

TCT-AP 2011

**Will bioabsorbable stents
transform PCI in the future?**

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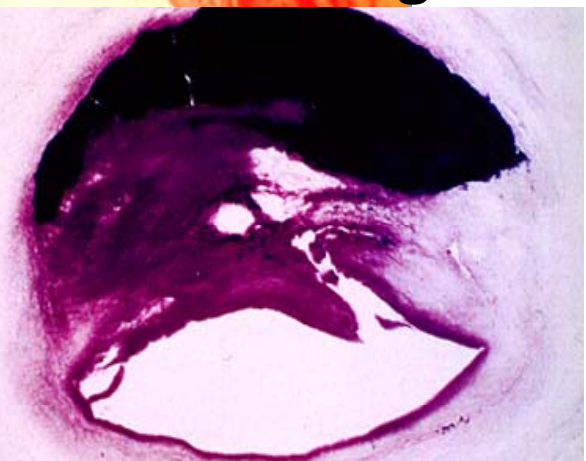
12:20-12:30 April 27th, 2011, 10 min.

Main Arena Level B2

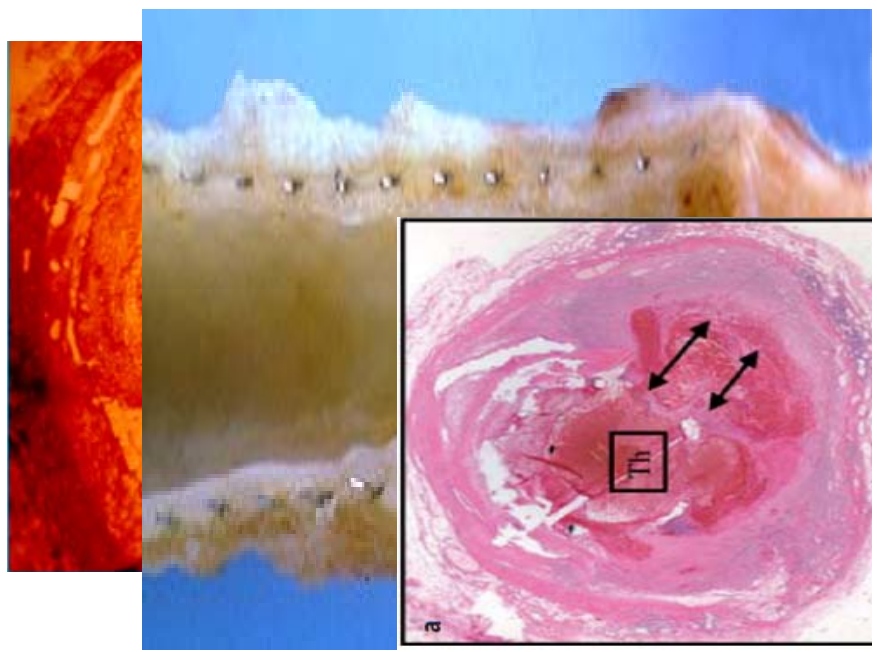
	POBA
Acute Occlusion	-
Acute ST	na
Subacute ST	na
Acute recoil	-
Constrictive remodeling	-
Neointimal hyperplasia	-
Expansive remodeling	+
Late Luminal Enlargement	+
Late ST	na

Post angioplasty



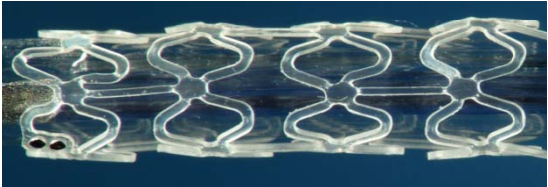
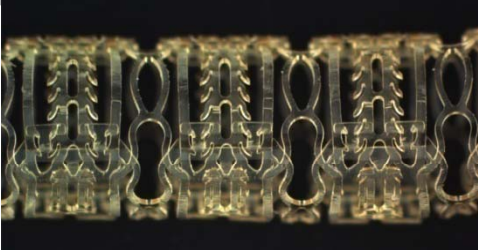

Dissection and intraparietal hemorrhage



4 mo



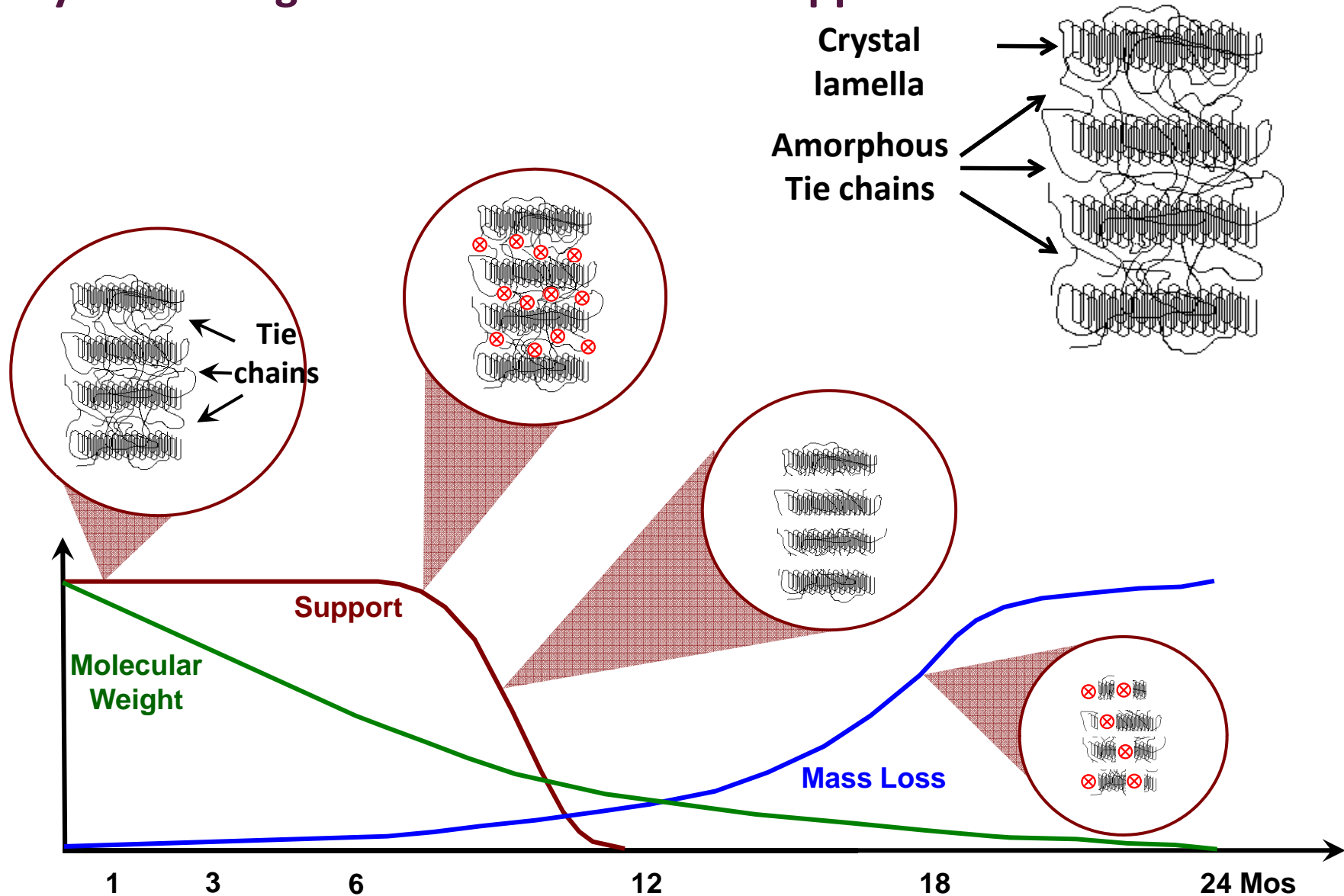
Overview of bioresorbable scaffolds in clinical arena

Company	Picture	Polymer/Drug	Features
Igaki-Tamai (2000)	 <p>IGAKI-TAMAI® STENT</p>	PLLA PLLA plus Tranilast	Zig-zag design deployed with a heated balloon
Biotronik (2006)		Mg alloy	Balloon expandable design
Abbott (BVS) (2006)		PLLA with everolimus	Balloon expandable
Reva Medical (2008)		Tyrosine poly carbonate with Iodine for radio-opacity	Design has ratchet links for deployment
BTI (2008)		Salicylic acid blended into polymer (PLA or adipic acid) with sirolimus	Balloon expandable

Clinical

Bioabsorbable Drug Everolimus Eluting Stent (BVS)

Polylactide Degradation versus Radial Support



Circulation



American Heart Association® | American Stroke Association®

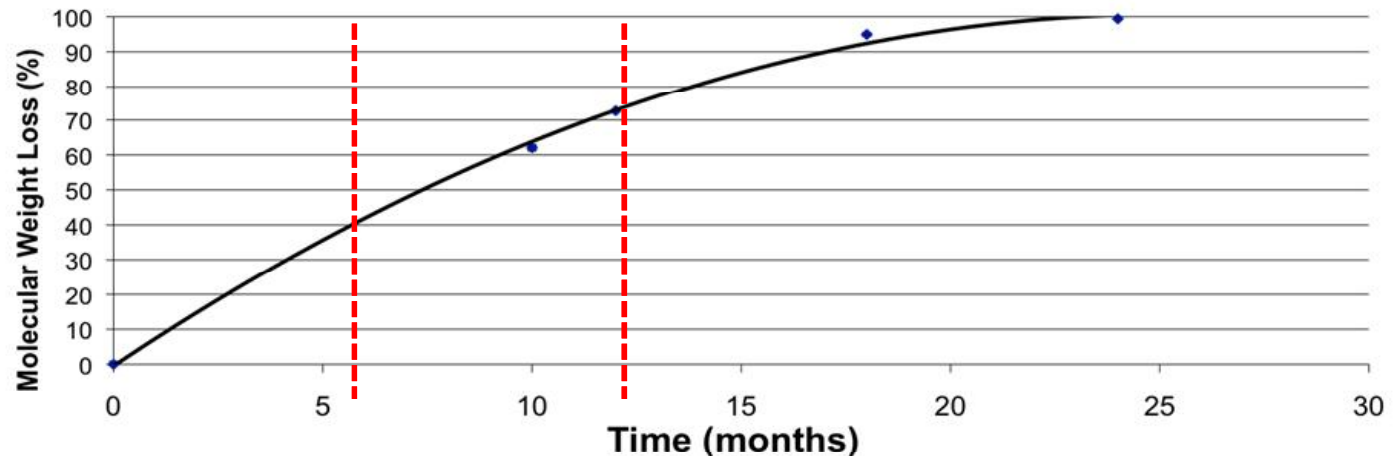
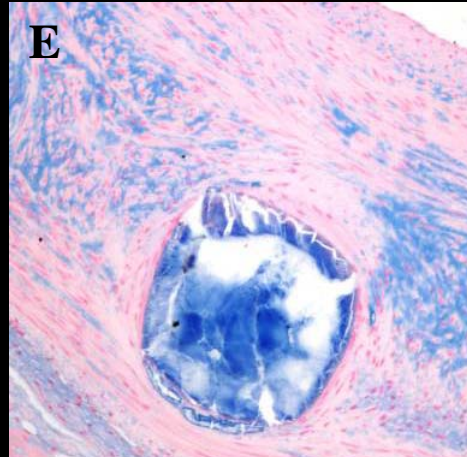
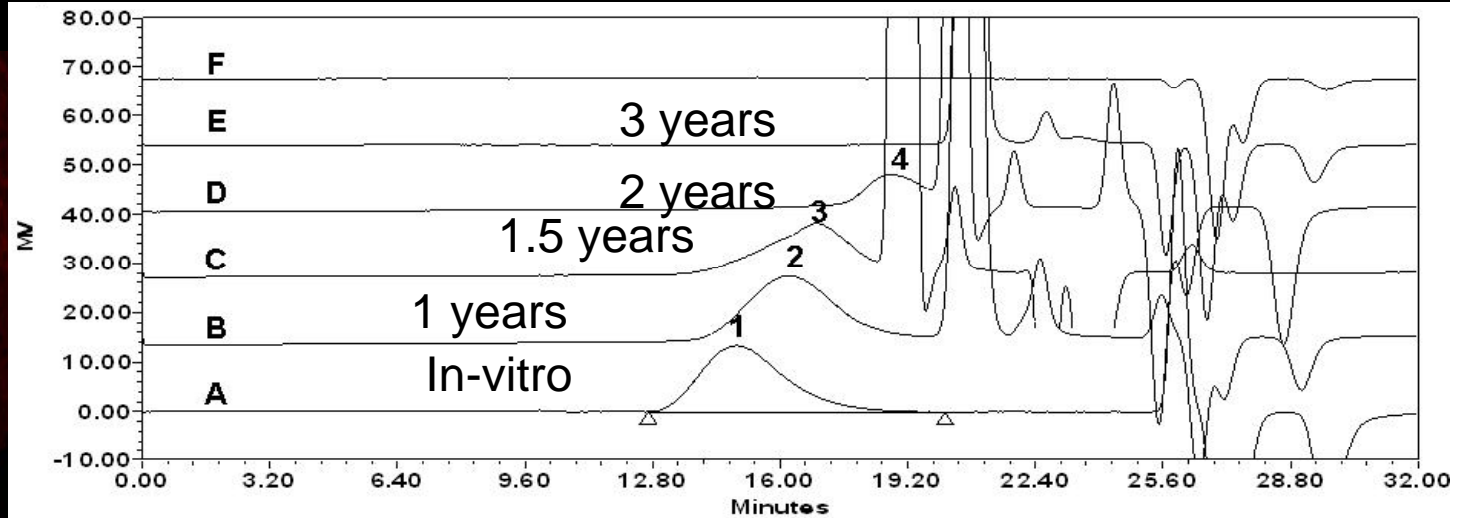
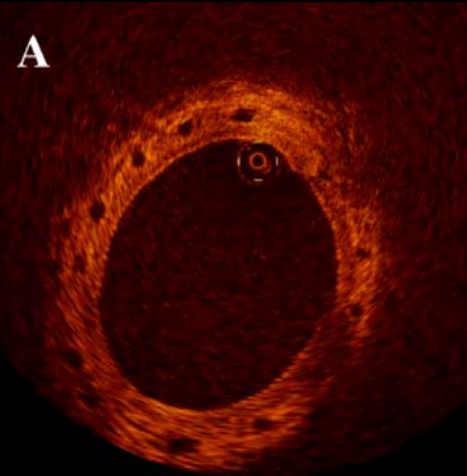
Learn and Live®

