

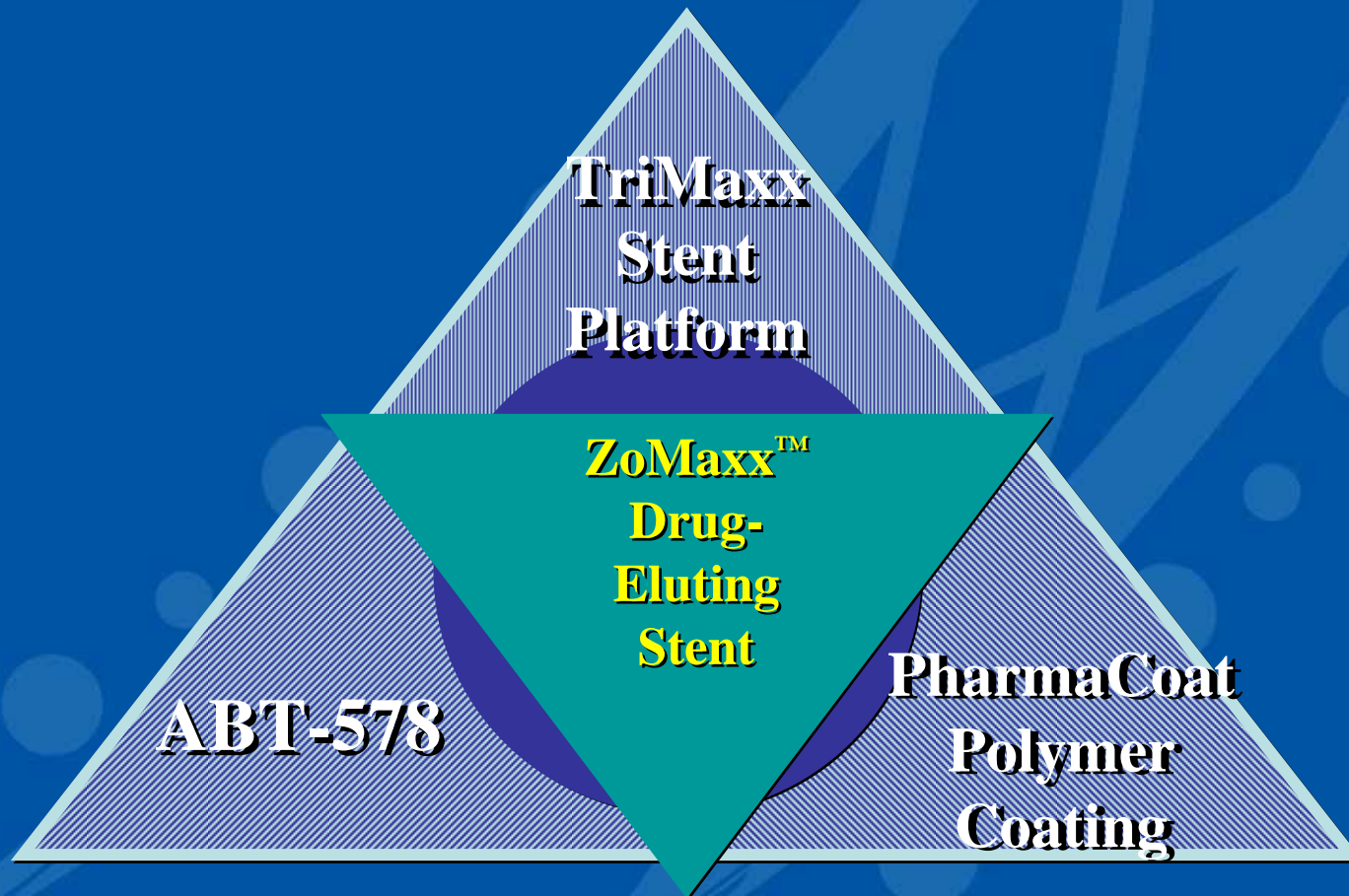
ZoMaxx: Abbott's Drug Eluting Stent Programme

John Ormiston

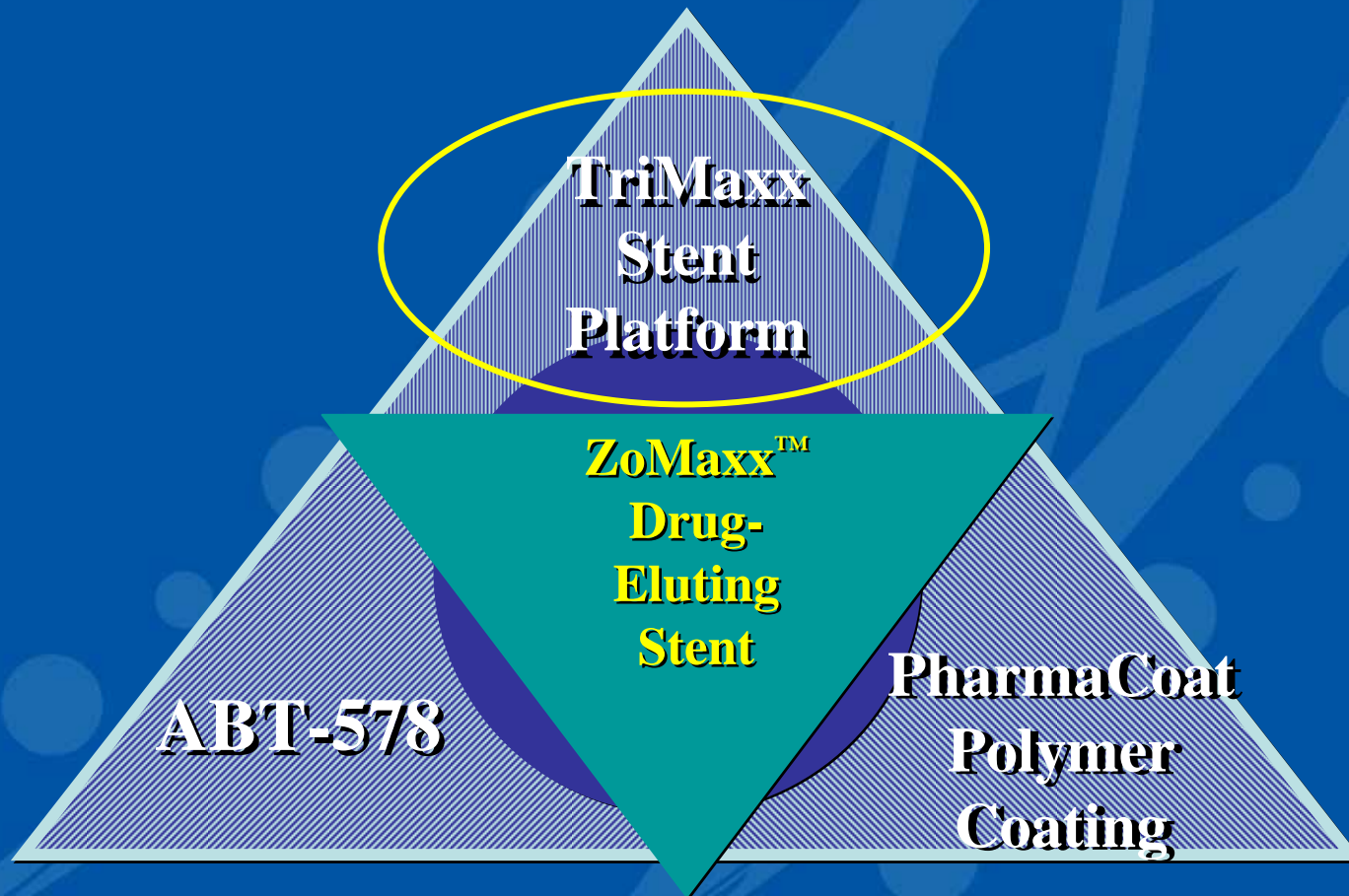
Green Lane and Mercy Hospitals

Auckland, New Zealand

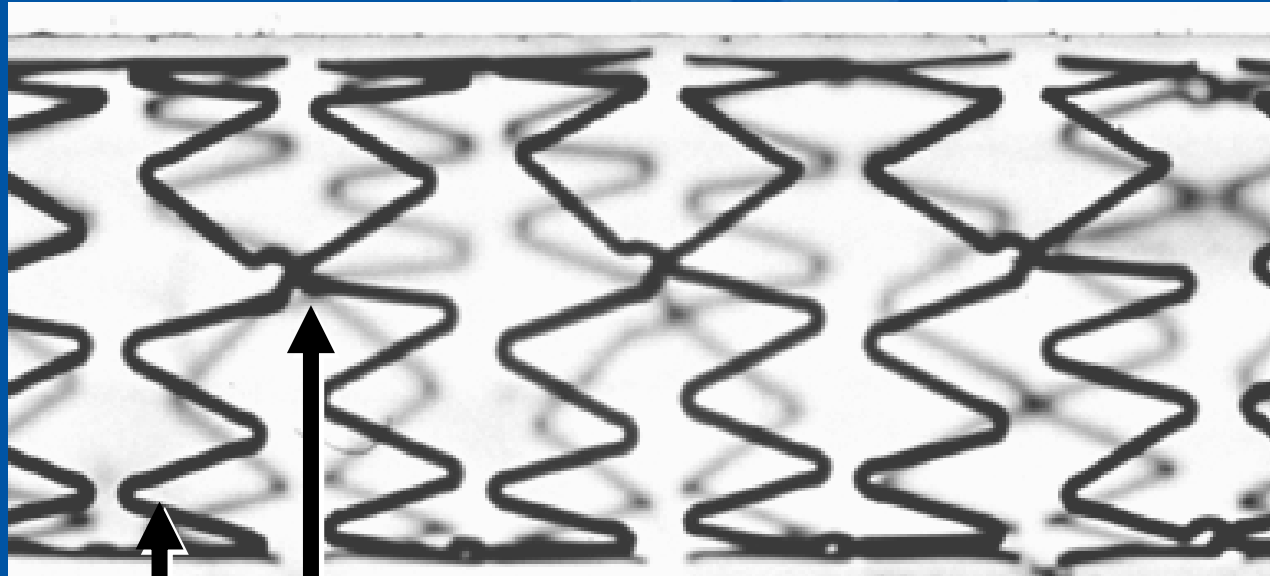
ZoMaxx Drug-Eluting Stent



ZoMaxx Drug-Eluting Stent



TriMaxx Stent Platform

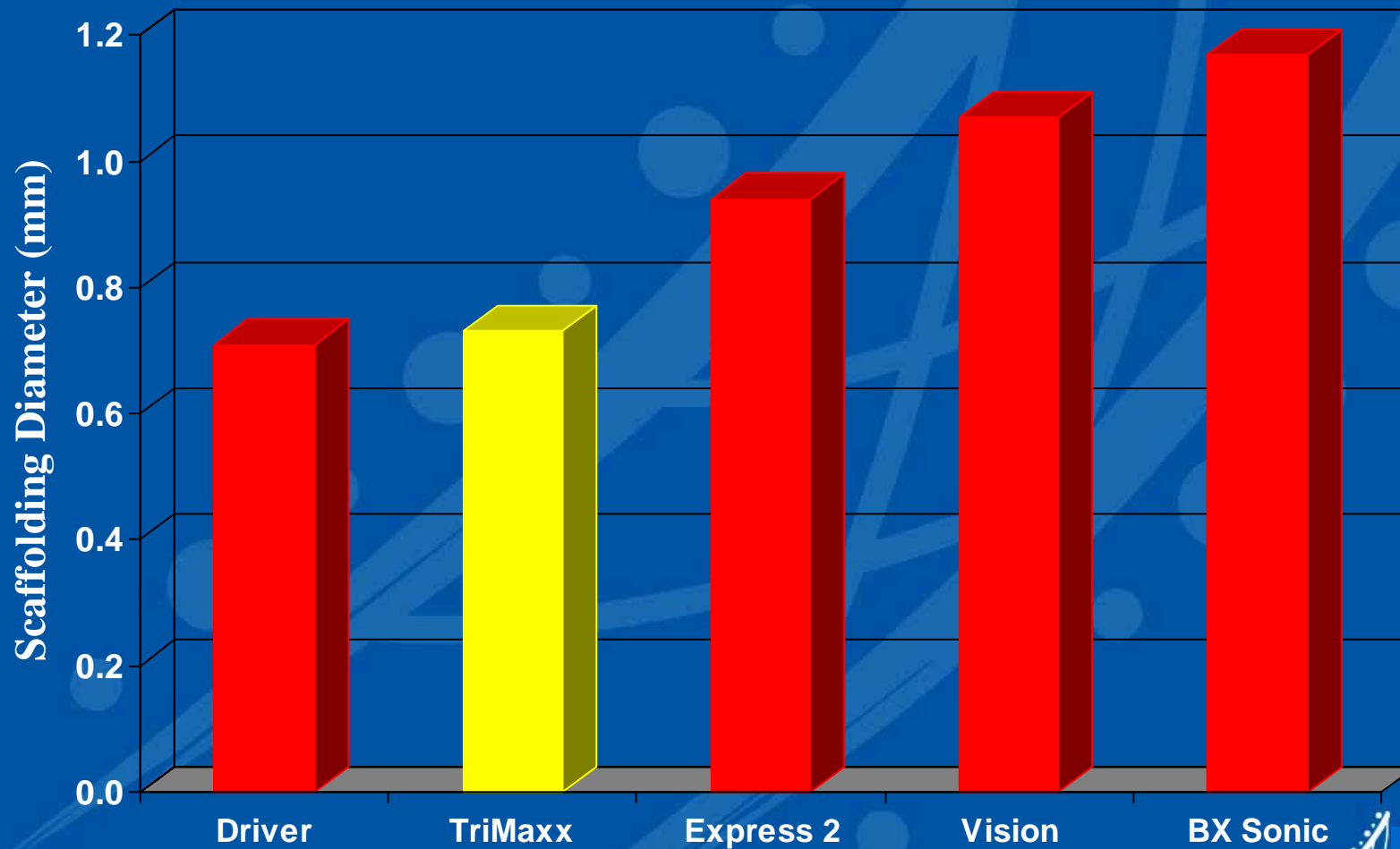
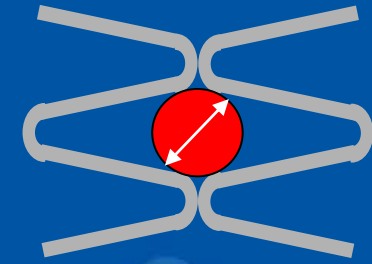


**8-10 cells/
perimeter**

**Off-set crown
connector**

**2 connectors/
circumference**

Stent Scaffolding (Mean interstrut diameter)

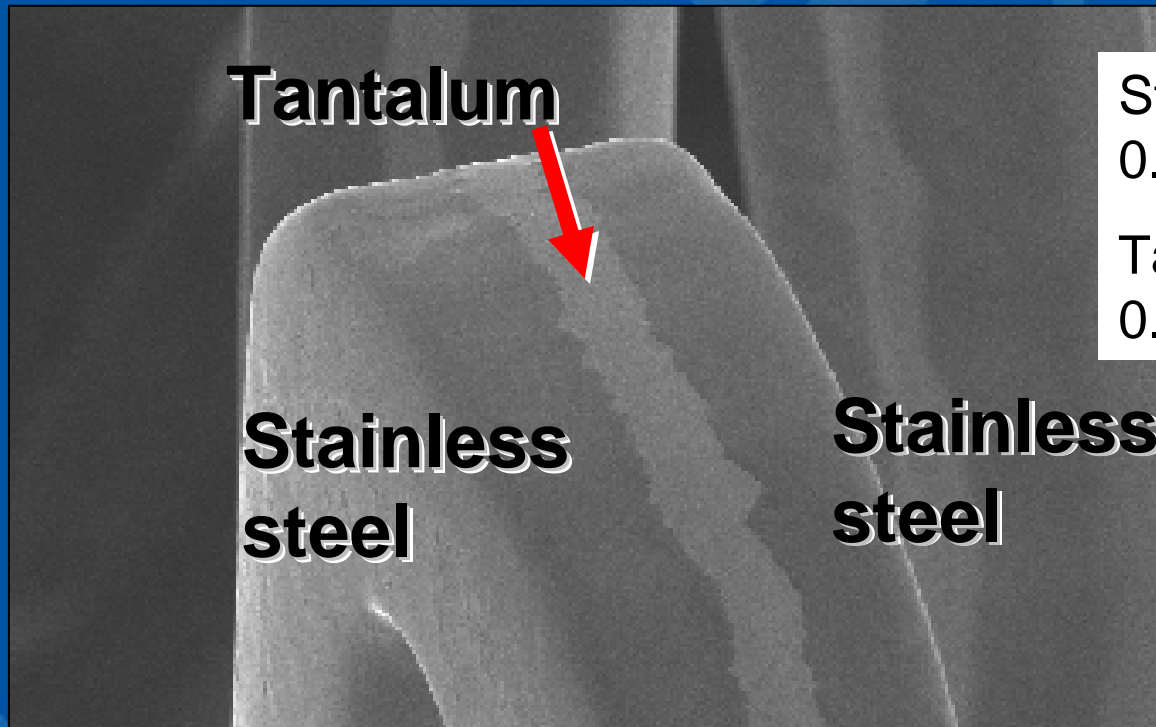


Driver is a trademark of Medtronic; Express² is a trademark of Boston Scientific;
Vision is a trademark of Guidant; Bx Sonic is a trademark of Johnson & Johnson



