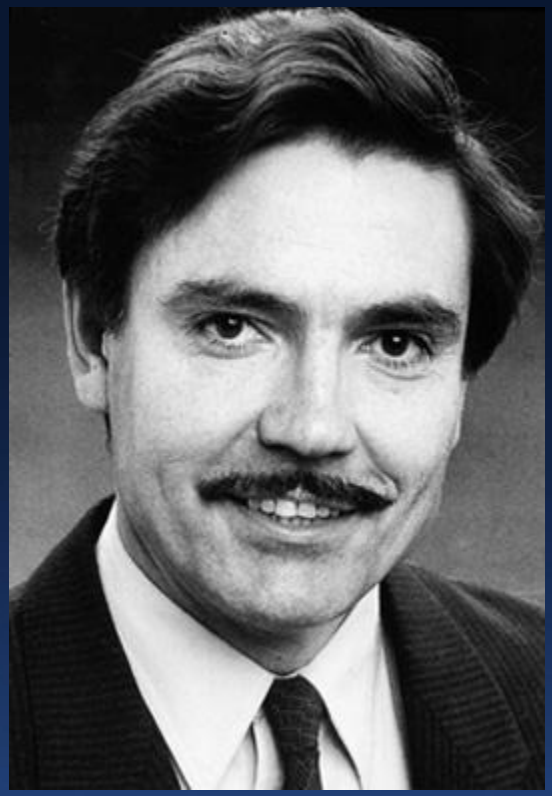
CVI SYMPOSIUM 2012

Old and New STENT Technology for CAD

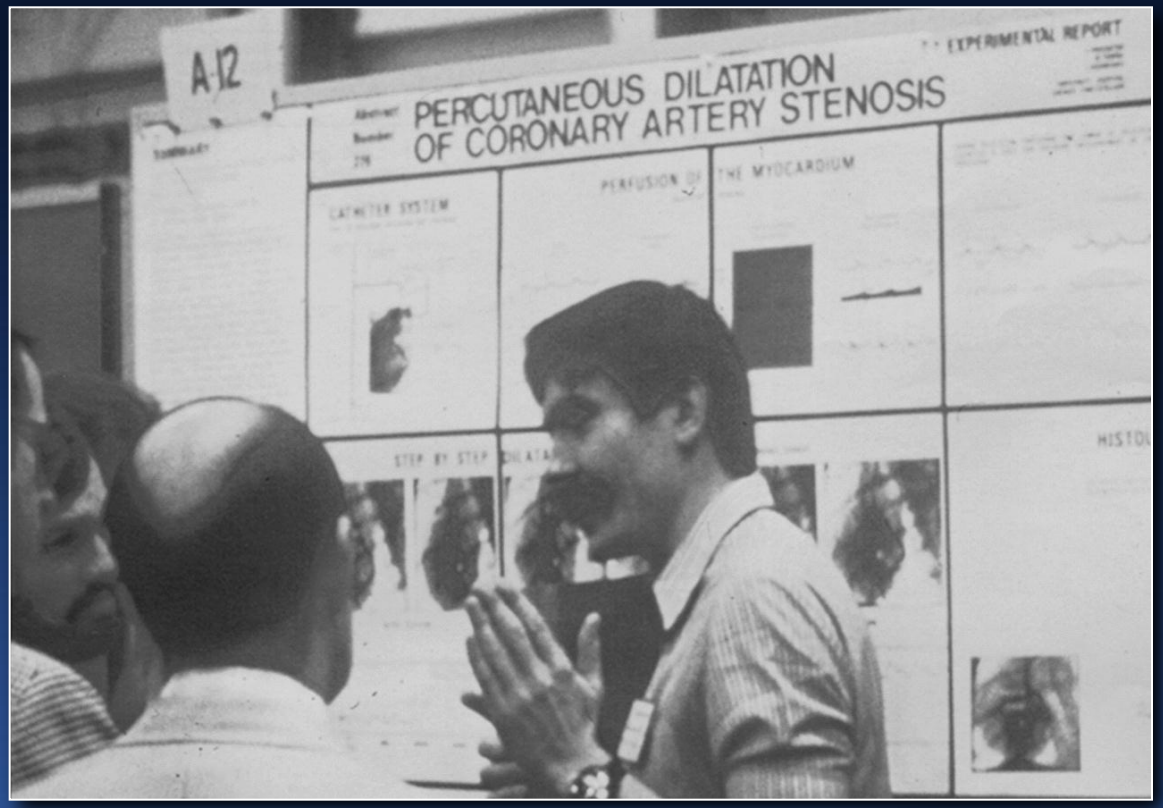
Luis F. Tami, MD

Cardiac Cath Lab Director
Memorial Regional Hospital

We began about 35 Years ago!



Andreas Gruentzig
1939 - 1985



AHA Meeting, Nov 1976, Miami, Florida

About Andreas Gruntzig's presentation at the AHA 1977

"……it was standing room only and after the presentation, the audience stood and applauded, almost unheard of at a scientific meeting."

First live demonstration in Zurich in 1978

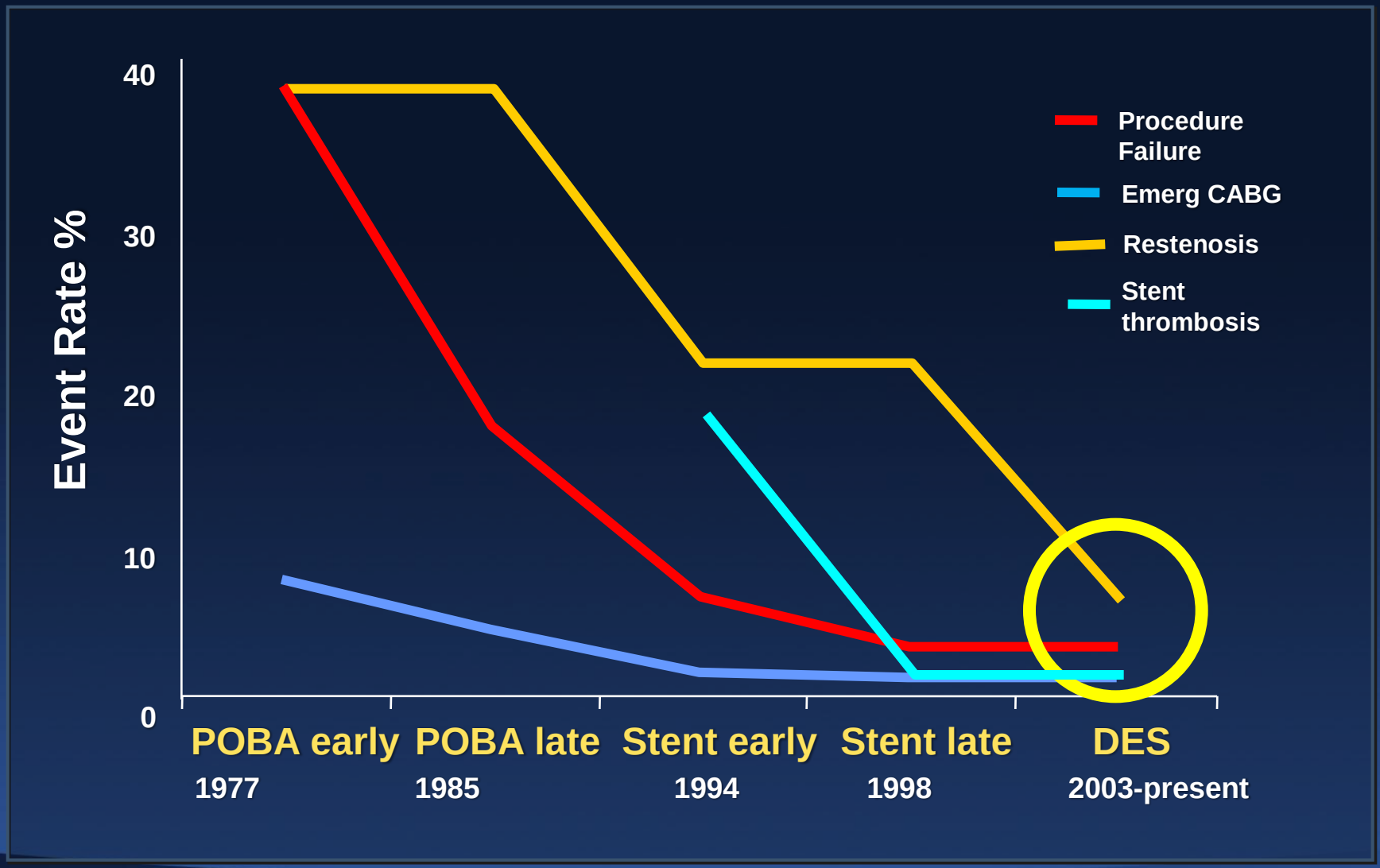
Gruntzig pioneered live demonstrations as a way to learn and master procedures.

..... And even today

Live Demonstration, Miami, Oct 2012

11,800 attendees from 52 countries. 46.5 hrs of life cases

PCI: Incremental Improvements



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.

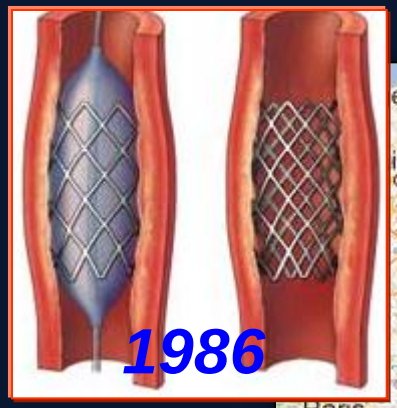
N Engl J Med 1987; 316:701-6

Ulrich Sigwarth (Lausanne, Switzerland 1986)

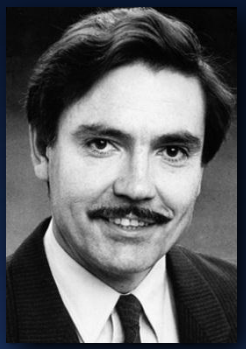
First human coronary implantation

Stents initially rejected due to stent thrombosis and bleeding due to anticoagulation

Coronary stents — implantation of foreign bodies into stenotic human coronary arteries: dream or nightmare?



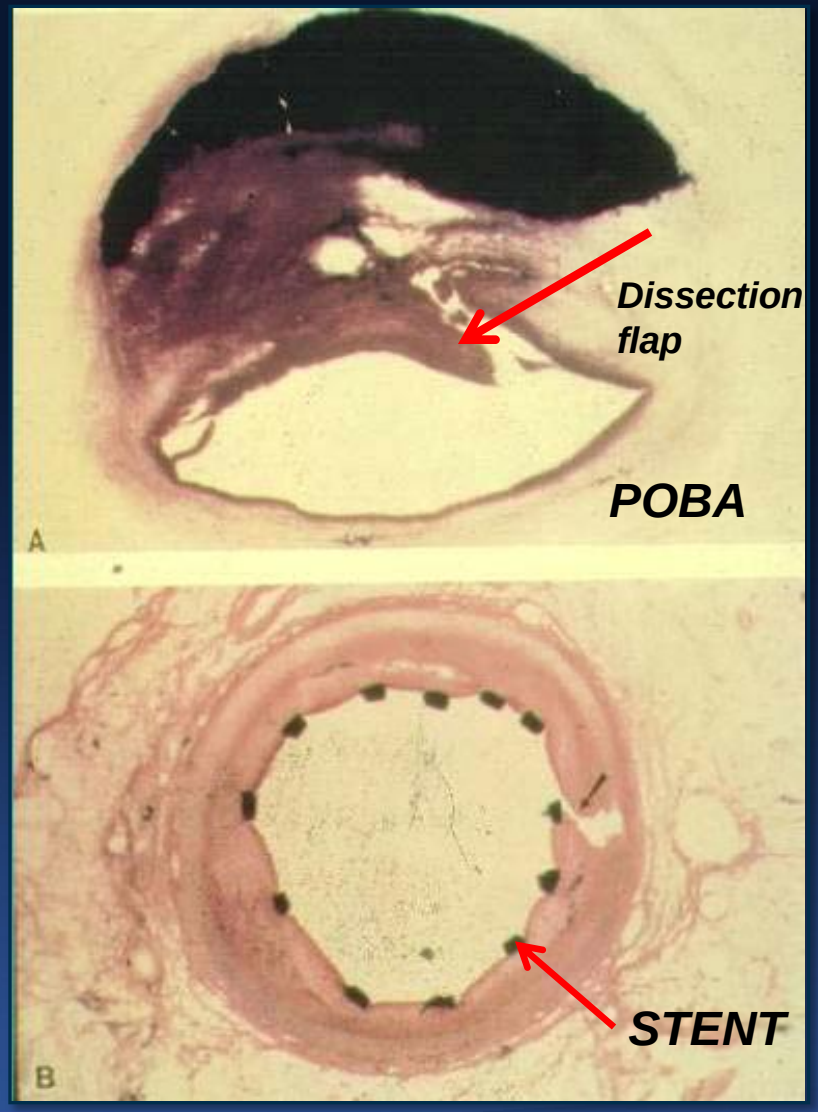
Ulrich Sigwart



Andreas Gruntzig

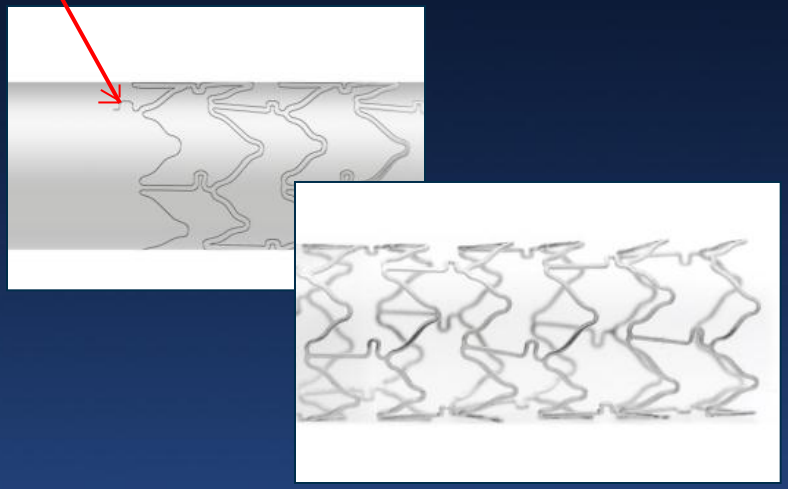
Why to Stent?

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

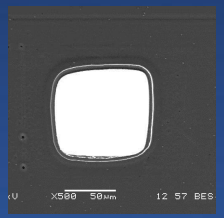


Basic strut types / Construction

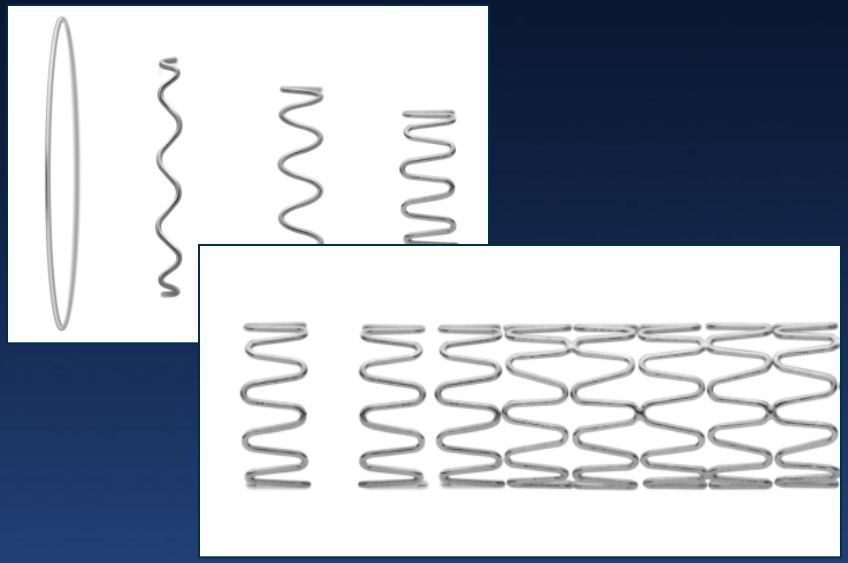
***1. Laser-cut stents** start as a tube, a laser removes material and a stent remains. Laser-cut stent production leaves square (blunt) edges.*



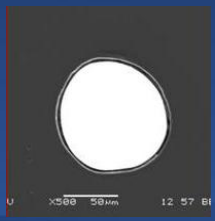
Squared edges



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



Ultrathin, smooth, rounded struts

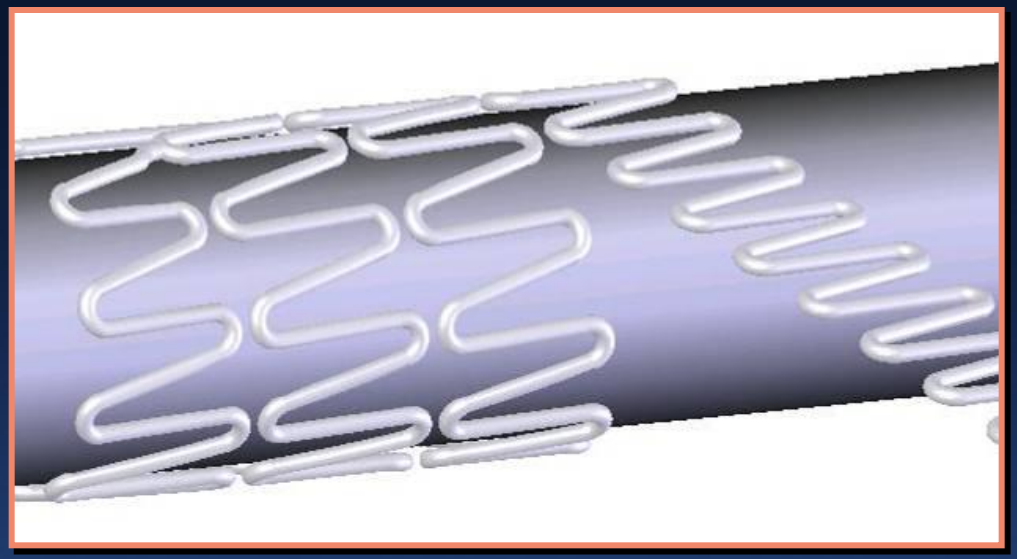


ALL OTHER STENTS

Driver, Endeavor

Continuous Helical Technology for stent strut construction

Continuous Helical Technology



0.0038"
↓
0.0034"
↓
0.0030"
↓
0.0025"
↓
0.0020"

- Enhance deliverability and conformability without compromising strength & opacity

→ Integrity, Resolute

AS A RESULTS OF STENTS…

Interventional Cardiologist sleep better at night

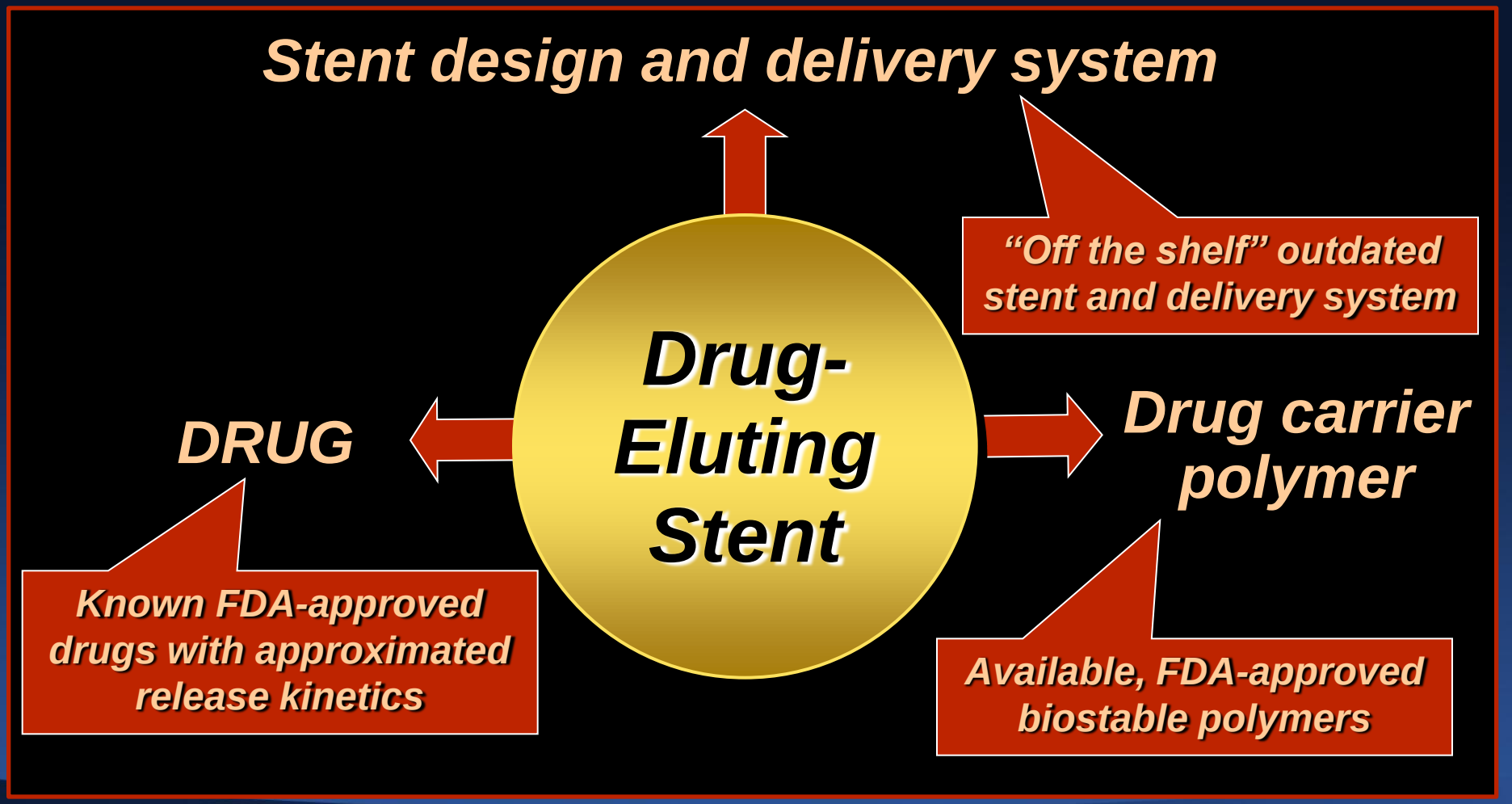
BUT ……..

