13th Angioplasty Summit 2008 – TCT Asia Pacific

The Future Landscape of DES: New Stent Platforms, Drug Carriers, and Recent Experiences

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Hospital Israelita Albert Einstein, São Paulo, Brazil
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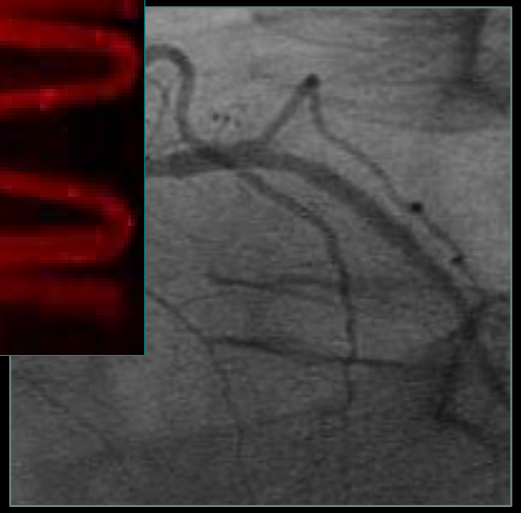
Other than that….

Drug-eluting Stents are Perfect!

Strategies to Improve Outcome with DES



Optimal Stent Design

Drug Duration

Optimal Procedural Result

Improved SAFETY

DES ‘Classification’

1st Generation DES

“2nd Generation DES”

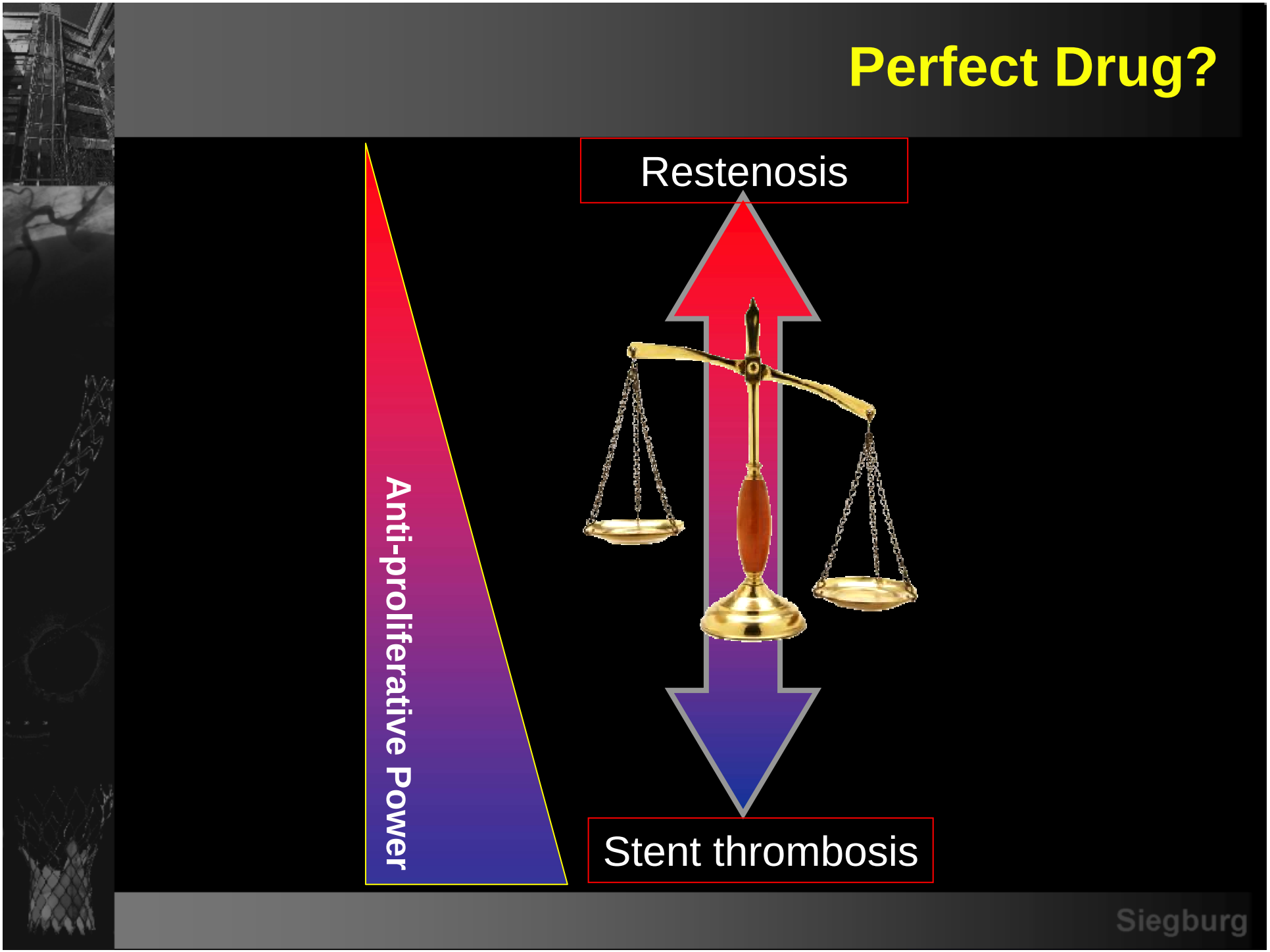
Lesion Dedicated DES

New DES Programs

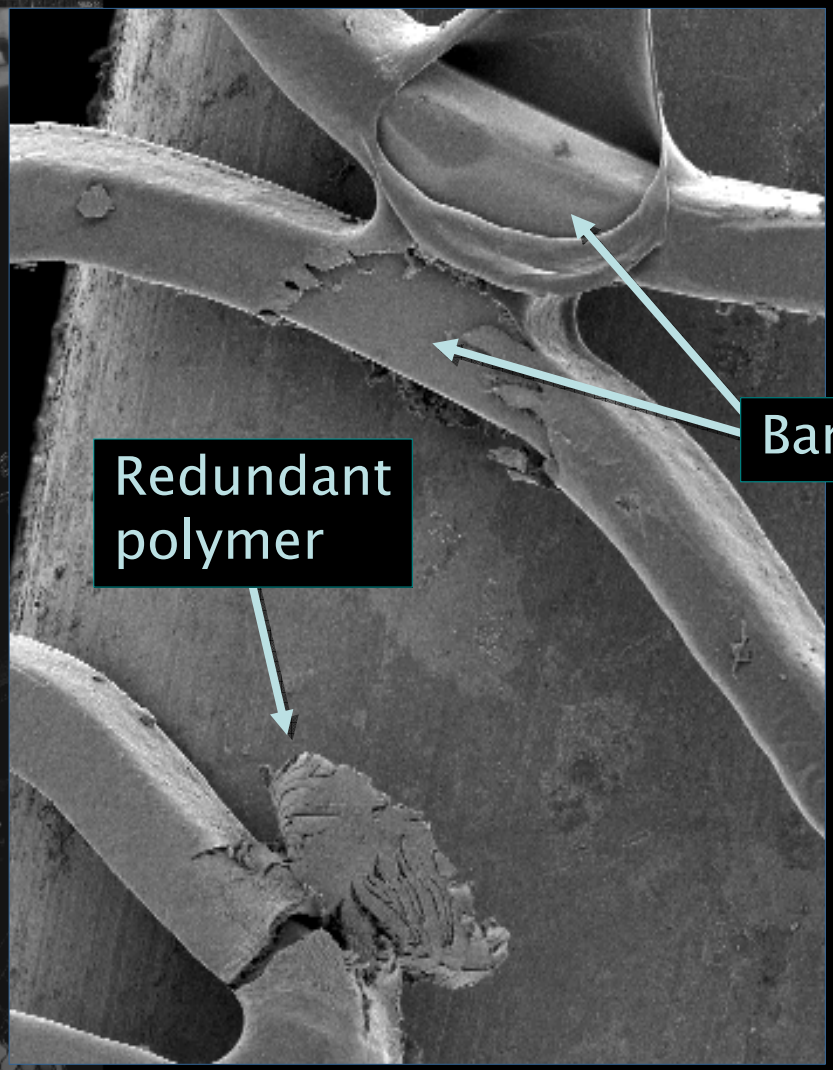
• Paclitaxel	BSC, Conor, Biosensors
• NO Donors	Blue Medical
• Biolimus A9	Biosensors, Terumo, Devax
• Zotarolimus	Zomax, Endeavor CR
• Pimecrolimus	Conor, Avantac
• Melatonin	Blue Medical
• Gleevec	Novartis
• Everolimus	Guidant
• Tacrolimus	Sorin
• EPC Progenitors	Orbus
• Restin-NG	AVI Biopharma
• Paclitaxel Balloon	B- Braun
• Bioabsorbable	Guidant, Biotronik, Reva

……

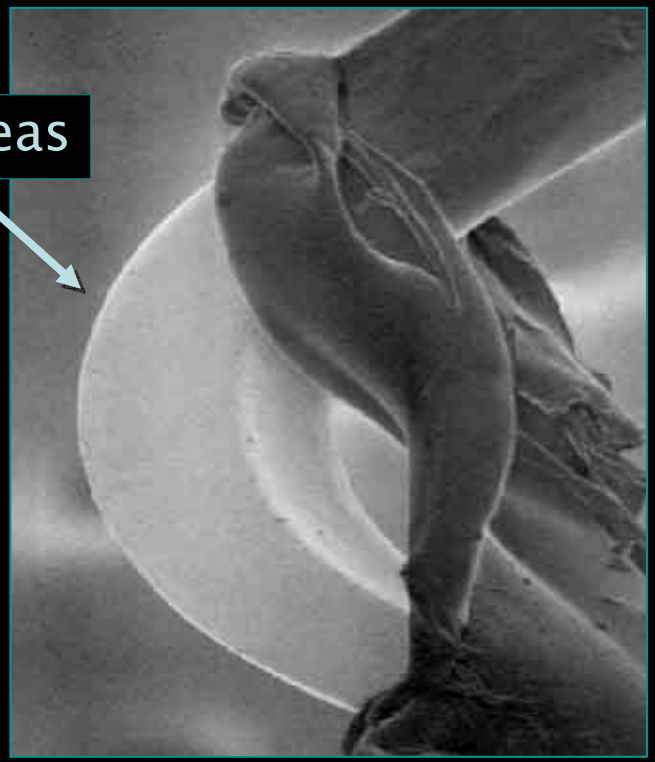
Perfect Drug?



Problems with polymers…

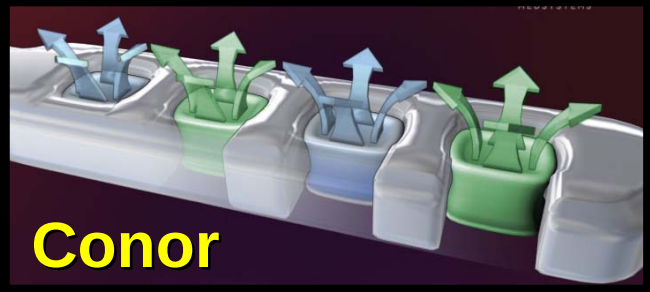


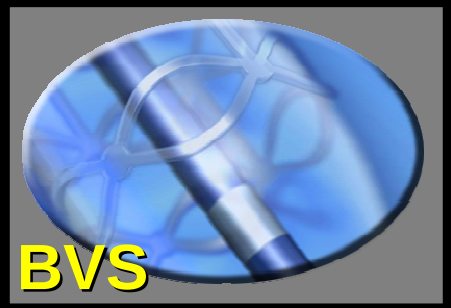
Polymer damaged by expansion in air at room temperature

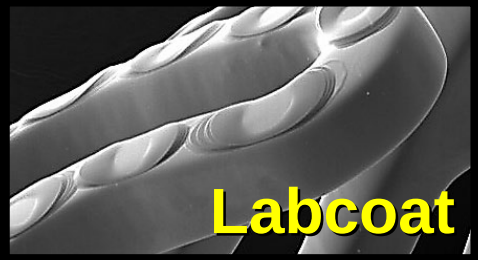


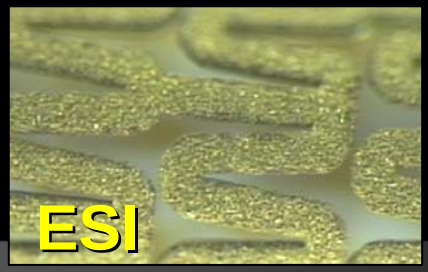
Advanced Approaches to Drug Release

- Bioabsorbable polymers
- Bioabsorbable stents
- Controlled polymer application
- Non polymer release