Triplex stent material

3 layered composite



Strut thickness
0.0029"

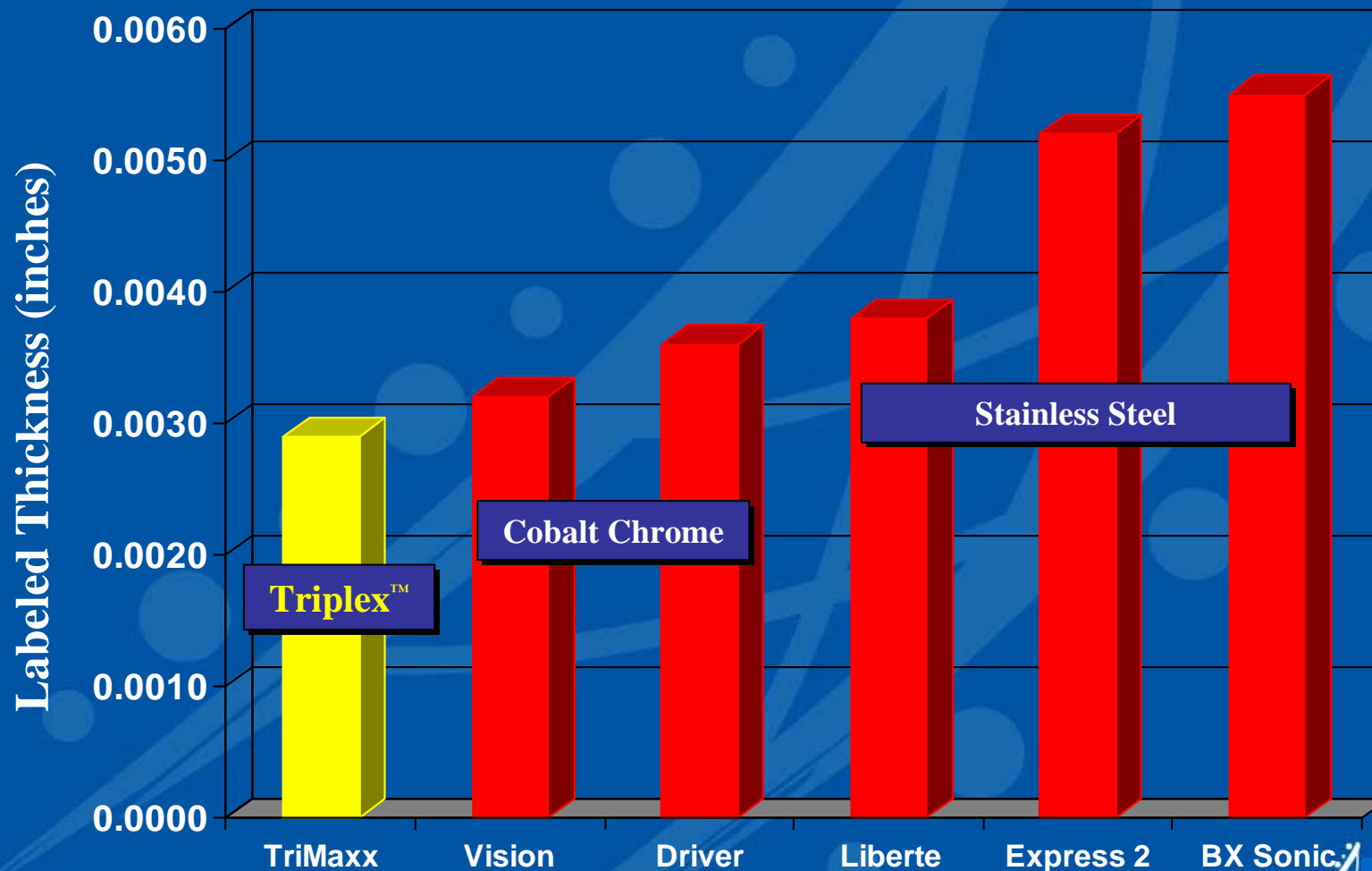
Tantalum layer
0.0029"

- ❑ **Tantalum provides strength and increased radioopacity**
- ❑ **It allows struts to be thinner without sacrificing strength or radioopacity**

Triplex is a trademark of Catheter Technology, Inc.

X

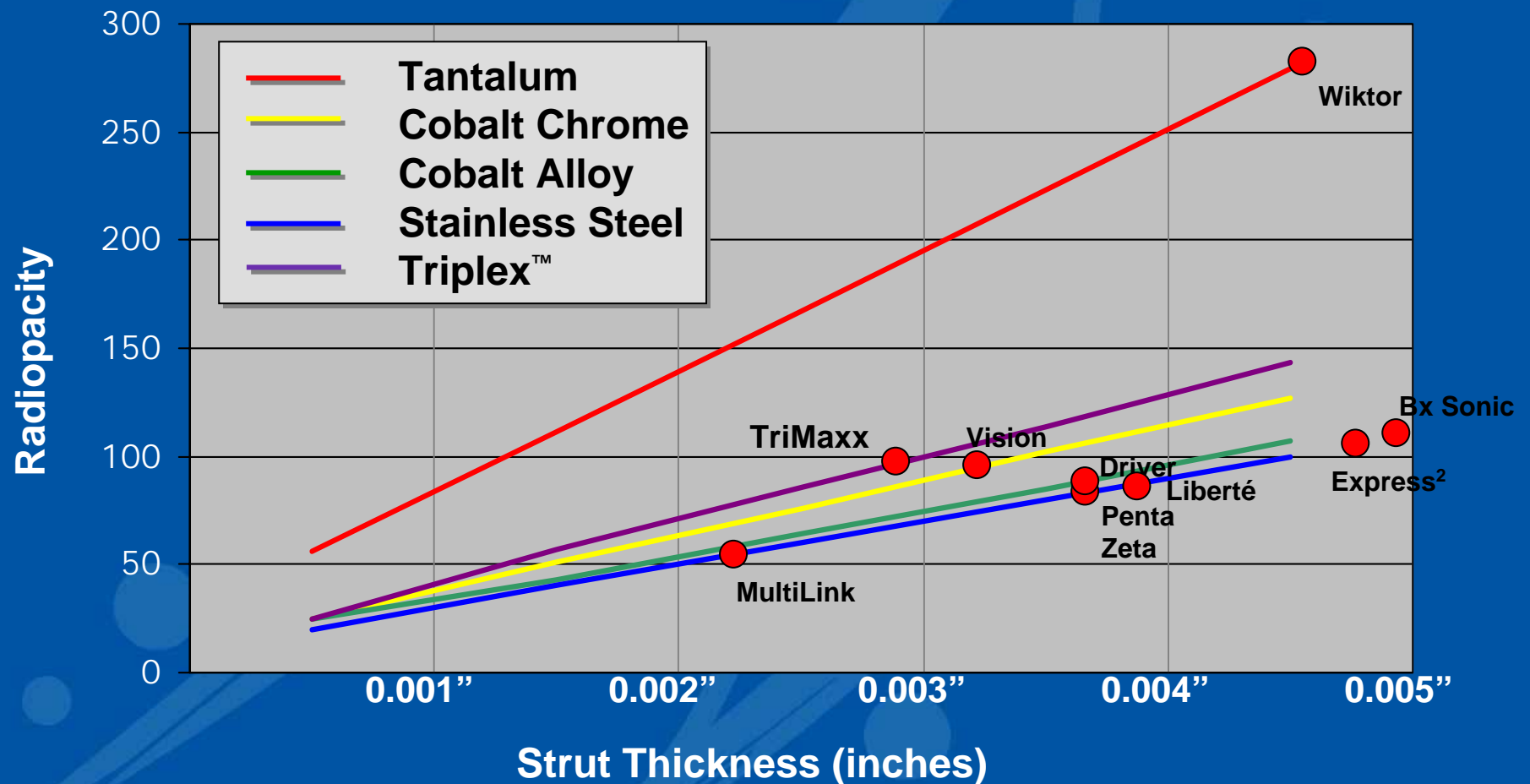
Stent Material and Strut Thickness



Driver is a trademark of Medtronic; Express² & Liberté are trademarks of Boston Scientific;
Vision is a trademark of Guidant; Bx Sonic is a trademark of Johnson & Johnson; Triplex is a trademark of Uniform Tubing, Inc.

Radiopacity

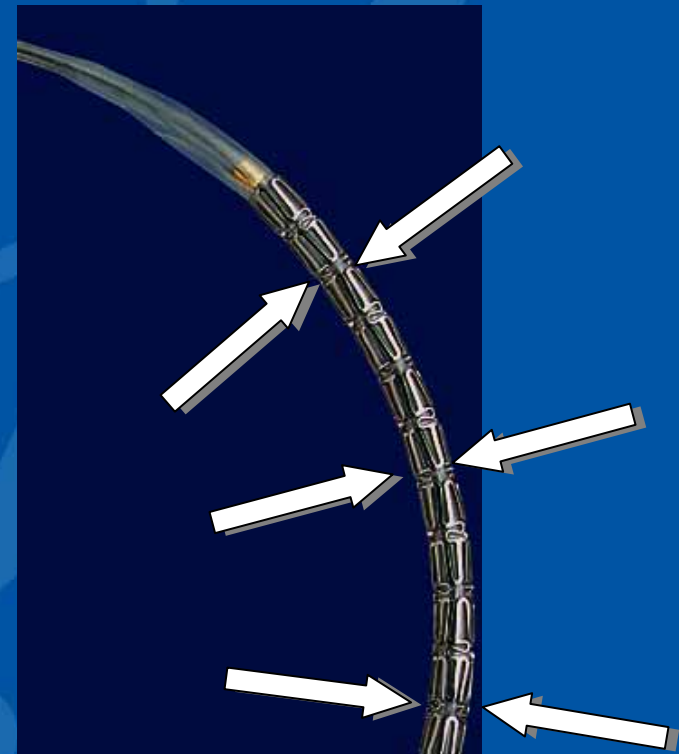
Strut thickness is less without sacrifice of radio-opacity



Driver is a trademark of Medtronic; Express² is a trademark of Boston Scientific;
Vision is a trademark of Guidant; Bx Sonic is a trademark of Johnson & Johnson; Triplex is a trademark of Uniform Tubing, Inc.

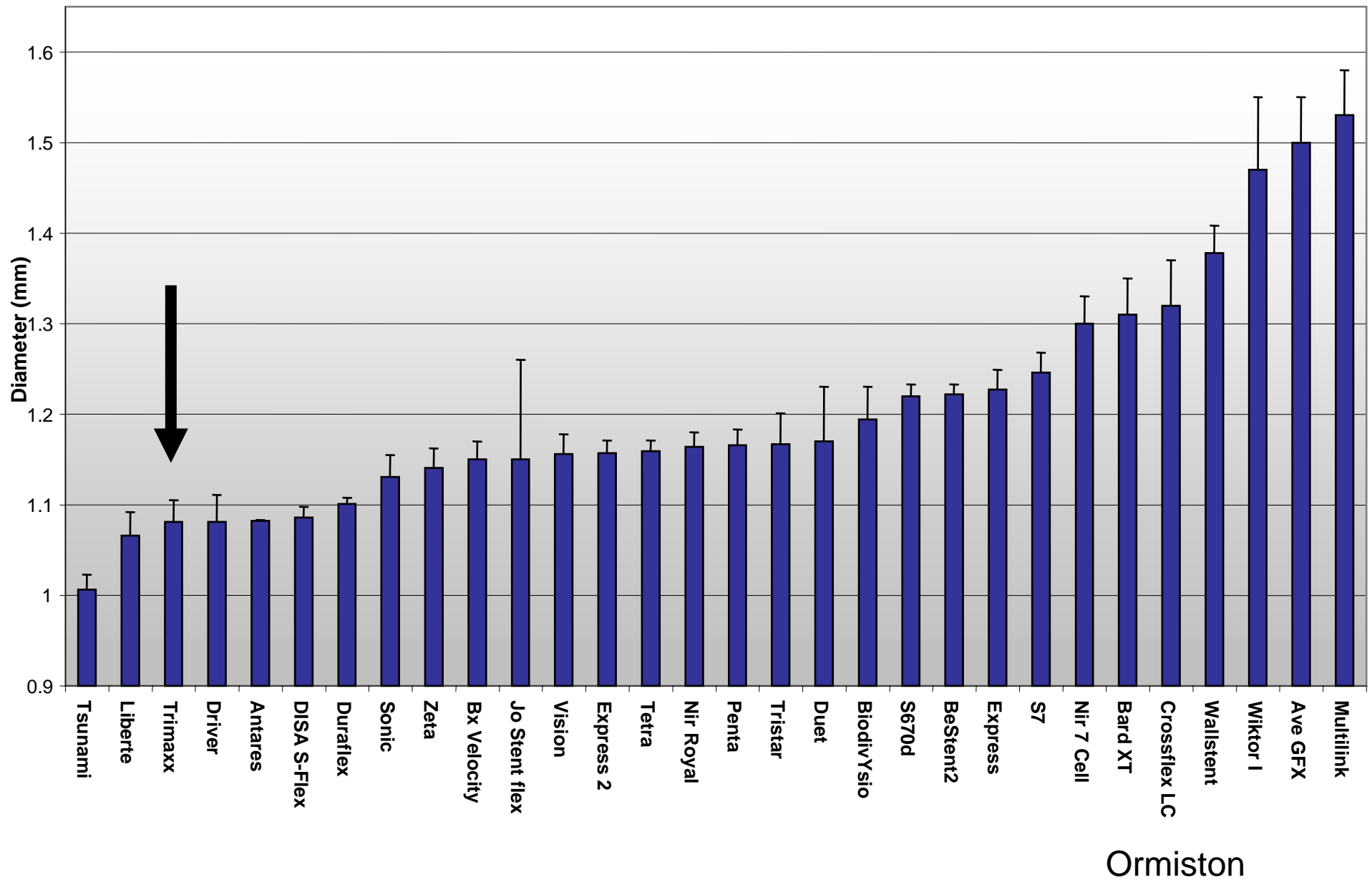
Independent Measurement of Stent/Delivery System Profile (Diameter)

- ❑ Calibrated travelling microscope
- ❑ 3 points along 3 examples of each stent/delivery system

