ABSORB Bioresorbable Vascular Scaffold System

- The 4th Revolution in Interventional Cardiology

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Abbott Vascular

17th Asian Harmonization Working Party Annual Conference
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Presentation Outline

- **Introduction and History of Interventional Cardiology**
- **The 4th revolution - Absorb Bioresorbable Vascular Scaffold System**
  - The Clinical Need for a Bioresorbable Vascular Scaffold
  - Design Goals of a Bioresorbable Vascular Scaffold
  - Device Design and Technology
  - ABSORB Clinical Program and Studies
  - Summary

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Introduction and History of Interventional Cardiology

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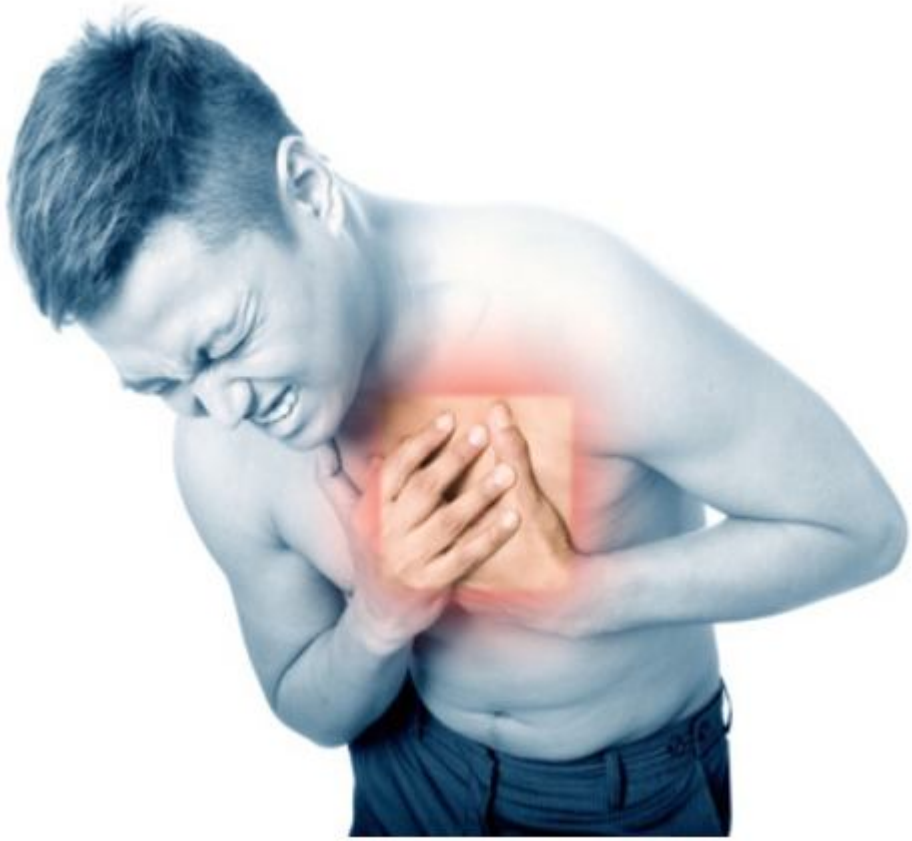
Coronary Artery Disease (CAD) and Chest Pain:
Chronic Angina, Unstable Angina or Acute MI



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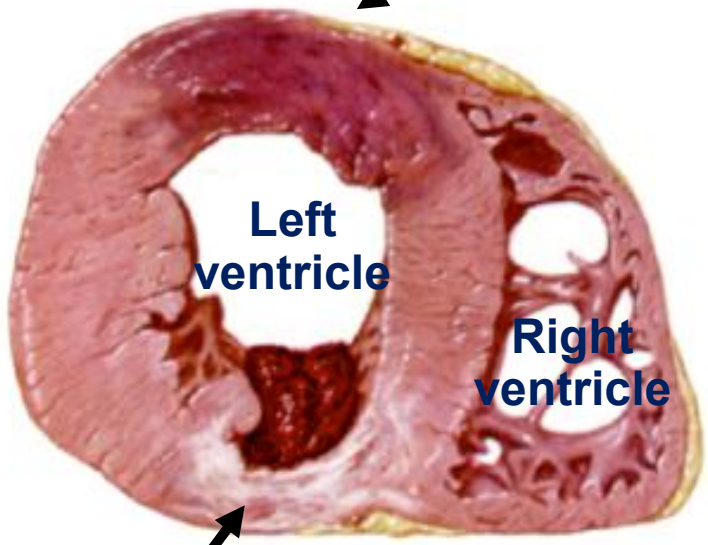
What a myocardial infarction looks like in the heart …

Acute anteroseptal infarction (Front)



Healed posterior infarction with overlying thrombus (Back)

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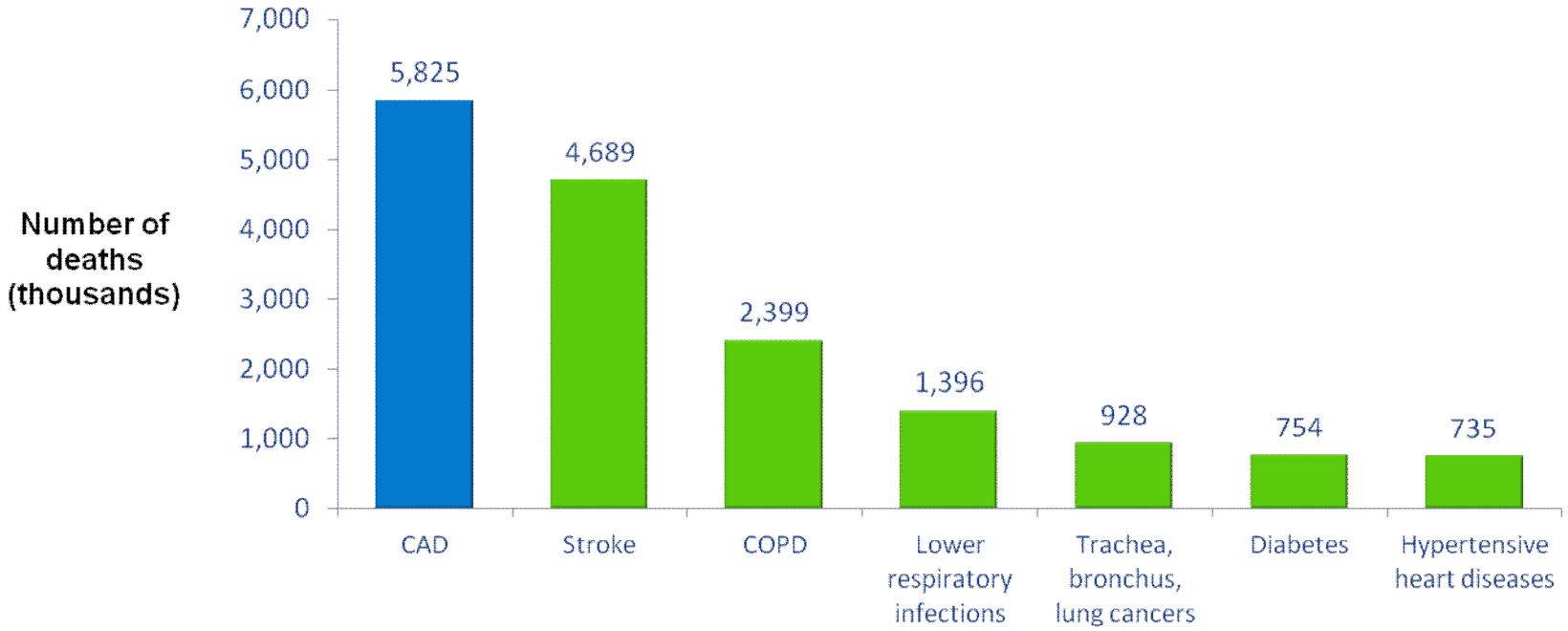
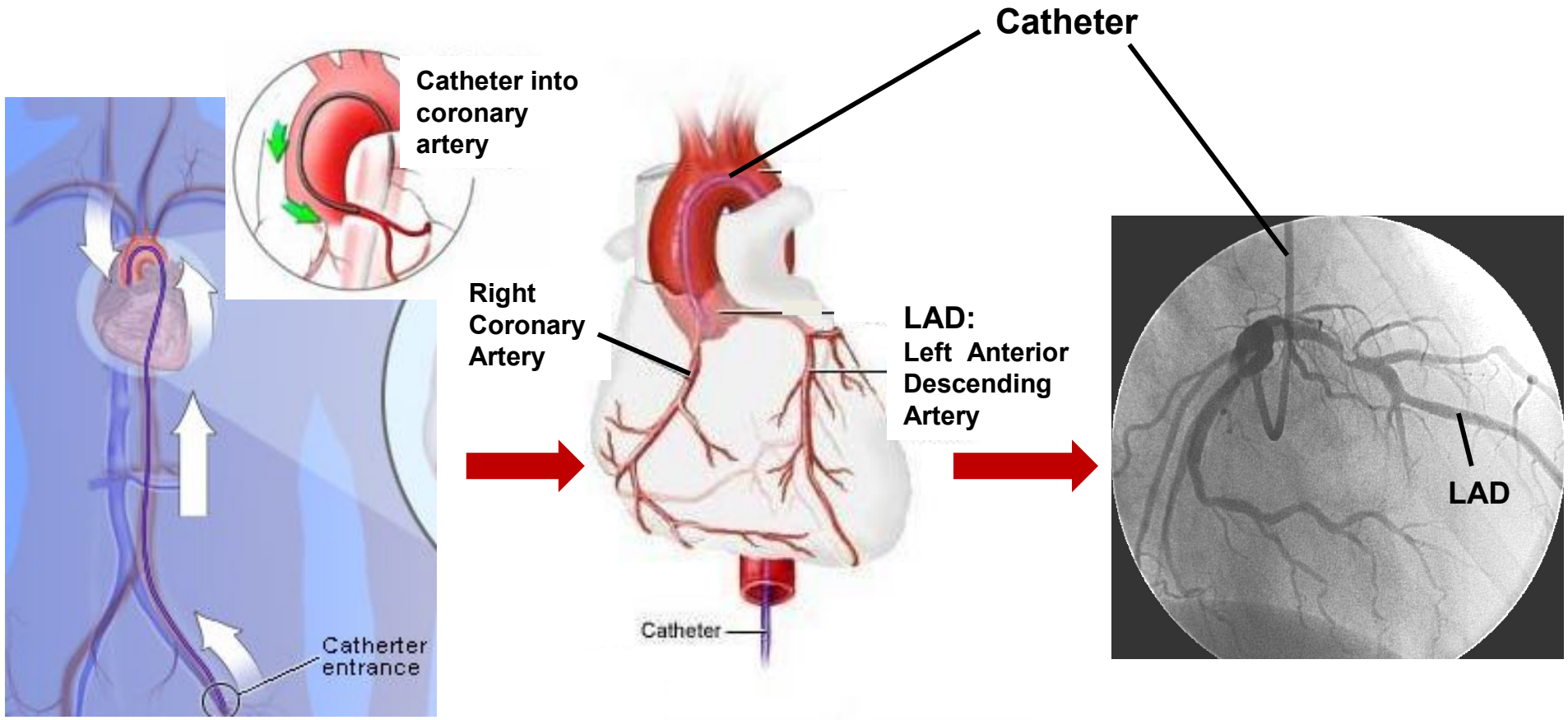
CAD is the number one leading cause of mortality worldwide for patients 60 years and older

Deaths in patients aged >60 years globally (2002)[1]



1. World Health Organization. Deaths from coronary heart disease. 2004. Available at: http://www.who.int/cardiovascular_diseases/en/cvd_atlas_14_deathHD.pdf. Accessed: Mar 2012. CAD=coronary artery disease; COPD=chronic obstructive pulmonary disease.

Gold standard to diagnose CAD: Coronary angiography



Technique **Anatomy** **Angiogram**

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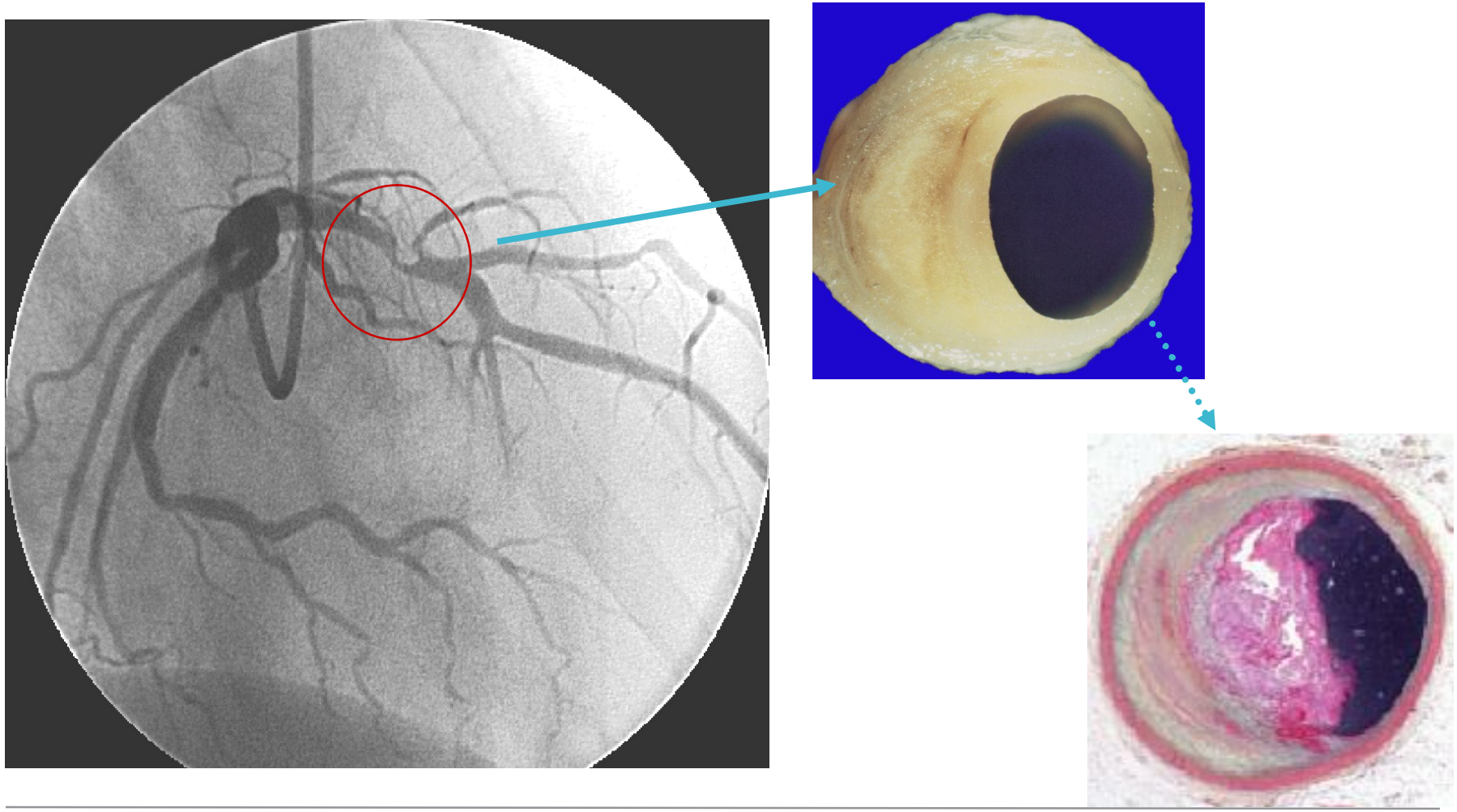
Left Coronary Artery with Atherosclerotic Stenosis



