

What Makes Endeavor Different?

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Conflict of Interest

Scientific Advisory Board to

- Abbott Vascular
- Boston Scientific Corp
- Cordis
- Medtronic

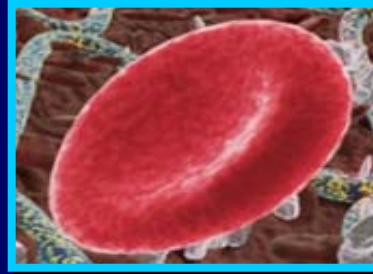
Endeavor is different by design

Components



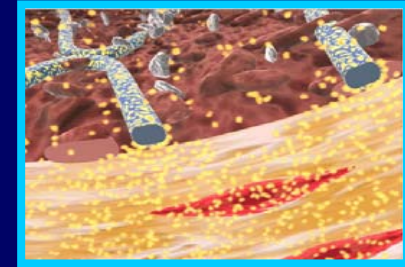
Stent Design

Modular stent with thin, round struts to help preserve endothelium during stent delivery



Biocompatible Polymer

Mimics red blood cell chemistry
Less platelets stick to polymer*



Lipophilic Drug

The most lipophilic limus drug that is rapidly absorbed by the arterial tissue**



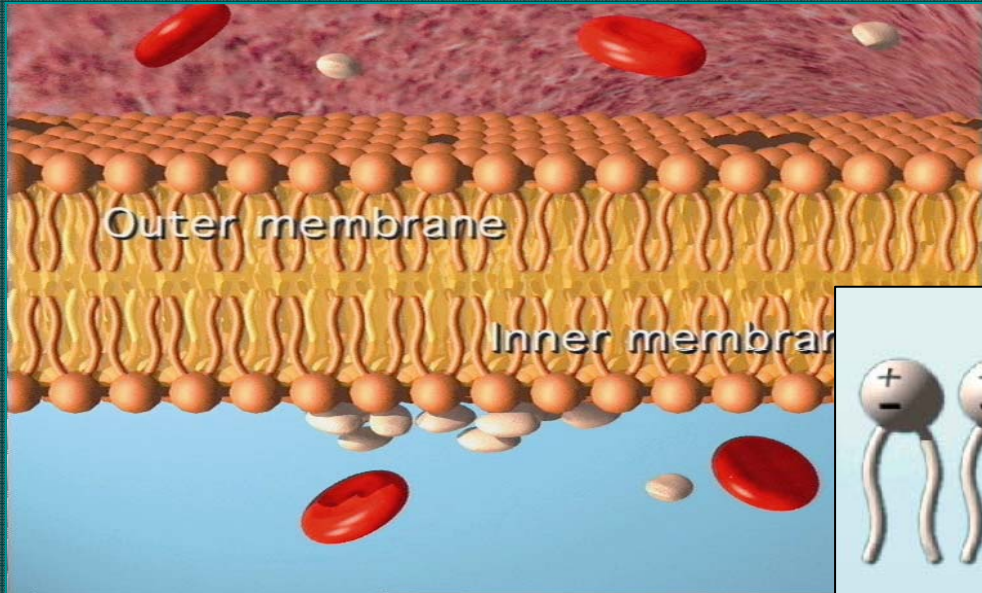
Design components of Endeavor allow for rapid, complete and functional healing

* pre-clinical studies on file at MDT comparing PC coated stents to uncoated stents