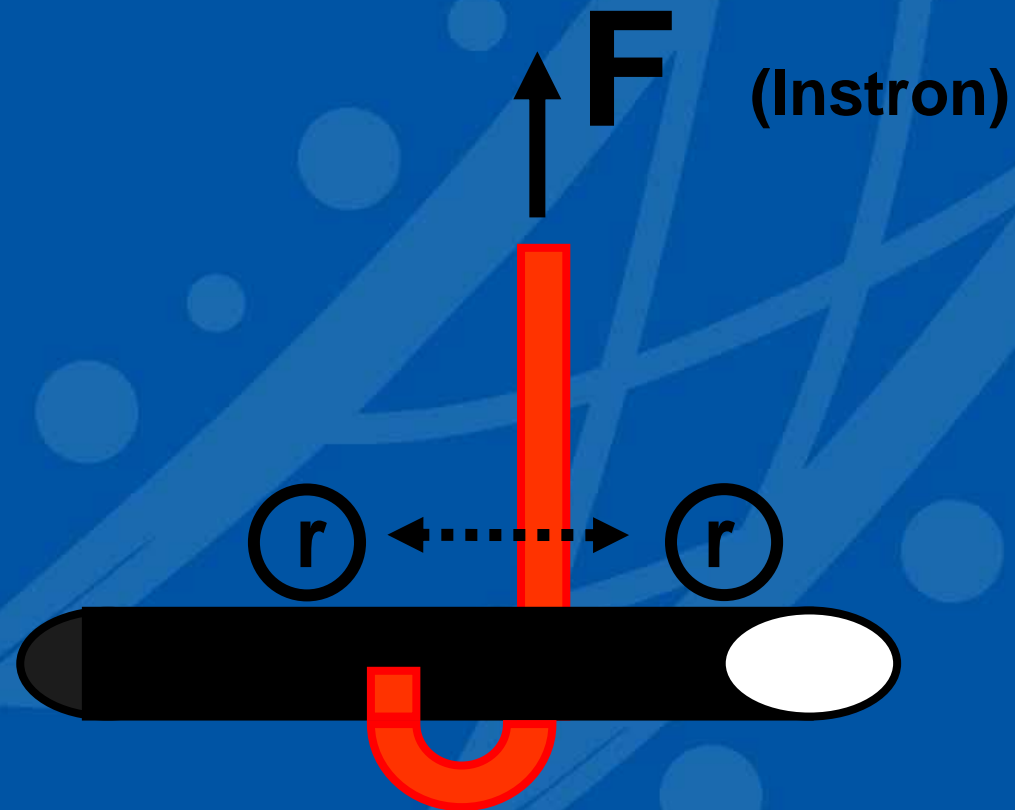


Ormiston CCVI 2000

Stent Delivery System Crossing Profile

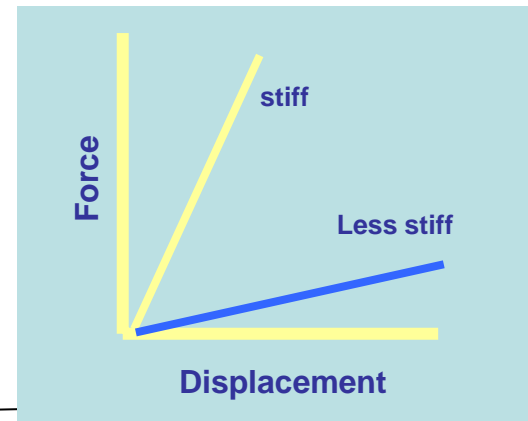


Stiffness was measured using a 3 point bend test



*Ormiston Cathet Cardio
Interv 2000*

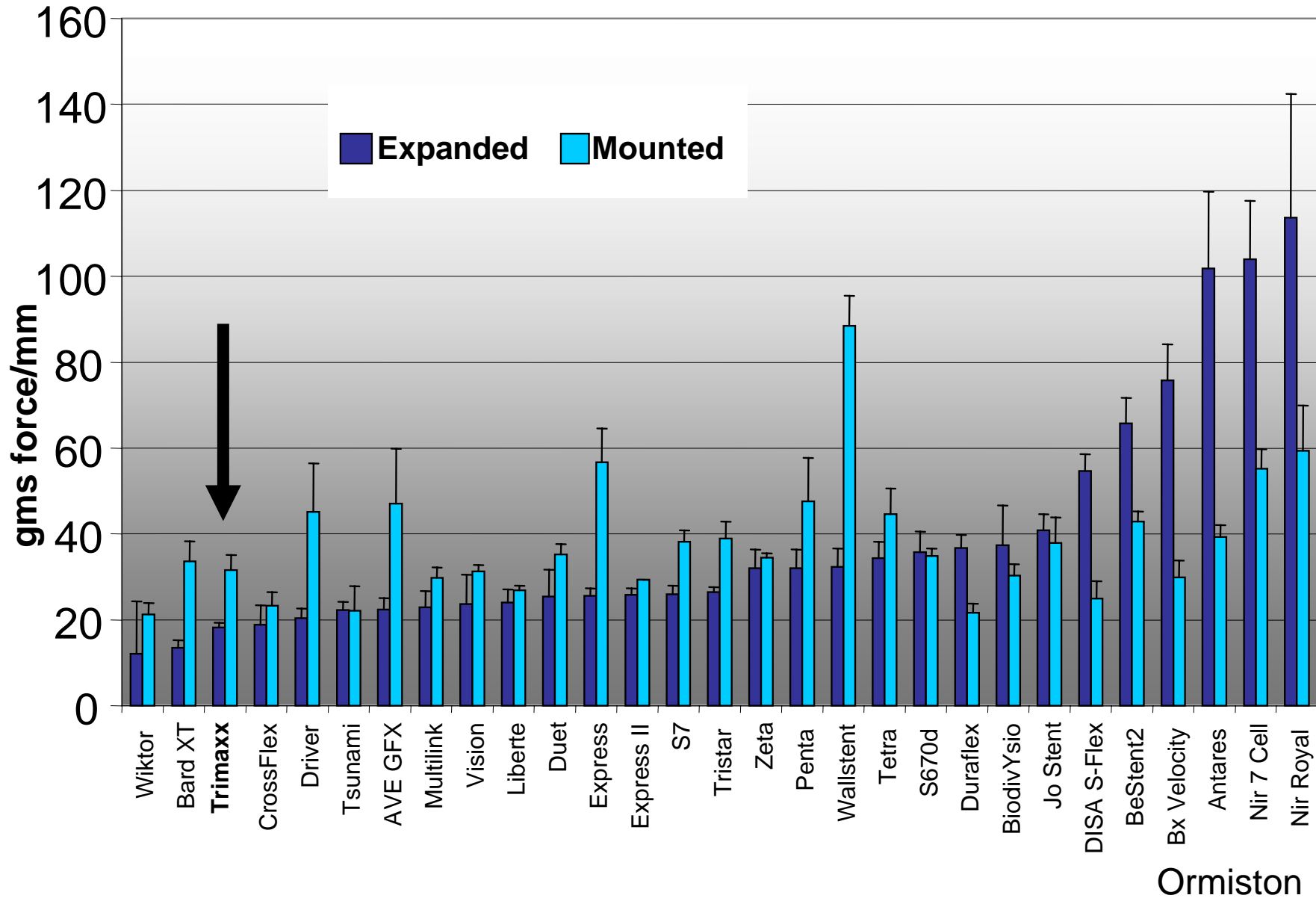
The slope of the Force/Displacement curve is Stiffness



Stiffness is the reciprocal of Flexibility

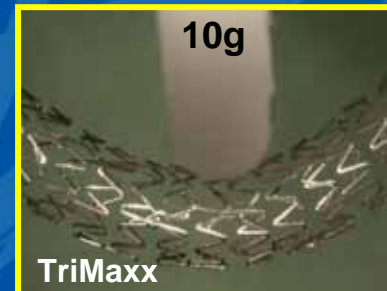
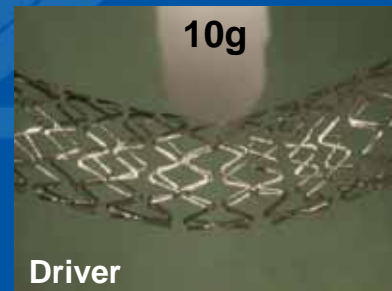
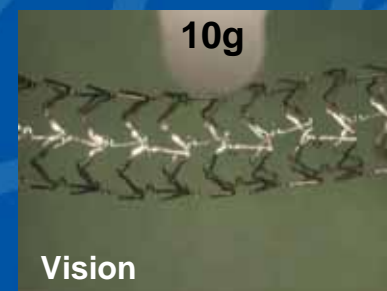
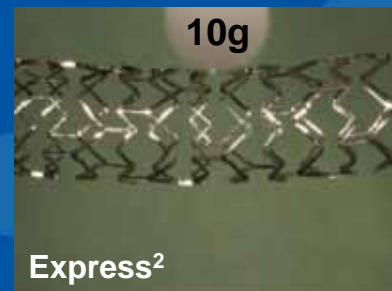
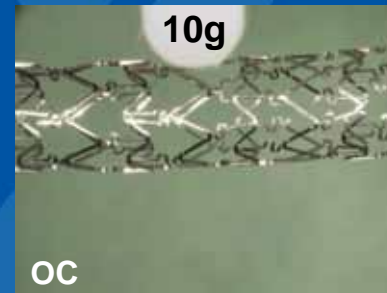
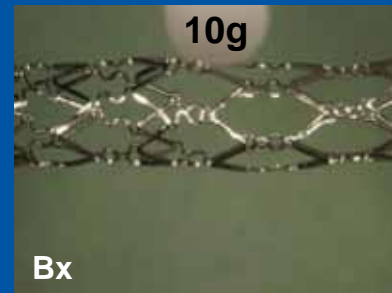
$$\text{Flexibility} = \frac{1}{\text{stiffness}}$$

Stiffness (reciprocal of flexibility)



Stent Flexibility

In Vitro Bench Testing



Driver is a trademark of Medtronic; Express² is a trademark of Boston Scientific;
Vision is a trademark of Guidant; Bx Sonic is a trademark of Johnson & Johnson

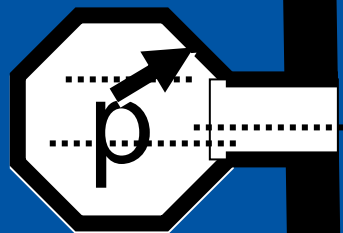


Data on file at Abbott Vascular Devices

Stent radial strength is needed especially in calcified, fibrotic, or ostial lesions to:

- Resist compressive forces
- Maintain size
- Maintain circular shape

PRESSURE CHAMBER



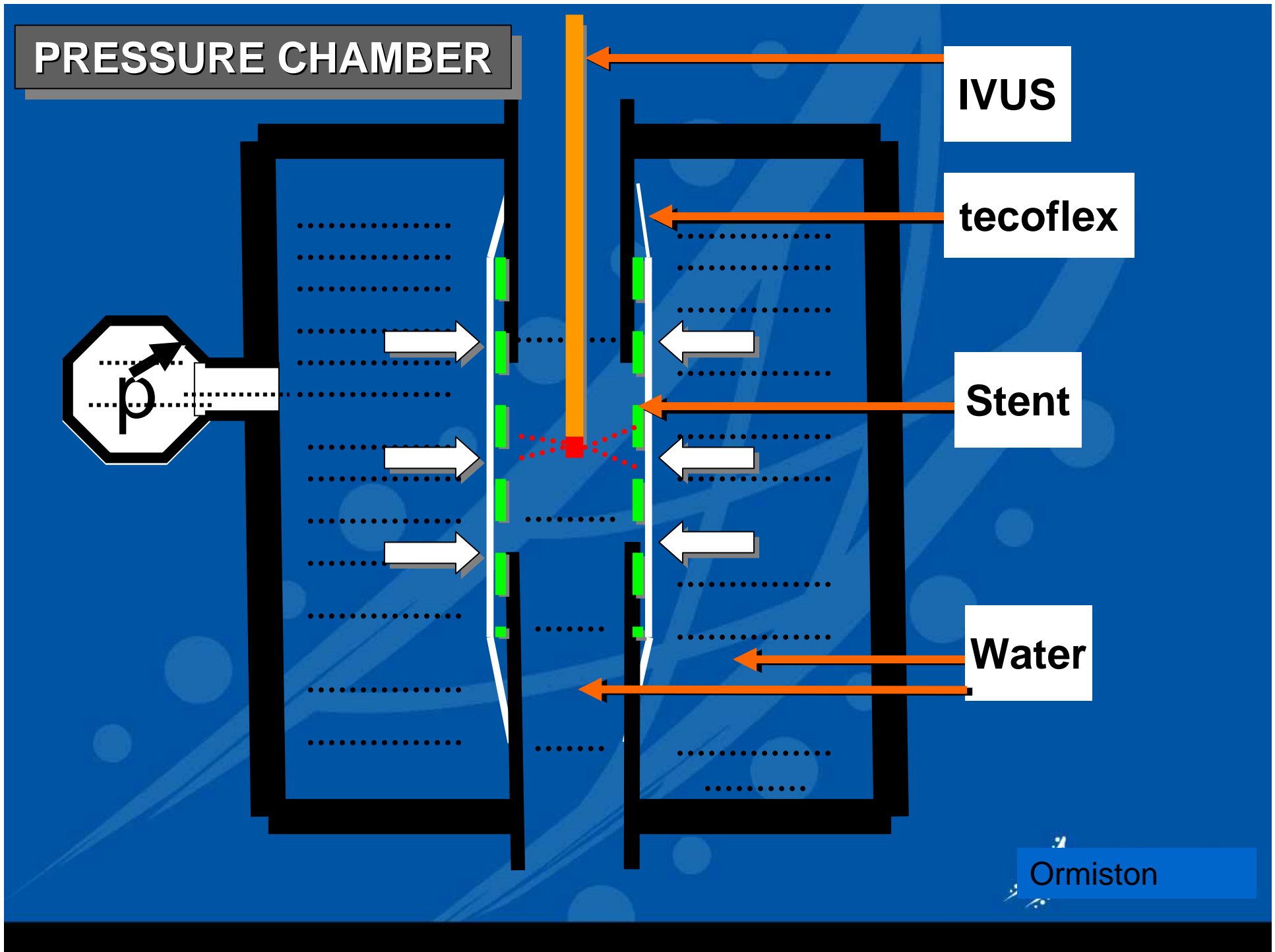
IVUS

tecoflex

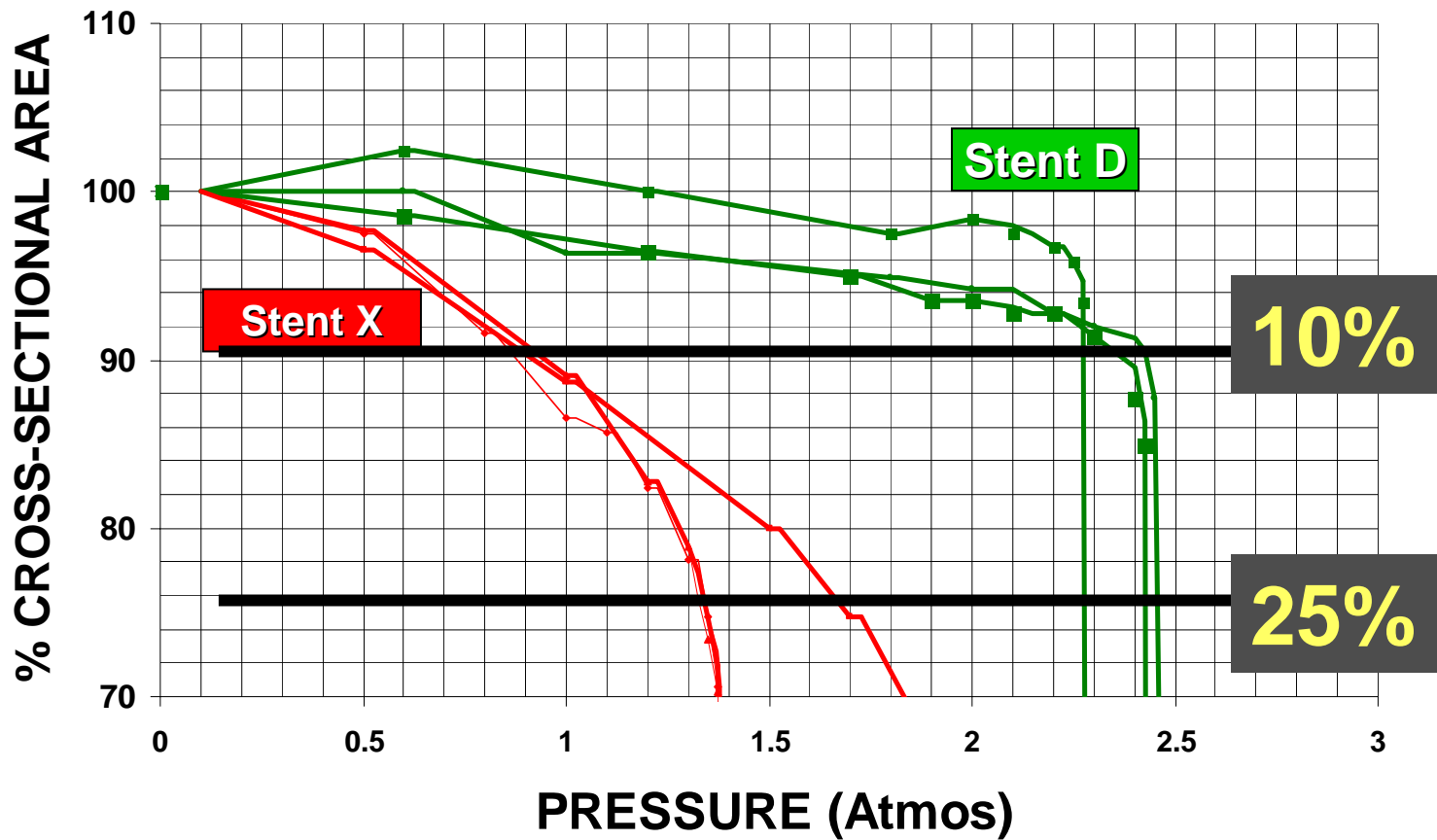
Stent

Water

Ormiston

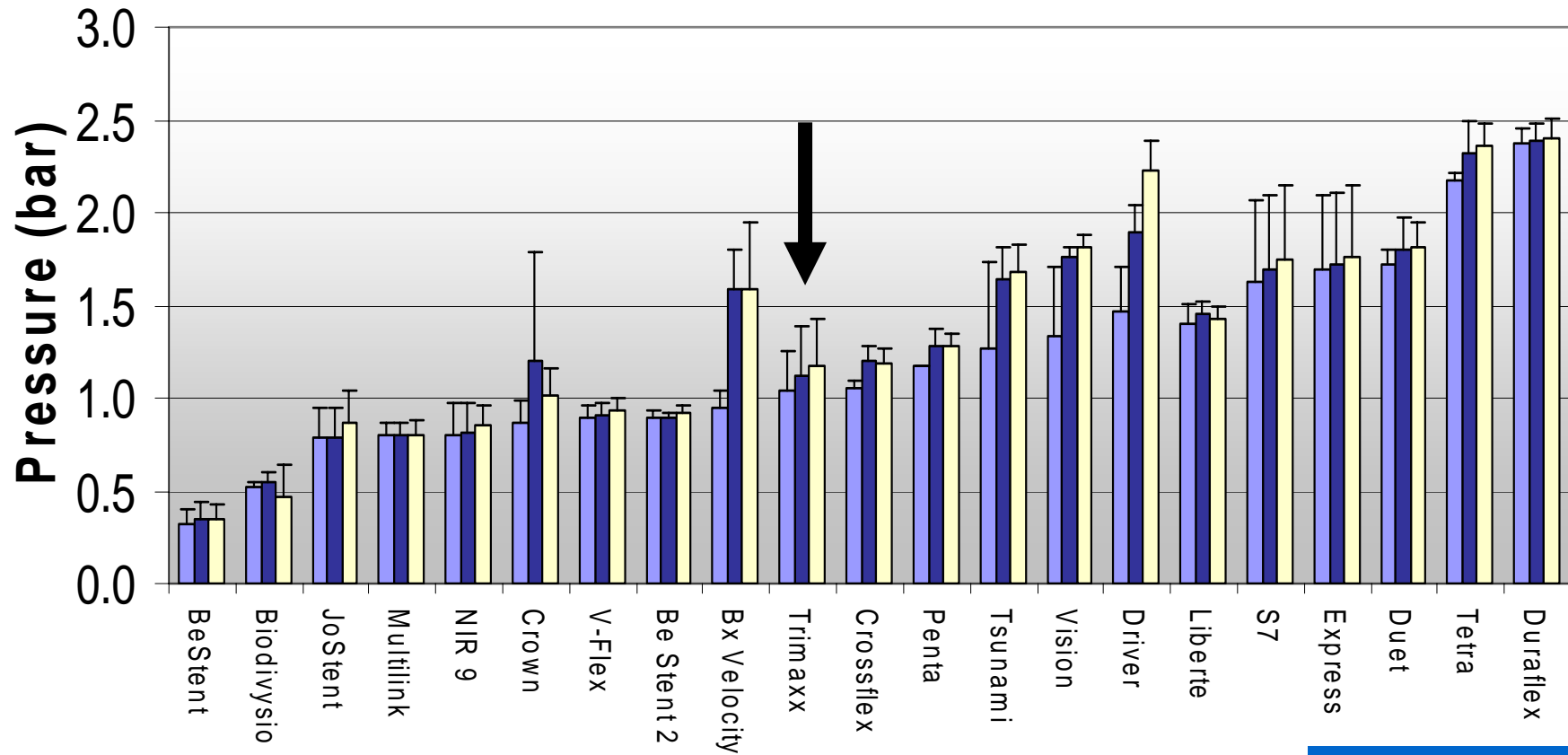


% AREA and EXTERNAL PRESSURE (IVUS on benchtop)



Radial Strength: External Pressure and Stent Cross-sectional Area Reduction

Mean 10% Mean 25% Collapse



Is the Zomaxx Stent Platform suitable for Bifurcation stenting in the DES era?

- Stents were deployed in a phantom using contemporary bifurcation techniques
- Stents were photographed externally and internally

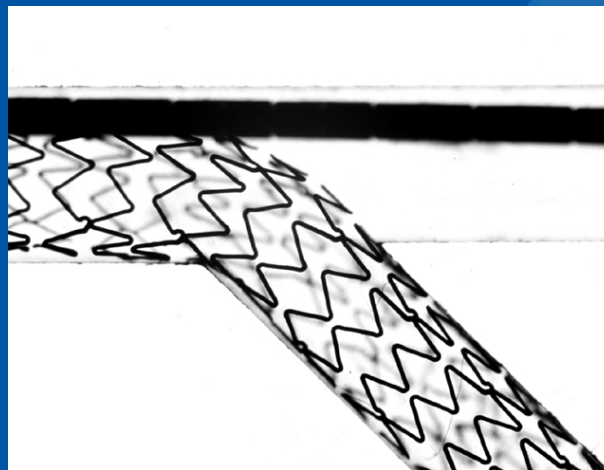
"Crush" Technique with Zomaxx



Main br

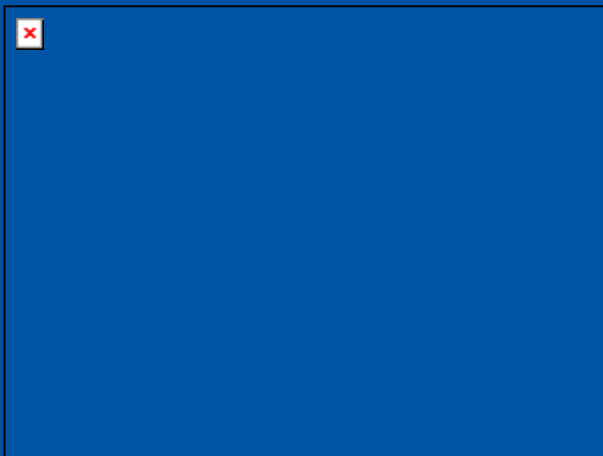
Side br

"Crush" Technique with Zomaxx



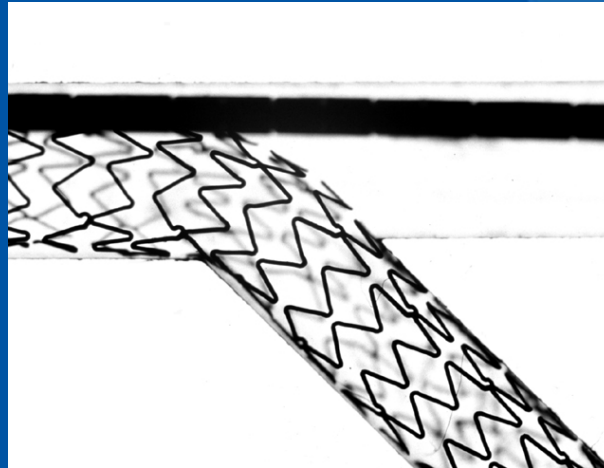
Deploy
side-br
stent

"Crush" Technique with Zomaxx

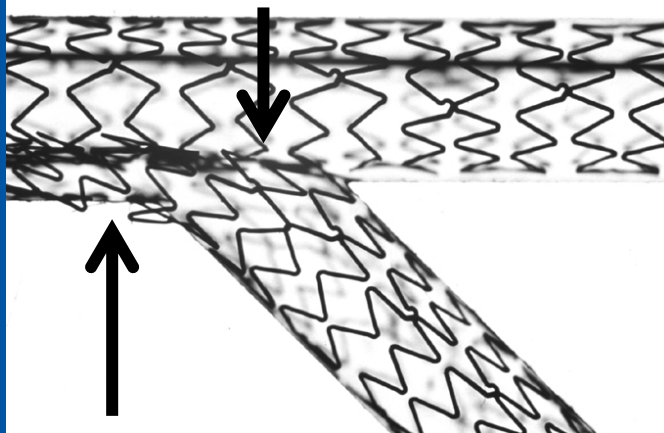


Deploy main br
stent crushing
side-br stent in
main br

"Crush" Technique with Zomaxx



2 layers

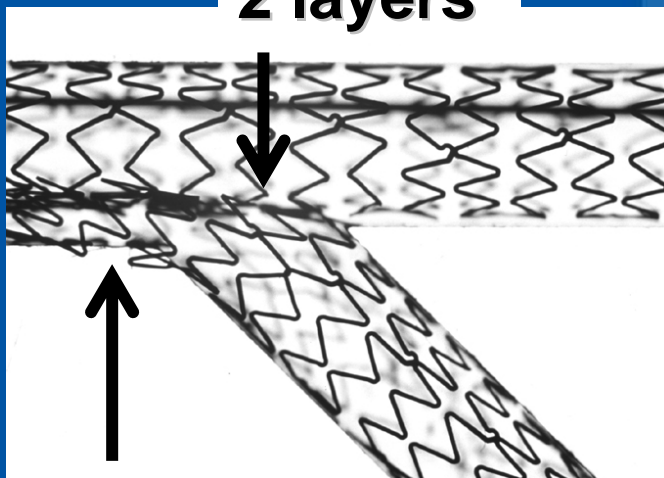


3 layers

"Crush" Technique with Zomaxx



2 layers

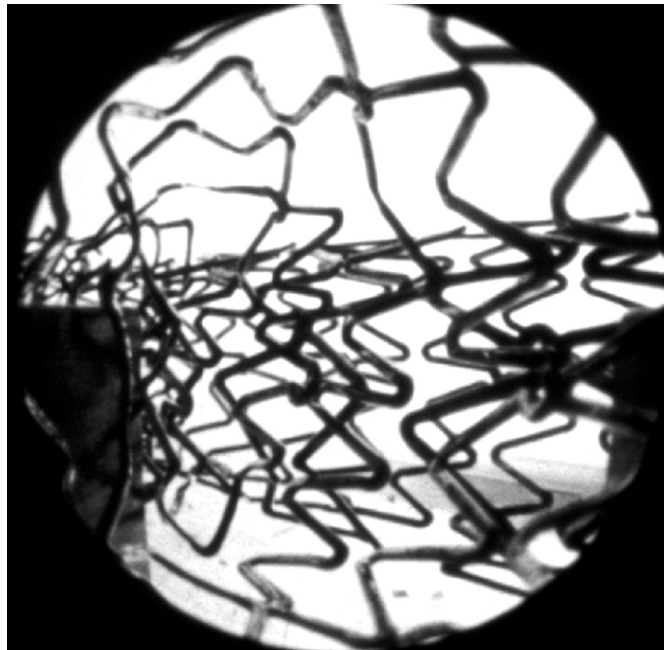
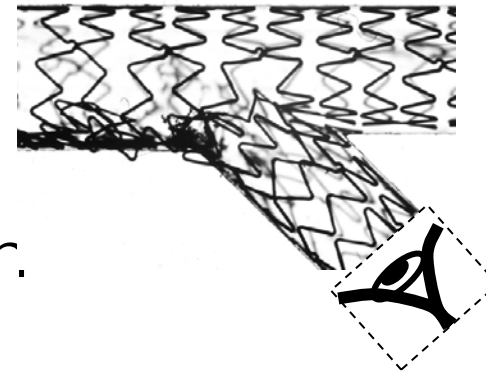


3 layers

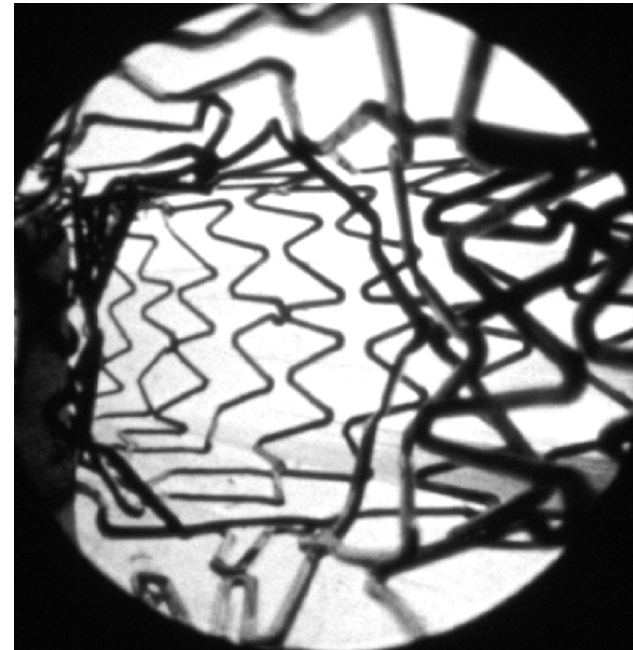


"Kissing" balloon
post-dilatation

Kissing balloon post-dilatation releases the side-branch from "jail" after "Crush" Bifurcation. Stenting



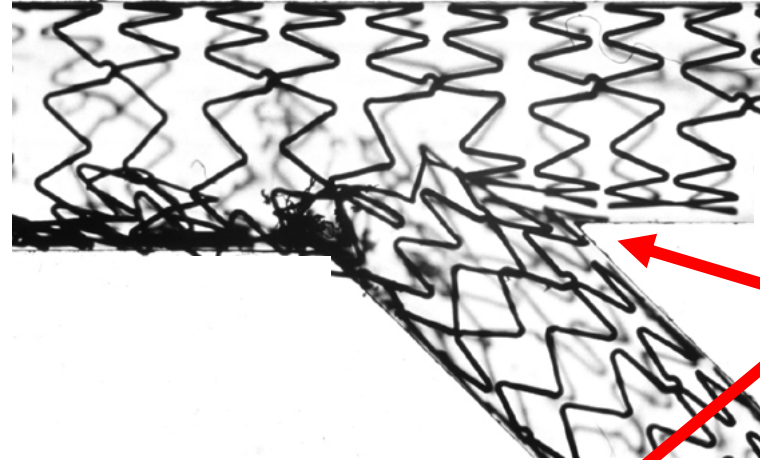
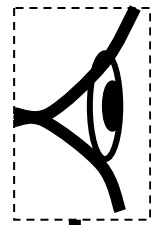
Before "kiss"
Side-br jail



