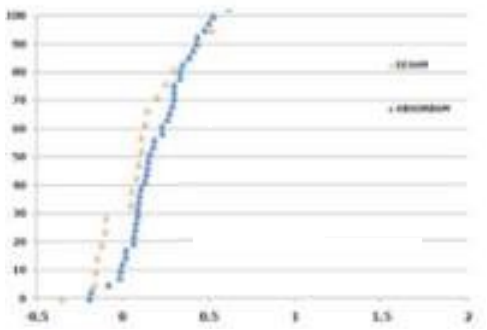


Ormiston JA et al. Lancet 2008

Absorb BVS clinical outcomes are comparable to best-in-class DES, XIENCE

- The Evolution of Cumulative Frequency Distribution Curves for Late Loss Over Time: BVS Cohort B and XIENCE V (Non-Matched 12 Population, ITT)

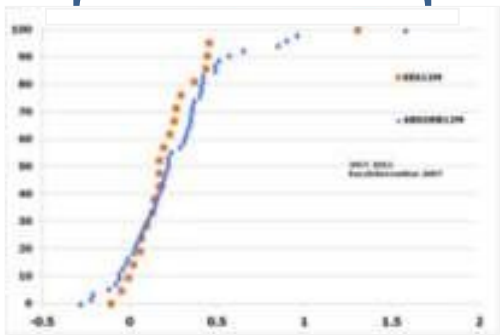
6 Months



BVS: 0.19 + 0.18 mm (n=42)

XIENCE V: 0.10 + 0.23 mm (n=22)

12 Months



BVS: 0.27 + 0.32 mm (n=56)

XIENCE V: 0.23 + 0.29 mm (n=22)

24 Months

BVS: 0.27 + 0.19 mm (n=38)

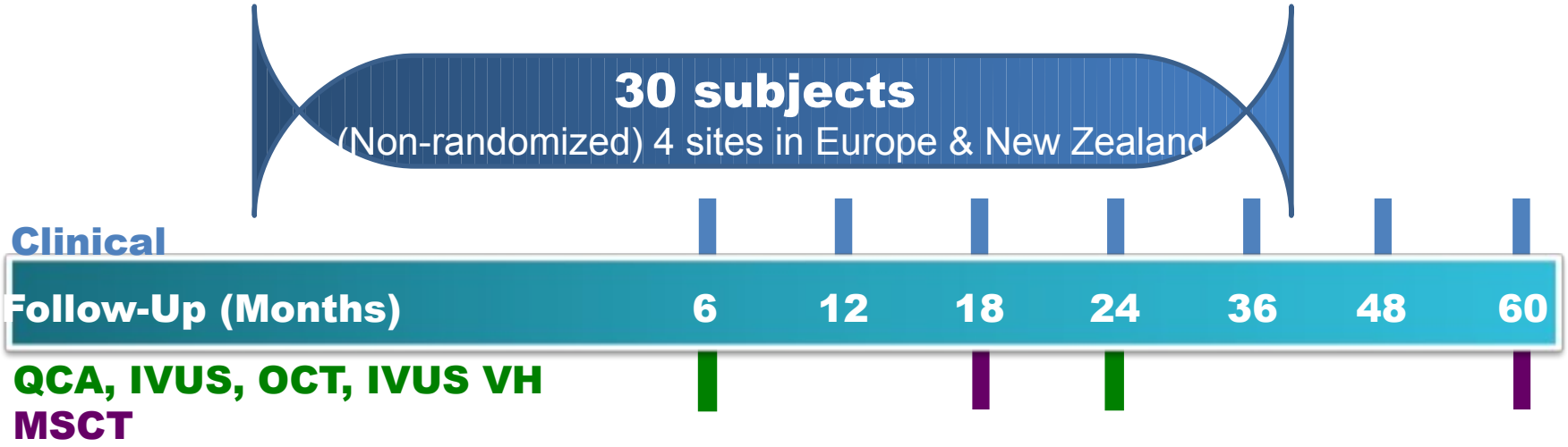
XIENCE V: 0.33 + 0.36 mm (n=100)

- Late Loss Unchanged Between 12 and 24 Months*

Serruys, PW., TCT 2011.

*One-year data is from ABSORB Cohort B Group 2 (n=56), two-year data is from Cohort B Group 1 (n=45)

Introduction
ABSORB Cohort A



Study Objective	**First In Man, Single Arm – safety/performance**
Endpoints	**Typical PCI clinical and imaging endpoints**
Treatment	**Single, de novo native coronary lesion in a vessel with a reference vessel diameter of 3.0 mm**
Device Sizes	**3.0 x 12mm scaffolds (3.0 x 18mm scaffolds available after enrolment start and used in 2 pts)**

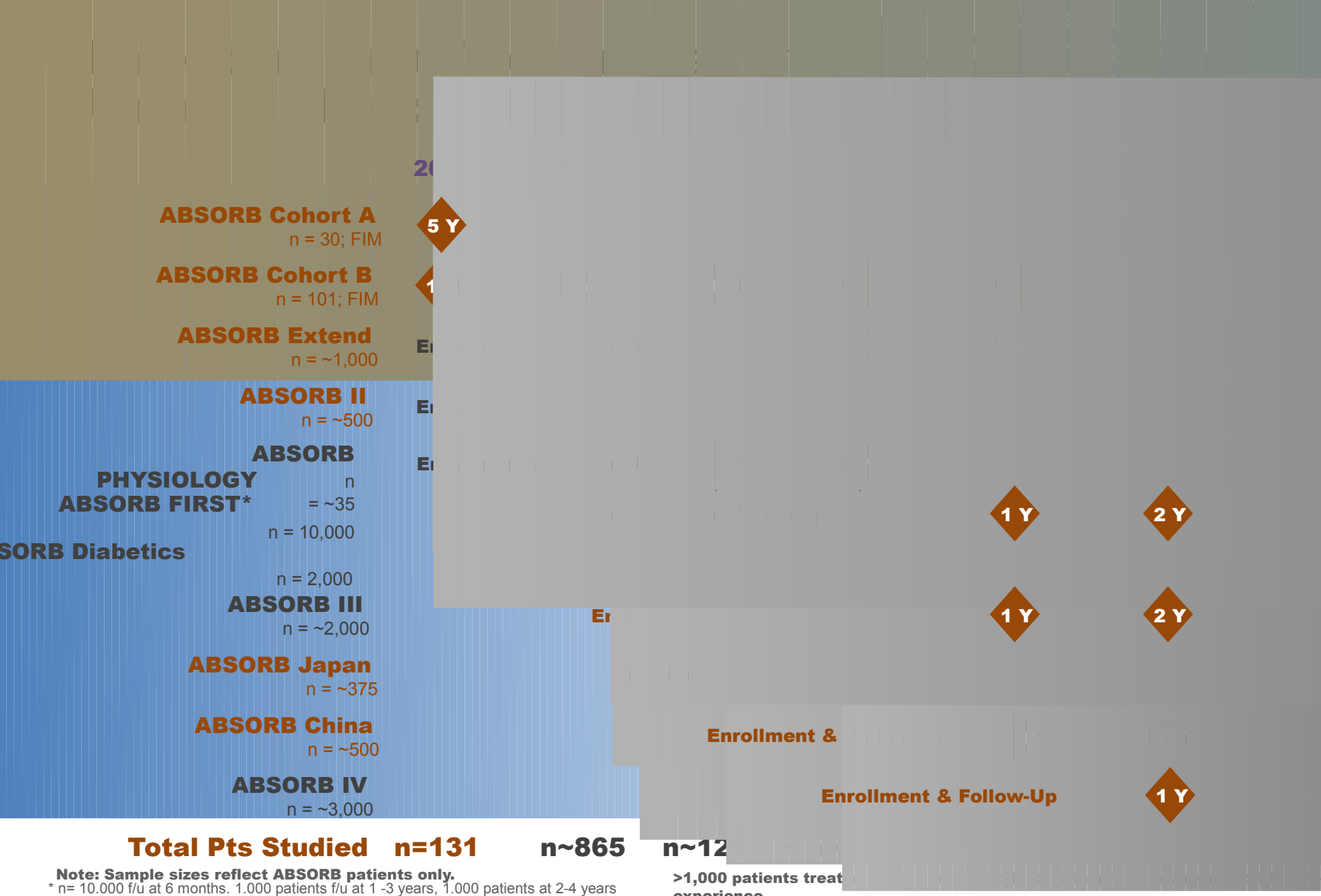
Four-year clinical follow-up of the ABSORB everolimus-eluting bioresorbable vascular scaffold in patients with *de novo* coronary artery disease: the ABSORB trial

Dariusz Dudek[1]*, MD; Yoshinobu Onuma[2], MD; John A. Ormiston[3], MD; Leif Thuesen[4], MD; Karine Miquel-Hebert[5], PhD; Patrick W. Serruys[2], MD, PhD

Table 1. Hierarchical major adverse cardiac events up to four years.