The Limitation of Bare Metal Stents: RESTENOSIS

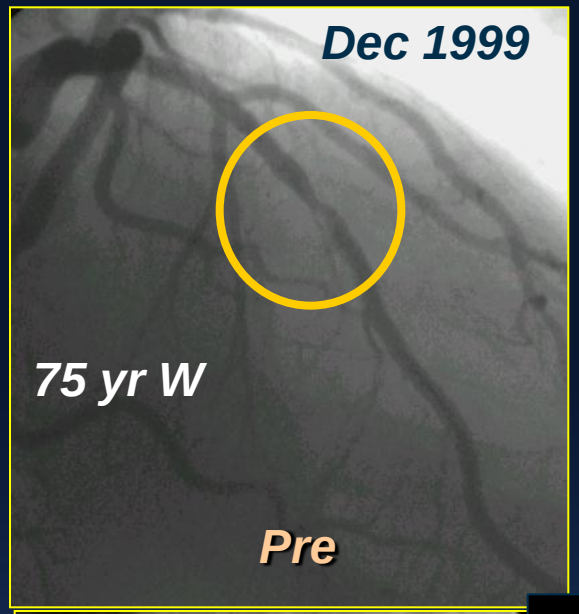
LATE LOSS = Intimal Hyperplasia

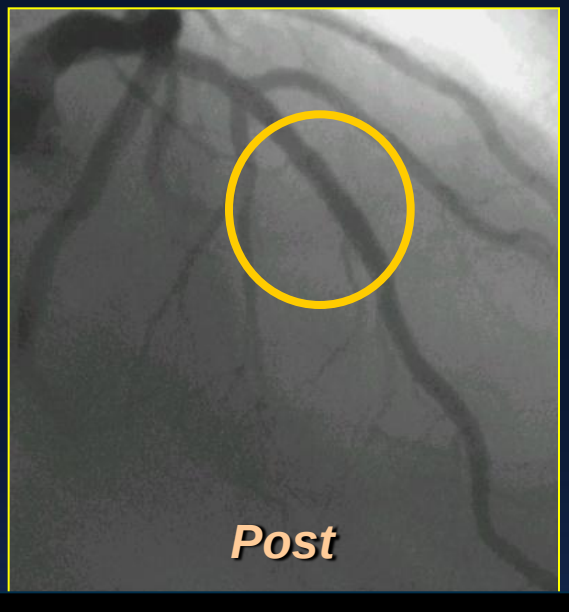
SOLUTION: Drug-Eluting Stents

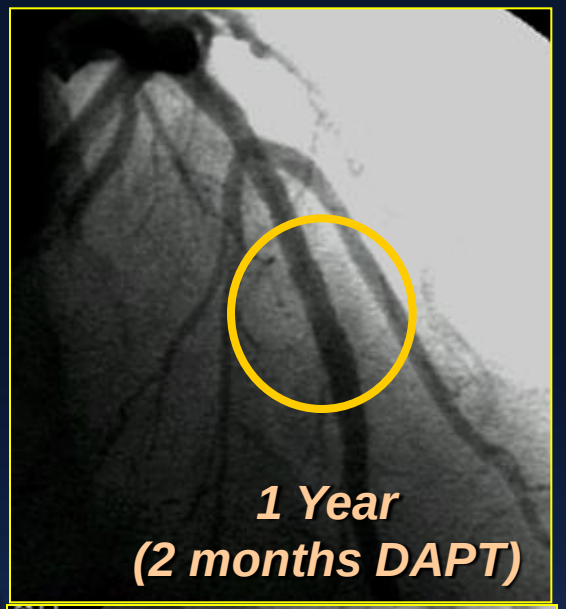
First Generation

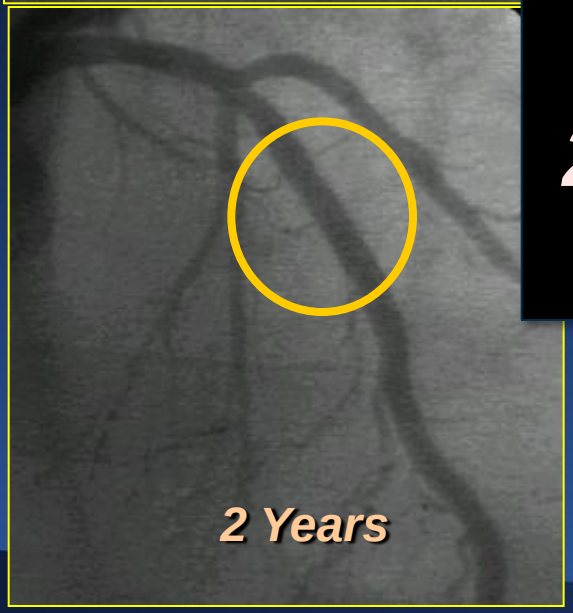


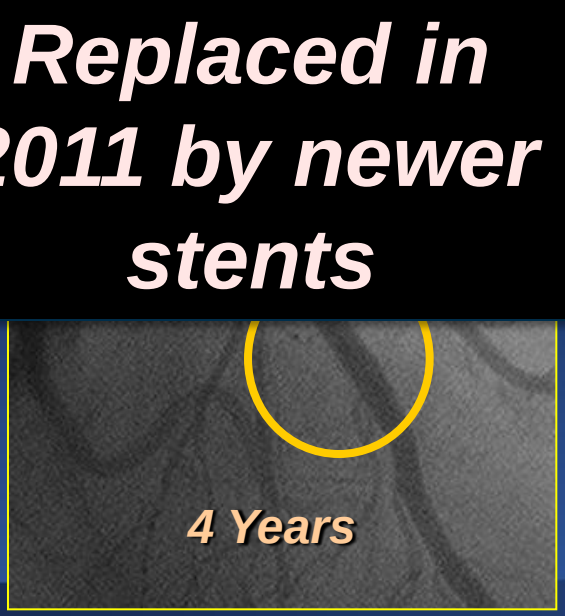
CYPHER Stent: First patient 10 Years



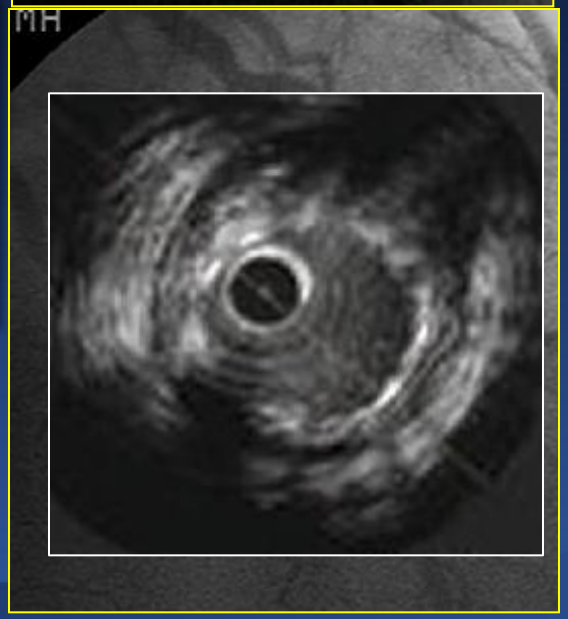






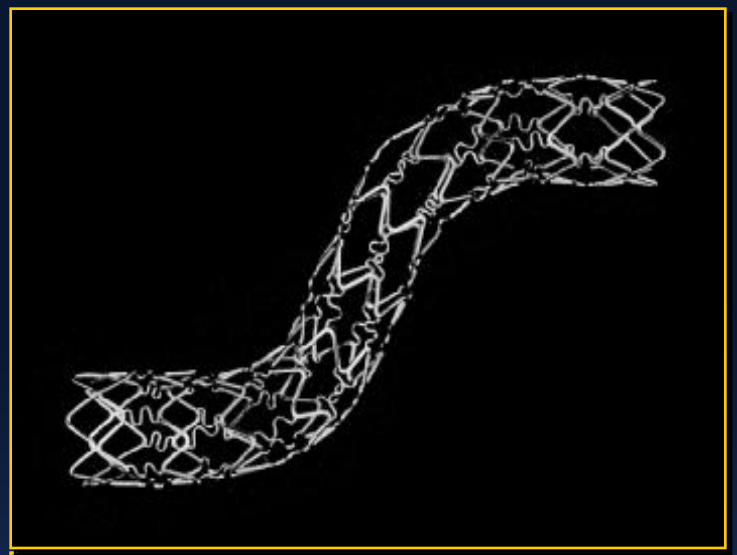


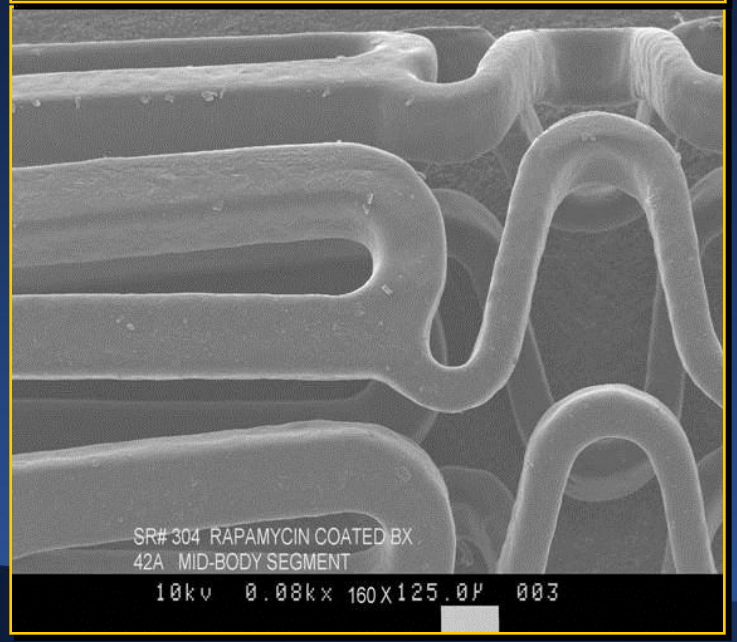
Replaced in 2011 by newer stents




Success over
In-Stent
Restenosis!!

The Sirolimus-Eluting Stent (Cypher)





FDA Approval in US: APRIL 2003

Bx VELOCITY™ Stent

- Stainless steel stent

Drug carrier:

- Blend of 2 polymers (PEVA + PBMA)

Sirolimus (~ 10um thick)

Cordis
a Johnson & Johnson company

One Year later: TAXUS Stent

Drug

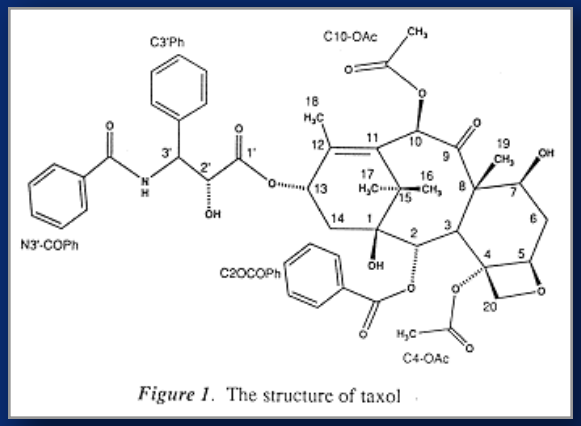
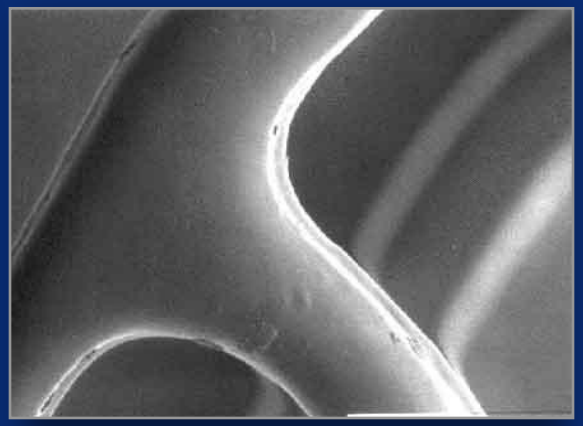
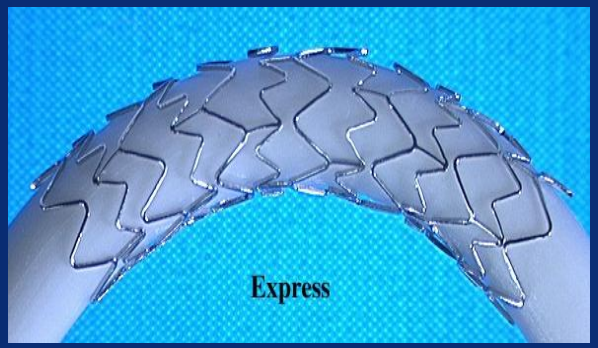


Figure 1. The structure of taxol

Polymer



Stent



Paclitaxel

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

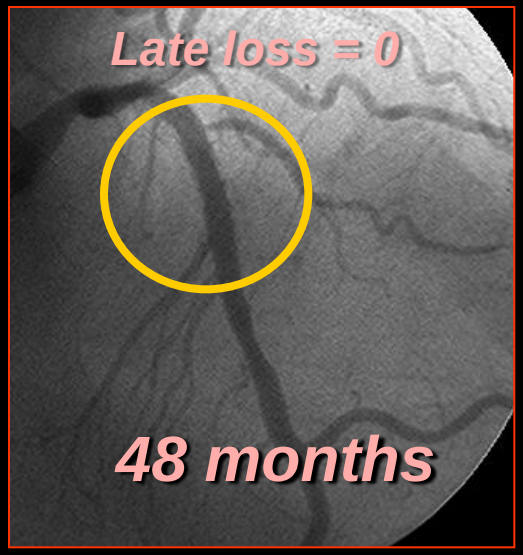
Translute™

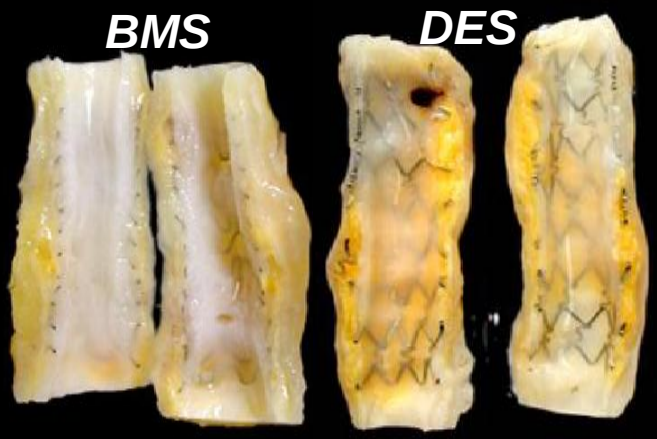
- *Polyolefin derivative*
- *Uniform*
- *Biocompatible*
- *Elastomeric*
- *Provides controlled release*

Express²

- *Stainless Steel*
- *Maverick balloon system*
- *Flexible*
- *Deliverable*

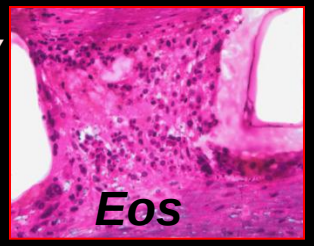
1st Generation DES….
the good, the bad, and the ugly!



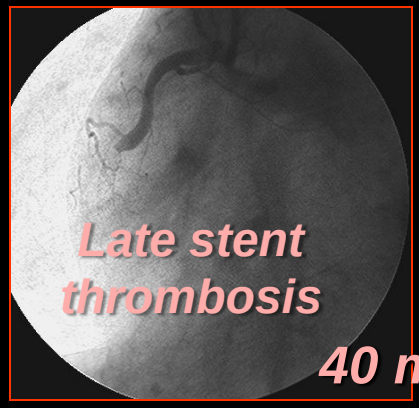


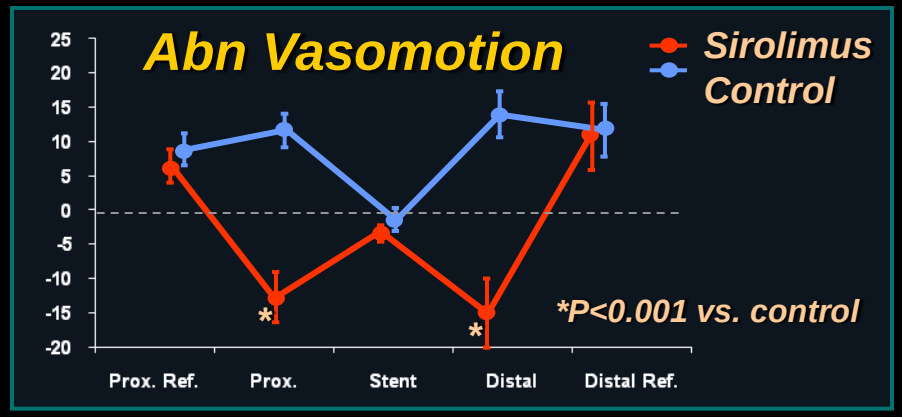
Delayed Healing!