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

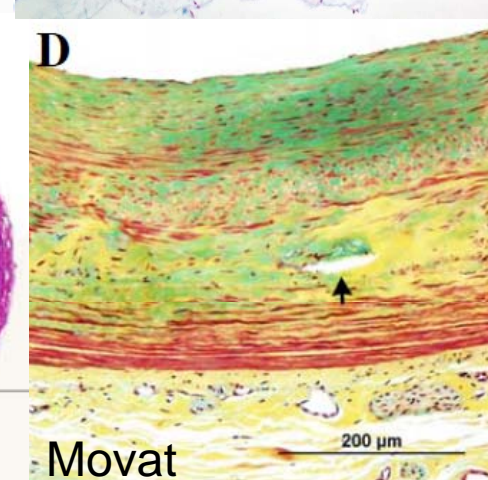
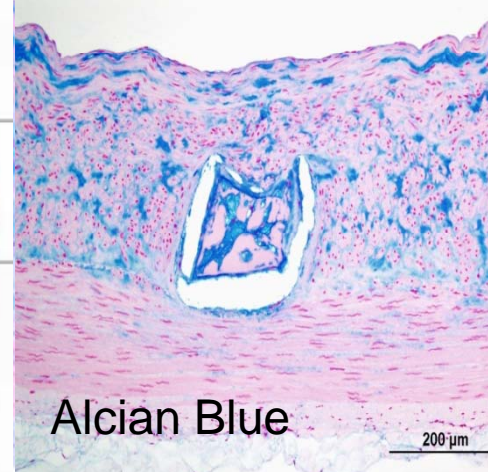
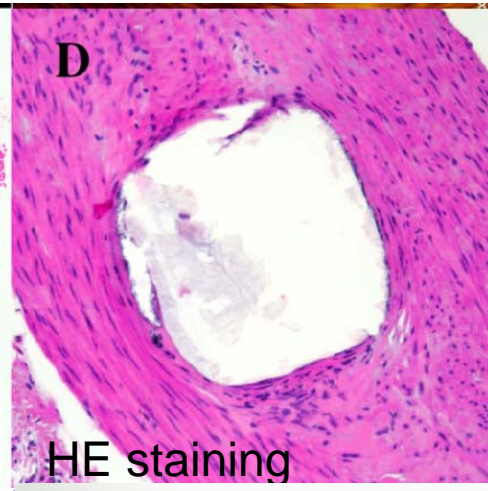
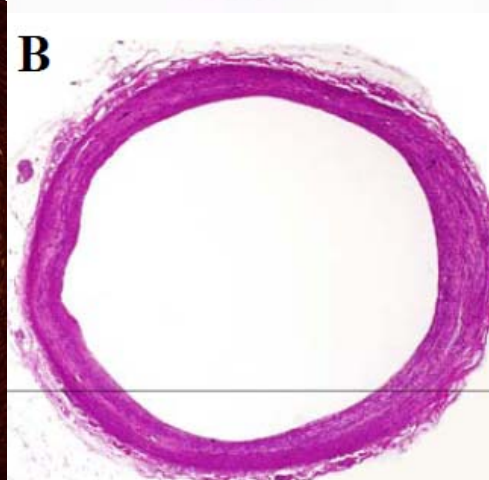
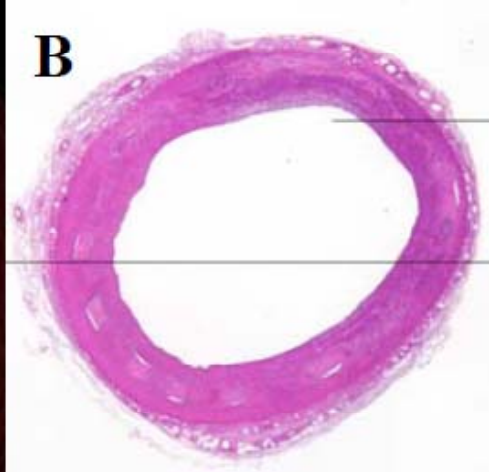
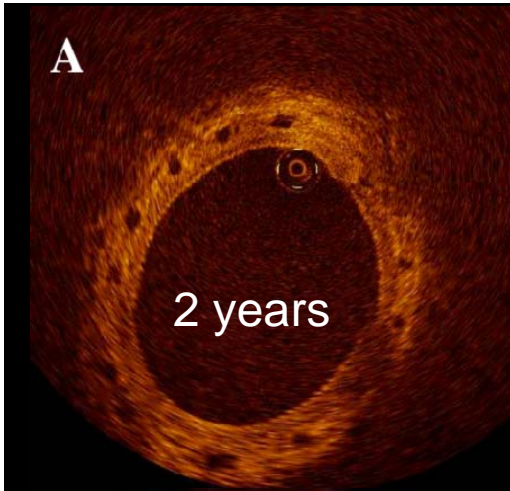
An Attempt to Decipher the Human Optical Coherence Tomography Images in the A Bioabsorbable Everolimus-Eluting Coronary Stent System (ABSORB) Trial

Yoshinobu Onuma, MD*; Patrick Serruys, MD, PhD*; Laura Perkins, DVM, PhD; Takayuki Okamura, MD; Nieves Gonzalo, MD; Hector M. Garcia-Garcia, MD, PhD; Evelyn Regar, MD, PhD; Marika Kamberi, PhD; Jennifer C. Powers, BS; Richard Rapoza, PhD; Heleen van Beusekom, PhD; Willem van der Giessen, MD, PhD; Renu Virmani, PhD

OCT and Histology: 2 years after Procedure



A, B: OCT: the "preserved box" appearance of struts
 C, D: Locations of bioresorbed struts readily visible in histological sections stained with HE
 E: Alcian blue fills in the regions previously occupied by the struts (proteoglycan).
 F, G: Neither collagen (red in Trichrome staining) nor smooth muscle (brown in smooth muscle actin immunohistochemical staining) were detected in the strut footprint .
 H: A small rim of calcification in von Kossa staining, corresponding to the location of the PDLLA coating (black arrows, H).



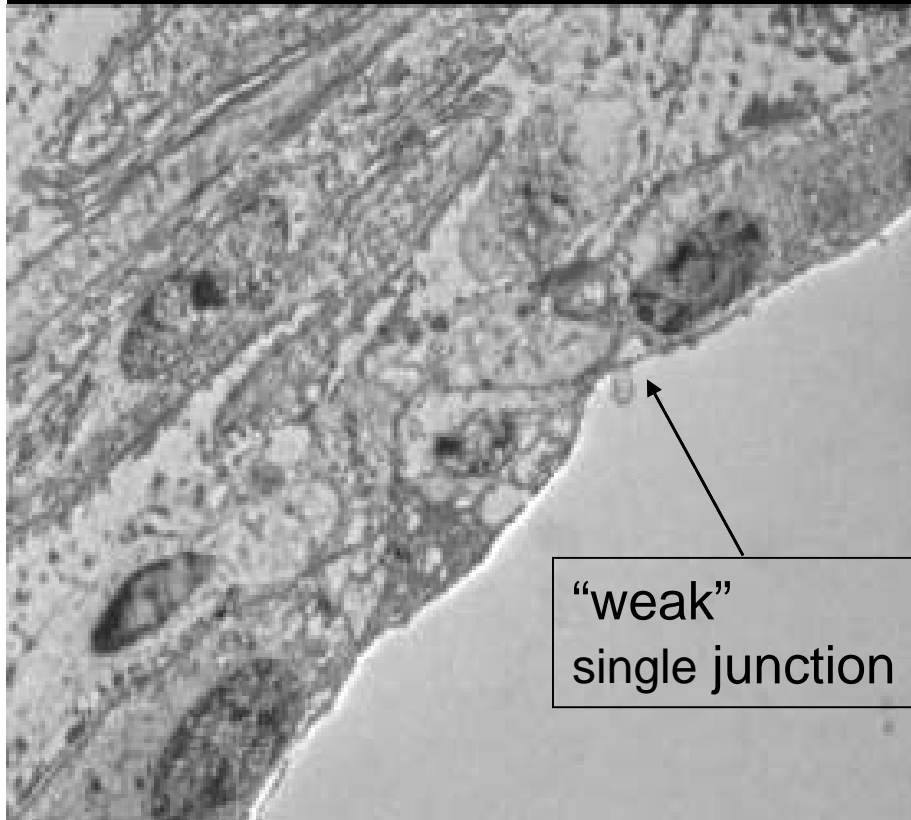
By chromatography, polymeric struts were no longer detectable

Strut voids were filled with young connective tissue and coalesced with vessel wall.

