

SOLACI 2012

**Bioabsorbable Scaffold:
Latest Clinical Performance**

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Bioresorbable Scaffold – Rationale and Goals

- Revascularize the vessel like a metallic DES, then resorb naturally into the body.
- Restore vascular response
- Reduce stimulus for chronic inflammation: reducing the need of long-term DAPT
- Facilitate future re-intervention
- Compatibility with non-invasive tests at follow-up (CT and MRI)

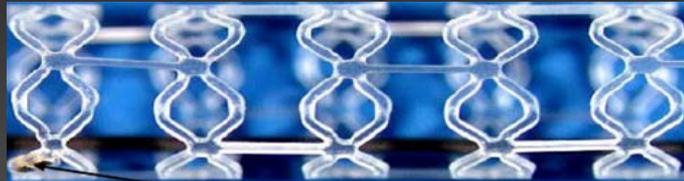
Bioresorbable Stents

Igaki-Tamai



PLA

BVS



PLLA

REVA



**Tyrosine-
Policarbonate**

Elixir



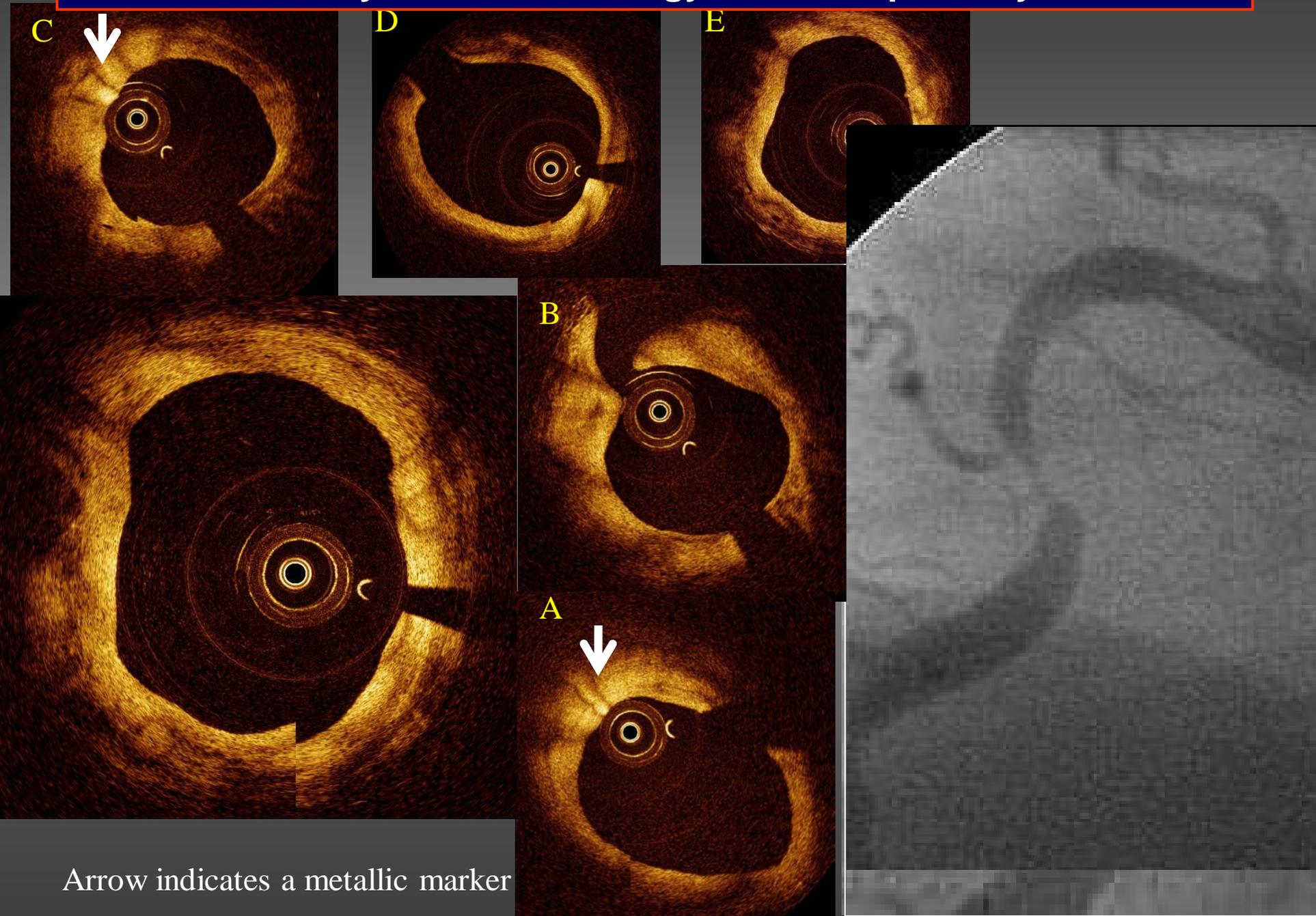
PLLA

Biotronik



Magnesium

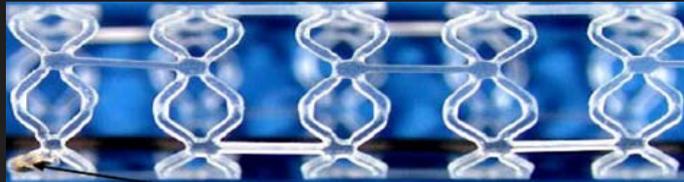
The safety of this technology remains up to 10 years.



Arrow indicates a metallic marker

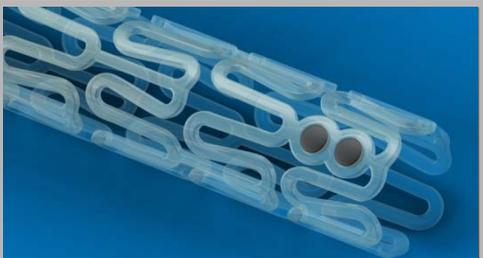
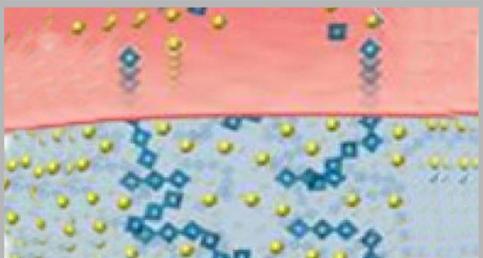
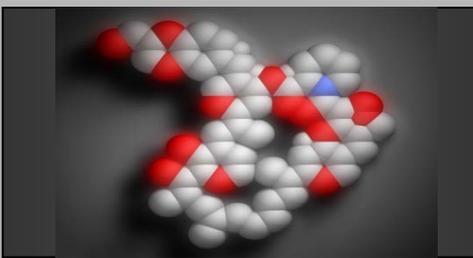
Bioresorbable Stents

BVS (Abbott)

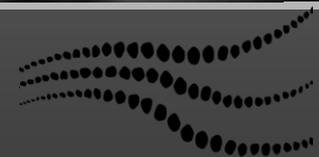


PLLA

Everolimus-Eluting Bioresorbable Vascular Scaffold

ML VISION Delivery System	Bioresorbable Device Platform	Bioresorbable Coating	Everolimus
<ul style="list-style-type: none">• Seven generations of MULTI-LINK success• World-class deliverability	<ul style="list-style-type: none">• Polylactide (PLLA)• Naturally resorbed, fully metabolized	<ul style="list-style-type: none">• Polylactide (PDLLA) coating• Fully biodegradable	<ul style="list-style-type: none">• Similar dose and release rate to XIENCE V
			

All illustrations are artists' renditions



ABSORB Global Clinical Program

Building Evidence

First in Man

- Cohort A
- Cohort B

Expanding Experience

- ABSORB Extend
- ABSORB BTK

Novel Endpoints

- ABSORB II
- ABSORB Physiology

Pivotal Trials and LandMark Analysis

- ABSORB RCT
- ABSORB Japan
- ABSORB China

ABSORB Cohort A

Completed

Principal Investigators:
Patrick Serruys, John Ormiston



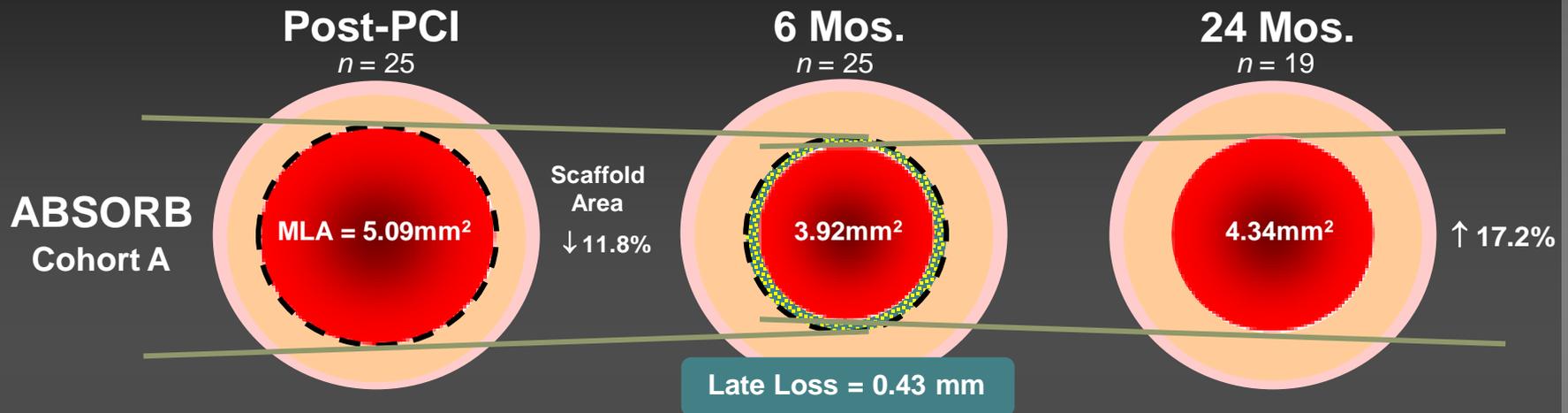
- Prospective, open label, single arm study.
- 30 patients enrolled at 4 sites
- Device sizes: 3.0 x 12 mm; 3.0 x 18 mm in two patients
- Treatment: single *de novo* lesion
- Follow-up schedule:

OCA, OCT, IVUS, VH

Clinical Baseline 6 mo 12 mo 18 mo 24 mo 36 mo 48 mo 60 mo

MSCT follow-up

Temporal Lumen Dimensional Changes, Per Treatment

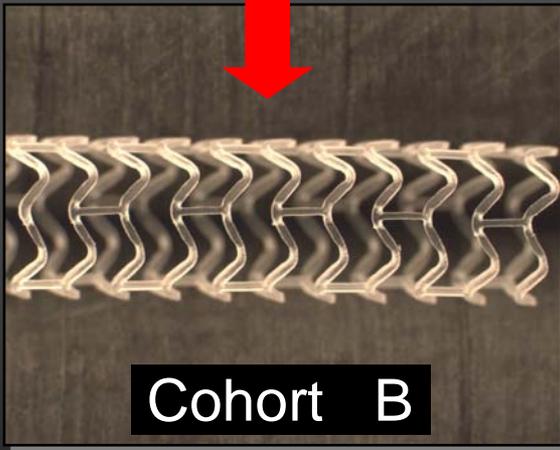
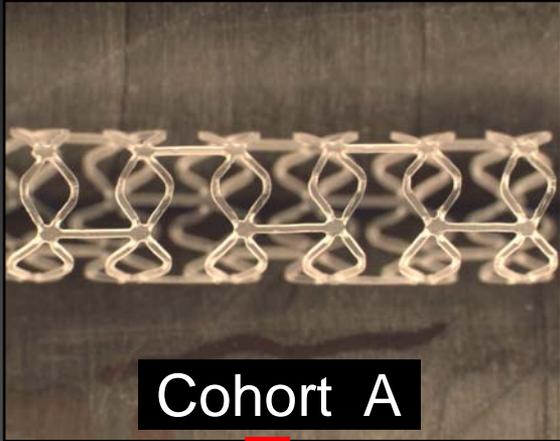


Late lumen loss at 6 months mainly due to reduction in scaffold area

Very late lumen enlargement noted from 6 months to 2 years

BVS Device Optimization

ABSORB



- More uniform strut distribution
- More even support of arterial wall
- Lower late scaffold area loss
 - Maintain radial strength for at least 3-4 months
- Storage at room temperature
- Improved device retention
- Unchanged:
 - Material, coating and backbone
 - Strut thickness
 - Drug release profile
 - Total degradation Time

ABSORB Cohort B

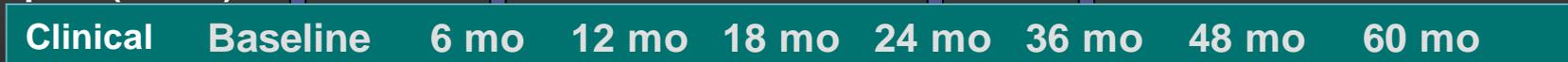
At 2-Year Follow-up

Principal Investigators:
John Ormiston, Patrick Serruys



- Prospective, open label, single arm study.
- 101 patients enrolled at 12 sites
- Device sizes: 3.0 x 18 mm
- Treatment: up to 2 *de novo* lesion
- Follow-up schedule:

Group B1 (n = 45)

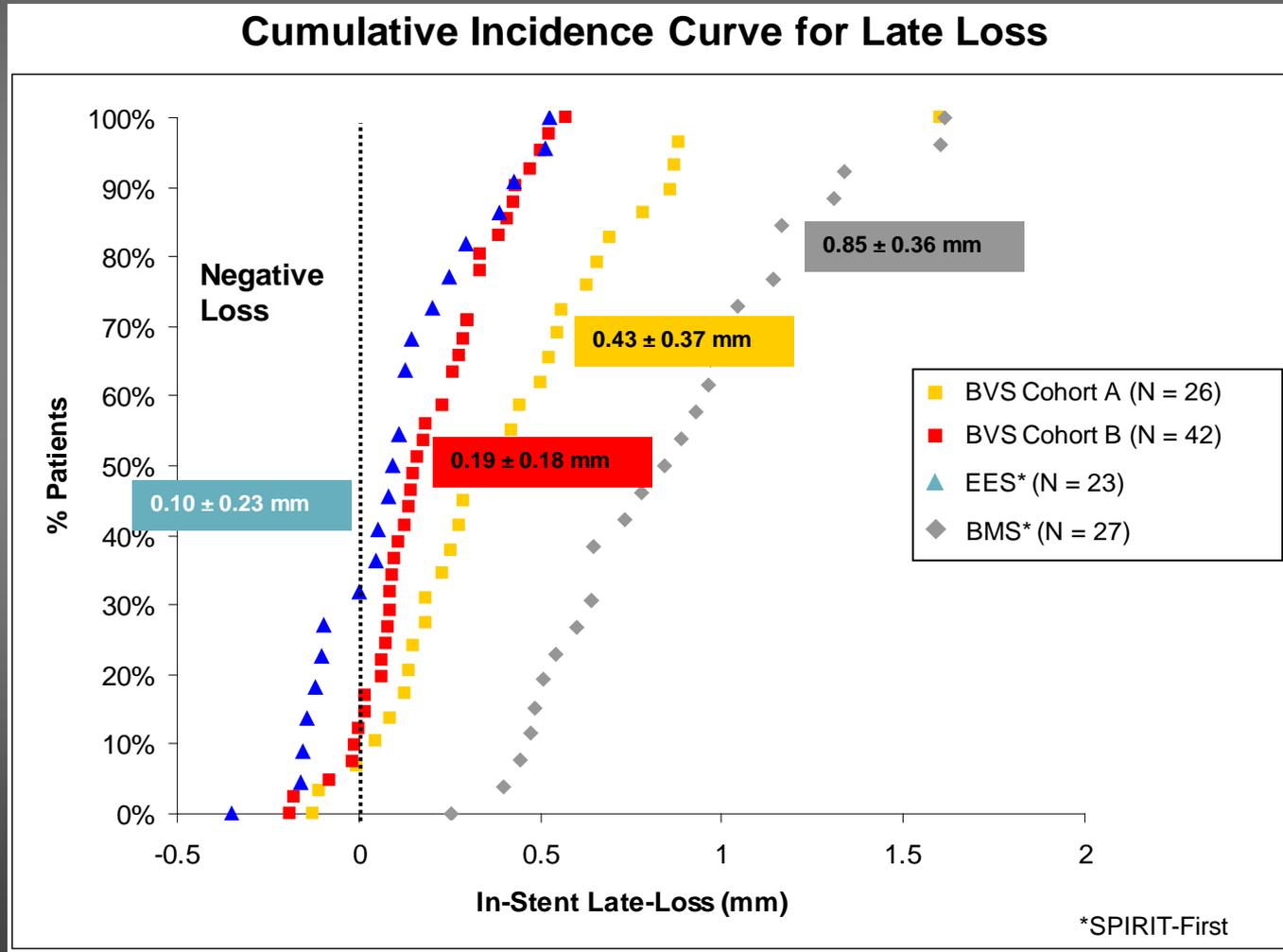


Group B2 (n = 56)

MSCT follow-up

B1 and B2 imaging: Angio, OCT, IVUS

6-Month QCA – Intent to Treat (Group)



ABSORB EXTEND

Expanding the Experience

Principal Investigator: Alexandre Abizaid

Co-PI: Antonio Bartorelli; Rob Whitbourn



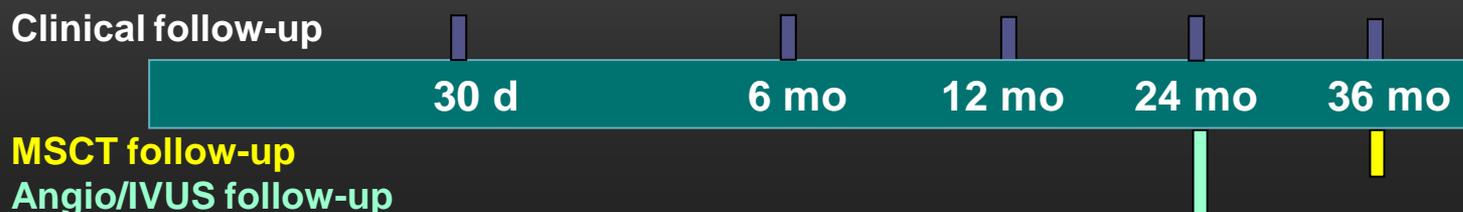
- Continued Access trial. FPI*: Jan 11, 2010
- No hypothesis-testing, typical PCI endpoints
- Device Sizes: 2.5, 3.0 mm (diameters); 18, 28 mm (lengths), or as available
- Lesion lengths ≤ 28 mm
- Planned overlap allowed
- Two imaging subgroups: OCT (n=50, planned overlap only); MSCT (n=100)
- Follow-up schedule:



ABSORB II

Therapy Differentiation: RECRUITING

- Prospective, multi-centered, single blind, randomized (2:1 ABSORB BVS: XIENCE PRIME) study in Europe and New Zealand
- Approximately 504 subjects will be enrolled in ~ 40 sites.
- Co-Primary Endpoints:
 - Vasomotion assessed by the change in mean lumen diameter between pre-and post-nitrate at 2 years by QCA (superiority)
 - Minimum lumen diameter (MLD) at 2 years post-nitrate minus MLD post-procedure post-nitrate by QCA (non-inferiority, reflex to superiority)
- Device sizes: Scaffold diameters: 2.5, 3.0 mm
Scaffold lengths: 18, 28 mm
- Treatment: Up to two *de novo* lesions; $D_{\max} \geq 2.25$ and ≤ 3.3 mm; lesion length ≤ 48 mm
- Follow-up schedule:



ABSORB EXTEND

Non-Randomized, Single-Arm, Continued Access Trial

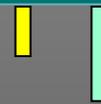


Clinical follow-up



MSCT follow-up (n=100)

OCT follow-up (n=50)

