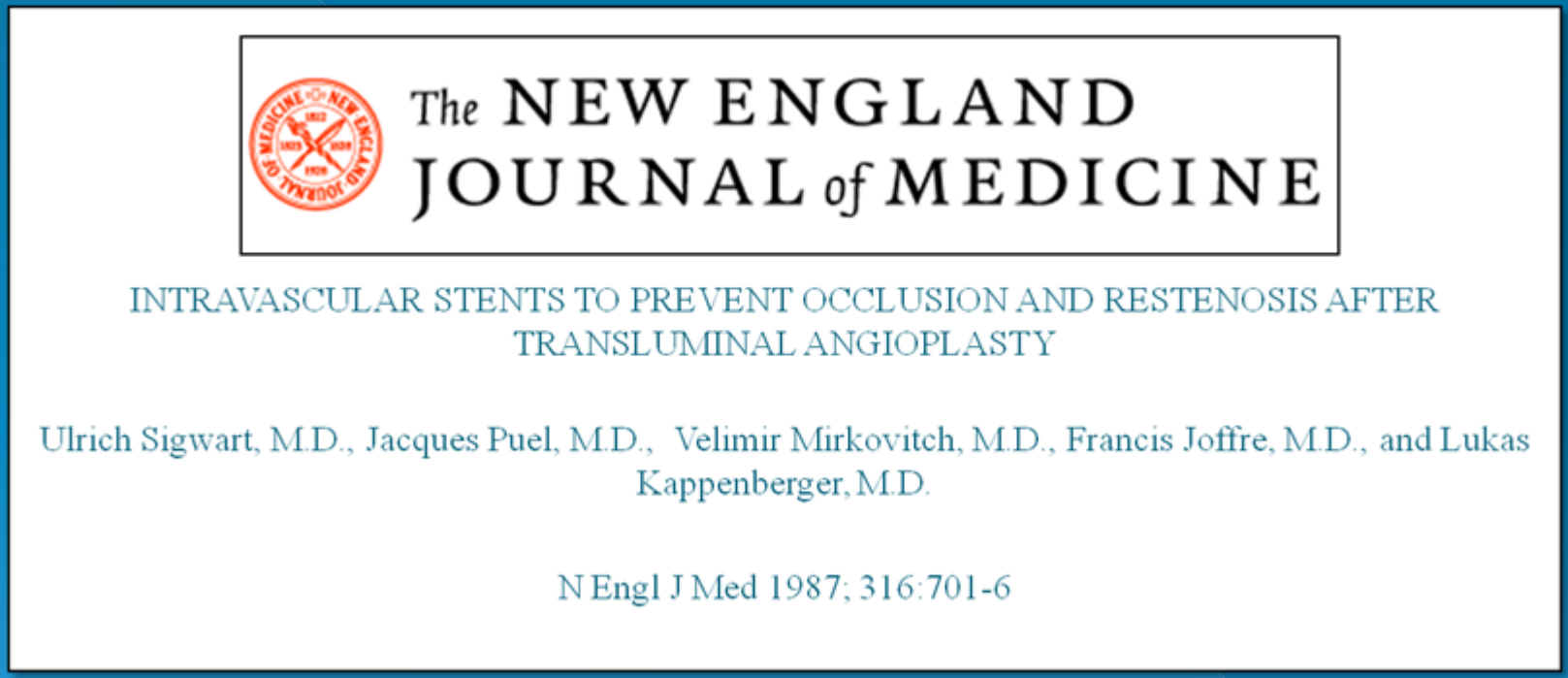
Stent Technology 2009

Luis F. Tami, MD
Cath Lab Director
Memorial Regional Hospital

First Report of Coronary Stenting in 1987



The NEW ENGLAND JOURNAL of MEDICINE

INTRAVASCULAR STENTS TO PREVENT OCCLUSION AND RESTENOSIS AFTER TRANSLUMINAL ANGIOPLASTY

Ulrich Sigwart, M.D., Jacques Puel, M.D., Velimir Mirkovitch, M.D., Francis Joffre, M.D., and Lukas Kappenberger, M.D.

N Engl J Med 1987; 316:701-6

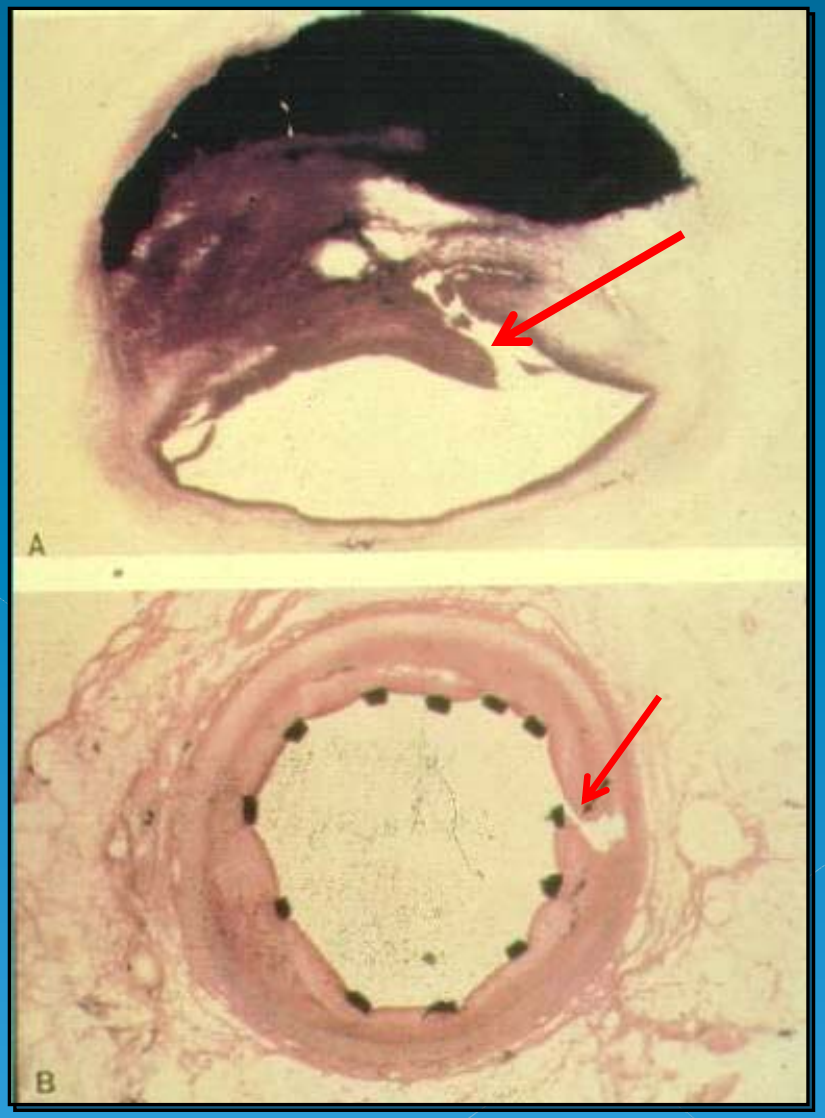
Ulrich Sigwarth (Lausanne 1986)

First human coronary implantation

Expon dvances
ars

Why to Stent?

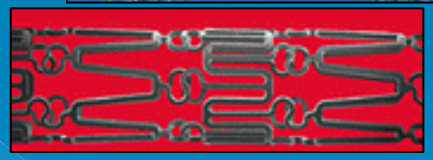
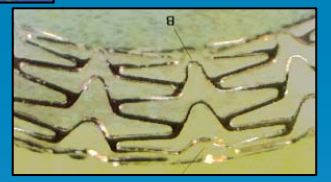
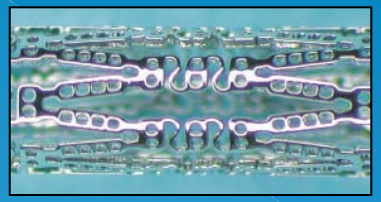
- Mechanically scaffold the artery and create a larger lumen predictably
- Prevent abrupt vessel closure
- Prevent restenosis



Stent Design

- Coil (Gianturco-Roubin)
- Slotted-tube (Palmaz-Schatz)
- Self-expanding mesh (Wallstent)
- multicellular or corrugated ring with flexible connections (majority of current stents)
- Open-cell or closed cell design

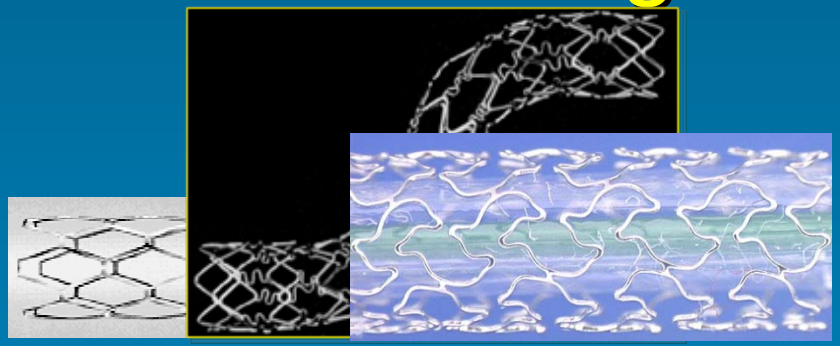


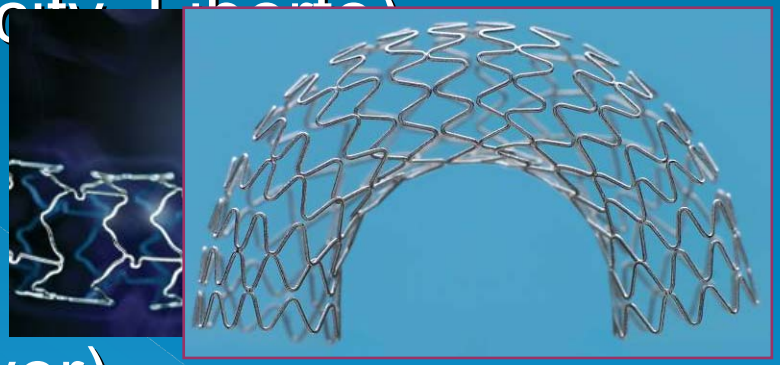



Features & Variables of Stent Design

Strut material

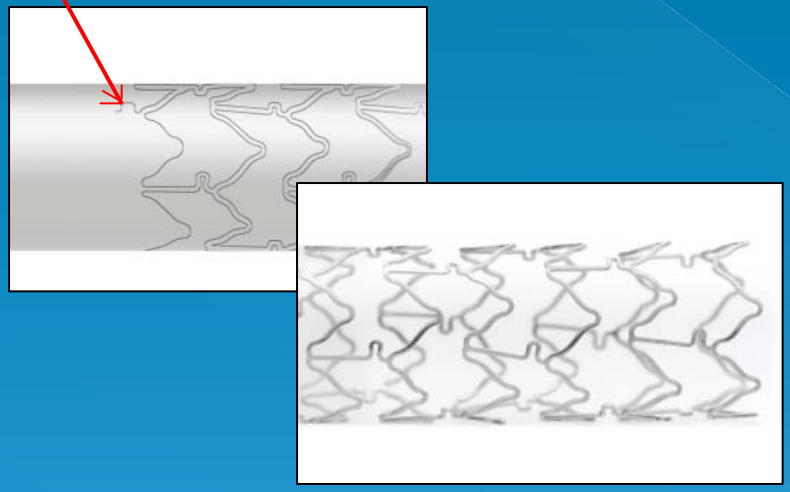


- Stainless steel 316 L (Palmaz-Schatz, Velocity, Liberte)
- Tantalum (Wiktor)
- Nitinol (ACT-One)
- Cobalt chromium (Multilink VISION, Driver)
- Platinum chromium (Taxus & Promus Element)

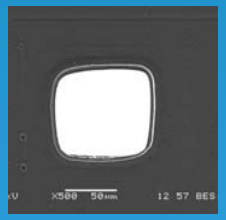


Basic strut types / Construction

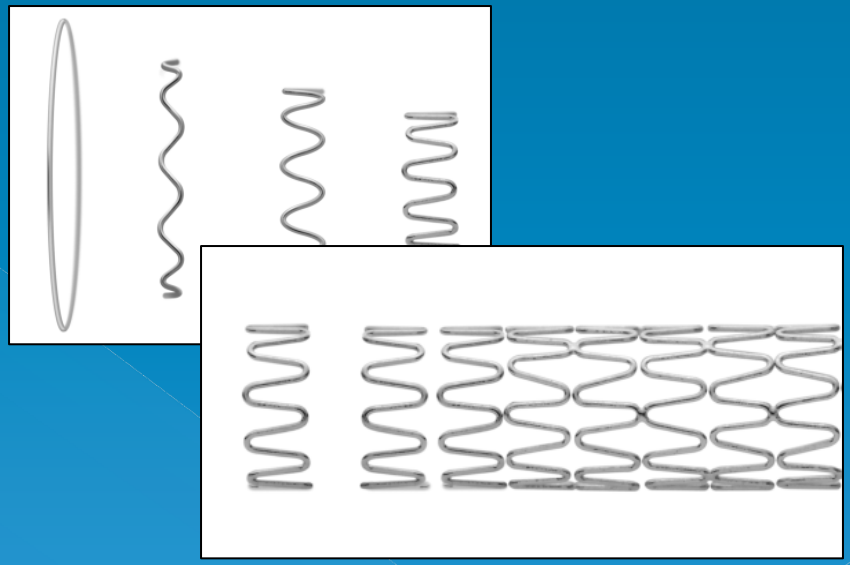
1. Laser-cut stents start as a tube, a laser removes material and a stent remains. Laser-cut stent production leaves square (blunt) edges.



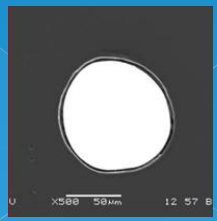
Squared edges



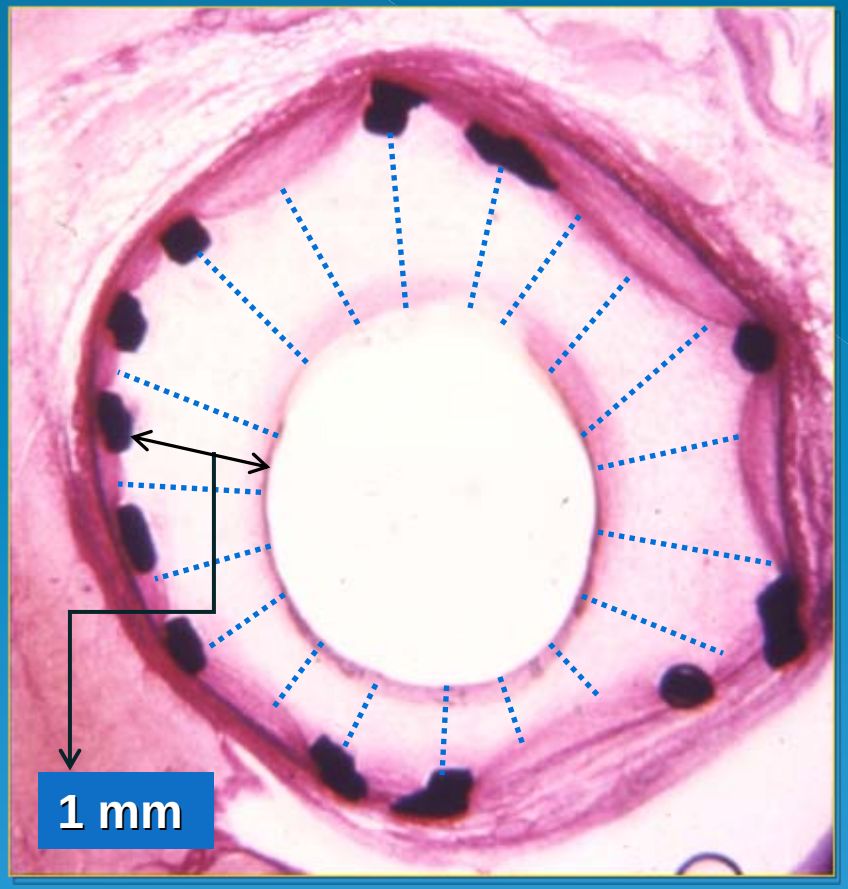
2. Metallic rings are formed into sinusoidal elements that are fused together to comprise a modular stent.