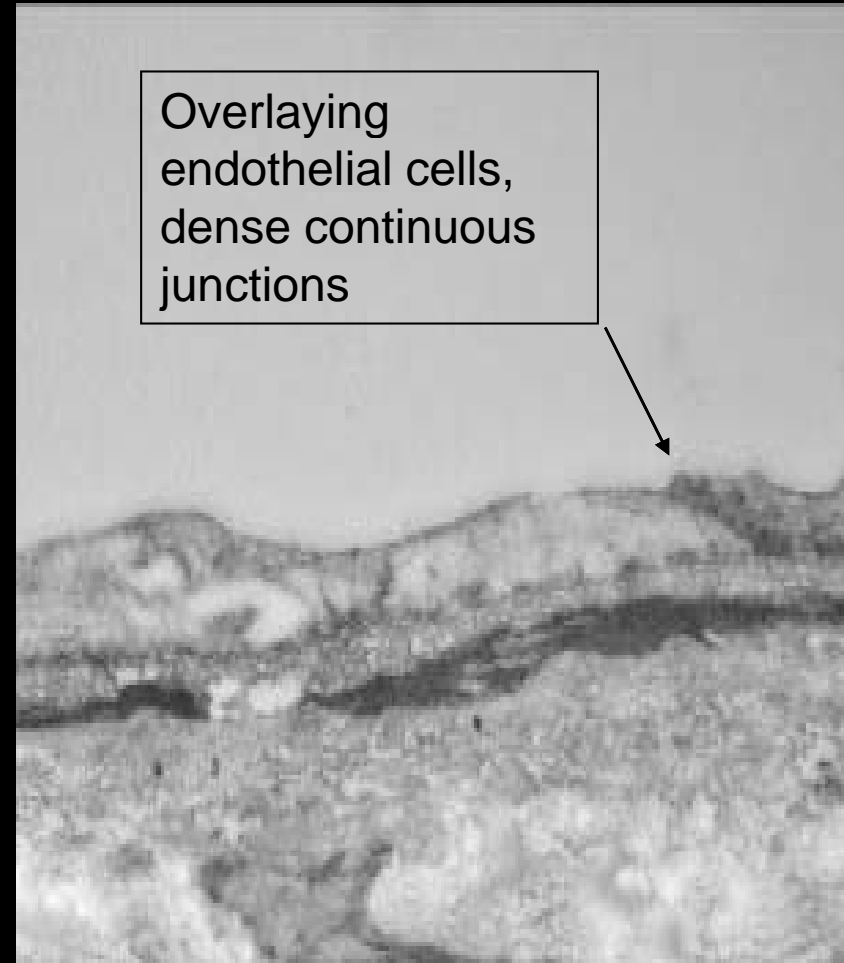
collagen = yellow
proteoglycans/muco polysaccharides = blue/green
SMCs = red
density of smooth muscle cells at the presumed site of polymeric struts.

Maturation of endothelial cell junctions

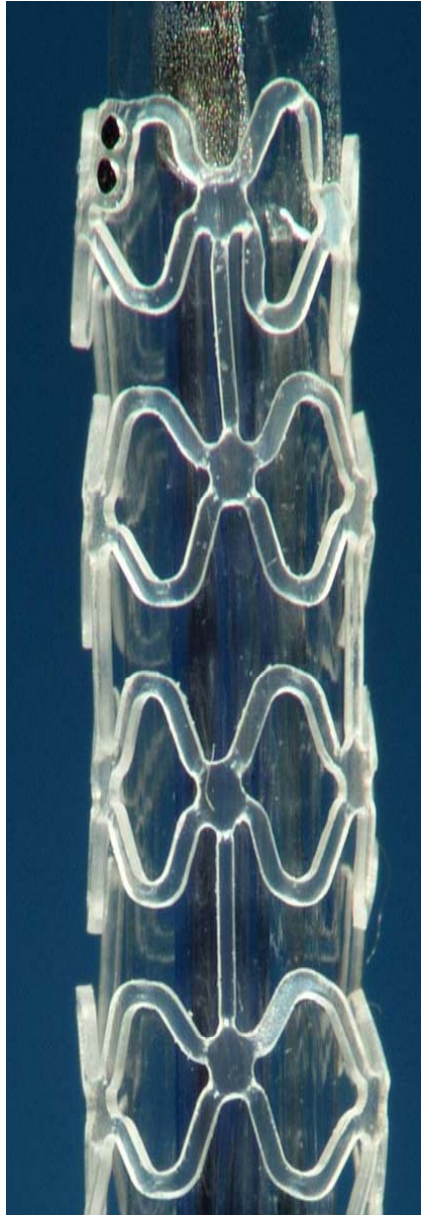
1 month BVS



48 month BVS

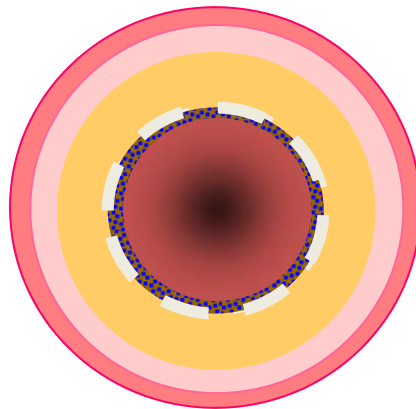


Background I: The first generation of everolimus-eluting bioresorbable scaffold (BVS1.0) showed signs of shrinkage at 6 months (dubbed “late recoil”) that contributed to the late luminal loss.



6 months

**ABSORB
BVS 1.0**



Late Loss = 0.43mm

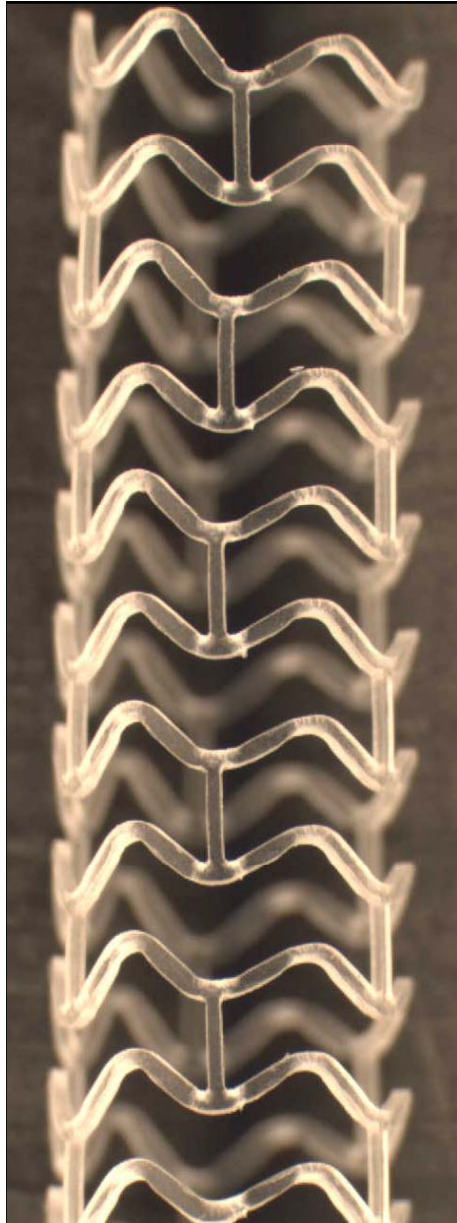
Δ Vessel Area = +0.3%

Δ scaffold Area = -11.8%

% Scaffold Obstruction = 5.3%

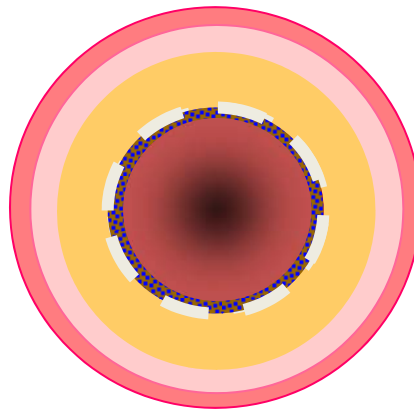
Δ Lumen Area = -16.8%

Background I: The second generation (BVS1.1) has a modified platform design and a different manufacturing process of the polymer.



6 months

**ABSORB
BVS 1.0**

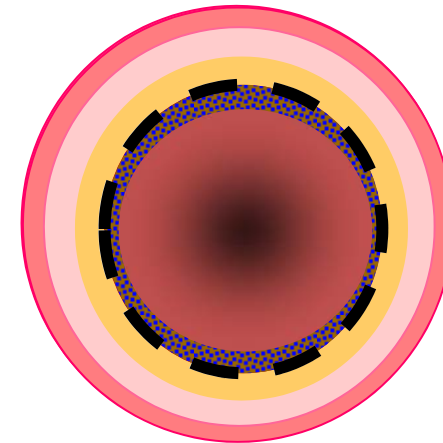


Late Loss = 0.43mm

Δ Vessel Area = +0.3%
 Δ scaffold Area = -11.8%
% Scaffold Obstruction = 5.3%
 Δ Lumen Area = -16.8%