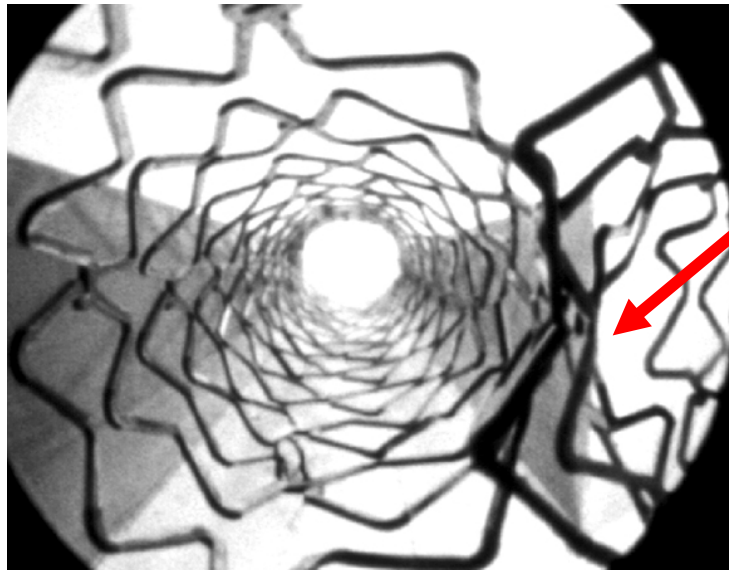
After "kiss"
No Side br jail

Ormiston

“Kissing” balloon post-dilatation after “crush” fully expands the Zomaxx stent at the side-br ostium and corrects any main br distortion



Well expanded at side-br ostium



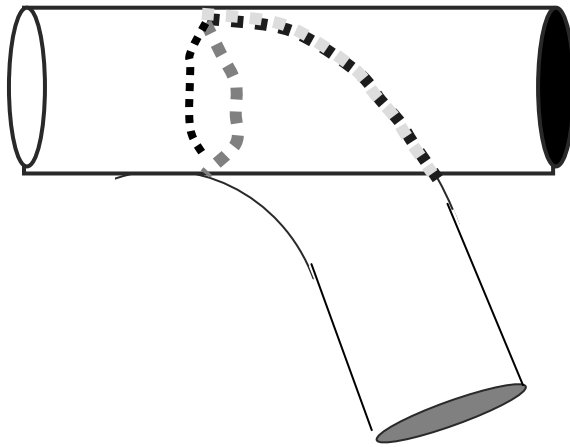
No obstruction to main br

No Side br jail

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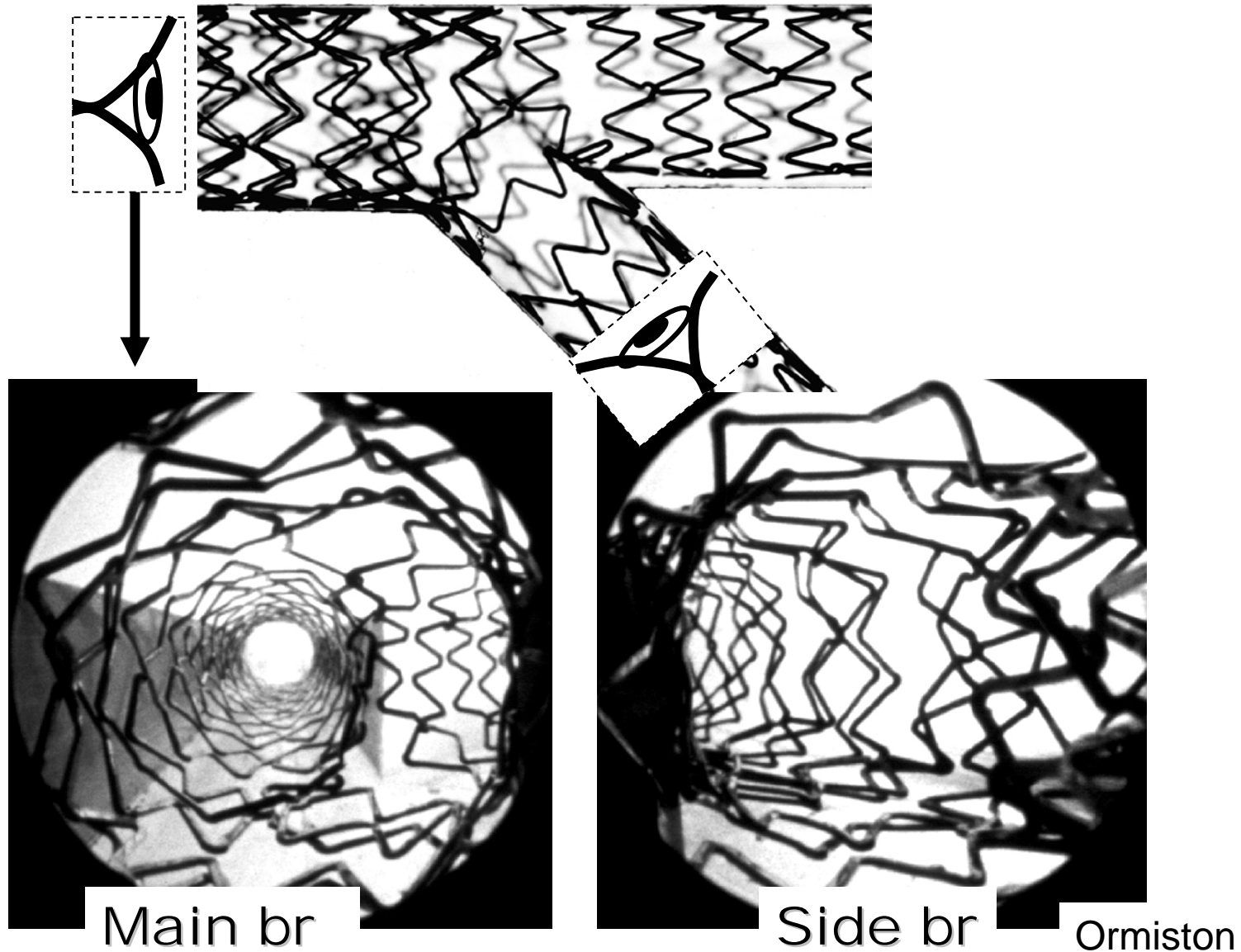
The "Culotte" Technique-

Provisional side-br stenting in the DES era

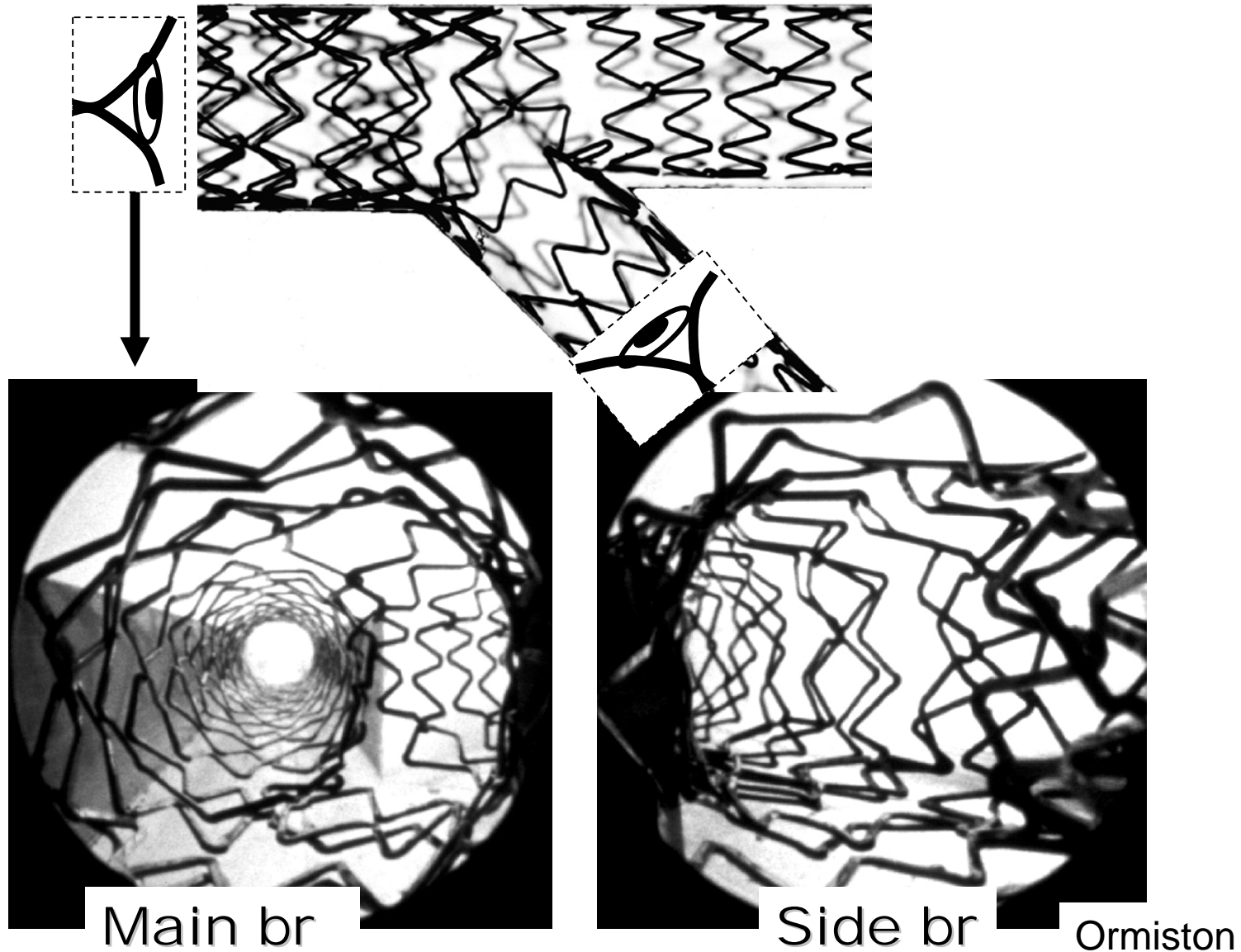


Ormiston 04

Trimaxx Stent after "Culotte" Bifurcation followed by "kissing" balloon post-dilatation



Trimaxx Stent after "Culotte" Bifurcation followed by "kissing" balloon post-dilatation

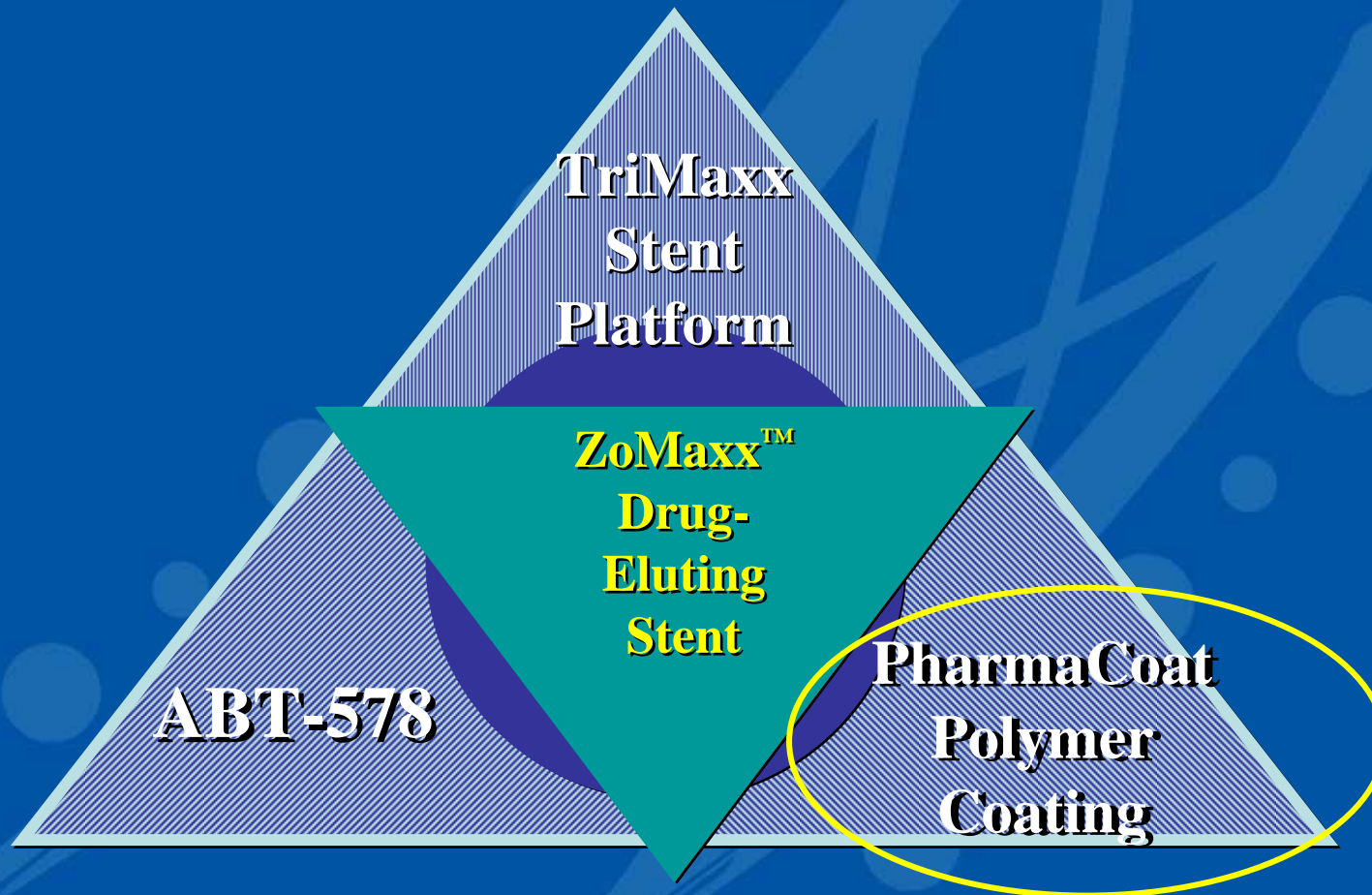


Trimaxx Trial (BMS)

- 100 patients to receive Trimaxx (BMS)
- Single-vessel, *de novo* coronary lesions (Type A-B), length ≥ 10 mm and ≤ 15 mm; RVD 3.0-3.75 mm
- Brazil, Germany
- PI: Alex Abizaid
- Primary Endpoint: MACE at 30 days
- Secondary Endpoints: MACE, TLR, TVR, ABR, Late Loss at 6 months