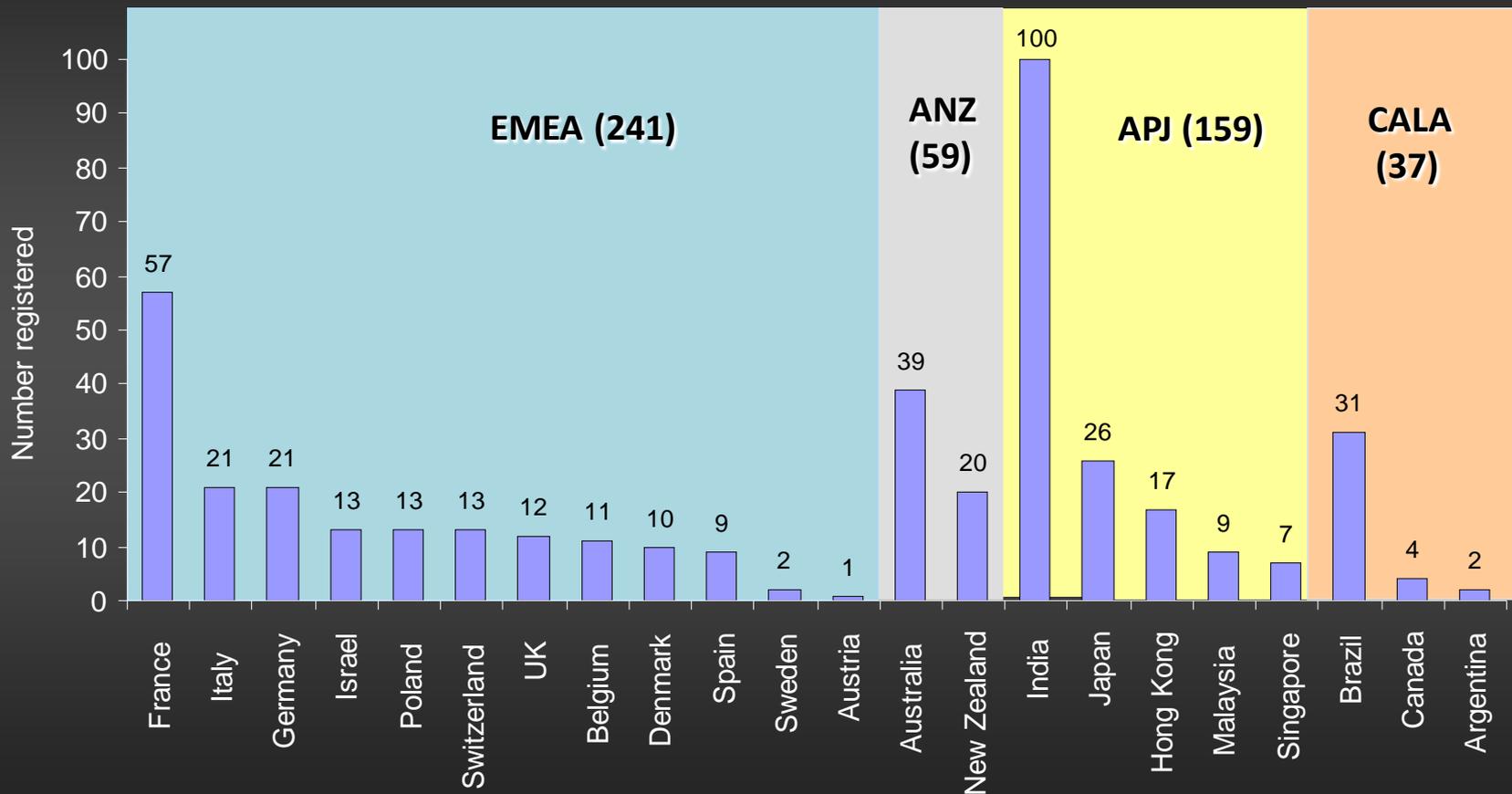


Study Objective:	Continued Access trial. FPI*: Jan 11, 2010
Endpoints:	No hypothesis-testing, typical PCI clinical endpoints
Treatment:	Up to 2 <i>de novo</i> lesions in different epicardial vessels Planned overlapping allowed in lesions >22 and ≤ 28 mm
Device Sizes:	Scaffold diameters: 2.5, 3.0 mm Scaffold lengths: 18, 28 mm

*FPI: First Patient In

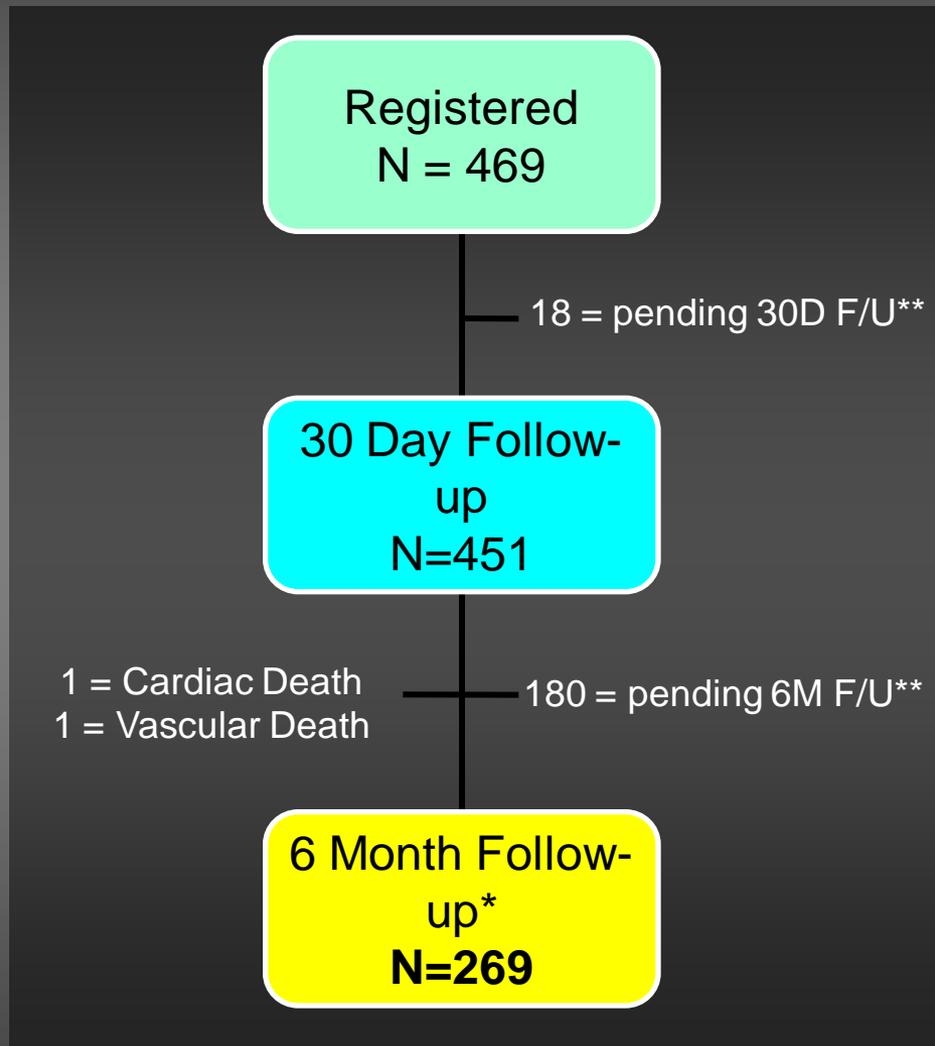
ABSORB EXTEND: Status as of February 27, 2012

- 54 sites are open; 27 actively registering
- 496 patients are registered, shown by country



6 Month Clinical Follow-up^o

(ITT Population)



^o Covers a registration period of January 11, 2010 to January 11, 2012

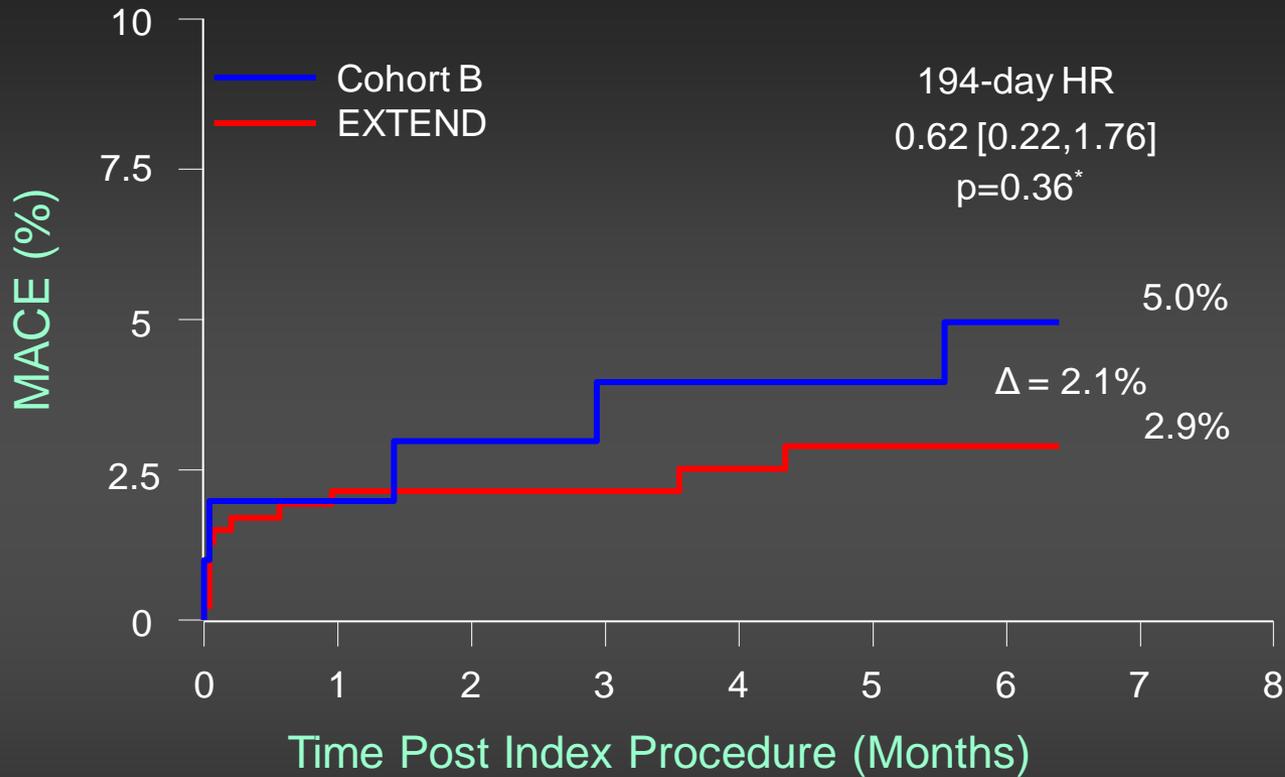
*F/U window ± 14 days

**As of the cut-off date of Jan. 11 '12

ABSORB BVS is neither approved nor available for sale in the U.S.

MACE Through 6 Months

(ITT – Interim Snapshot)



Number at risk

Time after index procedure (days)

	0	37	194
Cohort B	101	99	96
EXTEND	469	440	260

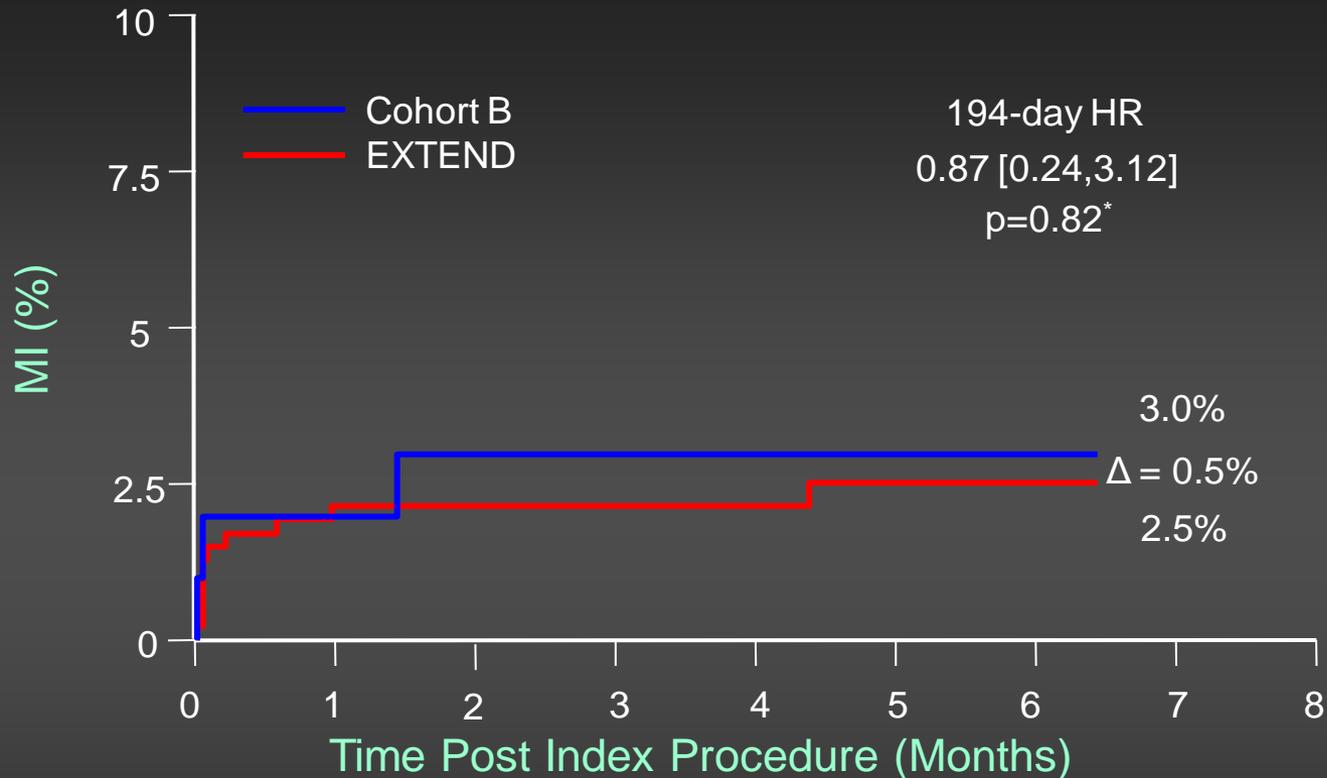
Note: MACE is defined as the composite of cardiac death, MI, and ischemia-driven TLR

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

ABSORB BVS is neither approved nor available for sale in the U.S.