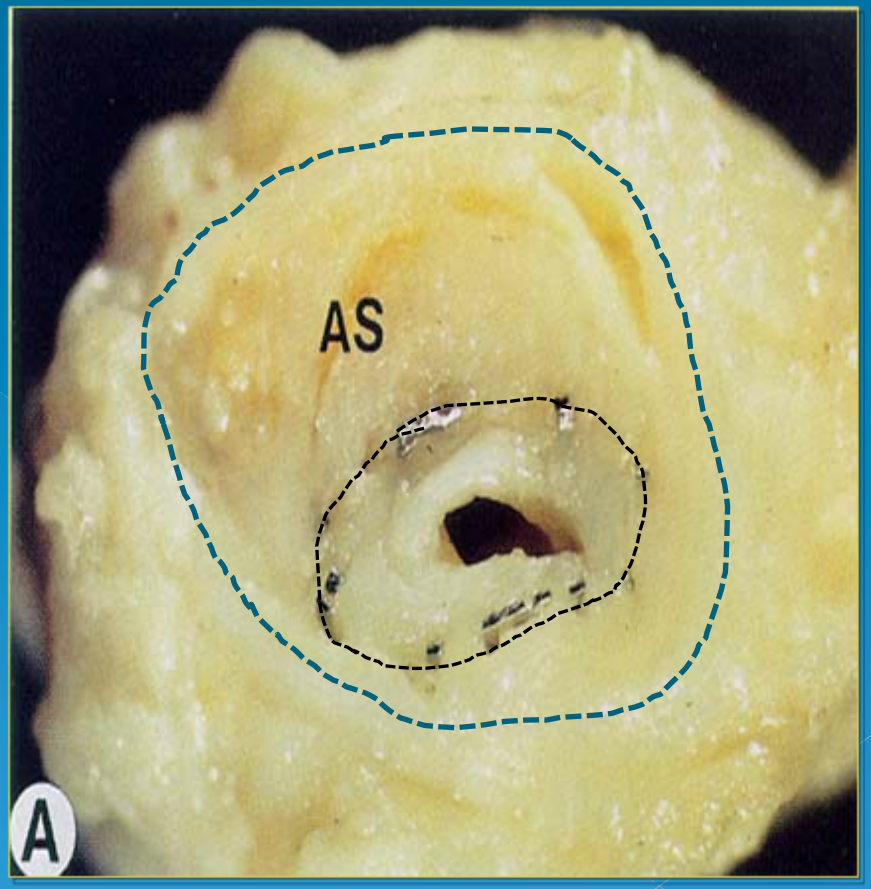


Ultrathin, smooth, edgeless struts



The Limitation of Bare Metal Stents

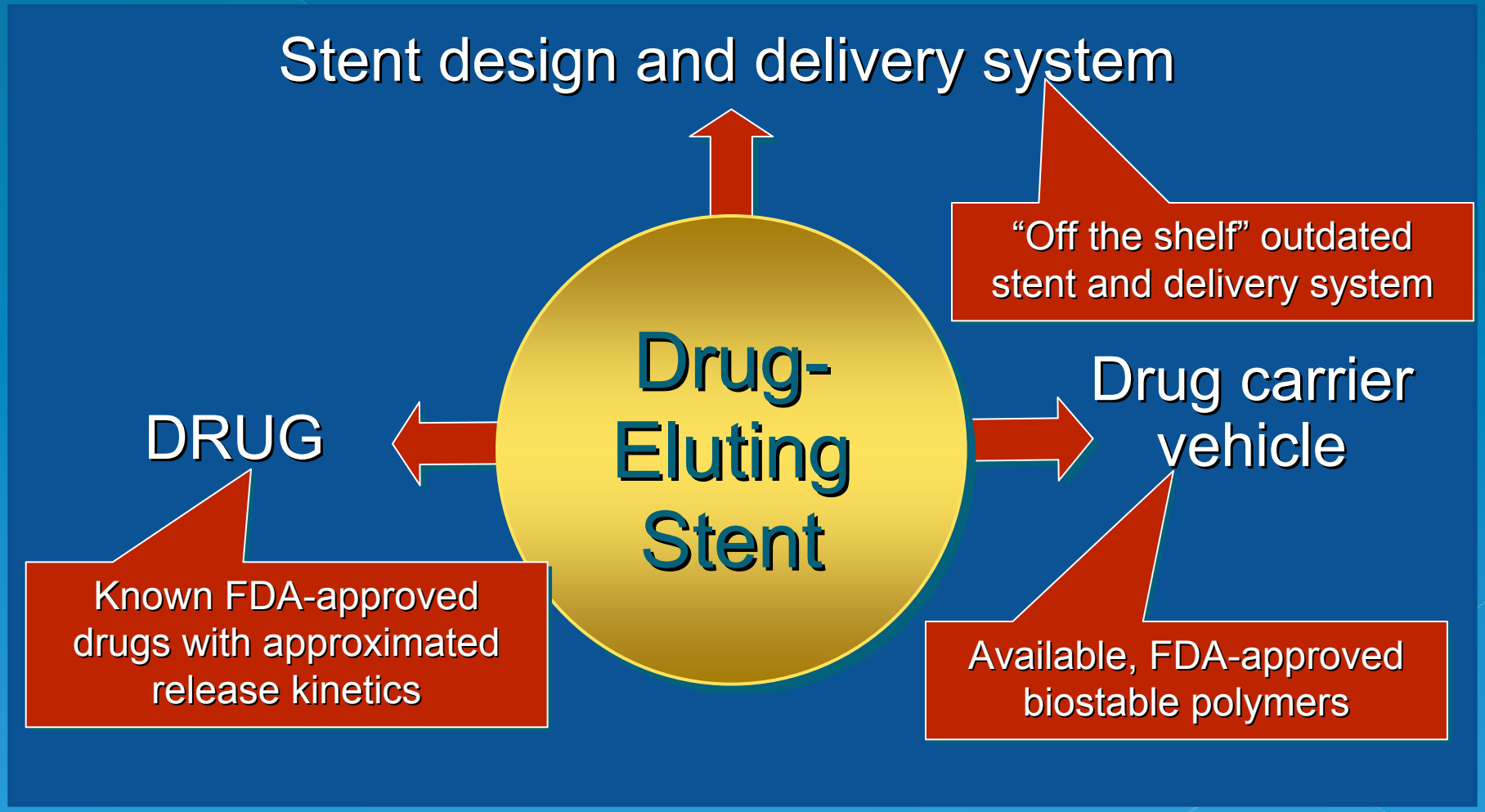




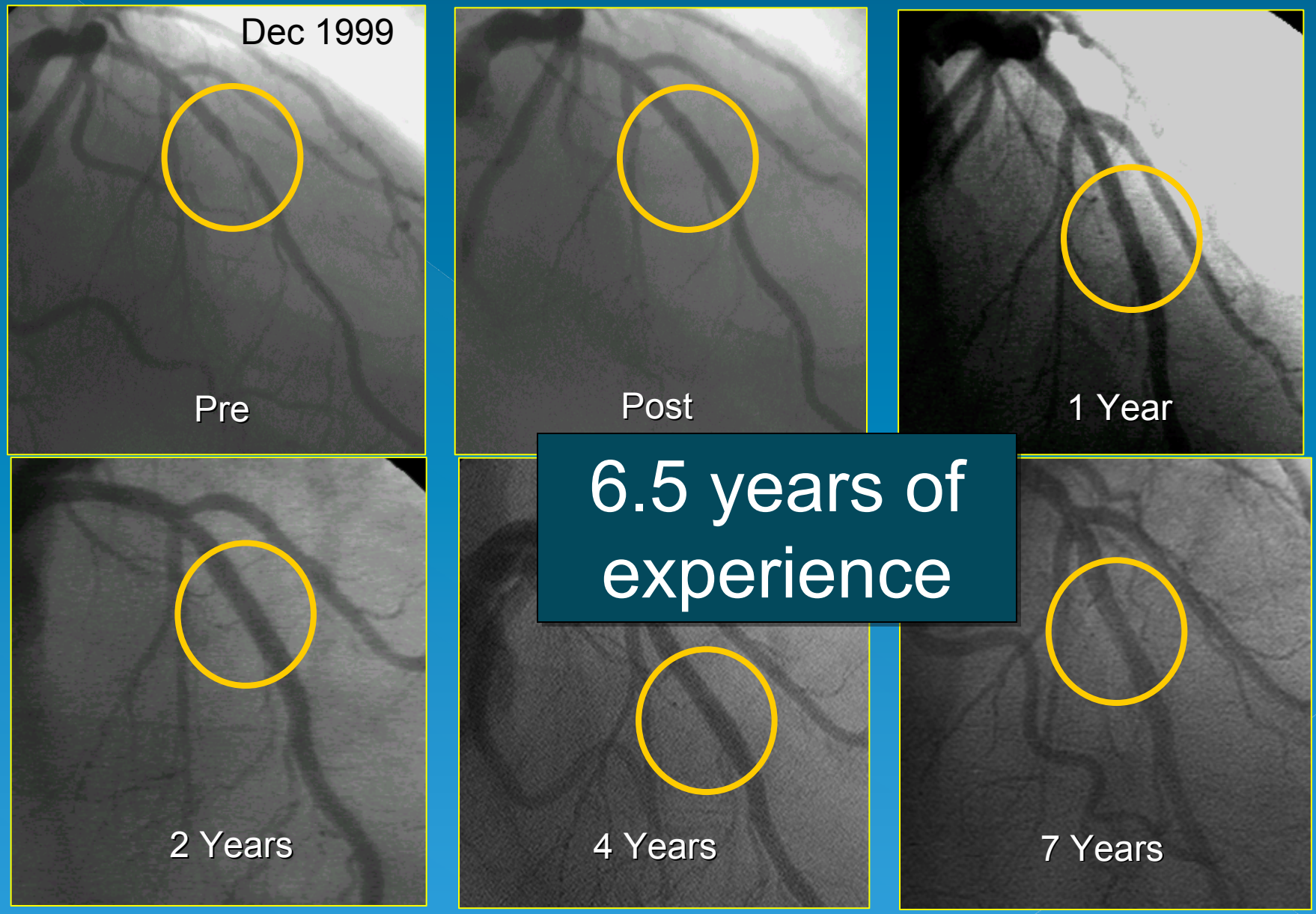
In-stent Restenosis = Intimal Hyperplasia

Drug-Eluting Stents

First Generation



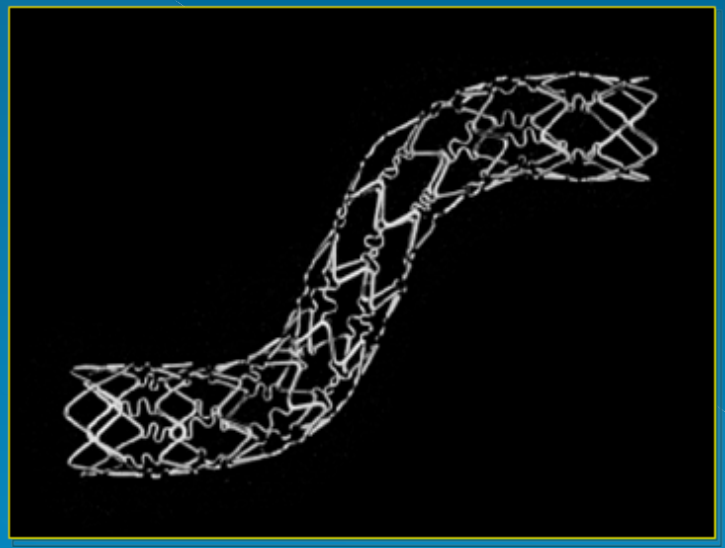
CYPHER Stent: First patient 7 Years FU

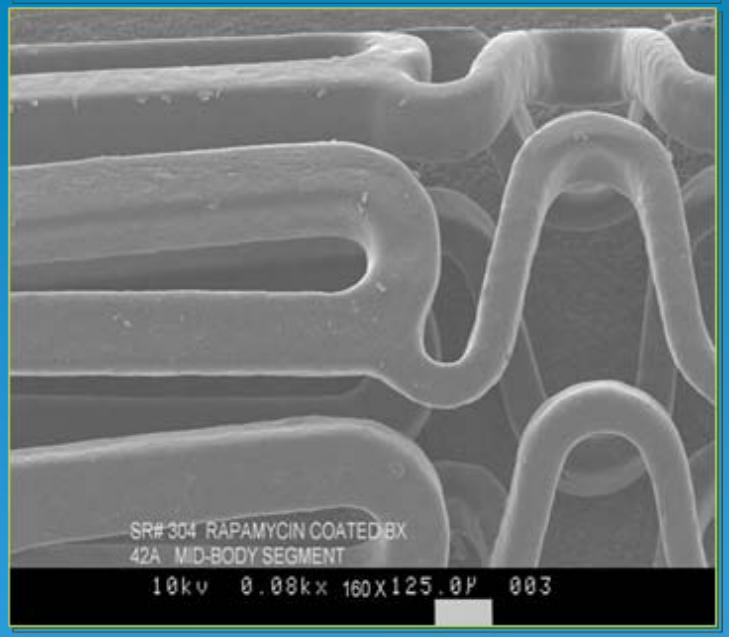


6.5 years of experience

Success over In-Stent Restenosis!!

The Sirolimus-Eluting Stent (Cypher)





- ***Bx VELOCITY™ Stent***

  Stainless steel stent

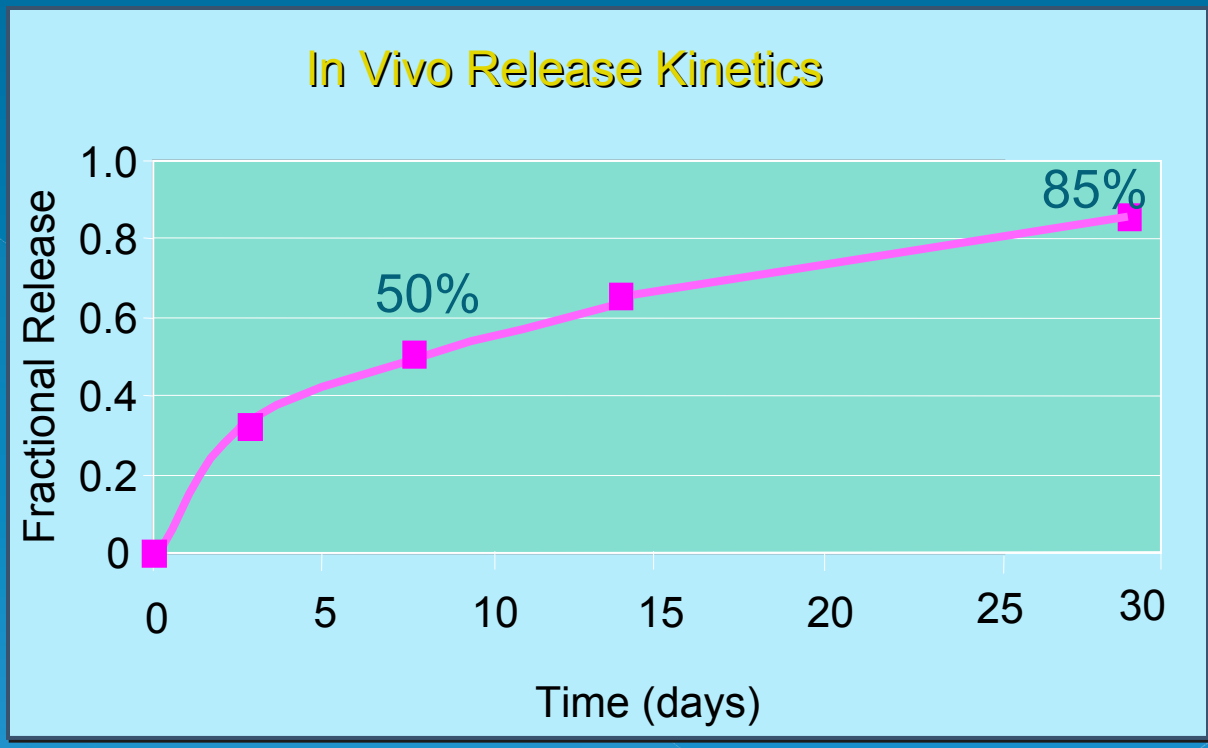
- Coating:

  Blend of 2 polymers (PEVA + PBMA) containing Drug: Sirolimus (~ 10um thick)

Sirolimus Eluting Cypher Stent

Topc

Basecoat = polymer/drug
+
Topcoat = polymer only
(diffusion barrier)



Sirolimus (Rapamycin): Cytostatic Agent

Released in a controlled manner from the polymer matrix (PEVA + PBMA)
ALL of the drug is released within 3 months

One Year later: TAXUS Stent

Drug

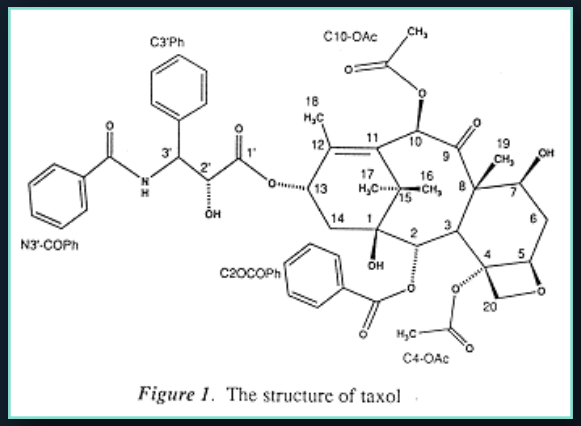
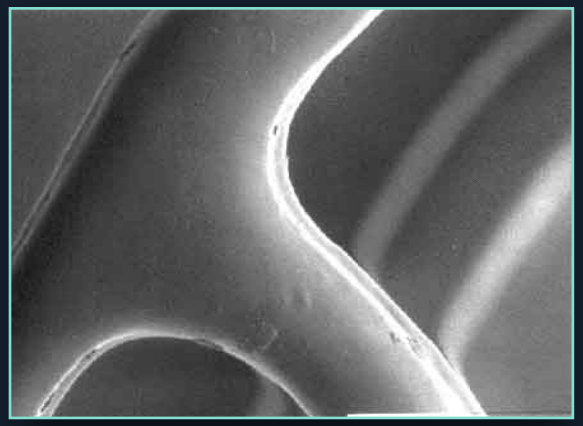


Figure 1. The structure of taxol

Paclitaxel

- Binds tubulin
- Stabilizes microtubular deconstruction
- Multi-cellular
- Multi-functional
- Cytostatic at low dose

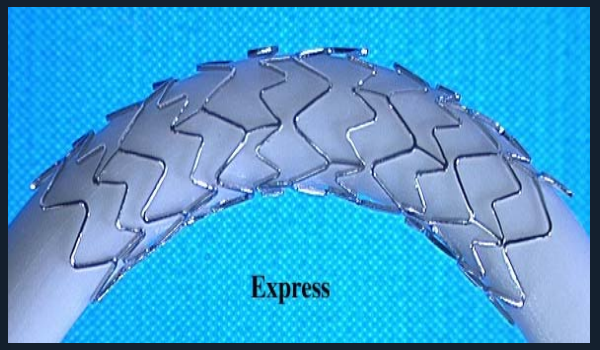
Polymer



Translute™

- **Polyolefin derivative**
- **Uniform**
- **Biocompatible**
- **Elastomeric**
- **Provides controlled release**

Stent

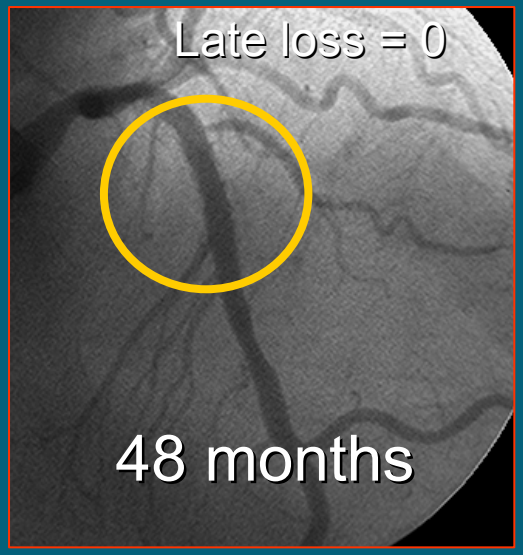


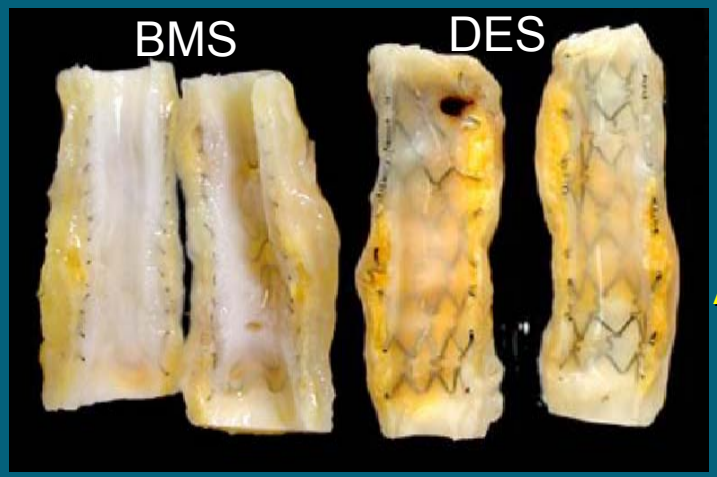
Express²

- **Tandem architecture**
- **Maverick balloon system**
- **Flexible**
- **Deliverable**

Look Carefully !!

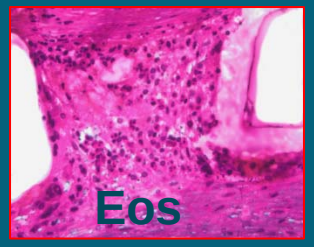
1st Generation DES…. the good, the bad, and the ugly!



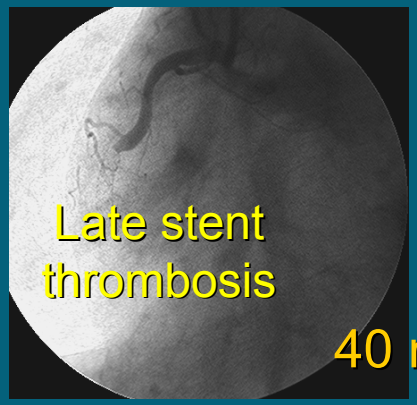


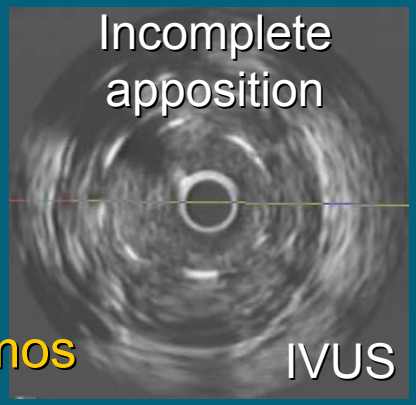
Delayed Healing!