ZoMaxx Drug-Eluting Stent

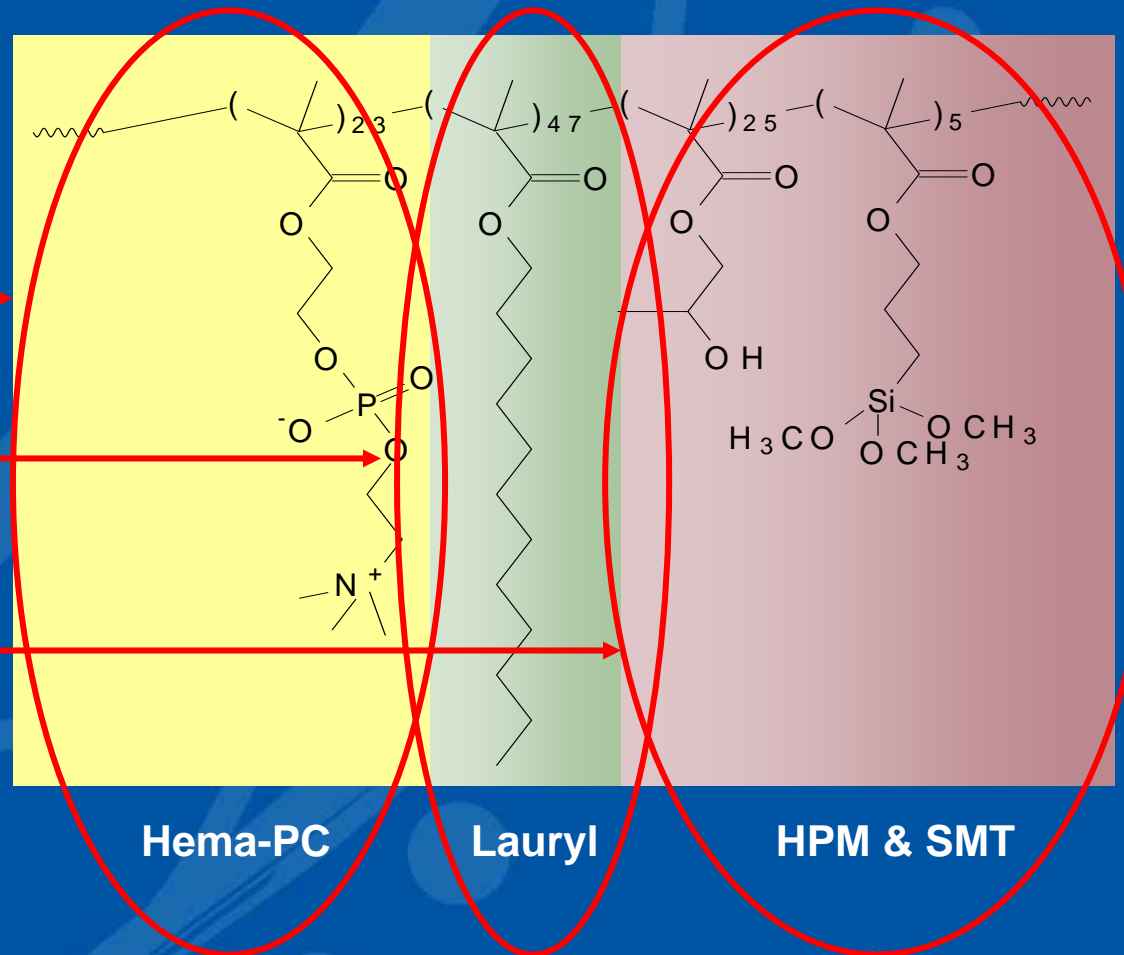


Polymer- PC Technology™

- **PC Technology™ mimics body's own chemistry**

- Hema-PC: Mimics outer membrane of red blood cell for biocompatibility
- Lauryl: Hydrophobic for stability and adhesion to the stent surface
- Hydroxypropyl Methacrylate (HPM) & Trimethoxysilyl Methacrylate (SMT): Cross-linking for durability

- **Following drug elution, PC coating remains bio-inert and non-inflammatory**

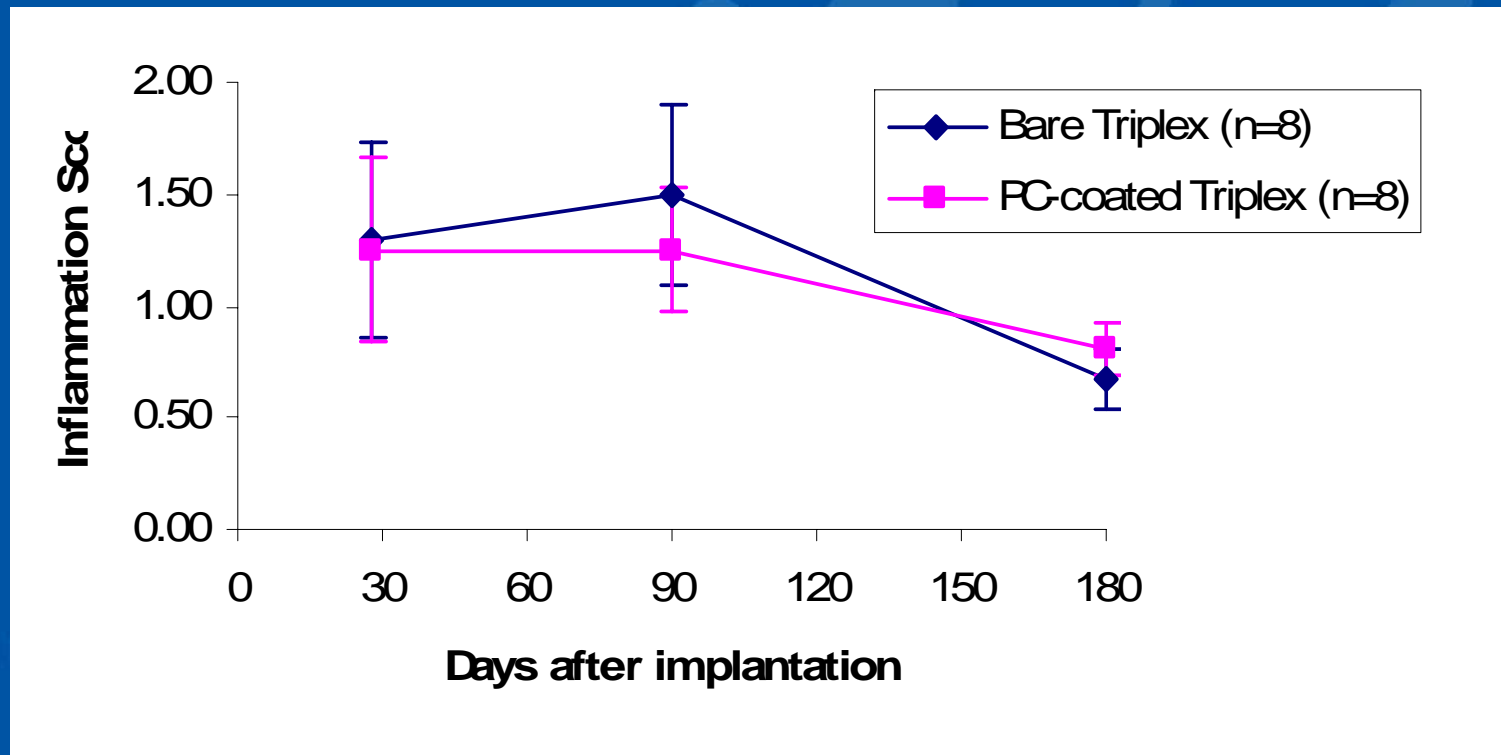


PC Technology is a trademark of Biocompatibles, Inc.

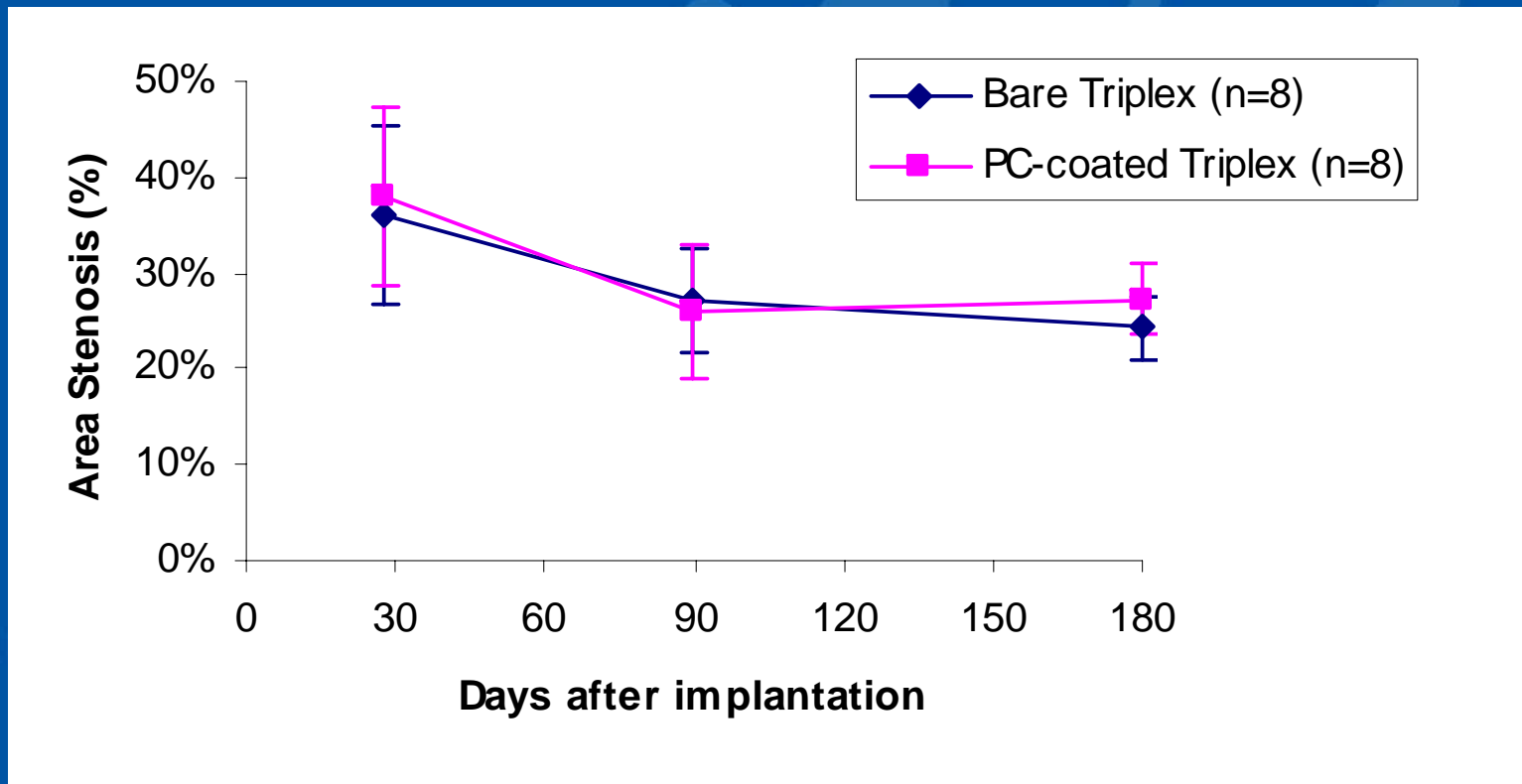
Presented by N. Chronos, TCT 2004, Washington, DC



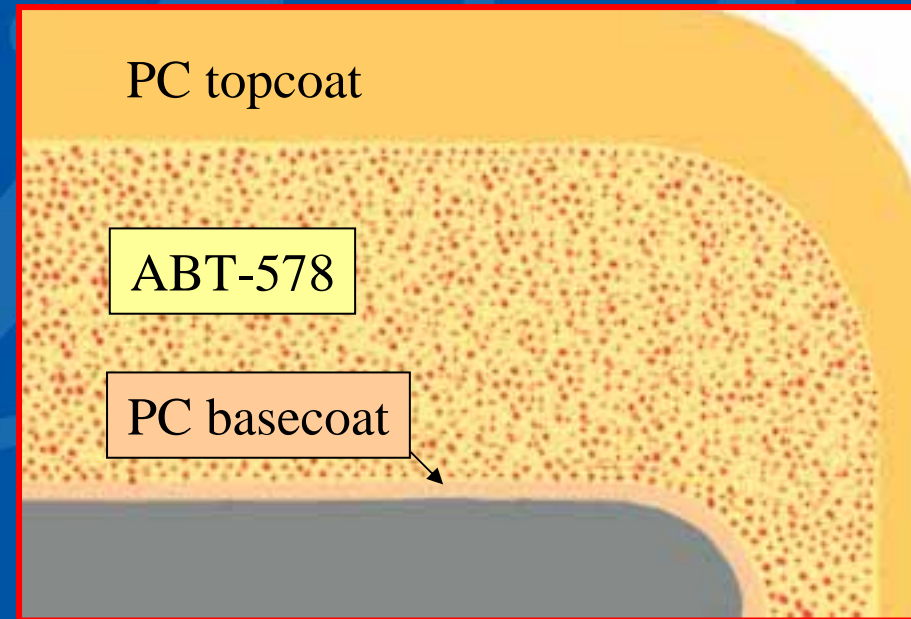
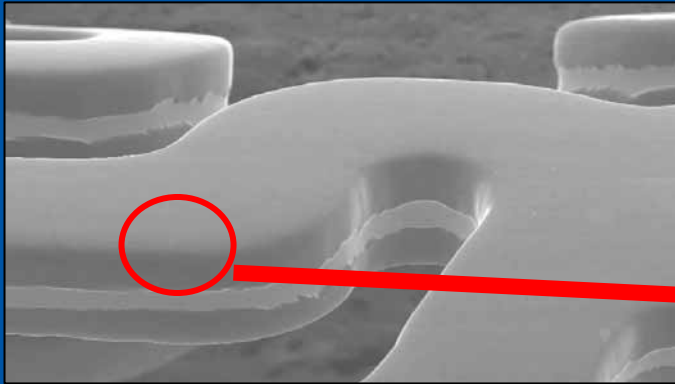
Effect of PC coating on Inflammation in Porcine Coronary arteries



Effect of PC coating on Neointimal Hyperplasia in Porcine Coronary Arteries



The ZoMaxx Stent - PharmaCoat

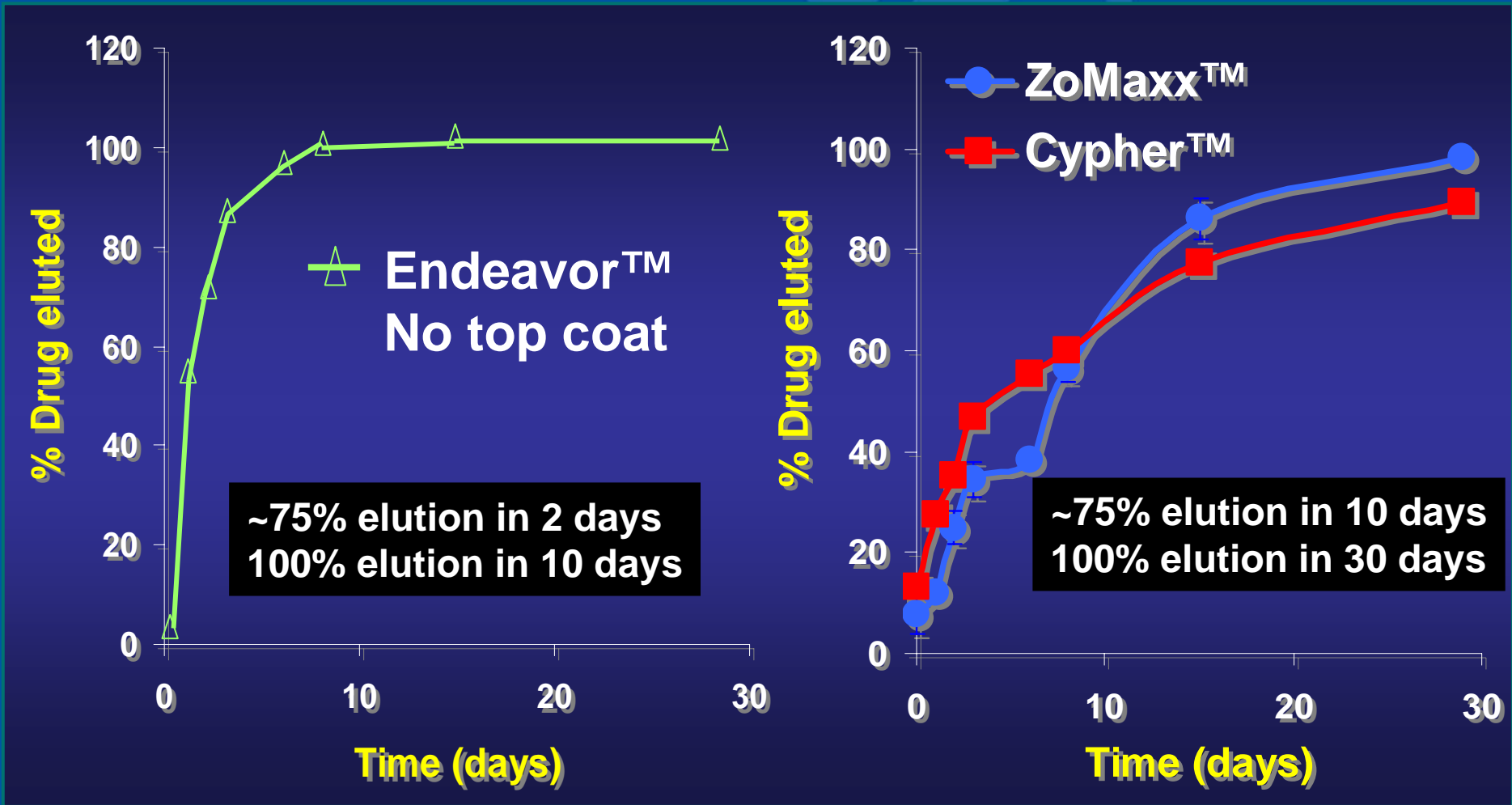


Not approved for sale in or
outside the United States.