Angioscopy

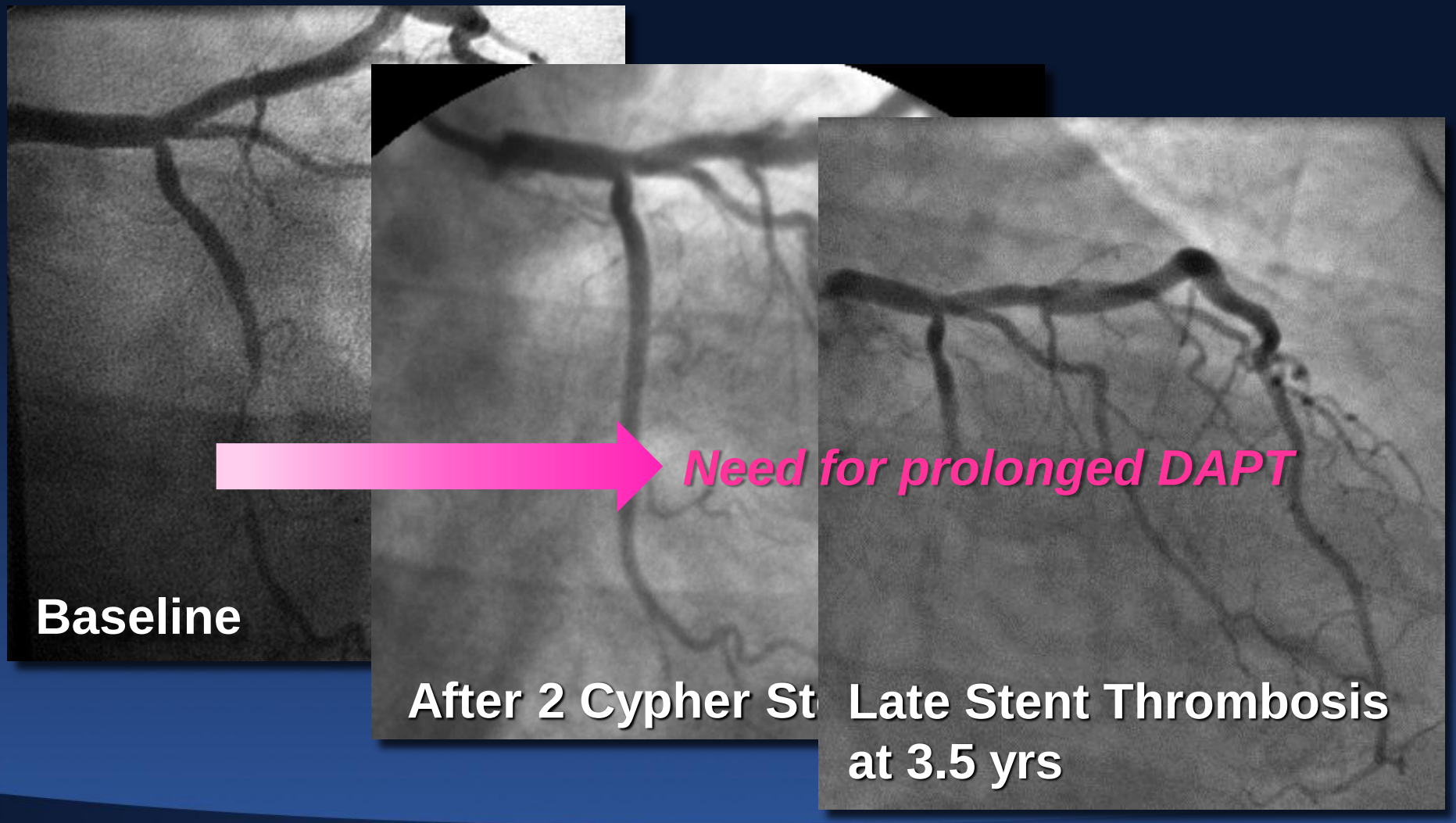


Inflammation





Late SES Stent Thrombosis

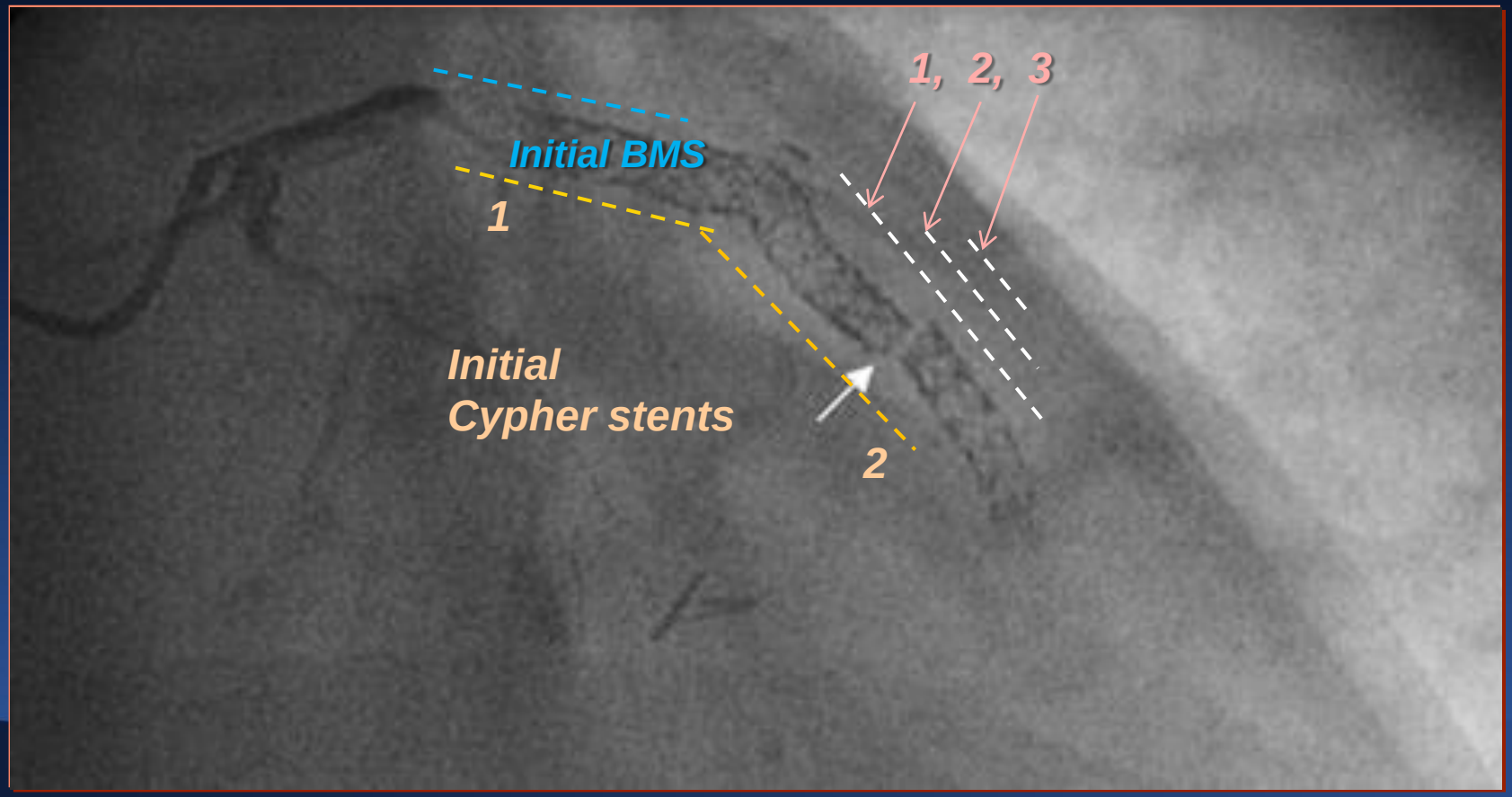


STENT FRACTURE

59 yr old LIMA to LAD. Graft failed and native LAD stent done in 1997 (initial) Native LAD stented with 2 Cyphers (1,2)

Subsequent restenosis

1. *Cypher 3.5 x 33*
2. *Cypher 3.5 x 13*
3. *Cypher 3.5 x 8*



ABNORMAL VASOMOTION DUE TO ENDOTHELIAL DYSFUNCTION

American Medical Journal 3 (2): 75-81, 2012
ISSN 1949-0070

Coronary Endothelial Dysfunction after Drug-Eluting Stent Implantation

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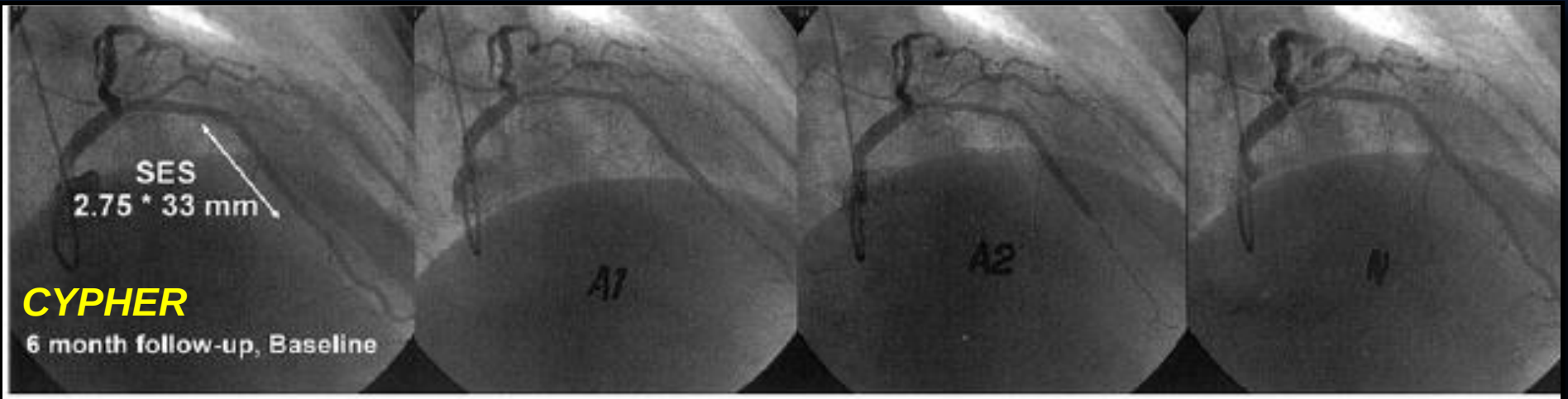
Nagoya City East Medical Center 1-2-23 Wakamizu,
Chikusa-Ku, Nagoya-Shi, Aichi-Ken, 464-857, Japan

STATE-OF-THE-ART PAPER

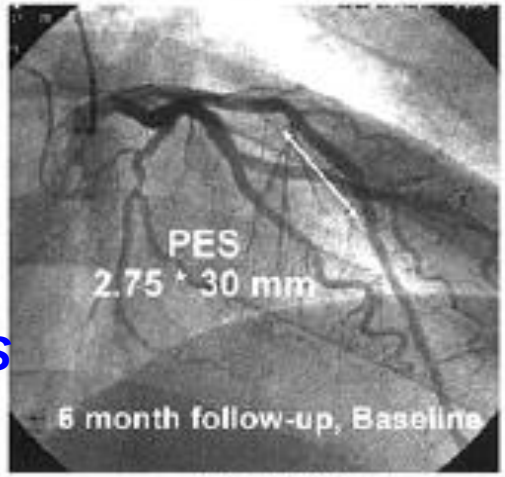
The First-Generation Drug-Eluting Stents and Coronary Endothelial Dysfunction

Lakshmana K. Pendyala, MD,* Xinhua Yin, MD, PHD,† Jinsheng Li, MD, PHD,†
Jack P. Chen, MD,† Nicolas Chronos, MD,† Dongming Hou, MD, PHD†
Louisville, Kentucky; and Atlanta, Georgia