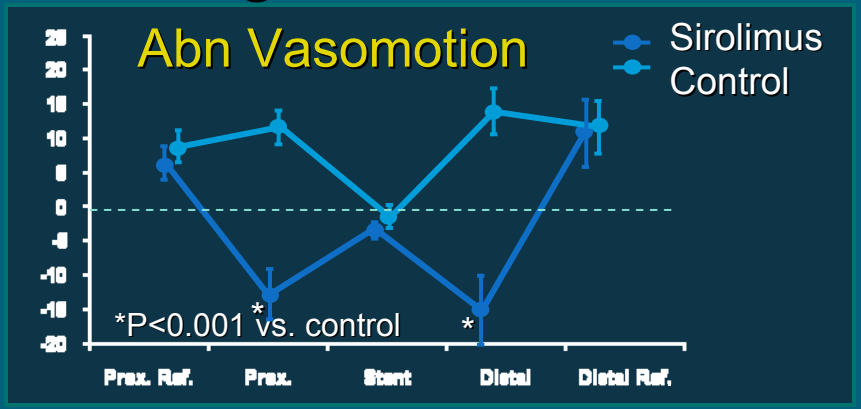
Angioscopy



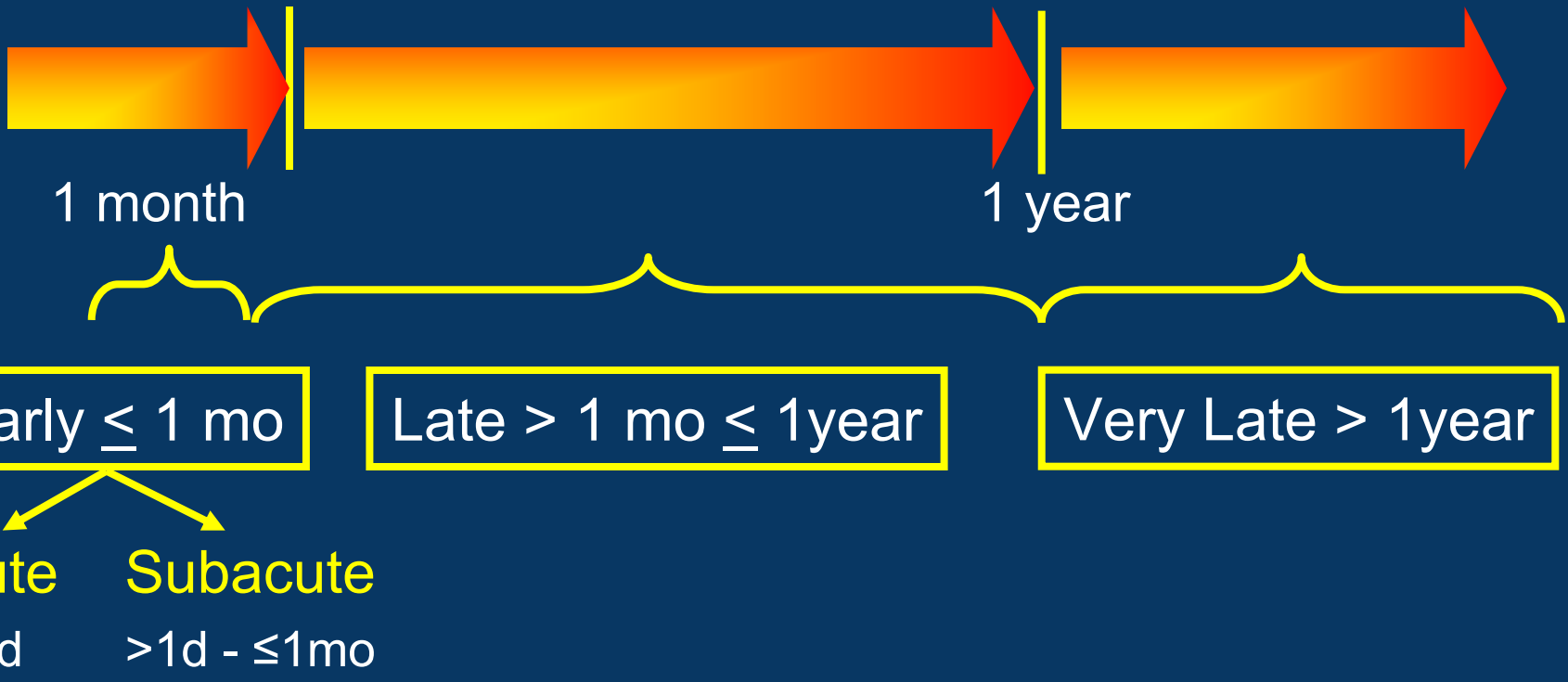
Inflammation





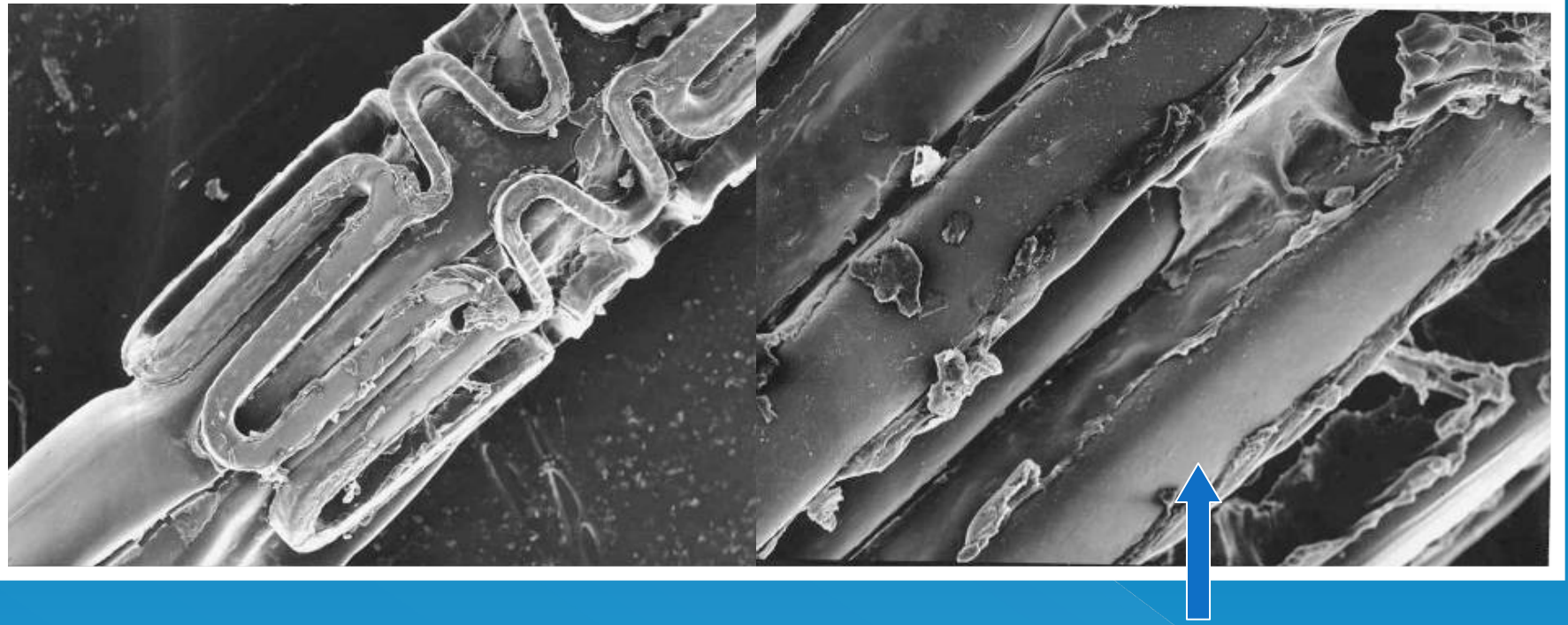


Stent Thrombosis

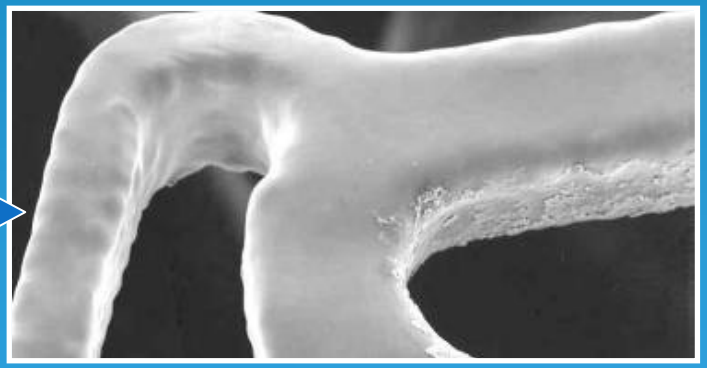


And still some restenosis…..

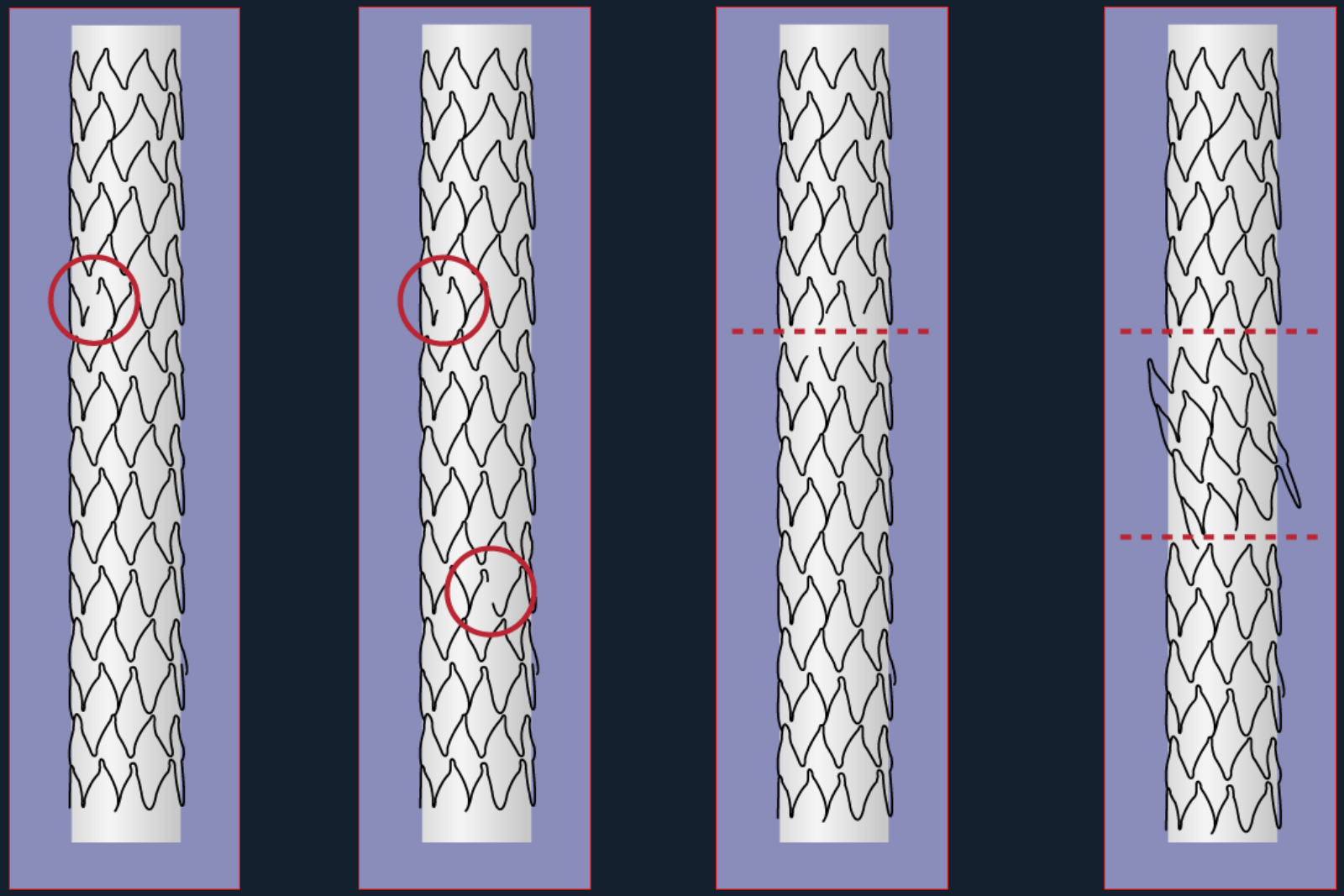
Polymer coating damage



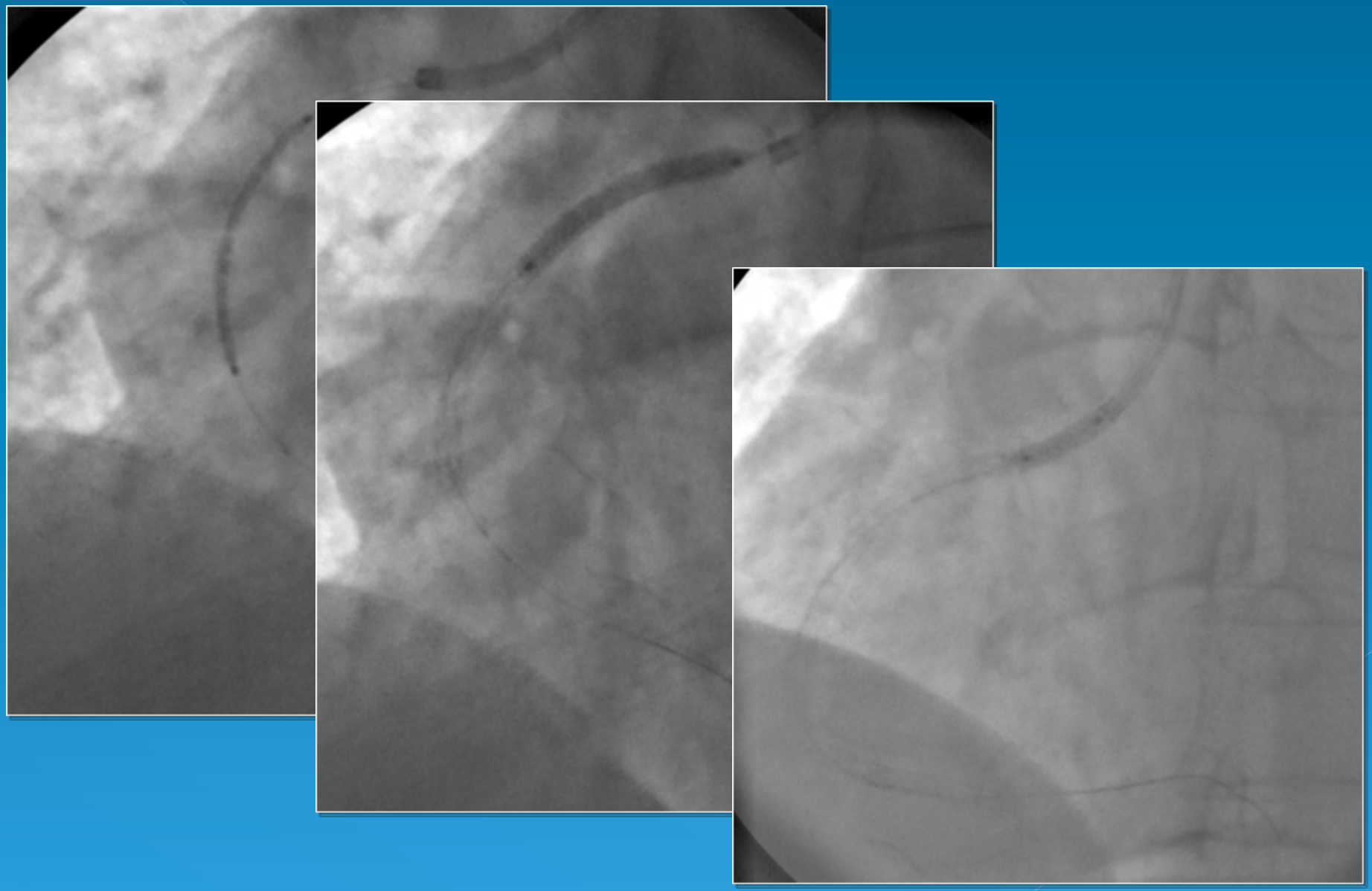
Failed to cross calcified lesion



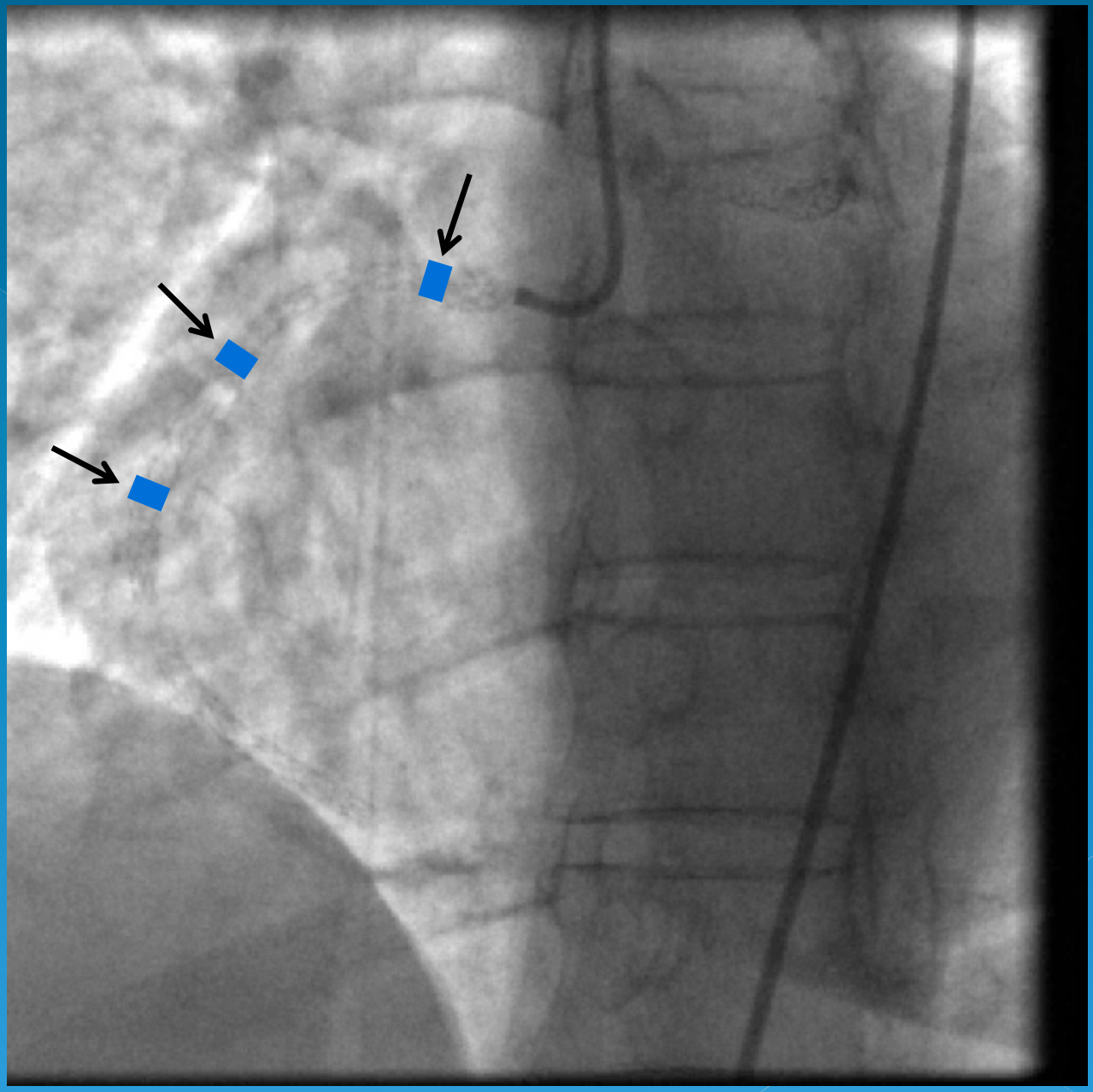
Undamaged polymer


Type I
Type II
Type III
Type IV
Single strut fracture
Multiple single stent fractures; different sites
Multiple stent fractures; complete transverse linear fracture
Complete transverse linear Type III fracture with stent displacement

RCA STENT PLACEMENT FOR DIFFUSE DISEASE



More than 2 yrs later, stops DAPT. One week later comes in with a inferior STEMI: Multiple Cypher stent Fractures

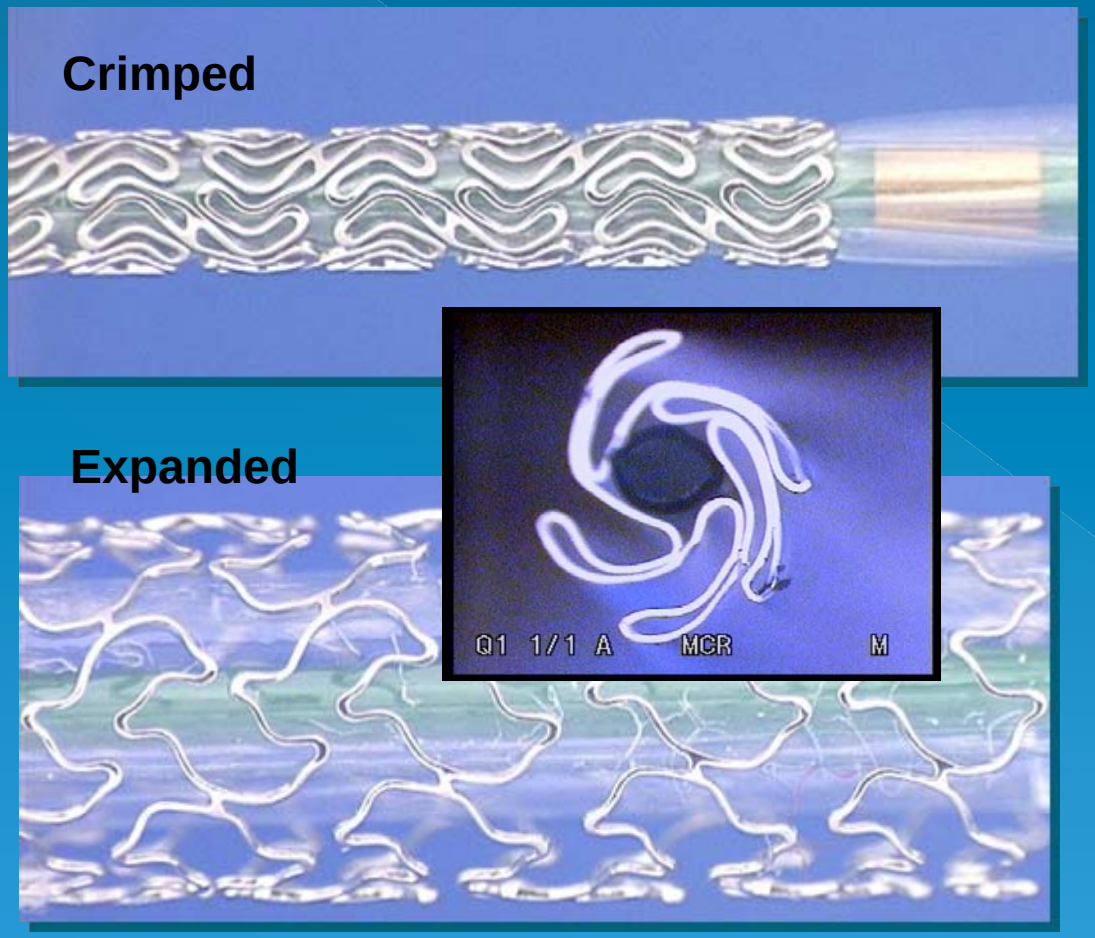


Second Generation DES:

Better designed to be drug eluting stents

Second Generation TAXUS Stent:

TAXUS Liberté™



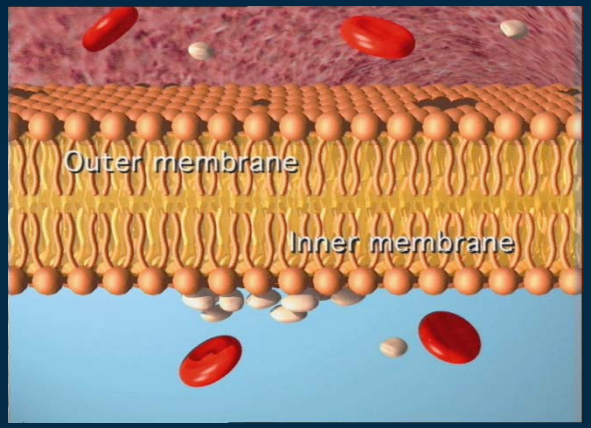
- *Polymer and drug are unchanged*
- *Maverick² balloon*
- *5-wing fold for improved re-wrap and less resistance to withdrawal*
- *Stainless steel 27%↓ in strut thickness - from 0.0052" (Express²) to 0.0038"*

Endeavor DES System

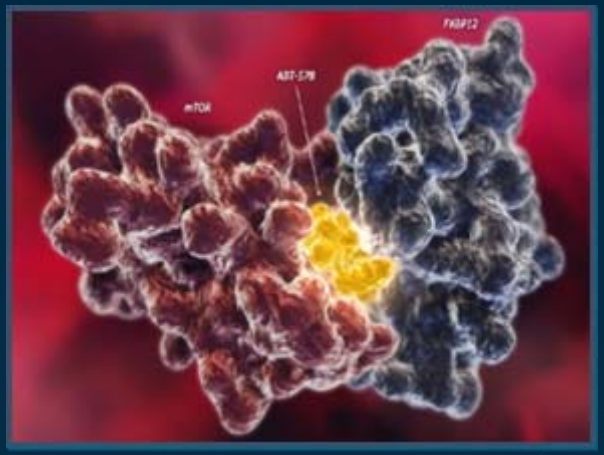
Driver Cobalt Alloy Stent

Stent Delivery

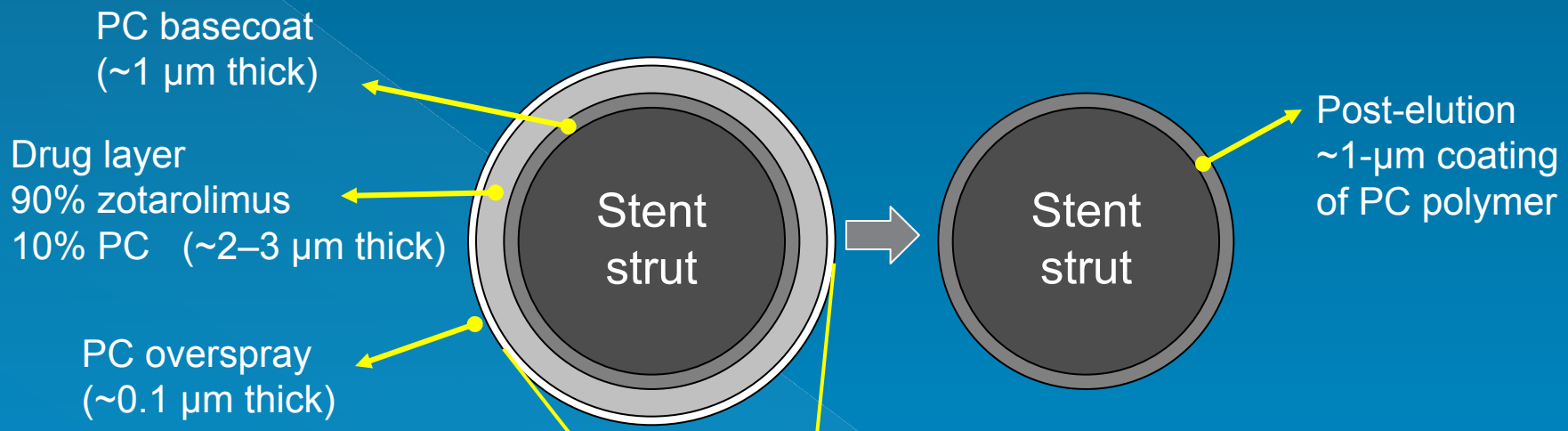
PC Technology



Drug: Zotarolimus



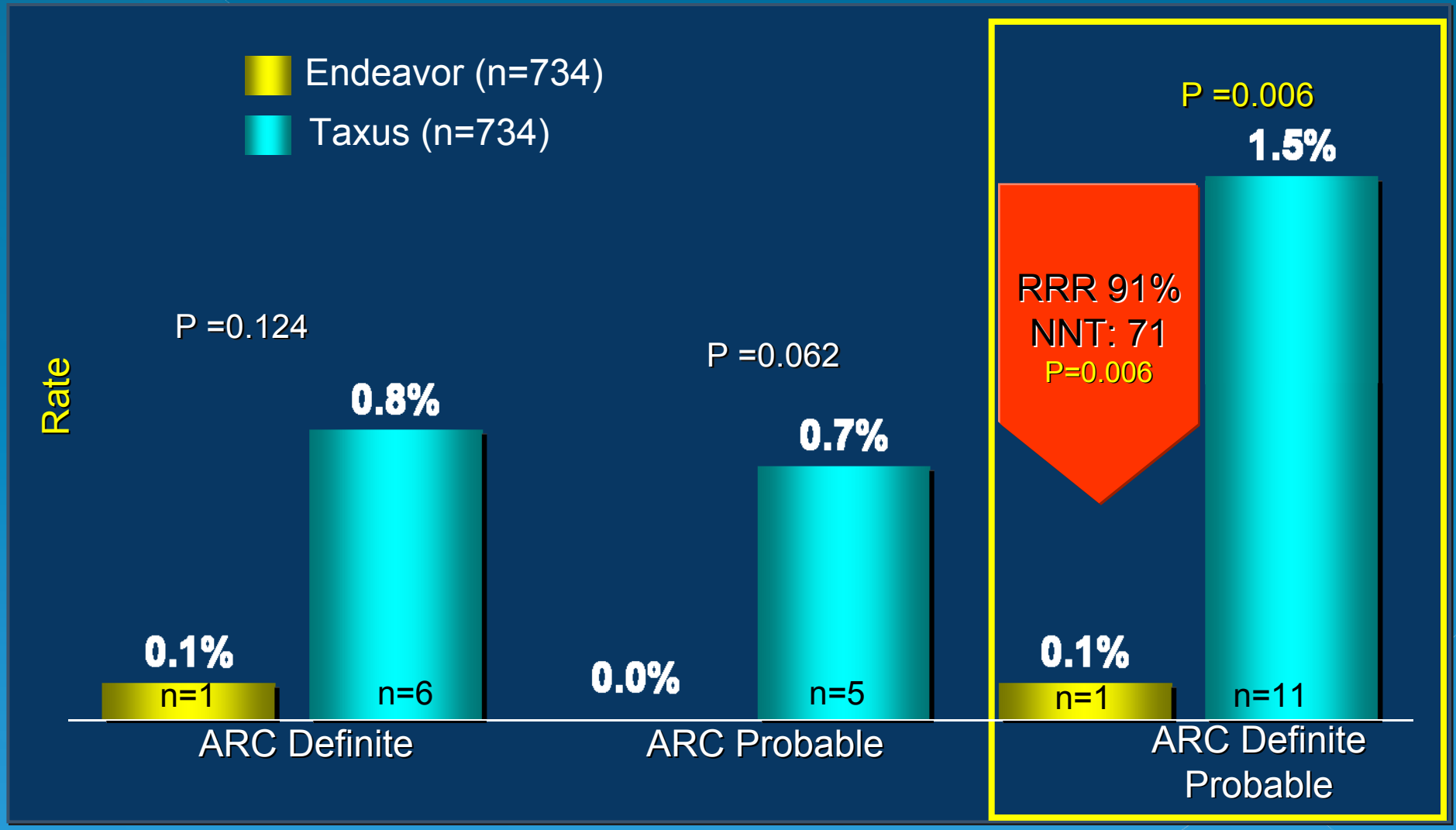
Endeavor Polymer + Drug Matrix



3.0-mm stents
500x magnification

Drug/polymer Strut thickness	Endeavor 4 µm 91 µm	Taxus® 16 µm 132 µm	Cypher® 13 µm 140 µm
Total thickness	95 µm	148 µm	153 µm

Very Late Stent Thrombosis (12-36 mos)
ENDEAVOR IV – 3yr FU

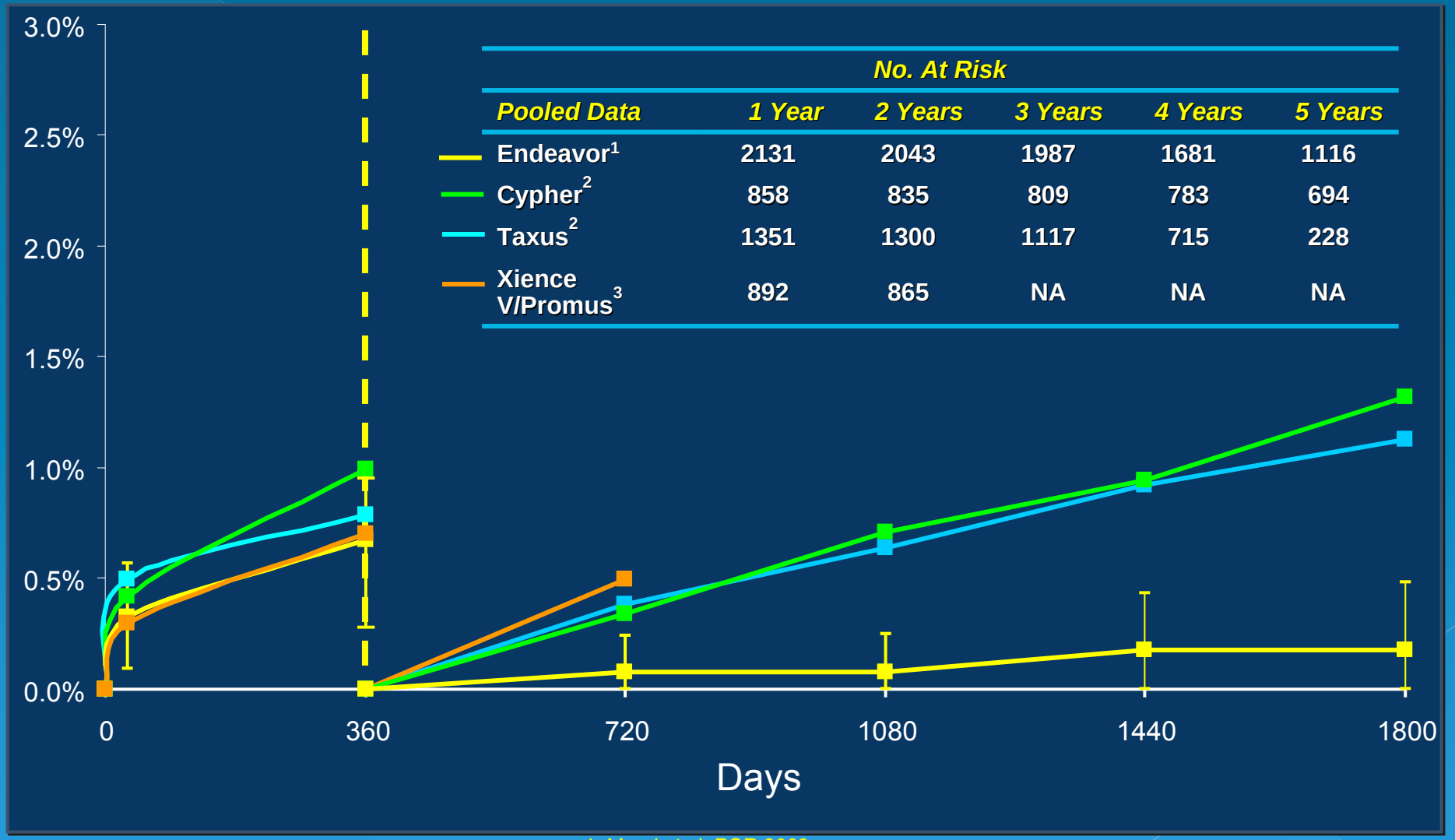


** ARC definition*

TCT Sep 2009

DES Pooled Programs

Definite/Prob ST* Landmark at 1 year to 5 Years



Pooled Data	No. At Risk 1 Year	2 Years	3 Years	4 Years	5 Years
Endeavor[1]	2131	2043	1987	1681	1116
Cypher[2]	858	835	809	783	694
Taxus[2]	1351	1300	1117	715	228
Xience V/Promus[3]	892	865	NA	NA	NA

*ARC Def

1. Mauri et al. PCR 2009.
2. 5 year Outcomes in the Sirius Trial, Weisz et al. JACC Vol. 53, No. 17, 2009
3. Mauri L et al. N Engl J Med. 2007;356:1020-1029.
4. Stone, G et al., New SPIRIT Clinical Data, ACC. 09.

OPTIMIZE (Brazil)

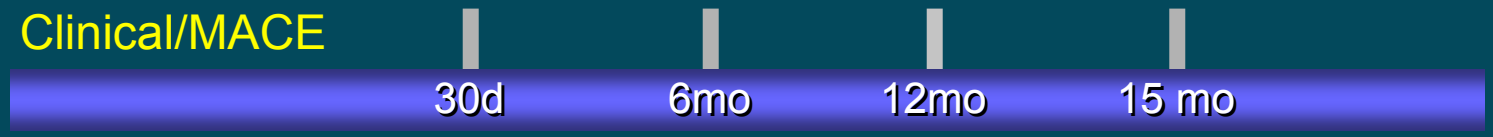
RCT 3 months DAPT vs 12 months

All comers (excluding STEMI)
Reference Vessel Diameter 2.25 mm-4.0 mm

Endeavor Stent
3 months DAPT
n = 1,600

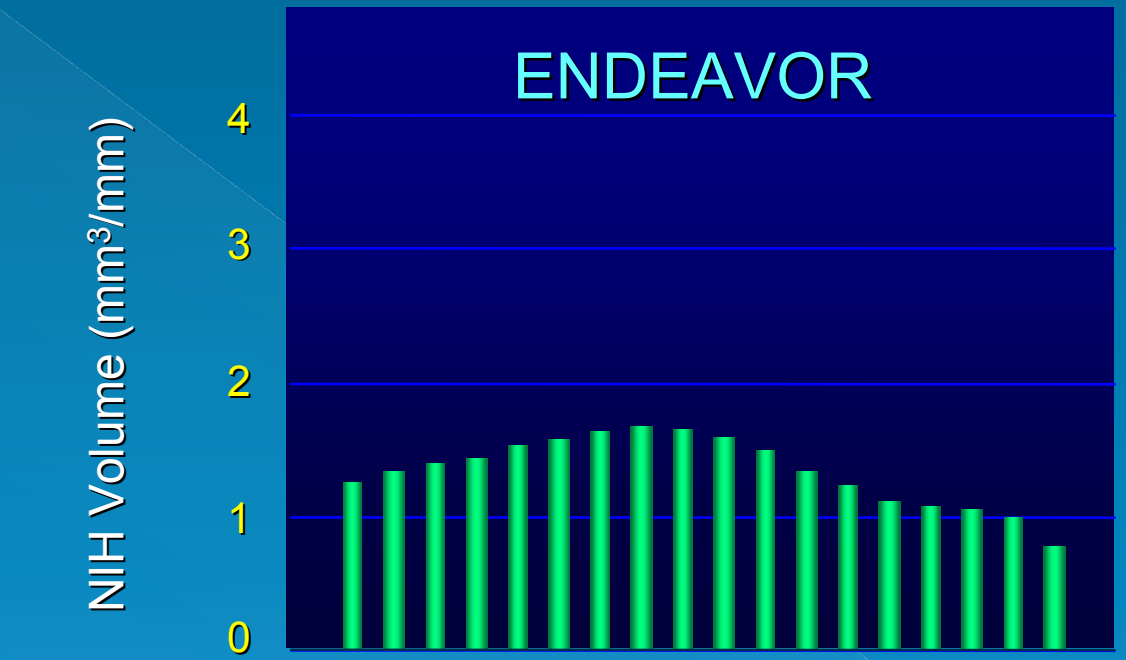
N = 3,200 patients
in
Brazil

Endeavor Stent
12 months DAPT
n = 1,600



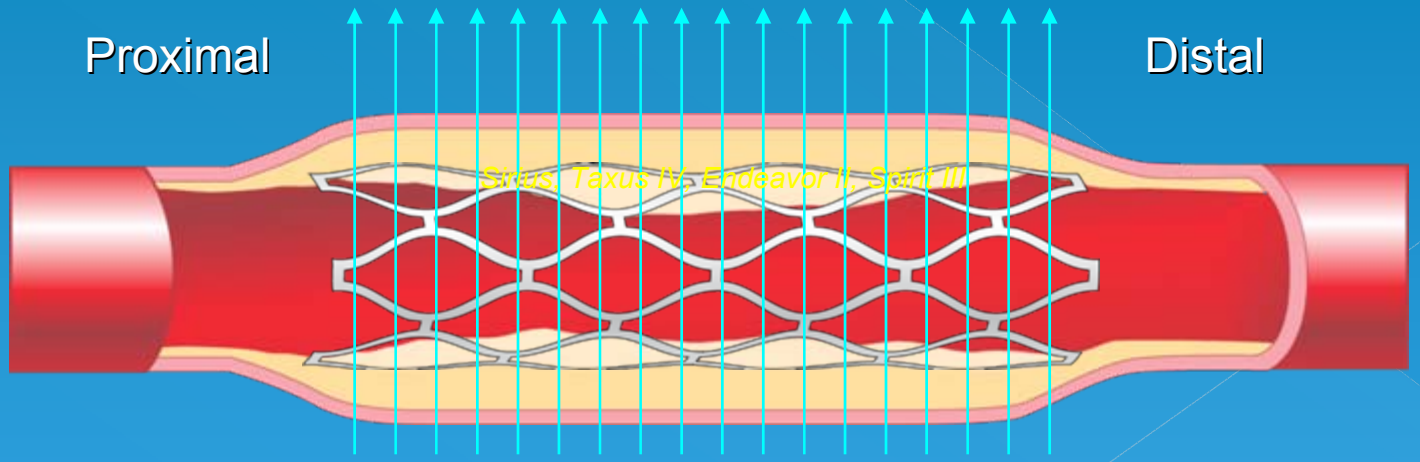
Primary Endpoint: TLF at 12 months
Secondary Endpoints: MI, Cardiac Death, ARC def/prob ST at 30 days, 6 months and 15 months
Drug Therapy: ASA and Clopidogrel 3 or 12 months

ENDEAVOR – IVUS

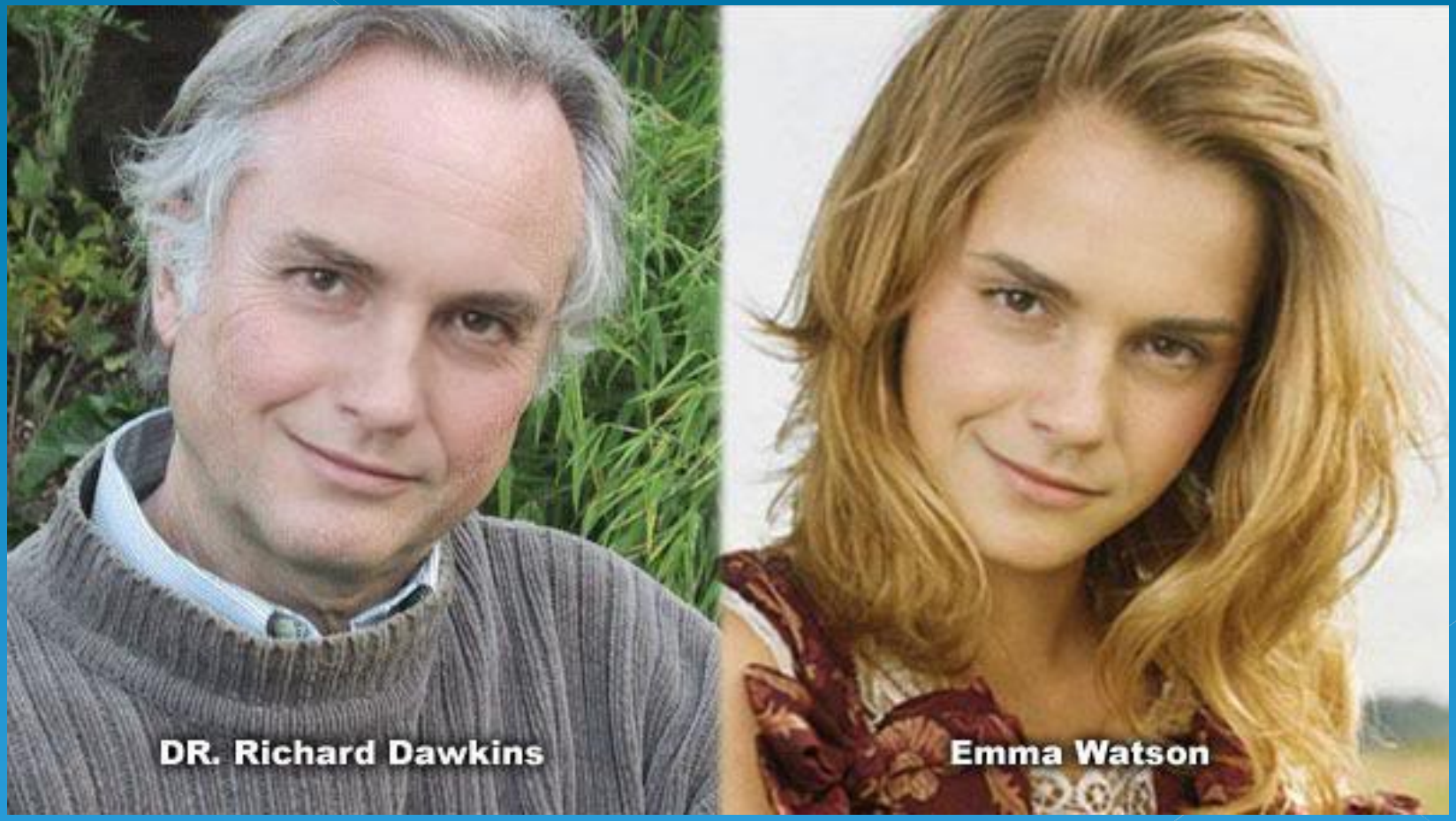


ENDEAVOR

(N=55)