Hierarchical	6-months 30 patients	4-years 29 patients*
Ischaemia driven MACE (%)	3.3% (1)*	3.4% (1)*
Cardiac death (%)	0.0%	0.0%
MI (%)		
Q-wave MI	0.0%	0.0%
Non-Q-wave MI	3.3% (1)**	3.4% (1)**
Ischaemia driven TLR (%)		
by PCI	0.0%	0.0%
by CABG	0.0%	0.0%

Dudek D. et al ., EuroIntervention 2011

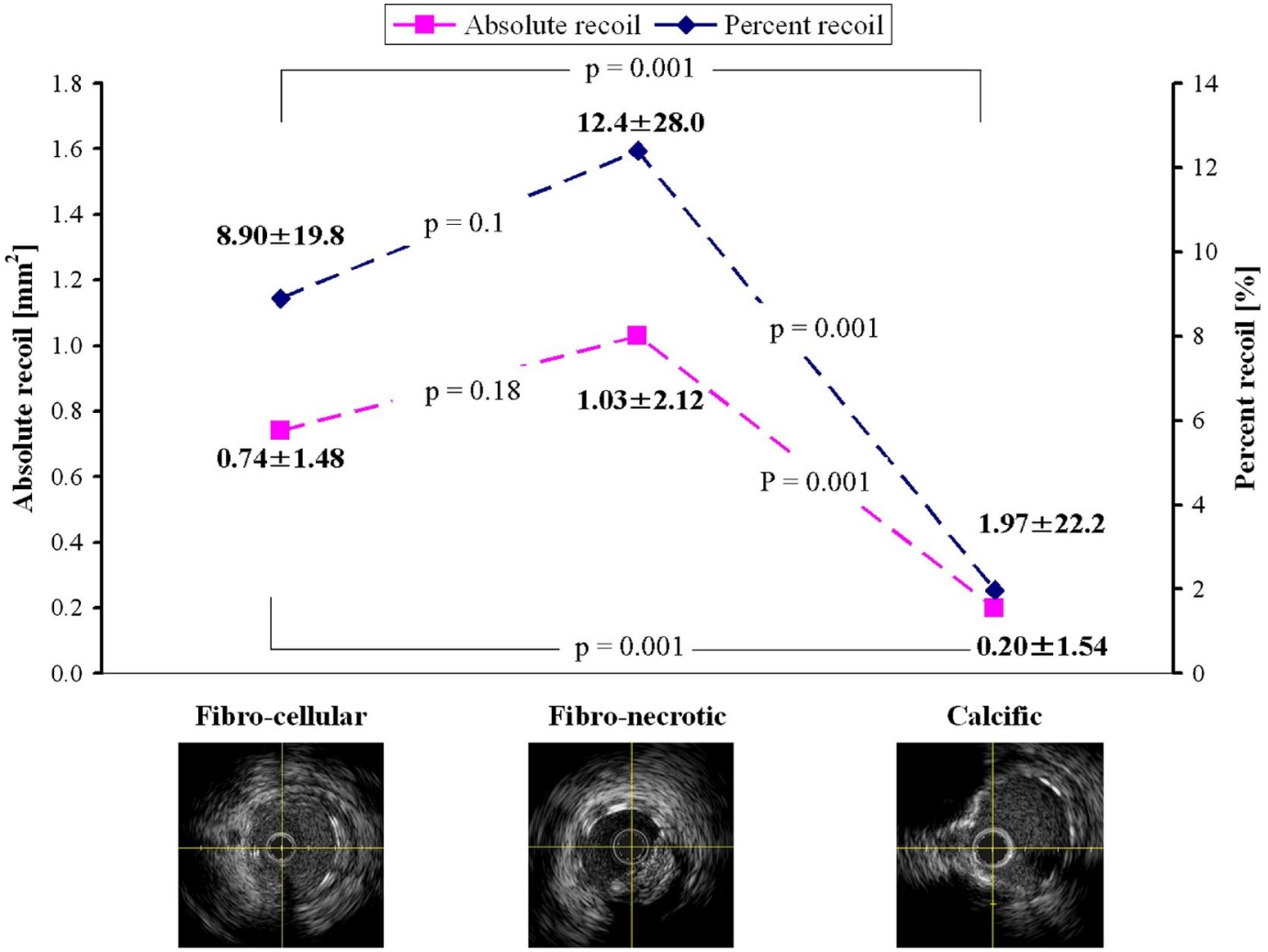


Note: Sample sizes reflect ABSORB patients only.

* n= 10.000 f/u at 6 months. 1.000 patients f/u at 1 -3 years, 1.000 patients at 2-4 years

>1,000 patients treat
experience.

VS-Recoil ist abhängig vom Plaque-Morphologie



Tanimoto S. et al., JACC 2007

First-in-Human Implantation of a Fully Bioabsorbable Drug-Eluting Stent: The BVS Poly-L-Lactic Acid Everolimus-Eluting Coronary Stent

John A. Ormiston,* MBChB, FRACP, FRACR, FCSANZ, Mark W.I. Webster, MBChB, FRACP, FCSANZ, and Guy Armstrong, MBChB, FRACP, FCSANZ

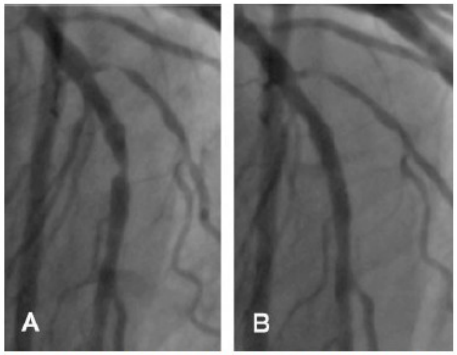


Fig. 1. Coronary angiography before (A) and after (B) BVS bioabsorbable everolimus-eluting stent implantation.

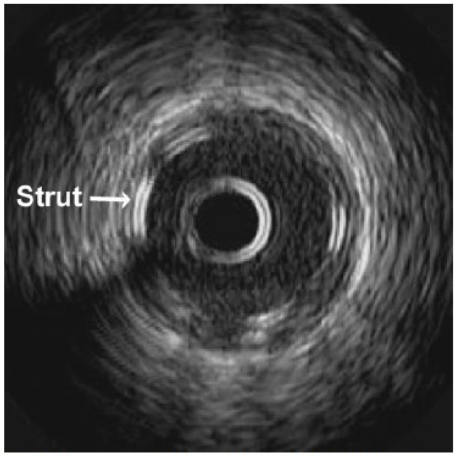
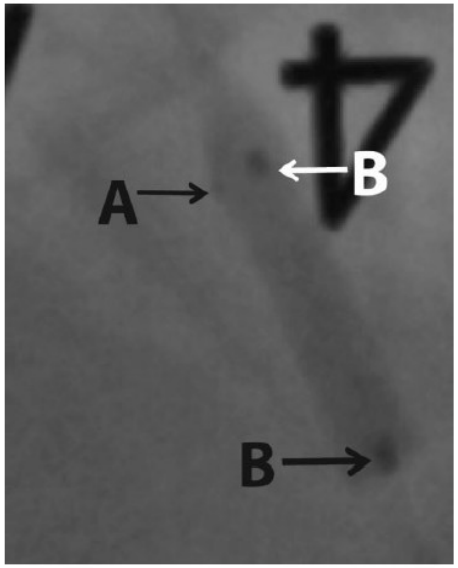
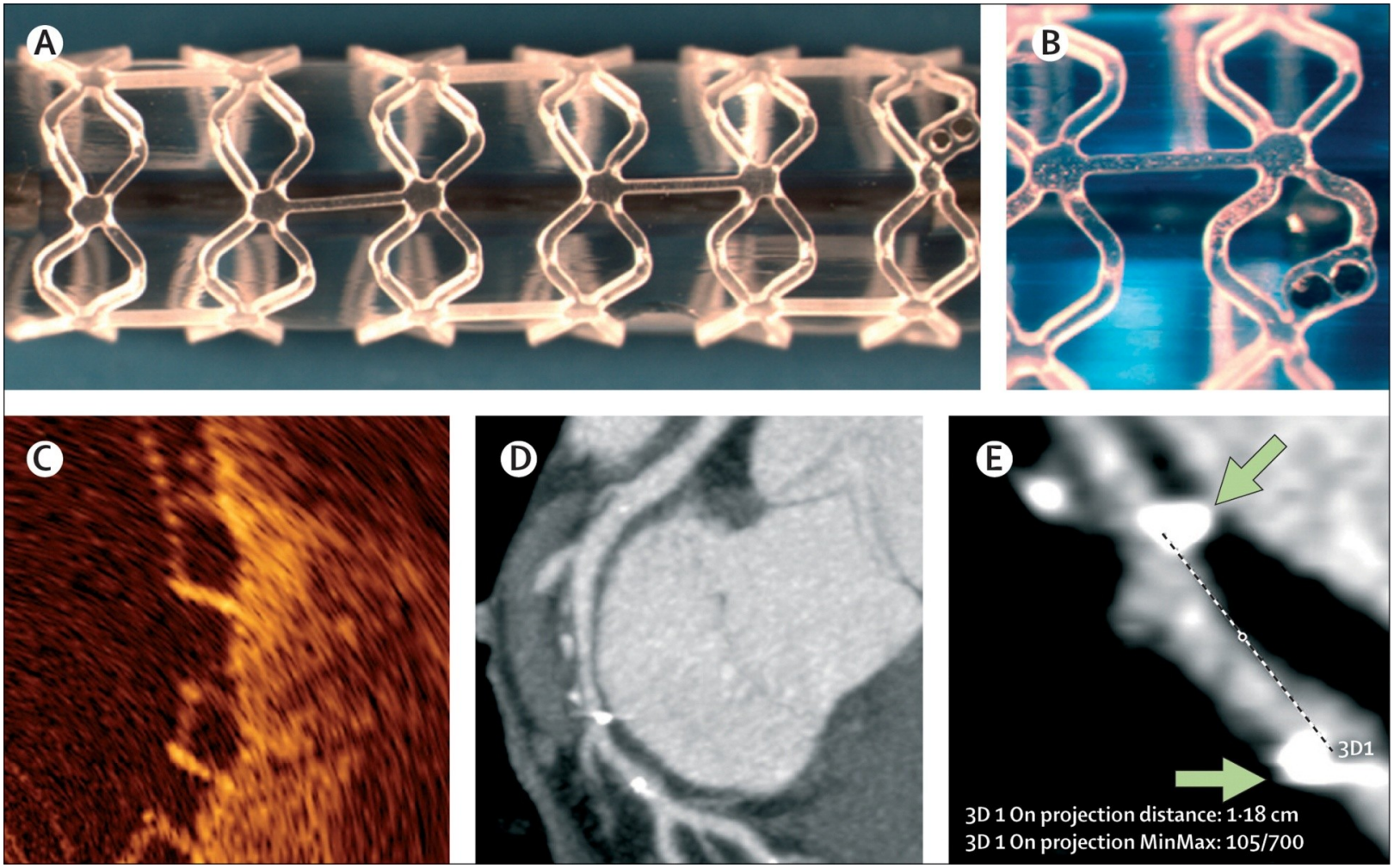