** Most lipophilic limus drug as compared to sirolimus and everolimus and paclitaxel

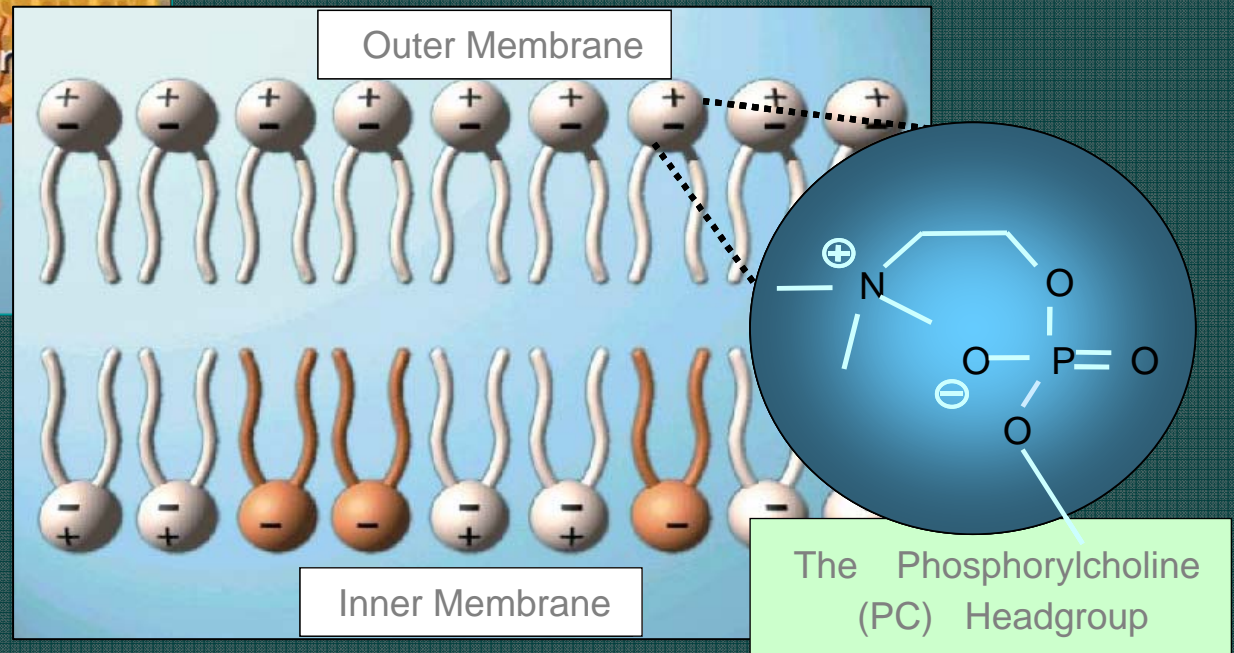
Endeavor DES System

PC Technology



90% of phospholipids in the outer membrane of a red blood cell contain the PC (Phosphorylcholine) headgroup

PC¹ mimics the chemical structure of the phospholipid headgroup



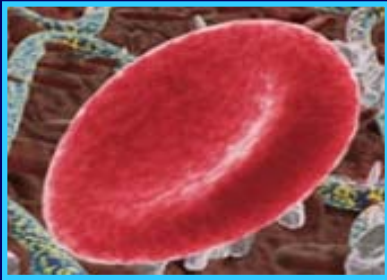
PC Advantage

- **Hydrophilic interface with blood**
- **Thromboresistance**
- **Minimal inflammation**
- **Mechanically stable at delivery**
- **Early endothelial coverage**
- **Functional endothelium**
- **Thin polymer**
- **Medtronic PC coating: polymer dissolution in 14 days**