MI Through 6 Months

(ITT – Interim Snapshot)



Number at risk

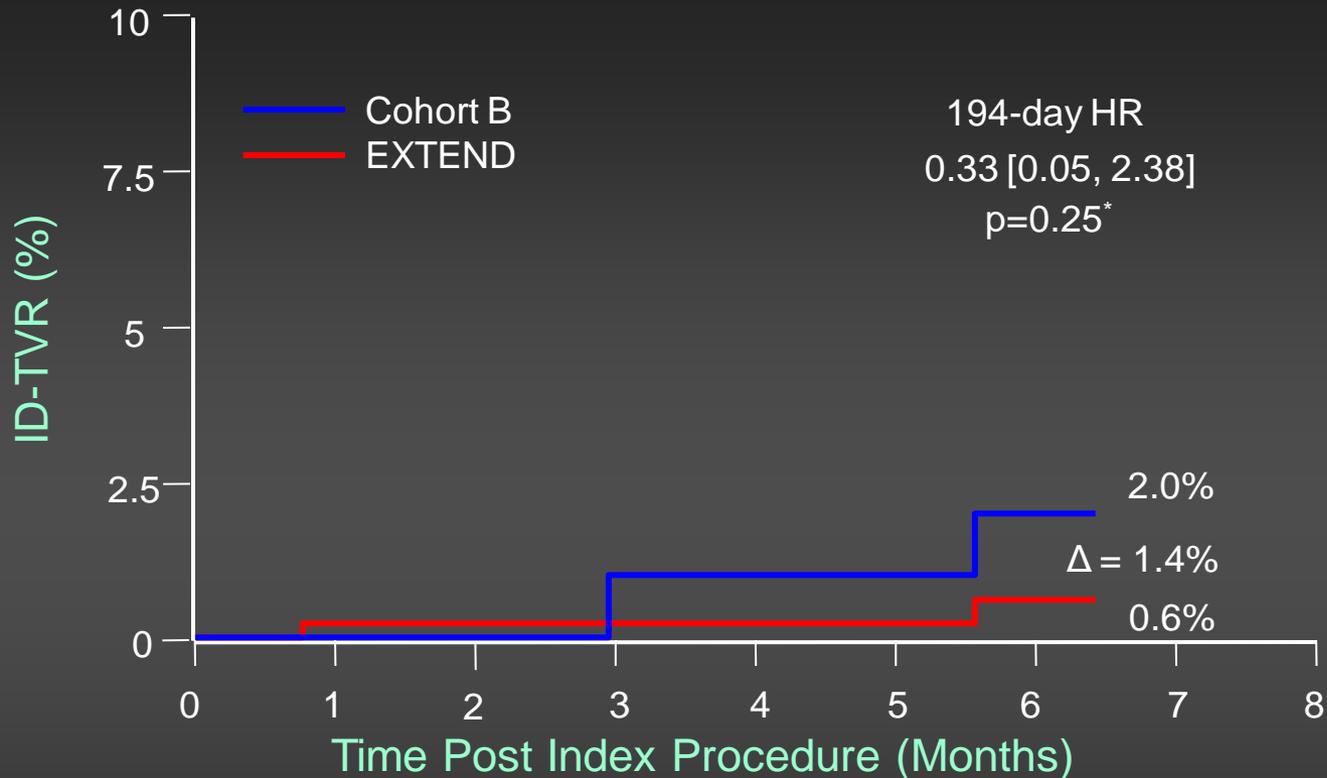
Time after index procedure (days)

	0	37	194
Cohort B	101	99	98
EXTEND	469	440	260

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

ID-TVR Through 6 Months

(ITT – Interim Snapshot)



Number at risk

Time after index procedure (days)

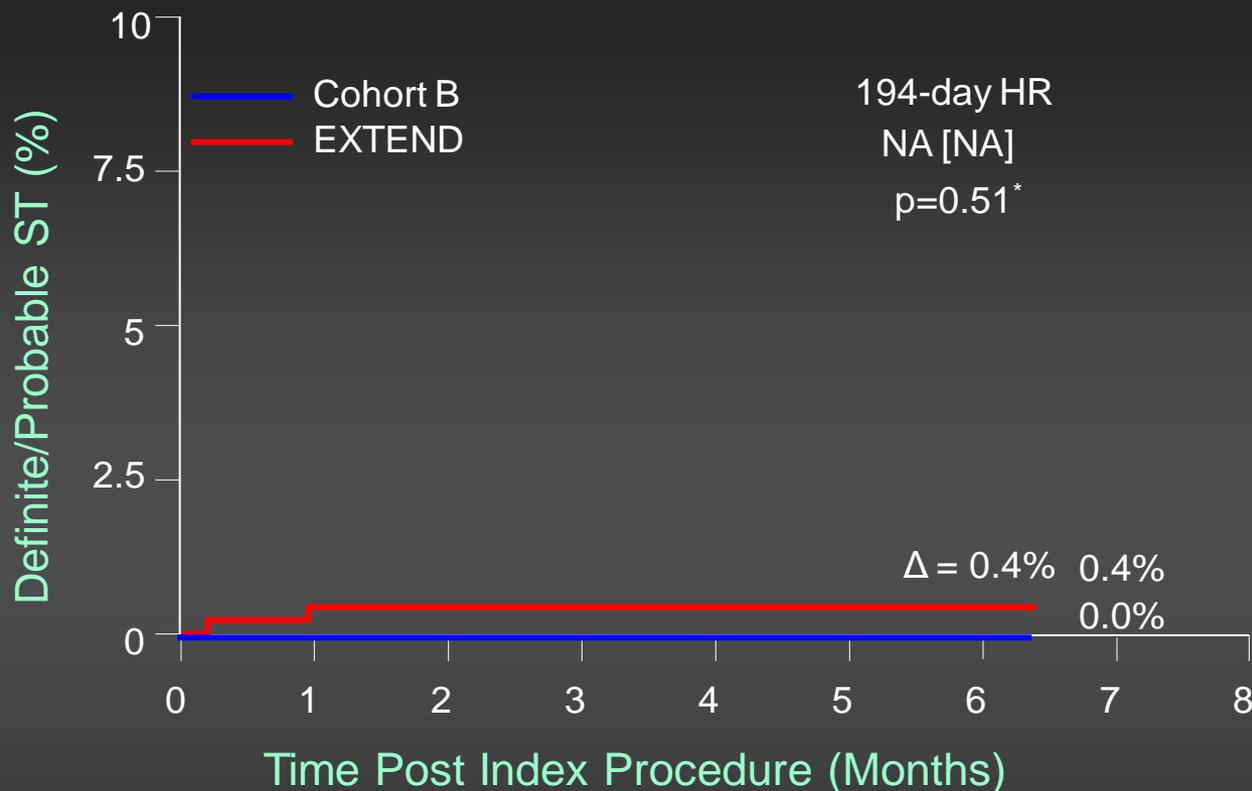
	0	37	194
Cohort B	101	101	99
EXTEND	469	449	265

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

ABSORB BVS is neither approved nor available for sale in the U.S.

ST (def/prob) Through 6 Months

(ITT – Interim Snapshot)



Number at risk

Time after index procedure (days)

	0	37	194
Cohort B	101	101	101
EXTEND	469	448	265

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

Questions and Potential Limitations

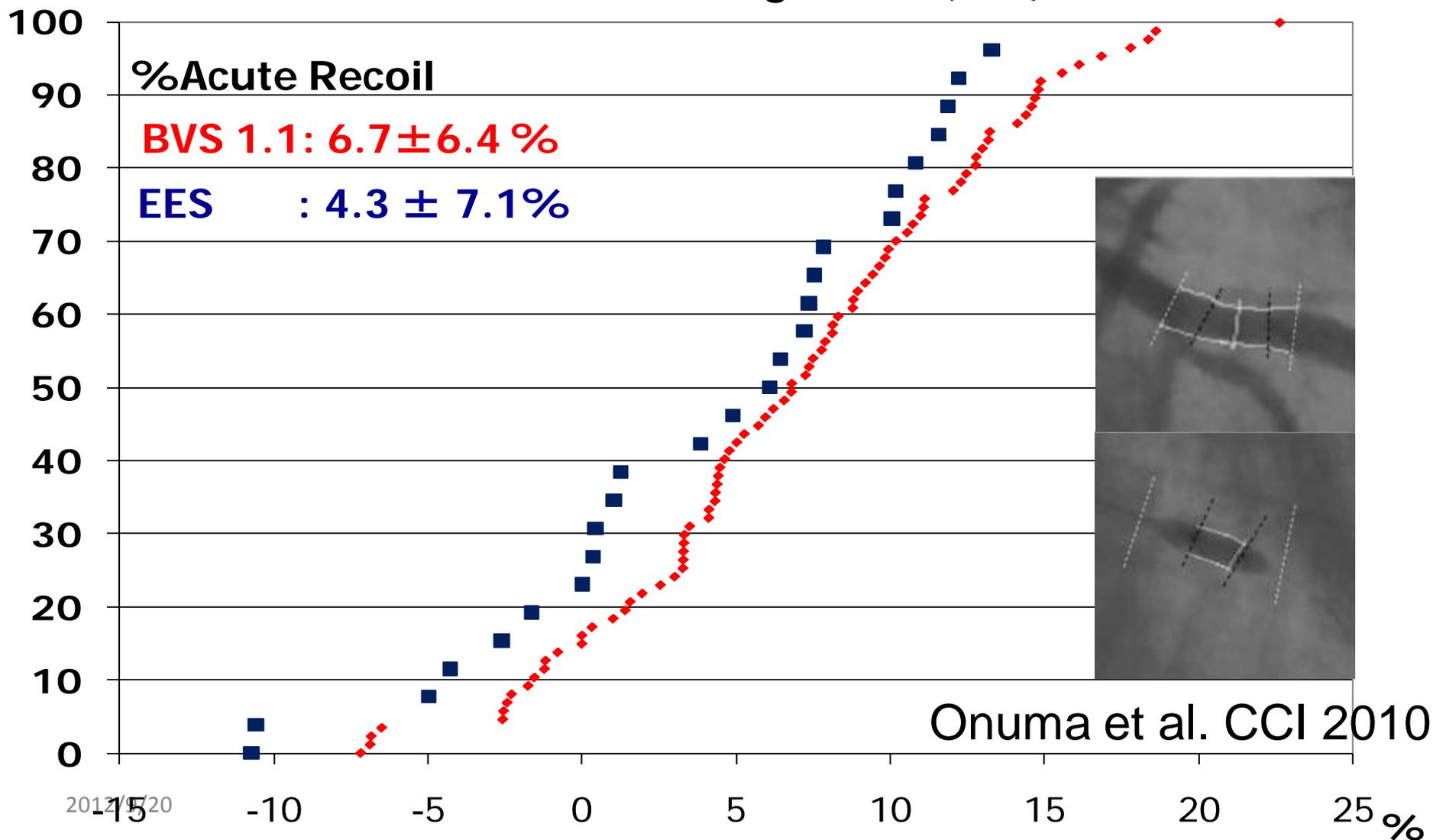
- Acute Recoil ?
- Conformability ?
- Bioabsorption is a real phenomenon?
- Restoration of vasomotion?
- Plaque stabilization / regression?