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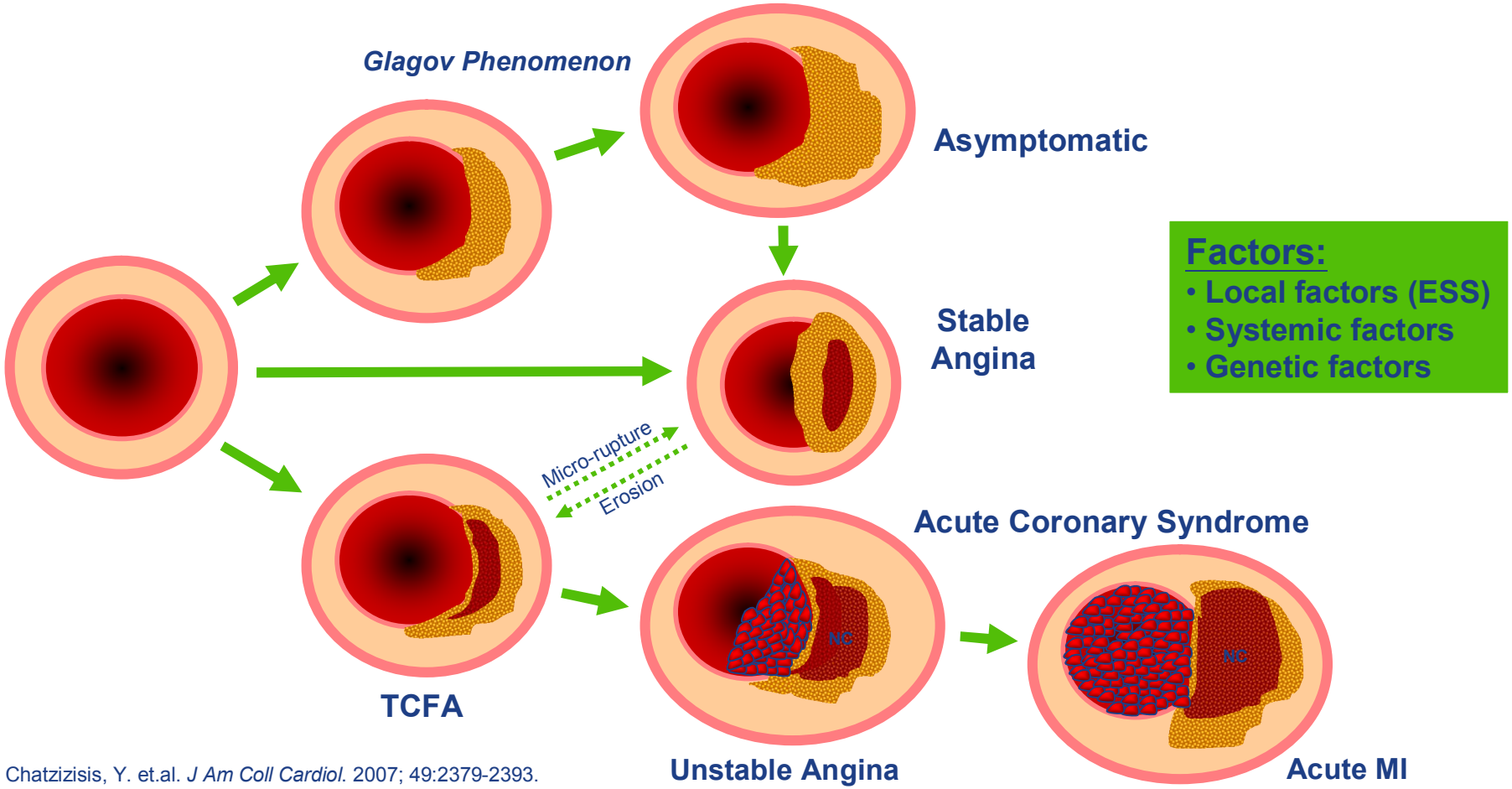
Natural Progression of Coronary Artery Disease



Chatzizisis, Y. et.al. *J Am Coll Cardiol.* 2007; 49:2379-2393.

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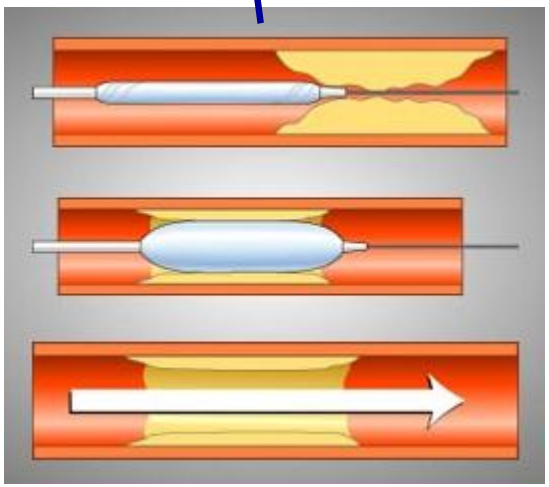
Interventional Cardiology – The beginning

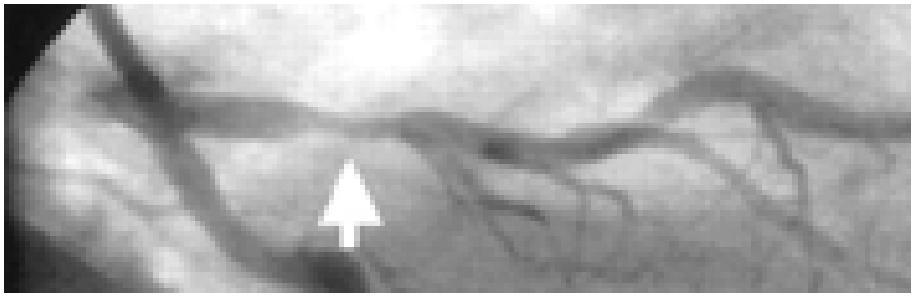
1977

1. Balloon (PTCA):
Andreas Gruntzig performs the first PTCA in Zurich, Switzerland

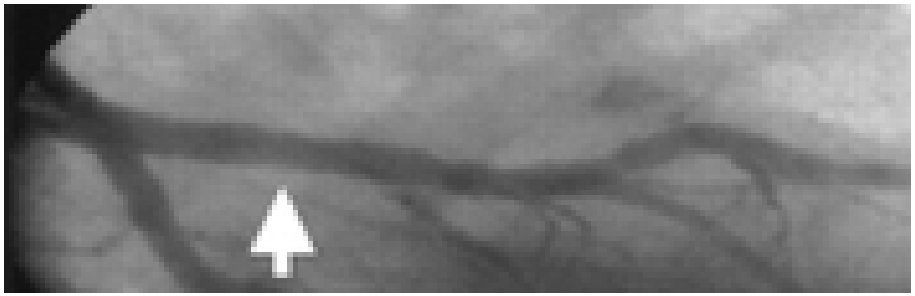


Restenosis after Balloon Angioplasty (PTCA)

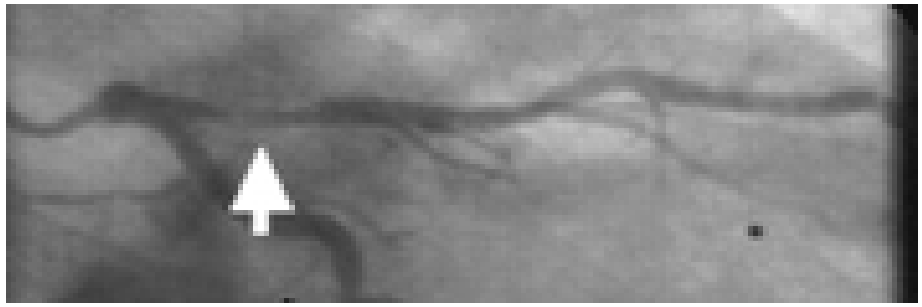
Pre PTCA

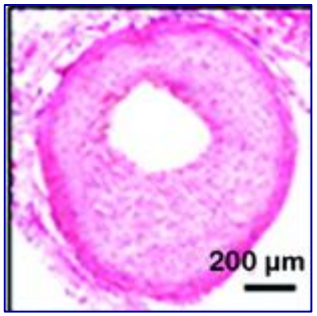


Immediately post - PTCA



6-month restenosis post - PTCA





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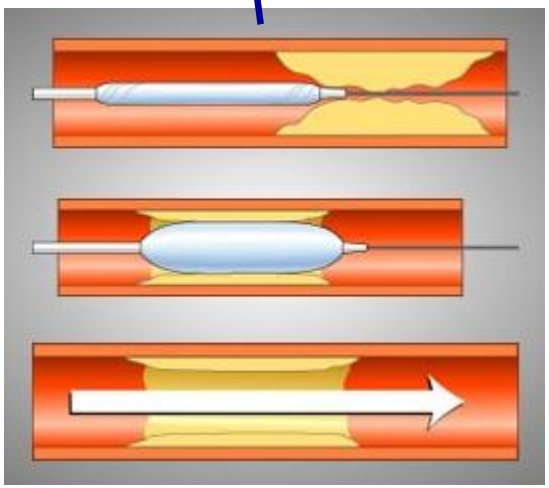
Interventional Cardiology – The 2nd revolution

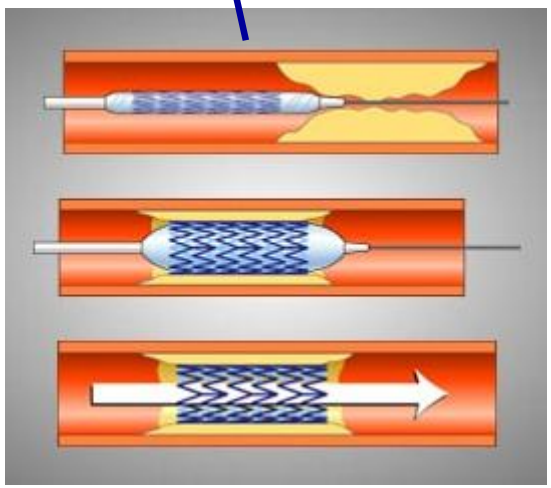
1977

1. Balloon (PTCA):
Andreas Gruntzig performs the first PTCA in Zurich, Switzerland

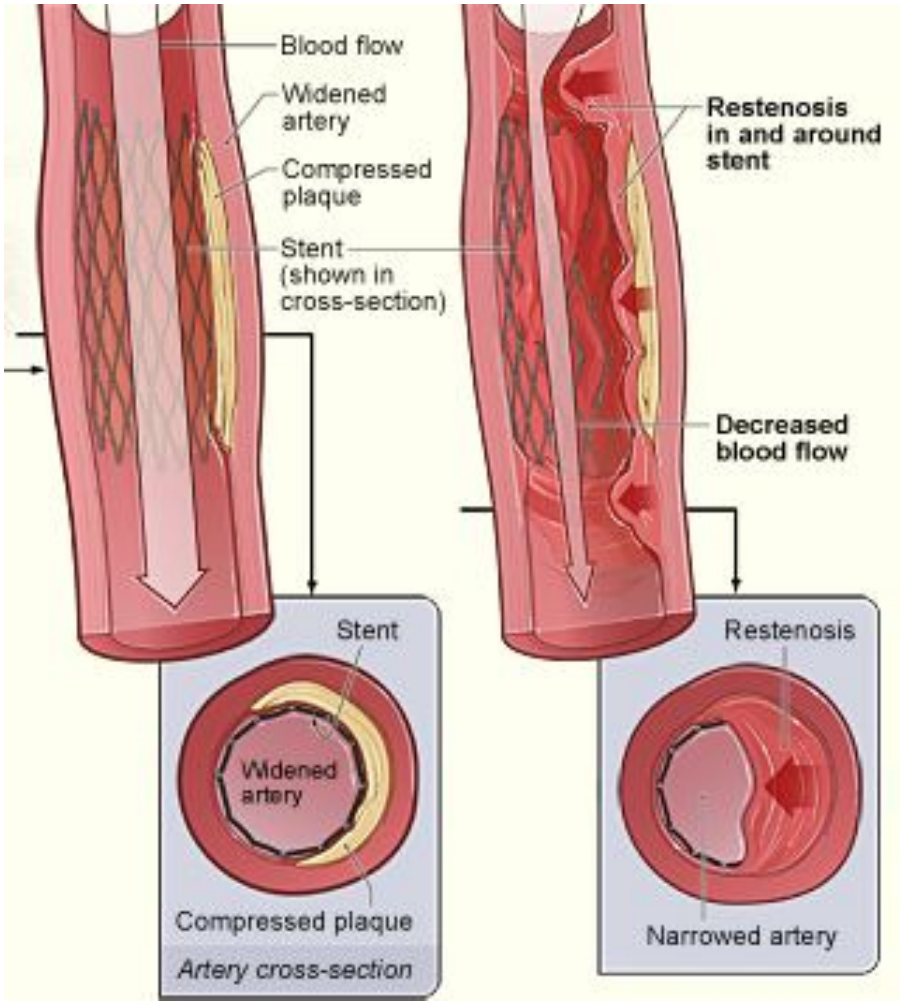
1988

2. Bare Metal Stent (BMS):
Julio Palmaz and Richard Schatz develop a stainless steel stent for coronary applications





Restenosis after Stenting



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Interventional Cardiology entering the 3rd revolution