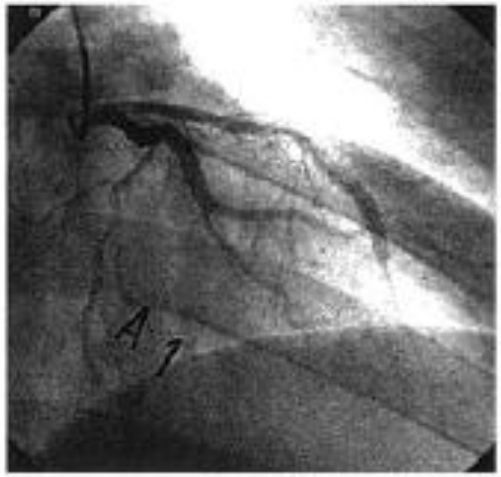


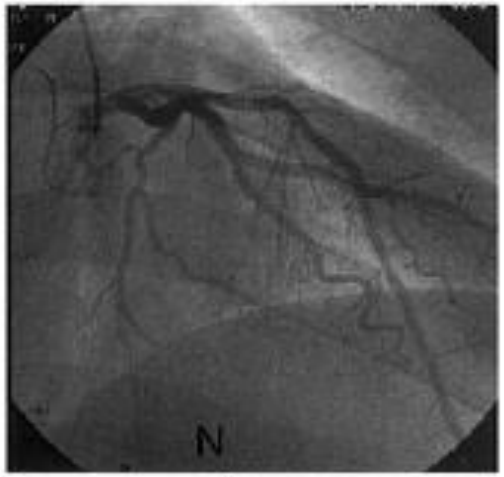
CYPHER

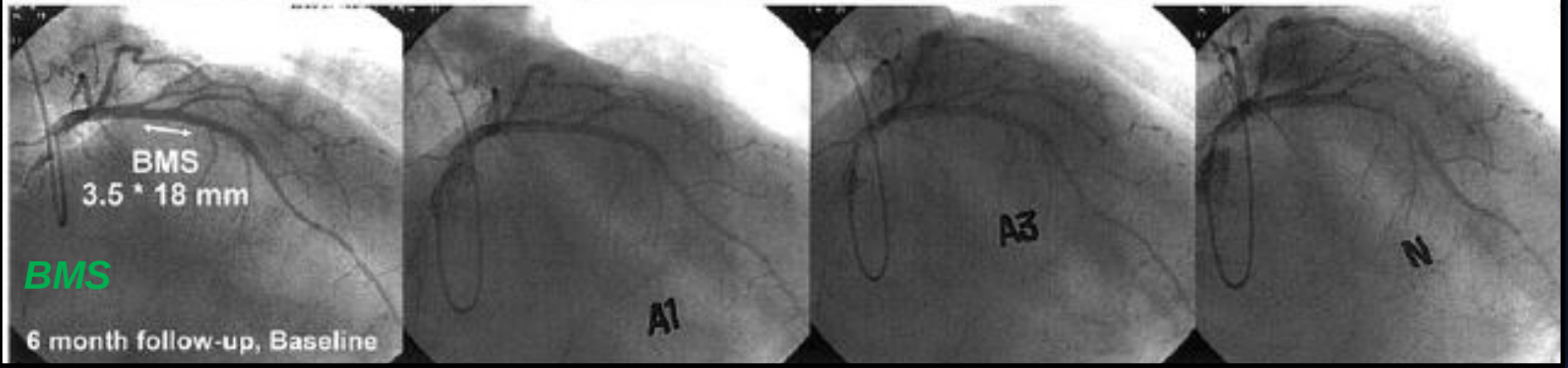
6 month follow-up, Baseline



TAXUS



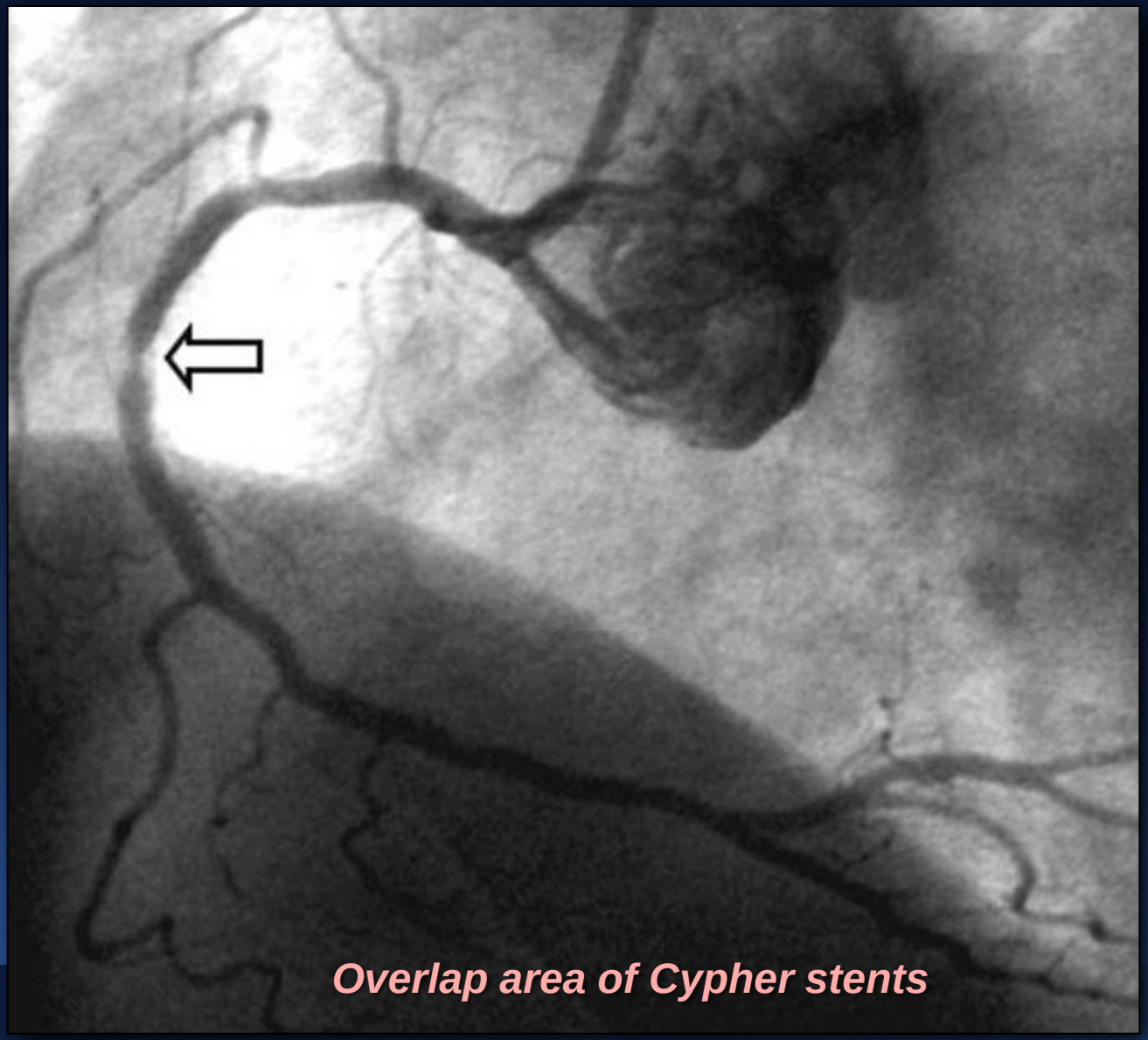


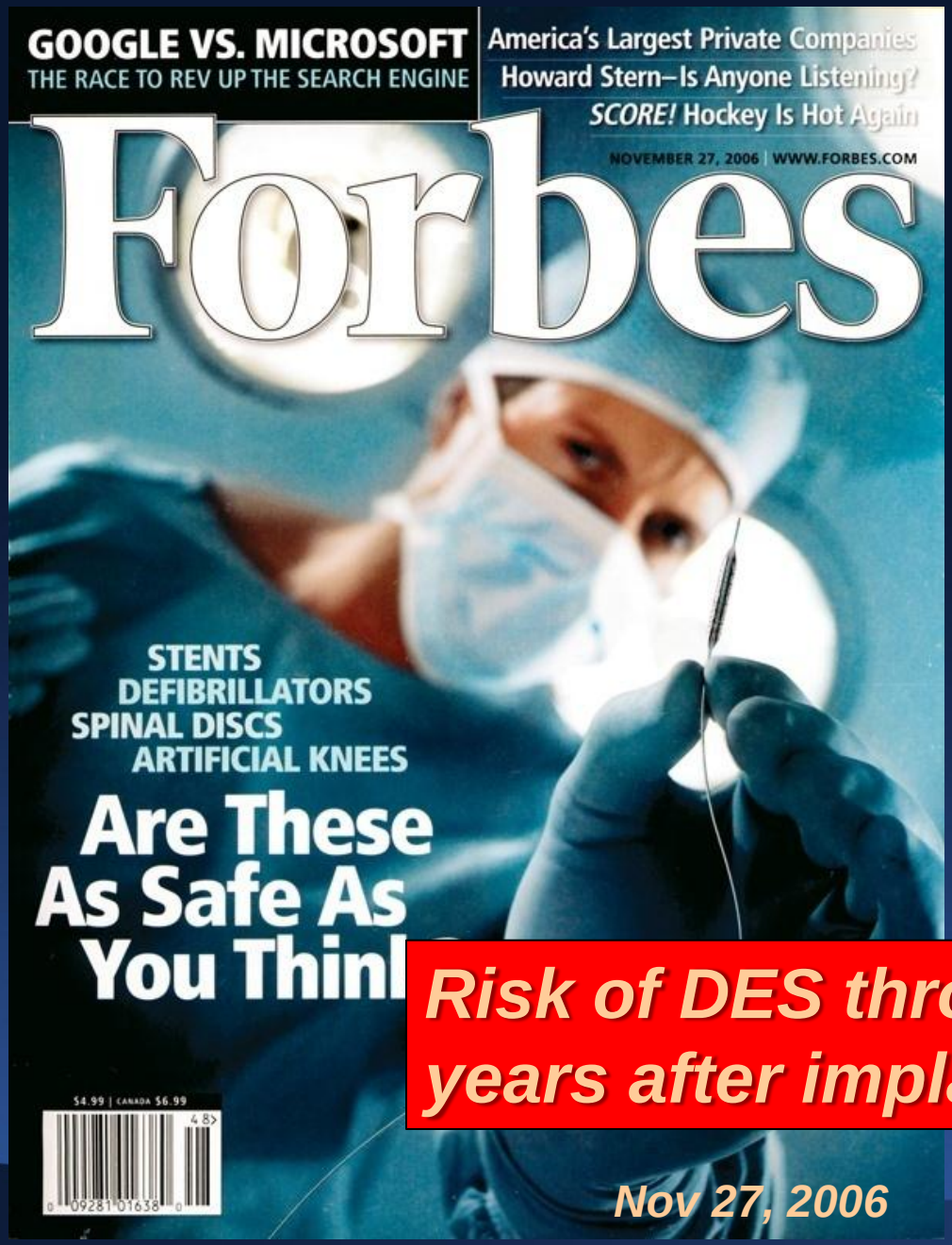


BMS

6 month follow-up, Baseline

DES RESTENOSIS



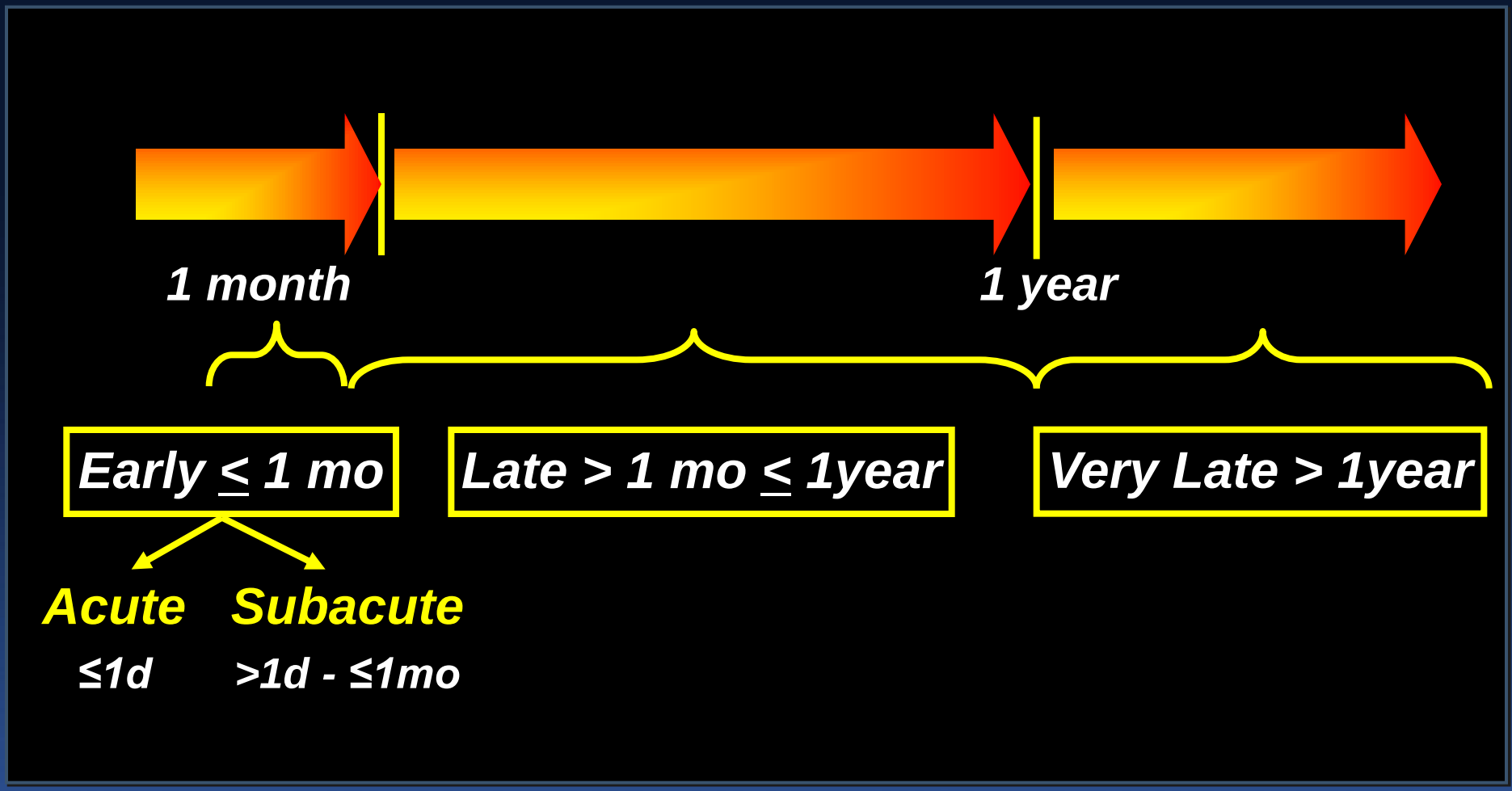


DES = "a million ticking time bombs"

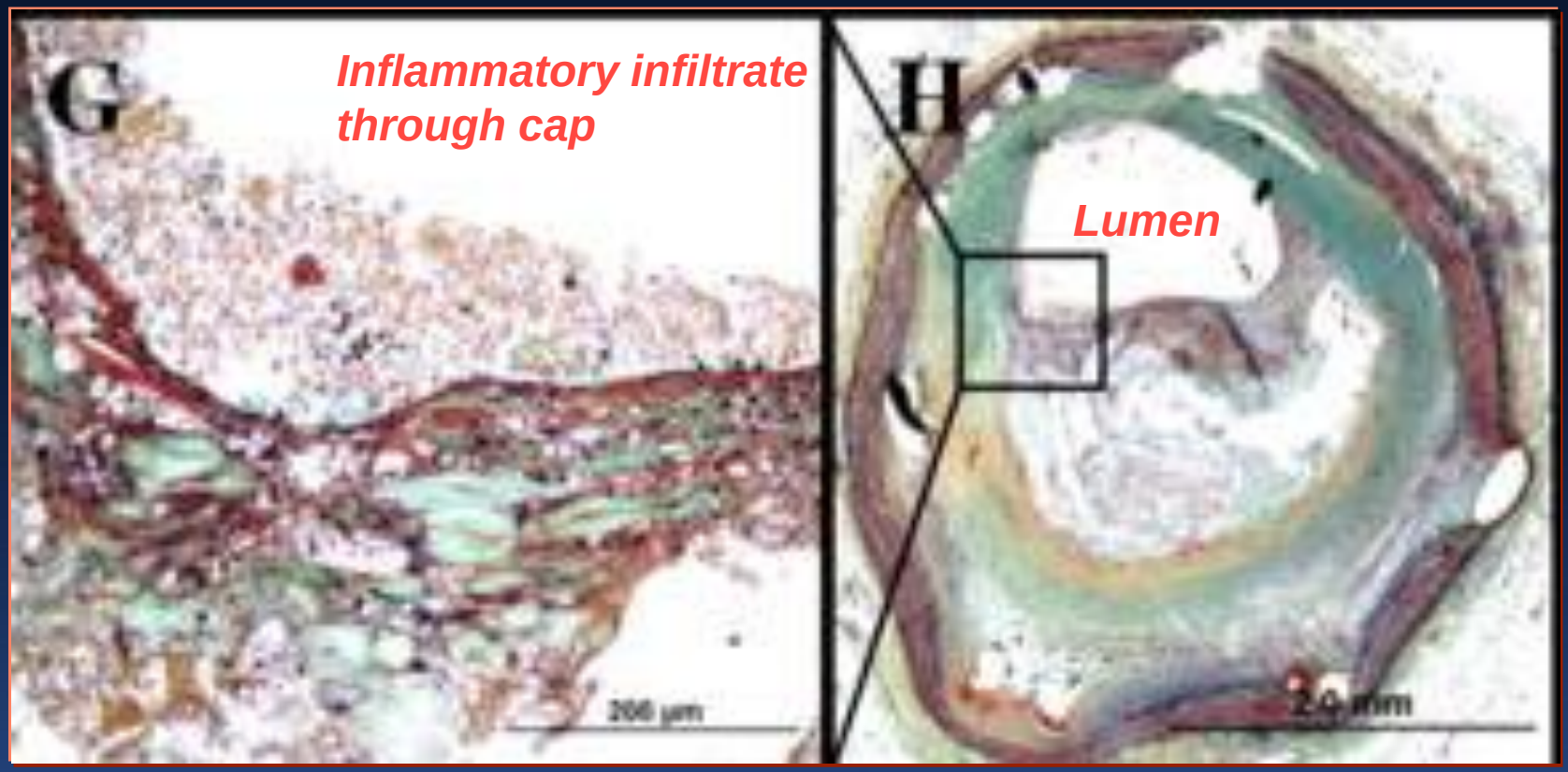
Risk of DES thrombosis even years after implantation

Nov 27, 2006

Stent Thrombosis



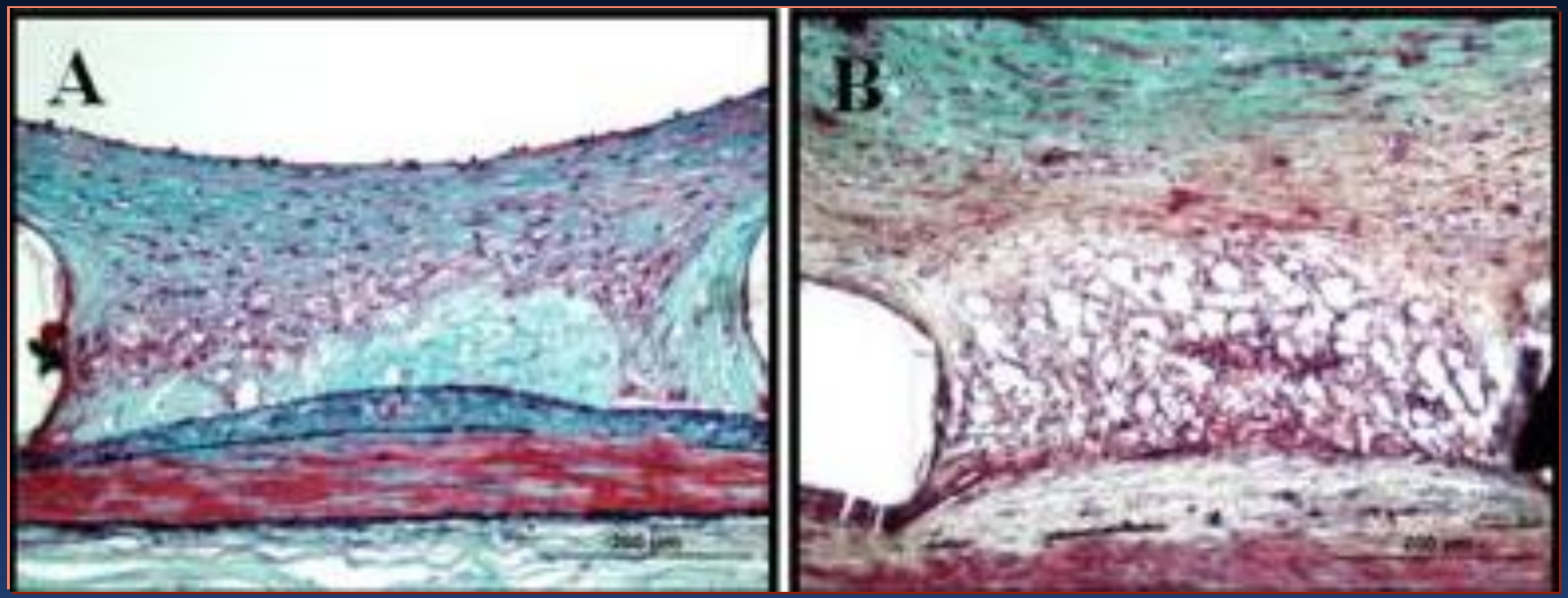
In-stent Neoatherosclerosis



Thin Cap Fibroatheroma 5 yrs after a BMS

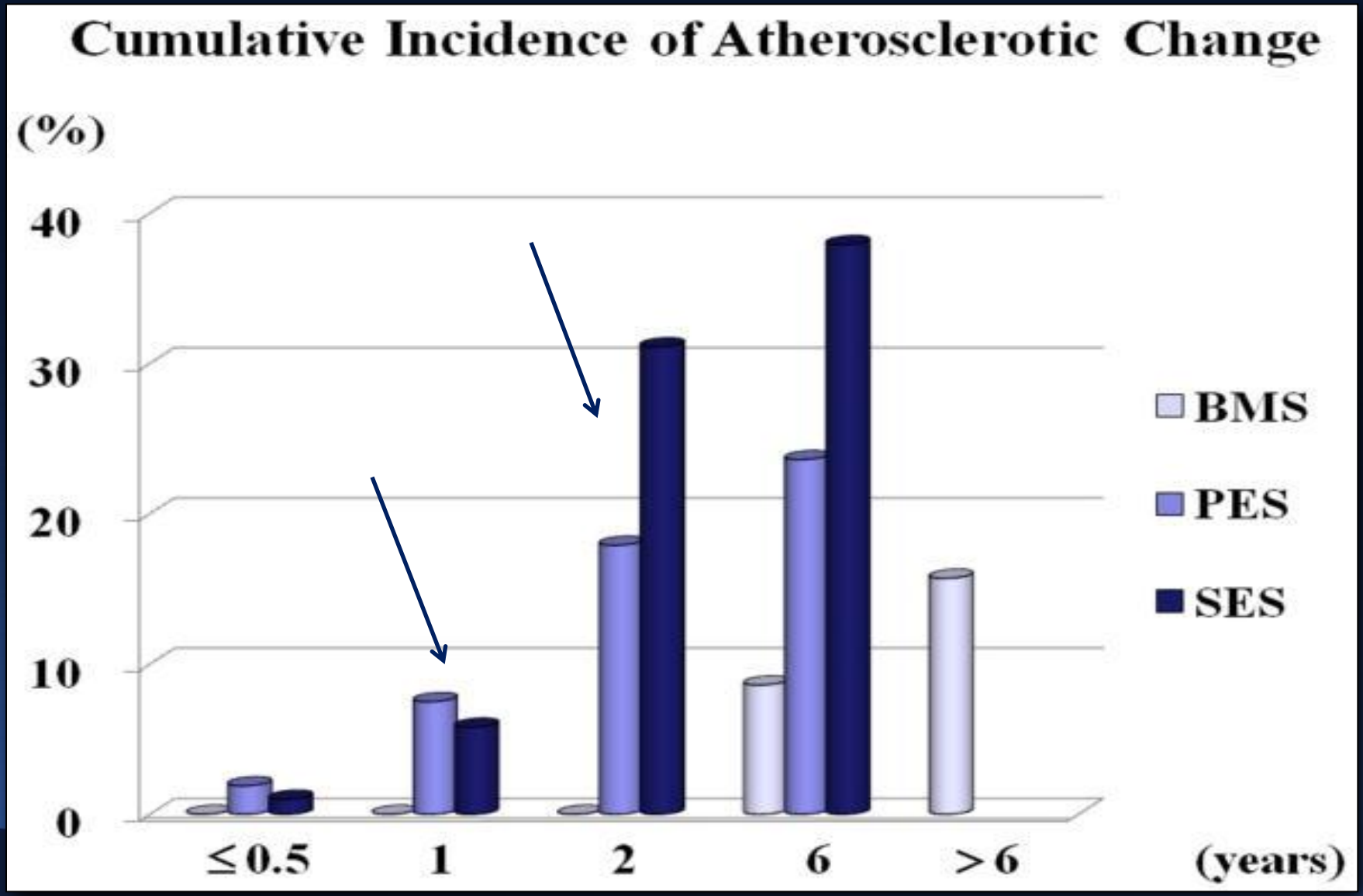
Left (Magnified view): Macrophages infiltrating thin fibrous cap

In-stent Neoatherosclerosis



Foamy Macrophages with early necrotic core in a Cypher stent after 13 months

Neoatherosclerosis: Earlier in DES

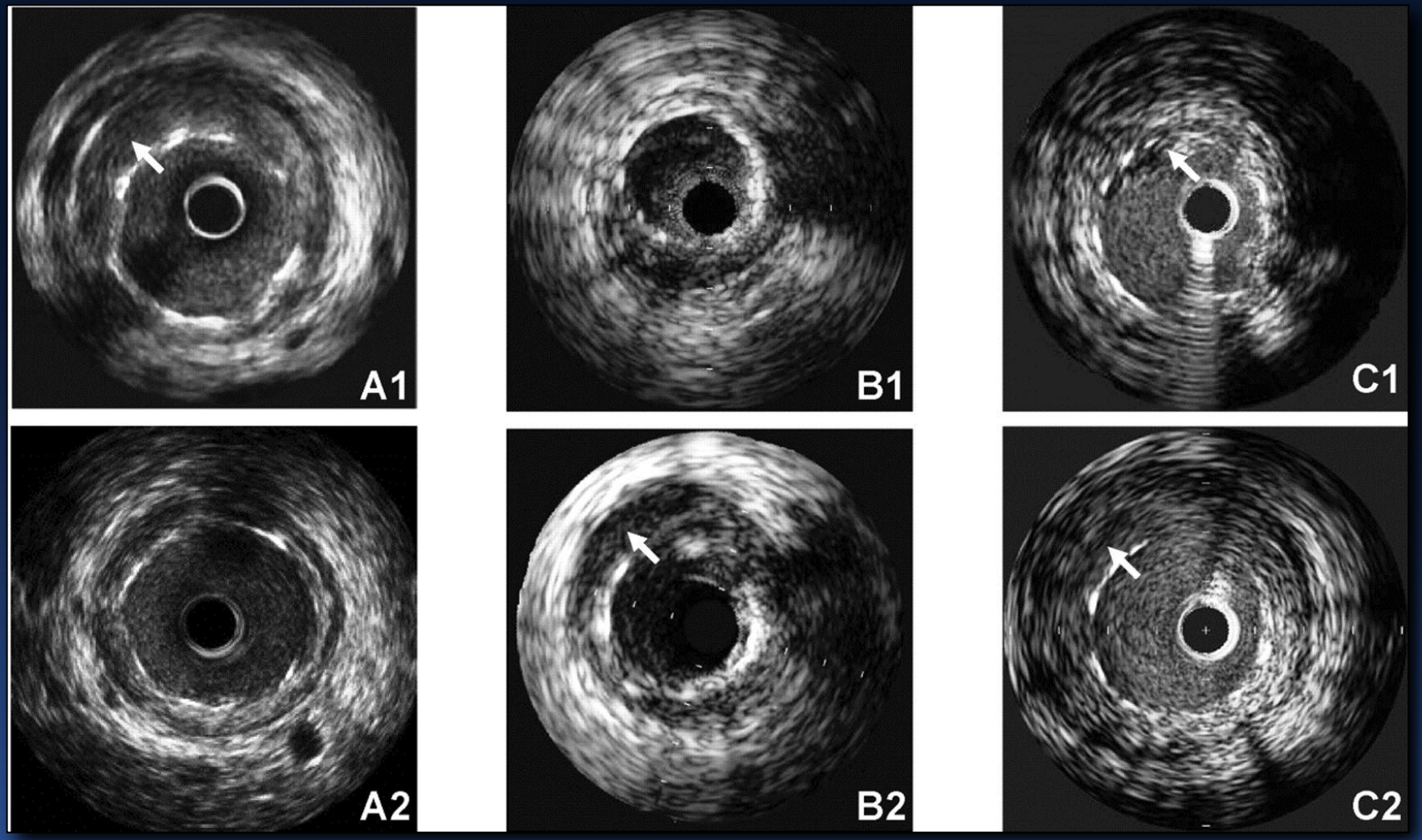


Blood Vessels change overtime:

IVUS images of stent malapposition

POST STENTING

FOLLOW UP



IVUS SUBSTUDY OF HORIZONS. Guo N et al. Circulation 2010;122:1077-1084

Current DES in the U.S.