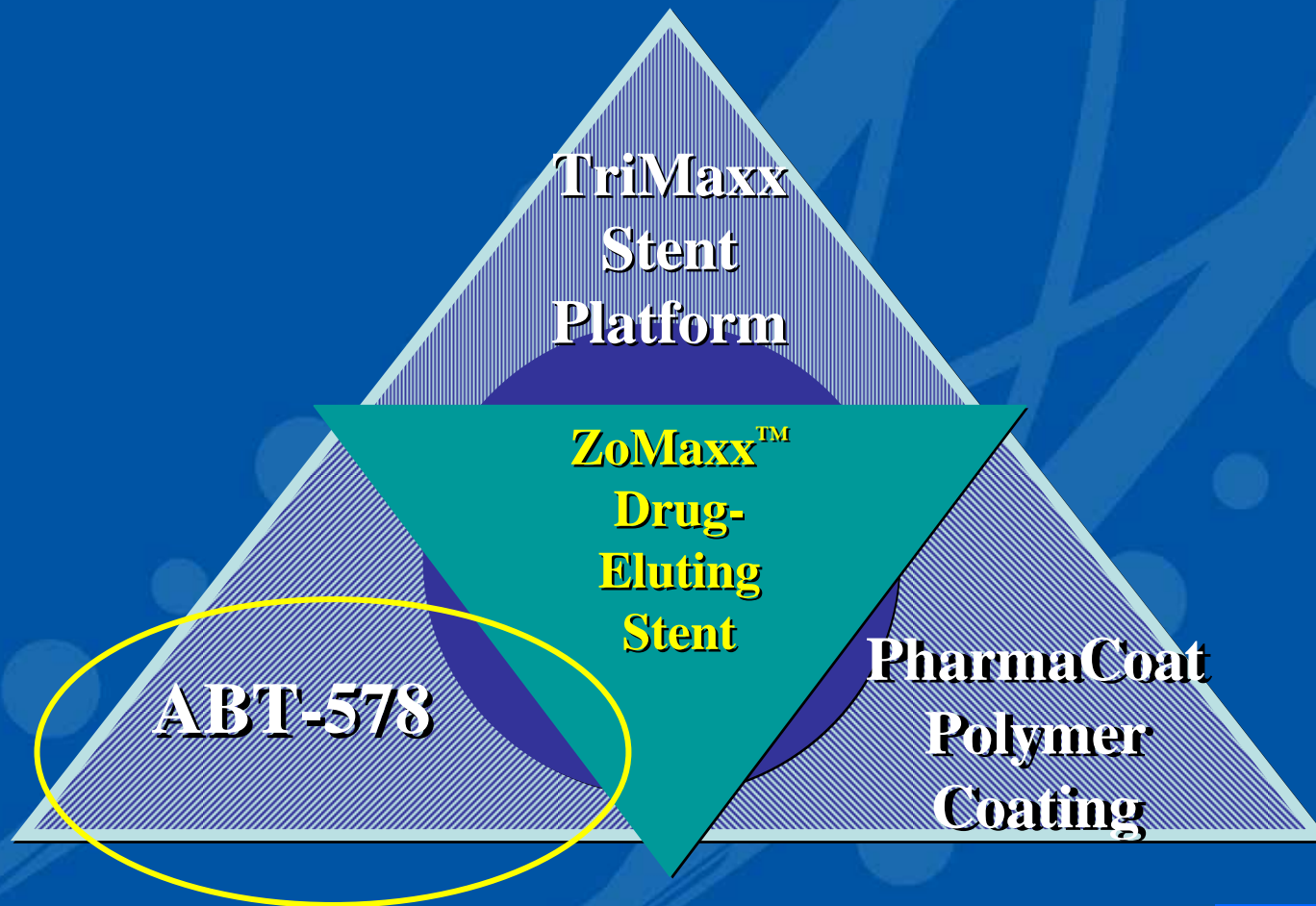


Comparison of *in vivo* Elution Rates

Rabbit iliac models

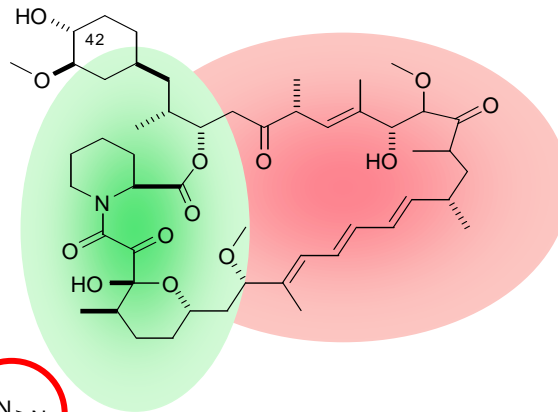


ZoMaxx Drug-Eluting Stent



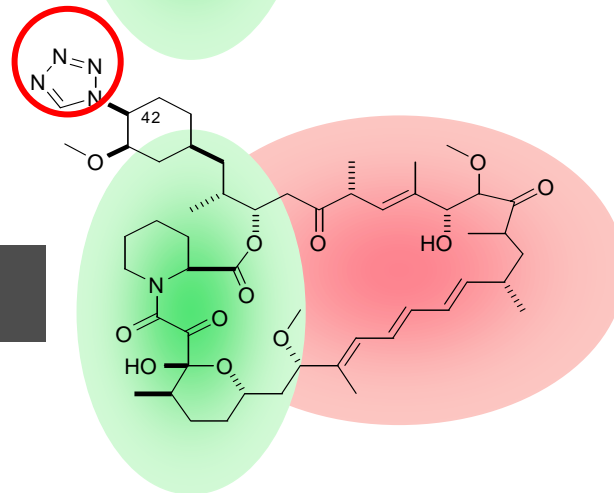
ABT 578 is different from rapamycin due to Tetrazole group on C42

Rapamycin



Tetrazole ring at C42

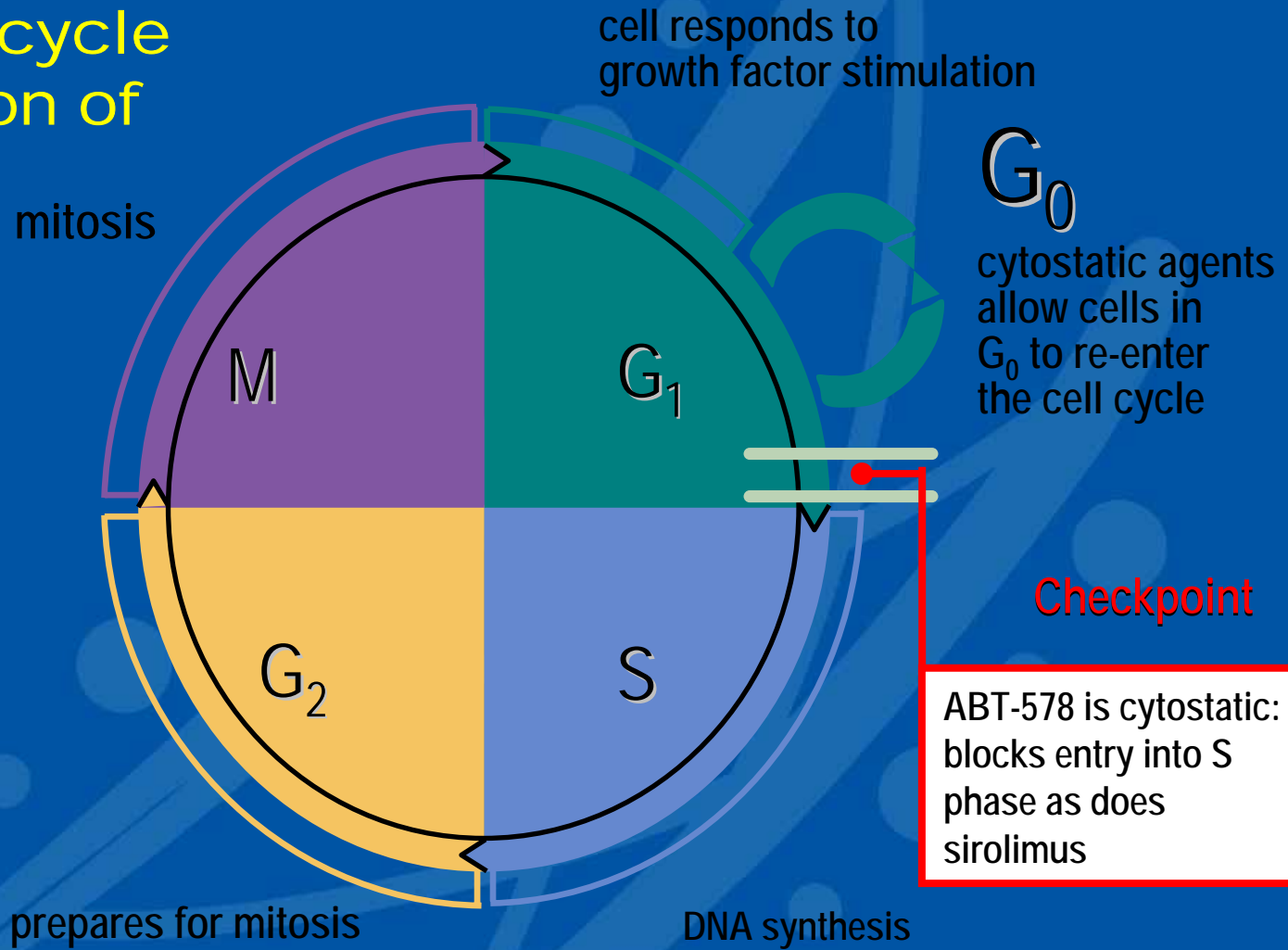
ABT 578



↑
FKBP Binding
Domain

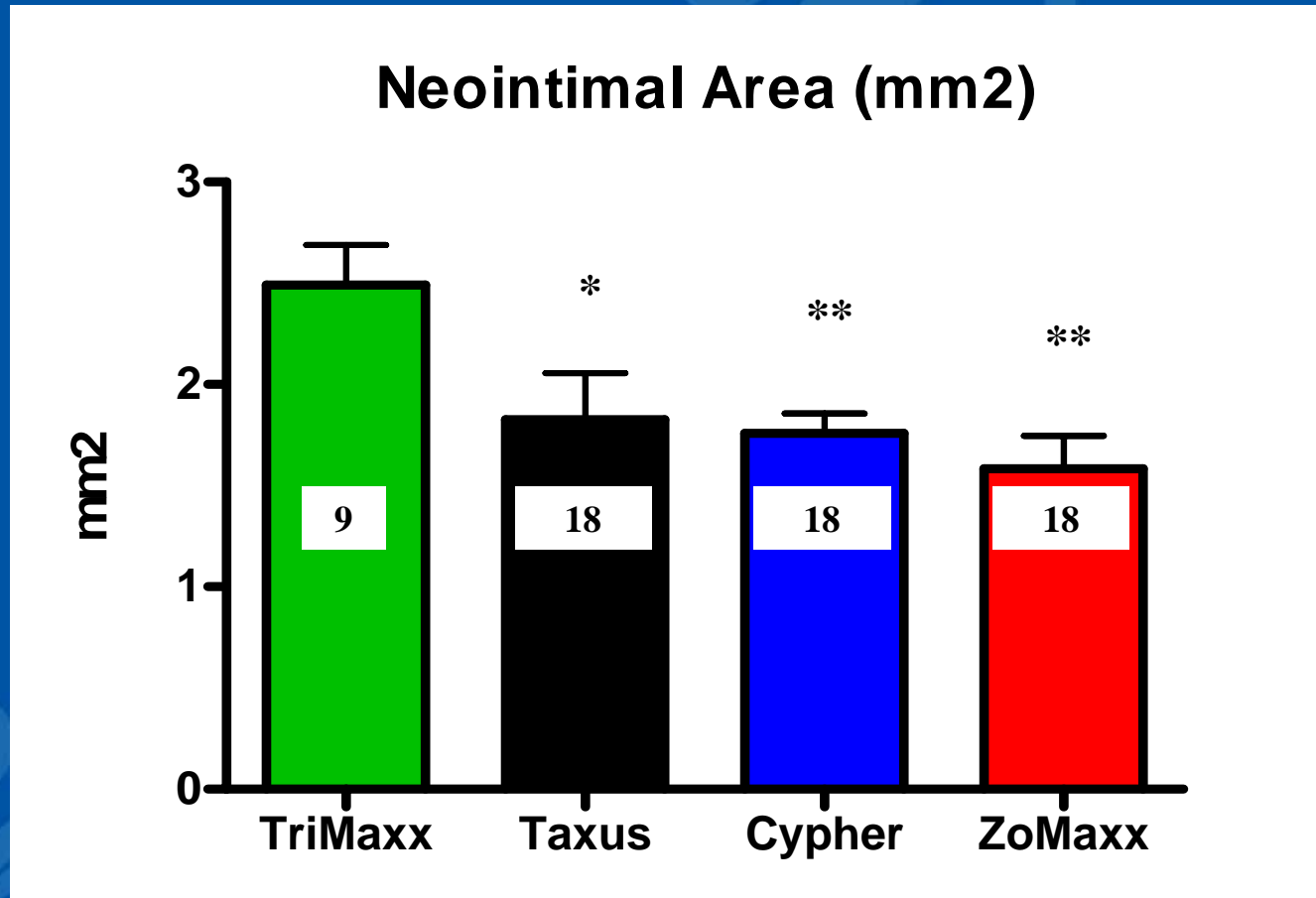
↑
mTOR Effector
Domain

The cell cycle and action of ABT 578



- ❑ **Delivered locally, ABT-578 inhibits inflammation and the proliferation of SMCs**
- ❑ **ABT-578 is cytostatic by halting the cell cycle in the late G_1 phase**

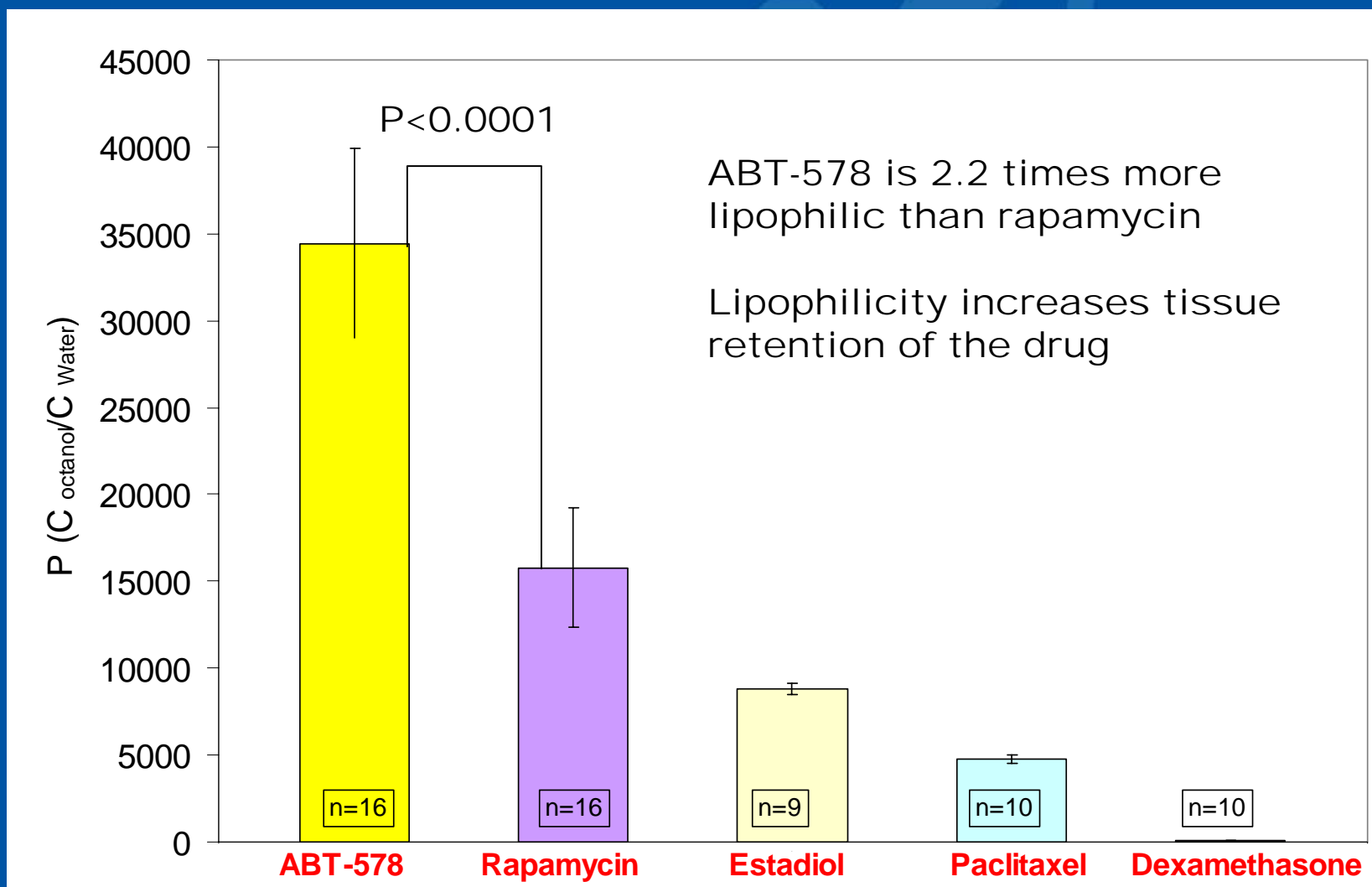
Effect of TriMaxx, ZoMaxx, Cypher, and Taxus Stents on Swine Coronary Morphometry at 28 days (mean \pm SEM)