Fig. 3. Intracoronary ultrasound image of a BVS stent. The parallel echoes represent reflected ultrasound from the blood/stent and stent/tissue interfaces. Because ultrasound can pass through a polymer stent in contrast to a metal stent, there is no acoustic shadowing behind the stent struts.



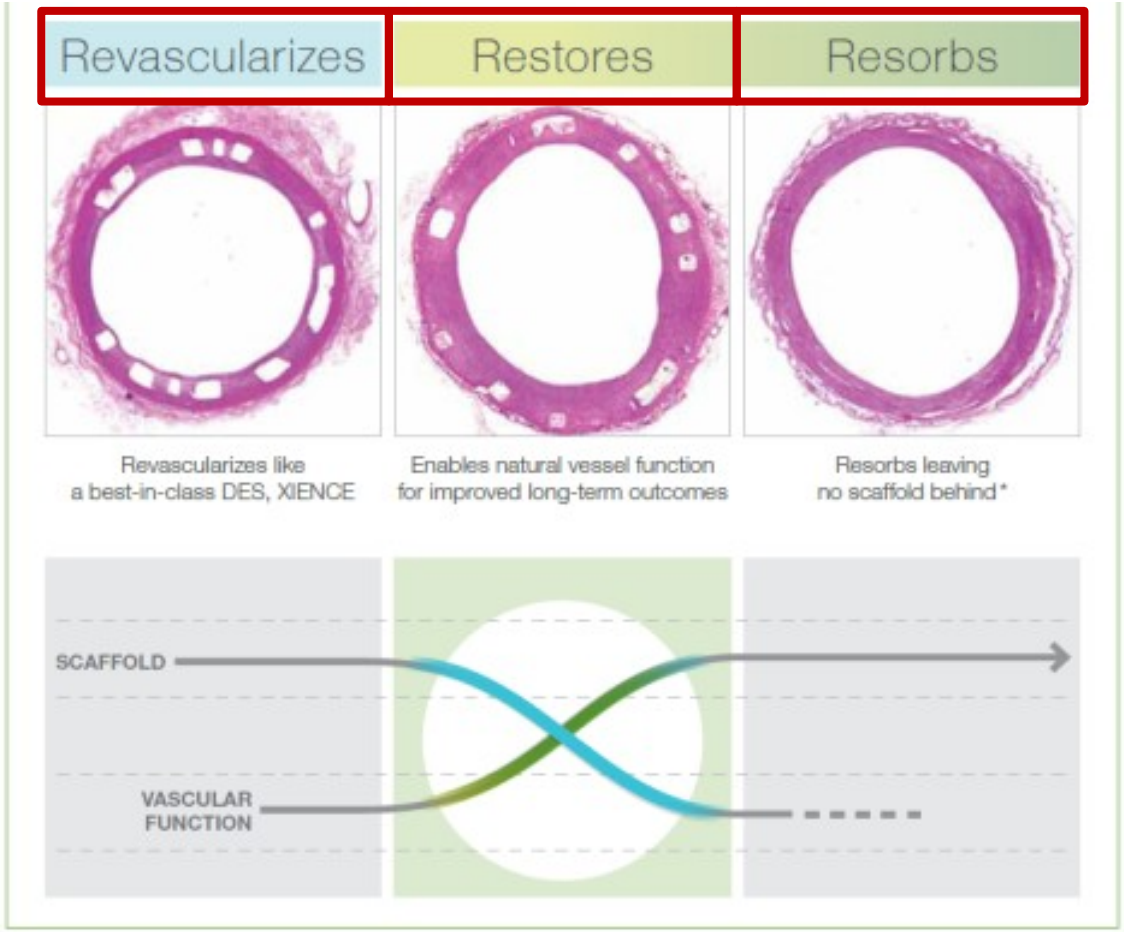
3 x 12mm BVS 1.0 PLLA

Ormiston J. et al., Cath Cardiovasc. Intervention 2007



Ormiston J. et al., Lancet 2008

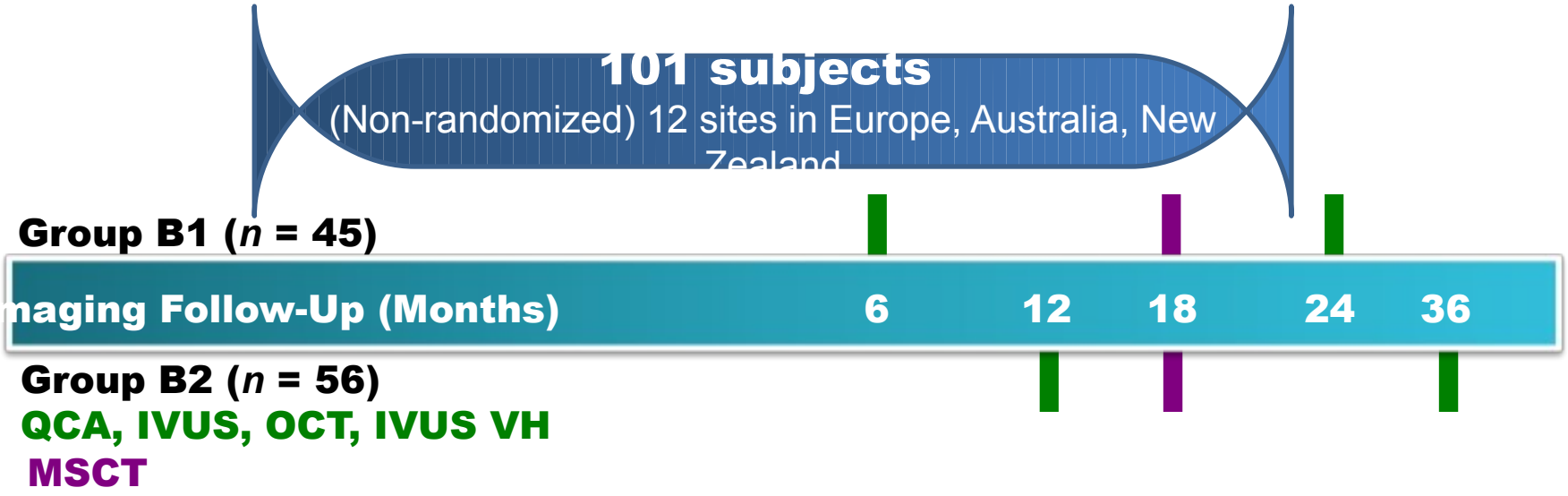
Absorb Works in 3 Phases to Deliver VRT



Histology images are from porcine animal models.