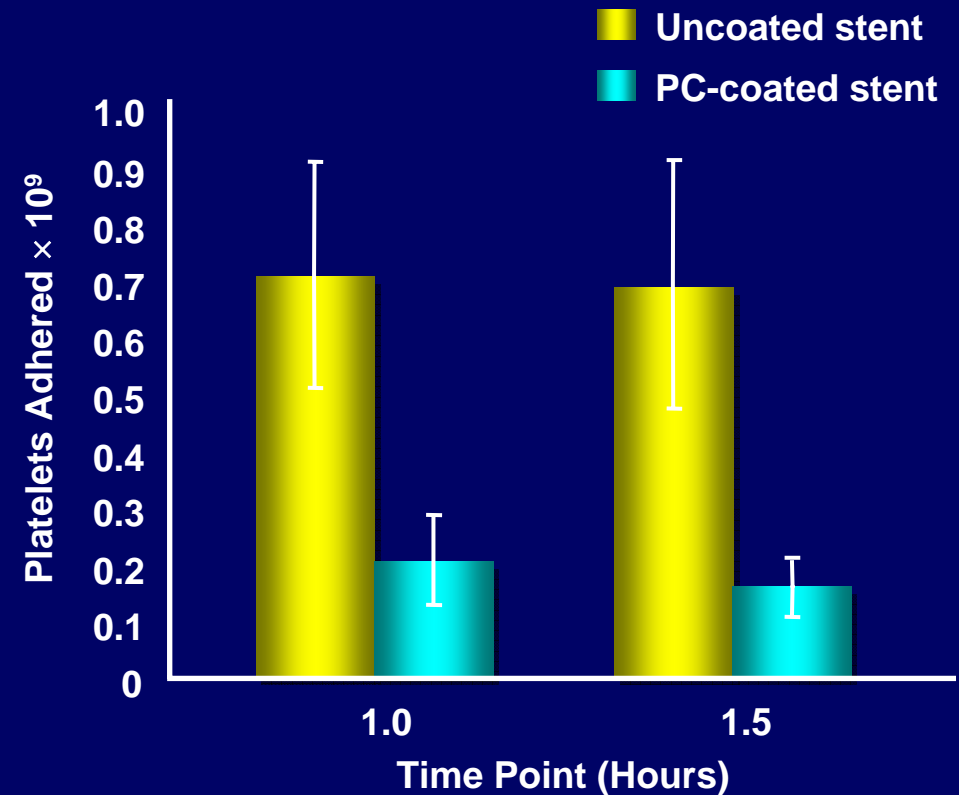


Endeavor PC Technology

Mimics the outside surface of the red blood cell

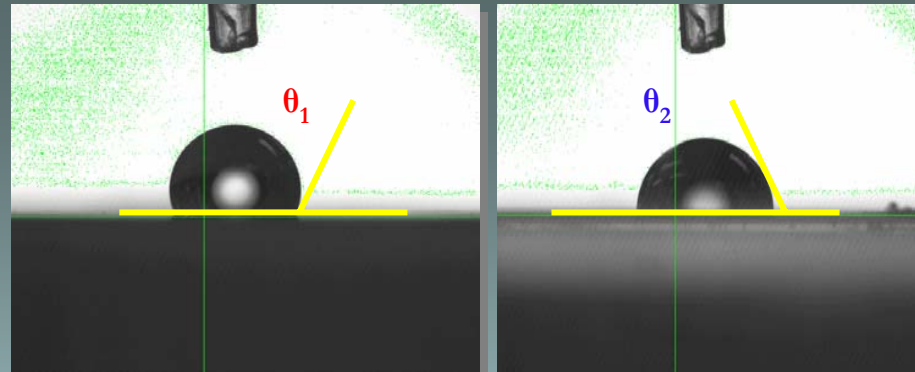


- Biocompatible and non-inflammatory
- In over 16 years of clinical experience and >150,000 stent implants, PC technology has been proven:
 - Safe
 - Durable
 - Benign
- Endeavor has the most hydrophilic coating reducing protein adhesion