Questions and Potential Limitations

- Acute Recoil ?
- Conformability ?
- Bioabsorption is a real phenomenon?
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#1. We do not have to worry about acute recoil

Cumulative distribution frequency curve
Relative Recoil of bioresorbable scaffolds (BVS) and metallic
Everolimus-eluting stents (EES)

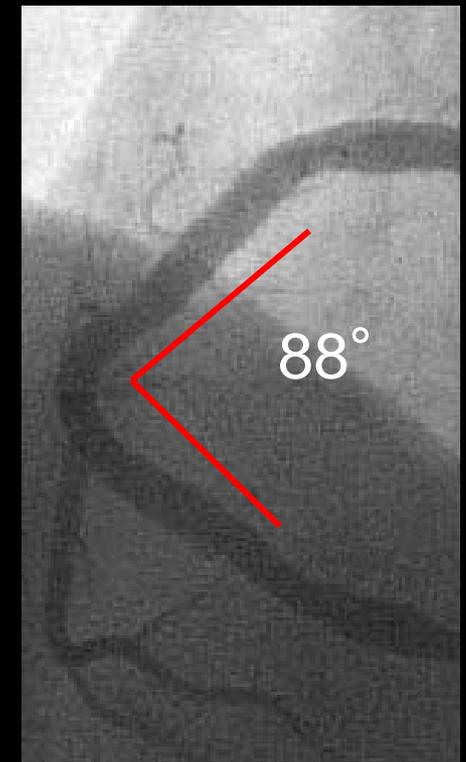
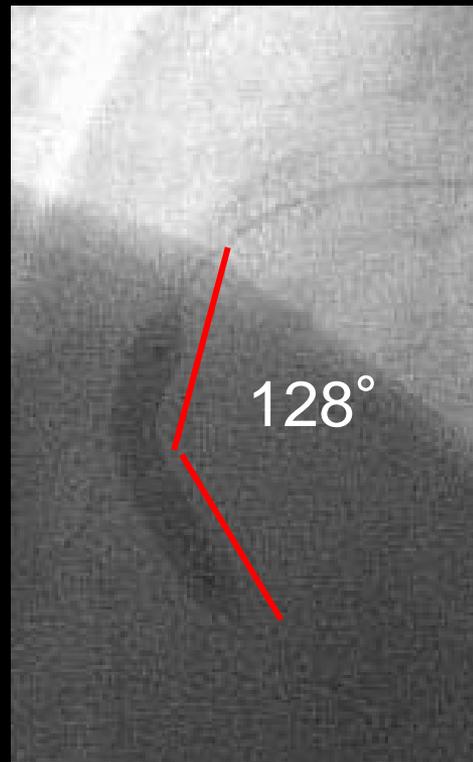
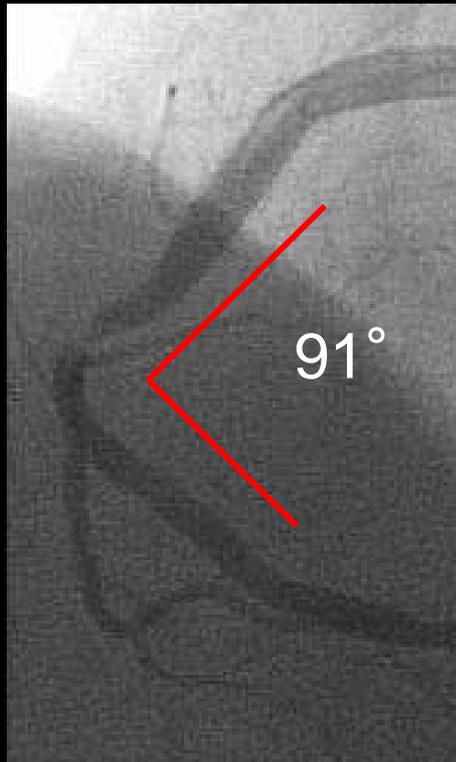


Questions and Potential Limitations

- Acute Recoil ?
- Conformability ?
- Bioabsorption is a real phenomenon?
- Restoration of vasomotion?
- Plaque stabilization / regression?

#2. Vessel curvature is respected after scaffolding In-vivo Conformability

Gomez et al. JACC int 2010



BVS has less impact on curvature in the scaffolded segment compared to metallic stents, and therefore (hypothetically) is associated with less influence on shear stress.

Questions and Potential Limitations

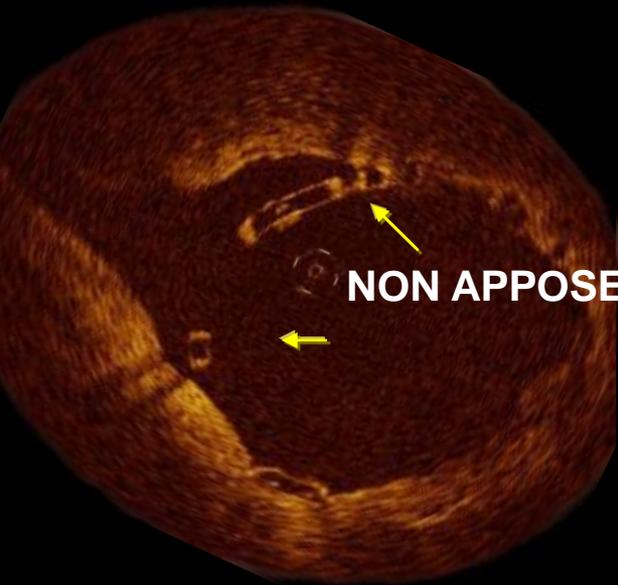
- Acute Recoil ?
- Conformability ?
- Bioabsorption is a real phenomenon?
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- Plaque stabilization / regression?

#3. Bioresorption is a real phenomenon

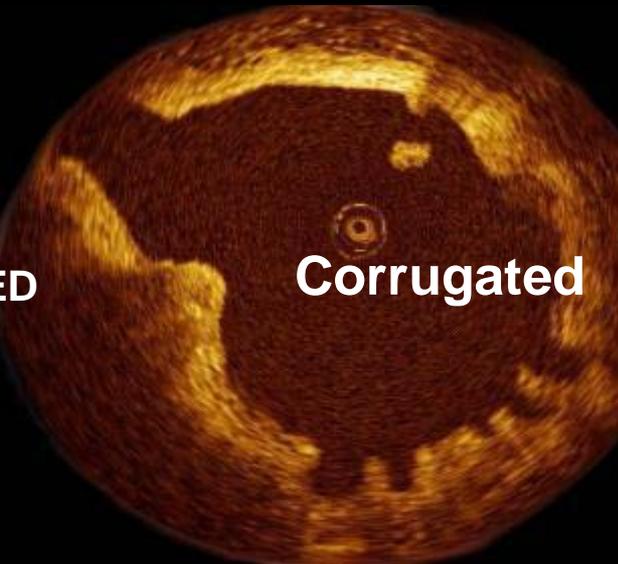
Post

6 months

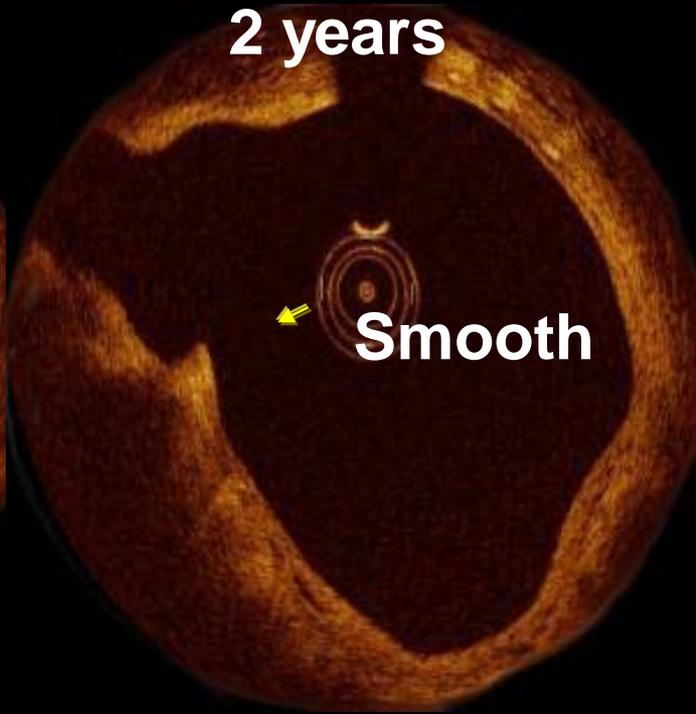
2 years



NON APPOSED



Corrugated



Smooth

Pre

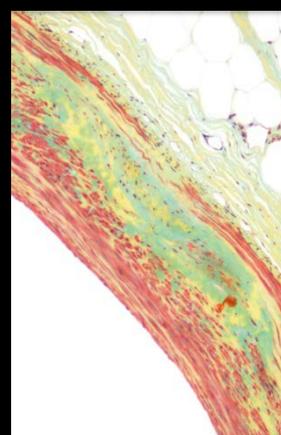
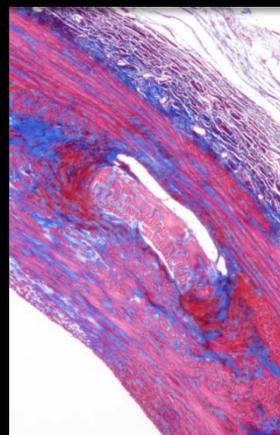
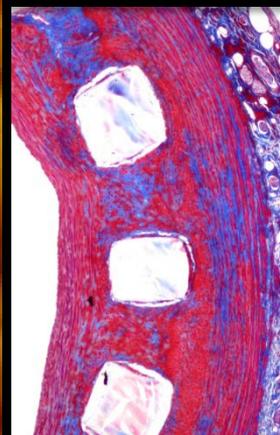
Post