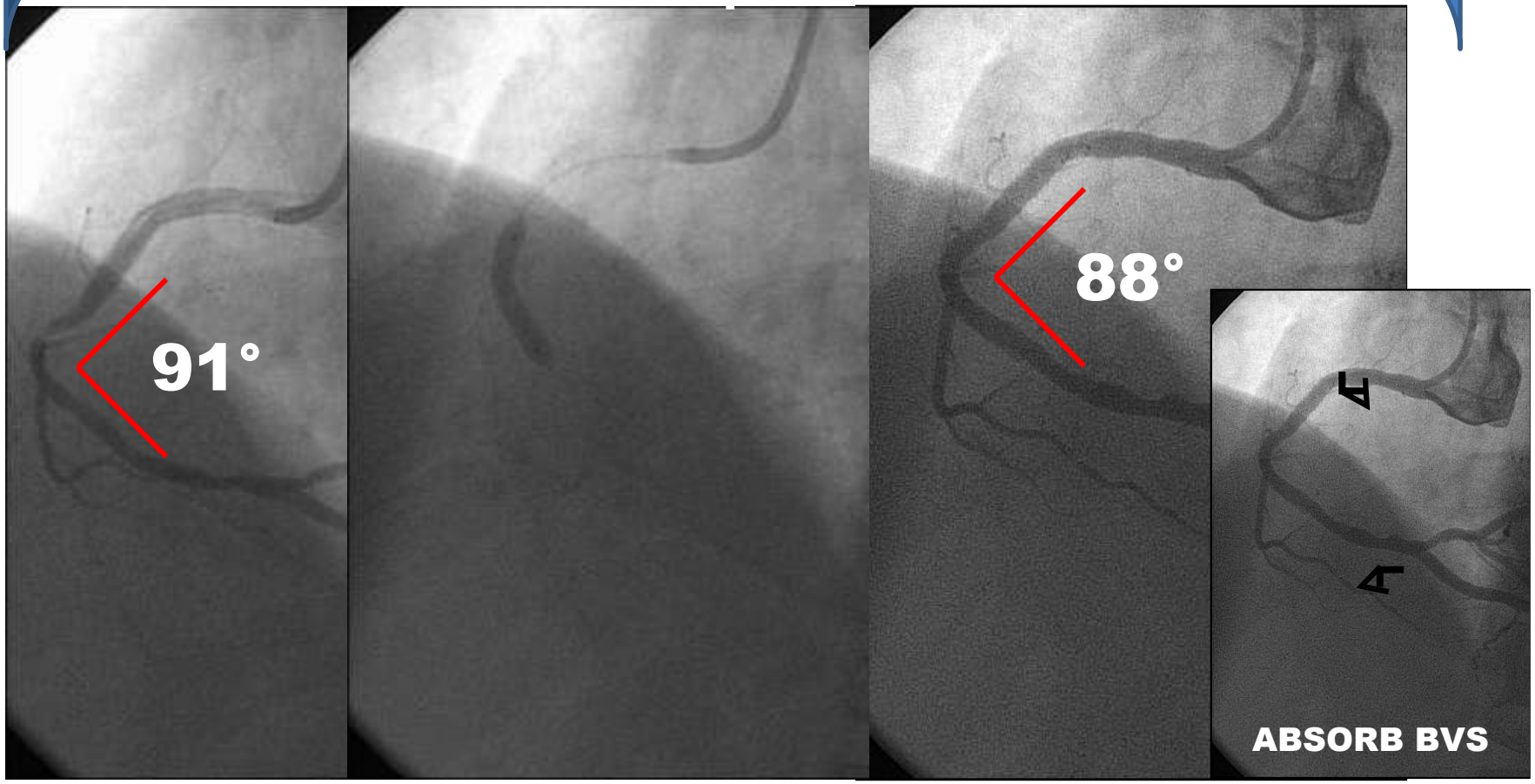
*Small platinum markers at scaffold edges remain for fluoroscopic landmarking.

Introduction
ABSORB Cohort B



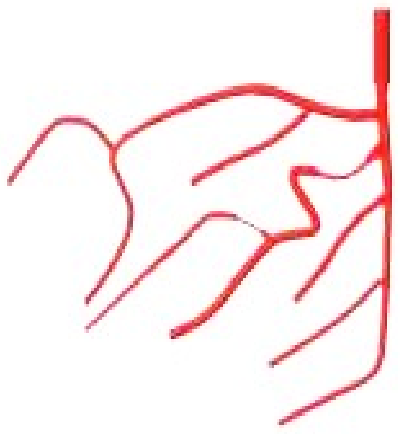
Study Objective	**First In Man, Single Arm – safety/performance**
Endpoints	**Typical PCI clinical and imaging endpoints**
Treatment	**Up to 2 *de novo* lesions in different epicardial vessels Reference vessel diameter of 3.0 mm, lesions ≤ 14 mm in length**
Device Sizes	**3.0 x 18mm devices**

Absorb provides better conformability compared to metallic platforms

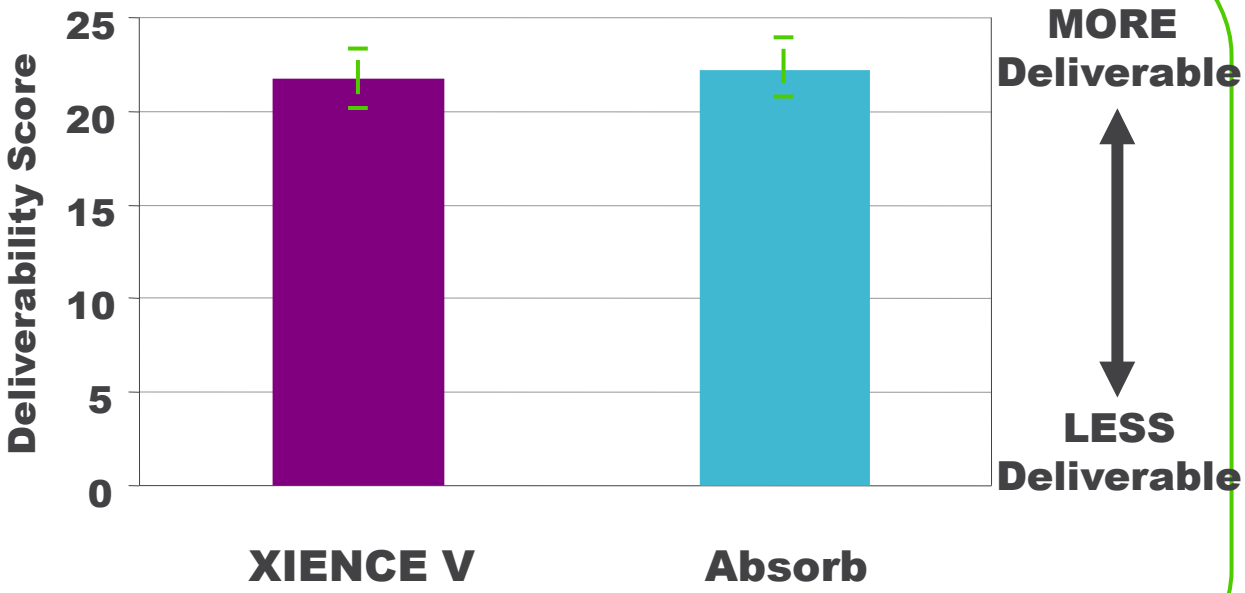


Serruys, PW. , TCT 2009; J. Gomez-Lara, JACC Cardiovascular Interventions

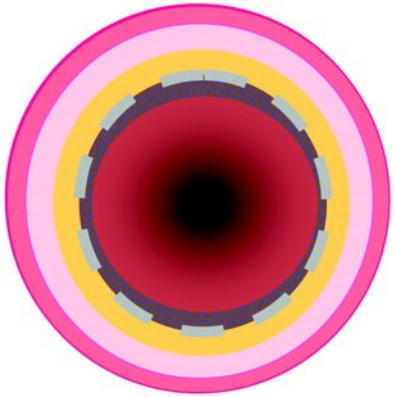
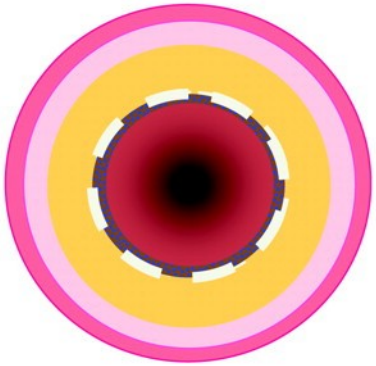
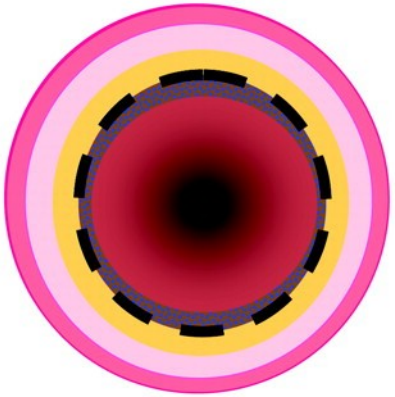
Deliverability in a Simulated Artery Model (SAM)