1977

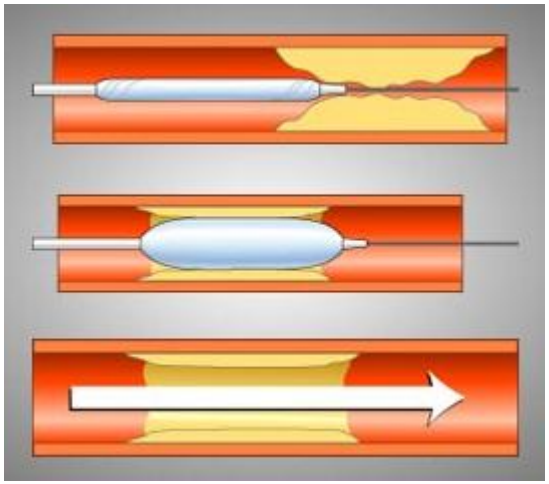
1. Balloon (PTCA):
Andreas Gruntzig performs the first PTCA in Zurich, Switzerland

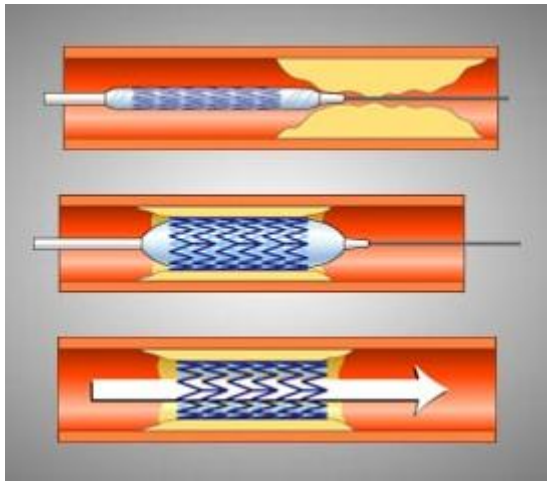
1988

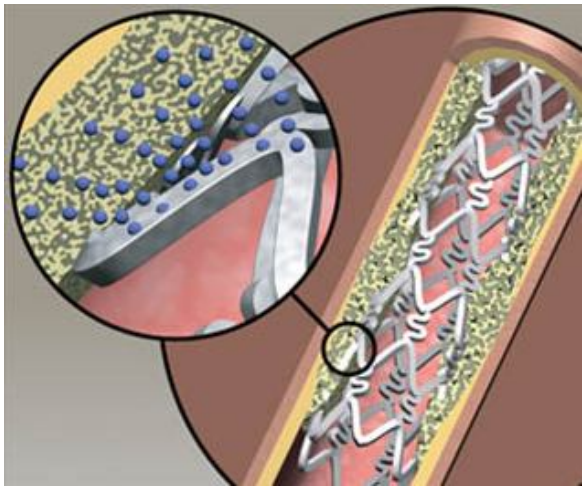
2. Bare Metal Stent (BMS):
Julio Palmaz and Richard Schatz develop a stainless steel stent for coronary applications

2002 - 2003

3. Drug-eluting stents (DES):
introduced to the European and U.S. markets







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Interventional Cardiology entering the 4th revolution

1977

1. Balloon (PTCA):
Andreas Gruntzig performs the first PTCA in Zurich, Switzerland

1988

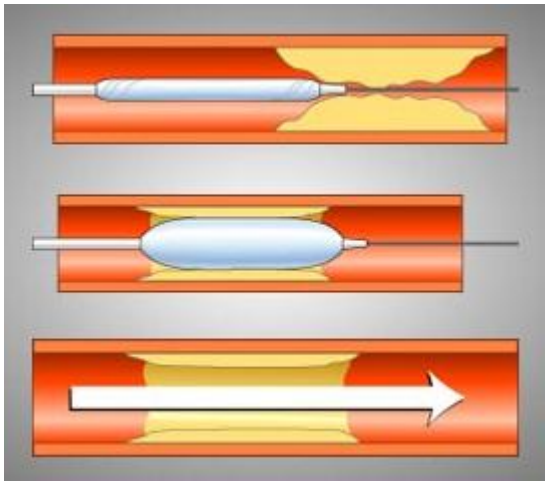
2. Bare Metal Stent (BMS):
Julio Palmaz and Richard Schatz develop a stainless steel stent for coronary applications

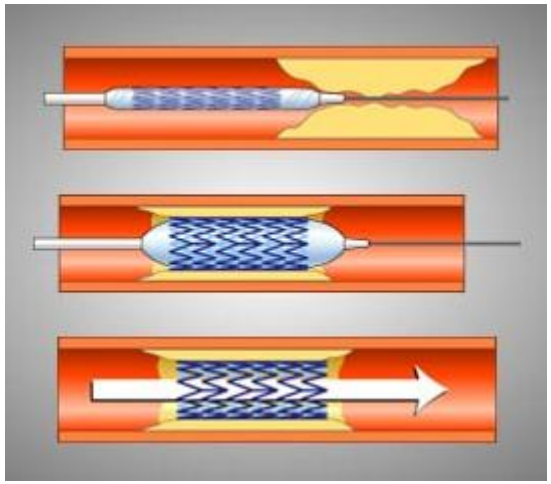
2002 - 2003

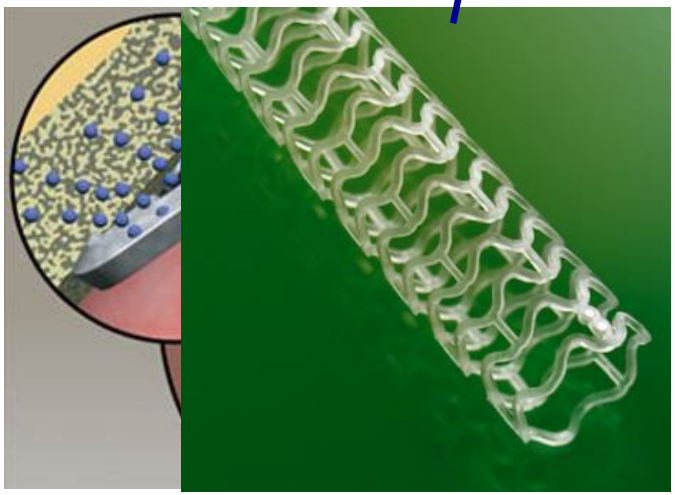
3. Drug-eluting stents (DES):
introduced to the European and U.S. markets

2011

4. Absorb
Bioresorbable Vascular Scaffold (BVS)







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Absorb Bioresorbable Vascular Scaffold (BVS) – The 4th Revolution

The Clinical Need for a Bioresorbable Vascular Scaffold

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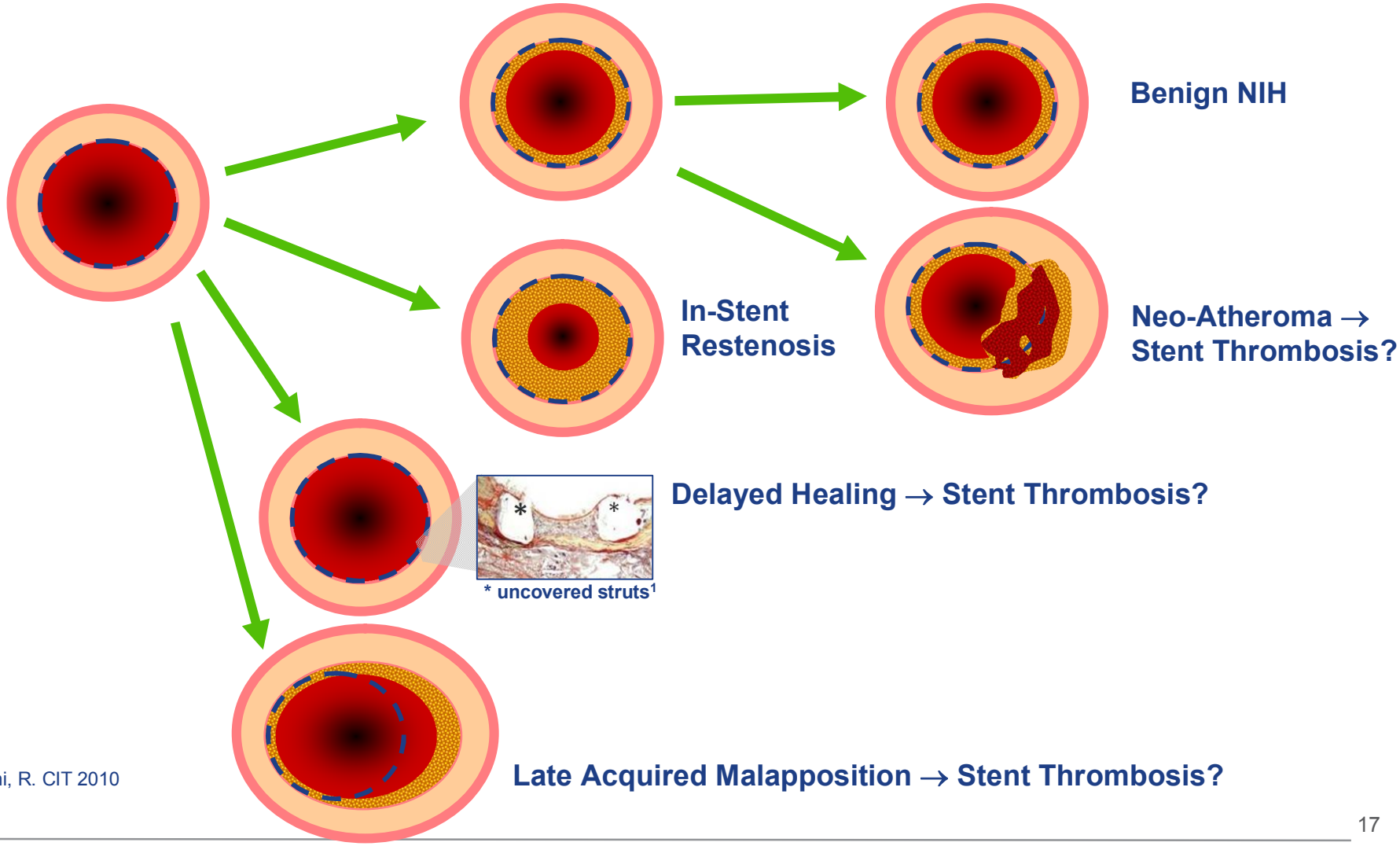
‘Caged’ (Stented) Vessel



1. Virmani, R. CIT 2010

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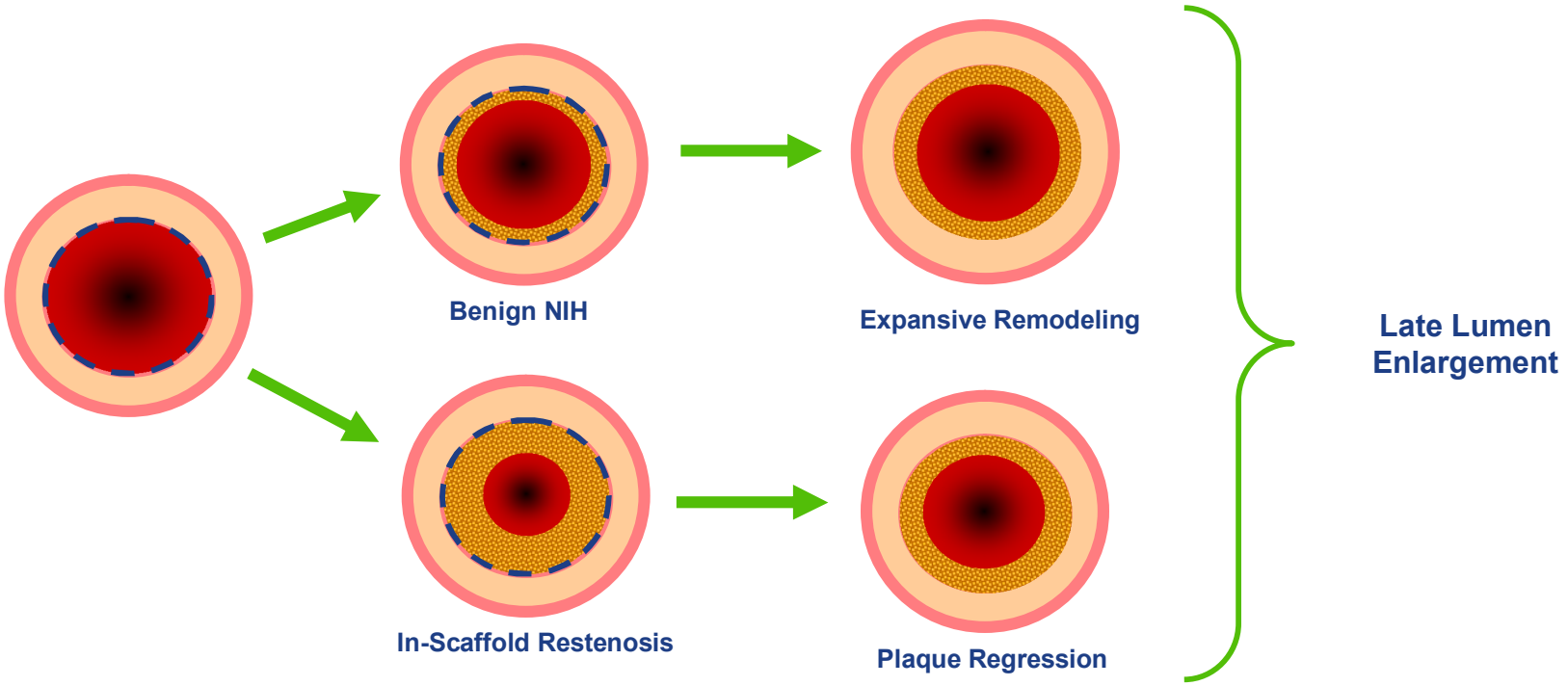
Potential of a Fully Bioresorbable Vascular Scaffold

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



The Clinical Need for a Bioresorbable Vascular Scaffold

Rationale

Vessel scaffolding is only needed transiently*

Vision

Improve Long Term Outcomes for Patients by Leaving No Scaffold Behind[1]

Potential Benefits

- 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.