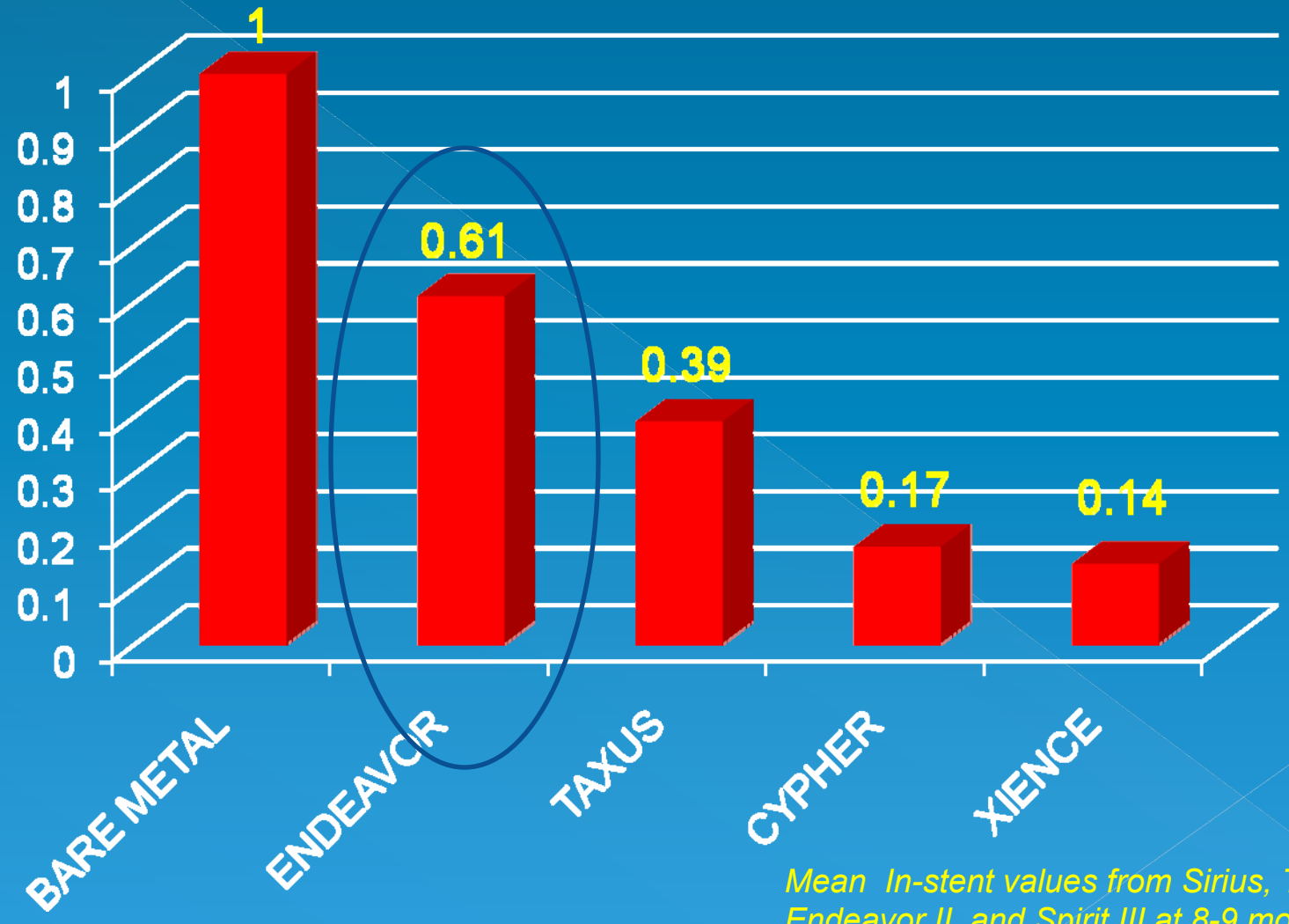


DES: They look similar but they are not the same



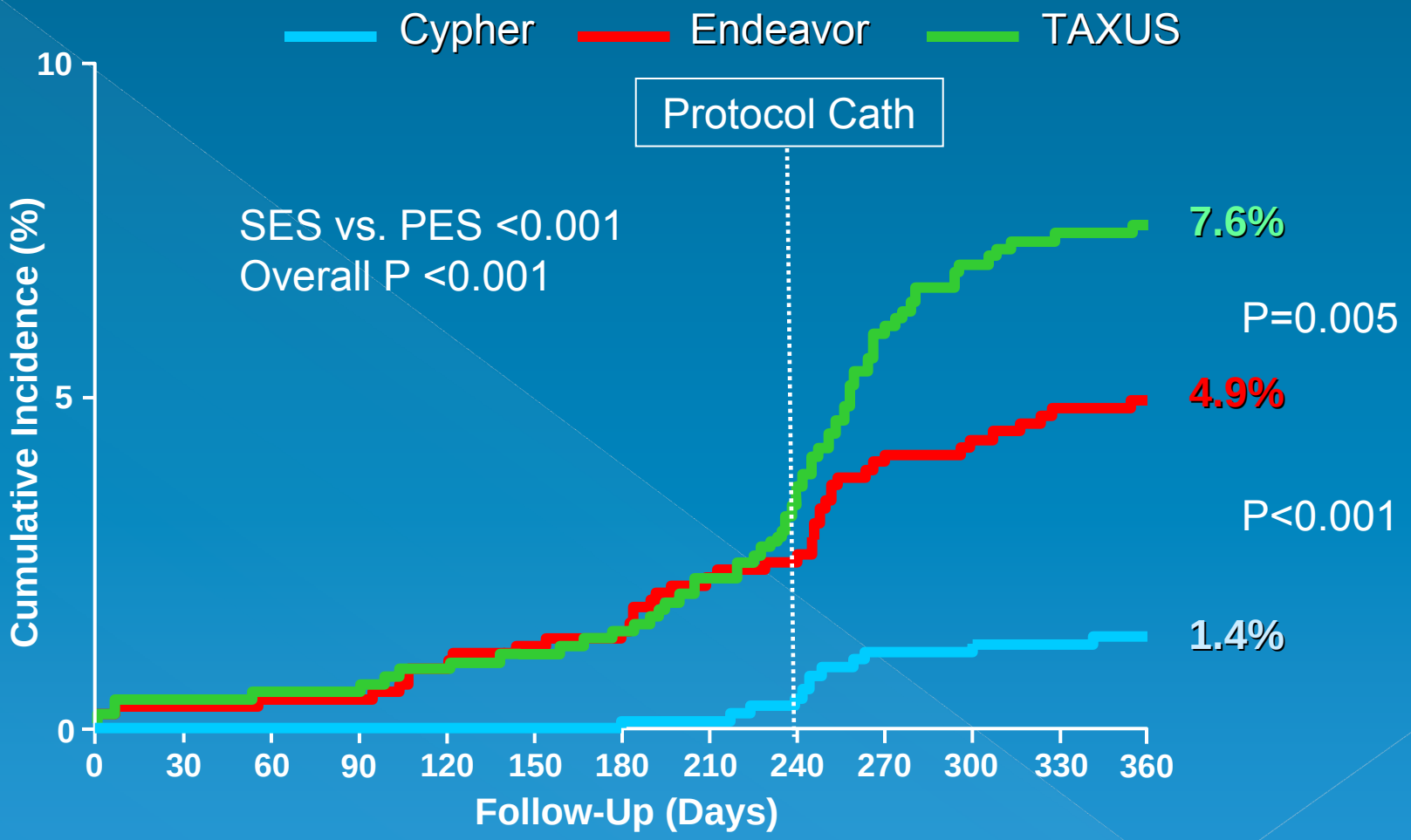
Late Loss* (mm)

An (imperfect) Index of Anti-restenotic Efficacy



Mean In-stent values from Sirius, Taxus IV Endeavor II, and Spirit III at 8-9 months

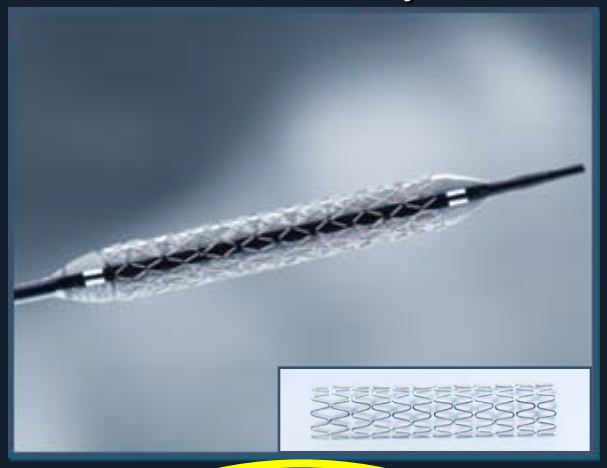
Ischemic driven TLR



Zest Trial, 2009

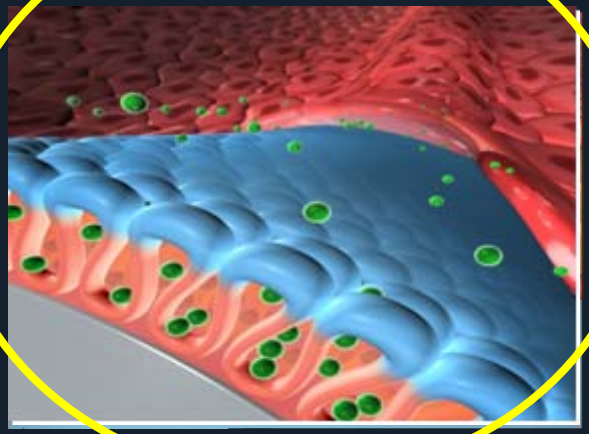
Solution: Resolute DES System

Driver Cobalt Alloy Stent

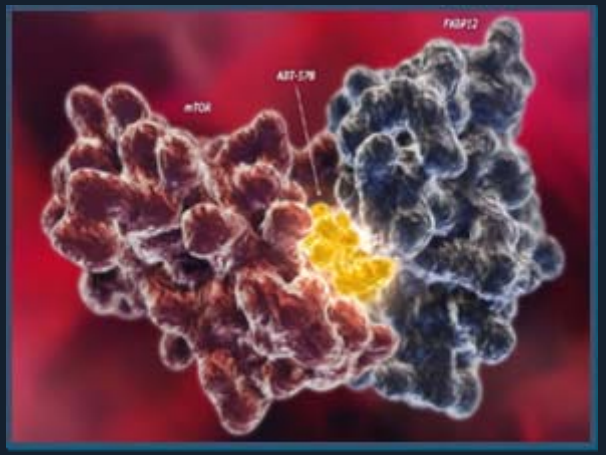


Stent Delivery System

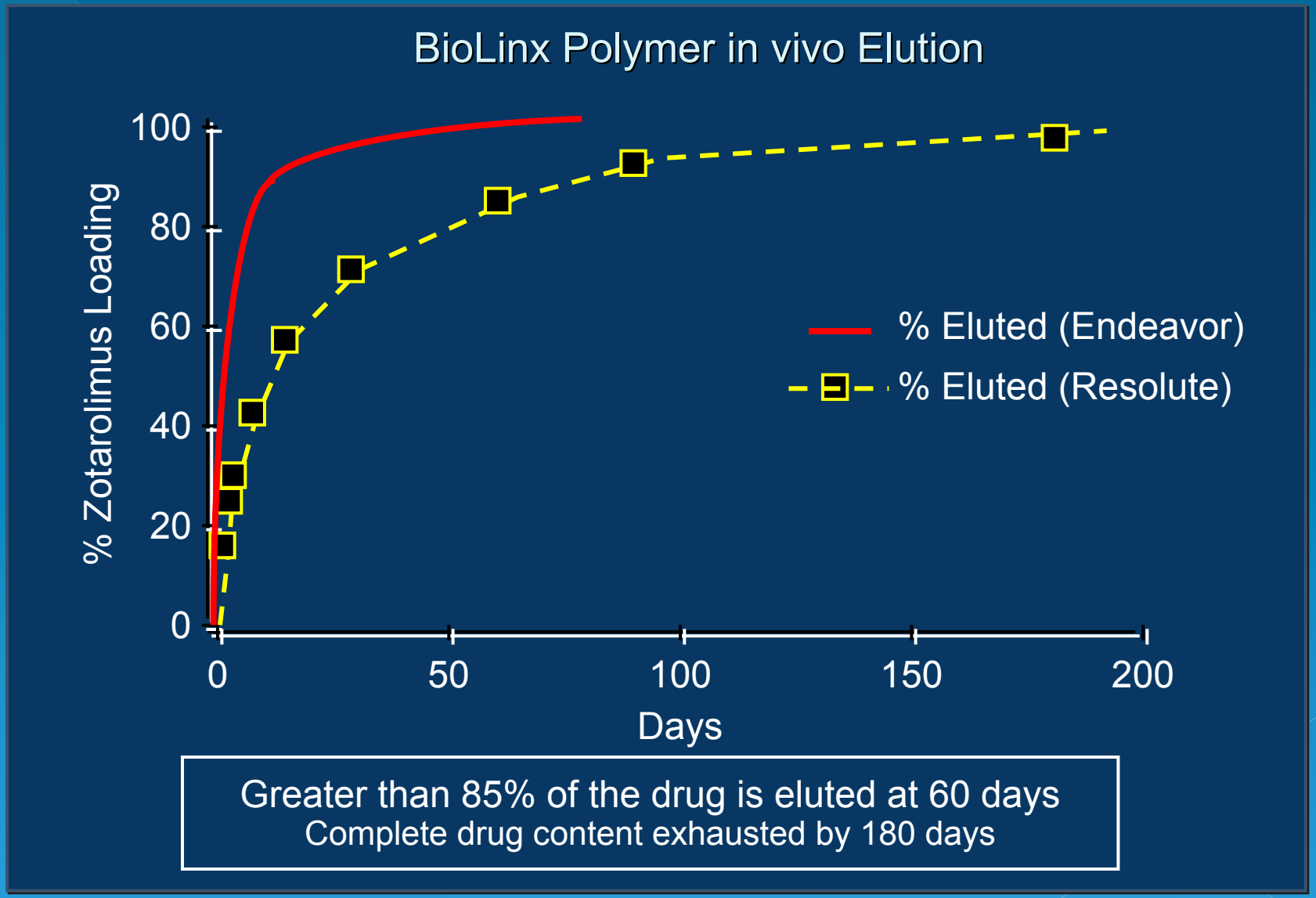
BioLinx Polymer



Drug: Zotarolimus



Resolute Elution Kinetics



Carter et al TCT 2006

Endeavor RESOLUTE

9 month Angiographic Results

n=96	In-stent	In-segment
Pre-procedure RVD (mm)		2.79 ± 0.40
Lesion Length (mm)		15.87 ± 6.51
MLD (mm) pre		0.82 ± 0.35
post	2.74 ± 0.41	2.33 ± 0.44
Acute Gain	1.91 ± 0.47	1.51± 0.50
Late loss (mm) ENDEAVOR	**0.67 ± 0.49**	**0.42 ± 0.50**
Late Loss (mm)	0.22 ± 0.27	0.12 ± 0.27
Late Loss Index	0.12 ± 0.16	0.08 ± 0.21
9 mo f/u % DS	10.13 ± 12.63	21.08 ± 10.62
ABR n (%)	1 (1%)	2 (2.1%)

*Meredith et al: EuroInterv 2007; 3:50-53

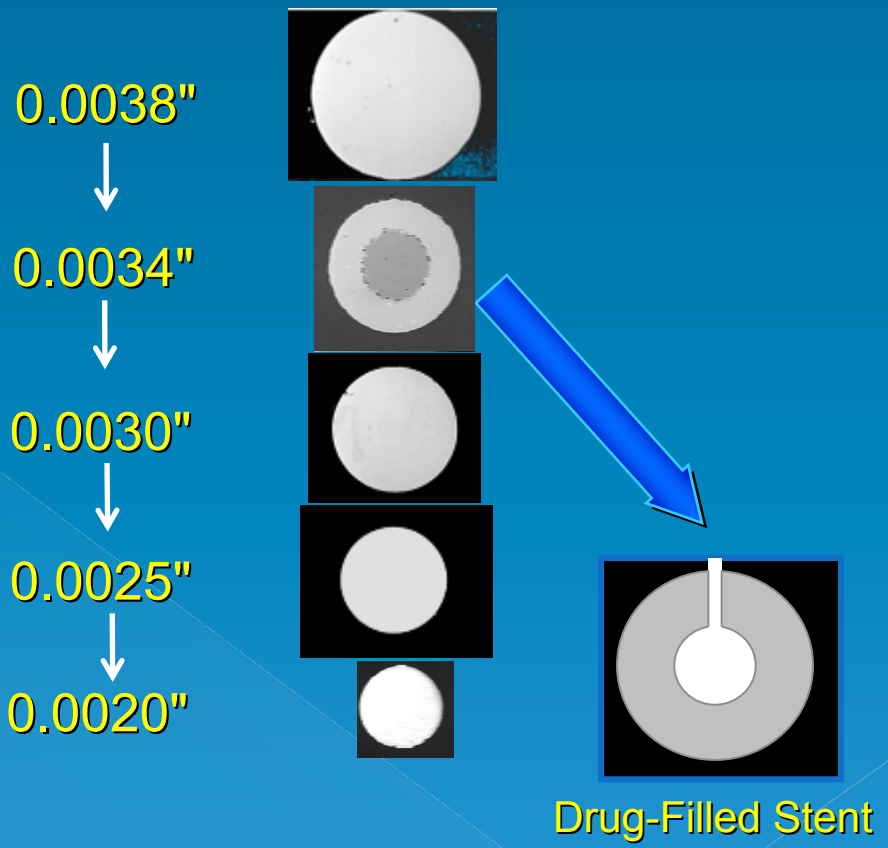
COMING SOON.....