Diffuse Disease PVA Vessel

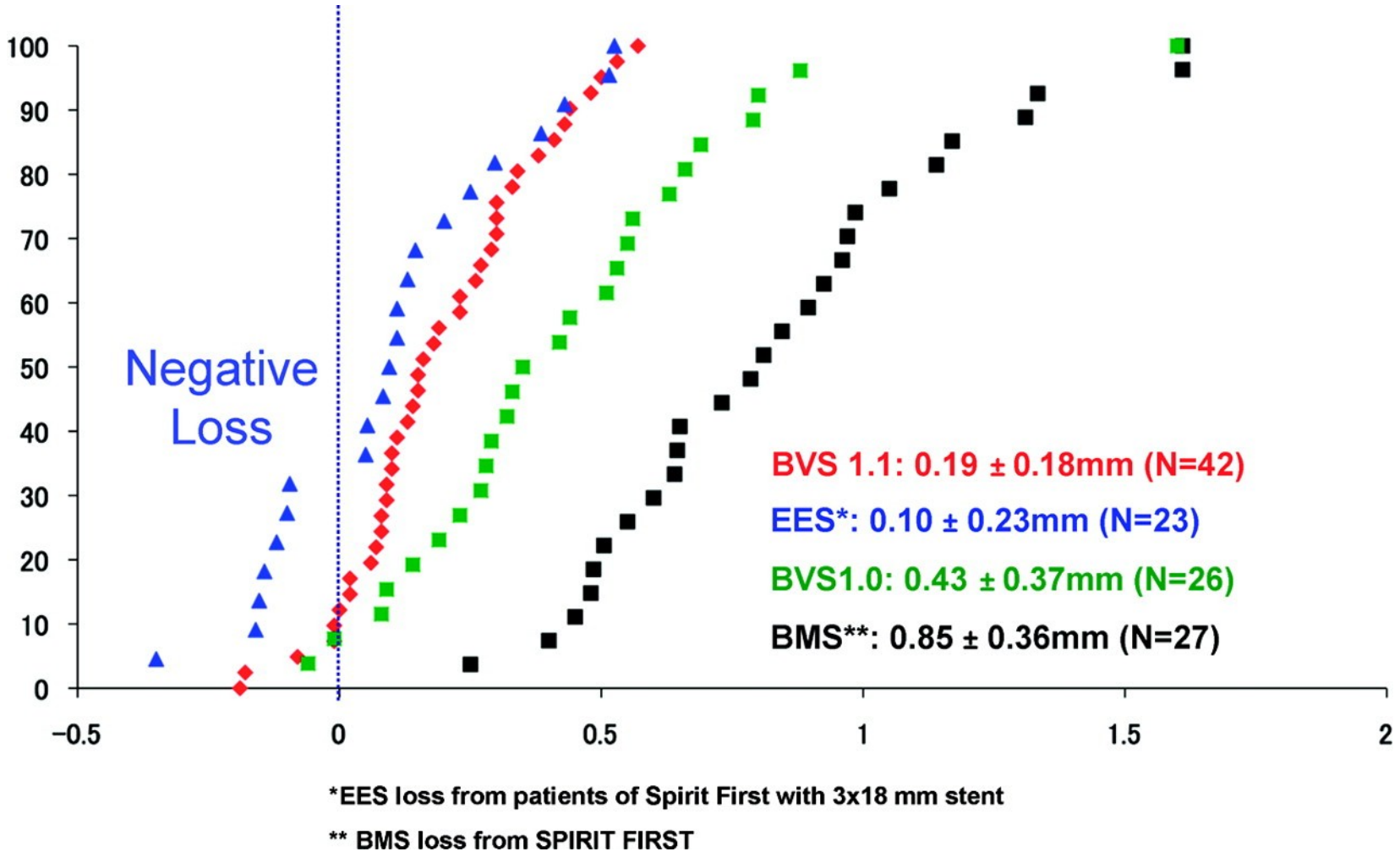


Tests performed by and data on file at Abbott Vascular.

SPIRIT-First Xience V Stent	ABSORB BVS 1.0	ABSORB BVS 1.1
		
Late Loss = 0.10mm	**Late Loss = 0.44mm**	**Late Loss = 0.19mm**
Δ Vessel Area = *+1.2%* Δ Stent Area = *-0.3%* Δ Lumen Area = *-7.2%* NIH Area (mm^2) = 0.50 % VO = 8.0%	Δ Vessel Area = *-0.4%* Δ Stent Area = *-11.7%* Δ Lumen Area = *-16.6%* NIH Area (mm^2) = 0.30 % VO = 5.5%	Δ Vessel Area = *+2.4%* Δ Stent Area = *-2.9%* Δ Lumen Area = *-4.0%* NIH Area (mm^2) = 0.07 % VO = 1.0%

6 Monats-FU

Onuma Y & Serruys PW Circulation 2011



*EES loss from patients of Spirit First with 3x18 mm stent

** BMS loss from SPIRIT FIRST

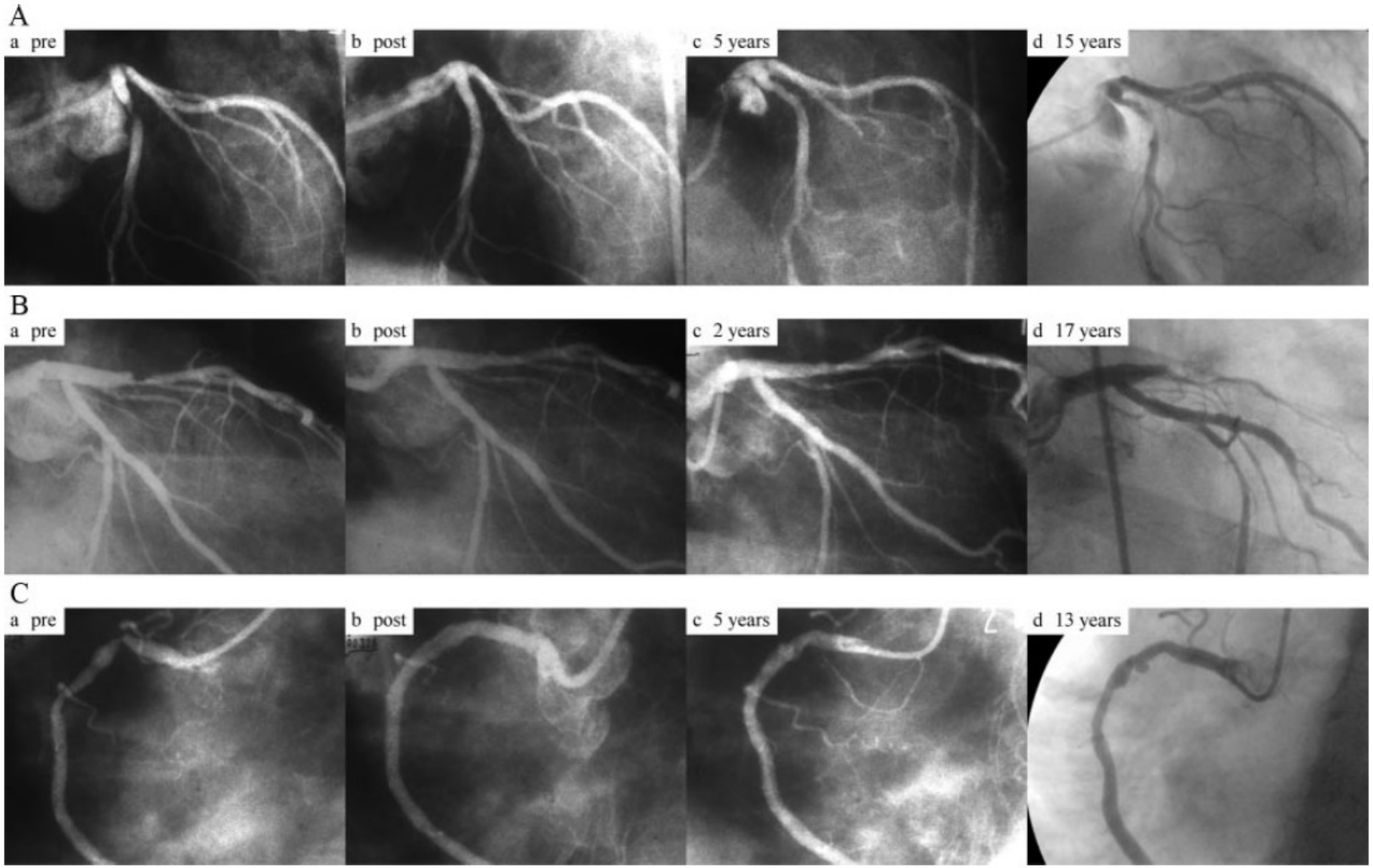
Serruys PW et al., Circulation 2010

BVS VERSUS BMS and DES

Same Parameters, Different Outcomes:

Very Subjective and Simplistic View from BMS

Preclinical Parameters	BMS	First Generation DES	Second Generation DES	Bioresorbable Scaffold
Mechanical injury severity	**standard**	**standard**	**standard**	**not worse**
Acute thrombus	**minimal**	**minimal**	**minimal**	**not worse**
Inflammation	**minimal**	**worse***	**better****	**not worse**
Acute recoil	**none**	**none**	**none**	**not worse**
Neointimal hyperplasia	**standard**	**better***	**better****	**not worse**
Endothelialization	**standard**	**worse***	**better****	**better****
Healing pattern	**standa**	**worse***	**better****	**better****