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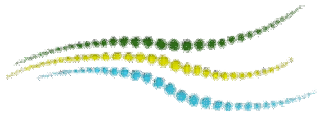
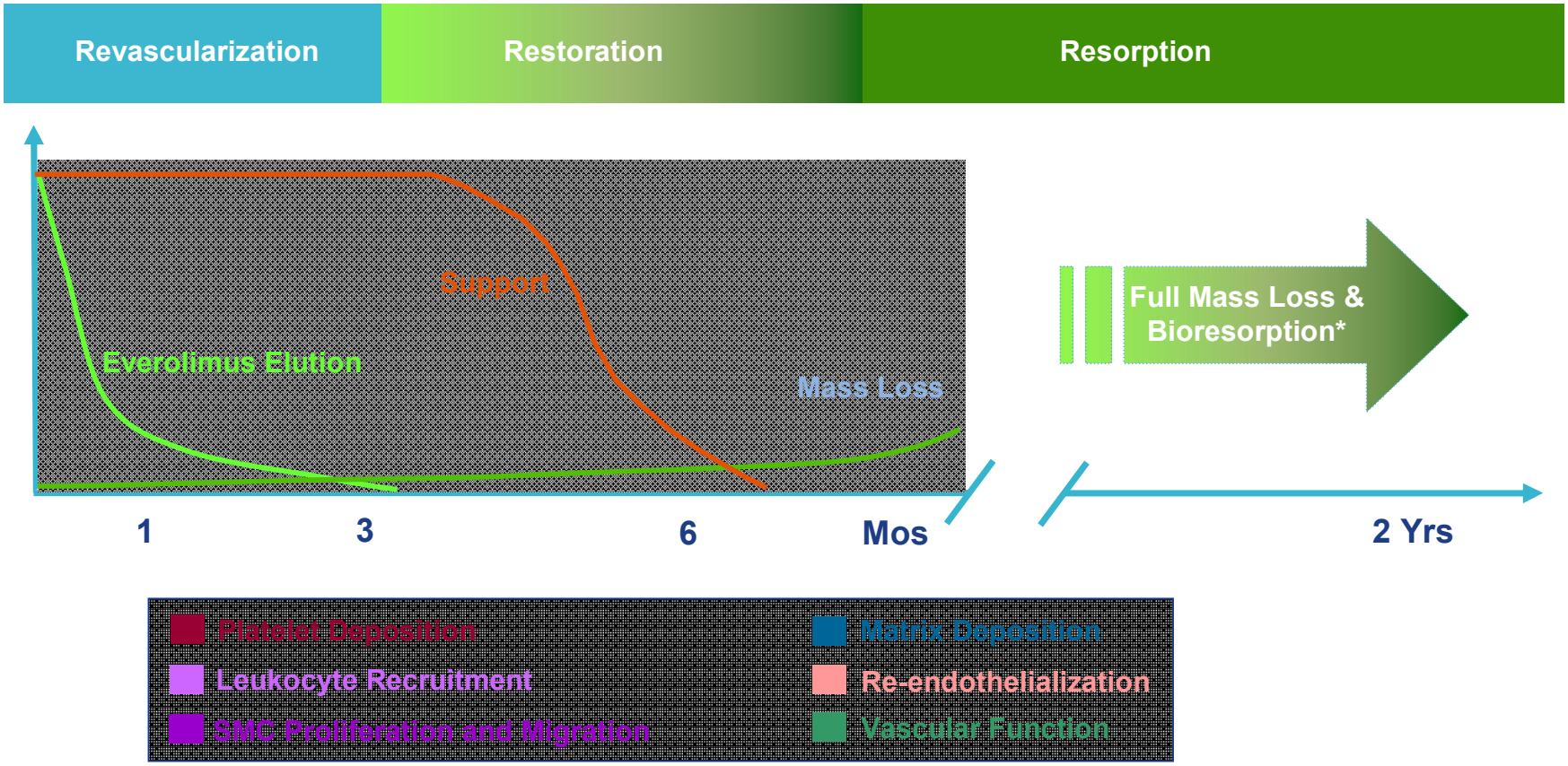
Absorb Bioresorbable Vascular Scaffold (BVS)

Design Goals of a Bioresorbable Vascular Scaffold



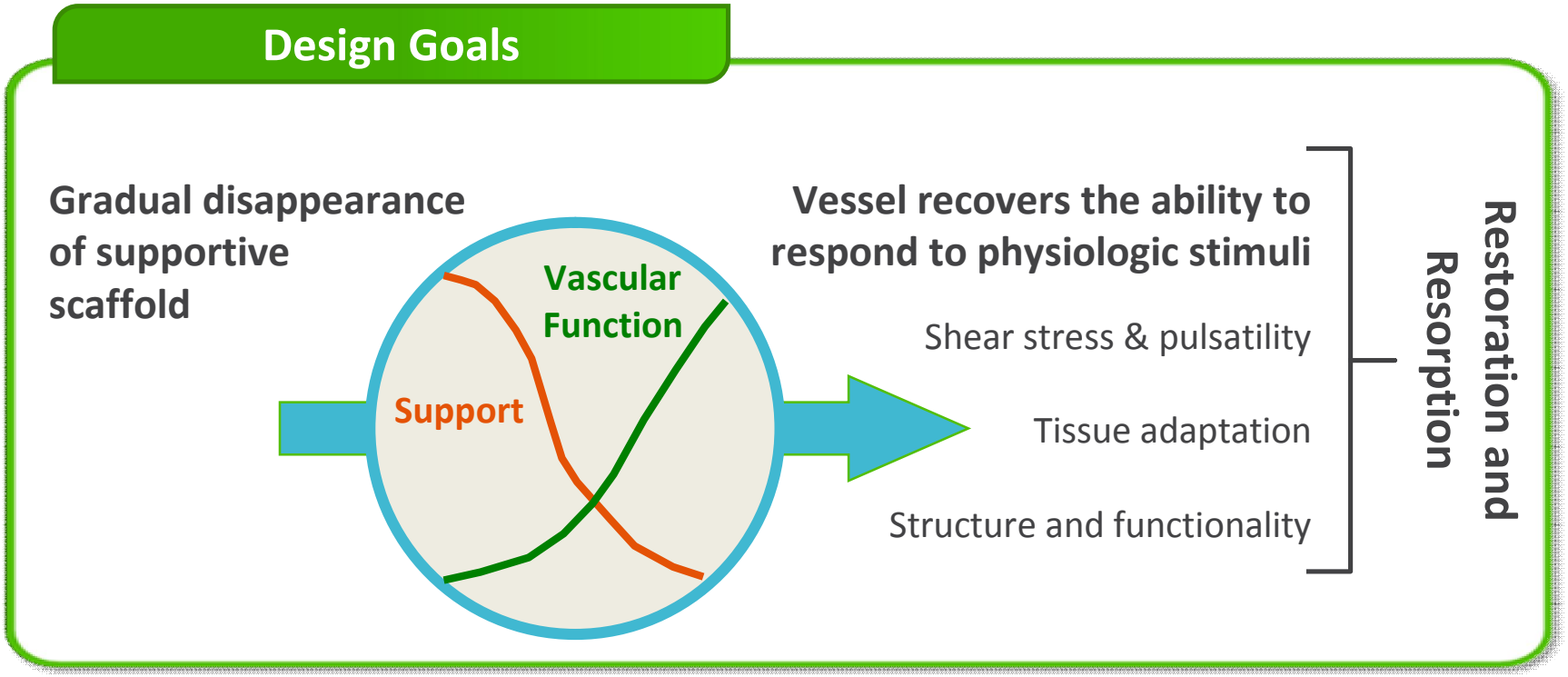
What is Required of a Fully Bioresorbable Scaffold ???



Forrester JS, et al., *J. Am. Coll. Cardiol.* 1991; **17:** 758.

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

Potential for Mechanical Conditioning



Mechanical conditioning may lead to improved cellular organization and vascular function

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

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Absorb Bioresorbable Vascular Scaffold (BVS)

Device Design and Technology

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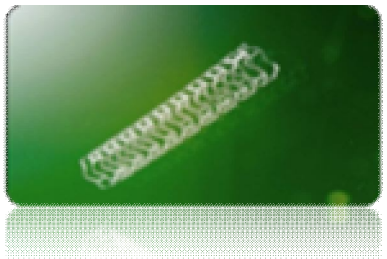
Abbott Vascular Everolimus-Eluting Bioresorbable Vascular Scaffold Components

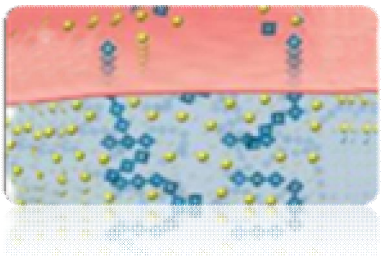
Bioresorbable Scaffold

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



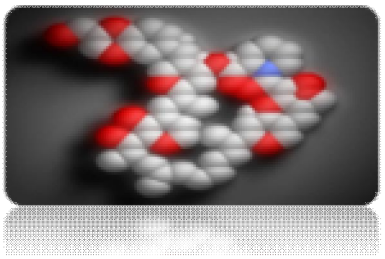
Bioresorbable Coating

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



Everolimus

- Similar dose density and release rate to XIENCE V



XIENCE V Delivery System

- World-class deliverability

*Except for platinum markers
All illustrations are artists' renditions

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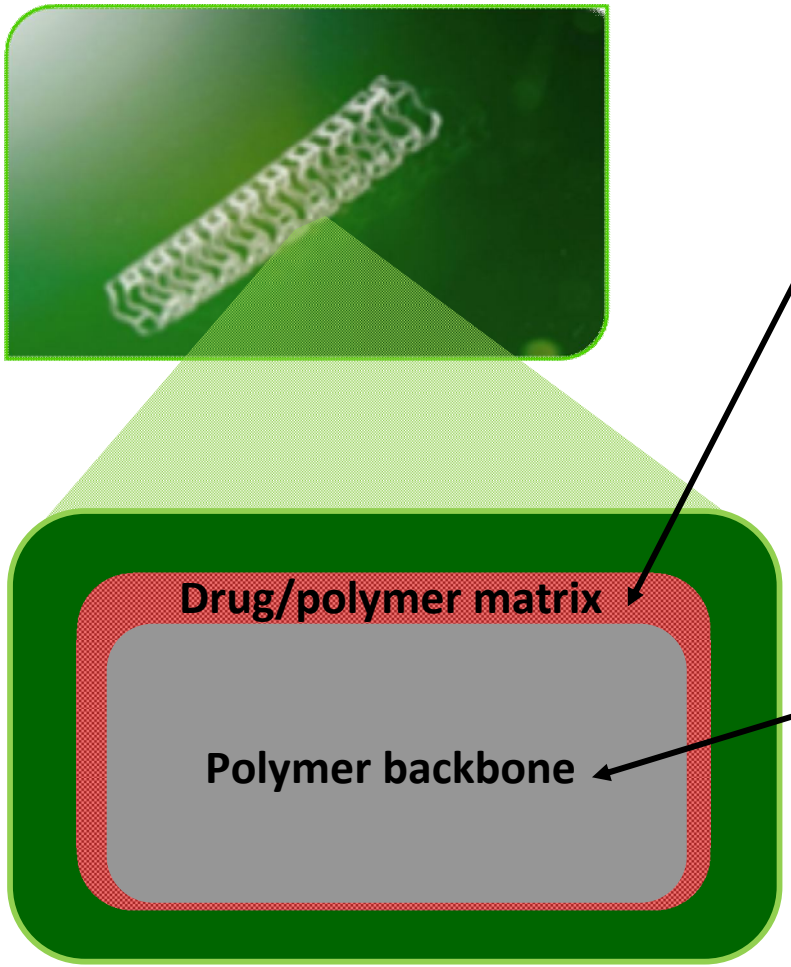
Bioresorbable Polymer



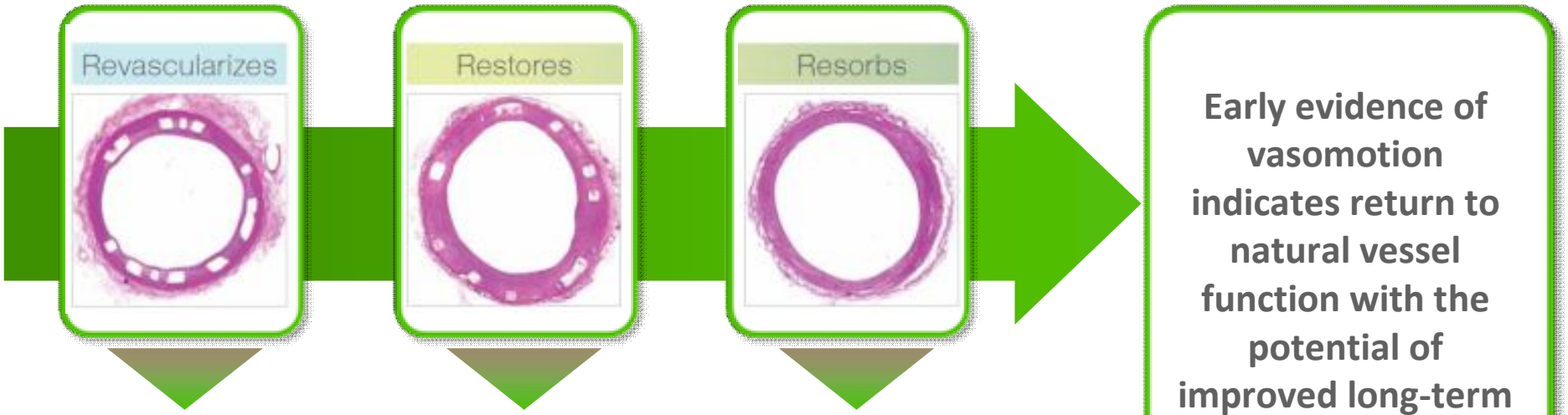
Everolimus/PDLLA Matrix Coating

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

PLLA Scaffold

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

Absorb Bioresorbable Vascular Scaffold: Three Phases of Functionality



Revascularizes like a best-in-class DES, XIENCE

Enables natural vessel function for improved long-term outcomes

Resorbs in a benign fashion with no inflammation or irritation, leaving no scaffold behind*