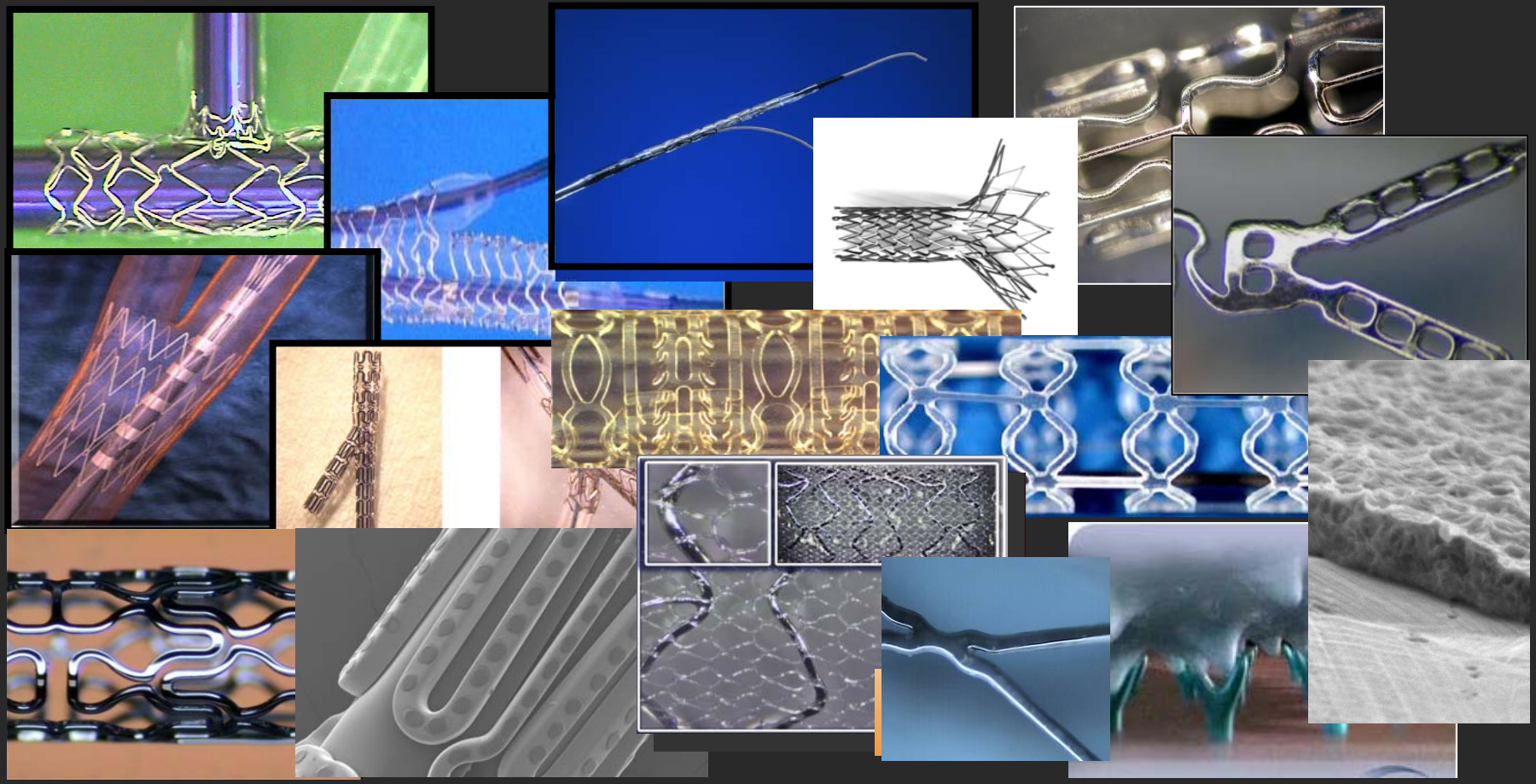




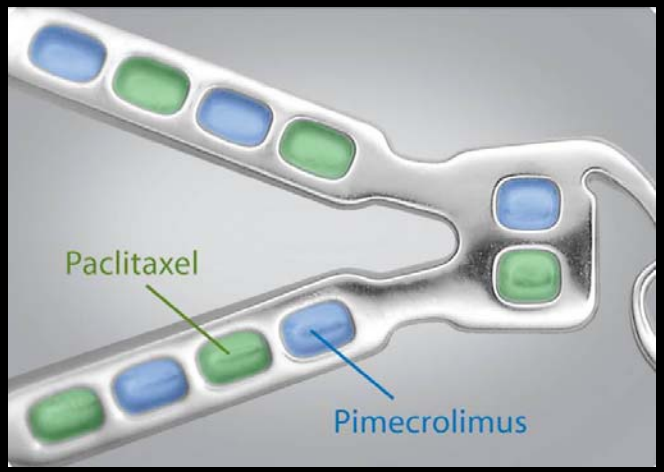




Multiple New Concepts



Conor/Cordis-
Drug Eluting Stent System



Independent, Controlled Drug Release from Adjacent Reservoirs

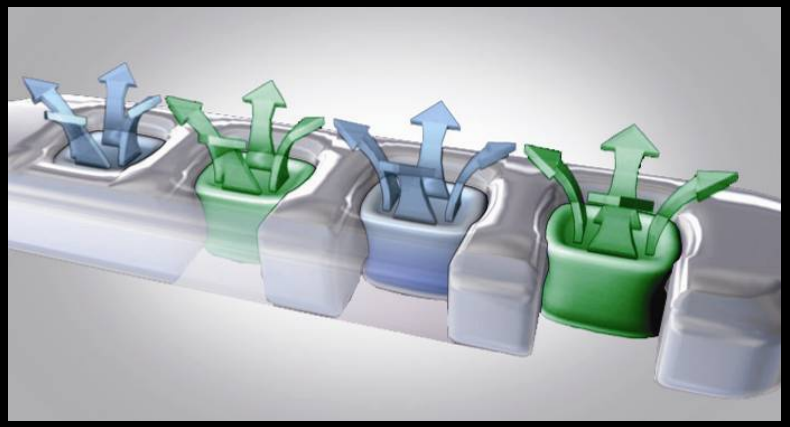
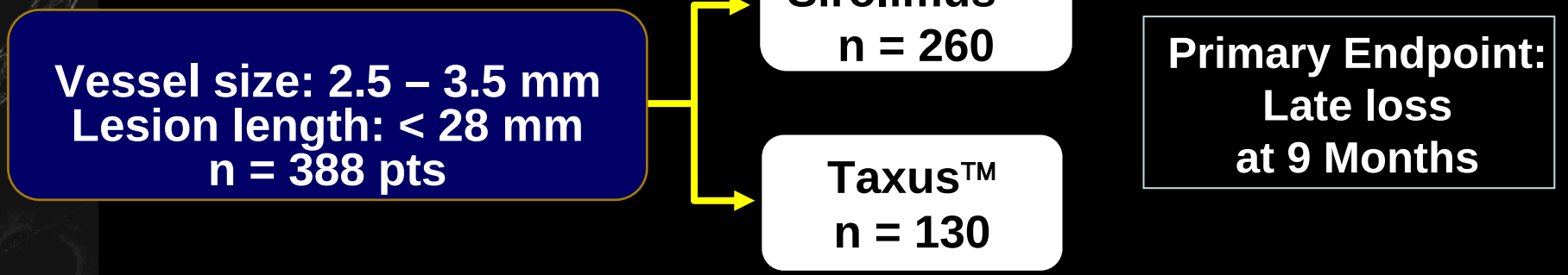


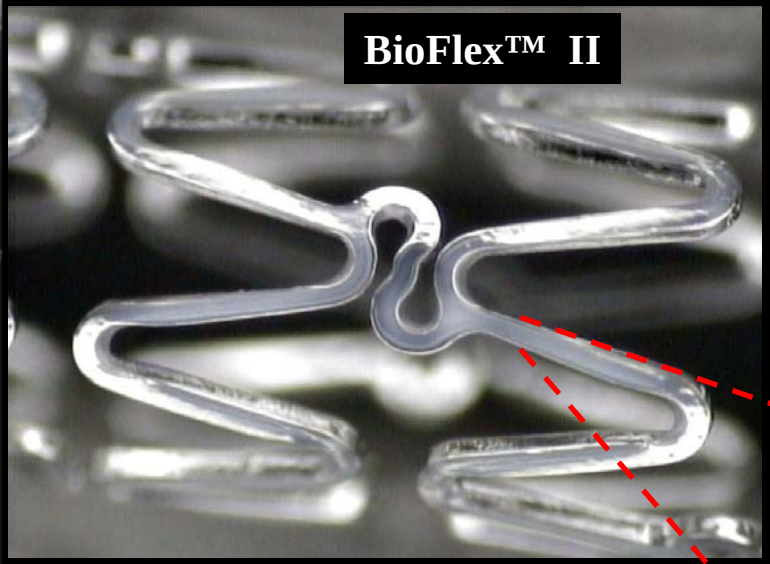
Illustration is an artistic rendering showing theoretical drug release; release is predominantly the direction of the vessel wall.

Res-Elution International Trial
(Abizaid, Ormston)



BioMatrix® III Stent Platform

BIOMATRIX



Biodegradable Drug/Carrier:

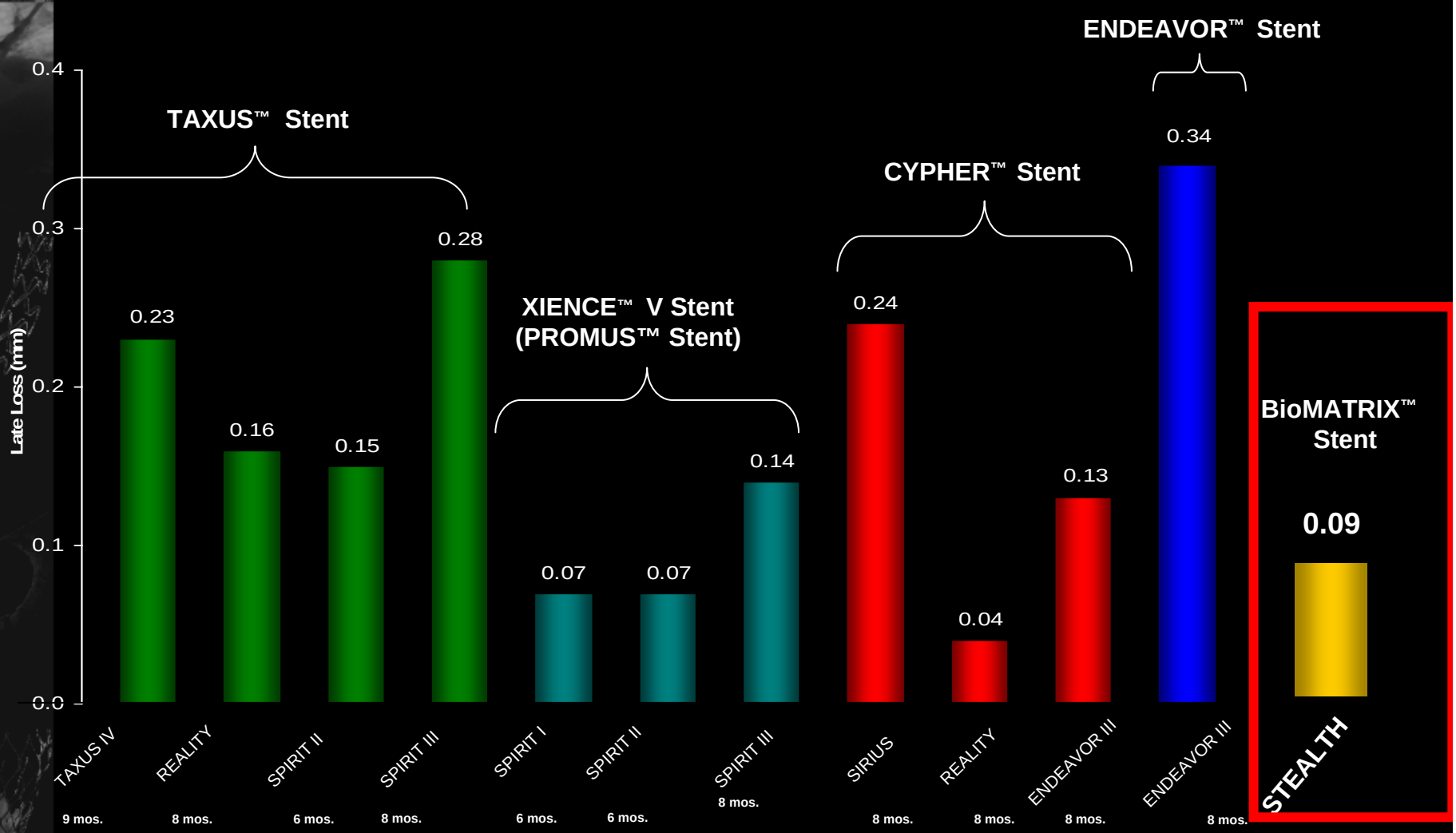
- Biolimus A9® / Poly (Lactic Acid) 50:50 mix
- abluminal surface only (contacts vessel wall)
- 10 microns coating thickness
- degrades in 9 months releasing CO_2+ water

Stent Platform:

- stainless steel (112 microns)
- corrugated ring, quadrature-link™ design
- radius link enhances axial fatigue resistance

Not available for sale in the United Sates.

In-Segment Late Loss
Across Multiple Randomized Clinical Trials



Data from trials that are not head-to-head are not intended to be comparative. SPIRIT is sponsored by Abbott. PROMUS Stent is a private-labeled XIENCE V Everolimus Eluting Coronary Stent System manufactured by Abbott and distributed by Boston Scientific Corporation. XIENCE is a trademark of Abbott Laboratories group of companies. PROMUS, TAXUS and Express² are trademarks of Boston Scientific Corporation or its affiliates. Cypher is a trademark of Cordis Corp. Endeavor is a trademark of Medtronic Vascular, Inc. For products, sponsors, and publications, refer to the Clinical Trial Glossary.