Yamaji Y. et al., Circulation 2010

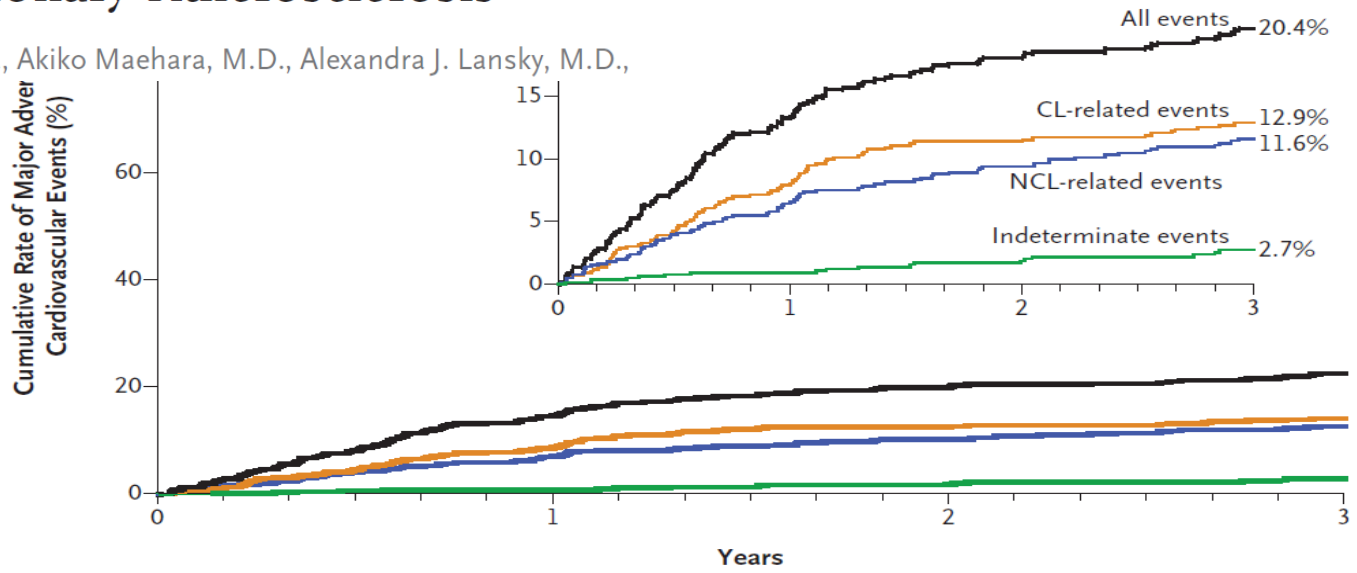
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

700 patients after ACS

A Prospective Natural-History Study of Coronary Atherosclerosis

Gregg W. Stone, M.D., Akiko Maehara, M.D., Alexandra J. Lansky, M.D.,

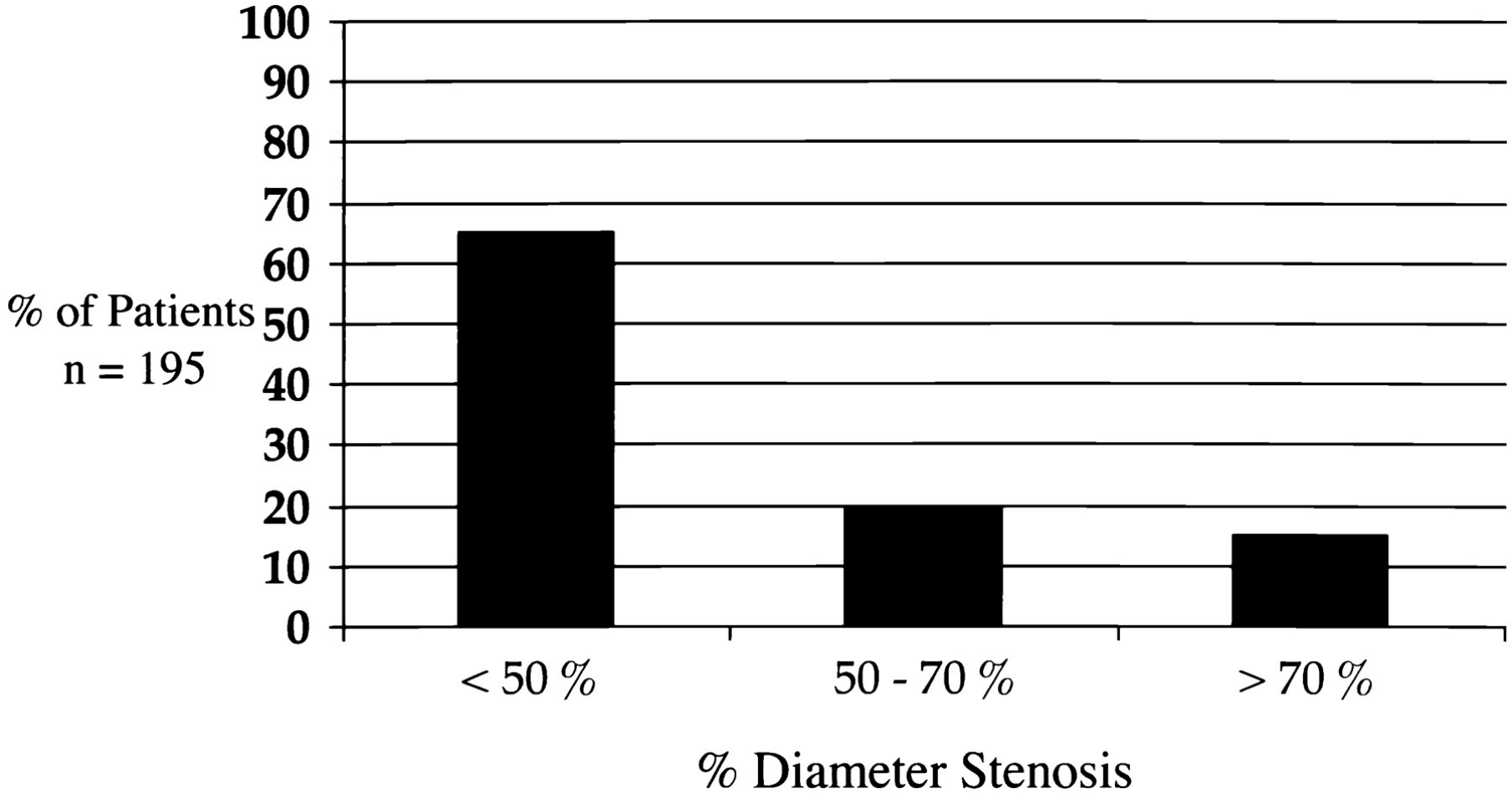


No. at Risk				
All patients	697	557	506	480
Patients with CL-related events	697	590	543	518
Patients with NCL-related events	697	595	553	521
Patients with indeterminate events	697	634	604	583

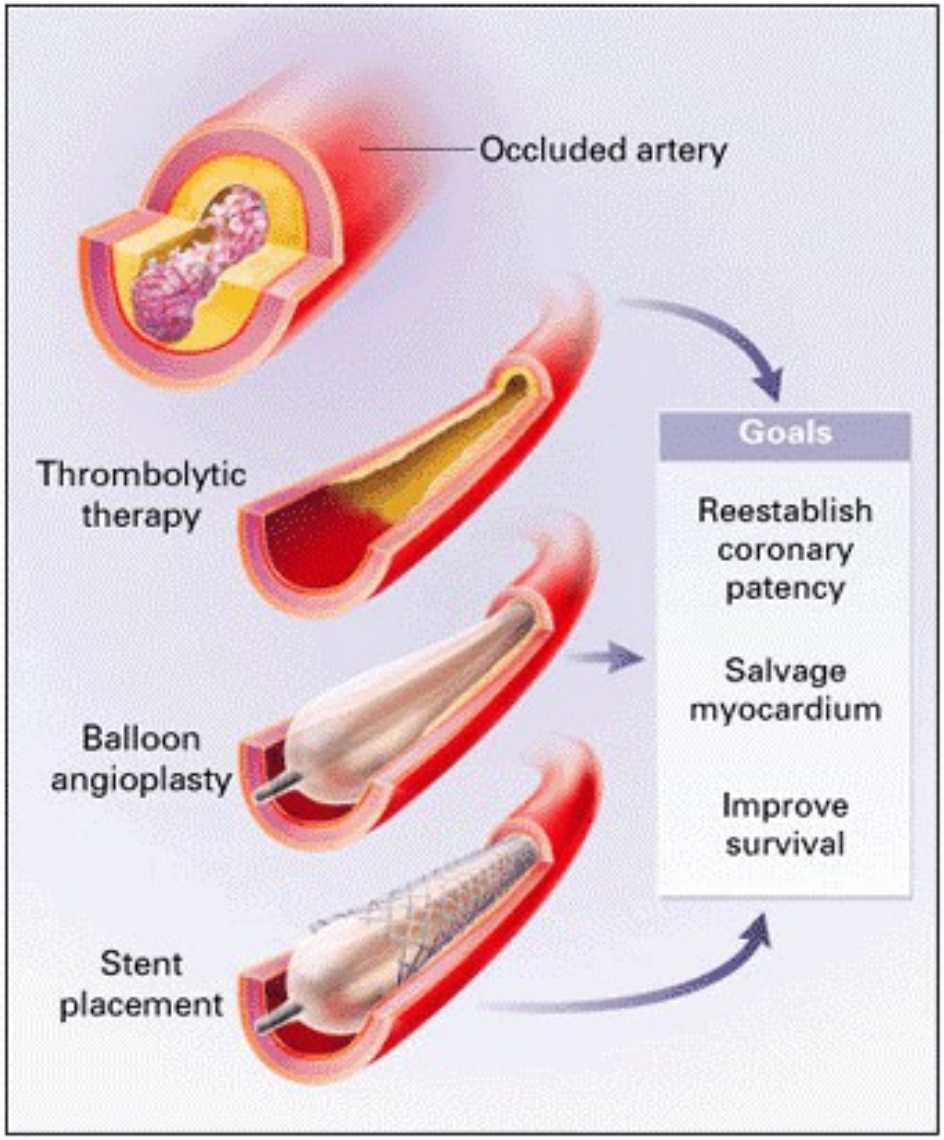
s not possible to stop the progression of atherosclerosis with the present treatment strategies