Vascular Reparative Therapy (VRT)

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

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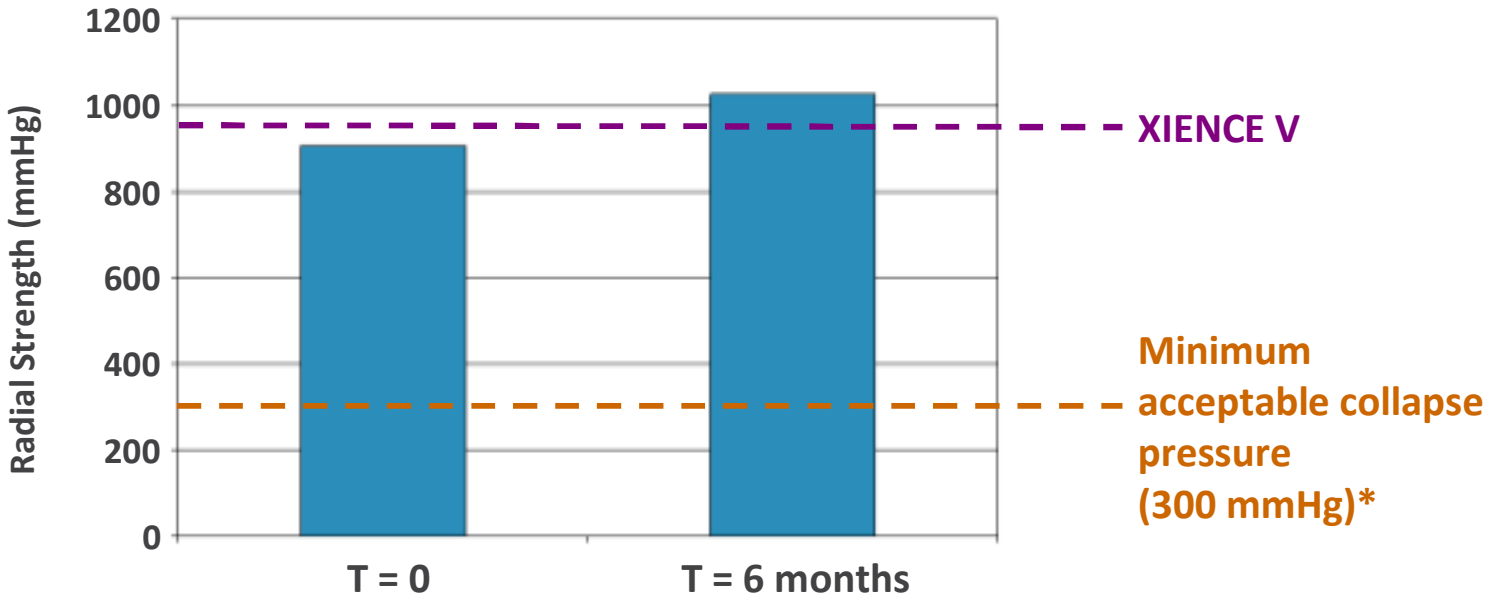
Absorb Vessel Support Over Time

Absorb Radial Strength



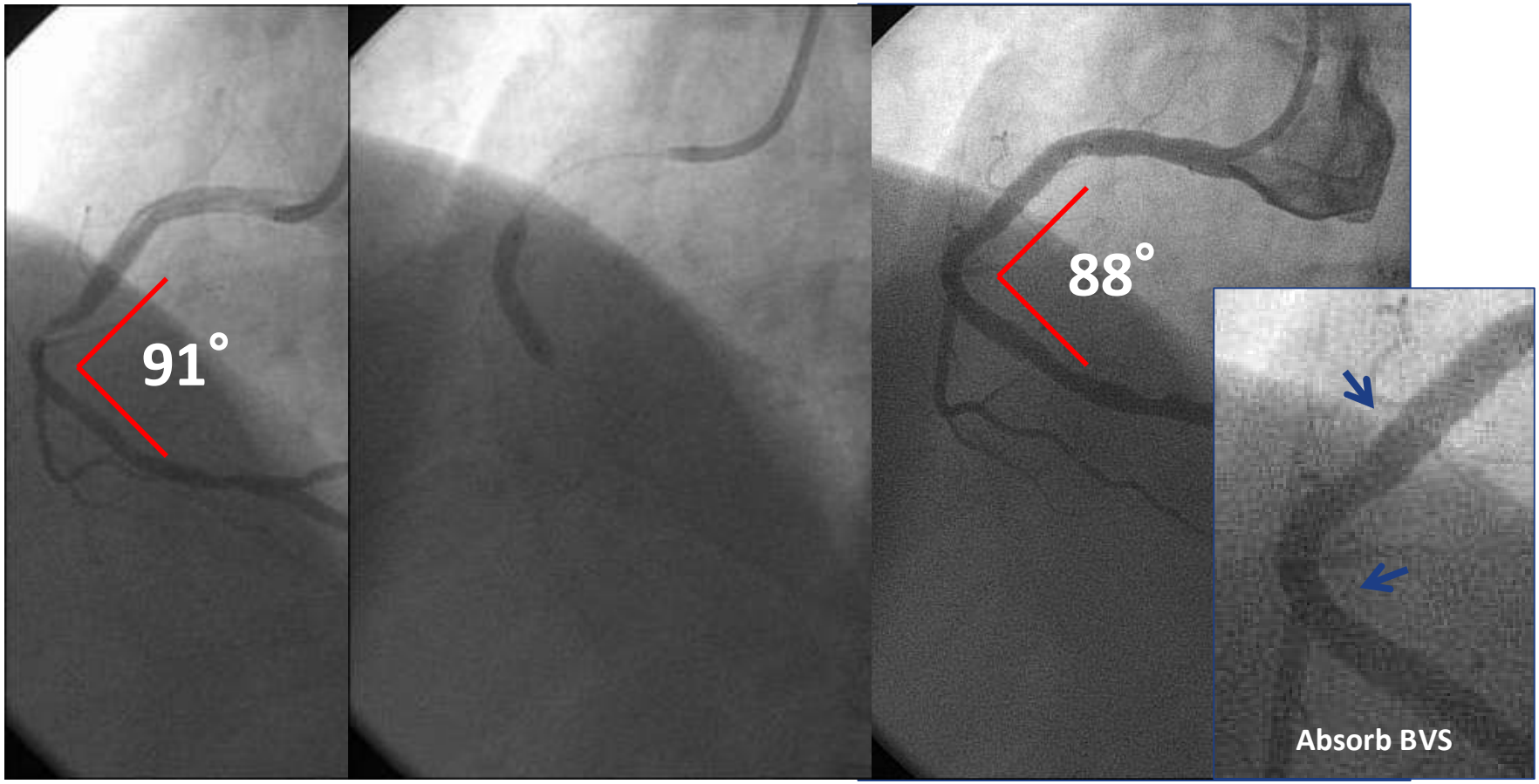
Absorb appears to maintain adequate support for at least as long as is needed

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.

Absorb Conformability

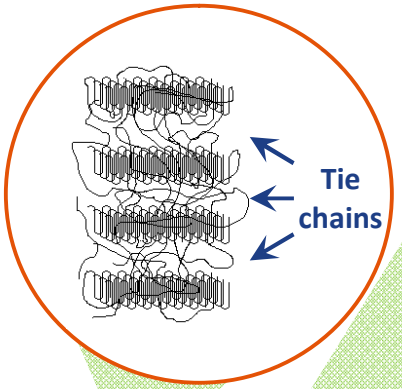
Absorb provides better conformability compared to metallic platforms

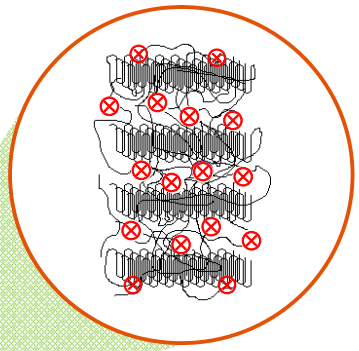


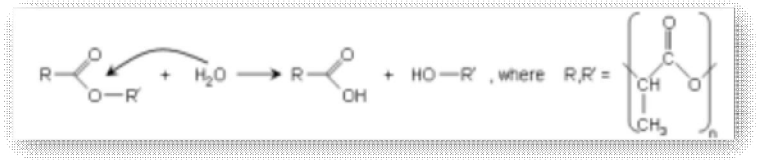
Serruys, PW. , TCT 2009; J. Gomez-Lara, JACC Cardiovascular Interventions

Polylactide Degradation vs. Radial Support

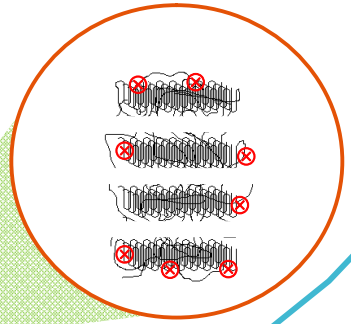
Hydrolysis occurs via random chain scission of the ester bond







Hydrolysis randomly cleaves amorphous tie chains, leading to a decrease in molecular weight without altering radial strength



When enough tie chains are broken, the device begins losing radial strength

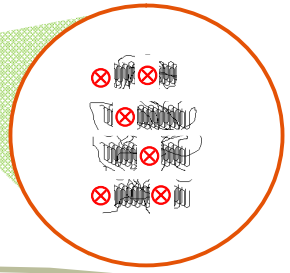
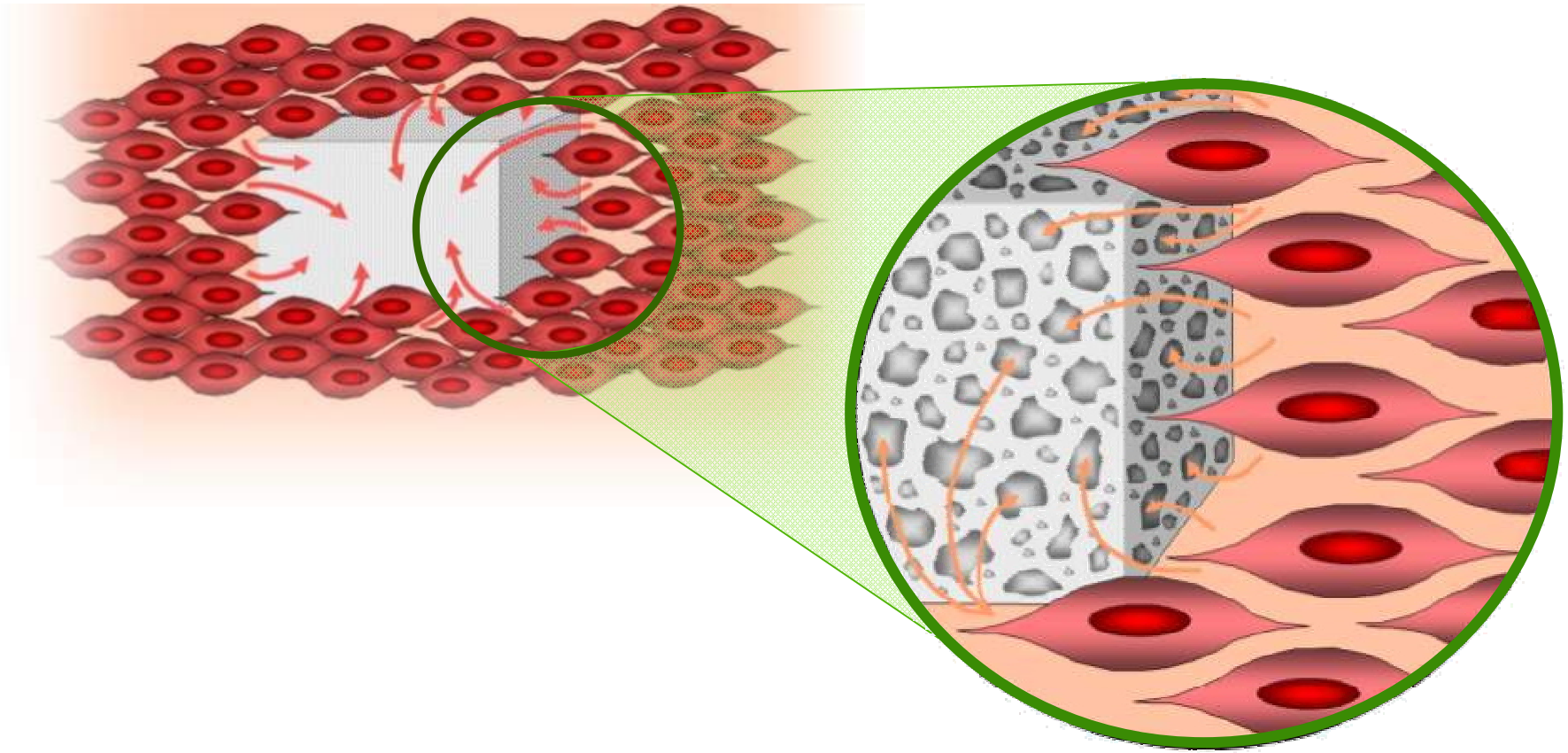


Illustration is artist's rendition. Data on file at Abbott Vascular.

The Absorb BVS Scaffold is Replaced by Functional Cellular Matrix



Based on preclinical histology evidence. Data on file at Abbott Vascular.