PSST 4128

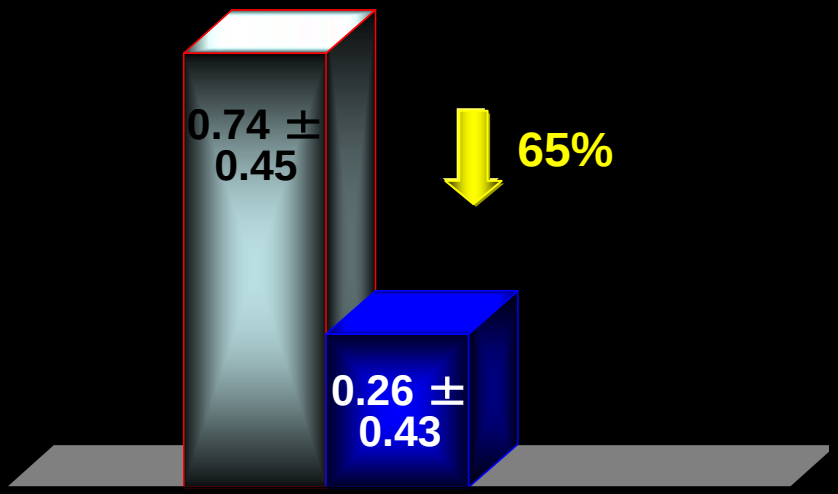
STEALTH I (Abizaid, Grube)

First In-Man
2:1 randomized
n = 120

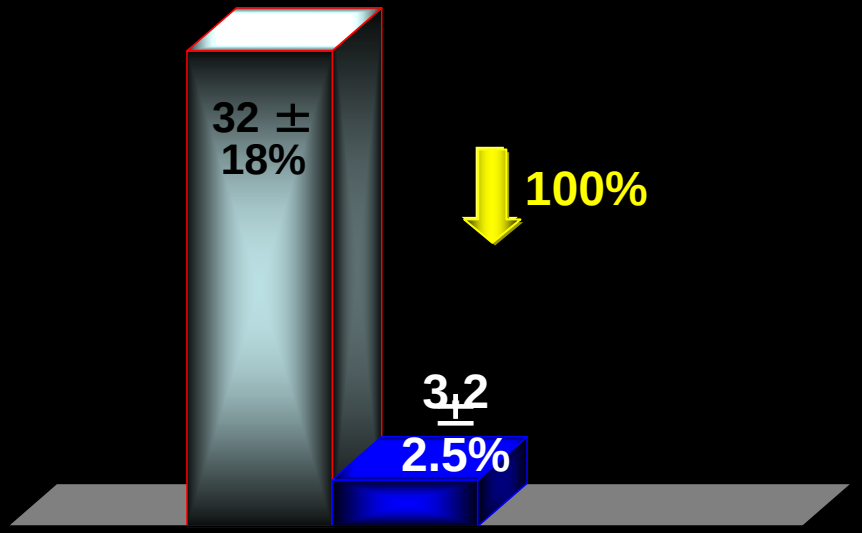
- Biolimus A9 Eluting Stent
  n = 80
- Control Bare Metal Stent
  n = 40

Primary Endpoint:
Late Loss at 6 Months

6-m In Stent Late Loss



6-m IVUS % obstruction



LEADERS Real World Randomized Study

All commers
Vessel size: 2.25 – 4.0 mm
Lesion length: no limit
n = 1700

- BioMatrix™ n = 850
- Cypher™ n = 850

Primary Endpoint:
MACE at 9 Months

STEALTH II Pivotal Study (D.Holmes)

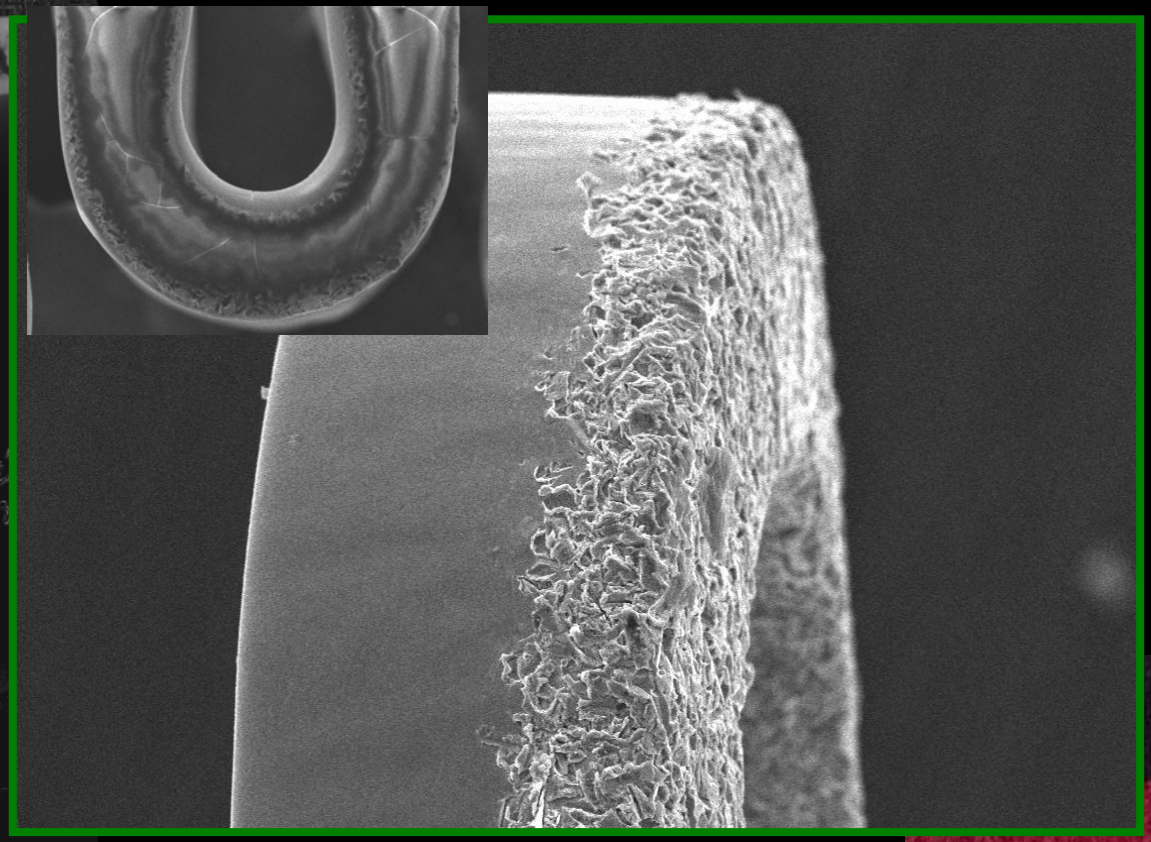
Vessel size: 2.5 – 3.5 mm
Lesion length: 10 – 24 mm
n = 1340

- BioMatrix™ II n = 670
- Taxus™ n = 670

Primary Endpoint:
Event-free TVF
at 9 Months

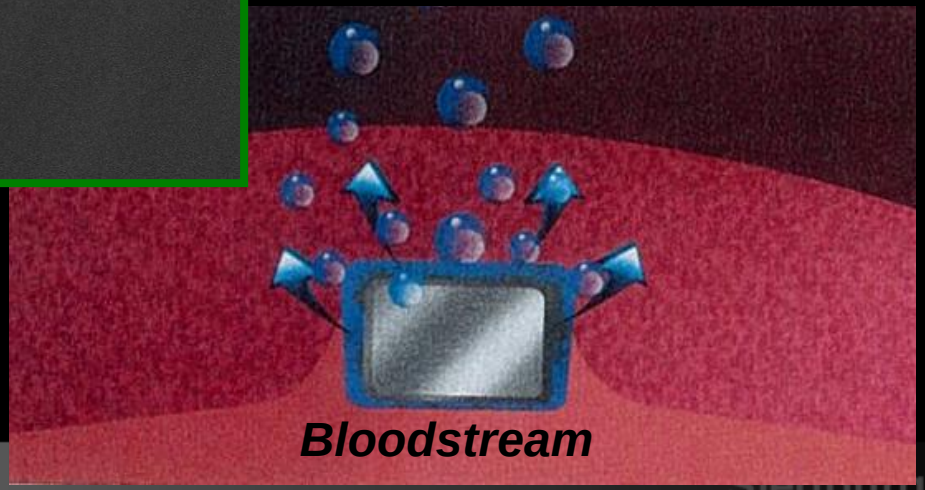
BioMatrix Freedom Stent
Biolimus A9® Drug

BIOMATRIX



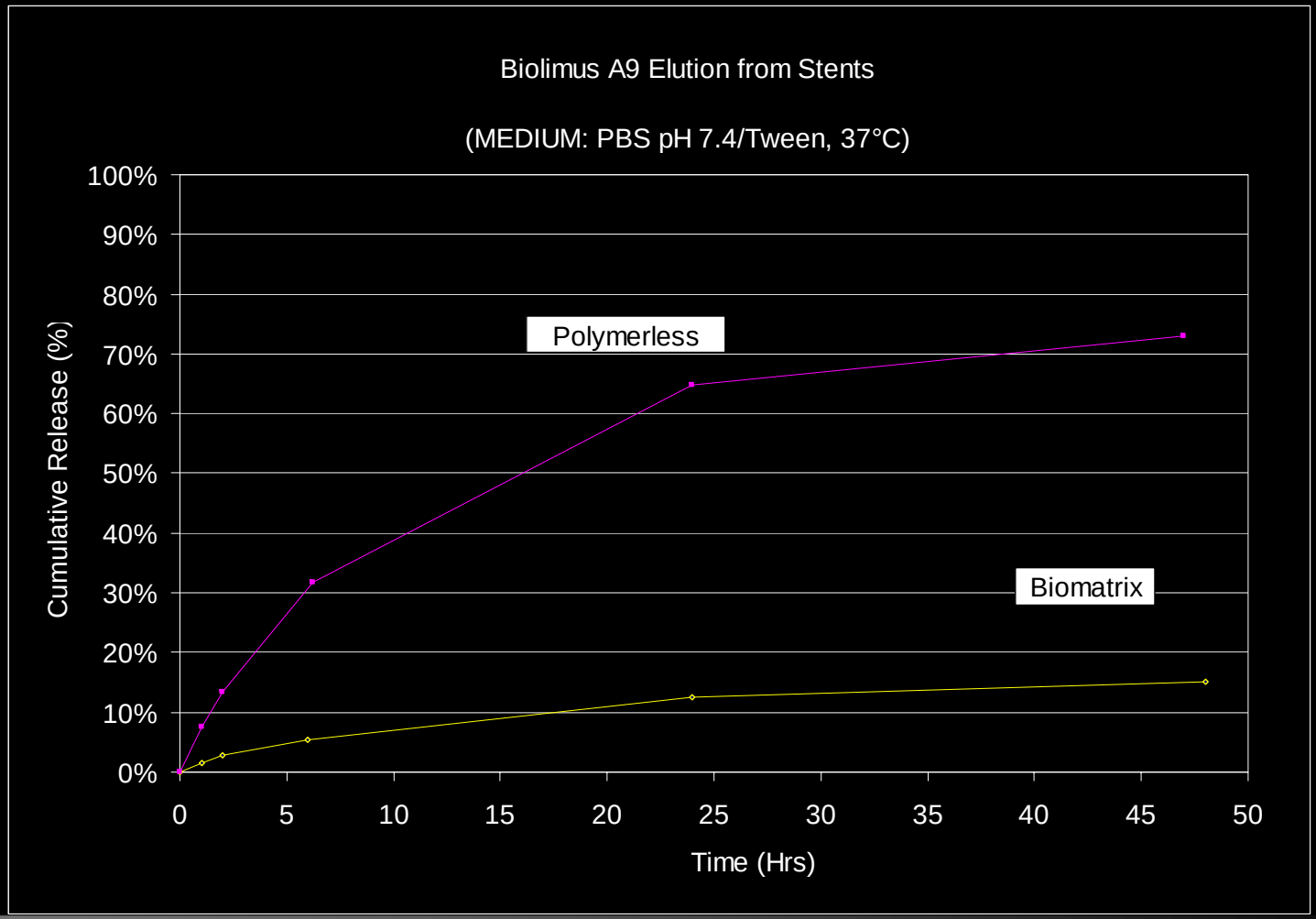
- Abluminal drug coating targets blood vessel walls
- Small amounts are released into circulation

Pure Biolimus A9 impregnated in metal stent surface



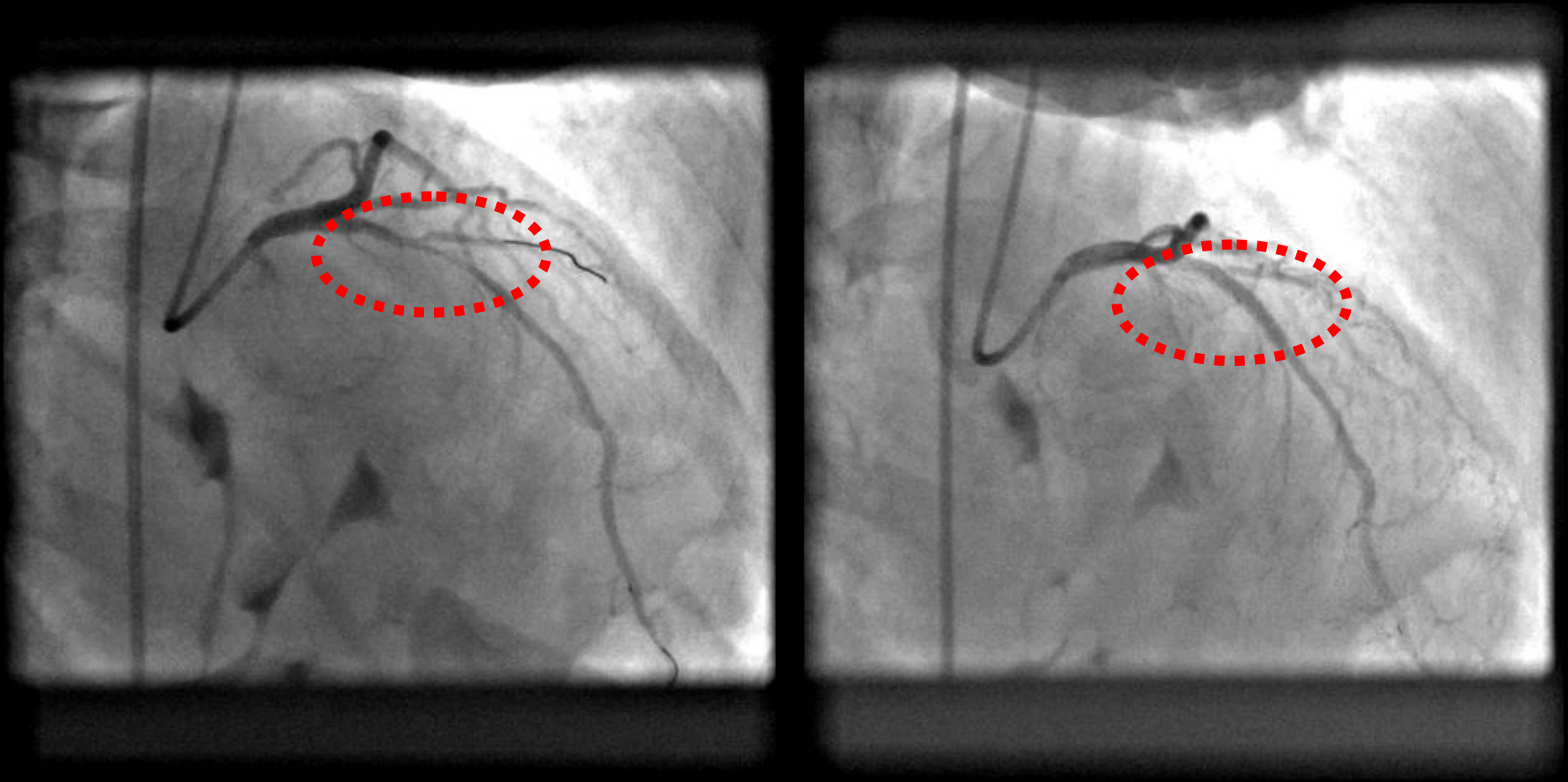
Biolimus A9 Release From Freedom Stent vs. BioMatrix® II