1Y

2Y

3Y

4Y

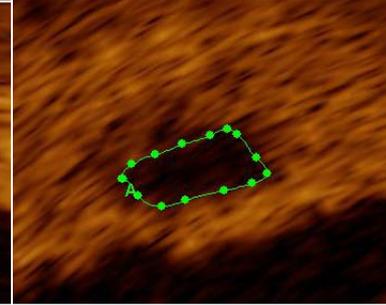
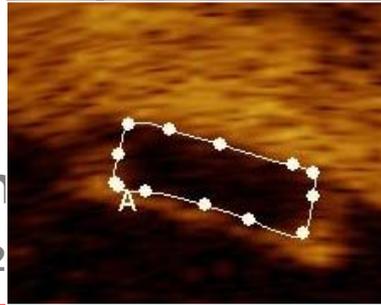


Results of Cohort B2 Quantitative OCT Analysis

22 Paired OCT in 21 pts

Post procedure 12 month % Difference P values

Mean scaffold area, mm²



66

0.30

Minimal scaffold area, mm²

05

0.33

Mean prolapse area, mm²

-

Mean strut core area, mm²

First signs of bioresorption

Mean Neointimal area, mm²

-

1.34

-

-

Mean flow area, mm²

7.51

6.13

-18.1

<0.001

Minimal flow area, mm²

5.95

4.51

-23.4

< 0.001

Lumen area stenosis, %

20.2

26.9

0.02

Uncovered struts, %

na

3.11

ISA area, mm²

0.41

2.94

(for patients with ISA)

(n=18)

(n=4)

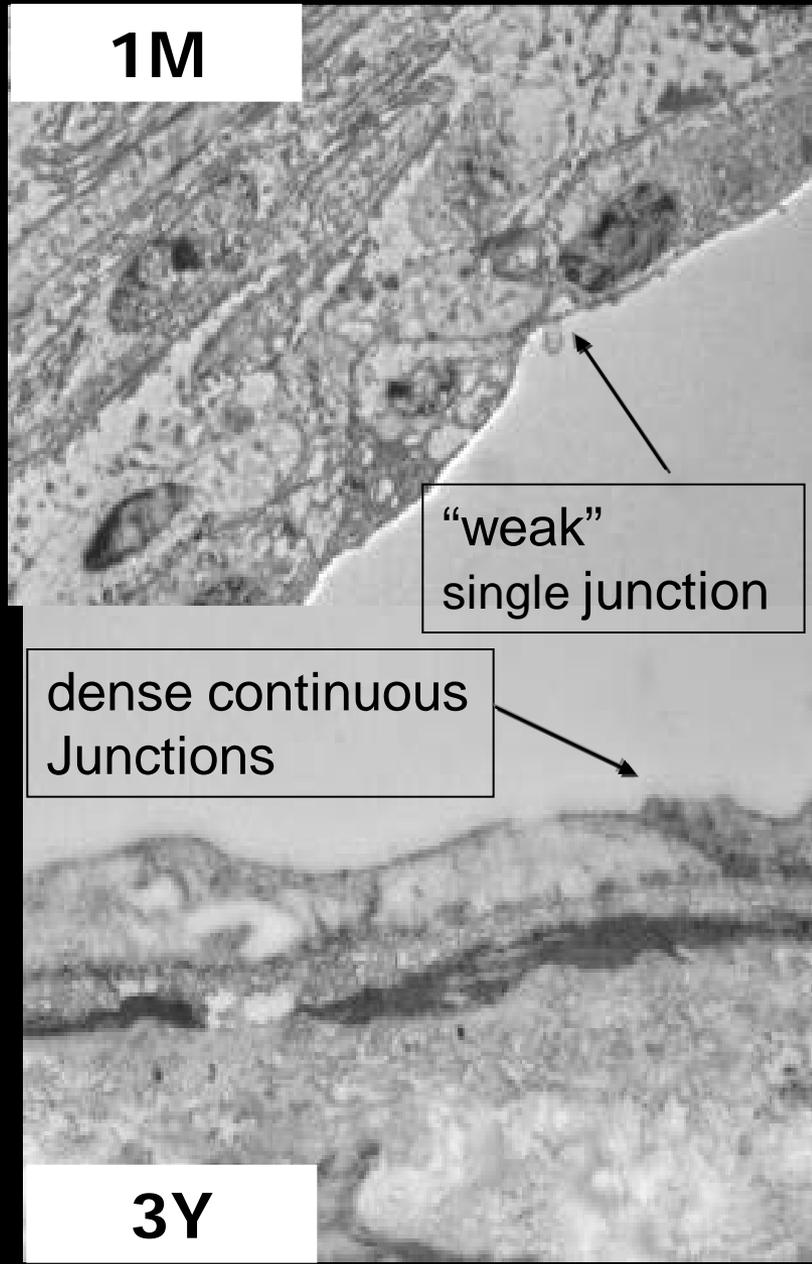
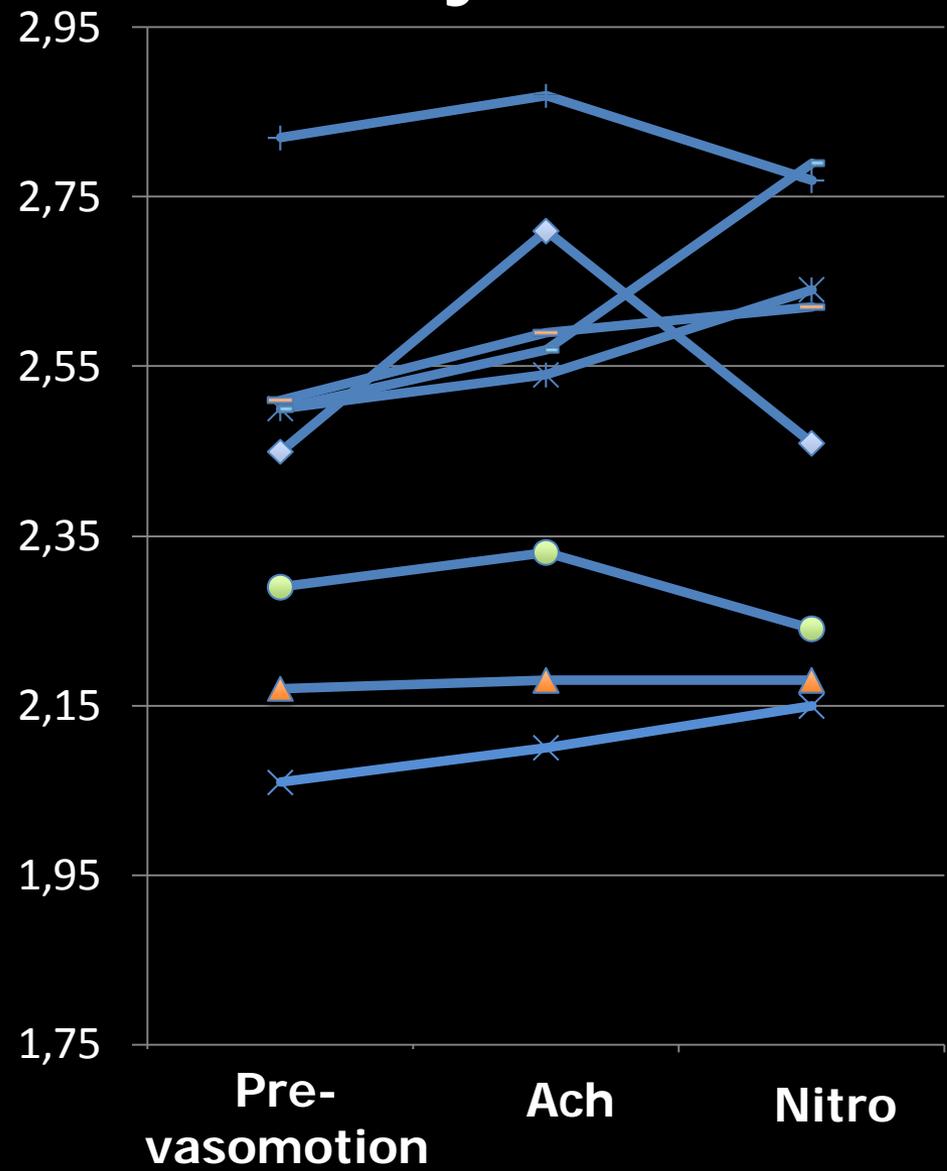
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Questions and Potential Limitations

- Acute Recoil ?
- Conformability ?
- Bioabsorption is a real phenomenon?
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- Plaque stabilization / regression?

#8. Restoration of the normal endothelial morphology and function with vasodilatation induced by intracoronary Acetylcholine

Acetylcholine



Questions and Potential Limitations

- Acute Recoil ?
- Conformability ?
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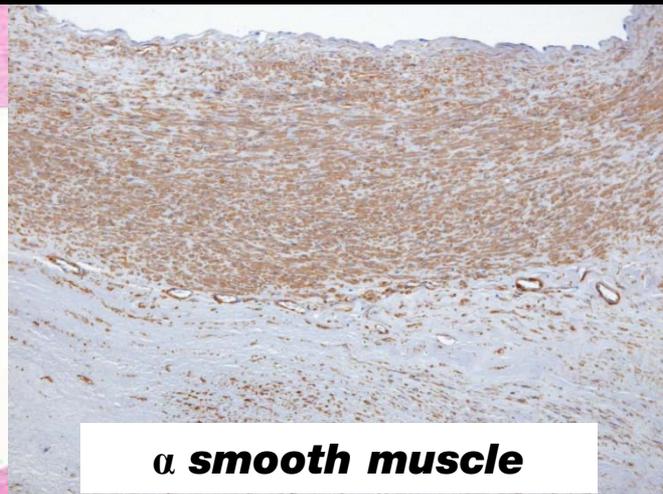
#5. Sealing and shielding of plaques as a result of scaffold implantation : can the scaffold cap the plaque?

Histology: 10 years stented LAD with an Igaki-Tamai stent

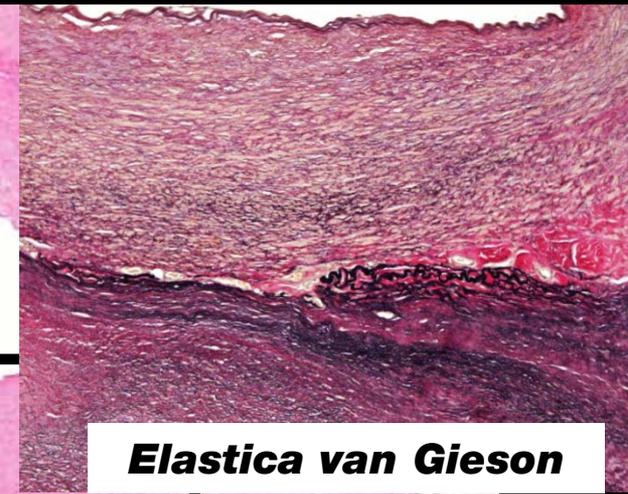
- There were almost no inflammatory cell infiltrations or foreign body reactions in 10-year histology.