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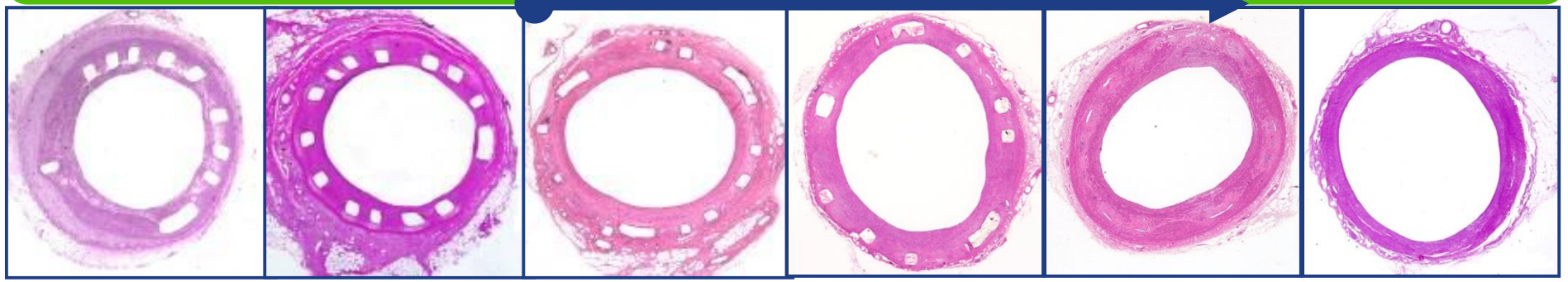
Porcine Coronary Artery Safety Study Demonstrates Biocompatibility

BVS Cohort A Device

Resorption Site

Polymer is replaced by provisional matrix



1 month | 6 months | 1 year | 2 years | 3 years | 4 years

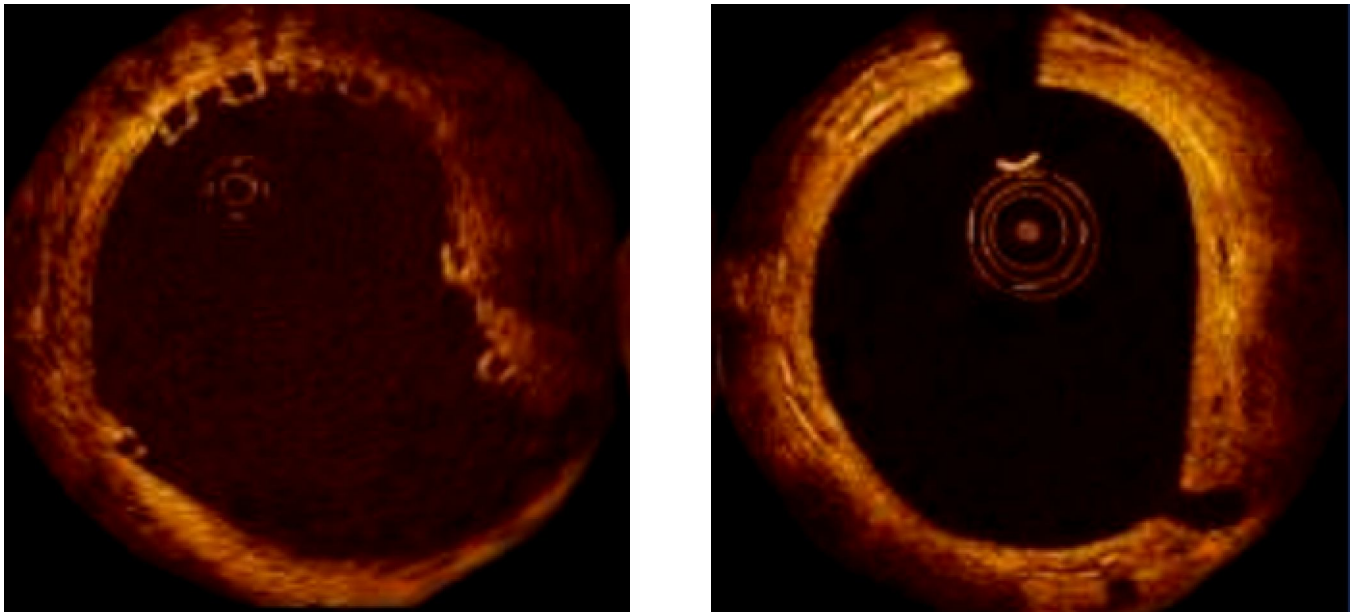
Representative Photomicrographs, Hematoxylin and Eosin, 2x objective

Tests performed by Abbott Vascular.
Data and images on file at Abbott Vascular.

The final golden tube – visualized by OCT (Optical Coherence Tomography)

After implantation

After resorption



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

Absorb Bioresorbable Vascular Scaffold (BVS)

ABSORB Clinical Program and Studies

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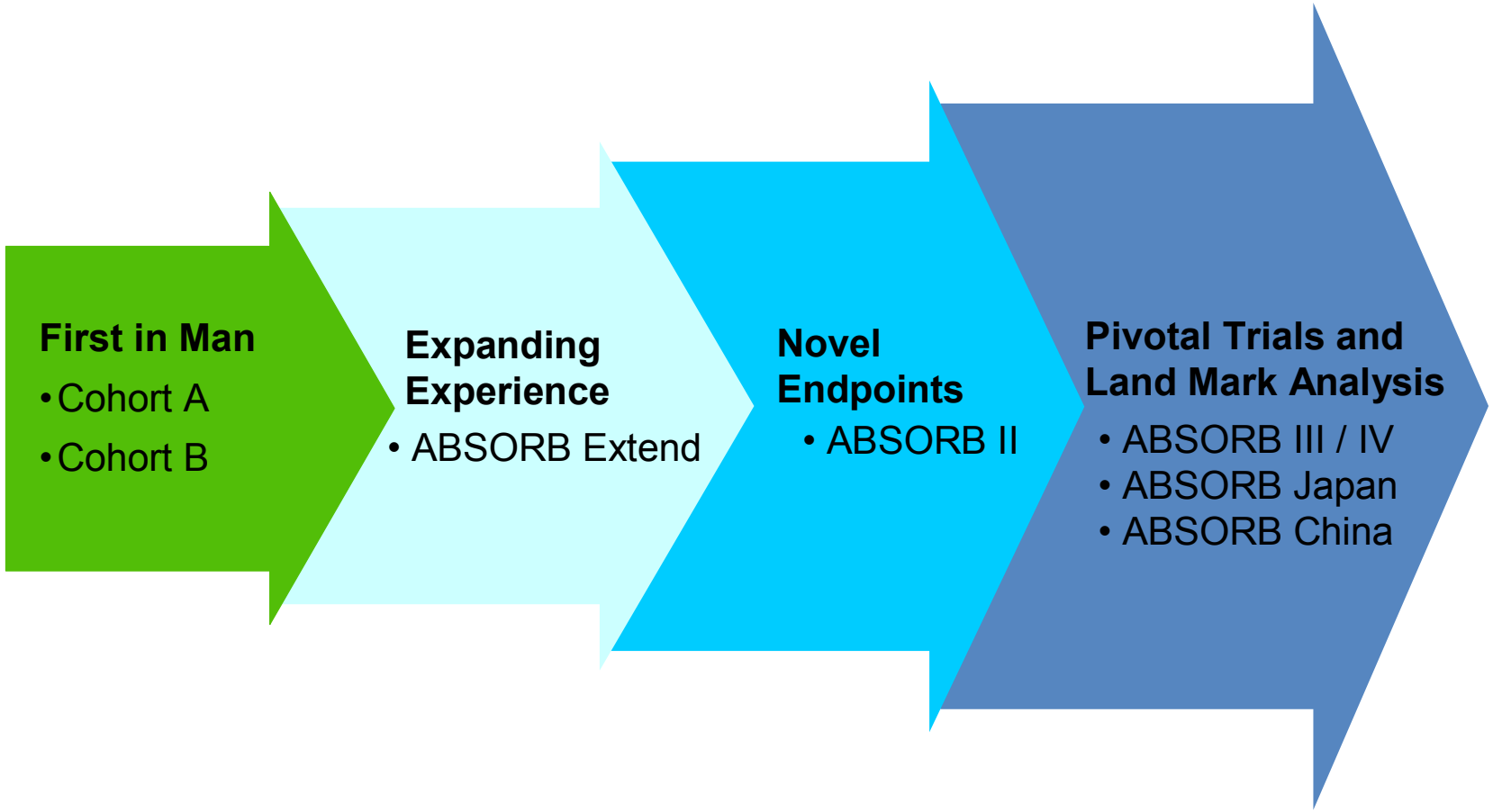
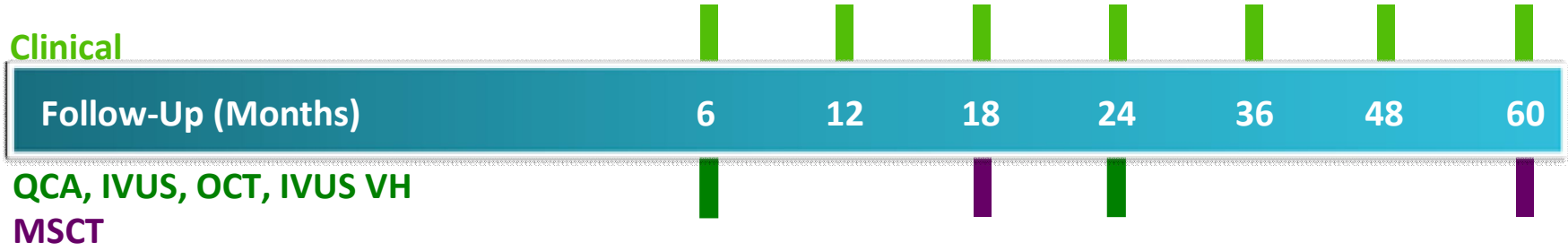
Absorb: A Revolutionary Therapy
Building Evidence



Introduction
ABSORB Cohort A

30 subjects
(Non-randomized) 4 sites in Europe & New Zealand



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 12 mm scaffolds (3.0 x 18 mm scaffolds available after enrolment start and used in 2 pts)

ABSORB Cohort A
Excellent Long-Term Data Out to 5 Years

- **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 withdrew consent and missed the 9, 12, 18 month and 2, 3, and 4 year visits; two patients died from a non-cardiac causes, one at 706 days and one at 888 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

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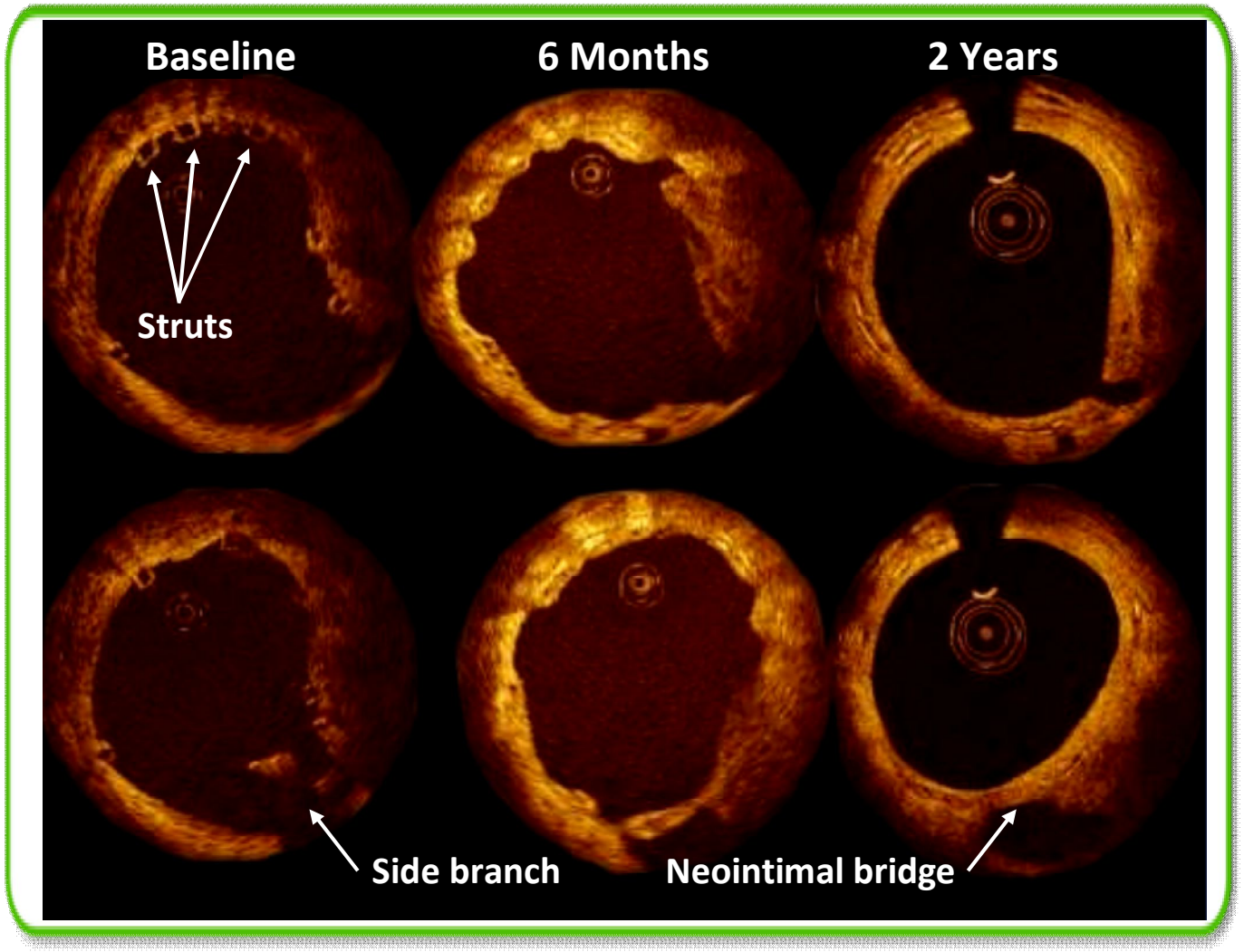
ABSORB Cohort A
OCT Images – Baseline, 6 months and 2 years



Serruys, PW., ESC 2008.