Stone G. et al., NEJM 2011

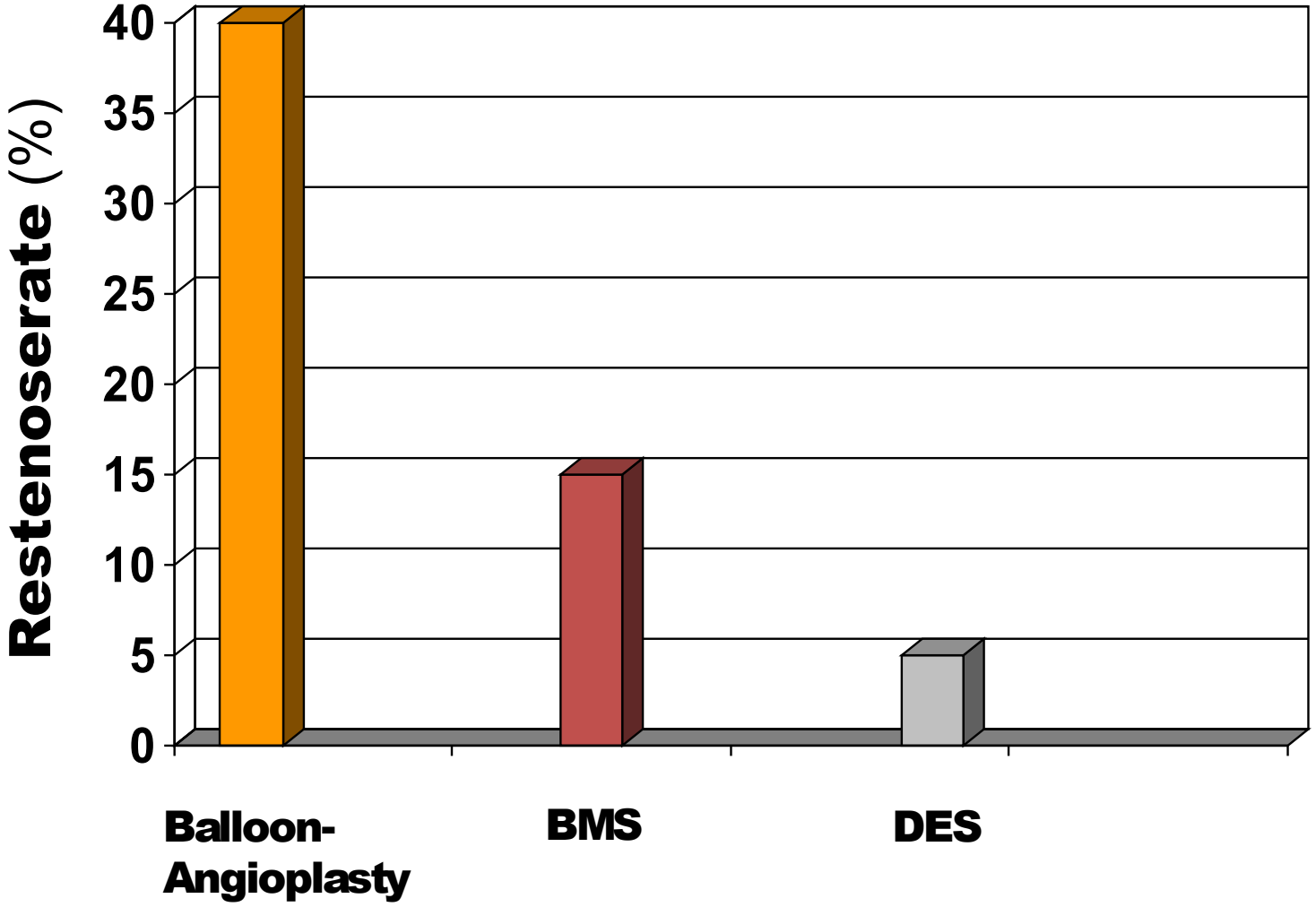
Severity of coronary artery stenosis before acute myocardial infarction

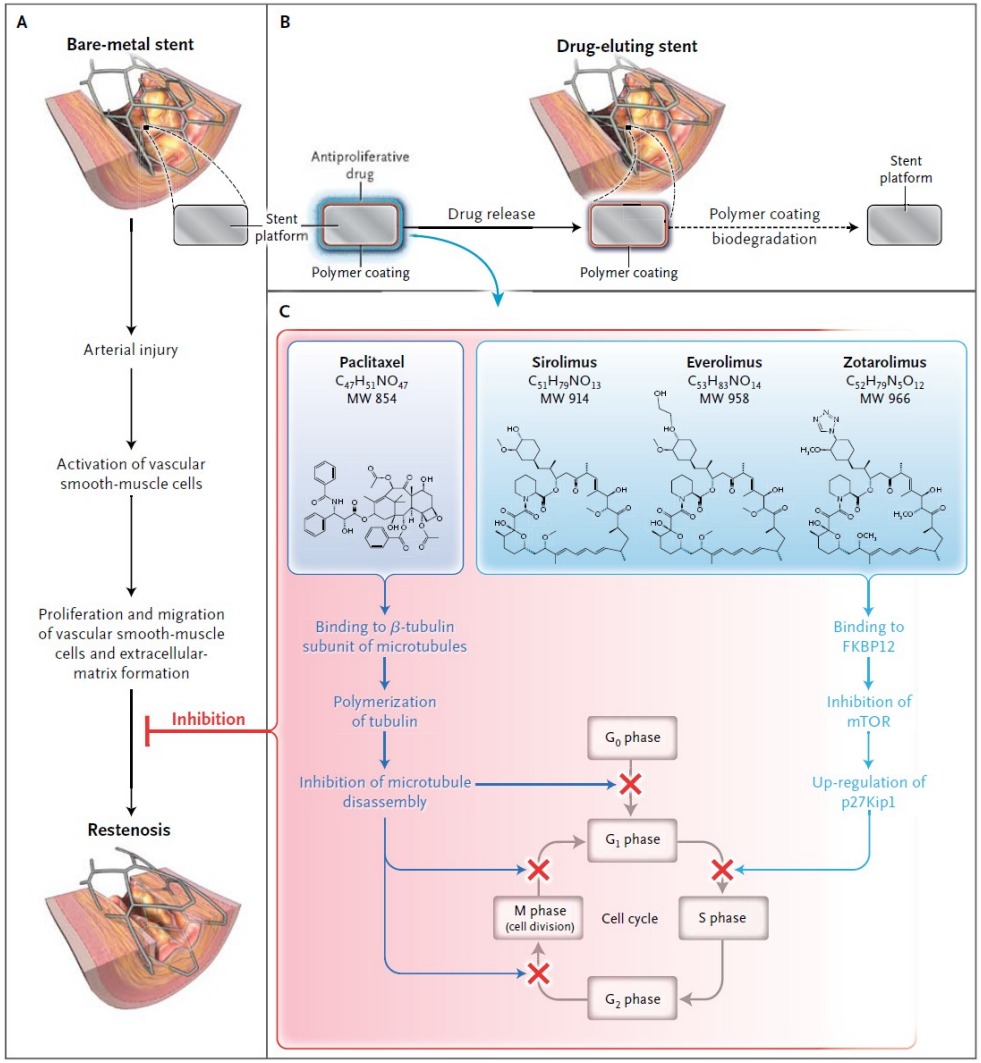


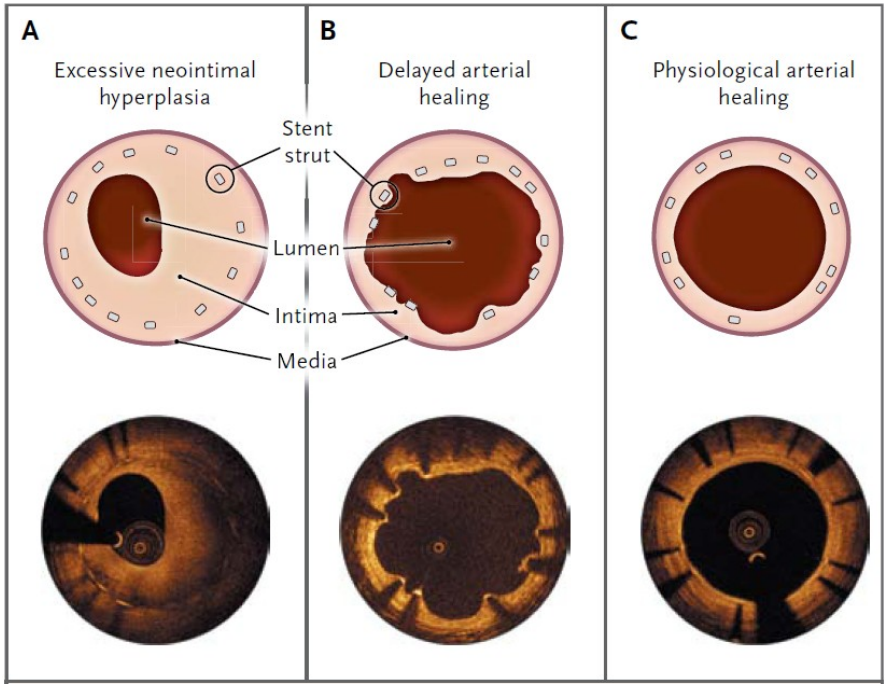
Smith SC, Circulation 1996


Occluded artery
Thrombolytic therapy
Balloon angioplasty
Stent placement
Goals
Reestablish coronary patency
Salvage myocardium
Improve survival