Haematoxylin Eosin



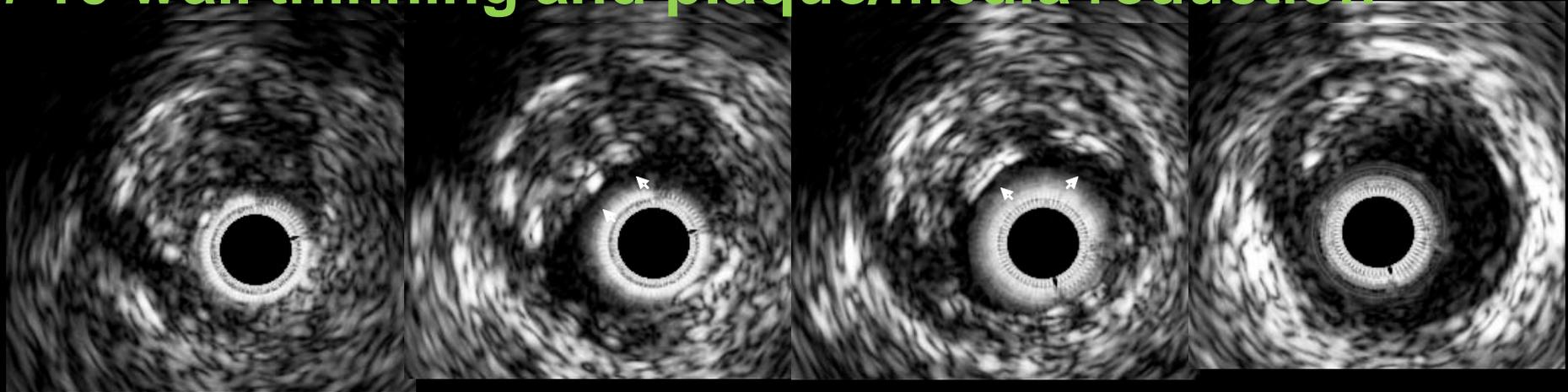
**α smooth muscle
actin**



Elastica van Gieson

- In intima, smooth muscle cells and fibrotic tissue were observed.

10 wall thinning and plaque/media reduction

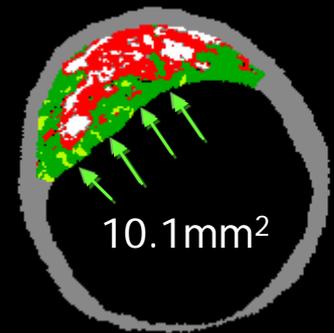
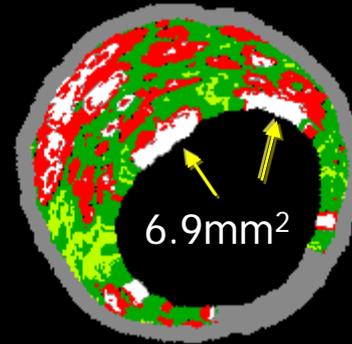
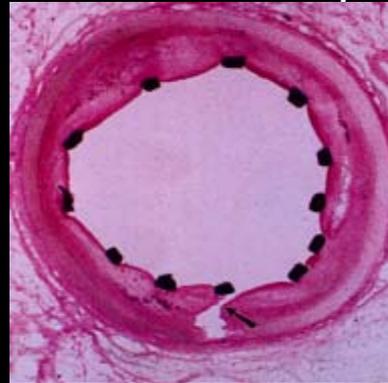


Pre-stenting

Post-stenting

6-month

24-month



Vessel (mm²)

13.49*

13.79

Δ-4%

12.68

Lumen (mm²)

6.04

5.19

Δ+11%

5.46

Plaque (mm²)

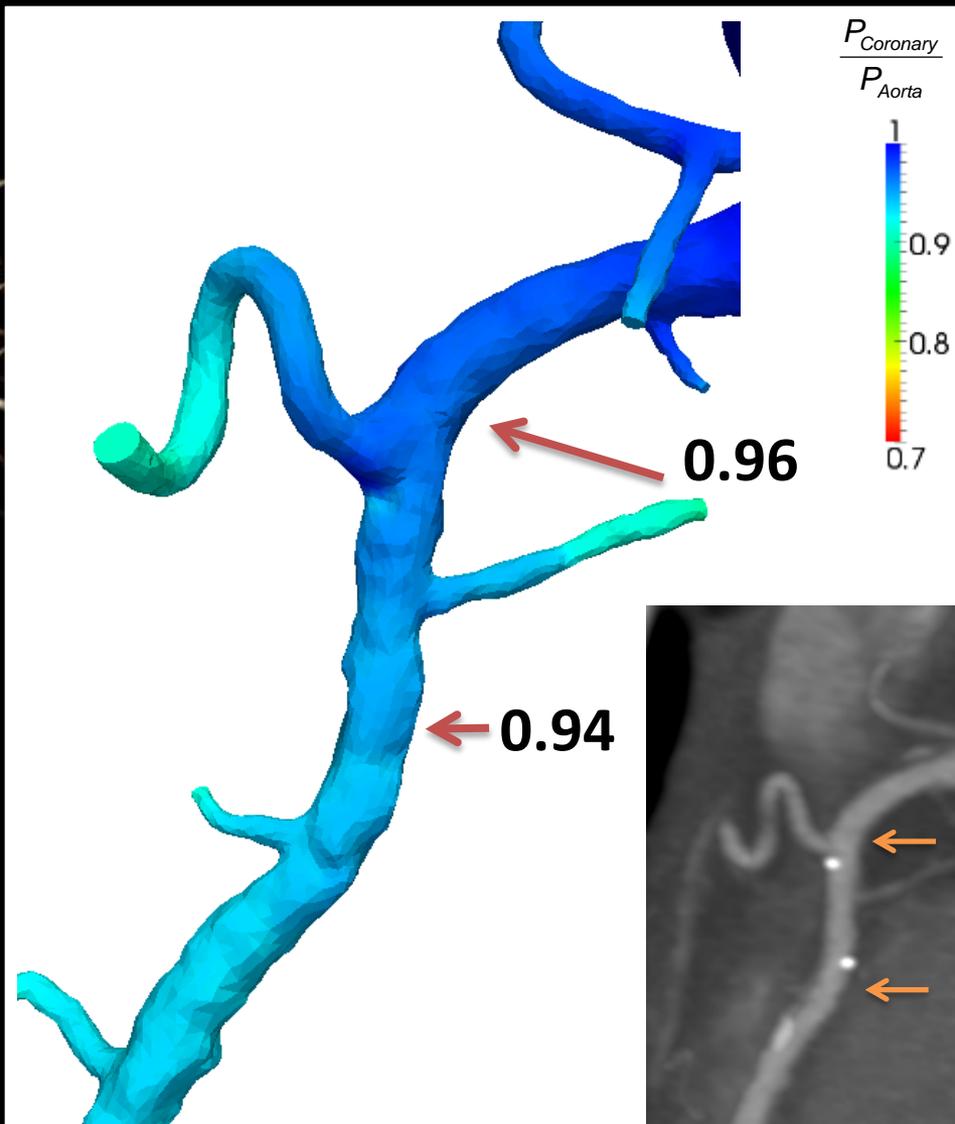
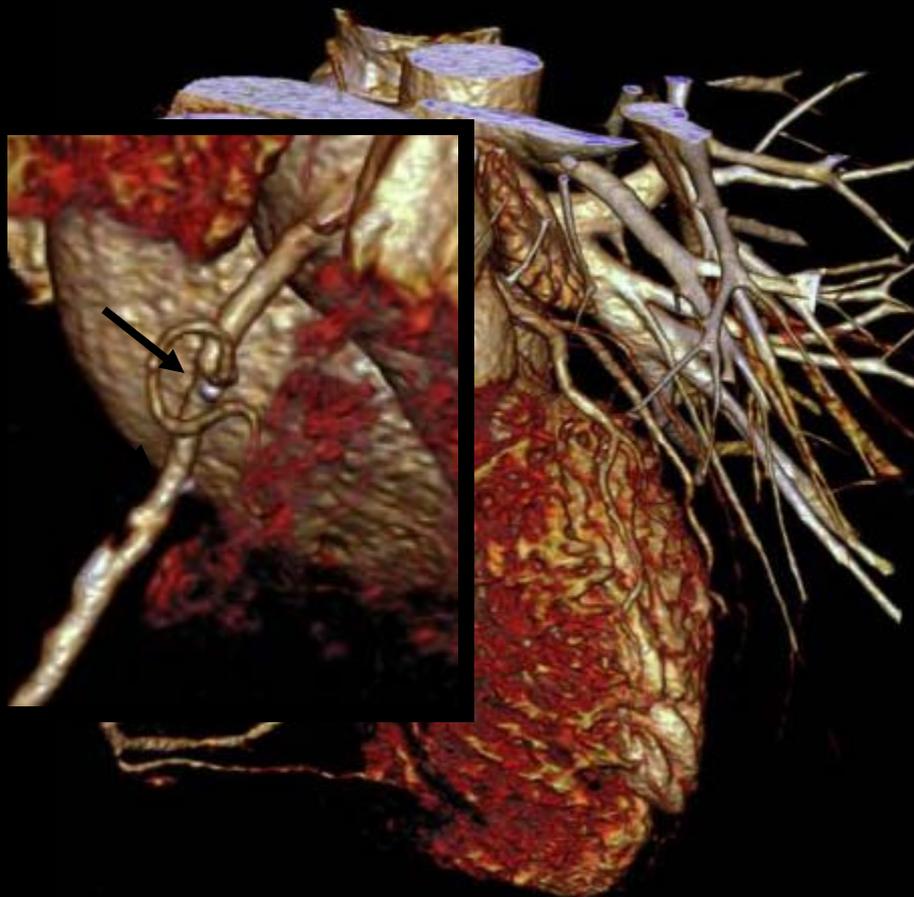
7.44*