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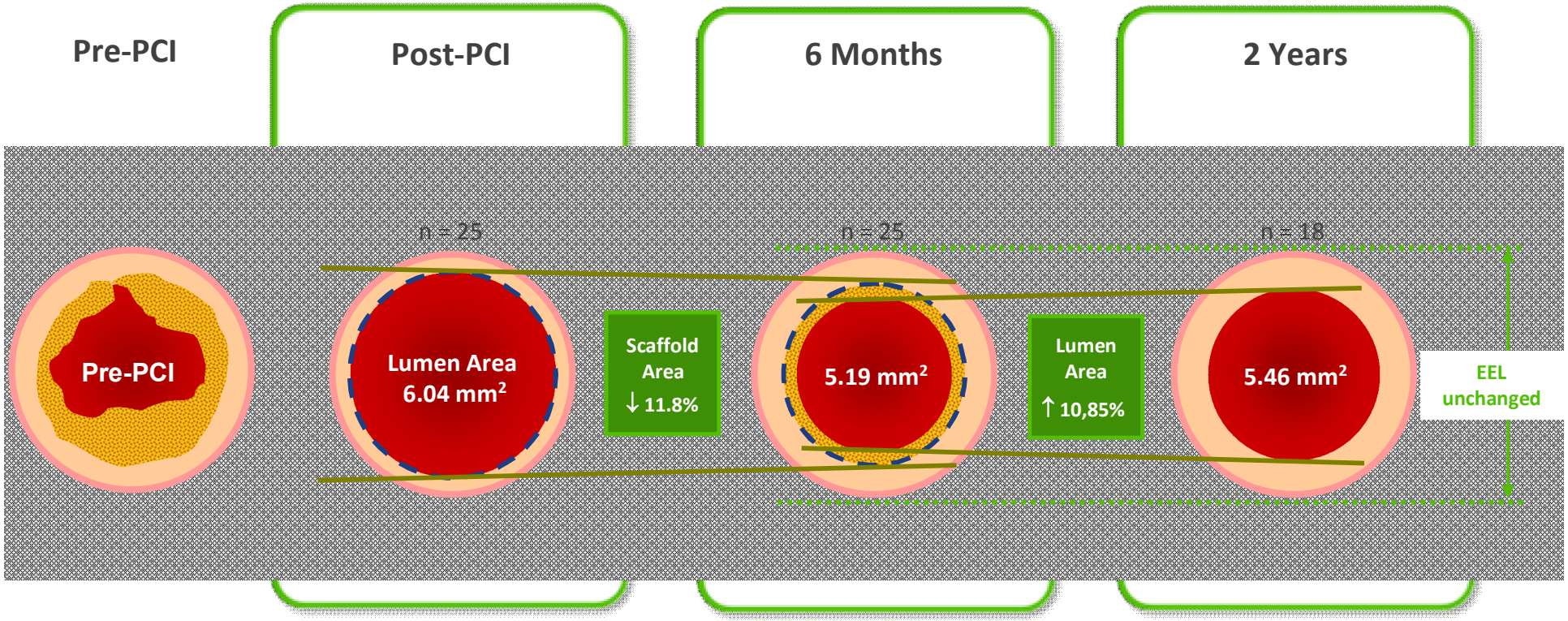
ABSORB Cohort A
Temporal Lumen Dimensional Changes, Per Treatment

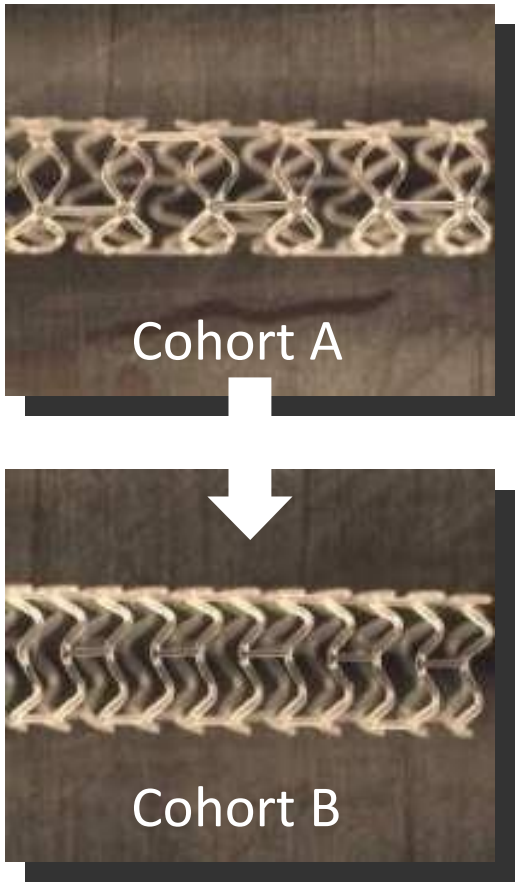


ABSORB Cohort A, Unpaired analysis*

- 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.

BVS Device Optimization Objectives



More uniform strut distribution

More even support of arterial wall

⇒ Lower late scaffold area loss (Late loss)

Maintain radial strength for at least 3 months

Unchanged:

Material, coating and backbone

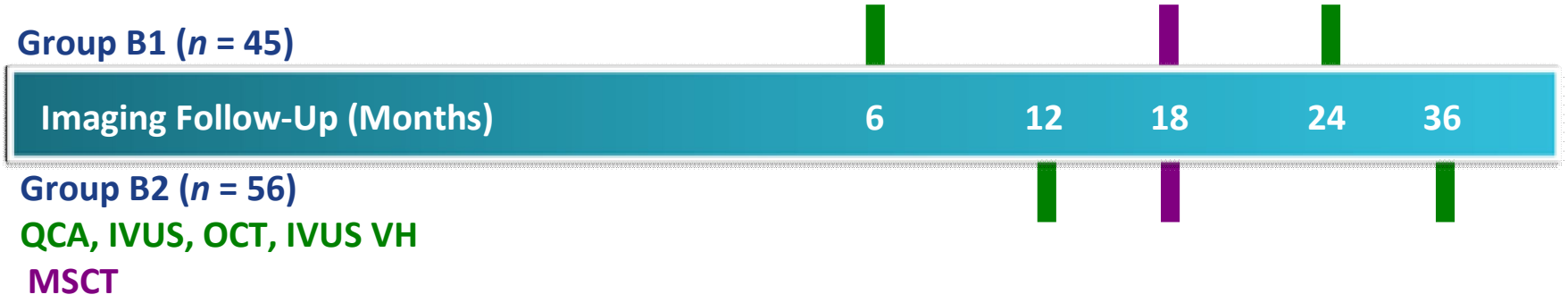
Strut thickness

Drug release profile

Photos taken by and on file at Abbott Vascular.

Introduction
ABSORB Cohort B

101 subjects
(Non-randomized) 12 sites in Europe, Australia, New Zealand



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 18 mm devices

ABSORB Cohort B Group 1&2
Clinical Results - Intent to treat

	30 Days	6 Months	1 Year	2 Years
Non -Hierarchical	n = 101	n = 101	n = 101	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

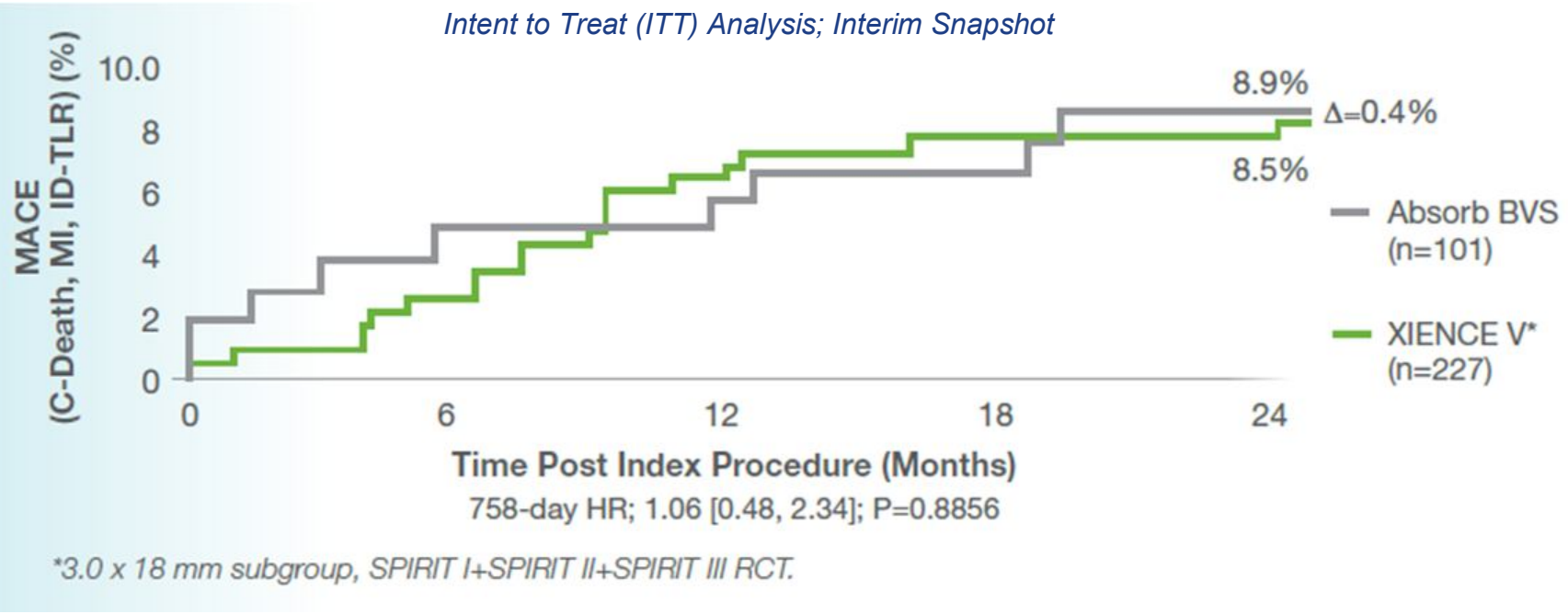
D. Dudek, ACC 2012 / *One patient missed the 2 year FUP

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

ABSORB Cohort B
Clinical Results - MACE

Similar Rates of MACE Compared to Historical XIENCE Data

Intent to Treat (ITT) Analysis; Interim Snapshot



**3.0 x 18 mm subgroup, SPIRIT I+SPIRIT II+SPIRIT III RCT.*

Dudek D. ABSORB Cohort B 2-year data, ACC 2012.

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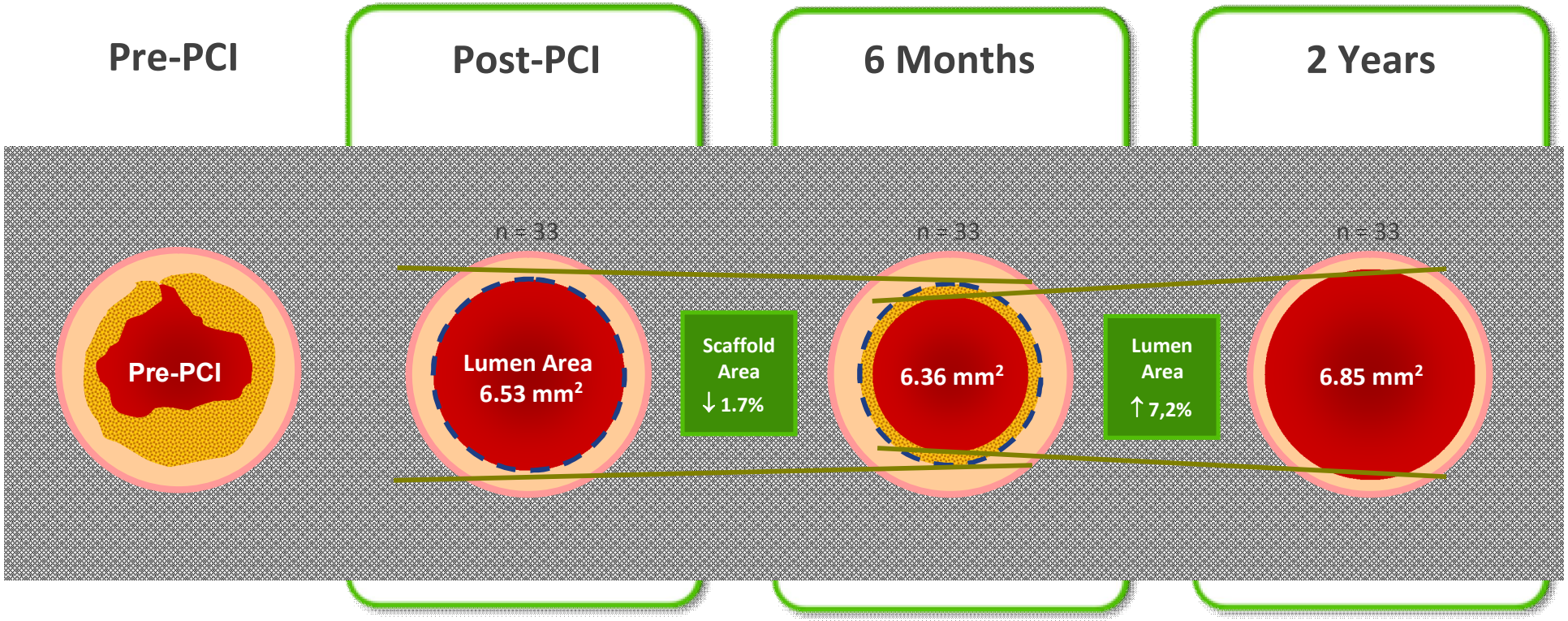
ABSORB Cohort B
Temporal Lumen Dimensional Changes