Second Generation stents

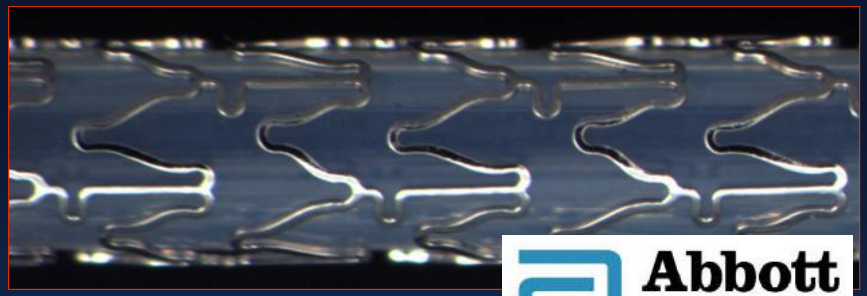
- **Promus** (Bsc) **/ Xience** (Abbott): **2008**
- **Promus Element** (Bsc): **2011**
- **Ion (Taxus with a new stent platform)**
- **Endeavor** ***(2008)*** **/ Resolute** ***(2012)*** (Medtronic)

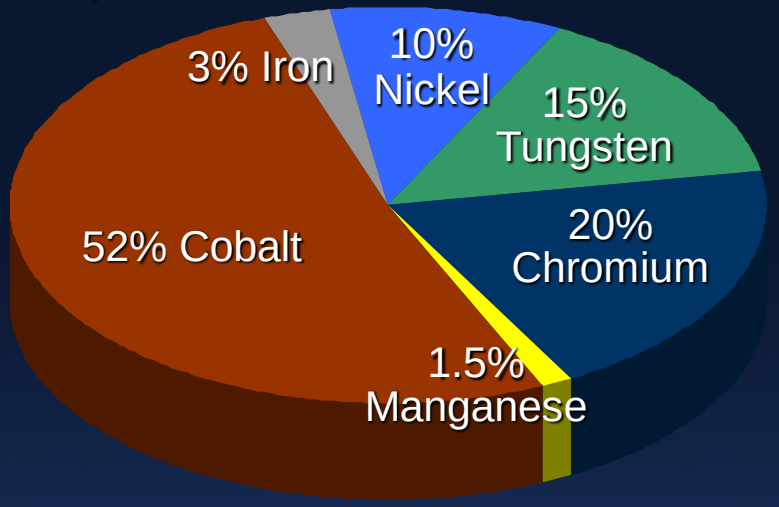
About 30 DES approved in Europe. About 80% DES used are the above listed. About 20% of market share are "other stents".

Everolimus-Eluting Stents: New standard

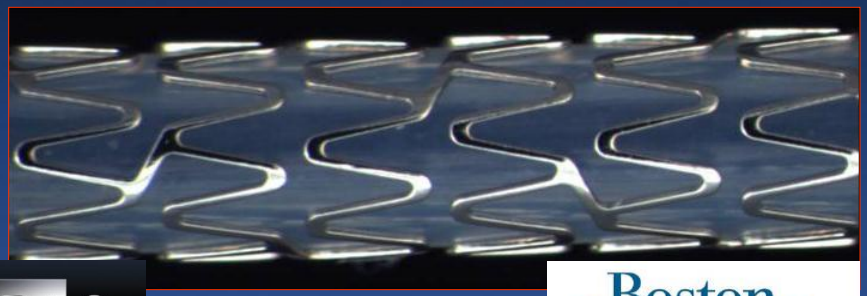
Polymer: PBMA & PVDF-HFP (7μm thickness)

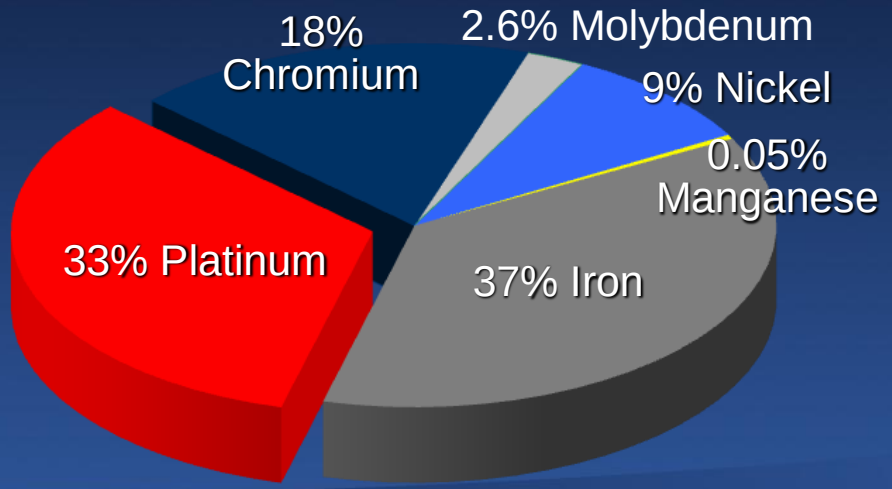
XIENCE V (CoCr-EES)





PROMUS Element (PtCr-EES)



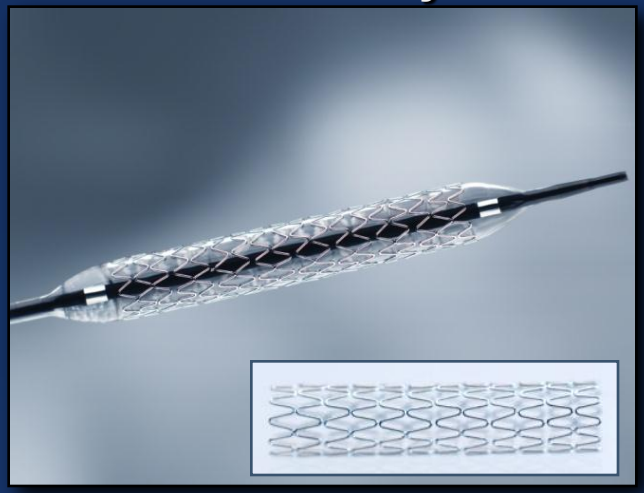


PBMA=poly (n-butyl methacrylate) (primer layer);
PVDF-HFP=poly (vinylidene fluoride-co-hexafluoropropylene) (drug matrix layer)

Stone GW et al. JACC 2011; 57:1700–8

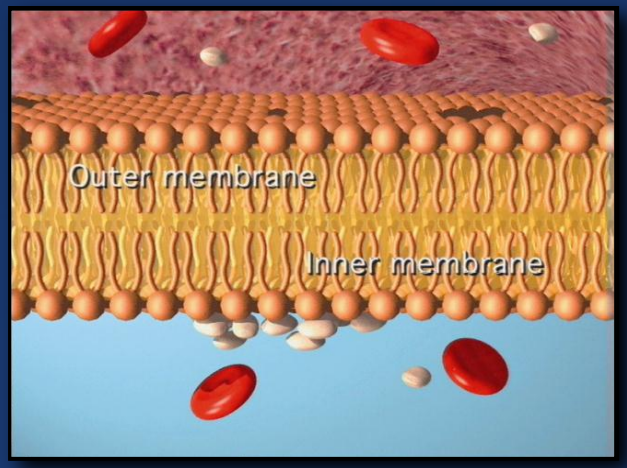
Endeavor DES System

Driver Cobalt Alloy Stent

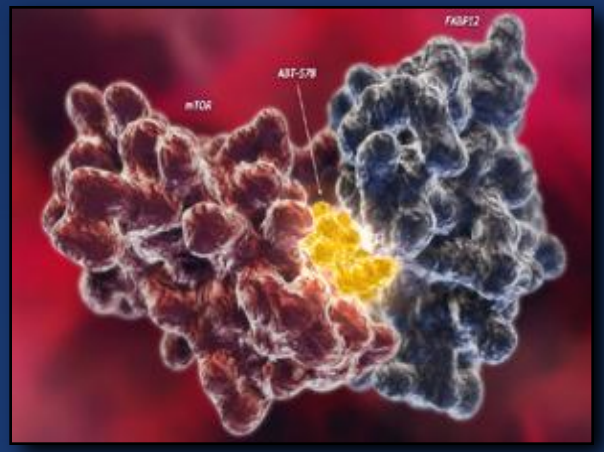


Stent Delivery System

PC Carrier



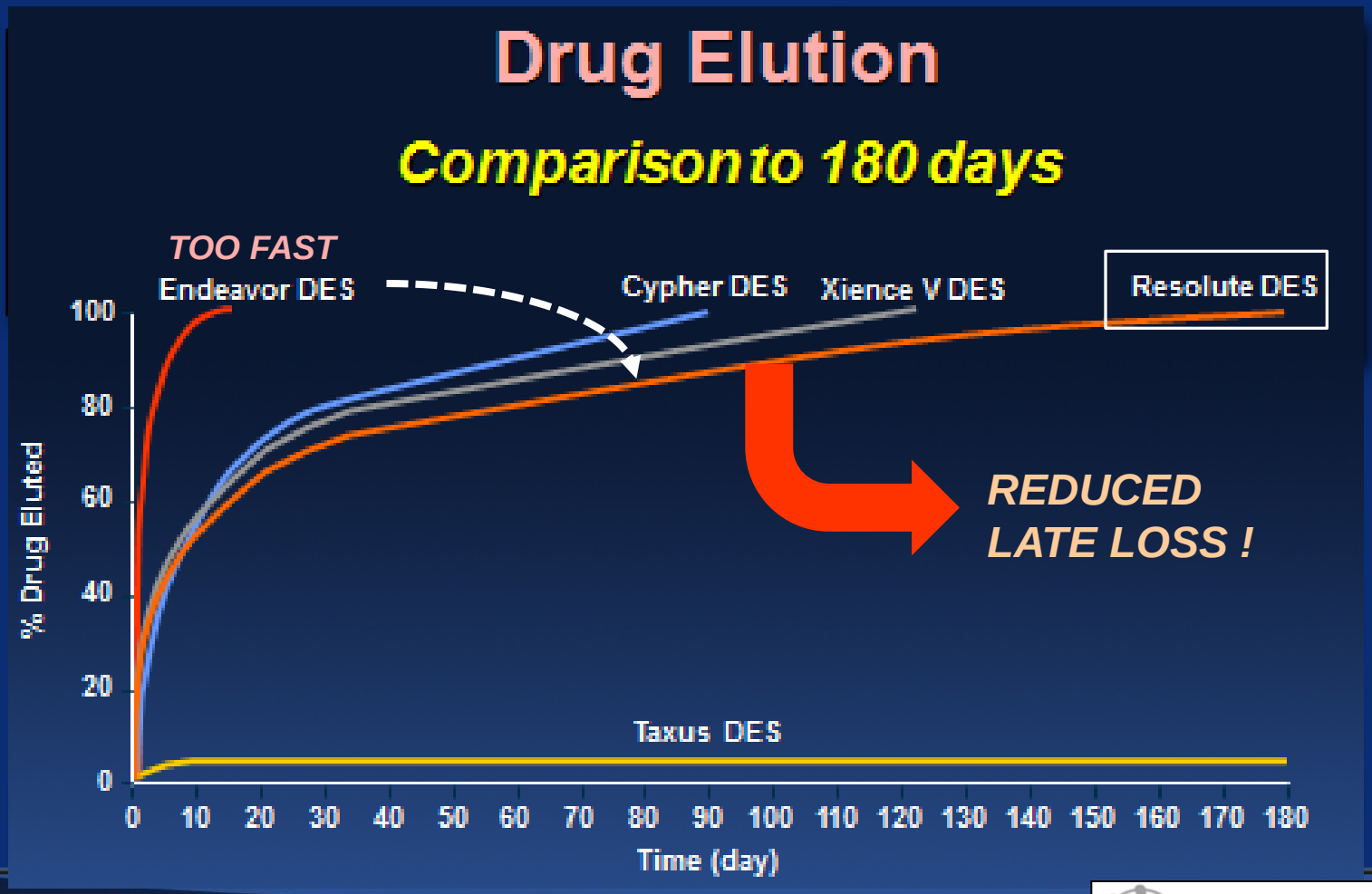
Drug: Zotarolimus



Medtronic

Resolute DES System

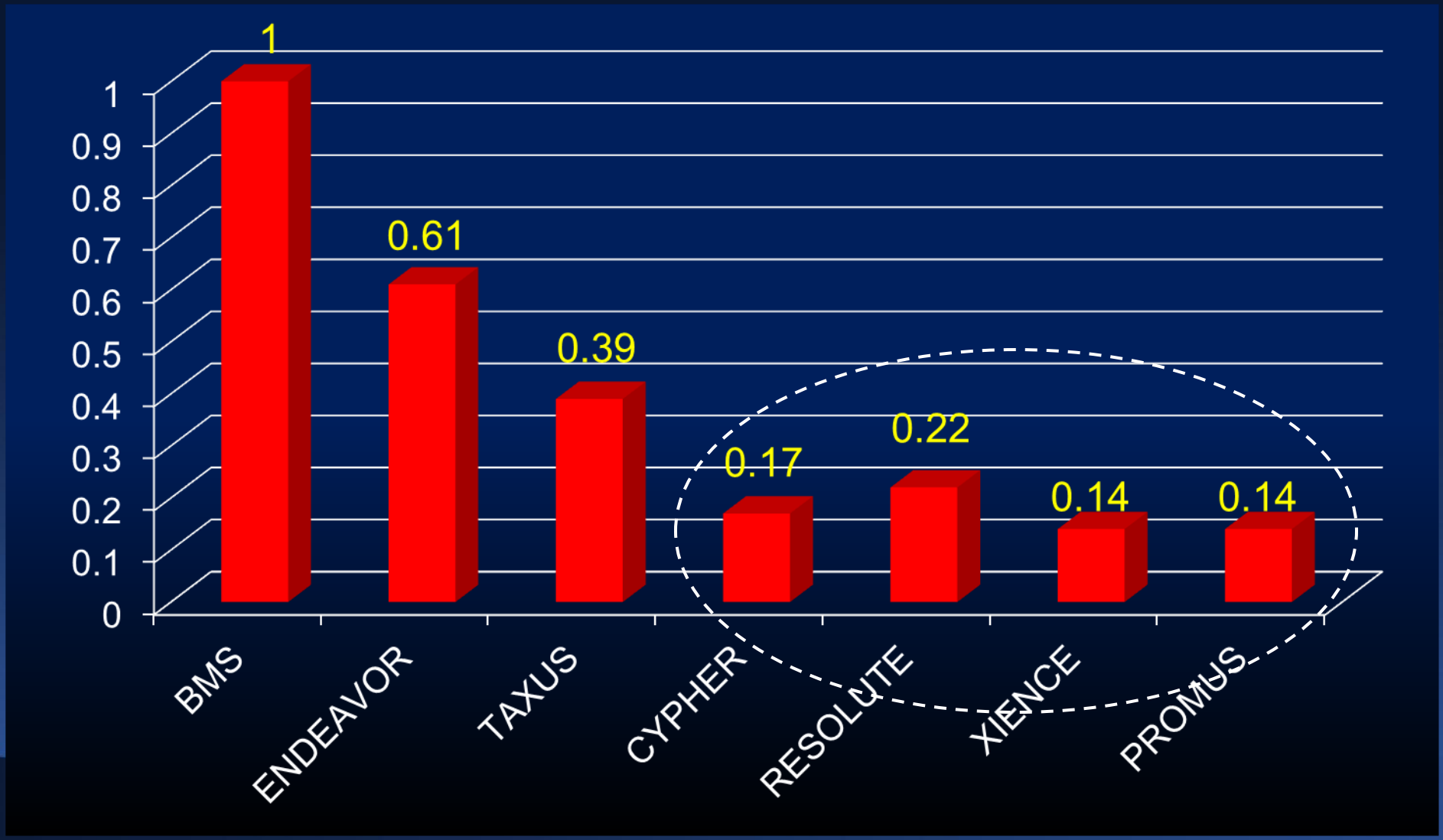
Integrity Cobalt Alloy Stent *Stent Delivery System*



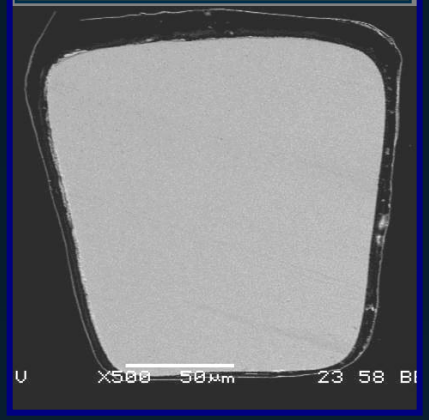
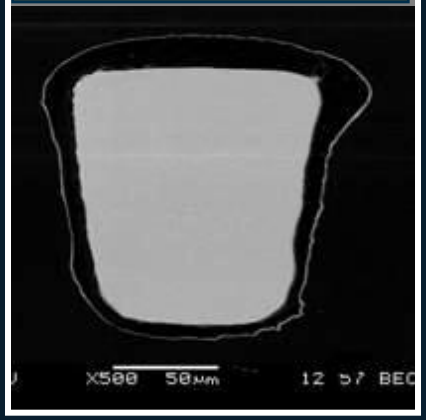
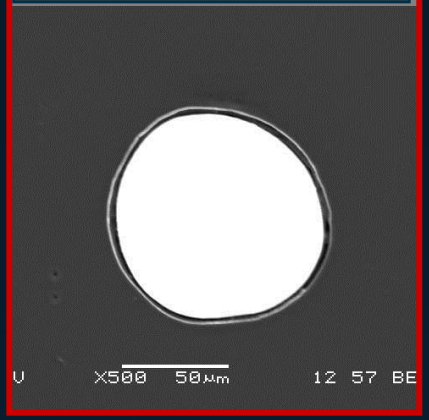
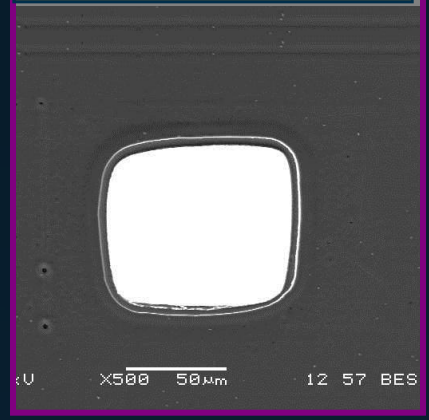
Medtronic

Late Loss* (mm) at 8-9 months

In-stent late loss



DES Strut and Polymer Thickness

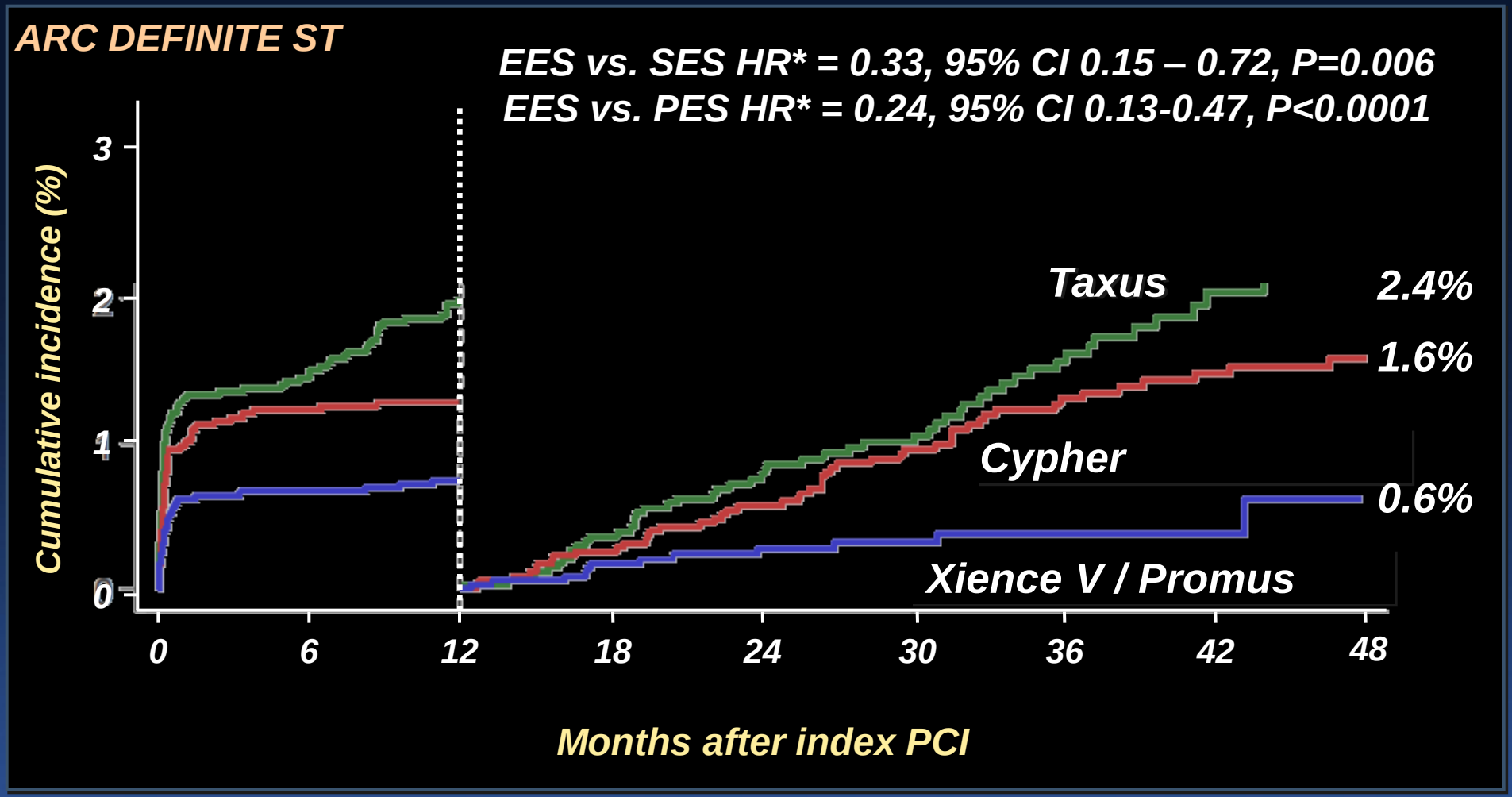
CYPHER®	TAXUS®	ENDEAVOR™	XIENCE™ V
			
Strut Thickness: **140 μm** Polymer Thickness: **12.6 μm** **Total:** **165.2 um**	Strut Thickness: **132 μm** Polymer Thickness: **16 μm** **Total:** **164 um**	Strut Thickness: **91 μm** Polymer Thickness: **5.3 μm** **Total:** **101.6 um**	Strut Thickness: **81 μm** Polymer Thickness: **7.8 μm** **Total:** **96.6 um**

3.0 mm diameter stents, 500x magnification

NOT ALL DRUG ELUTING STENTS ARE THE SAME !