6 months

**ABSORB
BVS 1.1**

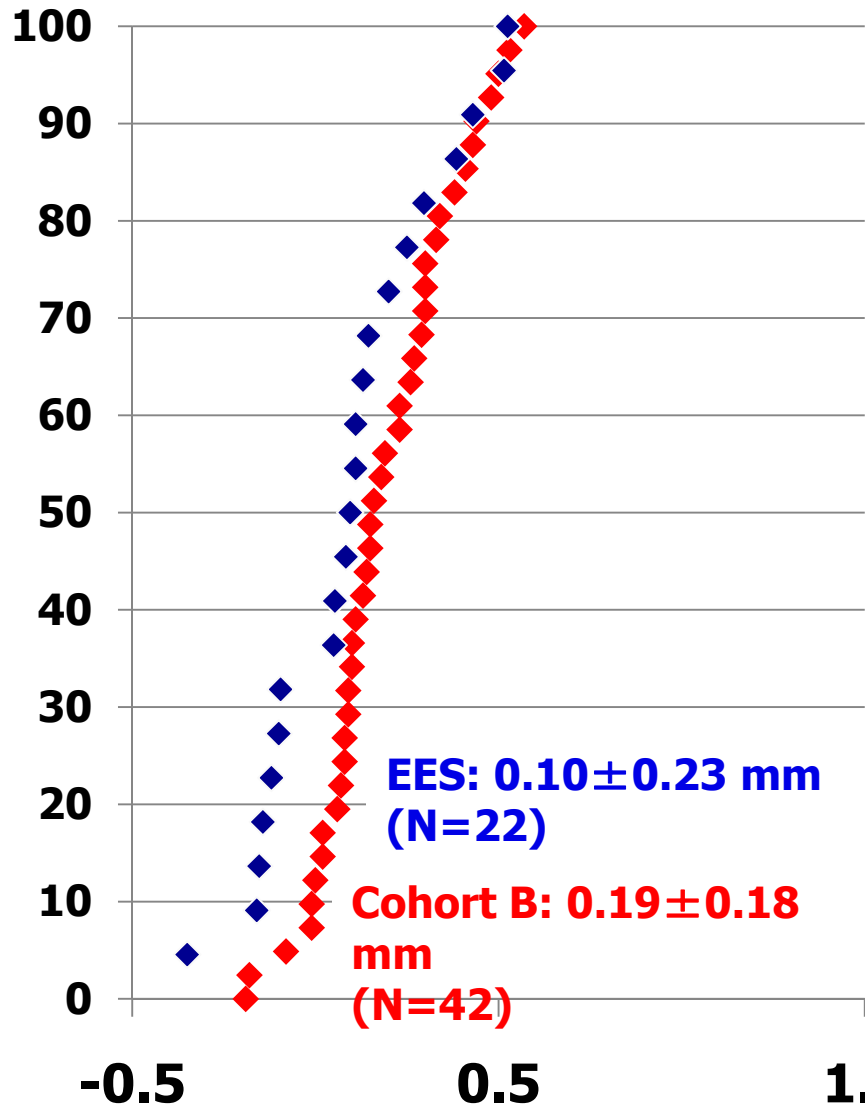


Late Loss = 0.19mm

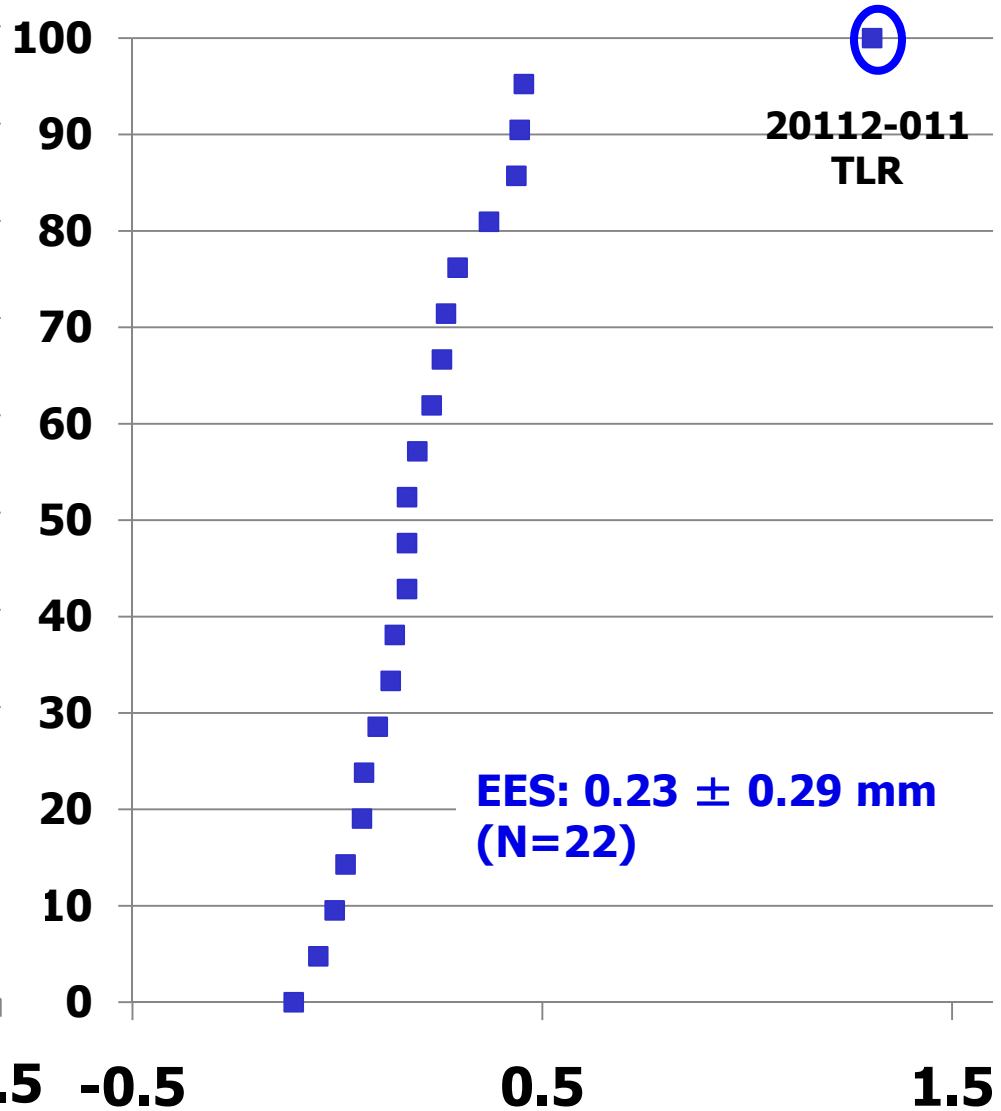
Δ Vessel Area = +2.4%
 Δ Scaffold Area = -2.0%
% Scaffold Obstruction = 1.2%
 Δ Lumen Area = -3.1%

Cumulative frequency distribution curves of Late loss/gain: BVS 1.1 (Cohort B) vs. Xience V (Spirit I)

6 Months (SPIRIT I vs. B1)

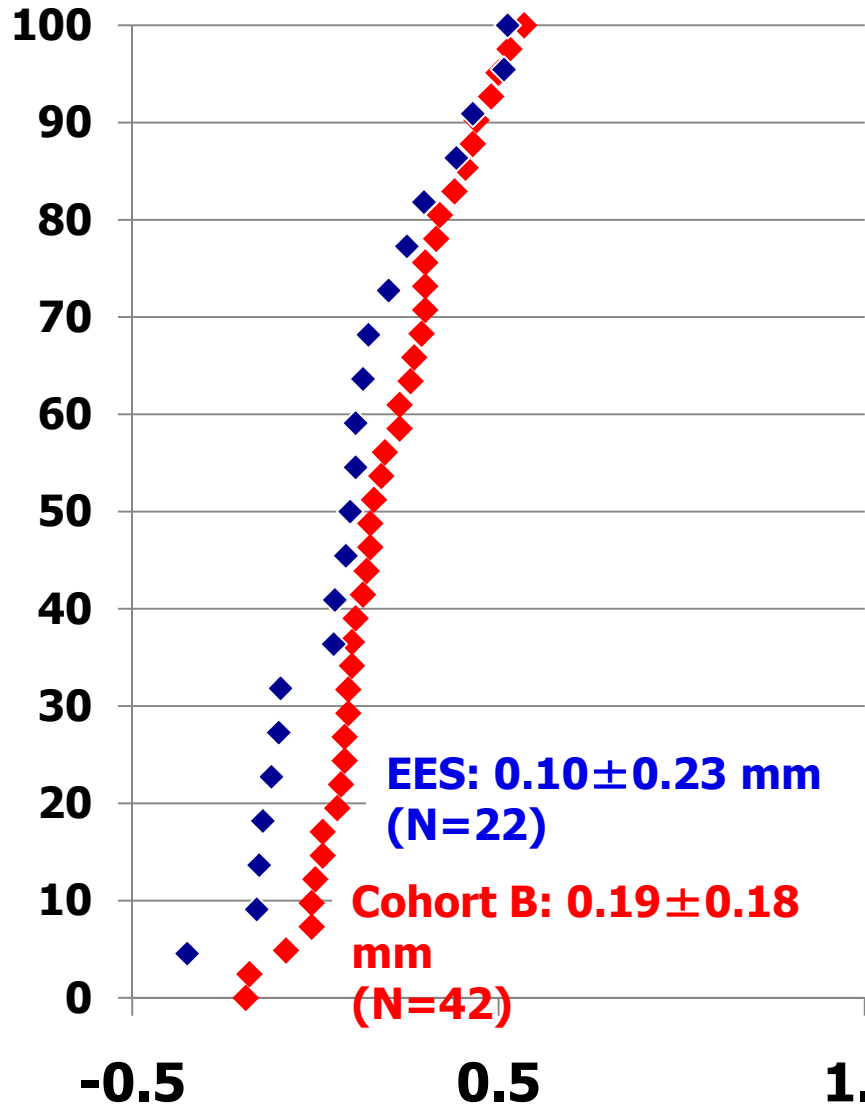


12 Months (SPIRIT I vs. B2)

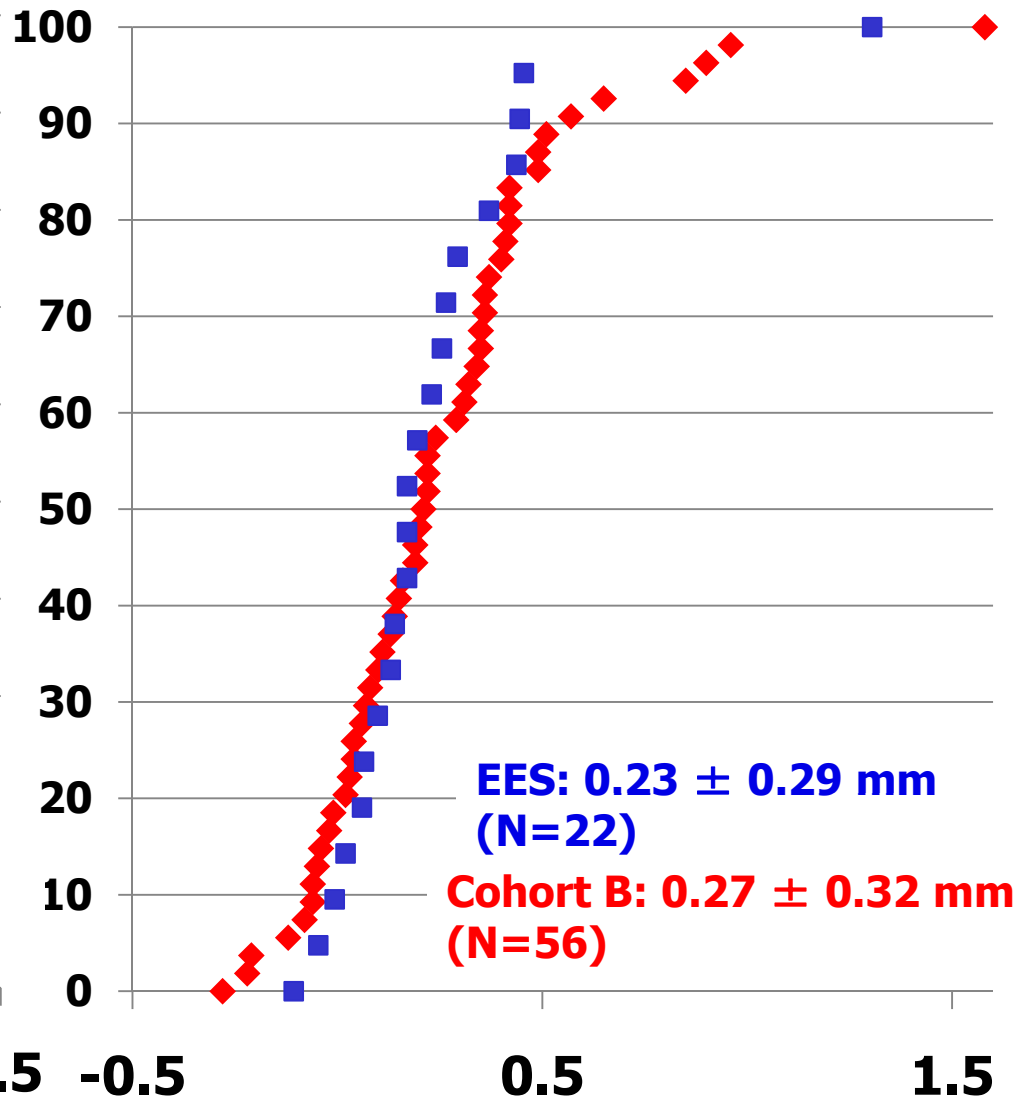


Cumulative frequency distribution curves of Late loss/gain: BVS 1.1 (Cohort B) vs. Xience V (Spirit I)