BIOMATRIX



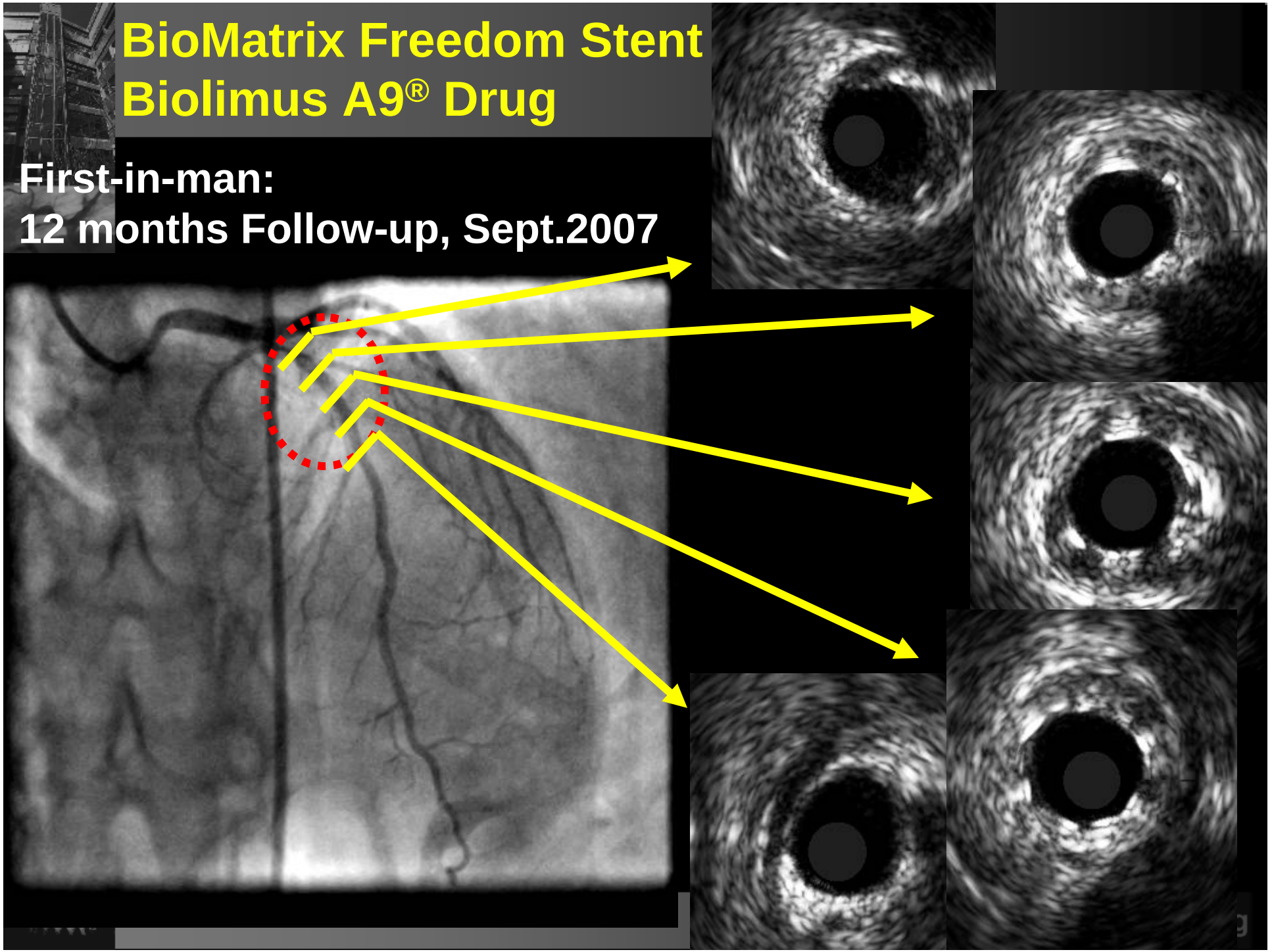
BioMatrix Freedom Stent
Biolimus A9® Drug

First-in-man: Baseline, Oct 2006

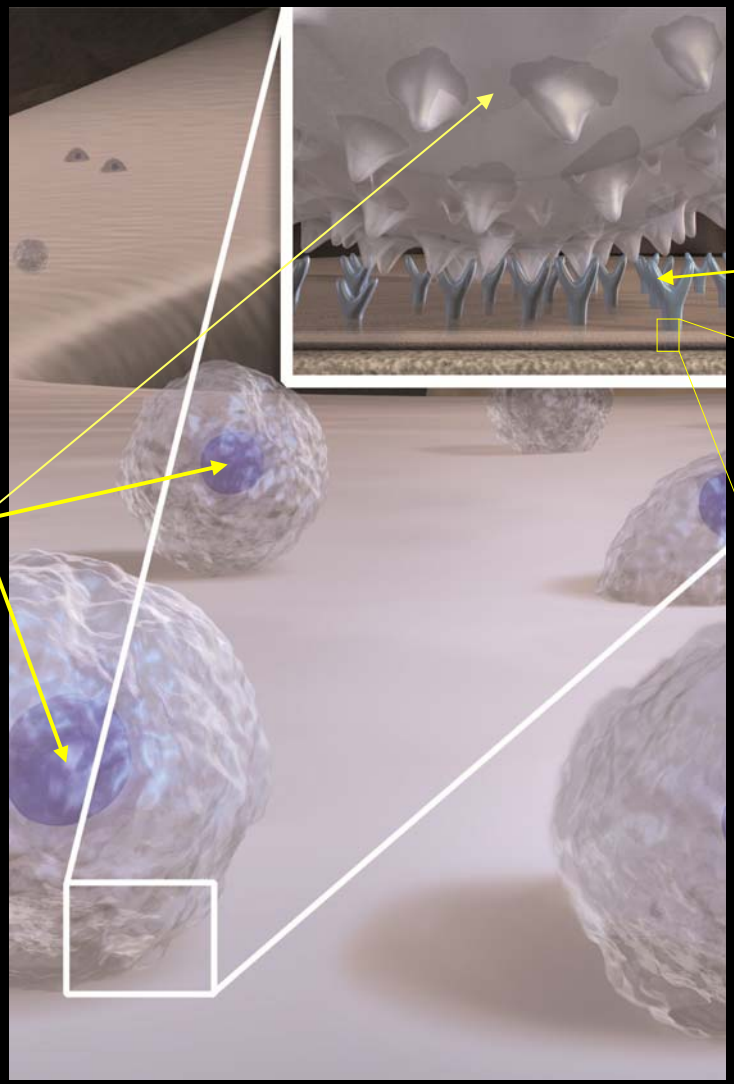


BioMatrix Freedom Stent
Biolimus A9® Drug

First-in-man:
12 months Follow-up, Sept.2007



Endothelial Progenitor Cell Capture Coating Technology - Orbus Neich Genesis



Captured EPC Cells on Surface

CD34 Antibody Layer

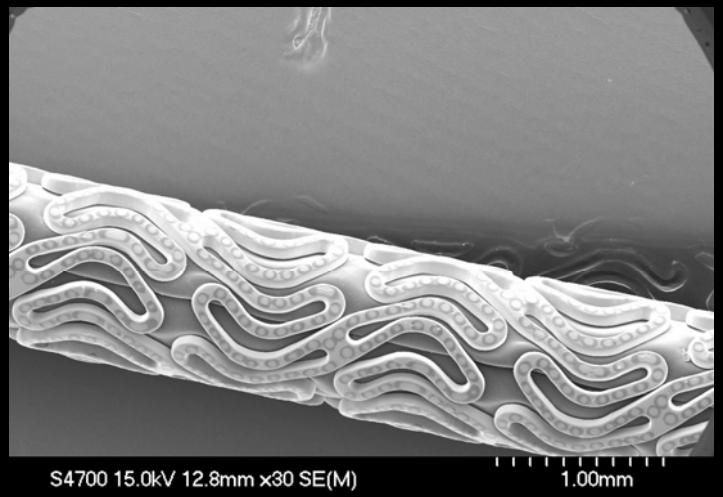
Intermediate Layer

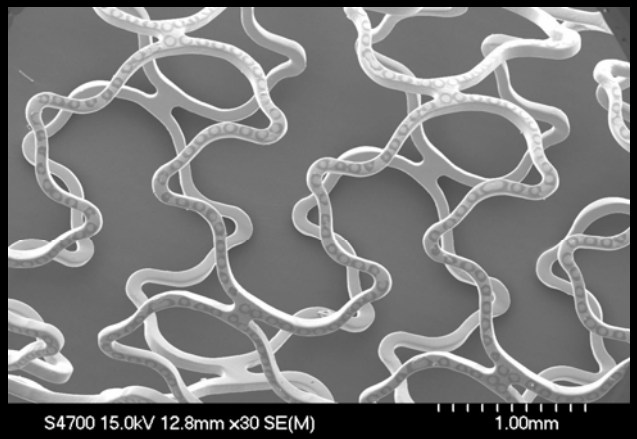
Stent Adhering Bottom Layer

Stent Surface

JACTax Stent –Labcoat Proprietary Technology/Product

- Liberte stent coated “out of the box”
- Exclusively Abluminal JACoating (no capping)
- 20 mcg of coating/16mm stent
- Coating contains 10 mcg of DLPLA and 10 mcg paclitaxel
- Approx. 2700 microdroplet surface structures/16 mm stent





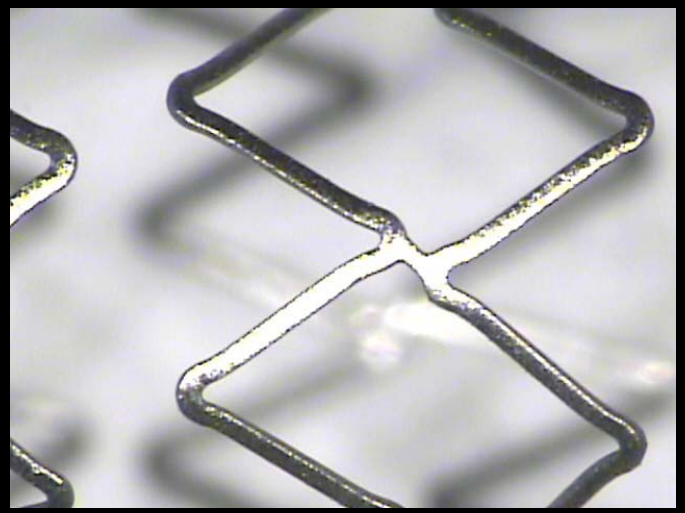
JACoating vs. Reservior - illustration

JACoating is approx. 1 micron thick vs Reservior polymer approx. 75 micron thick

The Elixir Stent
(Excella Stent + Novolimus)

Stent Design

- **Cobalt-Chromium alloy**
- **8 crown design for optimal scaffolding**
- **0.0032” strut thickness**



Controlled Release Technology

- **Methacrylate polymer family**
  - **Durable**
- **Biocompatible**
- **History of clinical use on vascular implants** dose
- Reduce dose (85 µg) and polymer load (<3 microns)

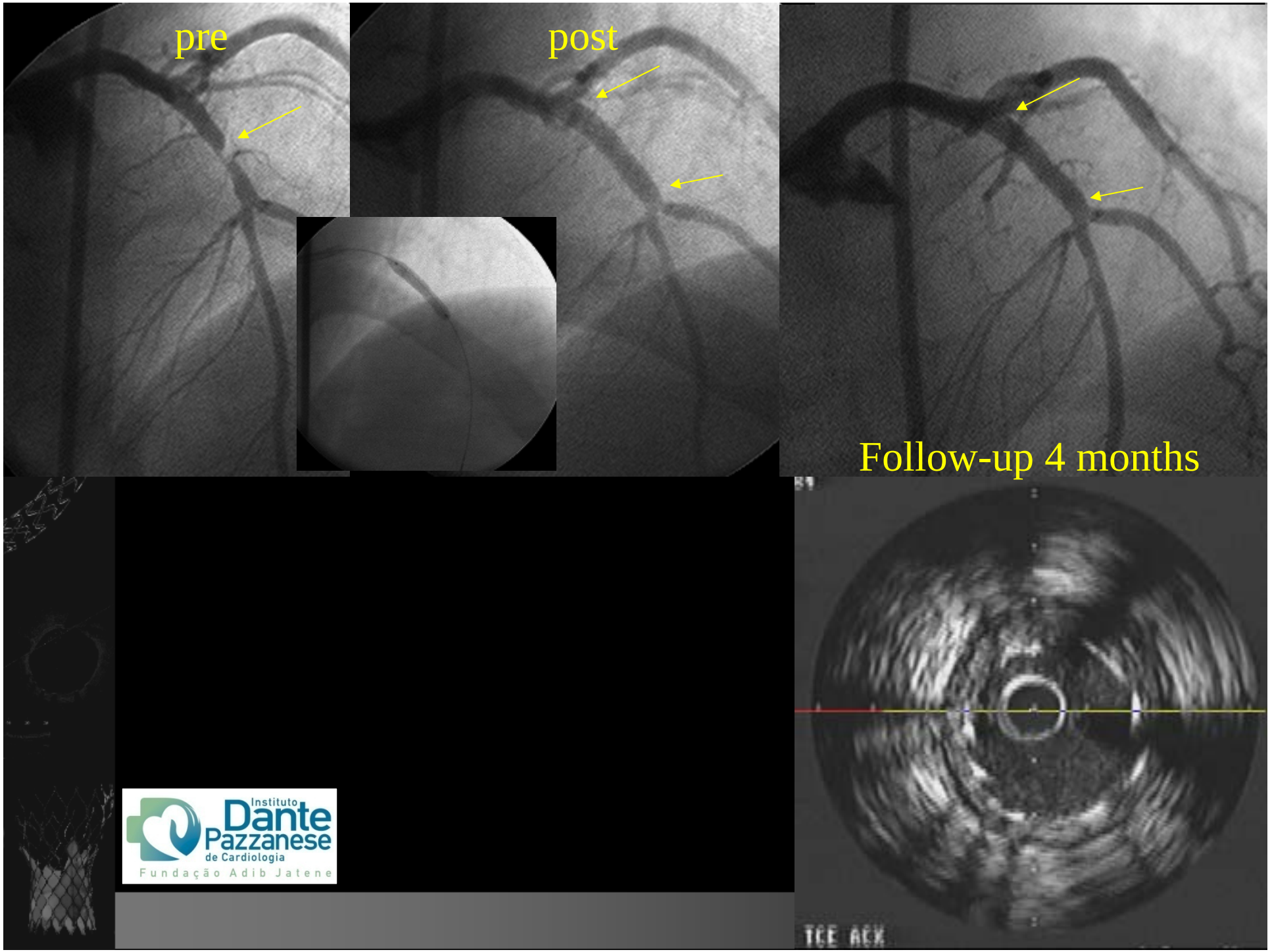
RESULTS

Quantitative Coronary Angiography

Variables	Lesions (n = 15)
Pre-procedure	
Reference vessel diameter, mm	**2.7 ± 0.4**
Lesion length, mm	**8.7 ± 3.7**
Minimum lumen diameter, mm	**1.0 ± 0.3**
Diameter stenosis, (%)	**62.5 ± 8.6**
Post-procedure	
Minimum lumen diameter, mm	**2.5 ± 0.3**
Diameter stenosis, (%)	**7.4 ± 9.6**
Acute gain, mm	**1.5 ± 0.3**
4-month follow-up	
Minimum lumen diameter, mm	**2.3 ± 0.4**
Diameter stenosis, (%)	**12.5 ± 13.1**
Lumen loss, mm	**0.15 ± 0.29**
Binary restenosis, n(%)	**0**