Continuous Sinusoid Technology and Stent strut construction

Continuous Sinusoid Technology

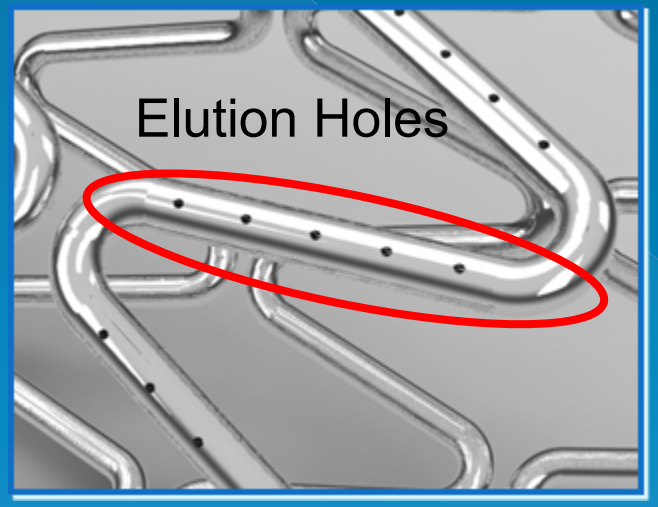
Program Targets:

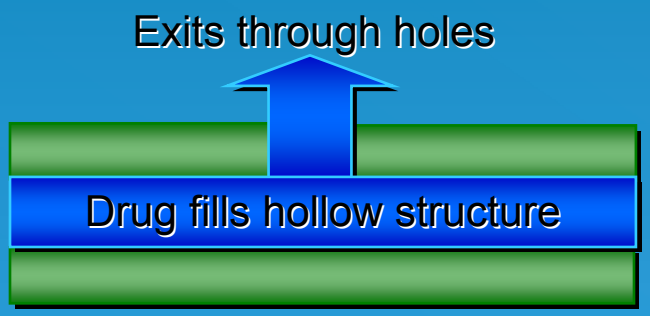
- Enhance deliverability and conformability without compromising strength & opacity
- Develop a platform for DES that enables optimized drug transmission



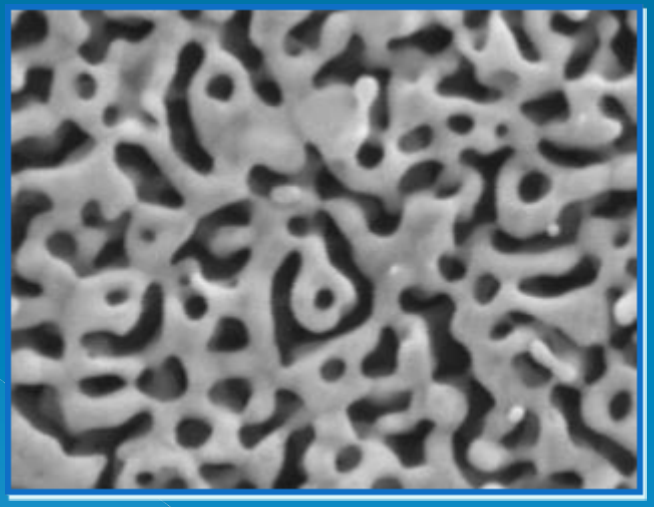
Non-Polymeric DES Approaches

Drug-Filled Stent





Nanoporous Surface Modification



Development Targets:

- Inhibit restenosis and cell proliferation without the use of a polymer
- Provide for rapid, healthy endothelialization

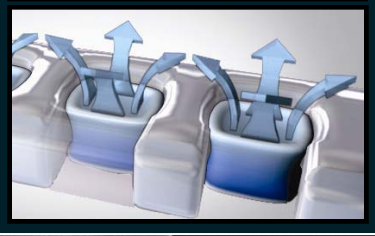
From Cypher to New Cordis RES Technology

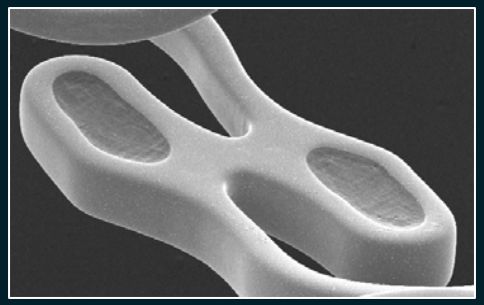
CoStar® Sirolimus-Eluting Coronary Stent System

A Stent Specifically Designed for Controlled Drug Delivery from a Bioresorbable PLGA Polymer

Costar Stent led Cordis to design the Nevo Stent

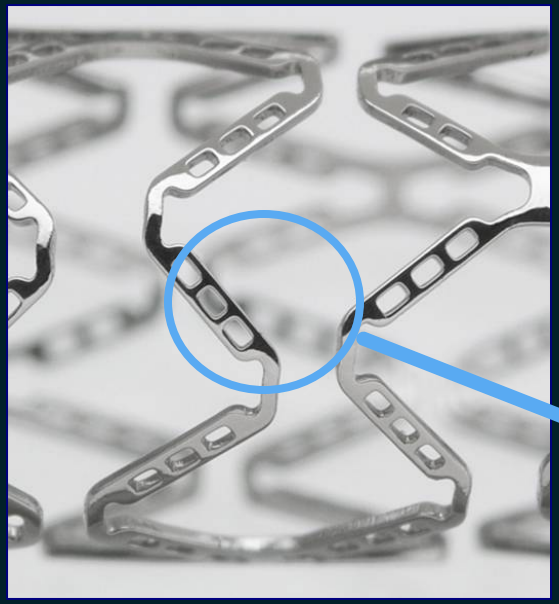
Reservoir inlays with PLGA bioresorbable polymers; reduced tissue-polymer contact area

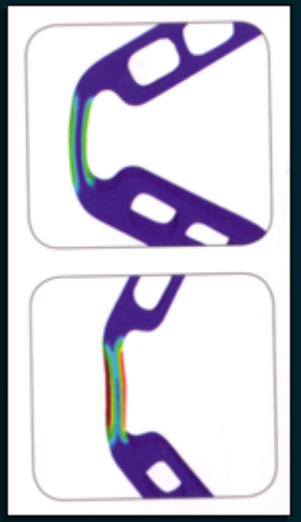


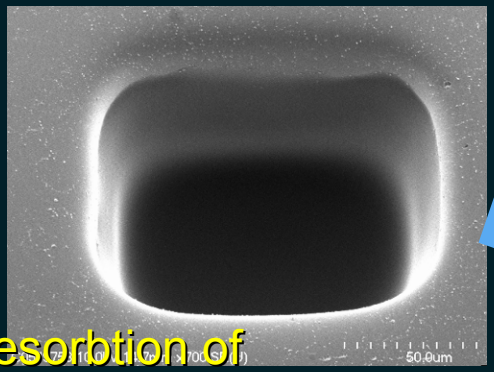


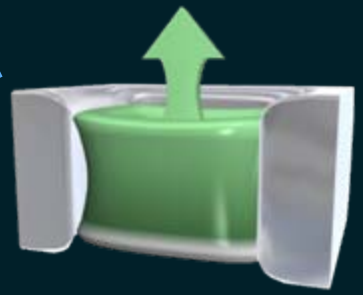
NEVO STENT: Low profile CoCr

Flexible Design with Non-Deforming Reservoirs





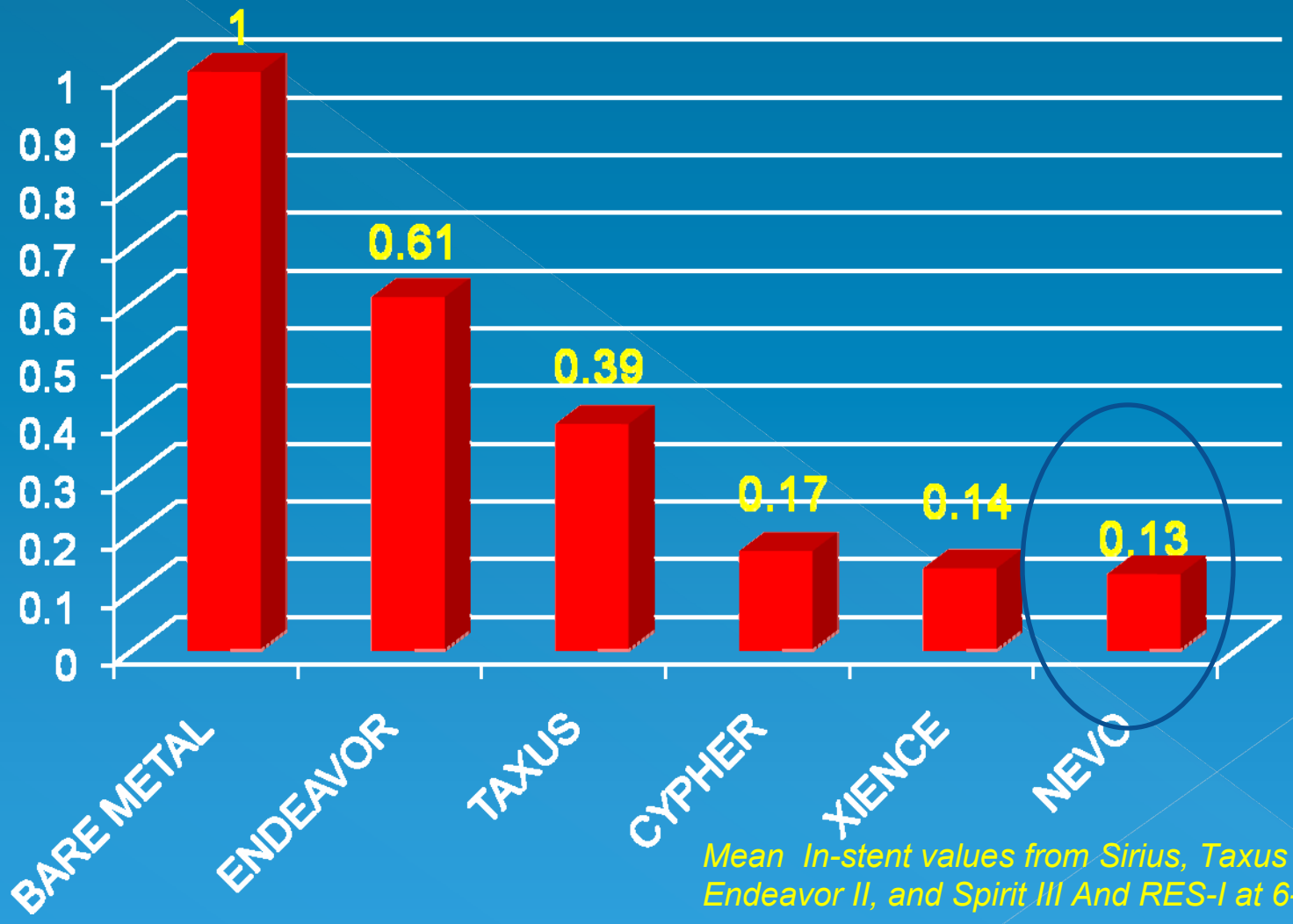




- Complete elution of the drug and resorbtion of the polymer from the reservoirs over time leave behind a bare metal stent

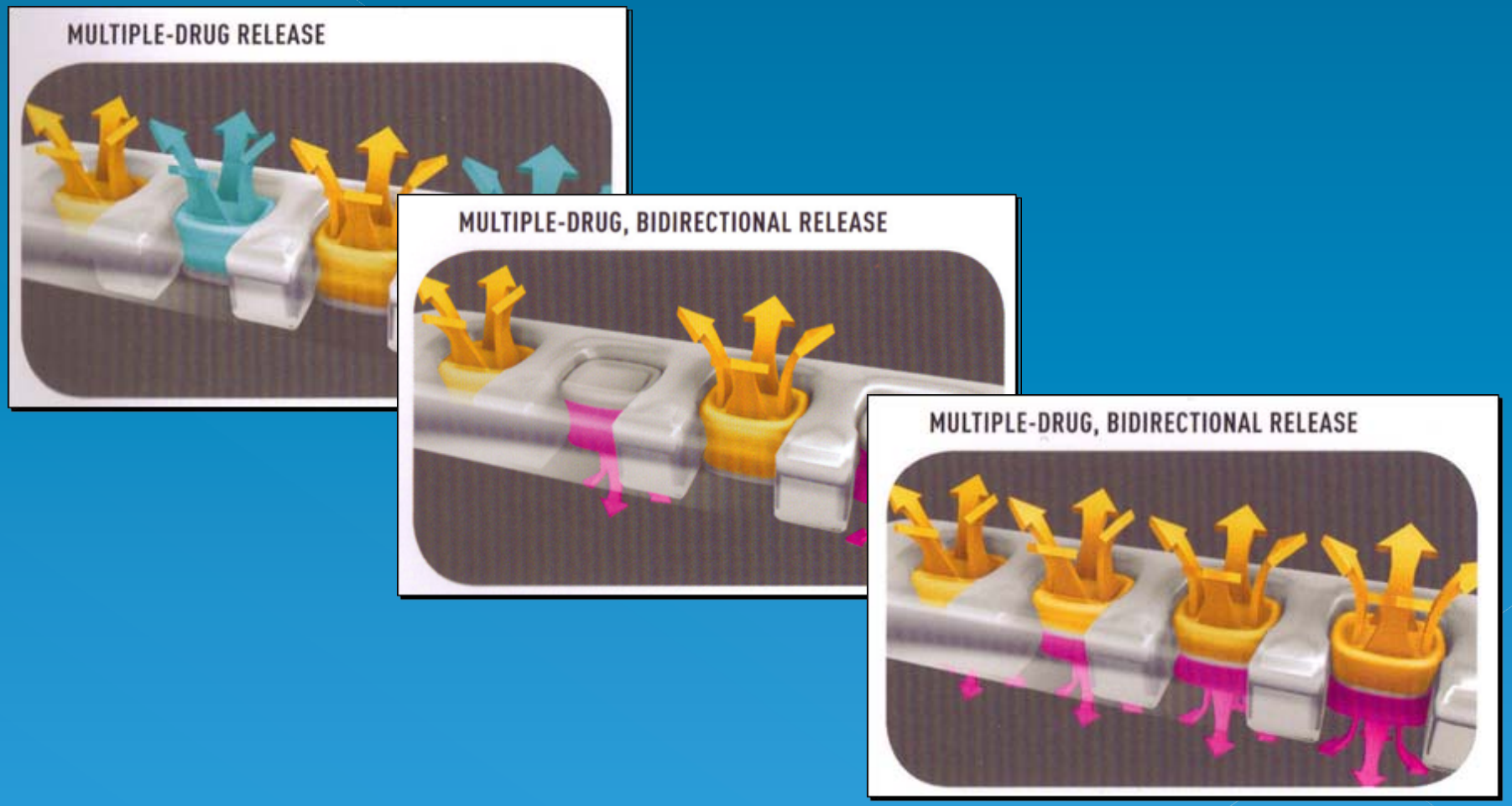
Late Loss* (mm)

An (***imperfect***) Index of Anti-restenotic Efficacy



Mean In-stent values from Sirius, Taxus IV Endeavor II, and Spirit III And RES-I at 6-9 months

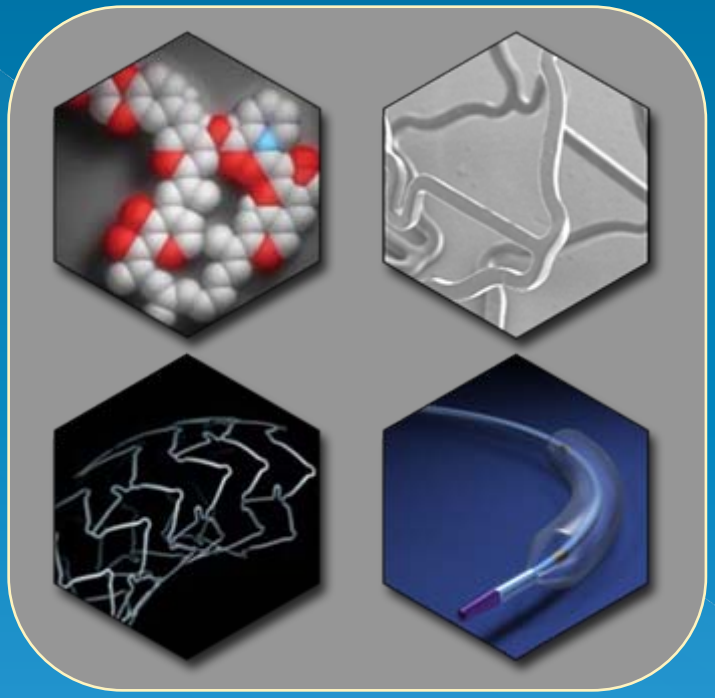
Nevo Stent: Future posibilities



XIENCE V / PROMUS
Everolimus-eluting Stent

Everolimus

ML VISION® Stent Platform

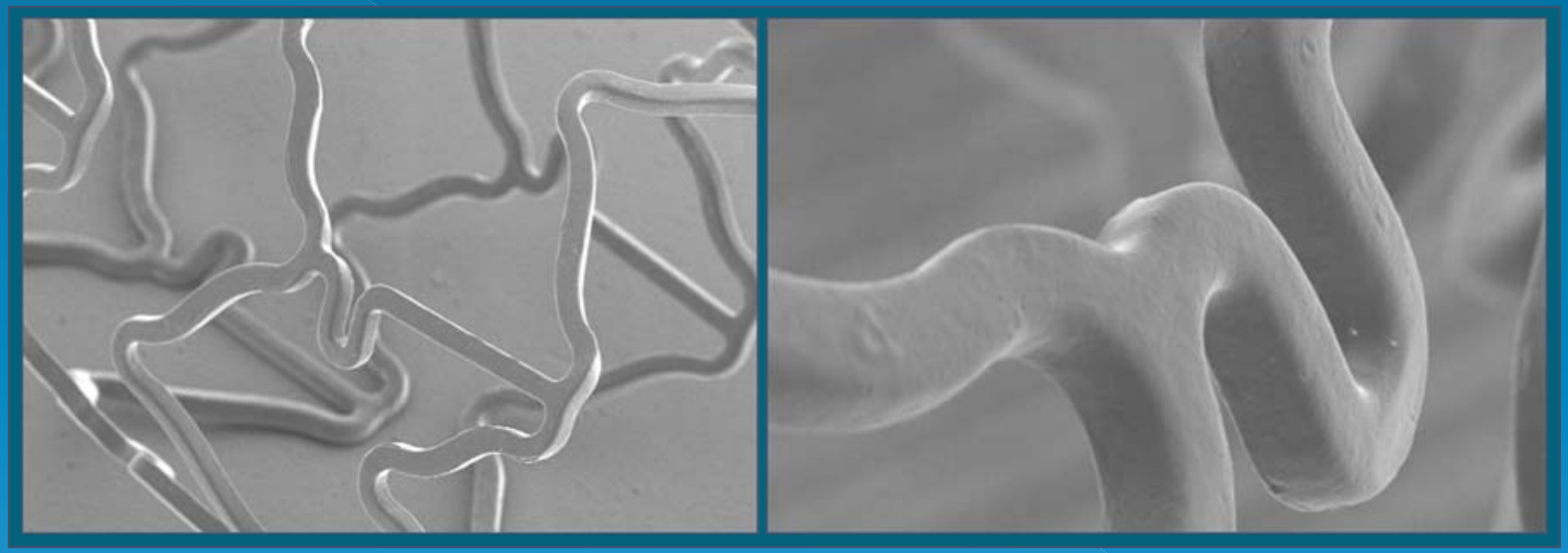


Durable Fluorinated Copolymer

ML VISION® Stent Delivery System

SPIRIT Clinical Trials

Coating Integrity – XIENCE™ V Fluoropolymer (7.8 um thick)

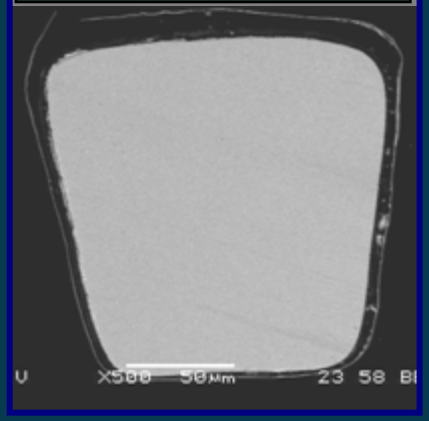


- Uniform, consistent coating integrity upon deployment
- Good adhesion to stent – no bonding, webbing, tearing
- Non-tacky drug matrix prevents “unwanted” adhesions

DES Strut and Polymer Thickness

3.0 mm diameter stents, 500x magnification

CYPHER®



Strut Thickness:

140 μm

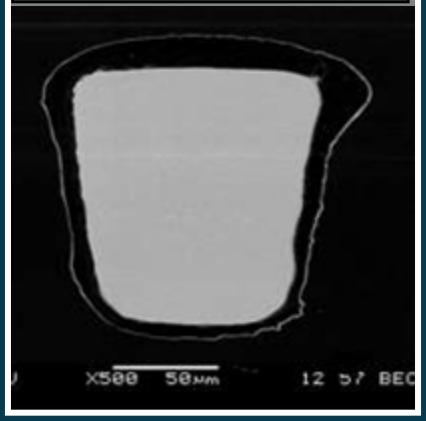
Polymer Thickness:

12.6 μm

Total:

165.2 um

TAXUS®



Strut Thickness:

132 μm

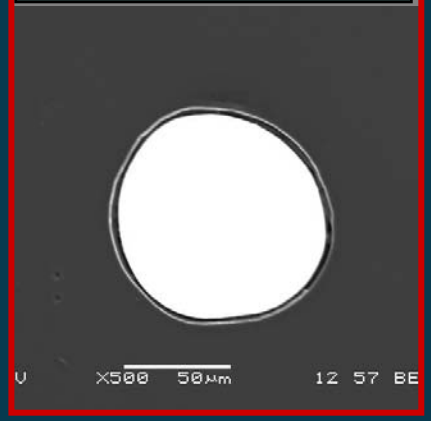
Polymer Thickness:

16 μm

Total:

164 um

ENDEAVOR™



Strut Thickness:

91 μm

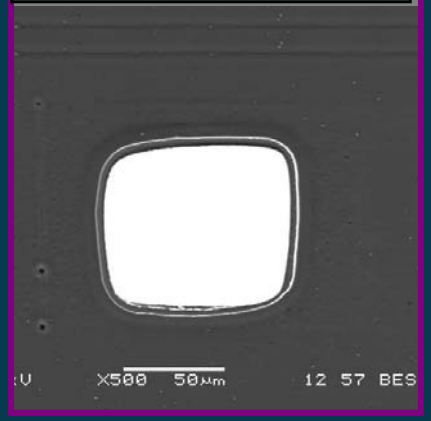
Polymer Thickness:

5.3 μm

Total:

101.6 um

XIENCE™ V



Strut Thickness:

81 μm

Polymer Thickness:

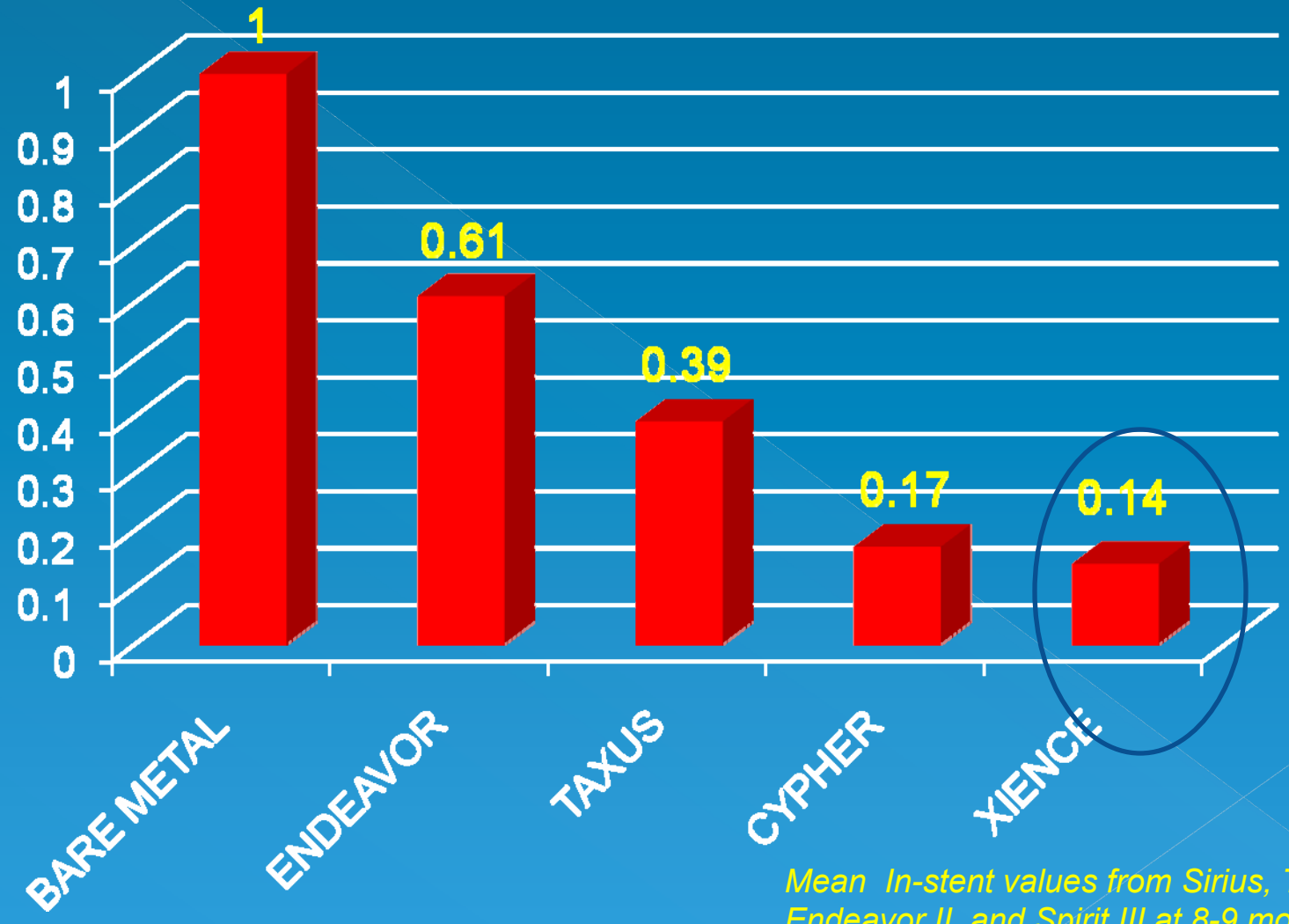
7.8 μm

Total:

96.6 um

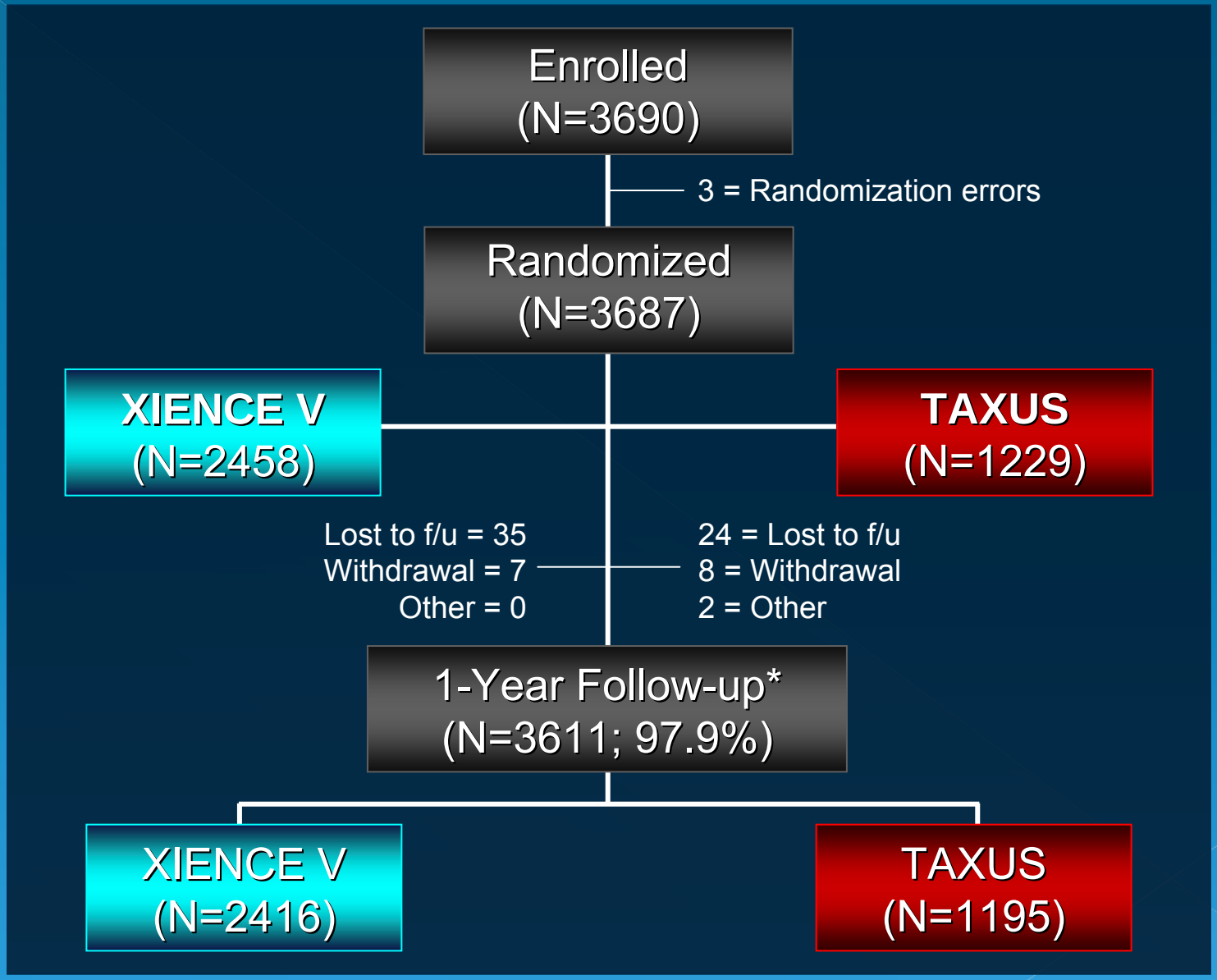
Late Loss* (mm)

An (imperfect) Index of Anti-restenotic Efficacy



Mean In-stent values from Sirius, Taxus IV Endeavor II, and Spirit III at 8-9 months

SPIRIT IV Study Protocol

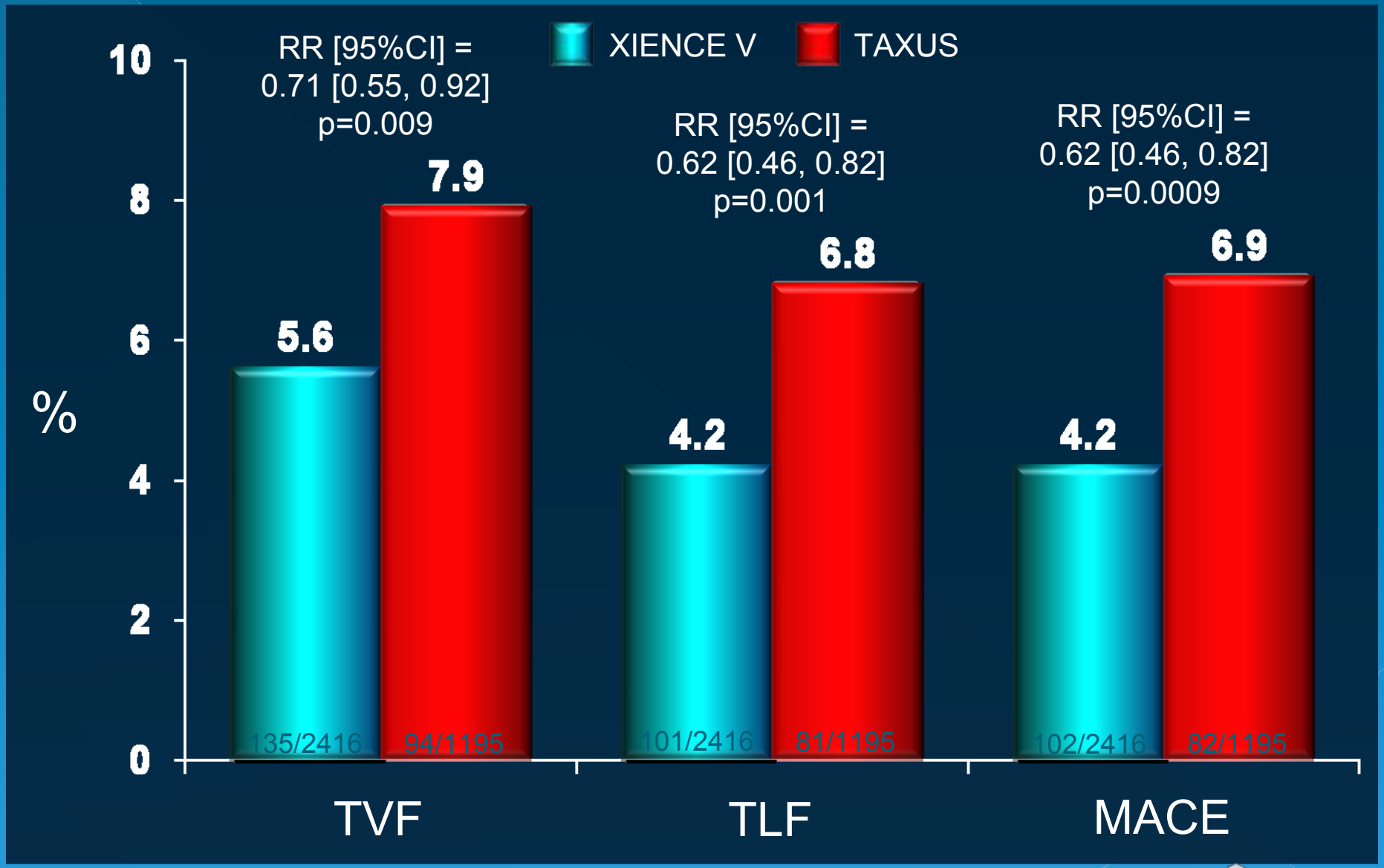


*F/U window: ± 28 days

TCT 2009

Spirit IV

TVF, TLF, and MACE Through 1 Year

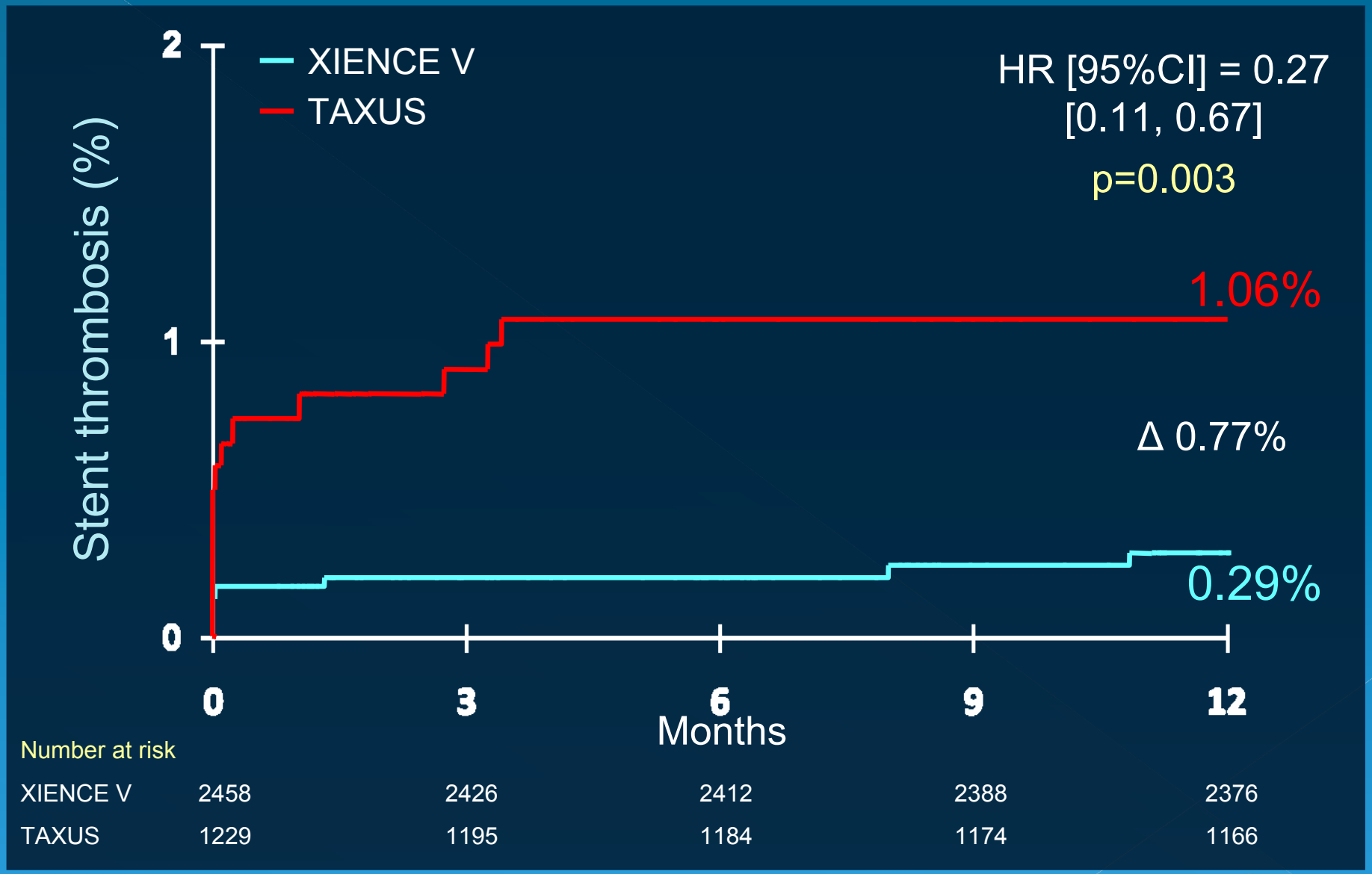


TLF = cardiac death, target vessel MI, or ID-TLR; MACE = cardiac death, all MI, or ID-TLR; TVF = cardiac death, all MI, or ID-TVR. 1 Year = 365 ± 28 days

TCT 2009

Spirit IV

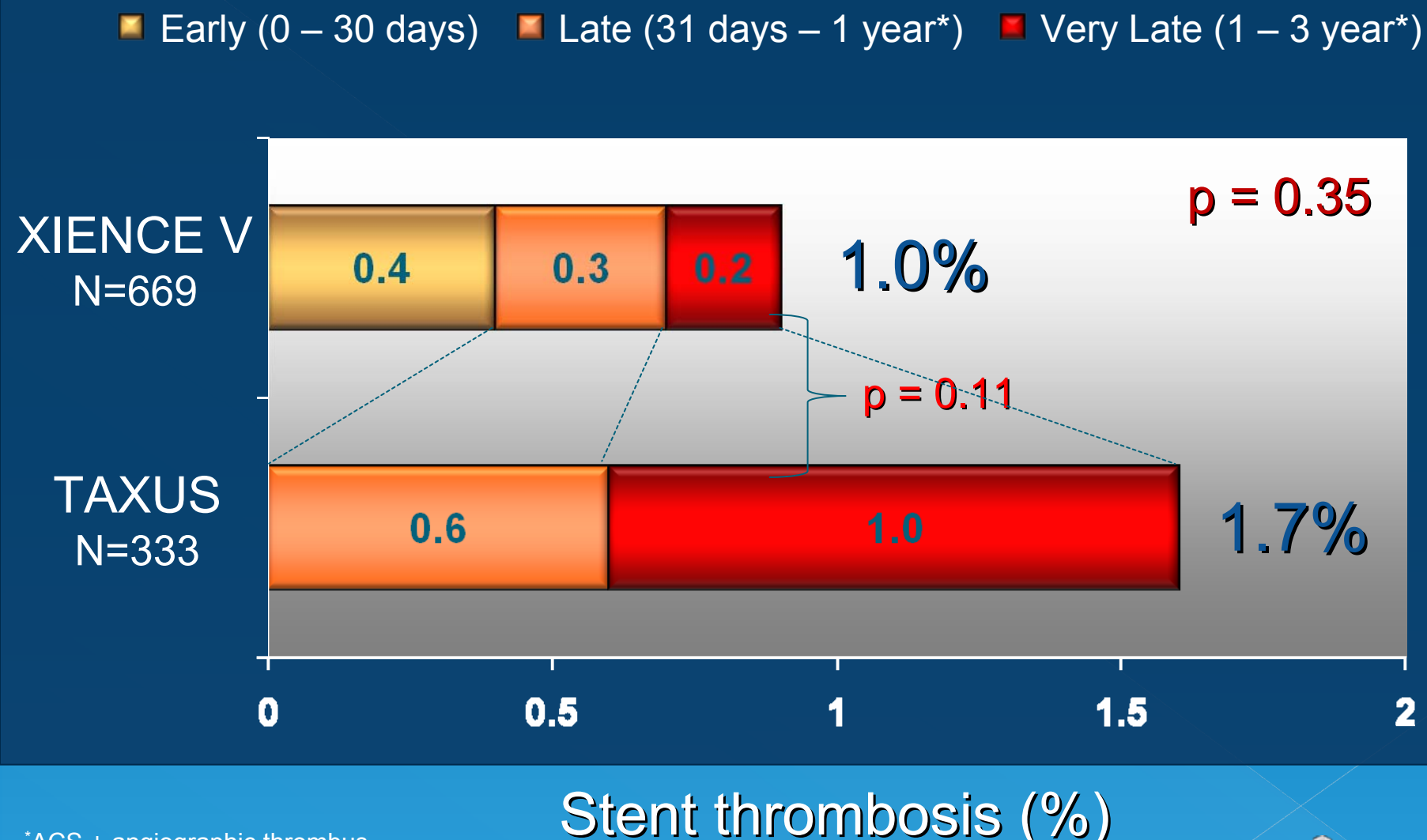
Stent Thrombosis (ARC Def or Prob)



TCT 2009

Spirit IV

Stent Thrombosis (Protocol Definition)*



*ACS + angiographic thrombus,
or unexplained death or STEMI/Q-wave MI
in target lesion distribution within 30 days
*Includes F/U window of ±28 days