6 Months (SPIRIT I vs. B1)

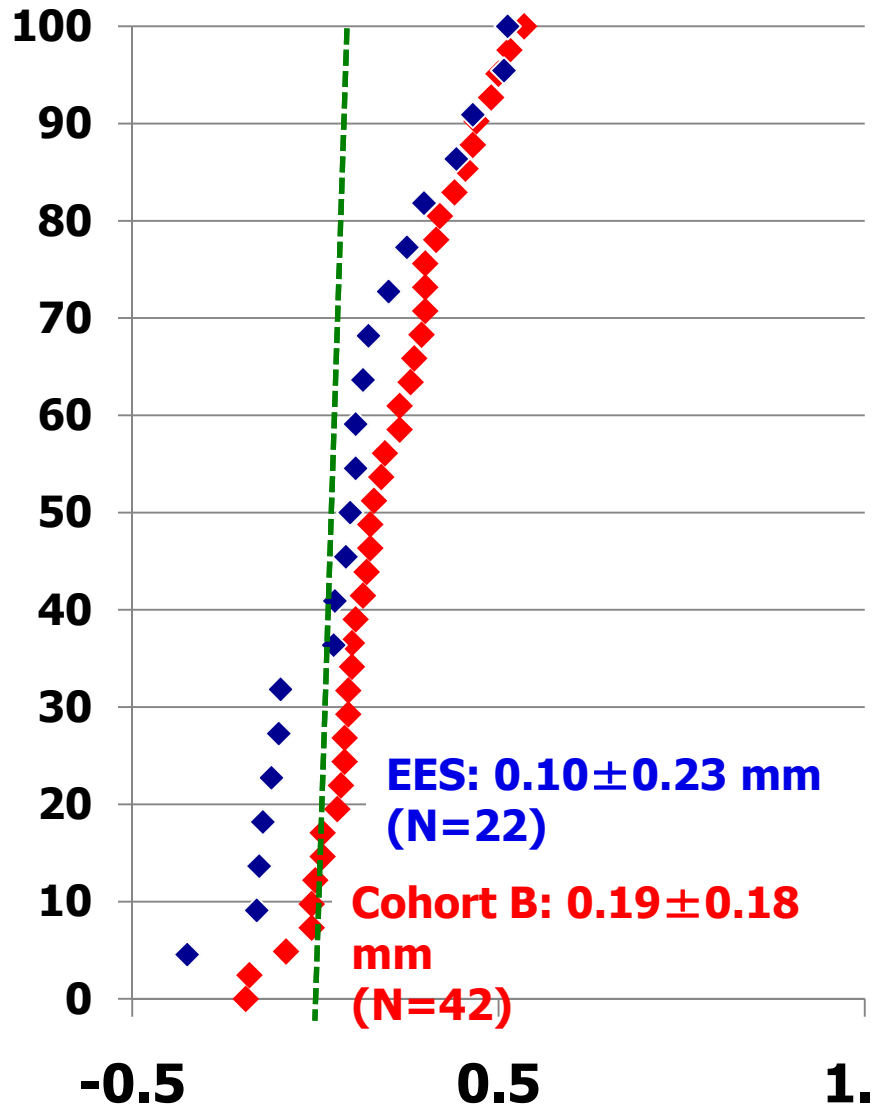


12 Months (SPIRIT I vs. B2)

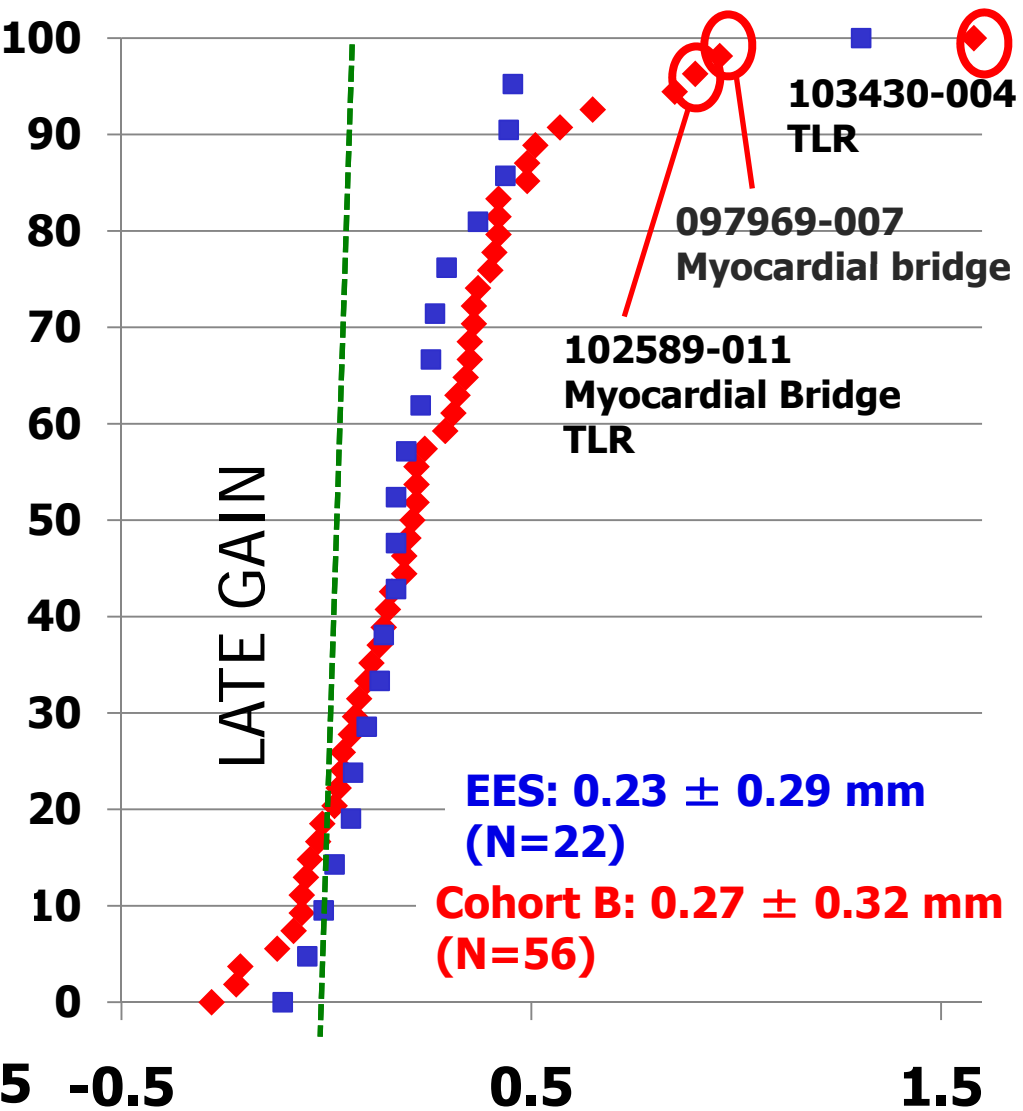


Cumulative frequency distribution curves of Late loss/gain: **BVS 1.1 (Cohort B)** vs. **Xience V (Spirit I)**

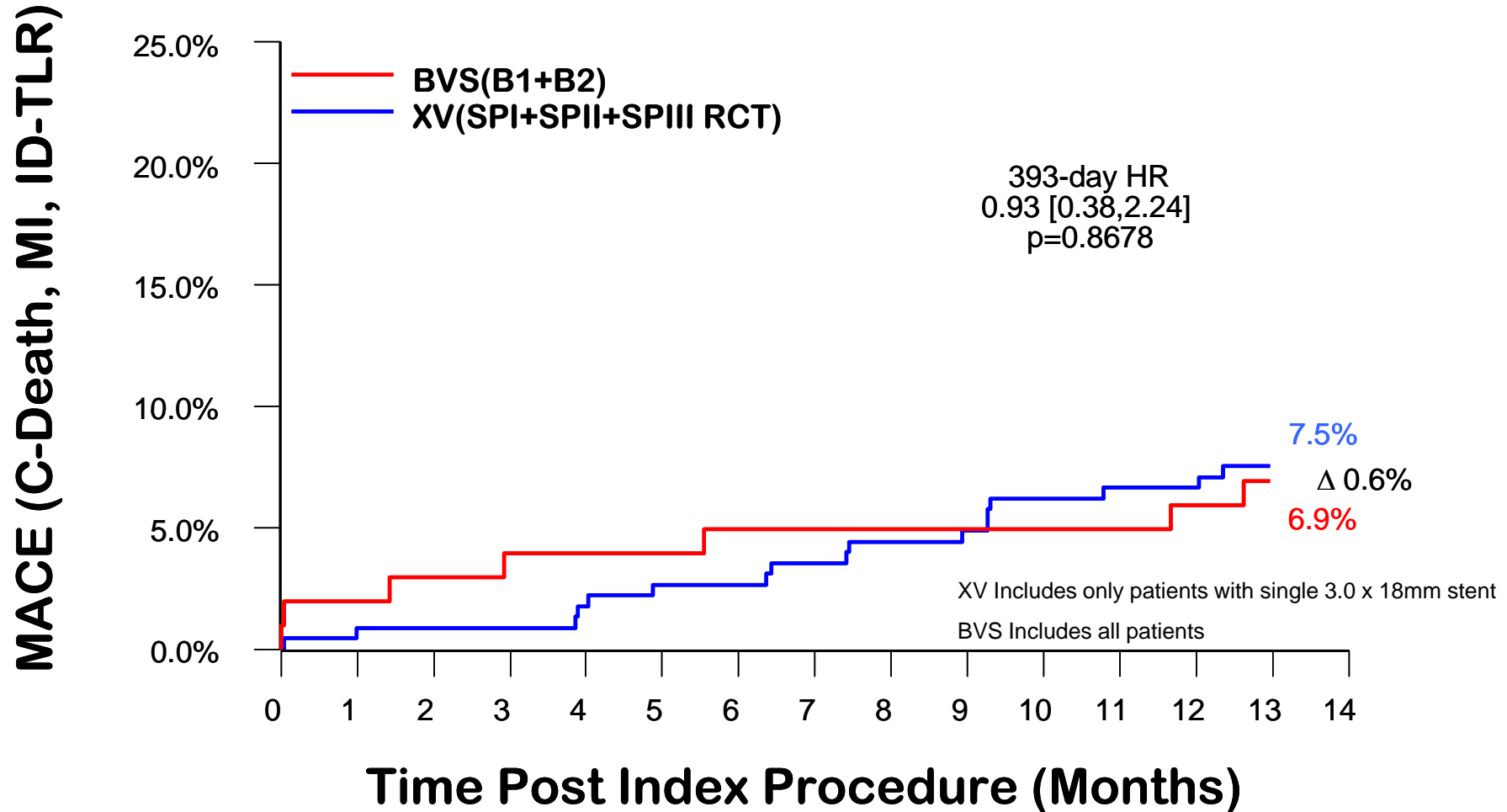
6 Months (SPIRIT I vs. B1)



12 Months (SPIRIT I vs. B2)



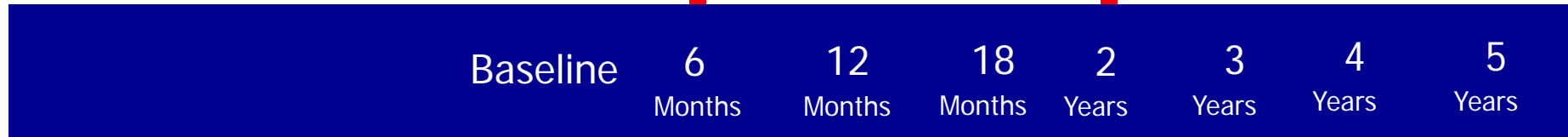
KM estimate of MACE rate in patients treated with BVS (Absorb Cohort B, n=101) vs. patients treated with a single 3x 18 mm metallic EES (Spirit I+II+III, n=227)



Patients at risk	0 days	37 days	194 days	284 days	365 days	393 days
BVS(B1+B2)	101	99	96	96	95	94
XV(SPI+SPII+SPIII RCT)	227	224	219	211	209	208

What did we learn from ABSORB cohort A (2006-2011)?


QCA, IVUS, OCT, IVUS VH



MSCT

A bioabsorbable everolimus-eluting coronary stent system for patients with single de-novo coronary artery lesions (ABSORB): a prospective open-label trial Lancet, 2008

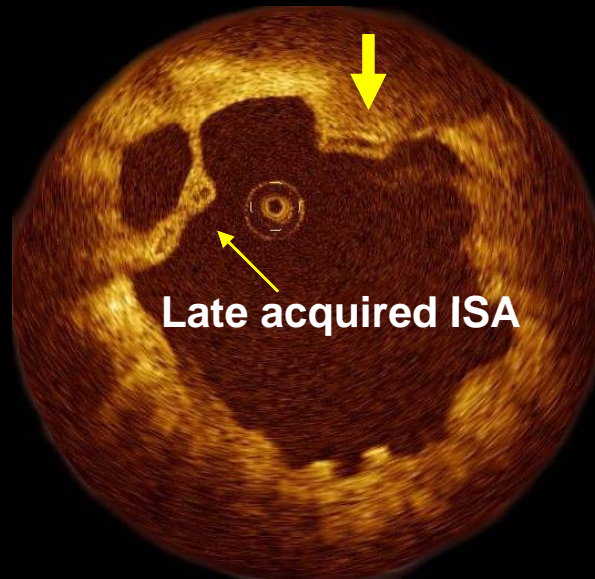
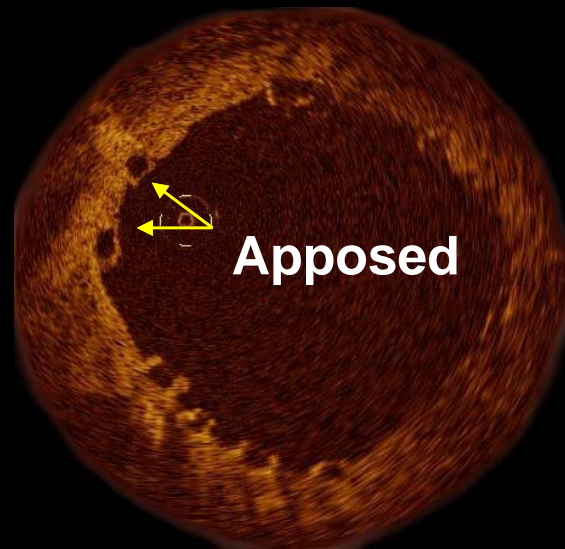
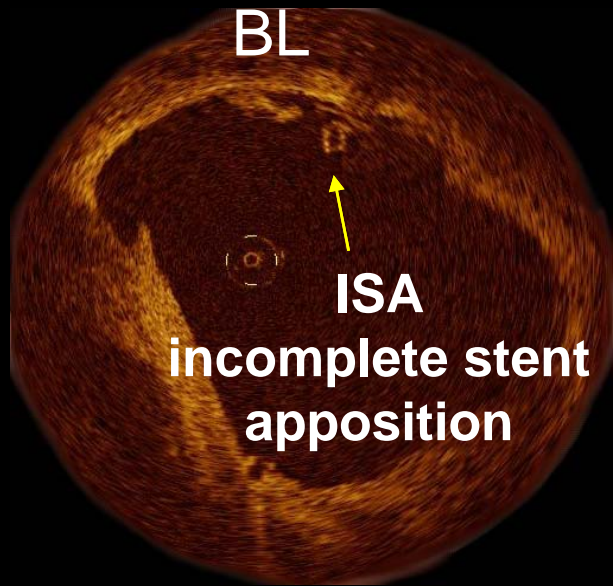
John A Ormiston, Patrick W Serruys, Evelyn Regar, Dariusz Dudek, Leif Thuesen, Mark W I Webster, Yoshinobu Onuma, Hector M Garcia-Garcia, Robert McGreevy, Susan Veldhof