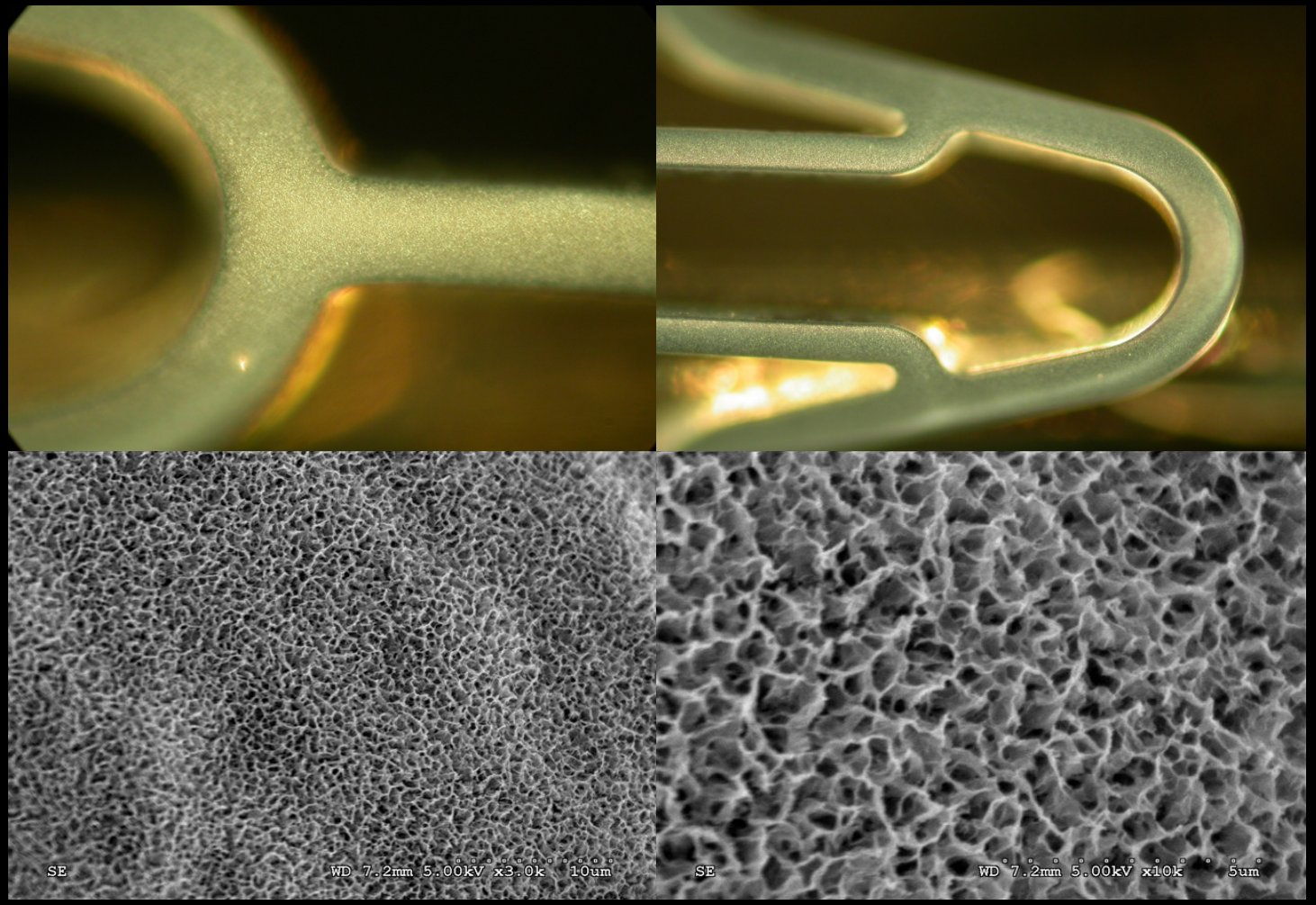
IVUS Volumetric Analysis
Baseline / 4 month follow-up

IVUS variables	Baseline N= 15 P	4-month follow-up N= 15 P
Vessel Volume (mm^3)	**251.2 ± 78.8**	**259.7 ± 86.1**
Stent Volume (mm^3)	**130.1 ± 39.7**	**134.0 ± 39.5**
Lumen Volume (mm^3)	**129.9 ± 39.7**	**130.8 ± 40.0**
NIH Volume (mm^3)	**N/A**	**3.2 ± 2.8**
% Stent Obstruction	N/A	**2.7 ± 2.7**


pre
post
Follow-up 4 months
Instituto
Dante
Pazzanese
de Cardiologia
Fundação Adib Jatene
TEE ACX

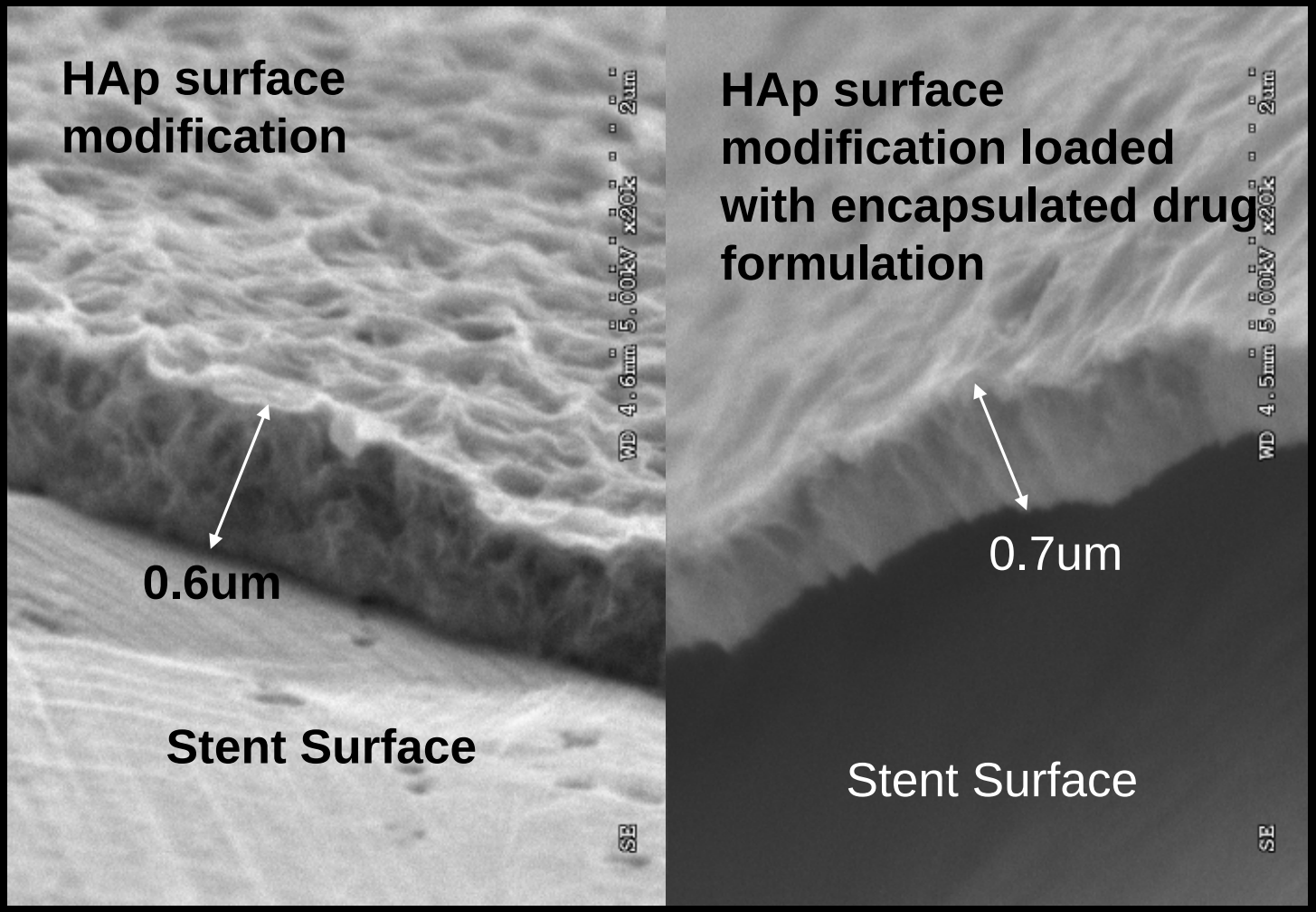
“MIV”

3D MicroPorous Nanofilm HydroxyHepatide (HAp)



HAp Drug Delivery System

(coated with Sirolimus)



Angiographic FU at 4 Months

Variable (N=13)	In-Stent	In-Lesion
MLD, mm	**2.34 ± 0.36**	**2.02 ± 0.37**
% Diameter stenosis	**10.4 ± 8.1**	**23.2 ± 8.7**
Late lumen loss, mm	0.27 ± 0.27	**0.18 ± 0.31**
Restenosis*, % (n)	**0.0 (0)**	**0.0 (0)**

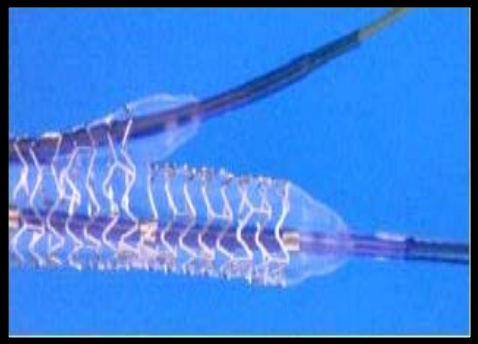
*Values are expressed as mean ± standard deviation. *Defined as diameter stenosis ≥ 50% at angiographic FU.*

IVUS Volumetric Analysis
Baseline / 4 month follow-up

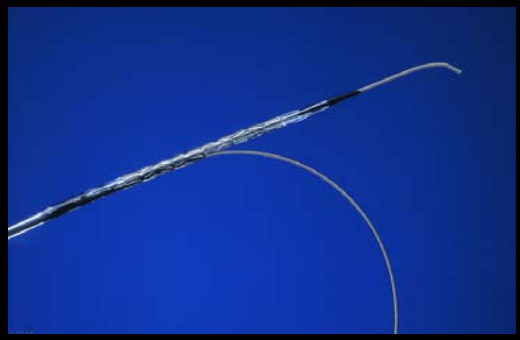
IVUS variables	Baseline N= 15 P	4-month follow-up N= 15 P
Vessel Volume (mm^3)	**276.7 ±**	**276.6 ± 84.8**
Stent Volume (mm^3)	**145.7 ± 14**	**142 ± 0.5**
Lumen Volume (mm^3)	**145.8 ±**	**138.8 ± 33.5**
NIH Volume (mm^3)	**N/A**	4.1 ± 3.4
Mallapposition Volume	**0.15 ± 0.5**	0.09 ± 0.3
% Stent Obstruction	N/A	2.8 ± 2.4

Lesion Specific Stent Designs, e.g. for bifurcations

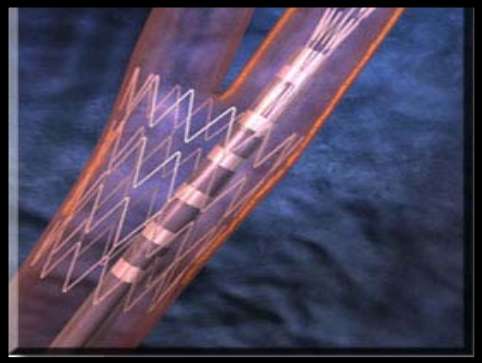
AST petal



Guidant frontier

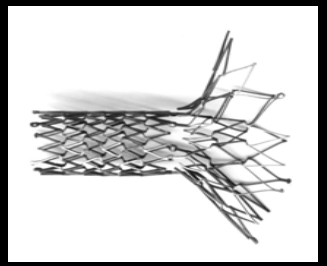


YMed sidekick



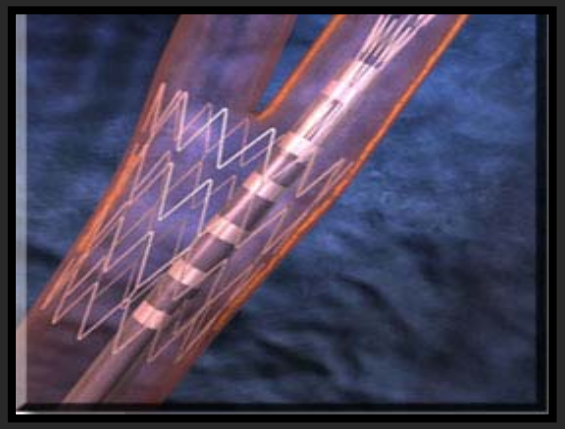
Devax (+ BA9)