Rate of Restenoses

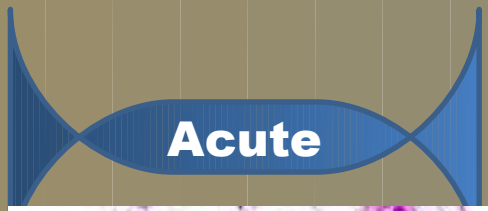


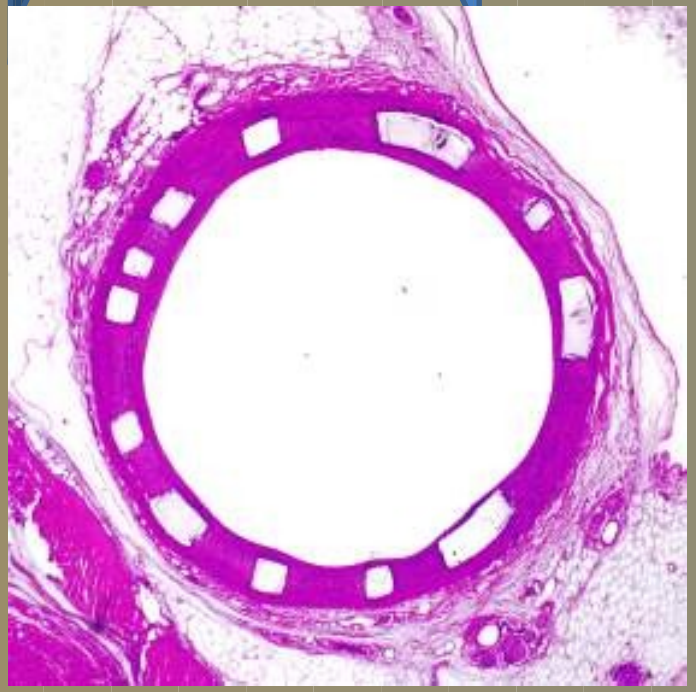


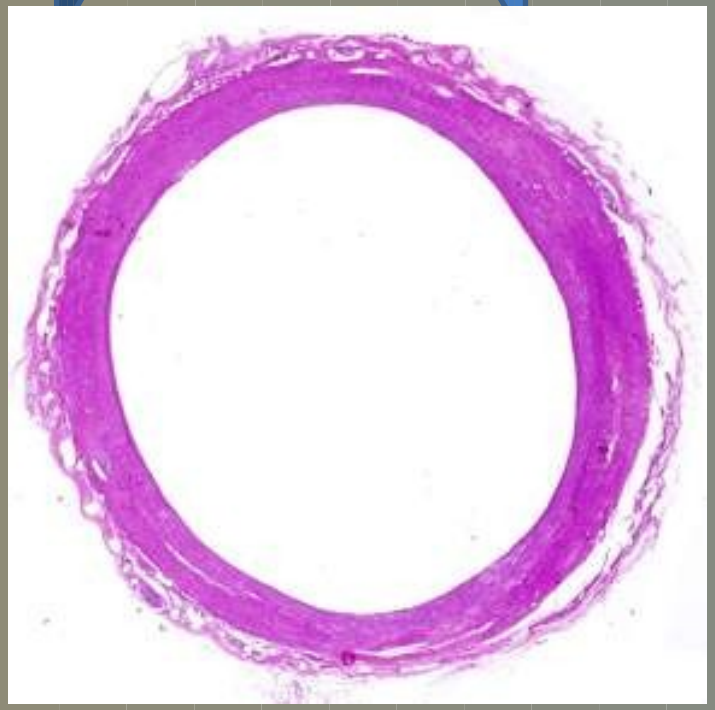


Stefanini G. et al., NEJM 2013

Bioresorbable Vascular Scaffold (BVS): Ideal of leaving nothing behind







Data and images on file at Abbott Vascular. Histology images are from porcine animal models.

Restoration of Vascular Integrity

18 months

12 months

6 months

Porcine coronary artery model

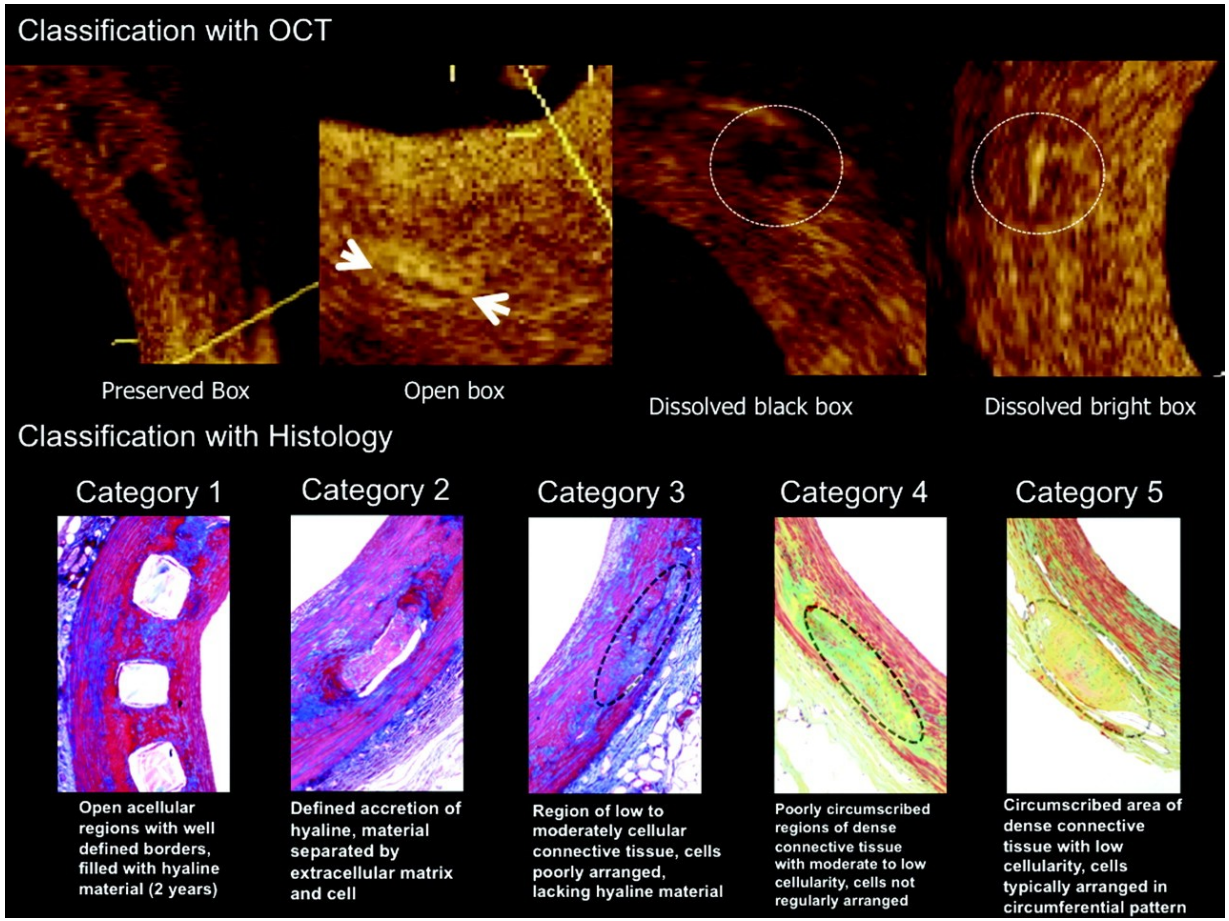
48 months

Data and images on file at Abbott Vascular. Histology images are from porcine animal models.

Intracoronary Optical Coherence Tomography and Histology at 1 Month and 2, 3, and 4 Years After Implantation of Everolimus-Eluting Bioresorbable Vascular Scaffolds in a Porcine Coronary Artery Model

An Attempt to Decipher the Human Optical Coherence Tomography Images in the ABSORB Trial

Yoshinobu Onuma, MD*; Patrick W. Serruys, MD, PhD*; Laura E.L. Perkins, DVM, PhD;



Onuma Y. et al., Circulation 2010