*p<0.05 vs. TriMaxx

**p<0.01 vs. TriMaxx

Lipophilicity of Some Clinical DES Agents

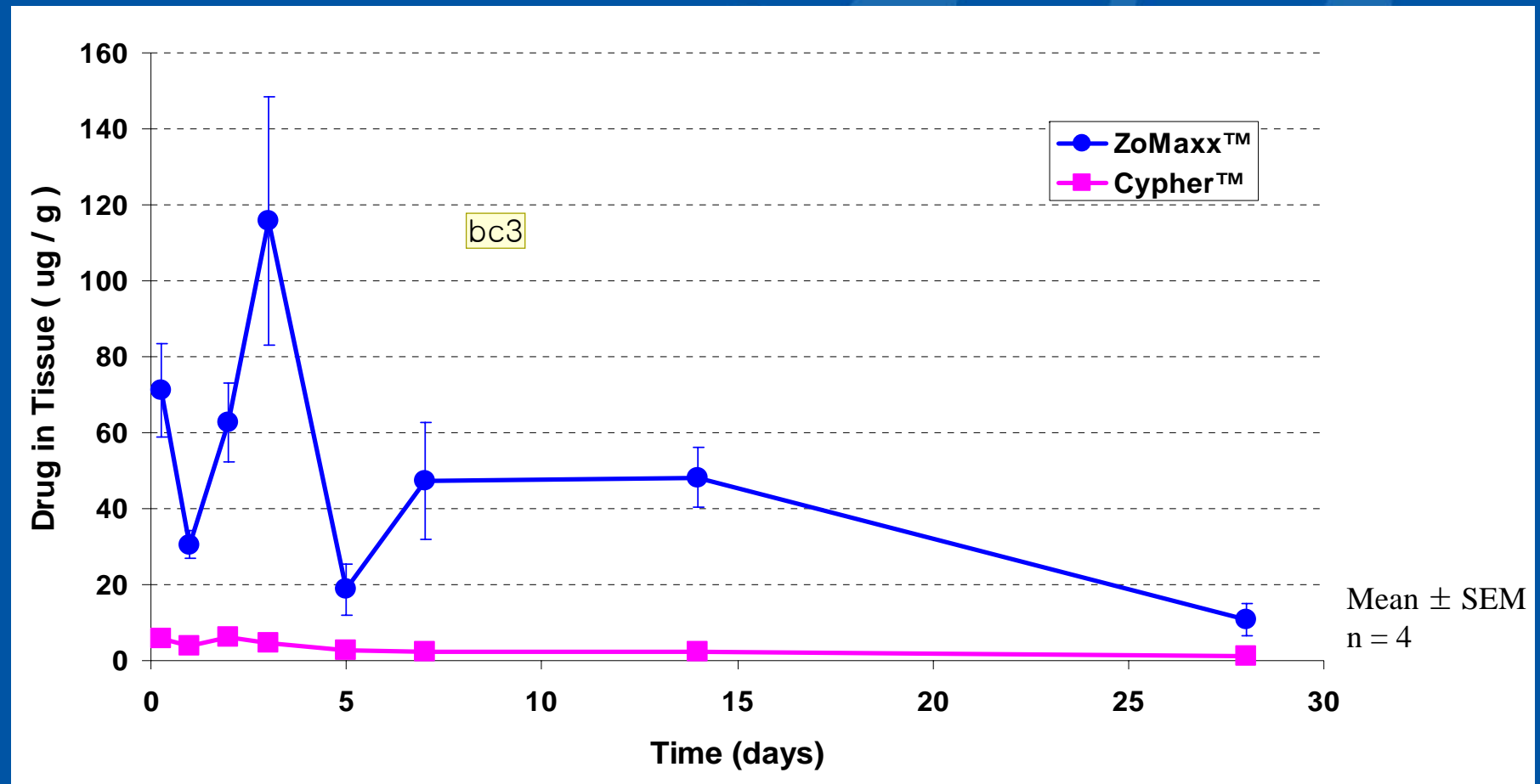


Determination of Partition Coefficients for ABT-578, Rapamycin, Paclitaxel, Dexamethasone, and Estradiol at 22 deg C, Abbott Laboratories Report on File, 2004



Rabbit Study - Preliminary results

Comparison of Drug Levels in Arterial Tissue for ZoMaxx Stent versus Cypher Stent



bc3

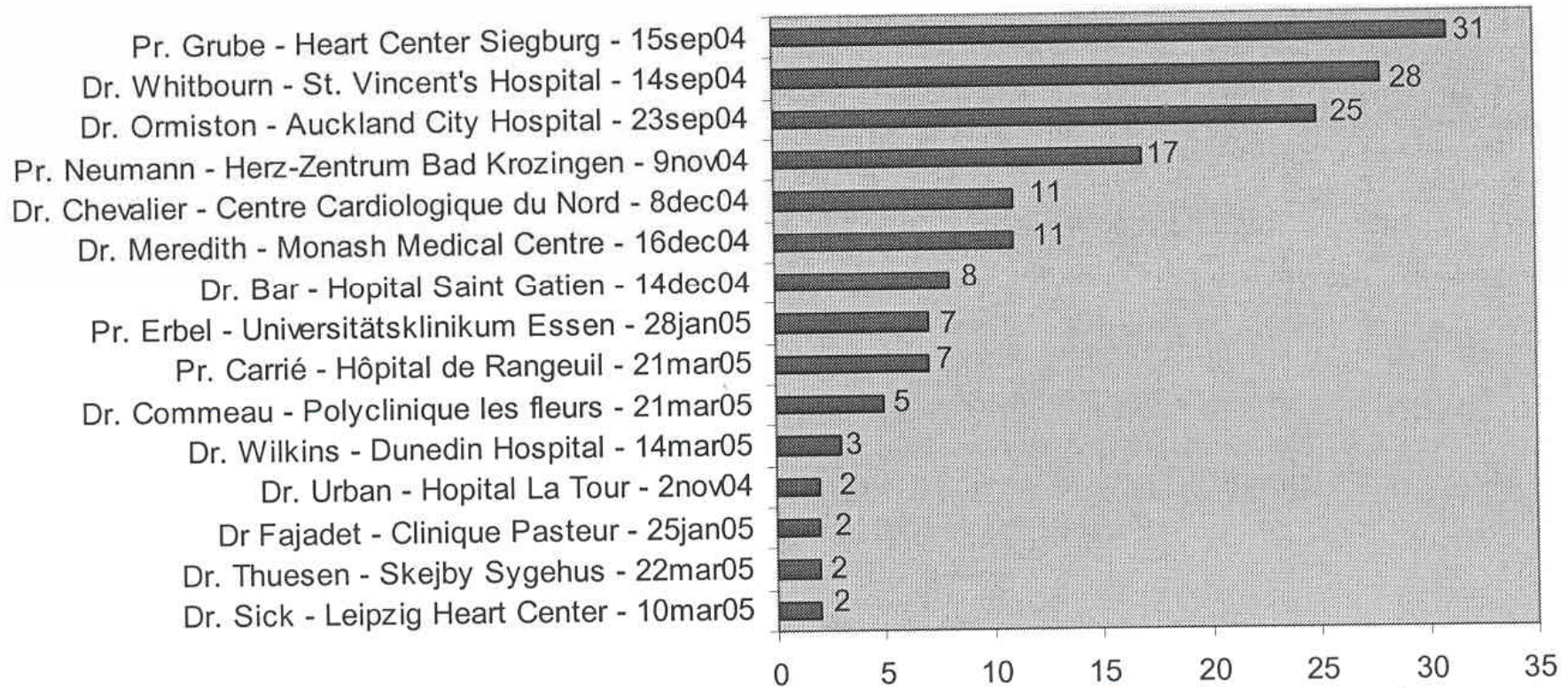
the ratio between abt and sirolimus uptake in the first 4 days is around 10:1, are we sure that is safe?
Bernard, 2004-05-12

Zomaxx I Trial

- 400 patients to be randomized to receive either a Zomaxx stent or a Taxus stent
- Non-inferiority trial
- Primary end-point is late loss 9 month angio
- Single de novo lesions
- **≥ 10 mm and ≤ 30 mm, RVD 2.5-3.5 mm**
- 35 sites New Zealand, Australia, Europe
- PI Bernard Chevalier



161 of 400 pts enrolled as of 15.4.05



Zomaxx II Trial

- 1670 patients will be randomized to receive either a Zomaxx stent or a Taxus stent
- Non-inferiority trial
- Primary end-point is TVR
- Single de novo lesions
- 75 sites USA and Canada



ZOMAXX I and II Core labs

Data Center

- Harvard Clinical Research Institute, Boston

QCA

- Brigham and Women's, Boston

IVUS

- Stanford Interventional Cardiology, Palo Alto

ECG

- Harvard Clinical Research Institute, Boston



Summary

- Zomaxx Stent
 - Trimaxx stent has excellent mechanical and physical properties
 - PharmaCoat polymer safe
 - ABT 578
 - Drug release rate similar to Cypher
- Trials -Zomaxx I underway, Zomaxx II planned

ZOMAXX I Trial

Randomized, Non-inferiority Trial vs Taxus

Single, *de novo* coronary lesions (Type A-B)
with length ≥ 10 mm and ≤ 30 mm,
and RVD 2.5-3.5 mm.
Pre-dilatation required

N=400
34 sites
Europe
Australia
New Zealand

Stent Diameters	Stent Lengths
2.5 mm	8, 18, 23, 28 mm
3.0 mm	8, 18, 23, 33 mm
3.5 mm	8, 18, 23, 33 mm

ZoMaxx™ Stent
N=200

TAXUS™ Stent
N=200

Clinical follow-up



Radiographic follow-up QCA/IVUS

Primary endpoint: 9-mos. in-segment late loss with equivalency limit of 0.25 mm, $\sigma=0.4$ mm; > 99% power; 1-sided $\alpha=0.05$

Secondary endpoints: MACE, TVF, TLR, TVR, binary restenosis, in-stent late loss, neointimal volume, neointimal volume obstruction

Medications: Clopidogrel 75 mg QD for at least 6 months, ASA 100 mg QD ≥ 12 months

Stratification: Site

ZOMAXX II Trial

Randomized, Non-inferiority Trial, Clinical Endpoint

Single, *de novo* coronary lesions (Type A-B)
with length ≥ 10 mm and ≤ 28 mm
and RVD 2.5-3.75mm
Pre-dilatation required

1670 subjects
~ 75 sites
USA and
Canada

Stent Diameters

2.5 mm

3.0 mm

3.5 mm

Stent Lengths

8, 13, 18, 23, 28 mm

8, 13, 18, 23, 33 mm

8, 13, 18, 23, 33 mm

ZoMaxx™ Stent
N=835

TAXUS™ Stent
N=835

Clinical follow-up



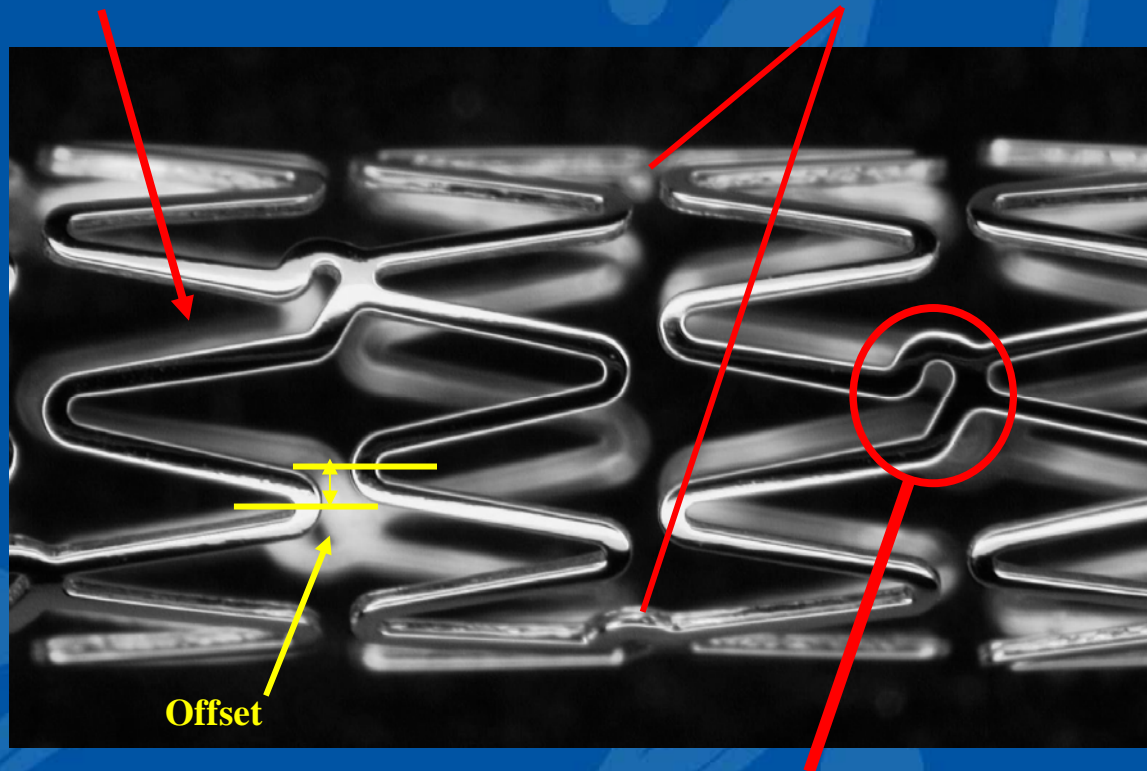
Radiographic follow-up QCA/IVUS

- Primary endpoint: Non-inferiority to TAXUS using 9-mo ischemia driven target vessel revascularization (TVR)
- Secondary endpoint: In-segment late loss at 9 mo. (QCA)
- Additional Analyses: Binary restenosis, MACE, TLR, TVR, in-stent late loss, neointimal volume, clinical outcomes by vessel diameter and lesion lengths
- Medications: Clopidogrel 75 mg QD for 6 months, ASA 325 mg QD for at least 12 months

TriMaxx Stent Pattern

8 or 10 cells around perimeter

2 connectors between rings



O.C.C.[™] (Offset Crown Connector): connecting foot pulls the rings closer together and offsets the apexes of the crowns for improved scaffolding

Distal →