8.60

Δ-13%

7.22

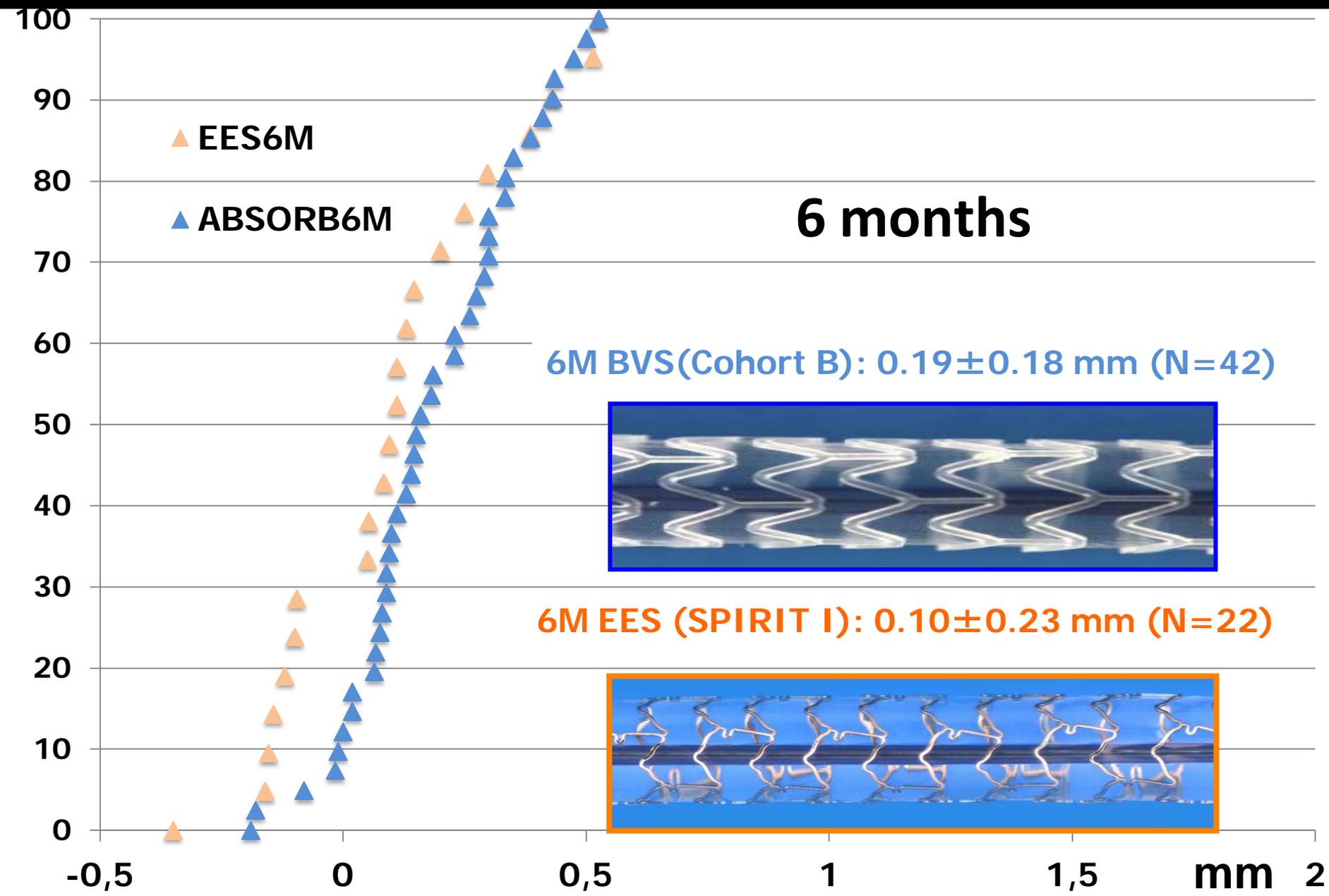
Non-invasive assessment of FFR at 5 years showed persistence of the normalization of coronary flow dynamics



Conclusion

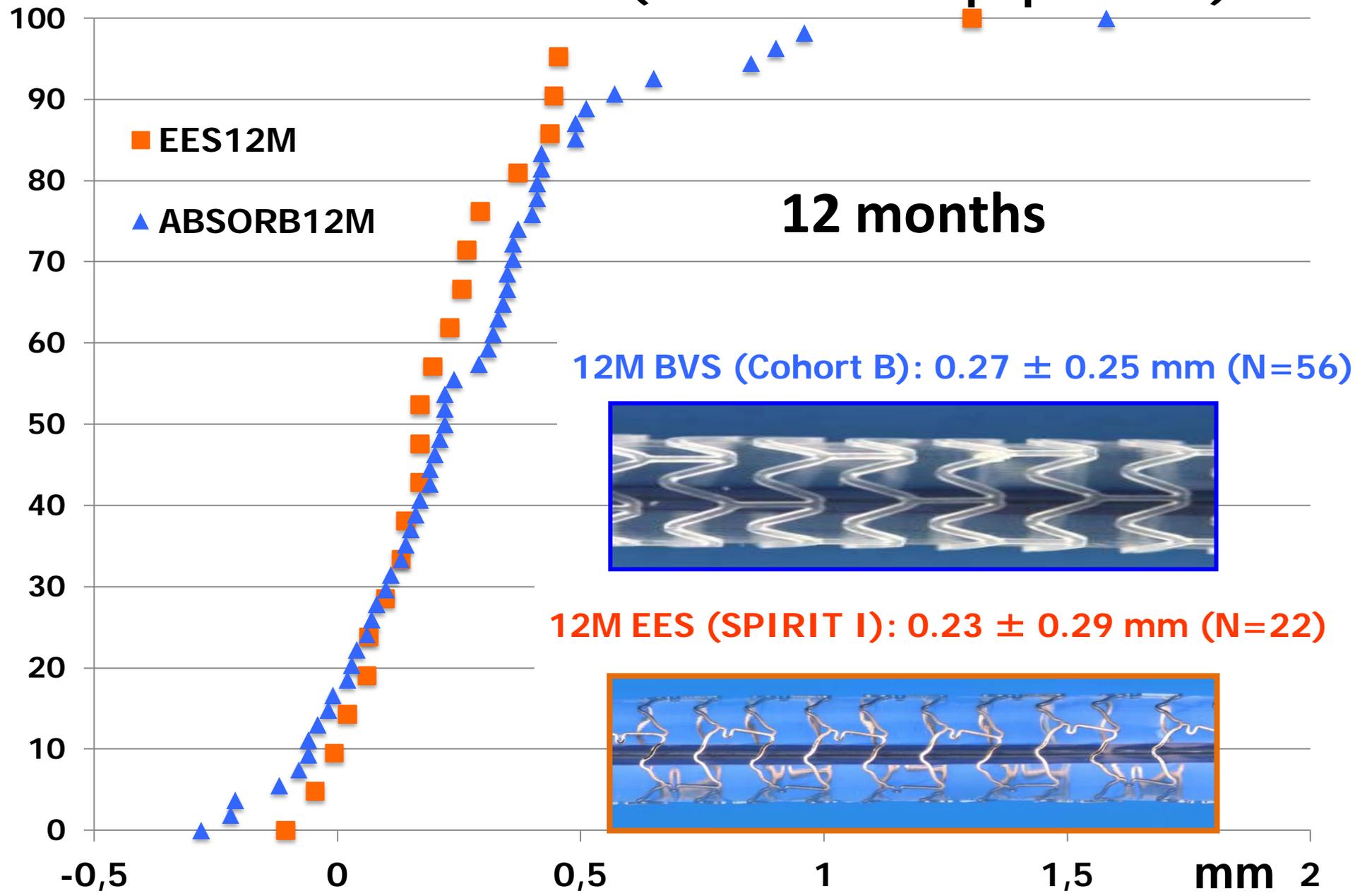
- A new era has began
- Major issues seams to be resolved (radial force, acute and chronic recoil, vascular vasomotion restauration)
- Larger studies with more complex patients are in enrollment phase and future randomized trials with unconventional design will be required for an universal penetration.

11 QCA : OTHER EVIDENCE OF LATE LUMEN ENLARGEMENT

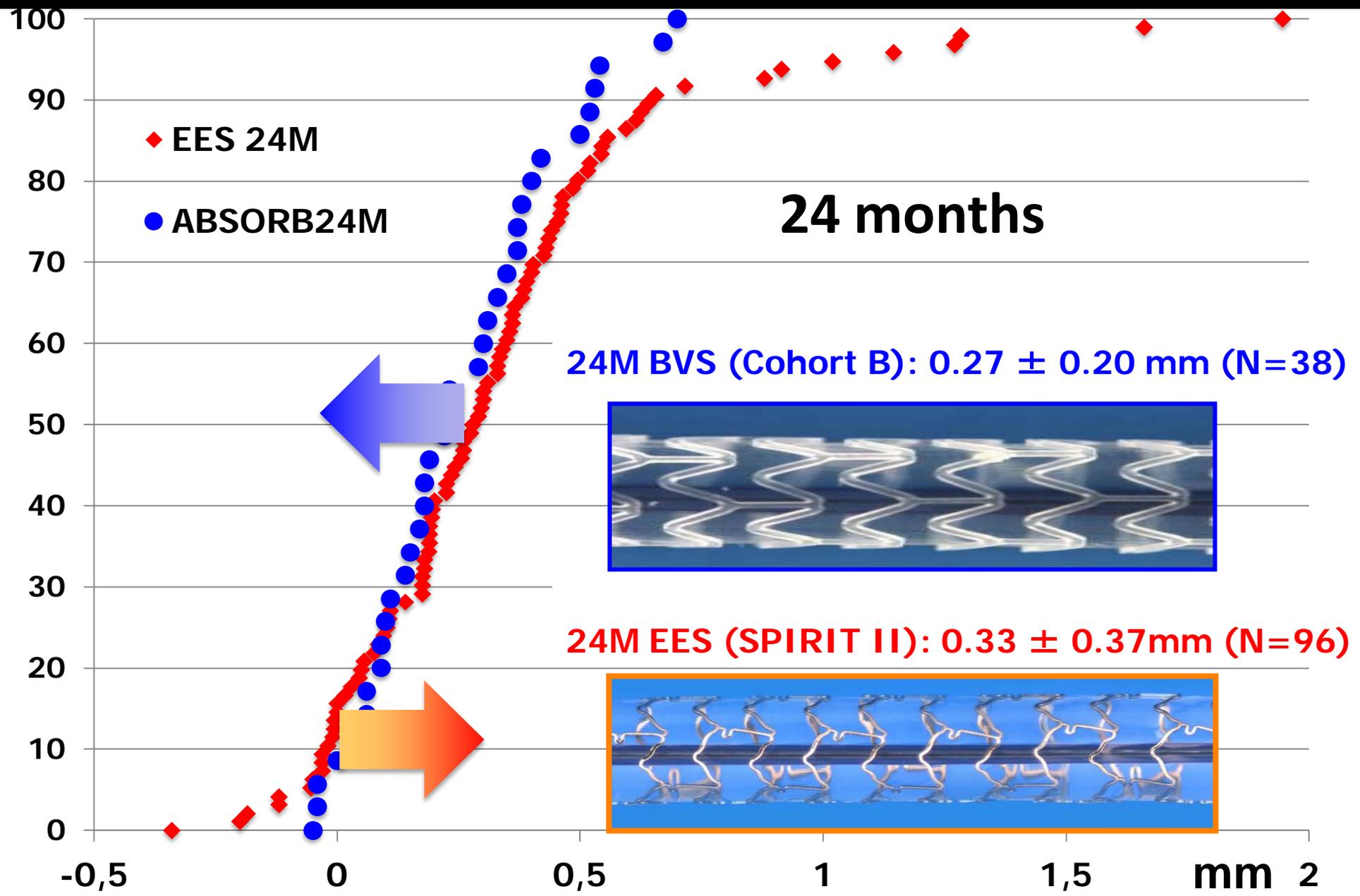


Insight on evolution of late luminal loss over times

BVS 1.1 and **Xience V** (non-matched population)



11 QCA : OTHER EVIDENCE OF LATE LUMEN ENLARGEMENT



Bioresorbable Scaffold – A new treatment Paradigm for Atherosclerotic Plaque

Compensatory Expansive Remodeling of EEM →