“true” bifurcation designs



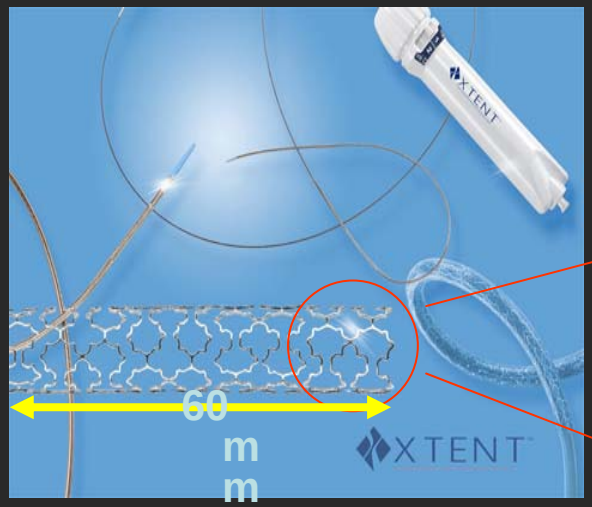
sidebranch designs

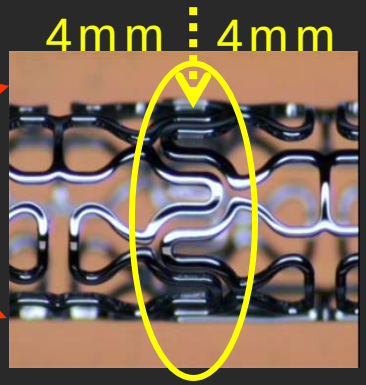
Dedicated Drug Eluting Stents to specifically address the needs of lesion subsets



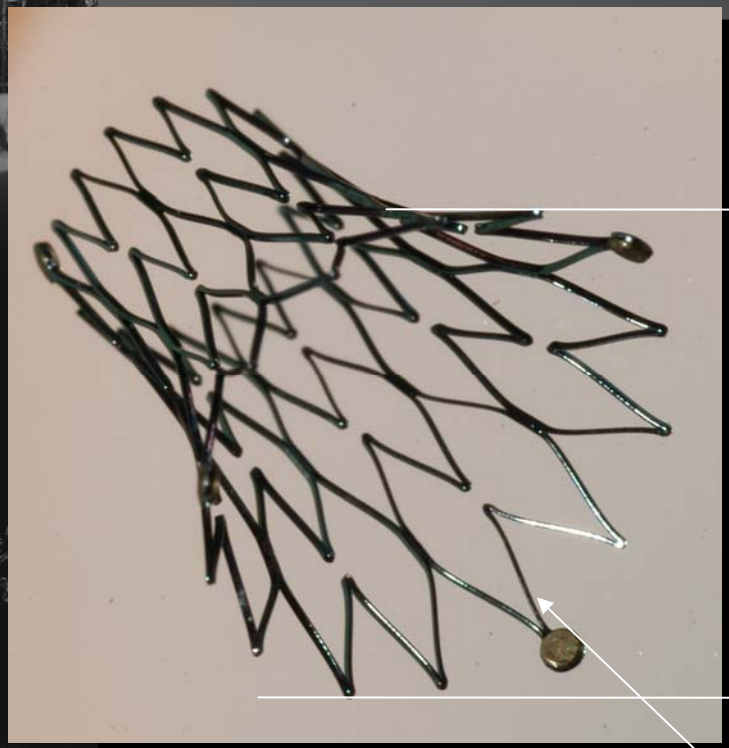
Devax (+ BA9)
(Bifurcation)

The Xtent System
(Multivessel/Multilesion)





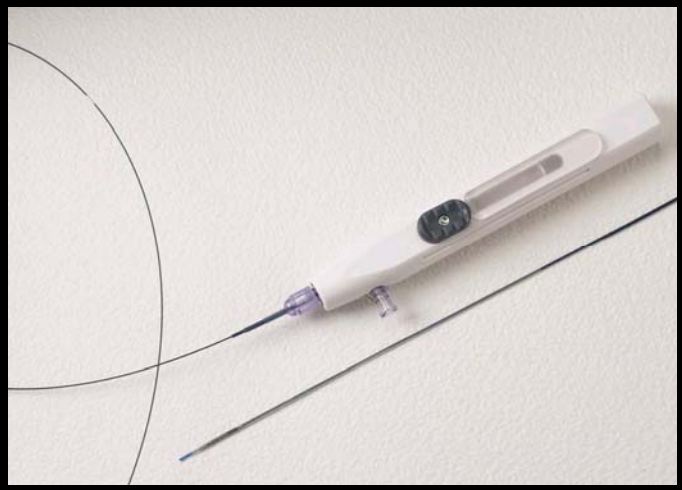
AXXENT™ Left Main Stent

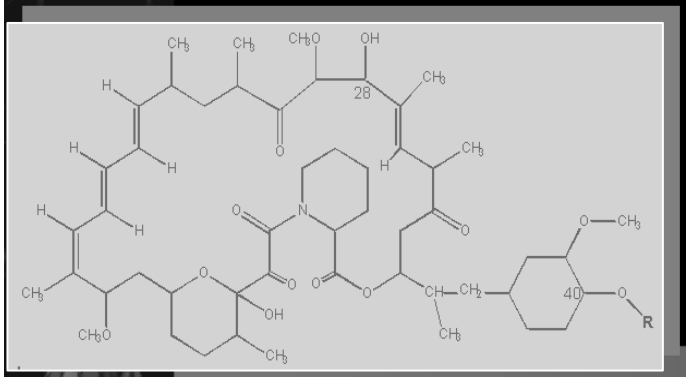


8, 10 & 12 mm
flare diameter

Material:	**Nitinol**
Vessel Range:	**3.75-4.75 mm**
Length:	**12 & 10 mm**

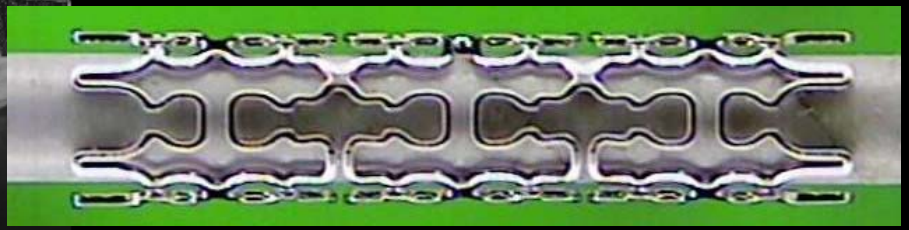
4.8F Rx Delivery System





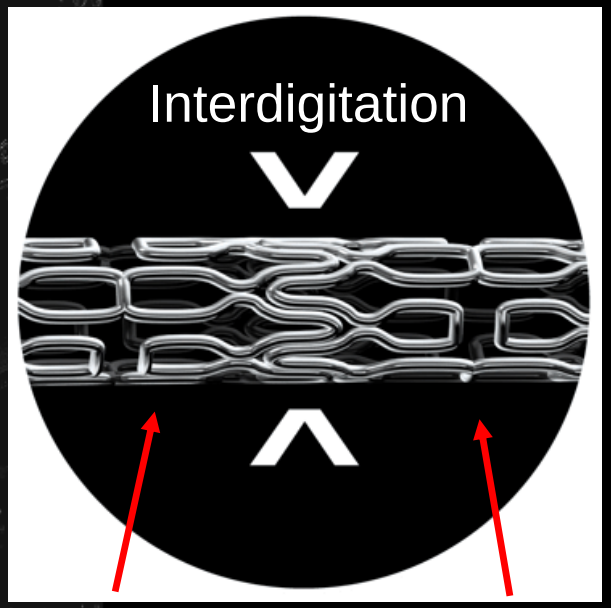
Biolimus A9® coating

XTENT Custom NX DES System



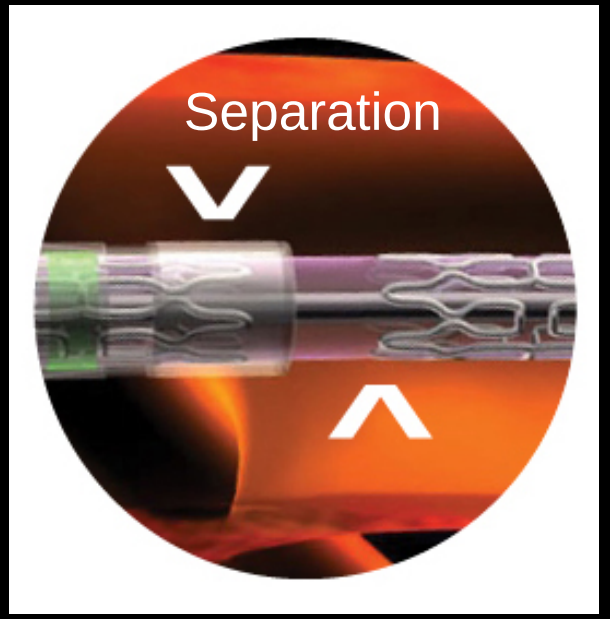
Single 6mm CoCr stent segment

6mm CoCr segments
Lengths: 60mm & 36mm
Diameters: 2.5, 3.0 & 3.5mm

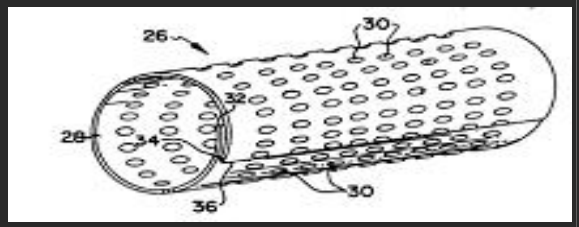
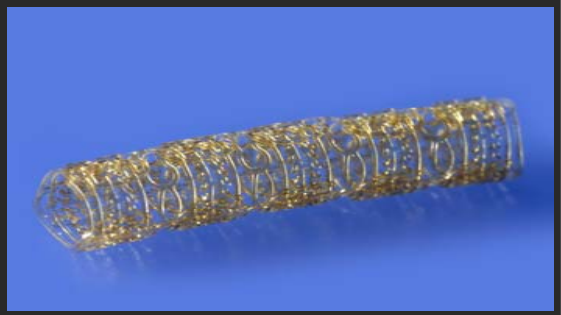


6mm stent 6mm stent

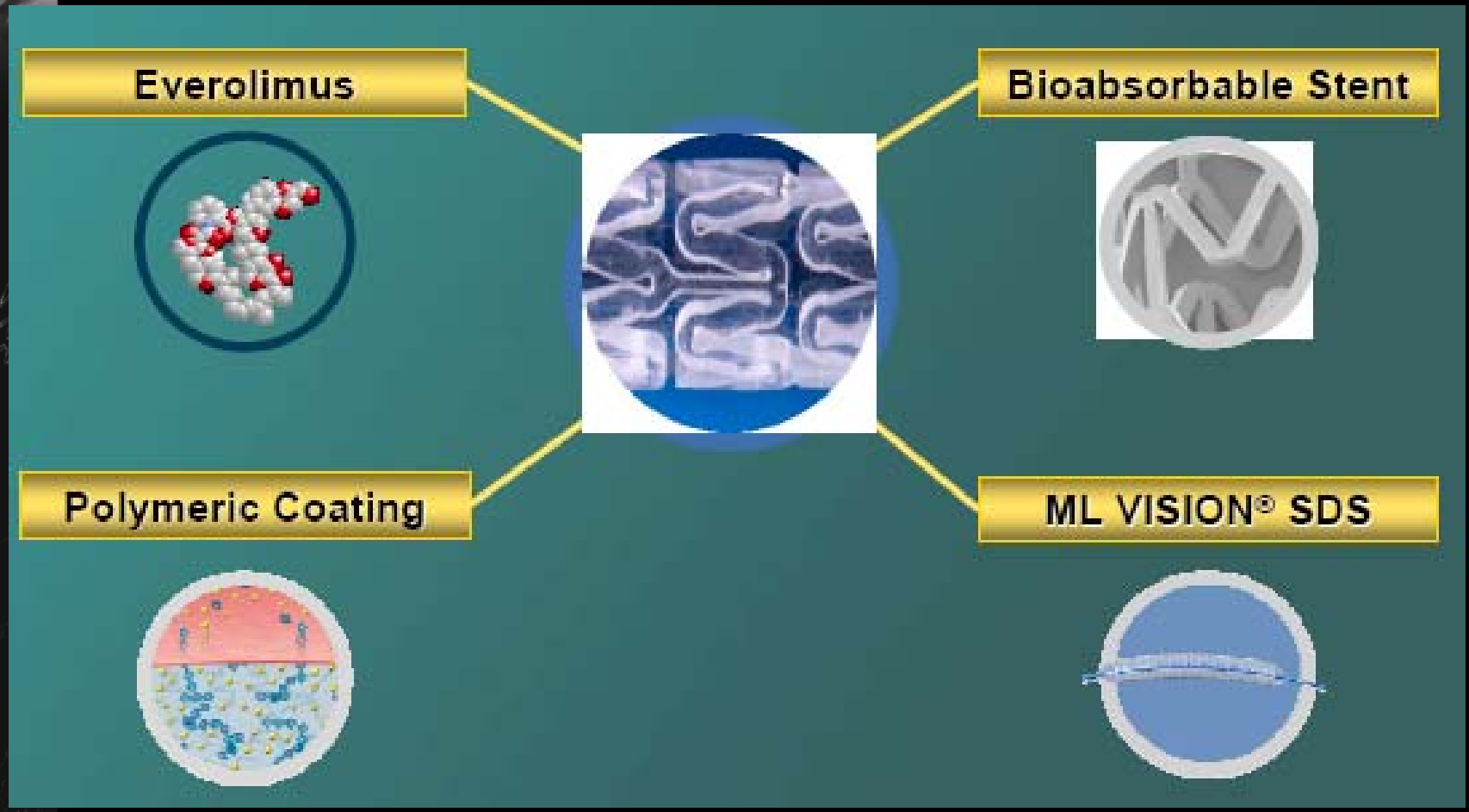
Custom stent lengths are created at points of interdigitation via valve separation mechanism



Biodegradable Stents

Company	Picture	Polymer/Drug	Features
Guidant (BVS)		All biodegradable polymers (PLLA) with everolimus	Self expanding and balloon expandable designs.
Igaki-Tamai		PLLA; Transilast	Zig-zag design deployed with a heated balloon FIM Trial; 50 pts
Reva Medical		Poly (DTE carbonate) with Iodine for radiopacity	Design has ratchet links for deployment
Biosensors		Poly (L or DL) lactide with BA9	Self expanding stent with a retractable sheath delivery catheter