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

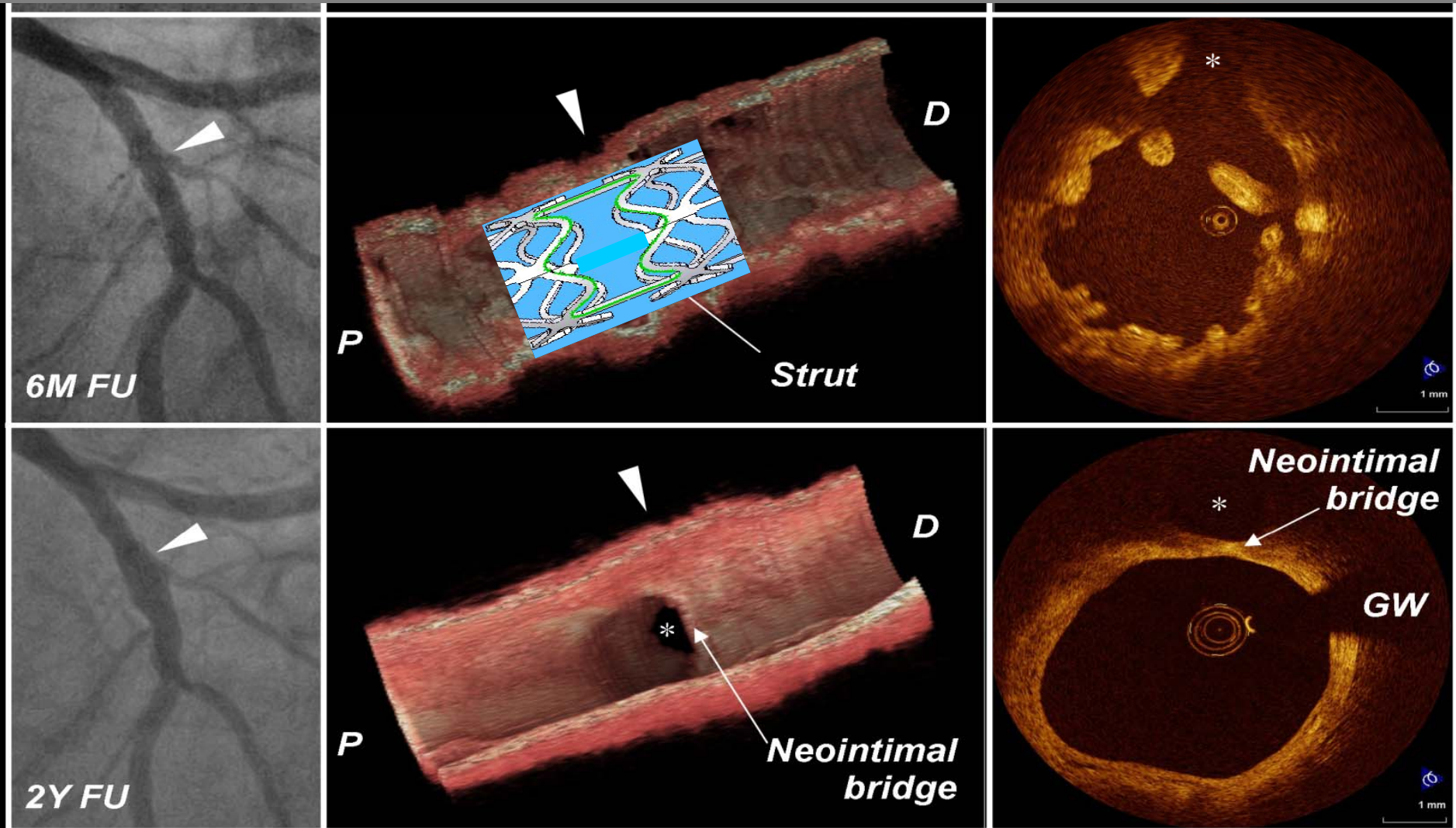
Lancet, 2009

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

#4. Bioresorption and vessel wall integration are real phenomena. (Lancet 2009)



#4. Bioresorption of jailed side branch are real phenomenon. (Okamura et al. EHJ 2010)

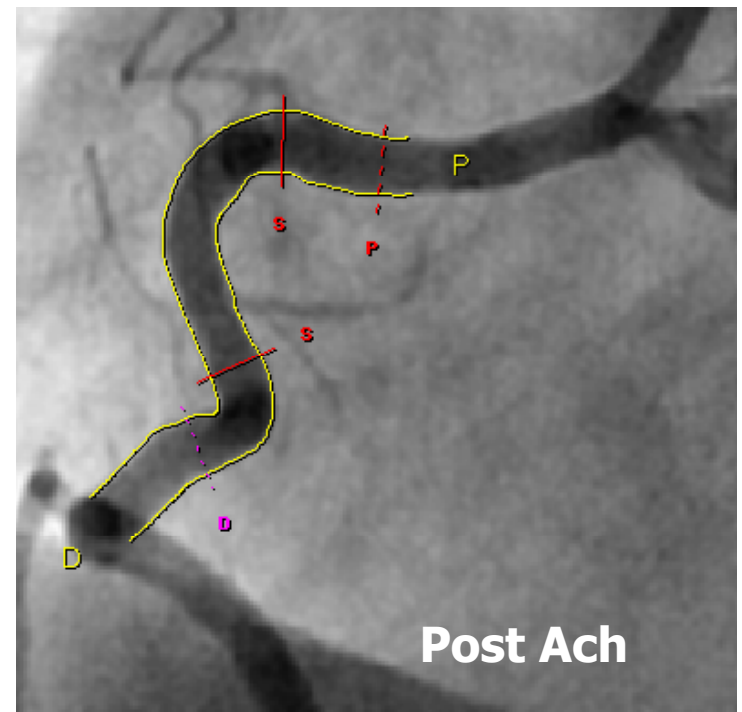
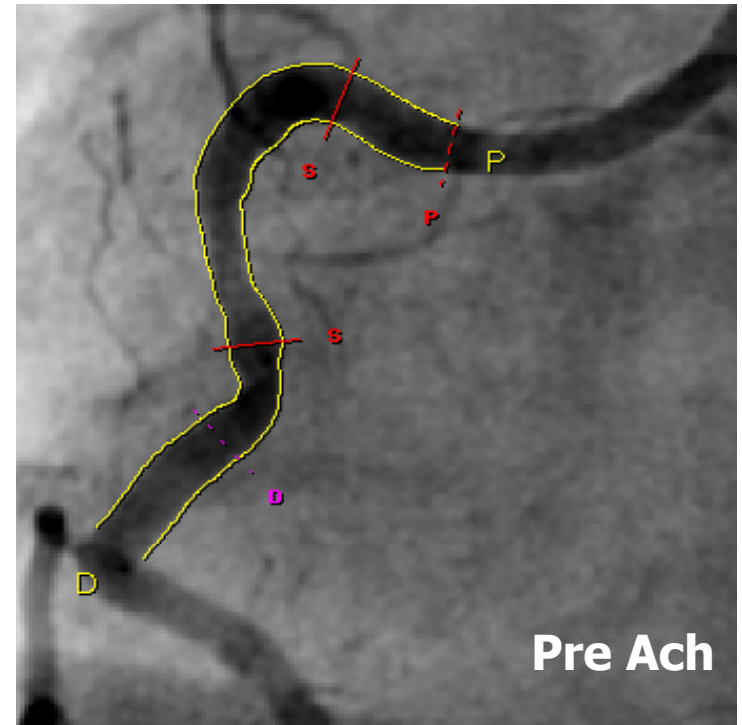
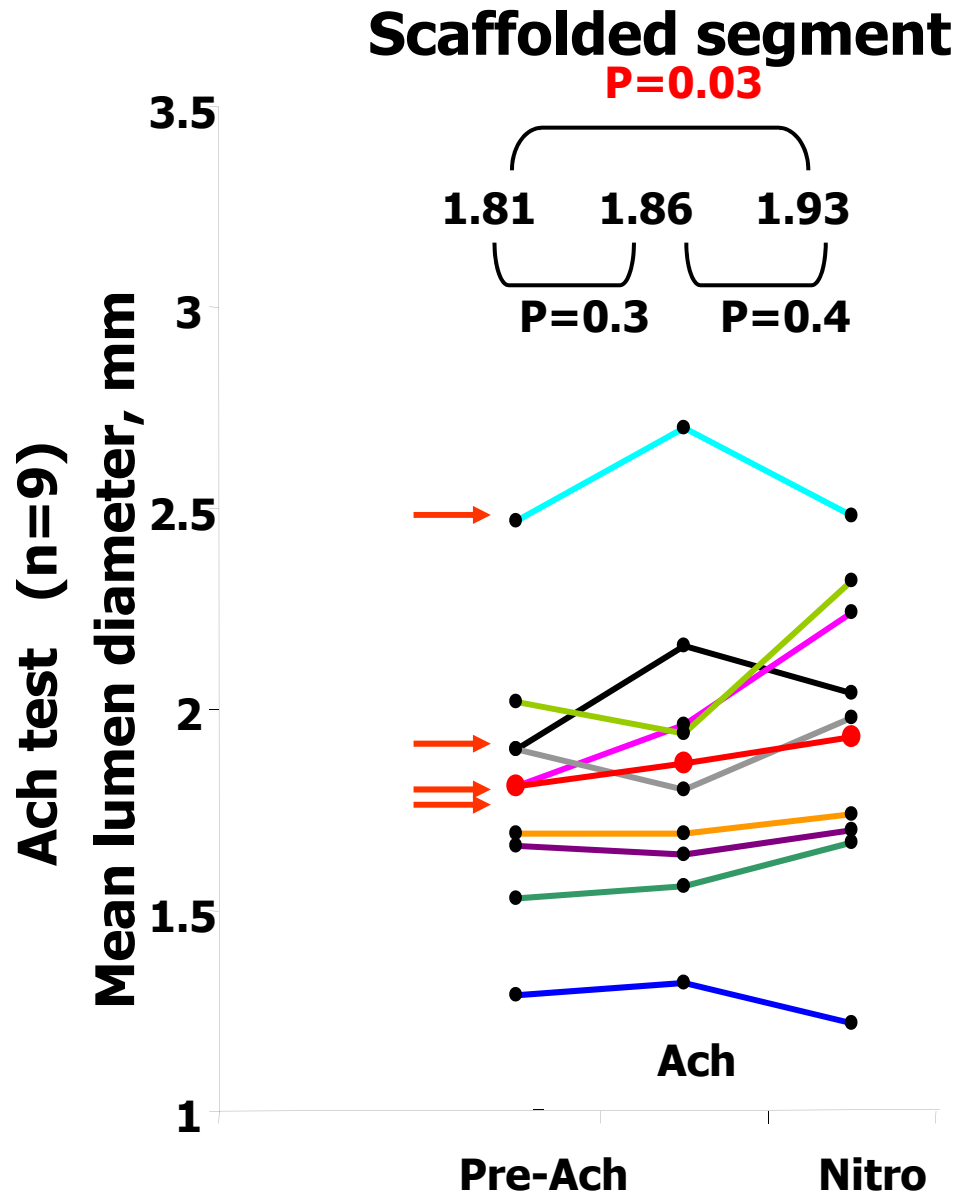