STENT THROMBOSIS: Landmark analysis

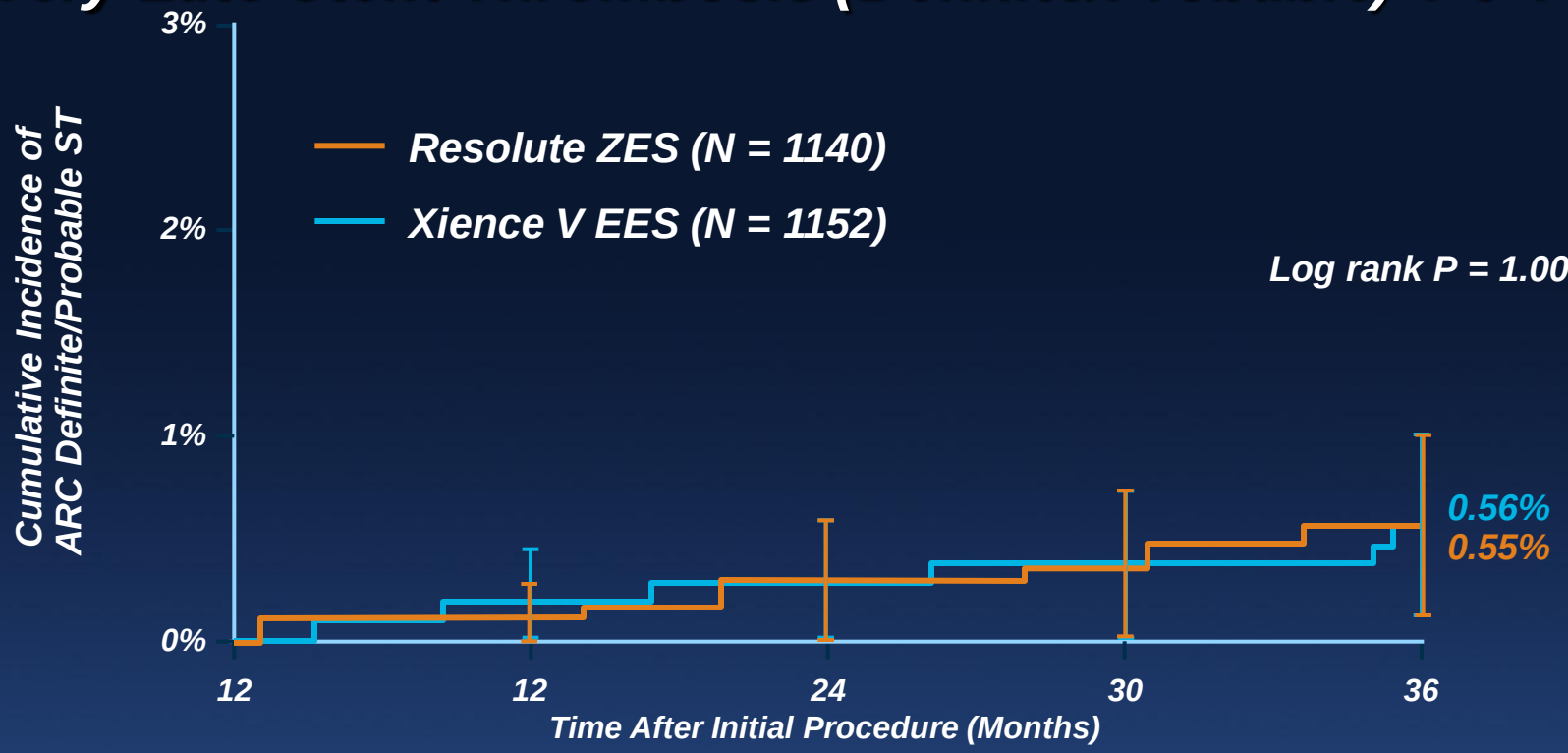
Bern Rotterdam (n=12,339 pts)



Räber et al, Circulation 2012

RESOLUTE All Comers Randomized Trial

Very Late Stent Thrombosis (Definite/Probable) 1-3 Years



Patients at Risk			
Resolute ZES	1140	1108	1081
CI%	0.00	0.27	0.55
Xience- ES	1152	1107	1083
CI%	0.00	0.27	0.56

%DAPT	*12mths*	*24mths*	*36mths*
Resolute ZES	*84.4*	*18.4*	*13.8*
Xience EES	*83.5*	*18.3*	*13.4*

TAKE HOME MESSAGES

Late Stent Thrombosis is a phenomenon of first generation DES (Cypher and Taxus). Evidence suggest safety of second generation DES (Xience, Promus Element and Resolute)

In fact, Xience has gained approval in Europe for 3 months of DAPT

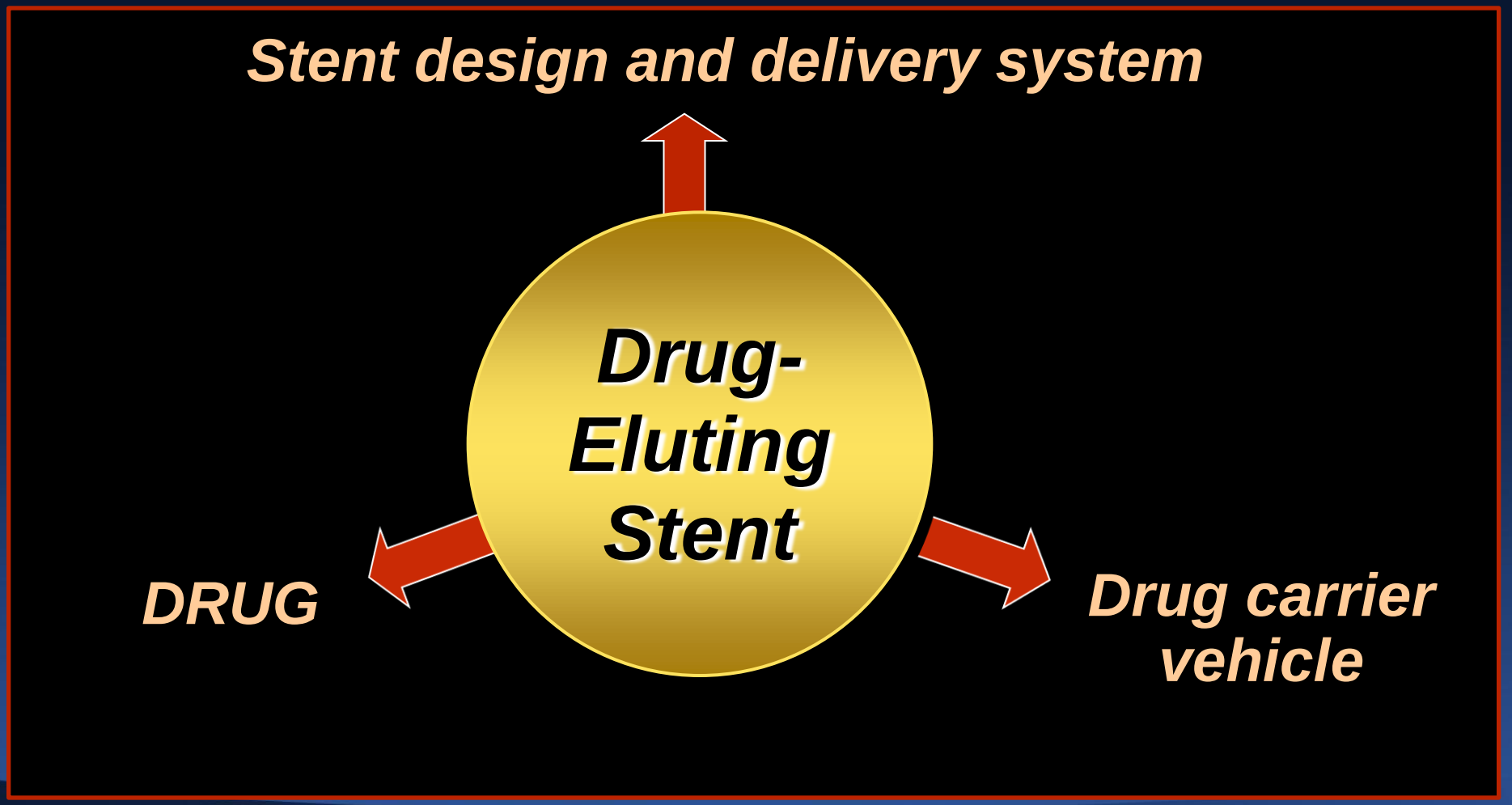
Reason: More biocompatible durable polymers:

-Fluoropolymers (Xience and Promus)

-Phosphorylcoline / BioLinx (Endeavor / Resolute)

Drug-Eluting Stents

WHICH NEEDS TO GO AND WHICH NEEDS TO STAY?



Polymer (drug carrier) has to go !

- *Bioabsorbable Polymers:* - Synergy
  - BioMatrix
  - Excella
  - Inspiron
  - EPC Combo
- *Polymer-Free:* - Drug-filled stent
  - BioFreedom
  - Translumina
  - Vestasyn
- *Special coatings*

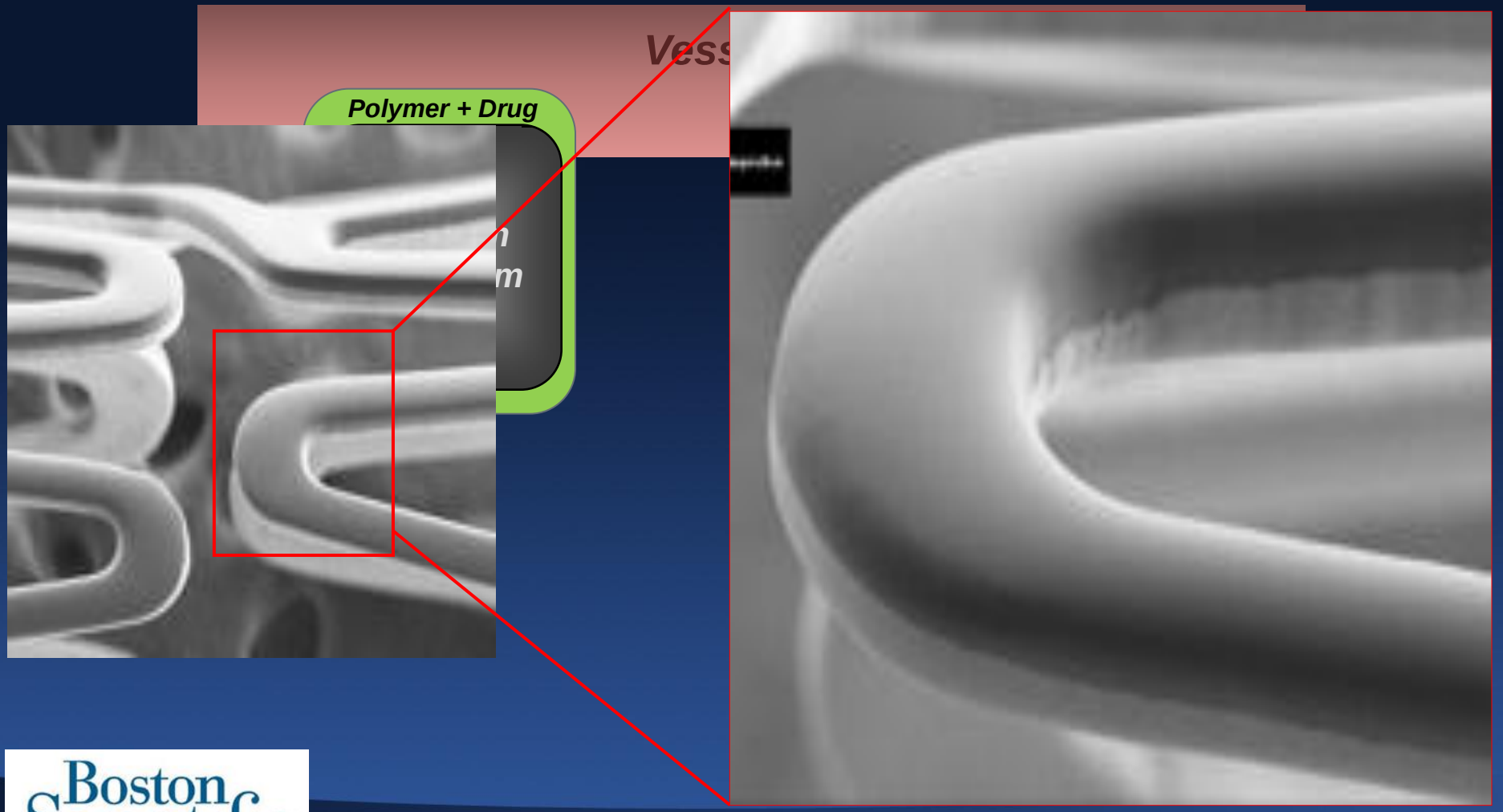
Drug-Eluting Technology Evolution

Current DES

Conformal Biostable Polymer

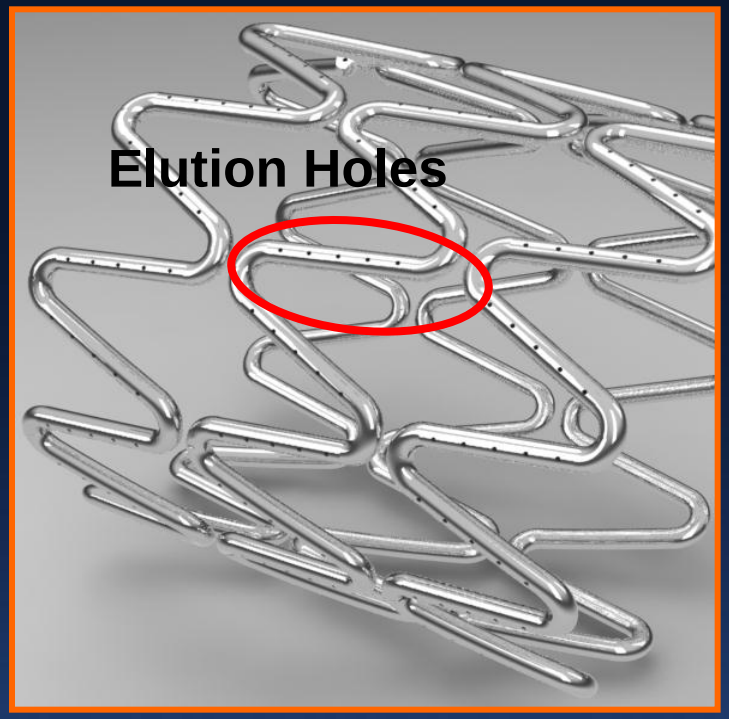
SYNERGY™ DES

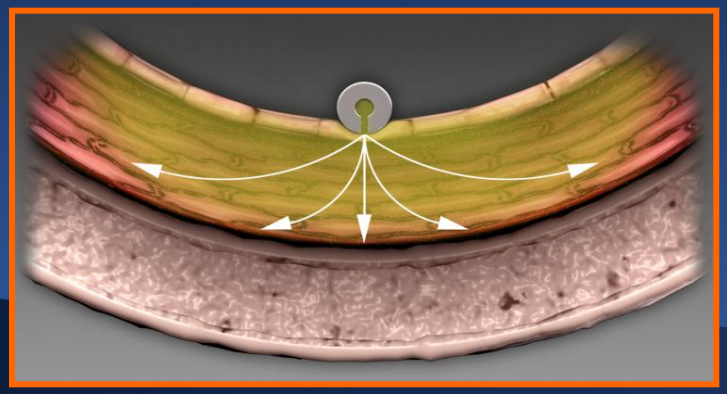
Abluminal Bioabsorbable Polymer

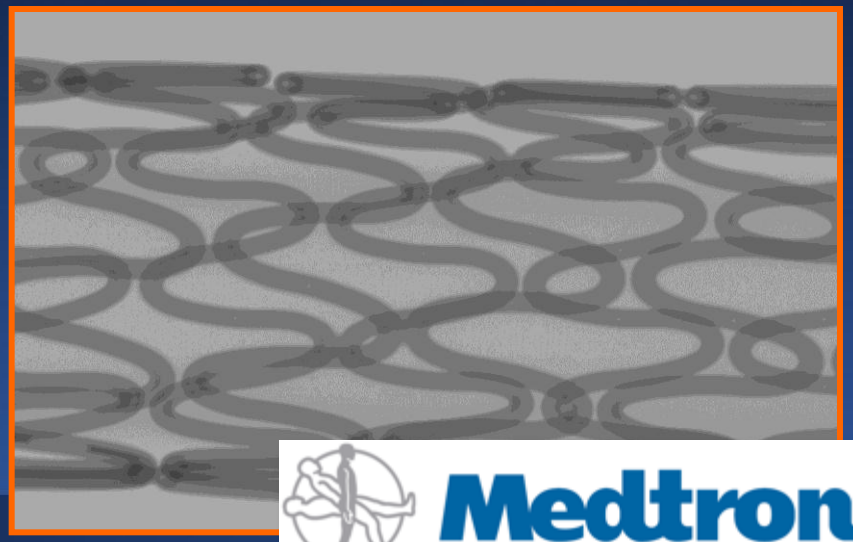


Boston Scientific

Drug elution controlled by diffusion
Drug Filled Stent without polymer





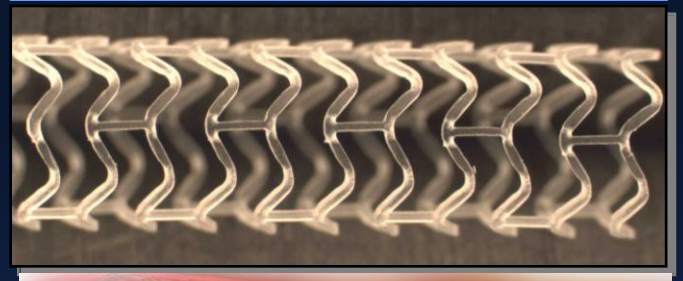
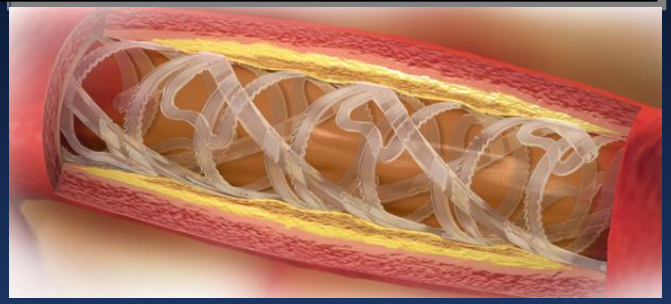


Medtronic

Bioabsorvable Vascular Scaffolds (BVS): New Scientific Breakthrough*

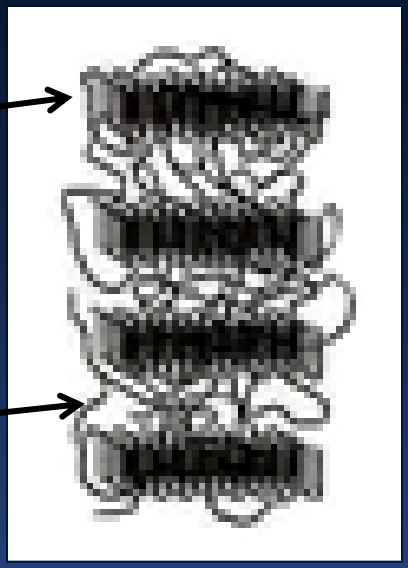
***Def.** Temporary vascular stent, termed "scaffold" due to its being based on a temporary bioresorbable platform.*