Absorbable DES
BVS Everolimus Eluting Stent



ABSORB Study
BVS Everolimus Eluting Stent

n=30	30 days	6 months
Cardiac Death (%)	0	0
MI (%)	0	3.3
Q-wave MI	0	0
Non Q-wave MI	0	3.3
Ischemia Driven TLR (%)	0	0
Ischemia Driven MACE (%)	0	3.3

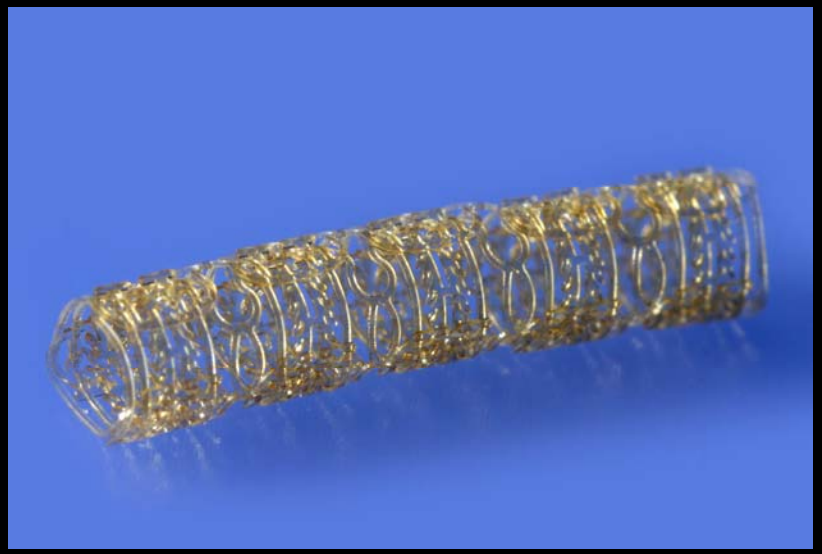
Serruys, i2 2007

ABSORB Study
BVS Everolimus Eluting Stent

	BVS Stent
Instent Late Loss (mm)	0.44 +/- 0.35
Prox Late Loss (mm)	0.25 +/- 0.32
Distal Late Loss (mm)	0.25 +/- 0.23
Diameter Stenosis (%)	27 +/- 14
Persisting Incomplete Apposition	4/26
Late Acquired Incomplete Apposition	7/26
Δ Vessel Area (%)	-0.4
Δ Stent Area (%)	-11.7
Δ Lumen Area (%)	-16.6
NIH Area (mm2)	0.3
%Volume obstruction	5.5

Serruys, i2 2007

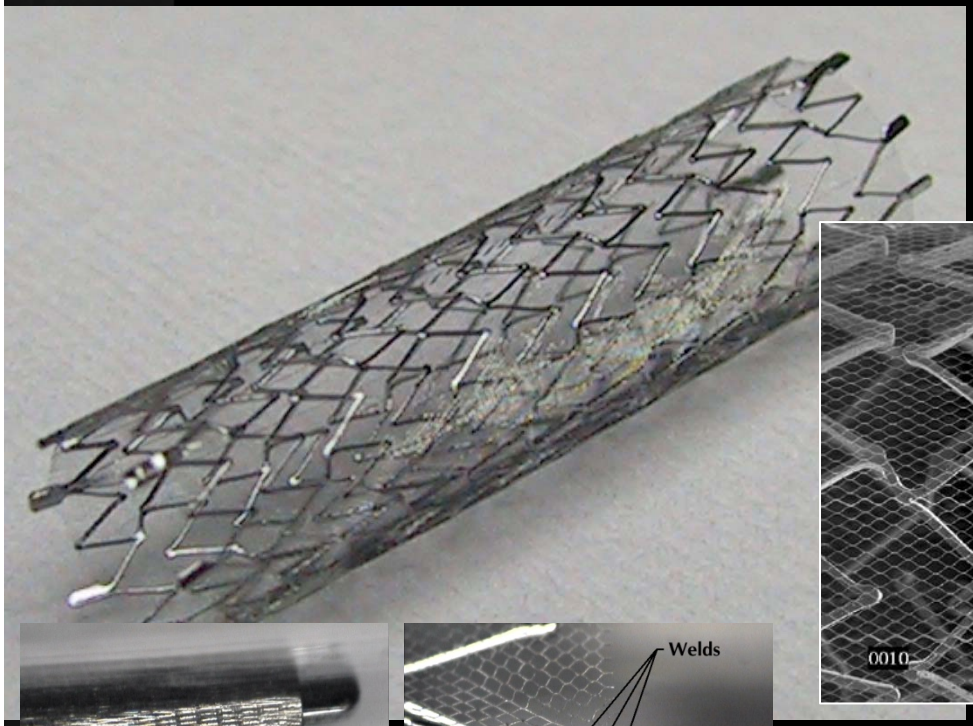
REVA Bioresorbable Stent

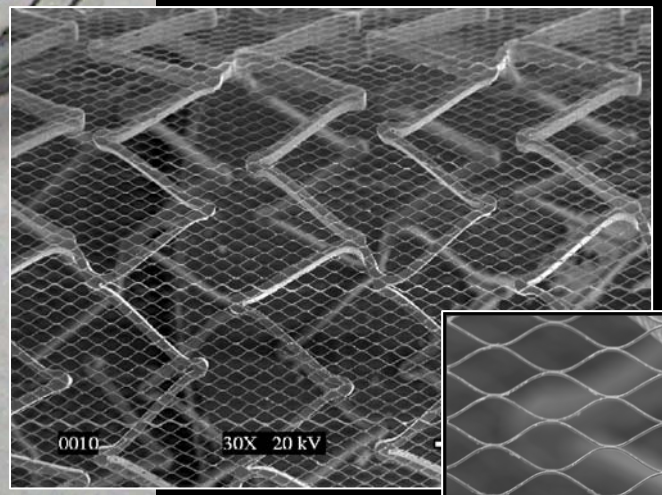


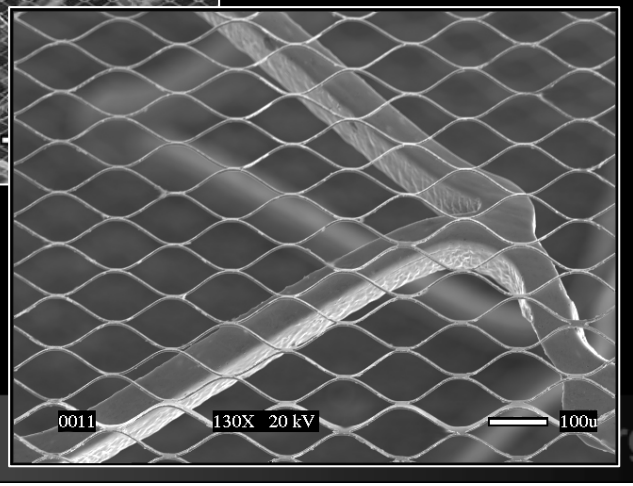
- Fully bioresorbable coronary stent system
- Integral bioresorbable drug-elution coating
- Paclitaxel-eluting

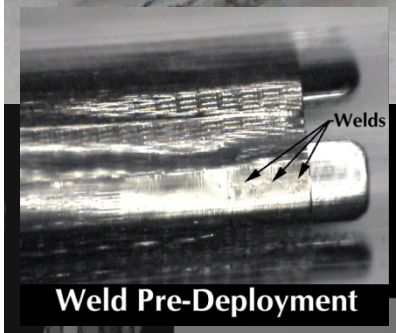
SVG / Thin Film Program

SESAME *e*Nitinol™ Covered Stent for SVG Therapy

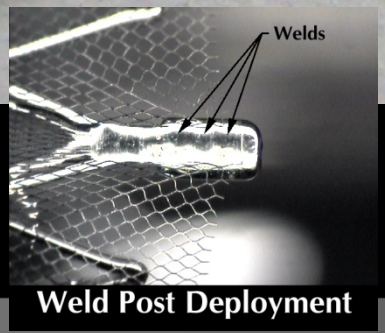








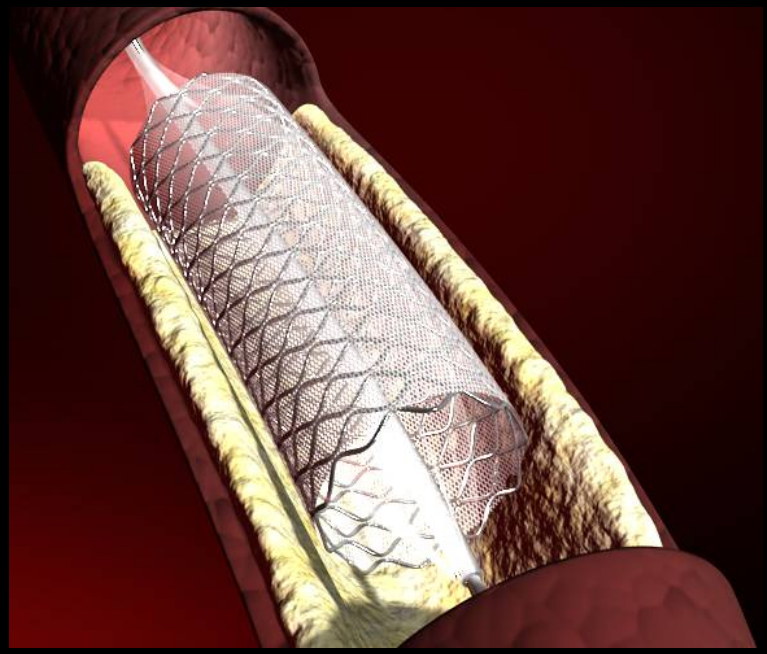
Weld Pre-Deployment



Weld Post Deployment

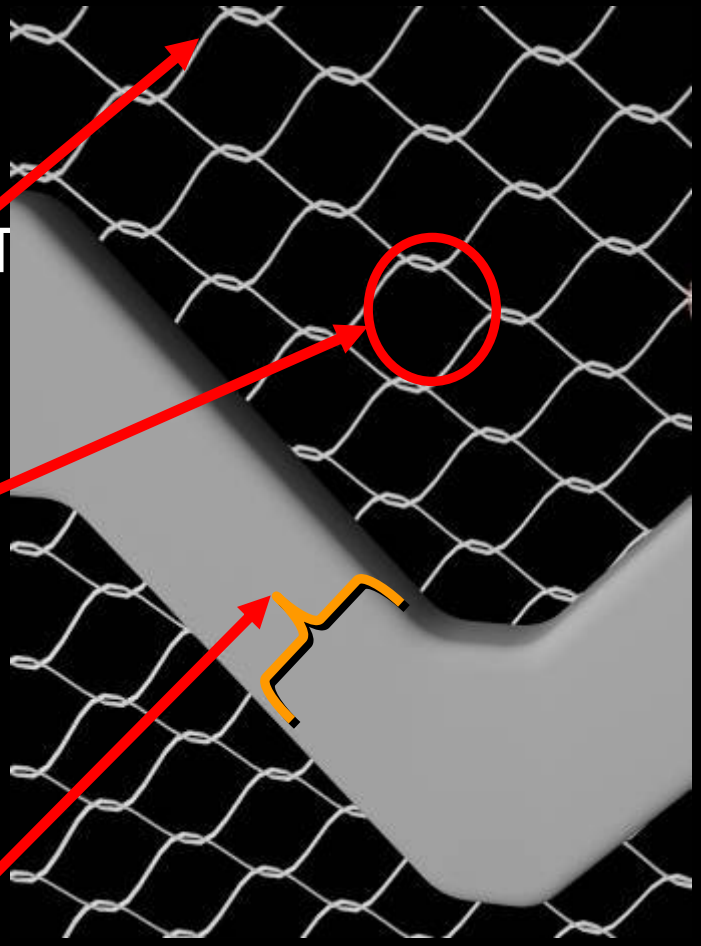
MGuard Stent

A stent wrapped with ultra-thin polymer mesh sleeve, knitted to the external surface