A

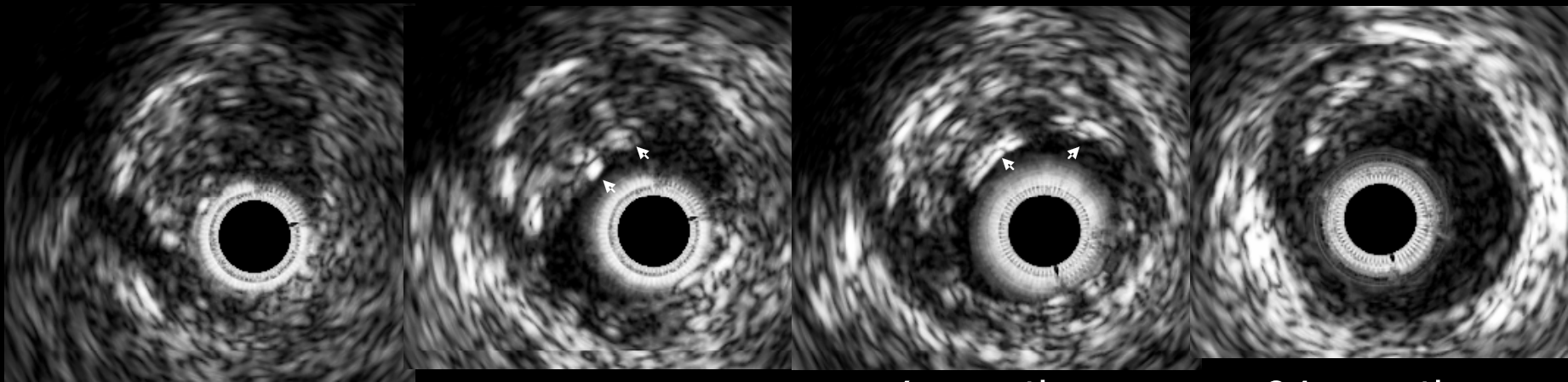
B

C

Endothelium-dependent vasomotion is restored (Lancet 2009)



Bioresorption and vessel wall integration are real phenomena. (Lancet 2009)

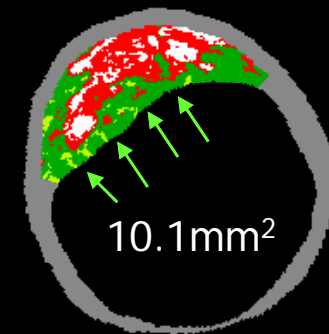
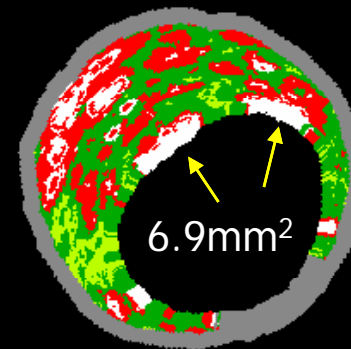
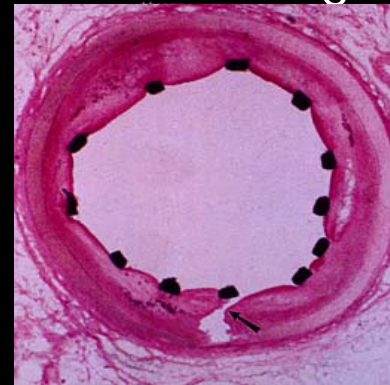


Pre-stenting

Post-stenting

6-month

24-month



Late plaque reduction and lumen enlargement have been documented.

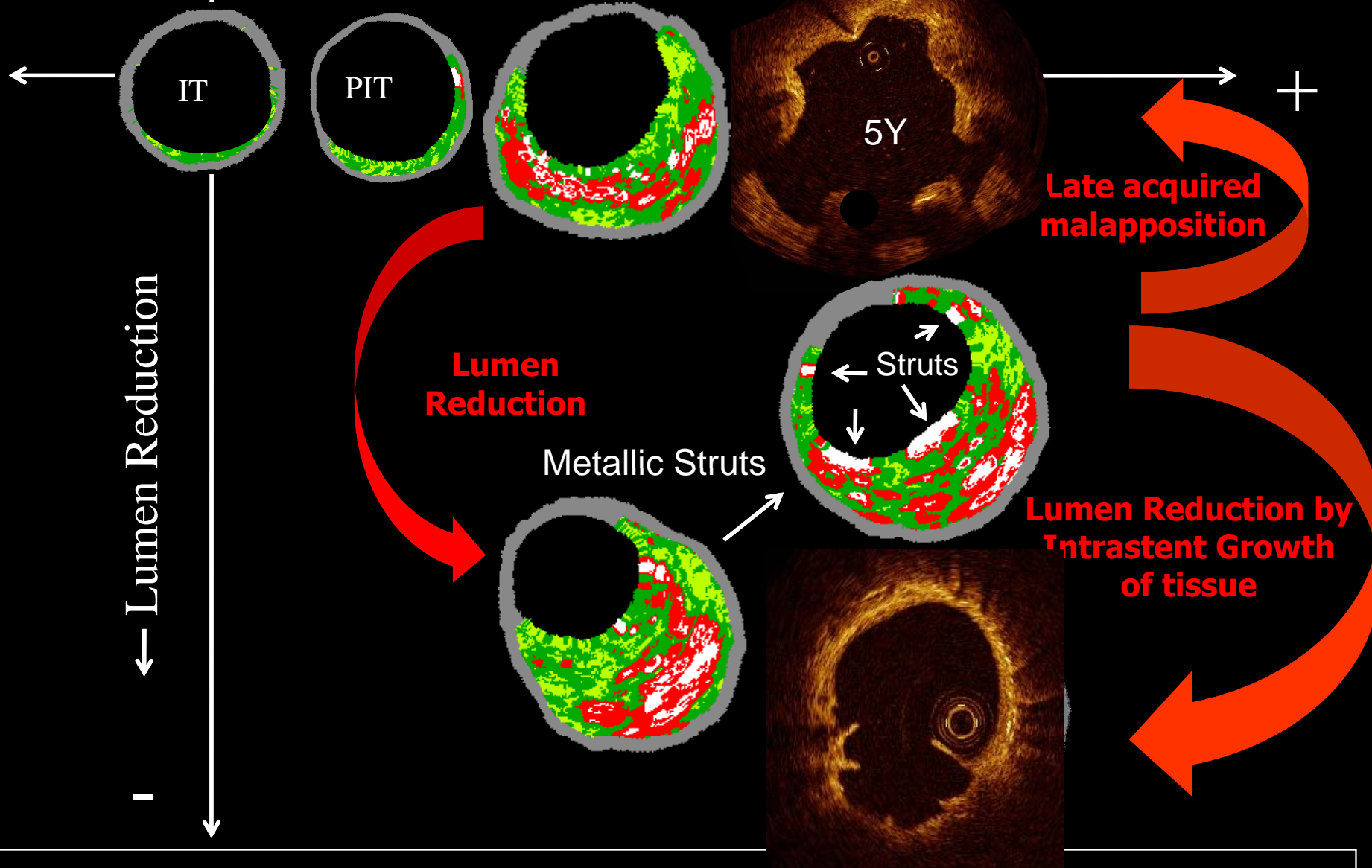
2-Year IVUS Unpaired (BVS1.0)

	Post-PCI n=25	6-month F/U n=25	2-year FU n=18	% Diff (6M to 2Y)	p-value
Vessel (EEM) area (mm ²)	13.49*	13.79	12.68	-3.91	0.08
Lumen area (mm ²)	6.04	5.19 ↗	5.46	+10.85	0.03
Minimal Lumen area (mm ²)	5.09	3.92 ↗	4.35	+17.24	0.005
Plaque area (mm ²)	7.44*	8.60 ↘	7.22	-12.74	<0.001

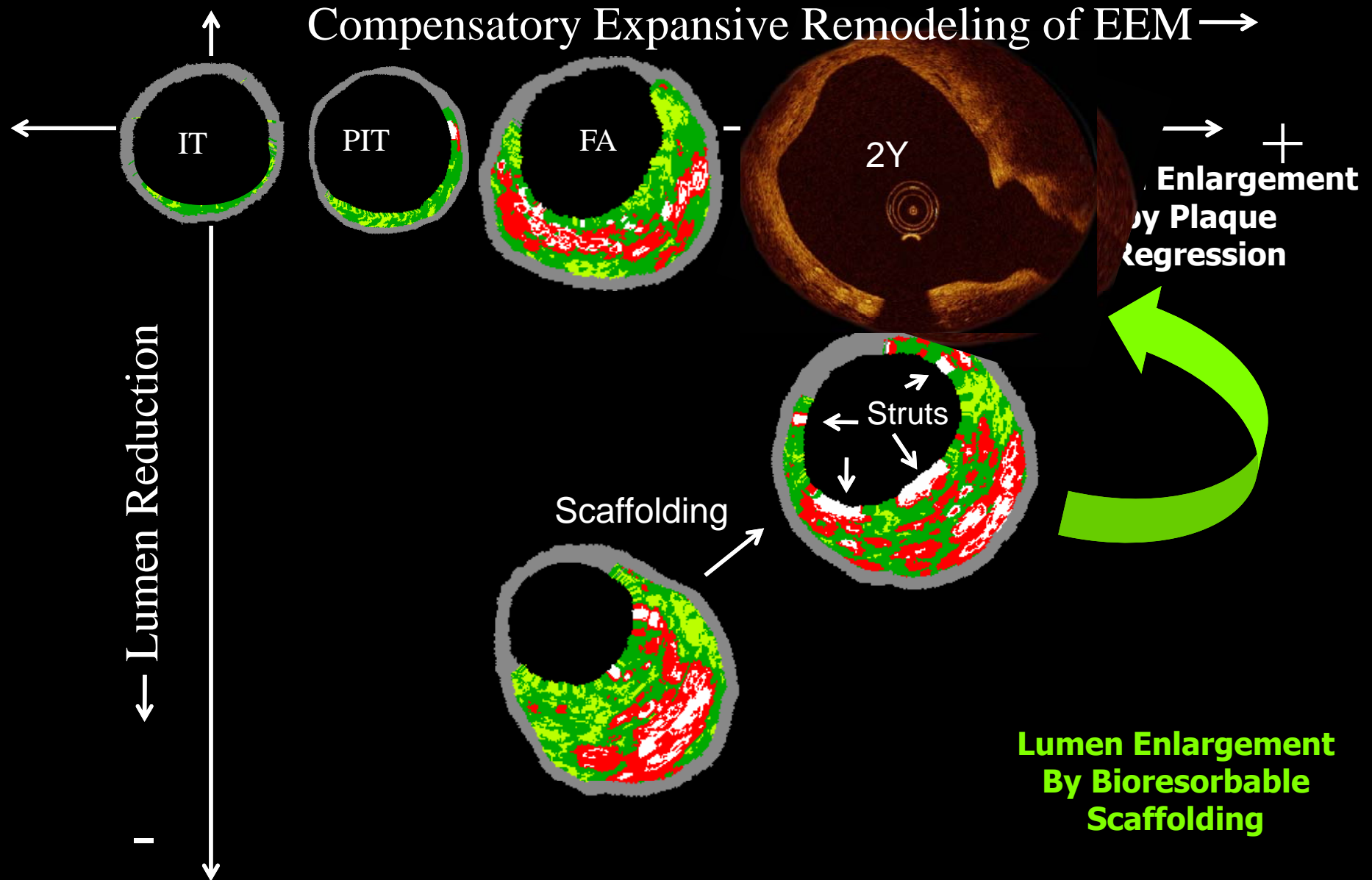
*n=24

P-values per Wilcoxon's signed rank test
% Diff based on paired values

Compensatory Expansive Remodeling of EEM →



Metallic Stent – A caged lumen doomed to get reduced, or a cage doomed to get malapposed