Relative Hydrophilicity of DES Polymers

Contact Angle Measurements Evaluate Surface Hydrophilicity



Lipophilic

Amphiphilic/Hydrophilic

Polymer

Contact Angle

C10

118°

C19

91°

C10+C19

84°

BioLinx

94°

PC

83°

PBMA

115°

SIBS

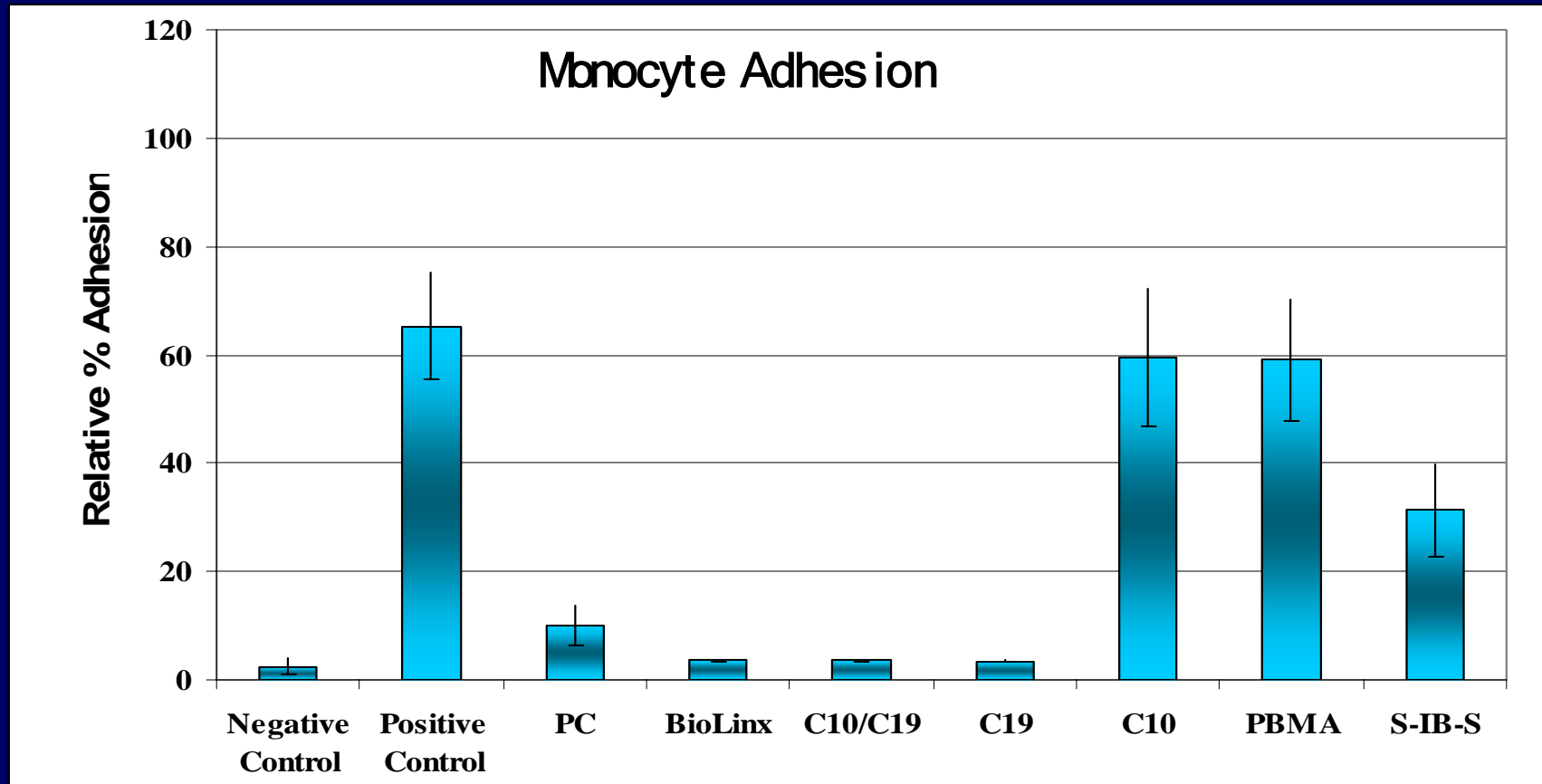
118°

SIBS: Styrene-Isobutylene-Styrene Triblock Copolymer [Taxus]

PBMA: Polybutyl methacrylate [Cypher cap coat]