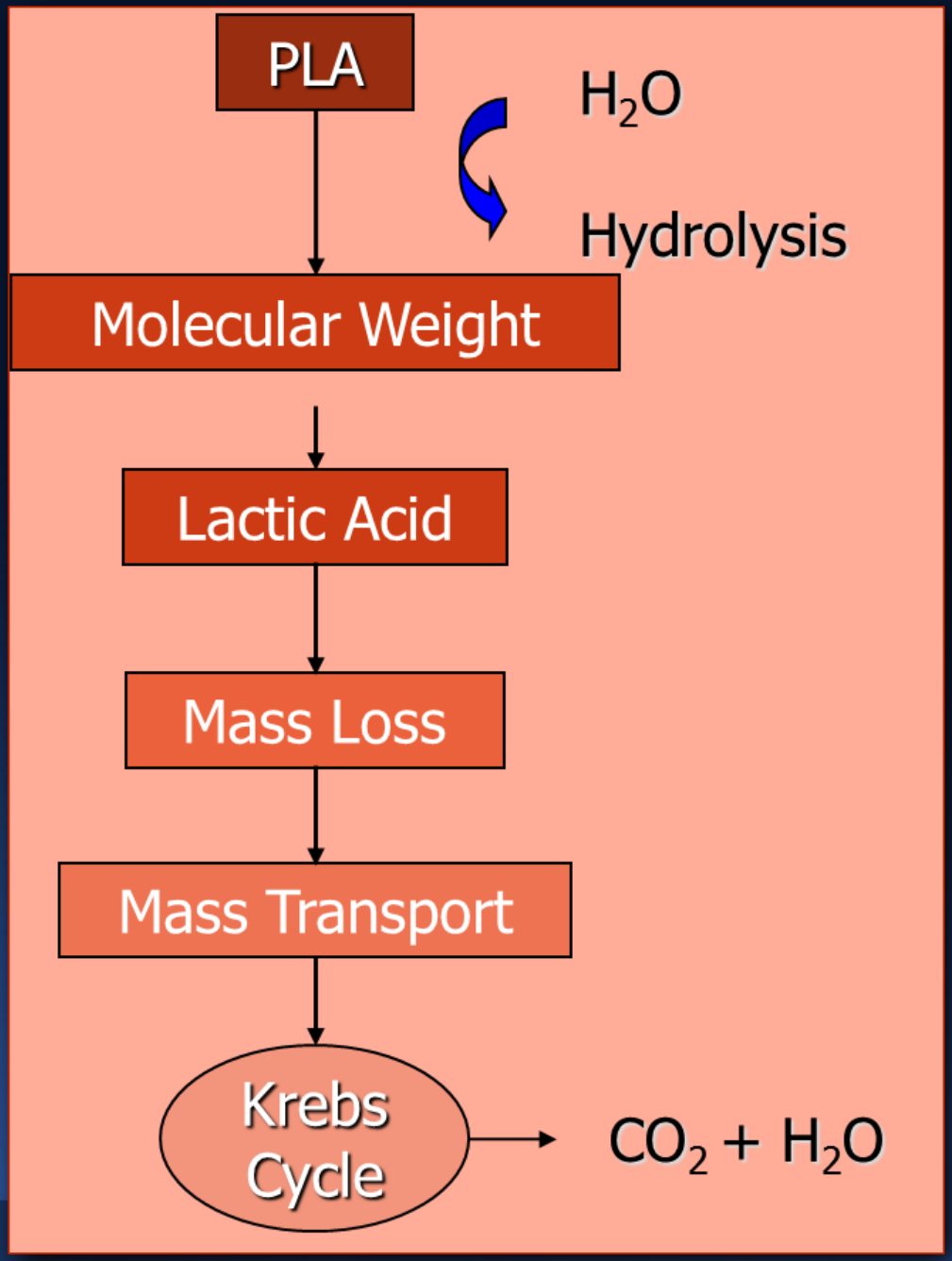
Fully Bioresorbable Stents (Scaffolds)

Igaki-Tamai		PLA
BVS		PLA (everolimus coat)
REVA		Iodinated tyrosine-polycarbonate (with PTX)
BTI		PAE-salicylate (with sirolimus)
Biotronik		Magnesium

PLLA = Poly (L-lactide)

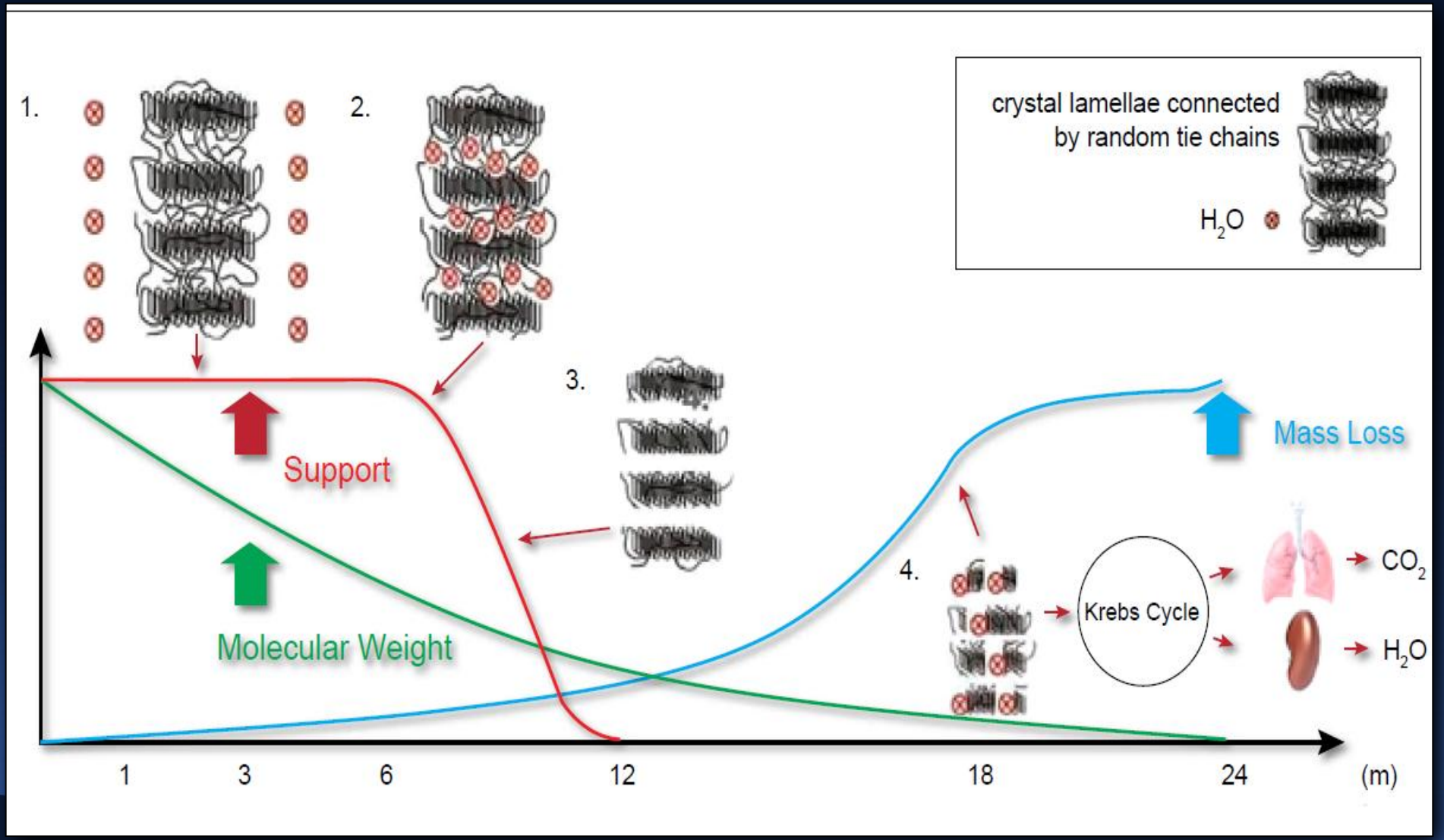
PLLA is used in numerous clinical items, such as resorbable sutures, soft tissue implants, orthopedic implants, and dialysis media.



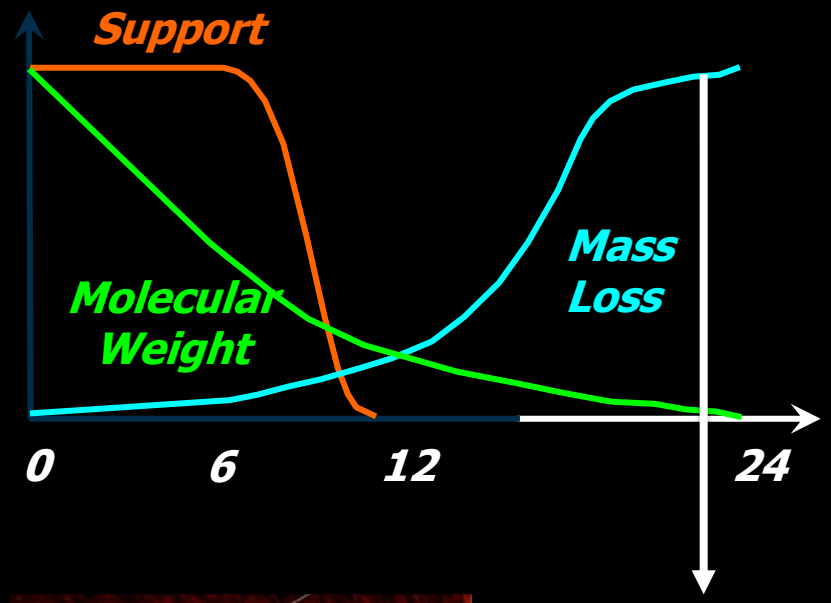


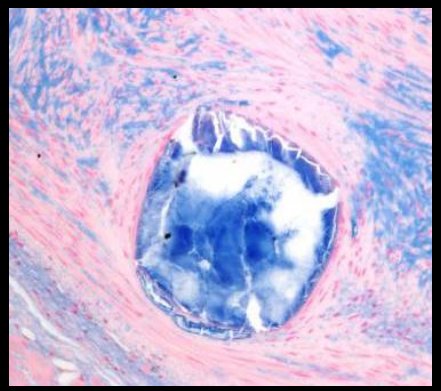
PLLA DEGRADATION PATHWAY

BVS Degradation



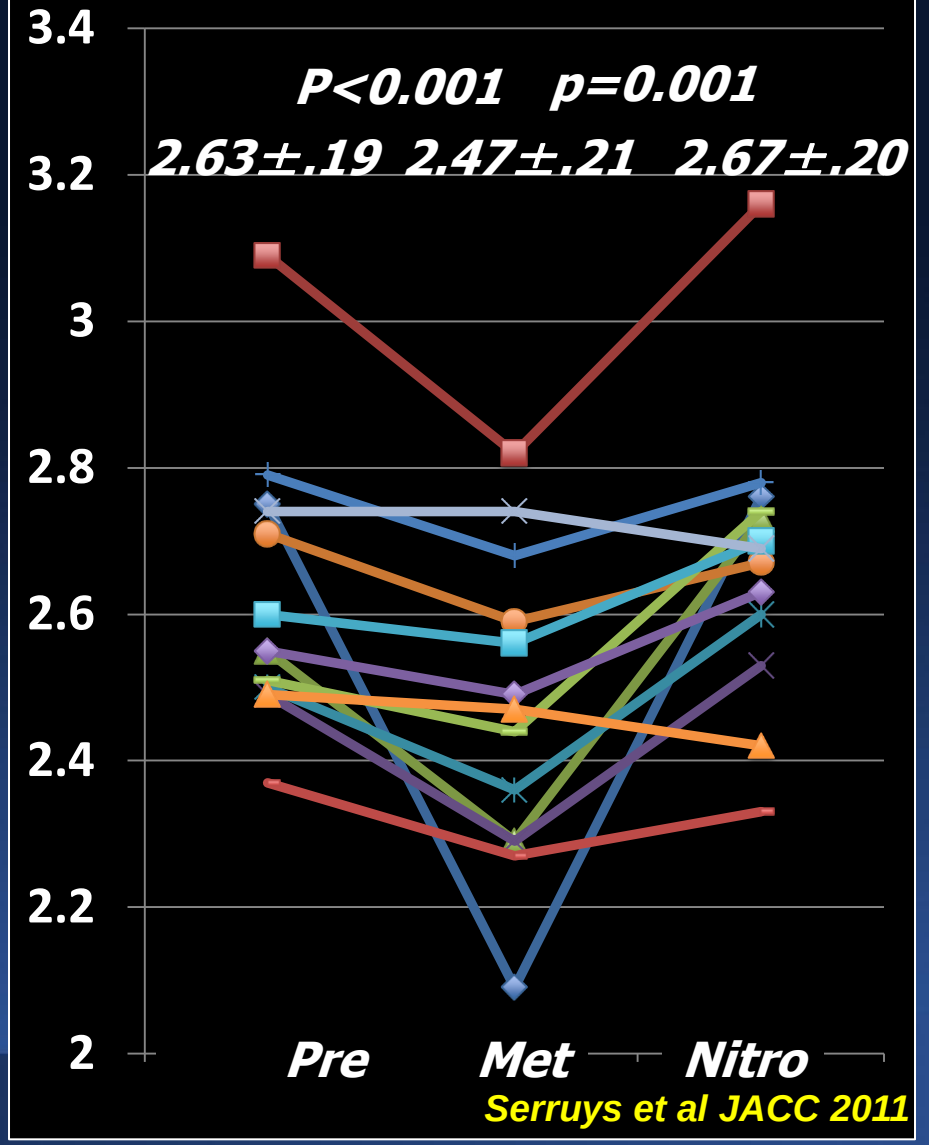
Mechanical integrity has disappeared by 12 months.



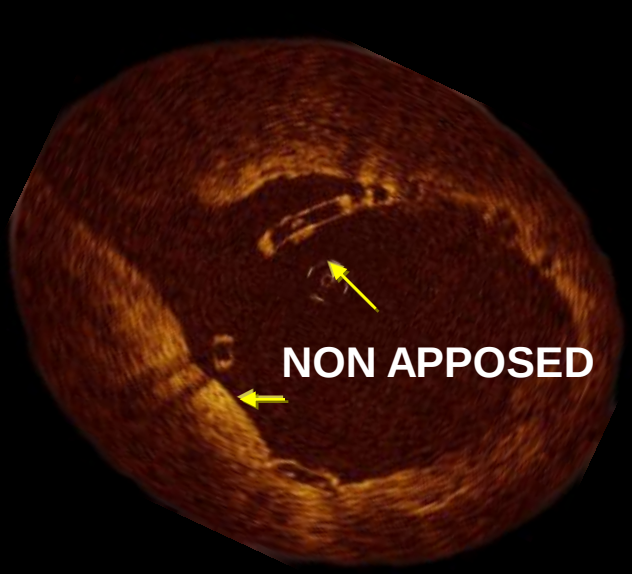


Restoration of vasomotion at 12 MONTHS

Ergonovine (n=13 patients)

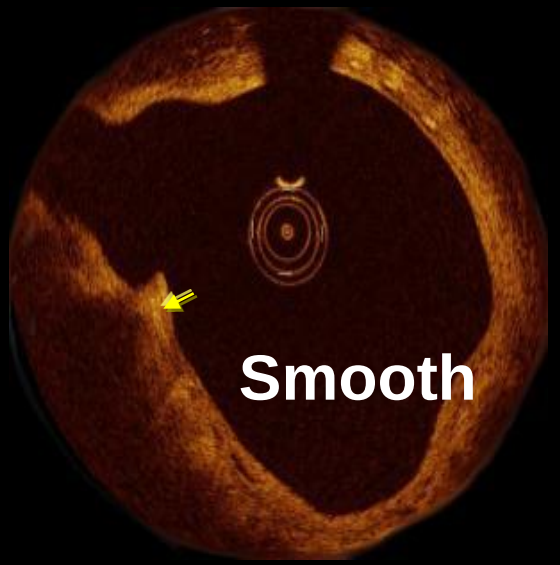


Bioresorption is a real phenomenon



Baseline

6 months

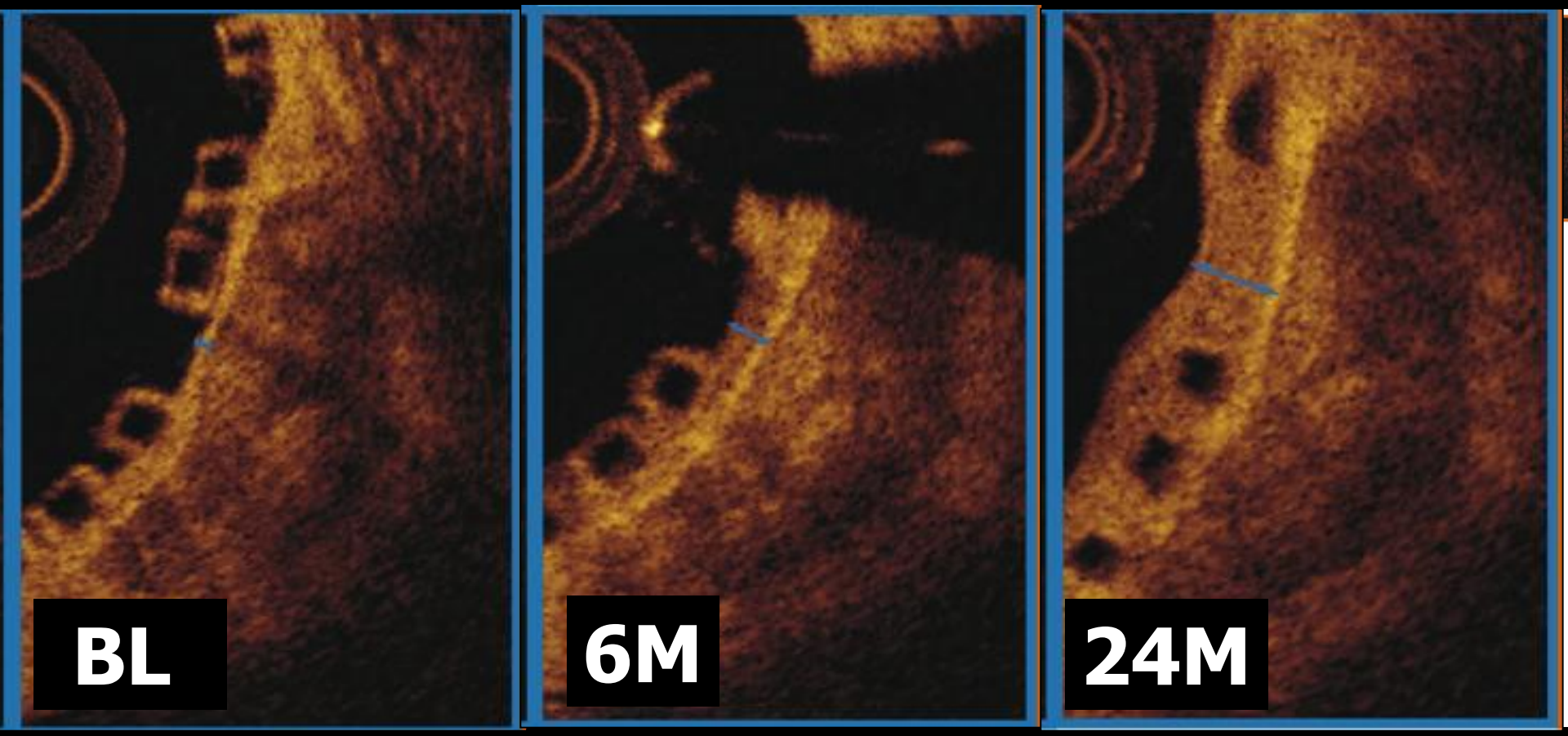


2 years

Serruys et al. Lancet 2009

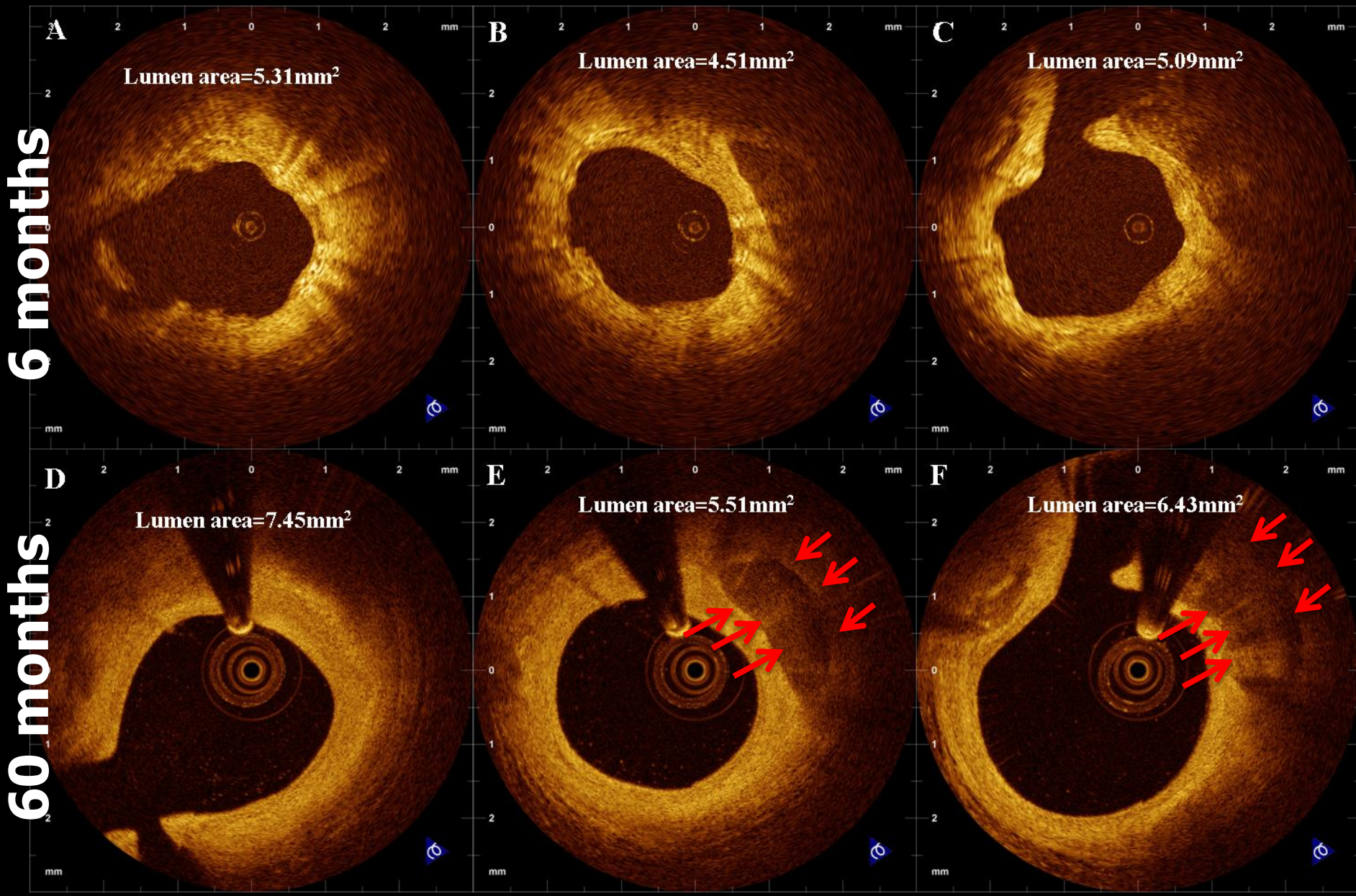
Scaffold healing results in plaque coverage: Can capping plaques prevent future Myocardial Infarctions?