ABSORB Cohort B, Serial analysis*

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

*Serruys, PW., TCT 2011

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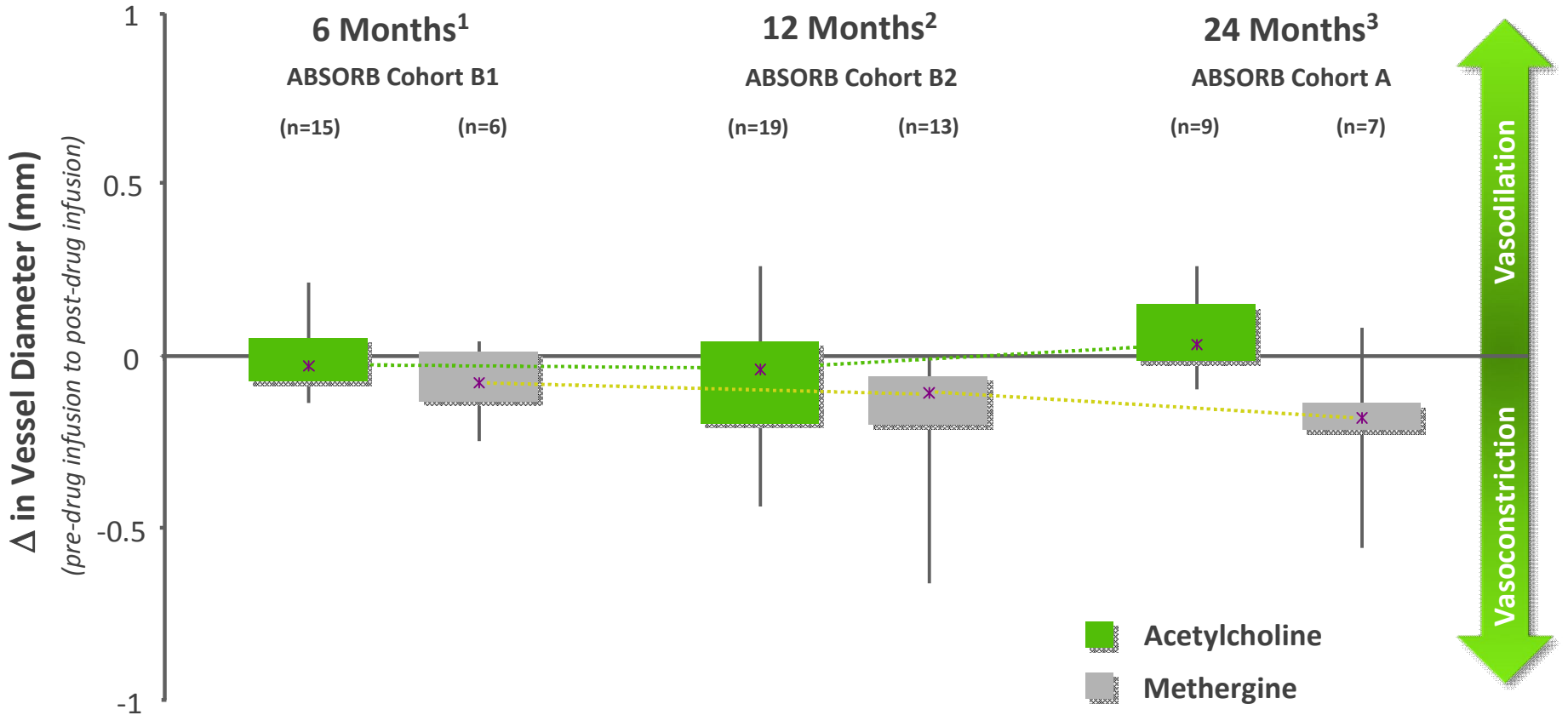
ABSORB Vasomotor Function Testing: Restoration of Vasomotion



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.

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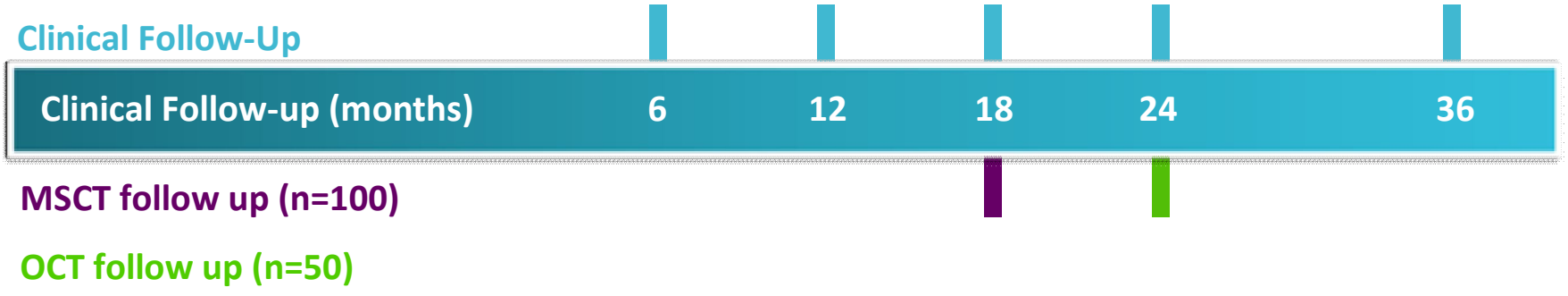
ABSORB EXTEND
Non-Randomized, Single-Arm, Continued Access Trial

~1,000 subjects
Up to 100 global sites (non-US)

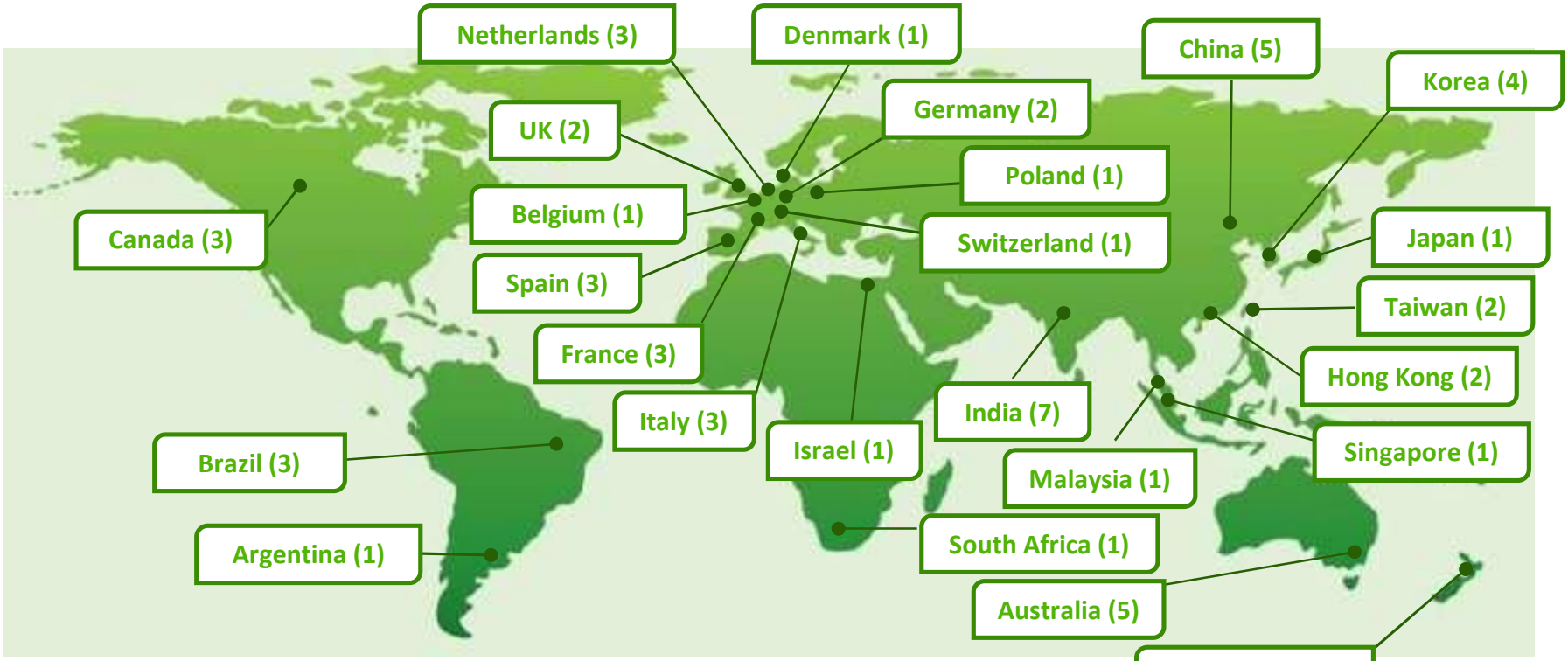


Study Objective	Continued Access trial. FPI: Jan 11, 2011
Endpoints	Typical PCI clinical endpoints
Treatment	Up to 2 *de novo* lesions in different epicardial vessels Planned overlapping allowed in lesions >22 and ≤ 28 mm
Device Sizes	Scaffold diameters: 2.5, 3.0, 3.5 mm Scaffold lengths: 12*, 18, 28 mm

* Sizes to be introduced into the trial once available.

ABSORB EXTEND
Planned Clinical Sites

Expansion in clinical sites, worldwide



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ABSORB Extend
Clinical Results - Intent to treat; Interim Snapshot

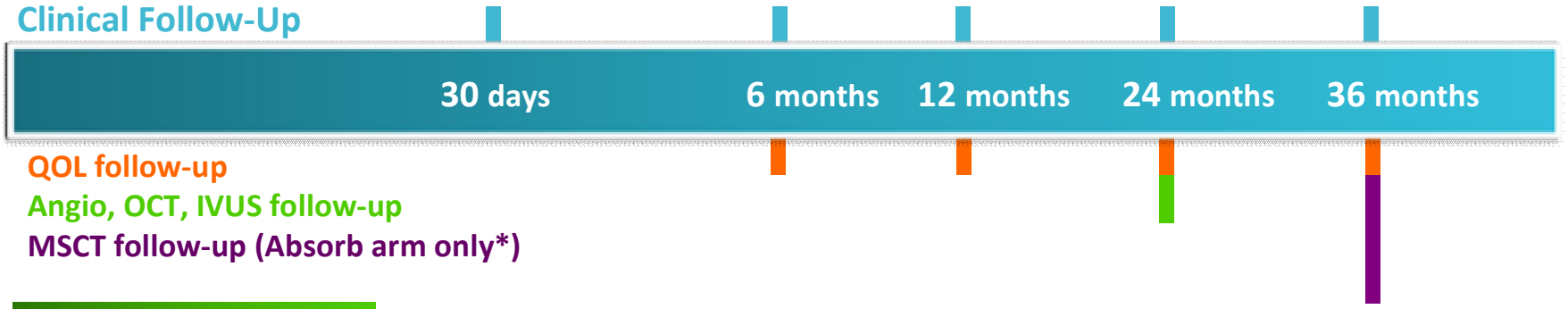
Non-Hierarchical	30 Days* n = 451	6 Months* n = 269
Cardiac Death (%)	**0 (0.0)**	**1 (0.4)****
Myocardial Infarction n (%)	**10 (2.2)**	**7(2.6)**
Q-wave MI	**3 (0.7)**	**3 (1.1)**
Non Q-wave MI	**7(1.6)**	**4 (1.5)**
Ischemia Driven TLR n (%)	**1(0.2)**	**1 (0.4)**
PCI	**1(0.2)**	**1 (0.4)**
CABG	**0**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

501 subjects
(Randomized 2:1 Absorb vs. XIENCE PRIME) Up to 40 European sites + New Zealand

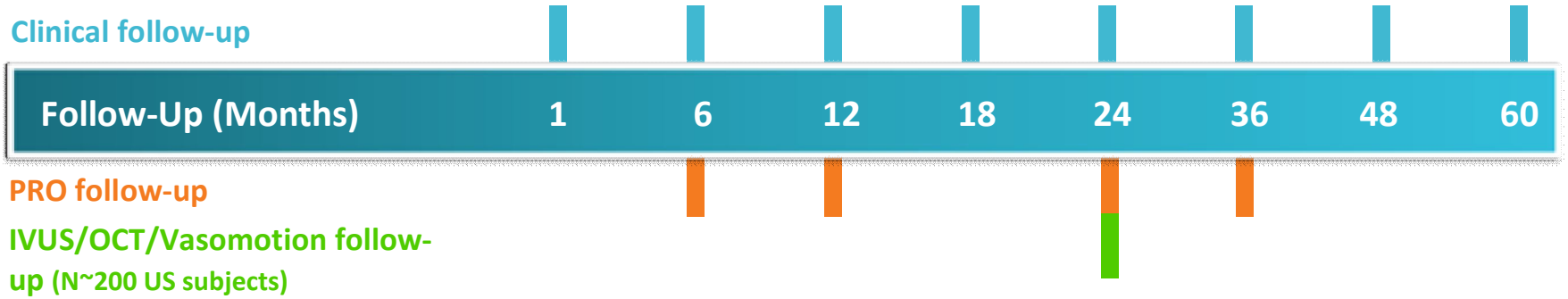


Study Objective	Randomized against XIENCE PRIME control. FPI 28-Nov-2011
Co-primary Endpoints	• Vasomotion assessed by change in Mean Lumen Diameter between pre- and post-nitrate at 2 years (superiority) • Minimum Lumen Diameter (MLD) at 2 years post nitrate minus MLD post procedure post nitrate (non-inferiority, 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, 3.5 mm Scaffold lengths: 12**, 18, 28 mm

* Non-German sites only.
** Sizes to be introduced into the trial once available.

ABSORB III
US Approval Trial

~2000 subjects (1267 Absorb, 733 XIENCE)
US and Australian sites. Follow-up out to 5 years



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

Summary

Current clinical data for the Absorb BVS suggest three phases of functionality:

1. ***Revascularization*** with comparable safety and efficacy outcomes to best in class DES (drug eluting stent)
   - No ST in ABSORB Cohort A (5 year follow up)[1] and Cohort B (2 year follow up)[3]; 0.4% ST at 6 months in ABSORB EXTEND[4]
   - Comparable MACE rates (3.4% at 5 years (Cohort A)[1], 9.0% at 2 years (Cohort B)[3], and 2.9% at 6 months – Extend[4])
2. ***Restoration*** **:** First signs by showing
   - Possible restoration of vasomotion function (19/33 patients had increasing MLD post Acetylcholine – Cohort B)[2]
   - Possible late lumen gain between 6 and 24 months (Cohort B)[1]
3. ***Resorption*** of Absorb has been shown on OCT, resulting in the final "golden tube"

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

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Thank you !

Questions?

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