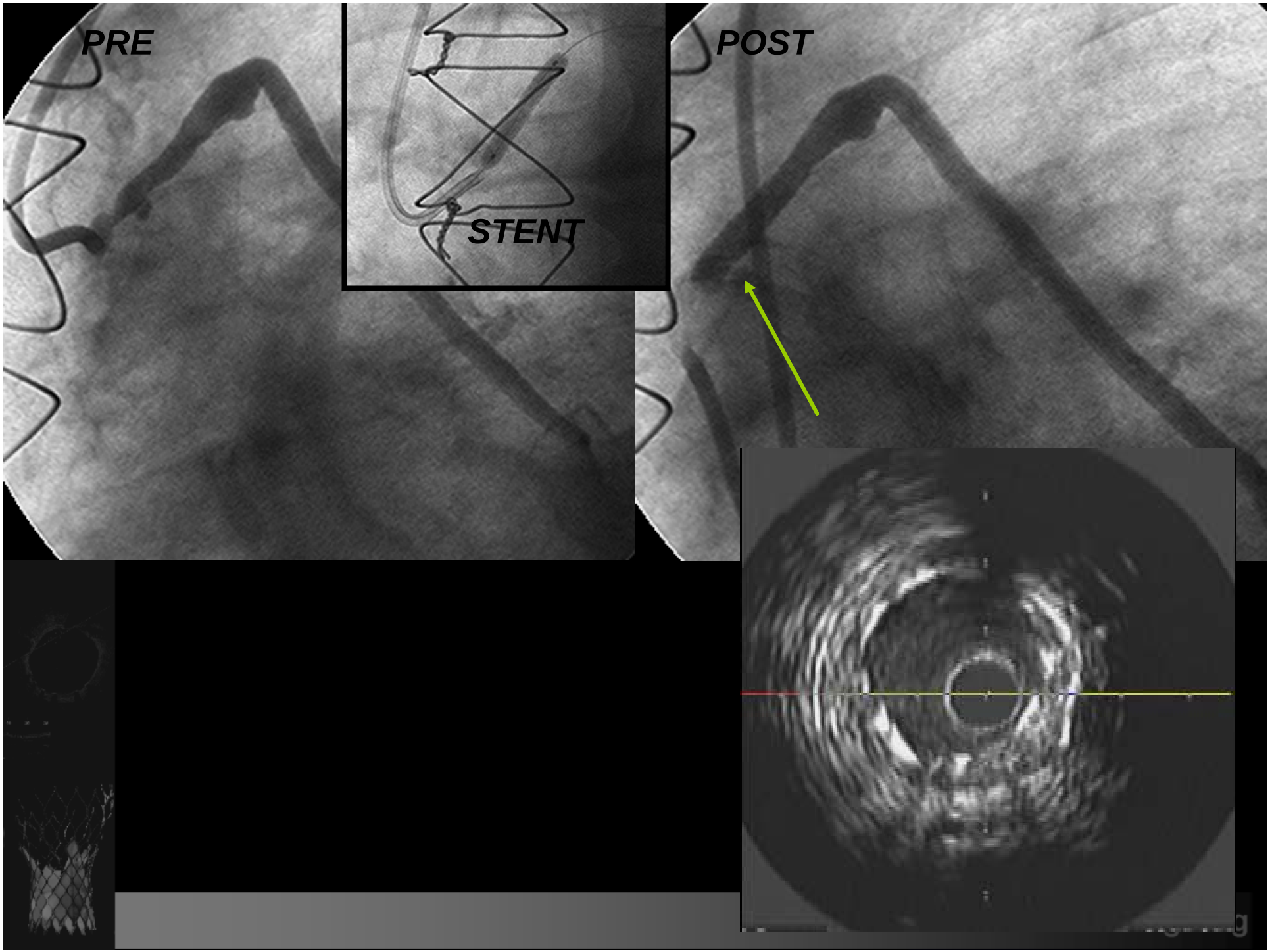


MGuard™

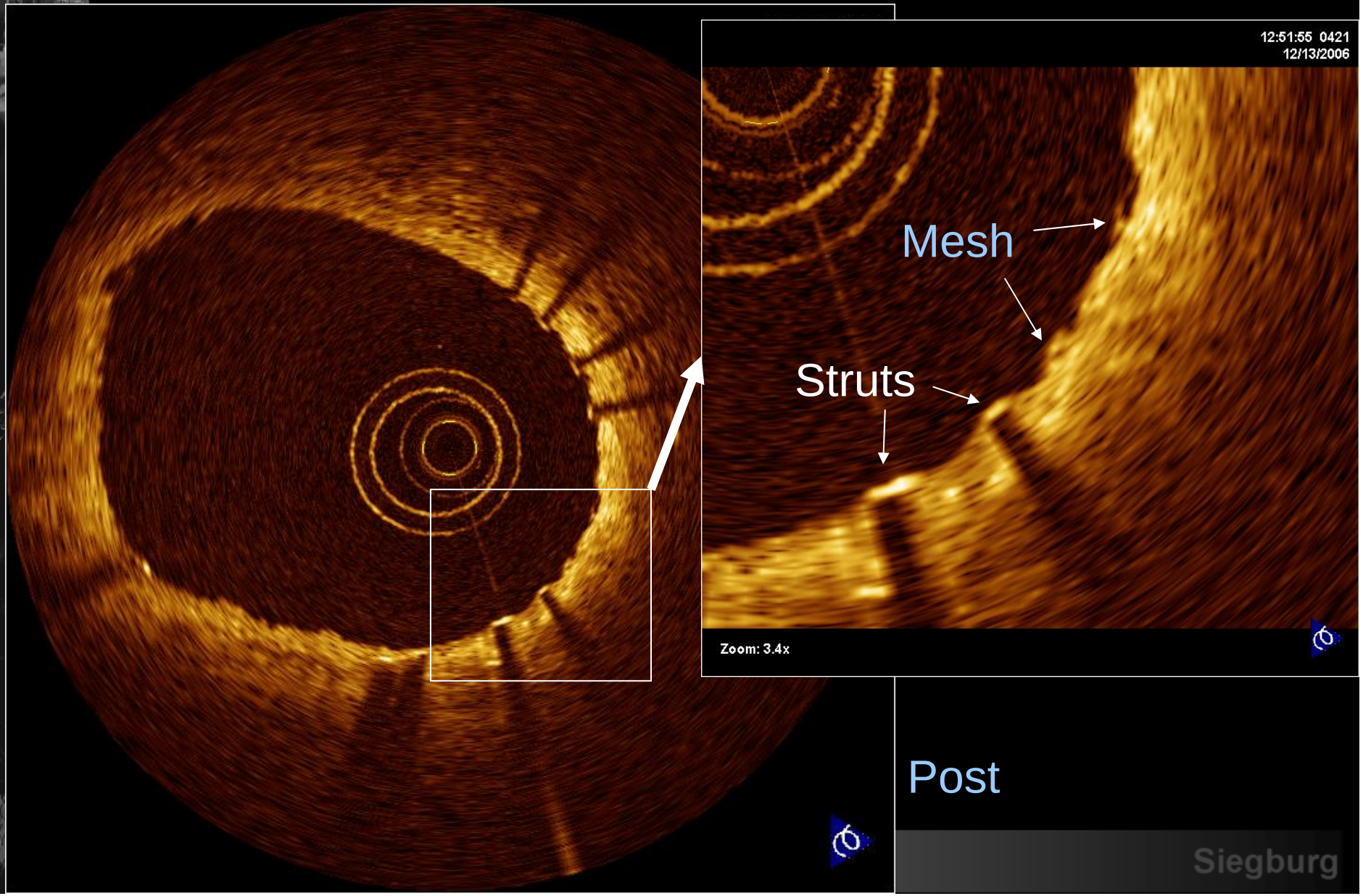
- A stent wrapped with a micron level fiber mesh
- 10-20 μm single, knitted PET fiber providing flexibility and strength
- ~180x150 µm apertures
- Same look and feel as a standard stent



Struts: (80-100 microns)


PRE
STENT
POST

MGuard (Inspire-MD) – Case Example

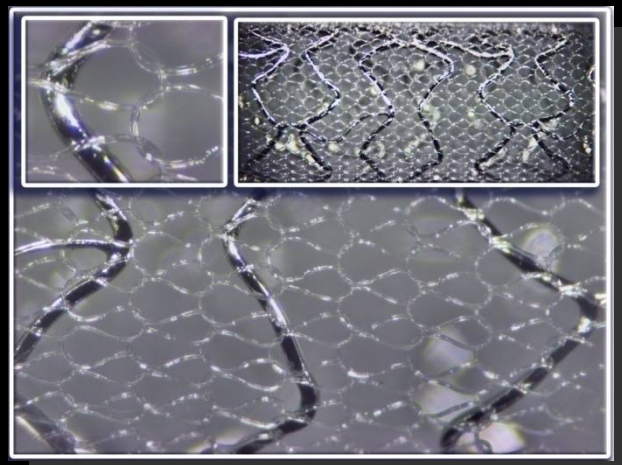


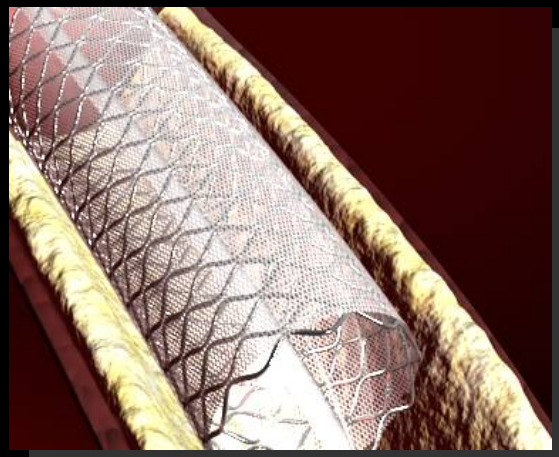
MGuard (Inspire-MD)

MGuard	InspireMD
Device description	Stent wrapped with a micron level knitted sleeve
Apertures size	150 x 180 microns
Fiber Thickness	10-20 microns
Indication	Coronaries
Approval status	CE Mark

Potential applications

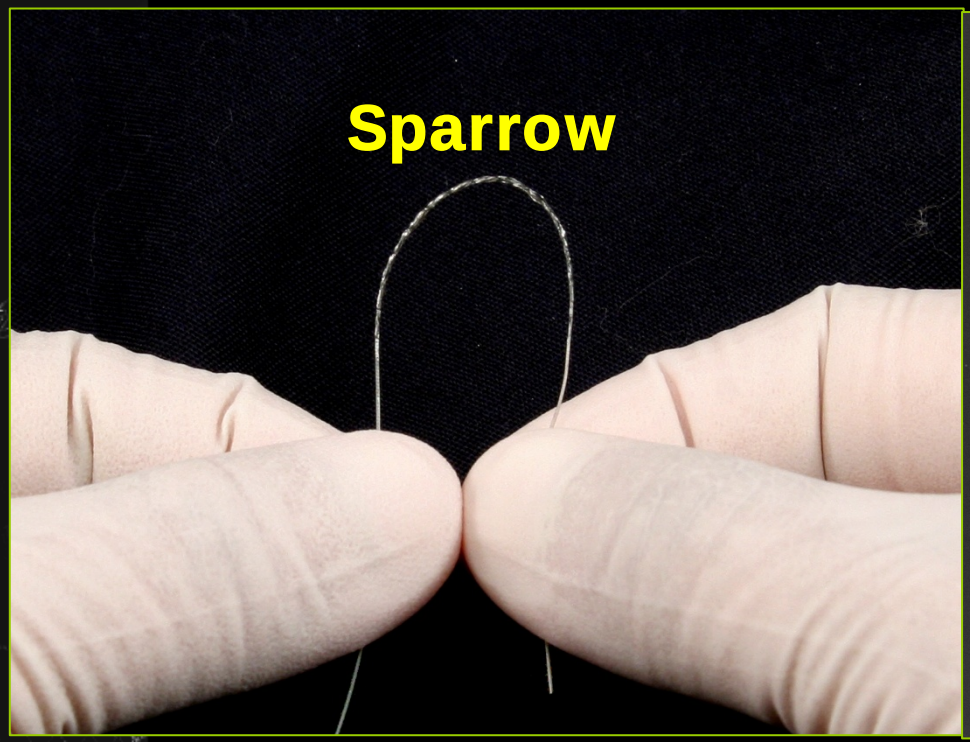
- Drug eluting mesh: An efficient drug delivery platform providing uniform coverage.
- Carotid : Protection during and post procedure
- Peripheral

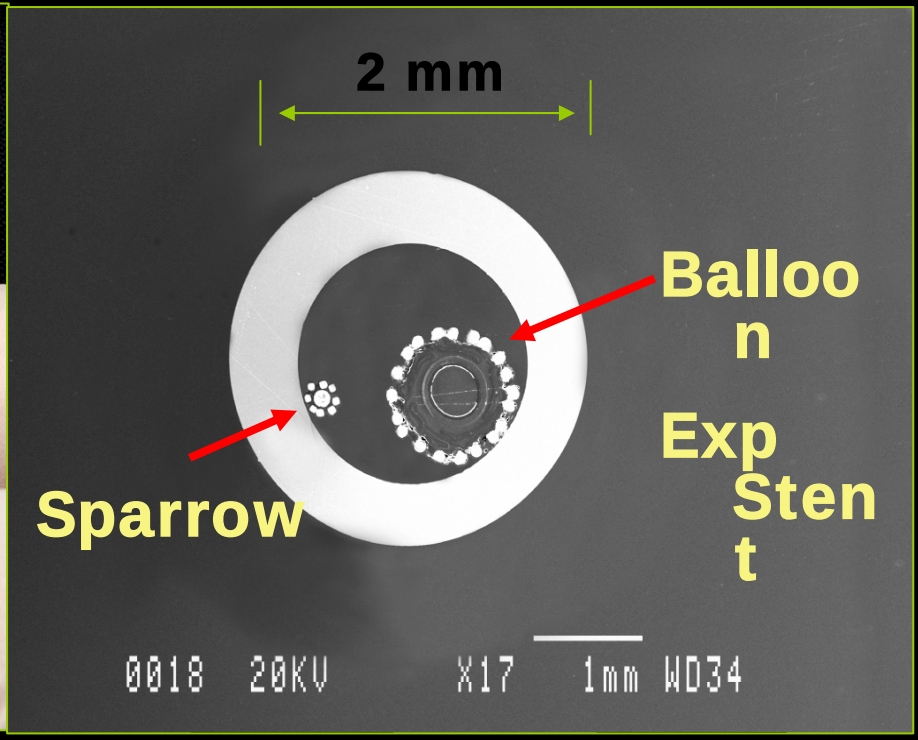




CardioMind

CardioMind Sparrow™ Stent Delivery System:
"Stent-in-a-Wire" .014" Guidewire Design





Investigational Device, Not for Sale in the US

CARE I
6 Month QCA Results

Characteristic	Aggregate (n=20)
In-stent % DS	38.12±26.77
In-segment % DS	39.87±24.51
In-stent MLD (mm)	1.35±0.60
In-segment MLD (mm)	1.31±0.54
In-stent LLL (mm)	0.73±0.57
In-segment LLL (mm)	0.61±0.51
Binary Restenosis	20% (4/20)

DES on the EU Market

Company	Stent	Drug - Coating	Comment
Abbott Vascular	Xience V	Everolimus - durable	CE Mark 2006
	ZoMaxx	Zotarolimus - durable	Development discontinued 10/06
	BVS (bioabsorbable)	Everolimus - bioabsorbable	ABSORB FIM
Biosensors International	Axxion	Paclitaxel	CE Mark 2005
	BioMatrix	Biolimus A9 - bioabsorbable	STEALTH FIM; expects CE Mark in 2007
Boston Scientific	Promus (equivalent to XIENCE V)	Everolimus - durable	CE Mark 2006
Conor Medsystems	CoStar	Paclitaxel - various	CE Mark 2006
Devax	Axxess (bifurcated)	Biolimus A9 - bioabsorbable	AXXESS PLUS; AXXENT FIM; CE Mark expected
JW Medical Systems	Excel	Rapamycin - bioabsorbable	MEDISTRA FIM
Medtronic	Endeavor	Zotarolimus - durable	CE Mark 2005
OrbusNeich	Genous Bio-engineered R Stent	Coated with antibody that captures endothelial progenitor cells	CE Mark 2005
Sahajan and Medical Technologies	Infinnium	Paclitaxel - durable	CE Mark 2005
Sorin Biomedica Cardio	Janus Flex	Tacrolimus	CE Mark
Xtent	Custom NX	Biolimus A9 - bioabsorbable	CUSTOM I and II FIM; CE Mark in 2007 expected


There are several additional new stars which will play an important role in the future;
But first they have to prove their benefit in carefully conducted adequate studies