Bioresorbable Scaffold – A new treatment Paradigm for Atherosclerotic Plaque

#8 No acute/Subacute/Late stent thrombosis up to 4 years

4 Year Clinical Results – Intent to Treat

Hierarchical	6 Months 30 Patients
Ischemia Driven MACE, %(n)	3.3% (1)*
Cardiac Death, %	0.0%
MI, %(n)	
Q-Wave MI	0.0%
Non Q-Wave MI	3.3% (1)**
Ischemia Driven TLR , %	
by PCI	0.0%
by CABG	0.0%

No new MACE events between 6 months and 4 years
No stent thrombosis up to 4 years (All patients off clopidogrel)

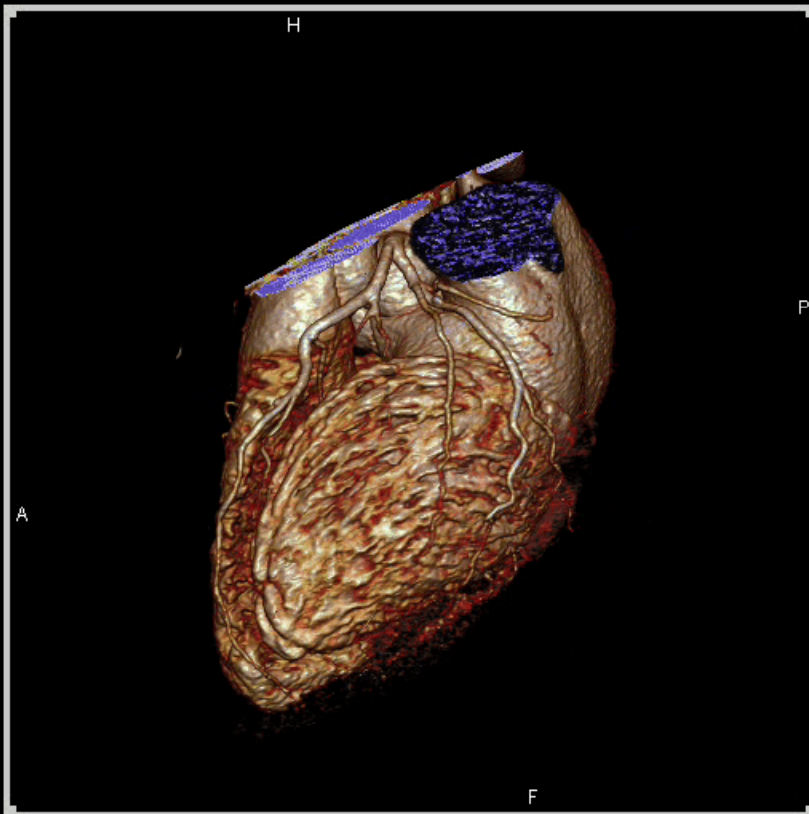
*One patient withdrew consent after 6 months but the vital status of the patients and absence of cardiac event is known through the referring physician.

**This patient also underwent a TLR, not qualified as ID-TLR (DS = 42%) followed by post-procedural troponin qualified as non-Q MI and died from his Hodgkin's disease at 888 days post-procedure.

Ormiston et al. 2008, Serruys et al. 2009, Onuma et al. 2010

Non-invasive imaging for early and late follow-up is now feasible.

Case 1 (5YR FU)

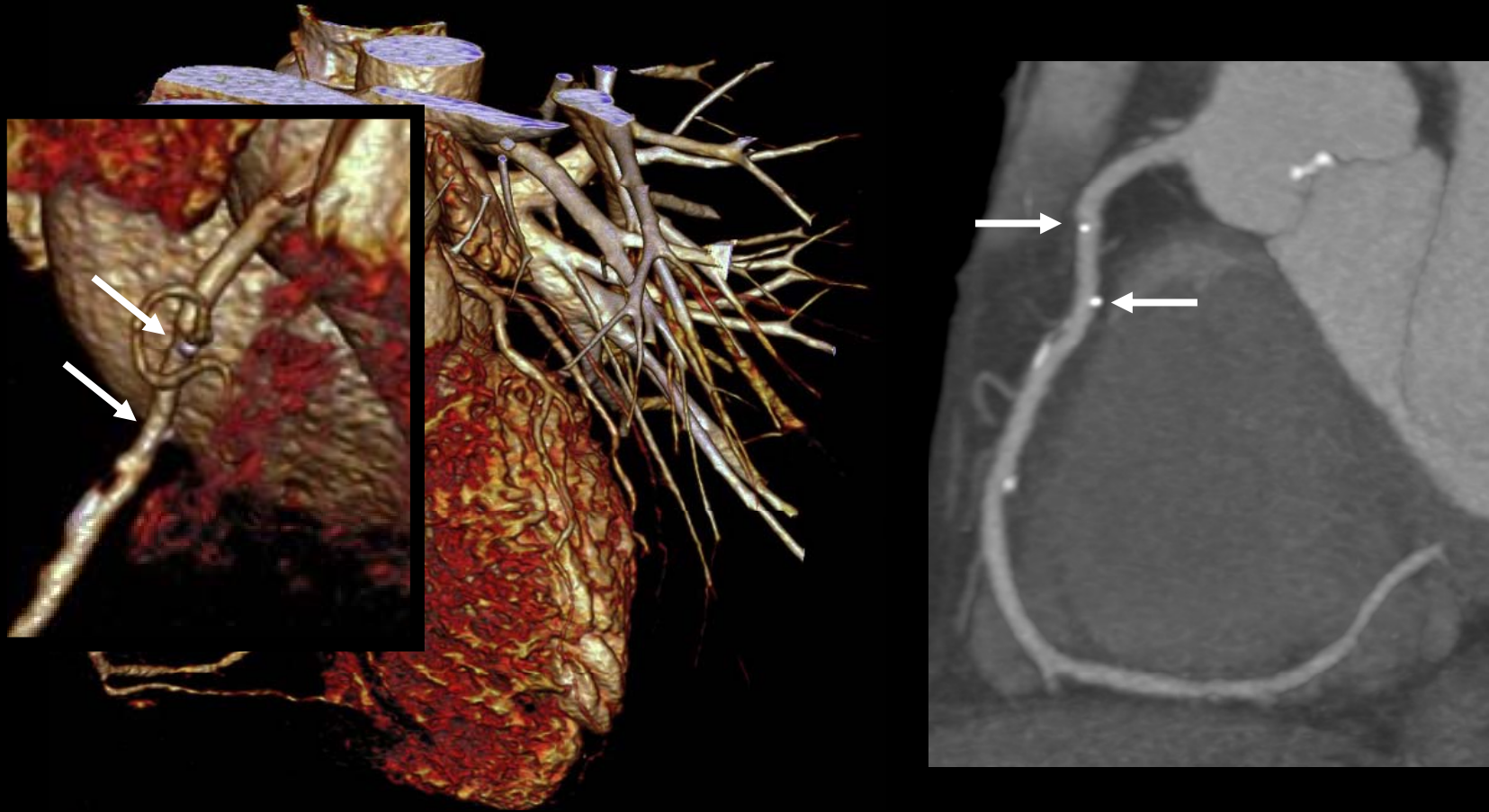


BVS proximal RCA

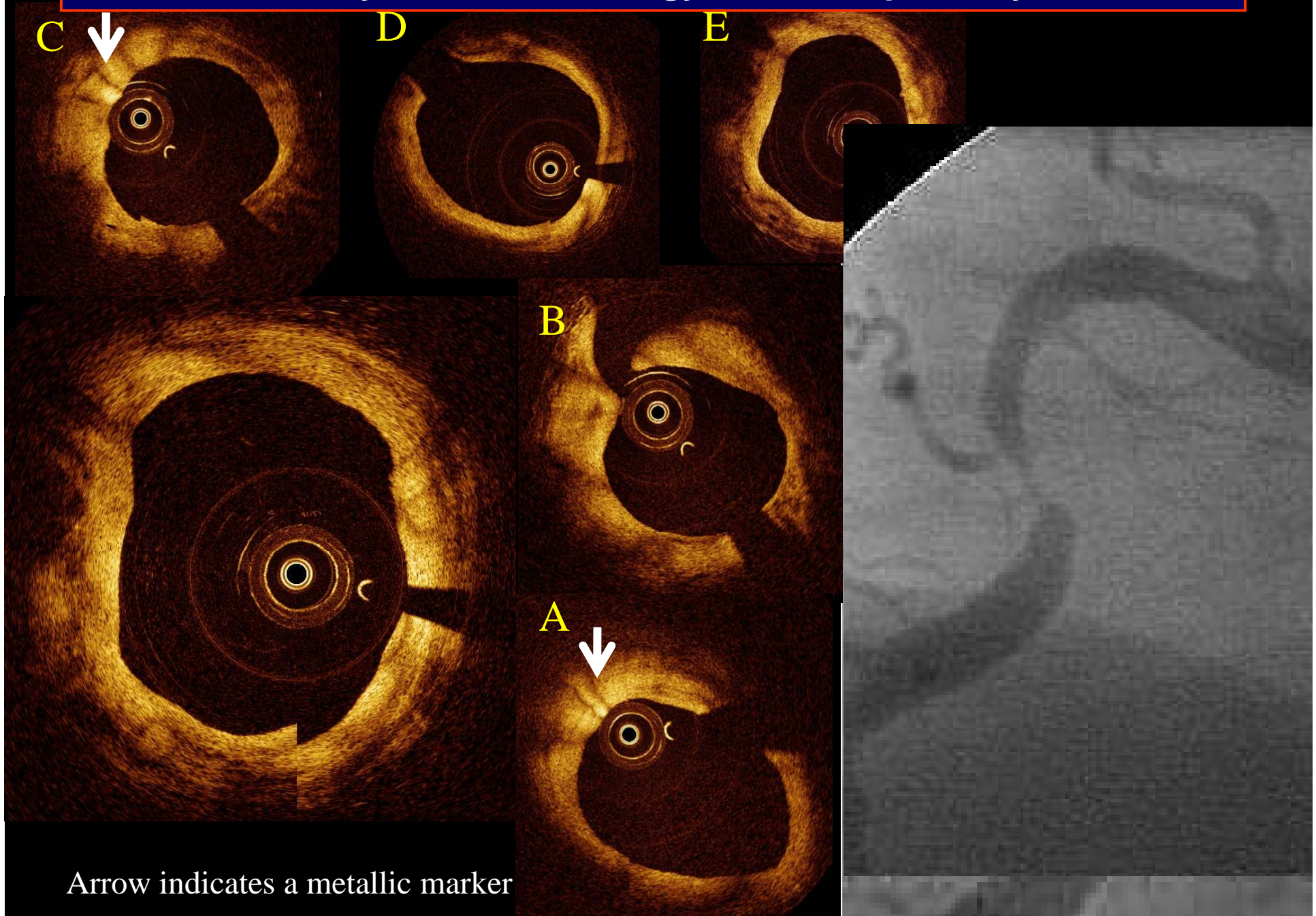
Prospective mode 128-DSCT
Diastolic exposure (HR 53)
100 Kv tube voltage
Effective dose 2.5 mSv



Case 1 (5YR FU)



the safety of this technology remains up to 10 years.



Arrow indicates a metallic marker

The Promise of biodegradable scaffolding as a vessel restoration device

- 1. Bioresorbable drug-eluting vascular scaffold treatment consists of implanting a transient scaffold made of the most common human molecule (lactic-acid). This scaffold is more flexible than Xience and is highly conformable to the vessel.**
- 2. Acute recoil is comparable to the metallic stents. Acute malapposition and jailed side branch fully disappeared within two years.**
- 3. BVS does not hinder shear stress from inducing late luminal enlargement and compensatory expansive remodeling.**