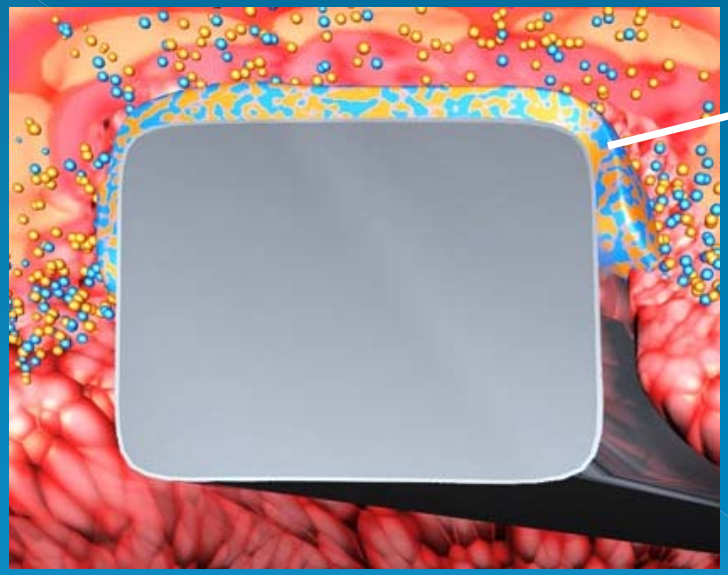
Spirit III

XIENCE PRIME : Next generation workhorse everolimus-eluting stent

OTHER DES PLATFORMS

- NOBORI BIOLIMUS
- BIOMATRIX BIOLIMUS

BioMatrix Biolimus-Eluting Stent

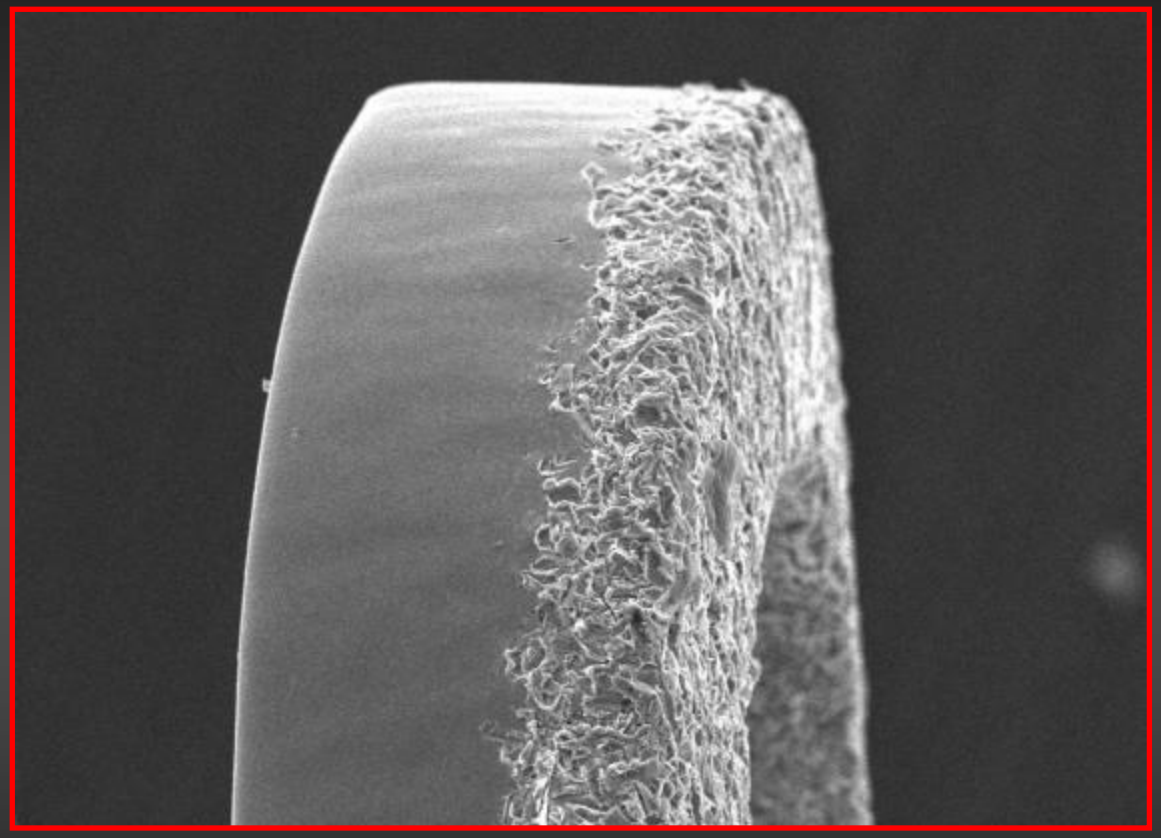


Biolimus (Sirolimus derivative) and PLA Biodegradable Polymer in Abluminal Stent Surface

Stainless steel stent platform has a strut thickness of 112 μm

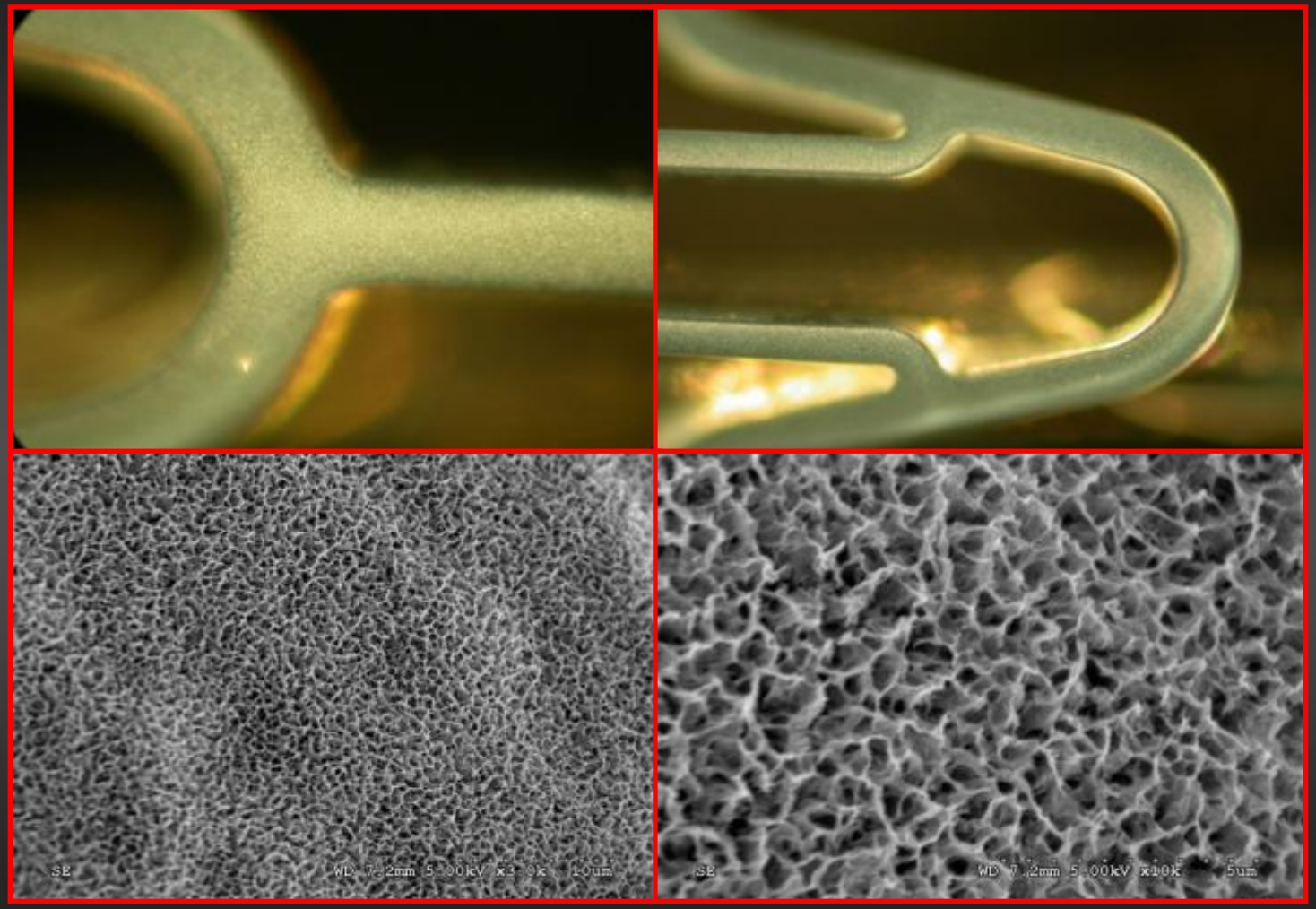
BioMatrix Freedom Stent

Micro-structured Surface



- Selectively micro-structured surface holds drug in abluminal surface structures

3D MicroPorous Nanofilm HAp



Dedicated Bifurcation Stents

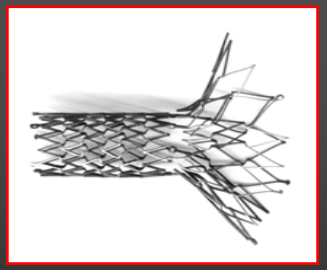
AST petal

Guidant frontier

Trireme

Devax (+ BA9)

“true” bifurcation designs

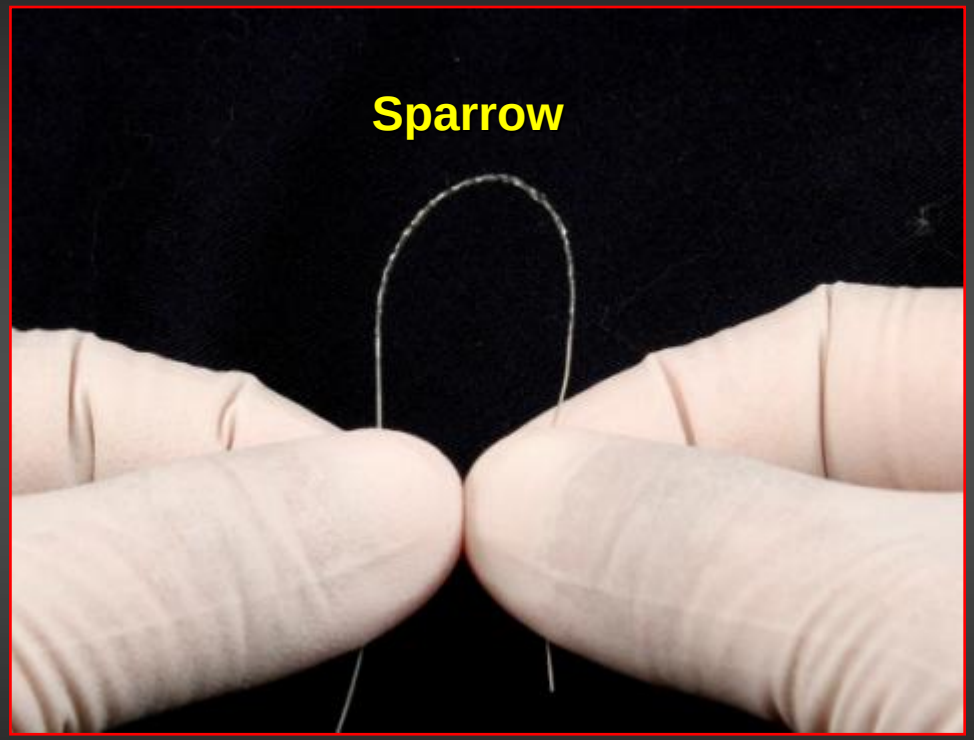


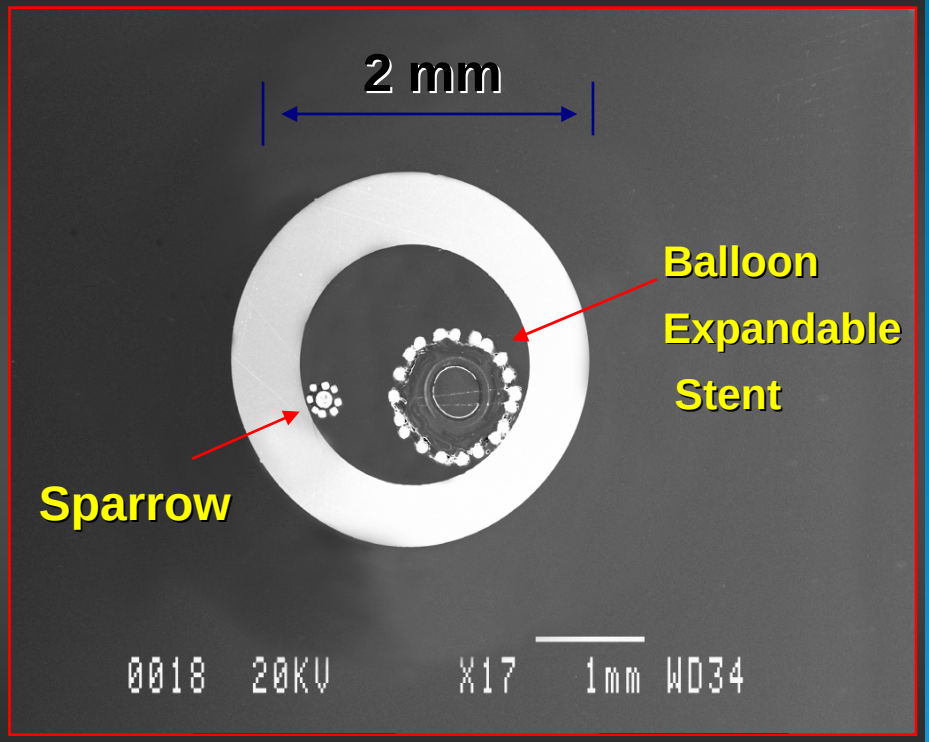
sidebranch designs

MGuard Stent

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

The CardioMind Sparrow™:
Stent on a .014” Guide Wire Platform

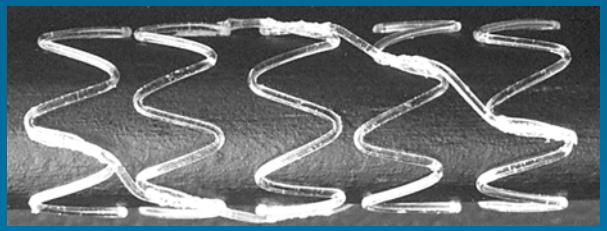




Bioabsorbable Stents

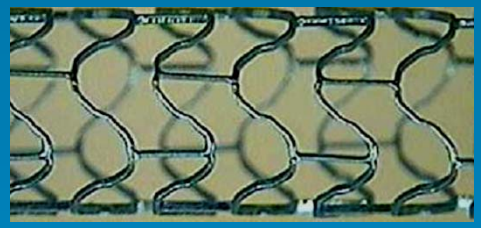
- Igaki-Tami (Igaki Medica Planning Co Ltd)
- Magnesium (Biotronik)
- REVA (REVA Medical)
- BTI (Bioabsorbable Therapeutics Inc)
- BVS (Abbott Vascular)

Igaki-Tamai stent

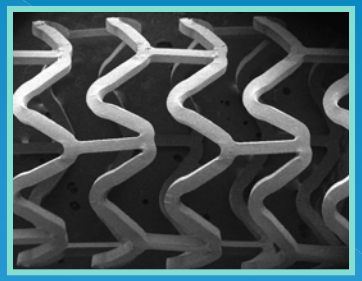


PLLA

Bioabsorbable Magnesium Stent



BVS (Abbott)



PLLA and
PDLLA
Everolimus

How about DRUG ELUTING BALLOONS (no stent or provisional stenting)?

Local Drug Delivery: Paccocath-DEB vs. DES

Drug-Eluting Balloon	Drug-Eluting Stent
Immediate release	Slow release
Short-lasting exposure	Persistent drug exposure
~ 300 - 600 µg dose	~ 100 - 200 µg dose
No polymers	Polymer
Wiped off the balloon surface	Diffusion from stent struts
Premounted stent optional	Stent mandatory

- Conventional angioplasty balloon catheters
- Coated with paclitaxel

  (+ contrast medium as matrix builder and release supporting additive)
- Controlled dose, homogeneity of coating, non-toxic excipients

Scheller et al., Circulation 2004;110:810. Speck et al., Radiology 2006;240:411. unpublished data

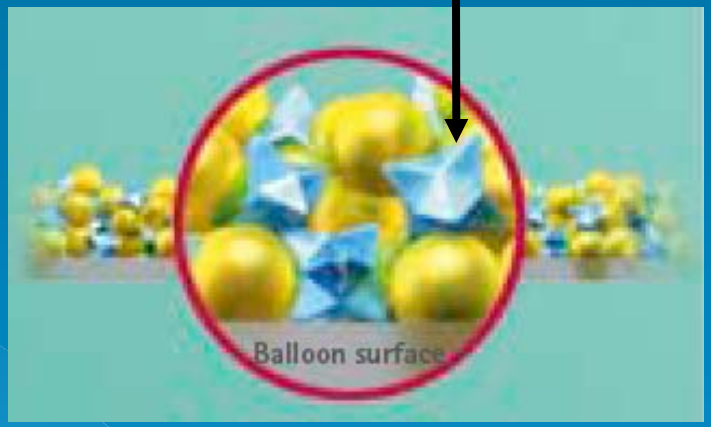
PACCOCATH®-Technology:
The Matrix Coating of SeQuent® Please

Pure paclitaxel

matrix coating:

paclitaxel + hydrophilic spacer

(iopromide = Ultravist®)



The hydrophilic spacer leads to:

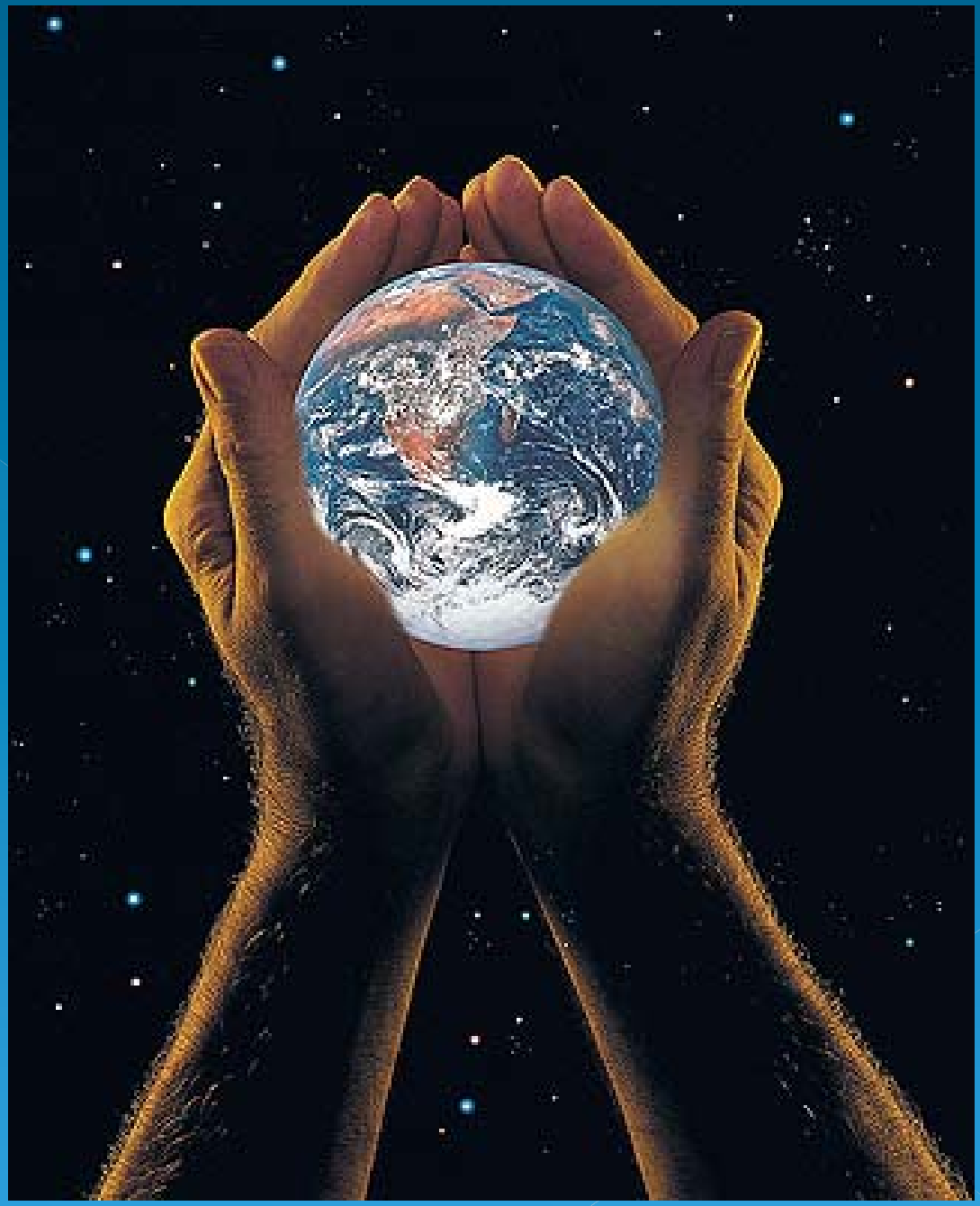
- Porous coating with a high contact surface between the lipophilic drug molecules and the vessel wall
- Uniform and complete release of the target drug dose after first balloon expansion that guarantees:
- A high bioavailability of paclitaxel on the target side for rapid drug absorption by the vessel wall

PEPCAD II ISR - Outcome, 6 months FU

n=126

	SeQuent Please	Taxus	p
n	66	60	
Follow-up	6.2 ± 0.8	6.2 ± 0.8	0.7
Control angiography	58 (87.9 %)	54 (90.0 %)	0.8
Late lumen loss	0.19 ± 0.38	0.47 ± 0.71	0.03
Binary restenosis in segment	**2 / 58 (3.4 %)**	**11 / 54 (20.4 %)**	0.007
TLR	2 / 64 (3.1 %)	10 / 60 (16.7 %)	0.02
Myocardial infarction	0 / 64 (0.0 %)	1 / 60 (1.7 %) NSTEMI due to side branch occlusion	1
Death	2 / 64 (3.1 %) 1 non-cardiac, 1 cardiac but not lesion related	1 / 60 (1.7 %) non-cardiac death	1
MACE (w / o noncardiac death)	3 / 64 (4.7 %)	11 / 60 (18.3 %)	0.02

Much more to come…



Thanks