Progressive sealing and shielding of calcified plaque



Magnified images at BL, 6M and 2Y, using the radio-opaque markers as a landmark.

Not only the BVS can cap the plaque…
late lumen enlargement is observed!!!



Bioabsorbable Vascular Scaffolds

Revascularization

- Provides transient mechanical support needed: 3-6 months
- Drug delivery that modulates healing

Vessel Restoration

- Normal vessel physiology is restored: Vasomotion, pulsatility and shear forces

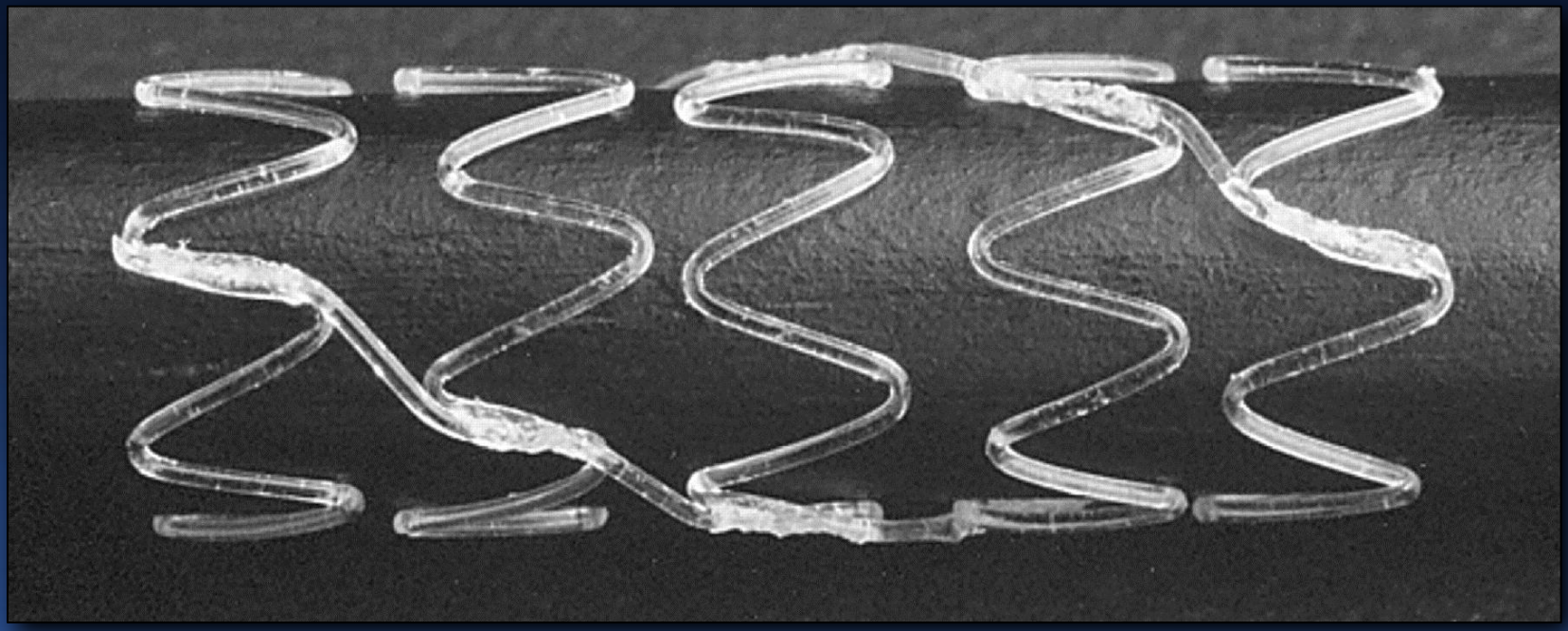
Resortion

- Gradual fading of stent without major inflammatory changes.
- Lumen dimensions are preserved or enlarge. Smooth endothelial surface is restored.

Igaki-Tamai bioabsorbable stent

Non-drug eluting

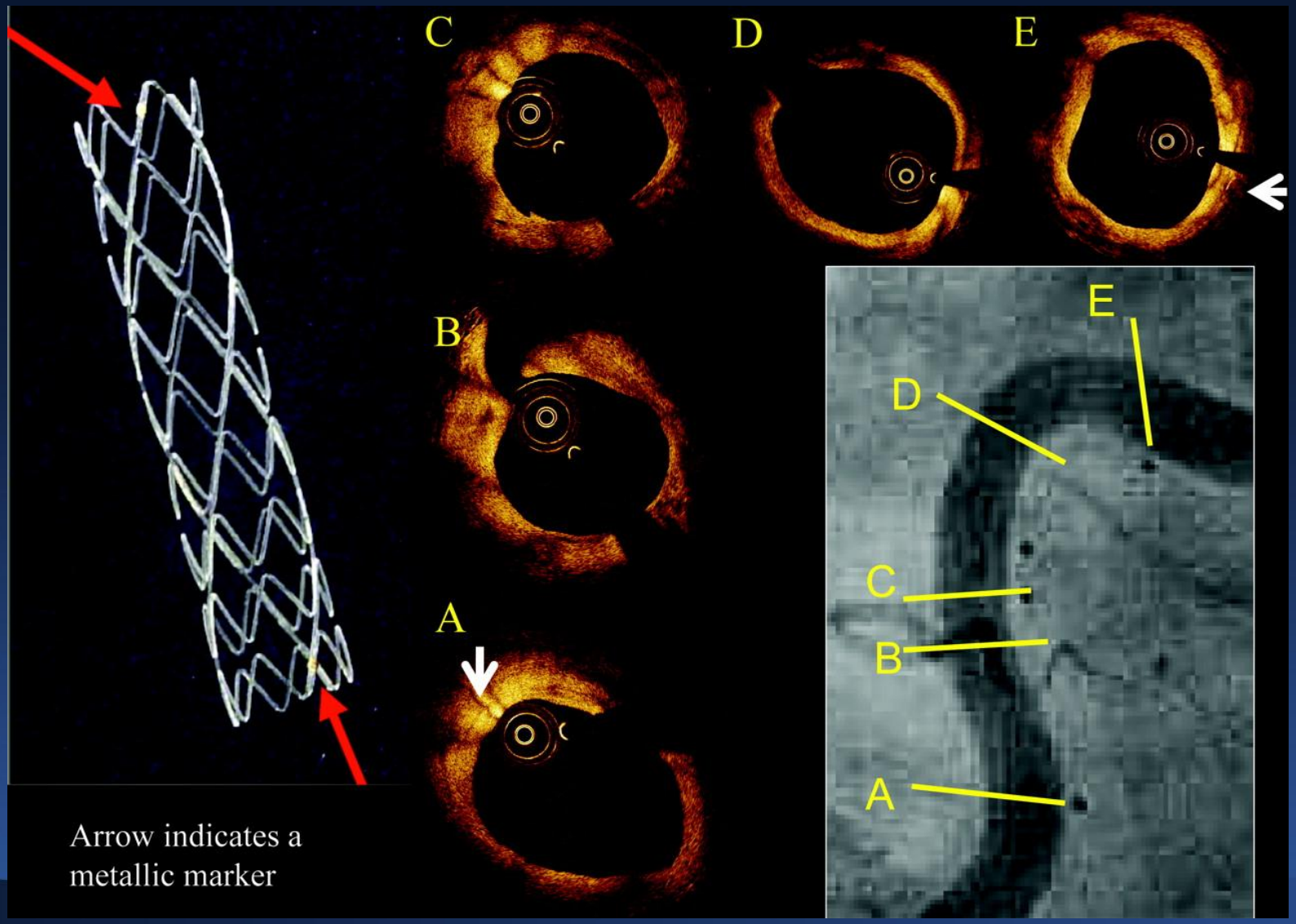
First BVS implanted in human in 2000 (50 pts)



Ormiston J A , Serruys P W Circ Cardiovasc Interv 2009;2:255-260

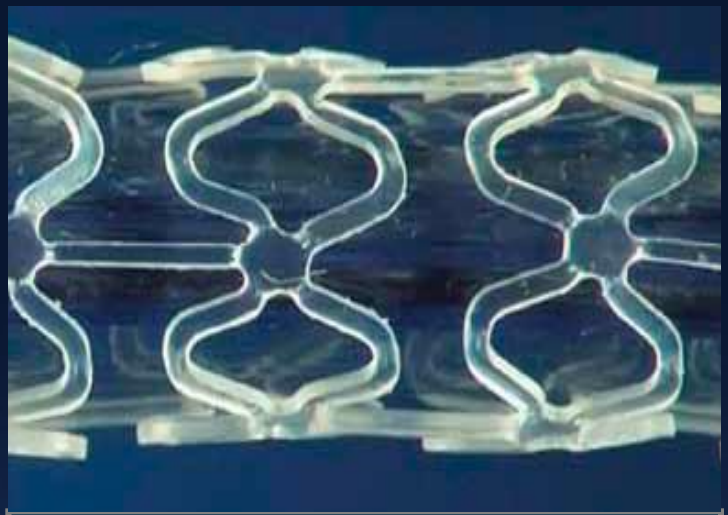
Igaki-Tamai PLLA stent

10 yr OCT images

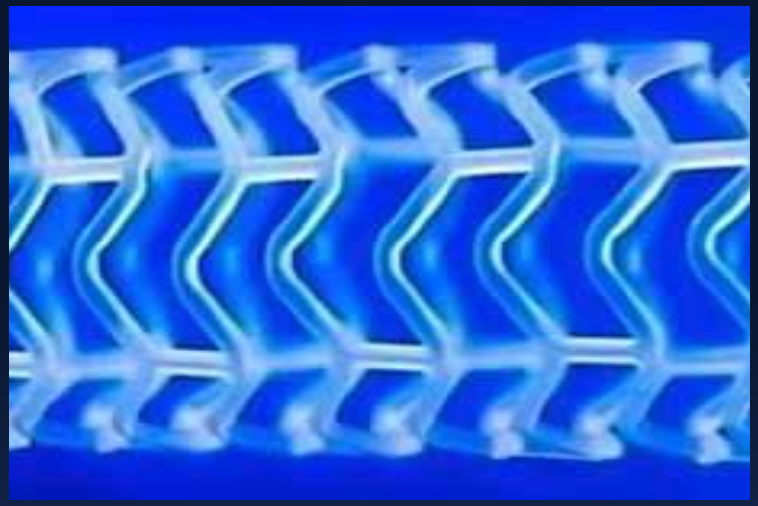


Onuma Y , Serruys P W Circulation 2011;123:779-797

Everolimus eluting BVS (Abbott)



SEM Gen 1.0 Cohort A clinical trial (2yr FU)

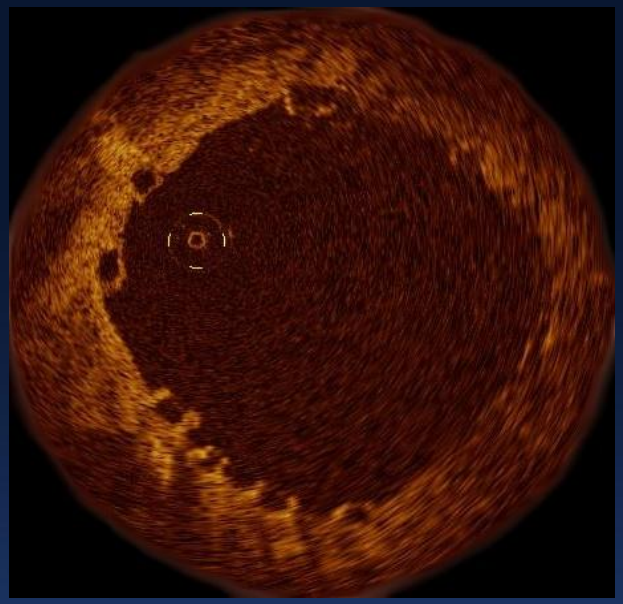


SEM Gen 1.1 Cohort B clinical trial (ongoing)

- More uniform support and drug application
- More radial strength and longer duration of support
- Storage room temp instead of refrigeration
- Delivery performance similar to metallic stent. Design like a Multi-Link stent
- Strut thickness 150 u and platinum markers at ends

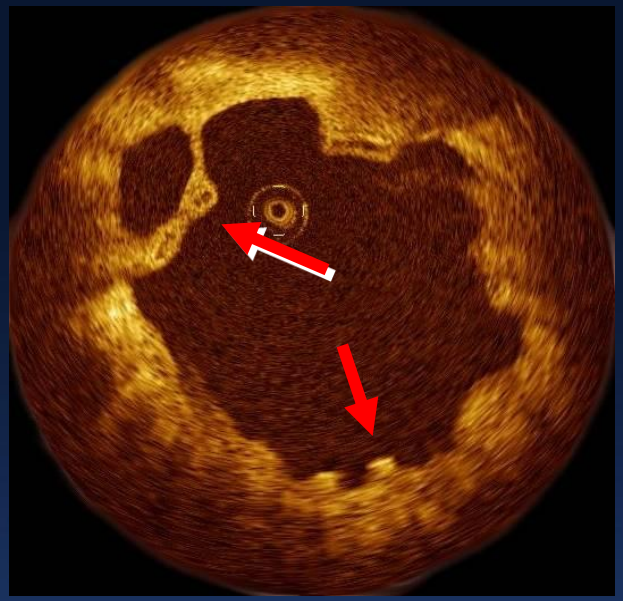
Absorb Trial: OCT Results

Post-stenting



Complete strut apposition

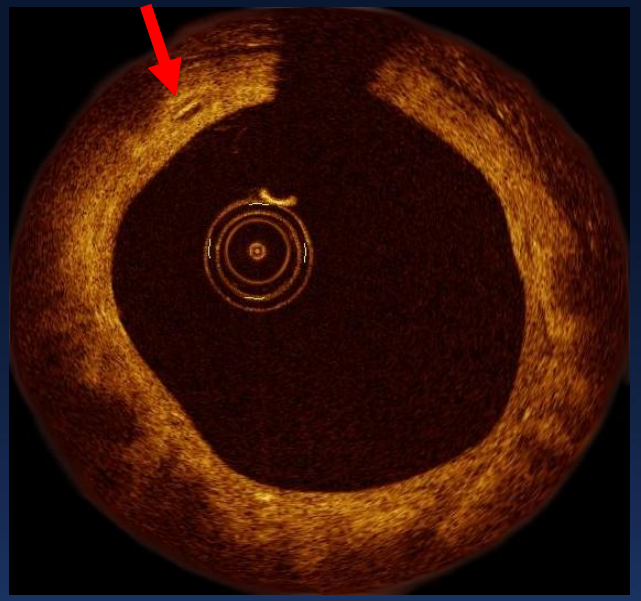
6-month



Late acquired incomplete stent apposition with tissue bridges between the struts

Corrugated endolumen

24-month



Smooth endoluminal lining

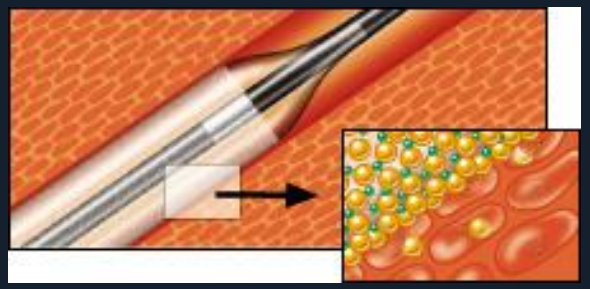
Struts largely disappeared although remnant just visible (arrow)

Serruys et al *Lancet* 2009

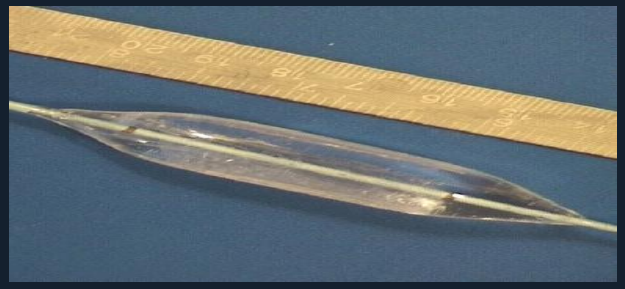
Drug-Eluting Balloons

SeQuent® Please
Paccocath® Technology – B. Braun

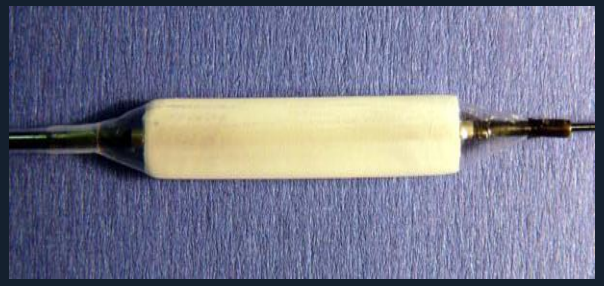
In.Pact
Invatec



DIOR® - EuroCor

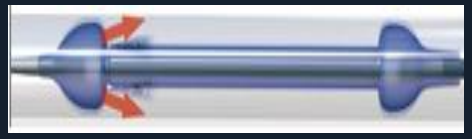


Elutax® - Aachen Resonance



Cricket™
Mercator

Genie™
Acrostak



ClearWay™
Atrium

CONCLUSIONS

- Stents are the standard of care in PCI
- DES eliminated restenosis in most patients
- First generation stents (Cypher and Taxus) are associated with LST / VLST, ED, SF, and accelerated neoatherosclerosis.
- Second generation stents (Xience, Promus and Resolute) have resolved some of these safety issues (and *should not carry the stigma of first generation stents*)
- Further safety with new DES designs (absorbable polymers or no polymers)
- BVS is the next frontier
- The delivery of drugs (DEB) and “scaffolding” arteries will become more common than “stenting” arteries

Thank you !