Endeavor PC Technology

Hydrophilic and Highly Biocompatible

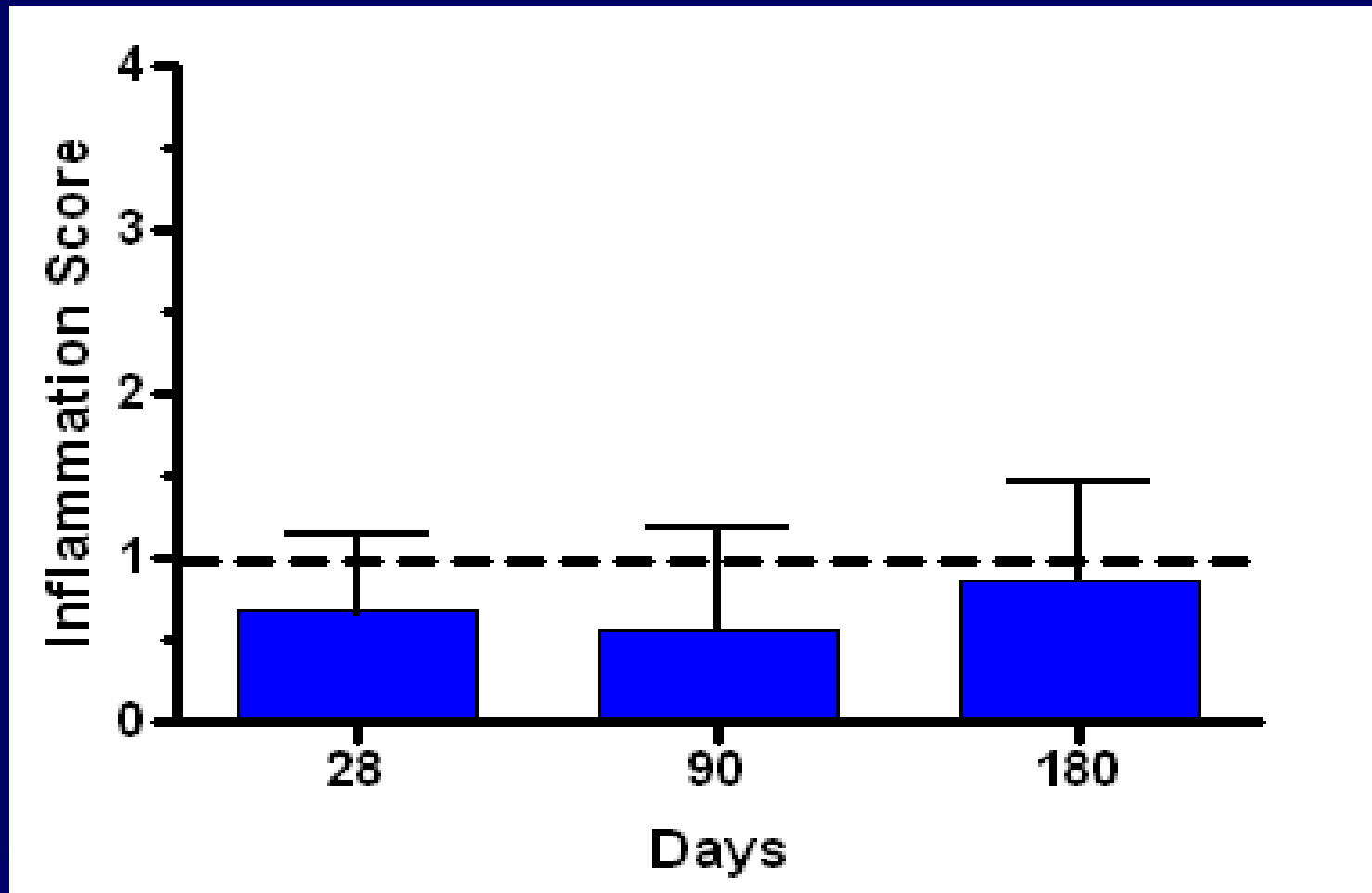


SIBS: Styrene-Isobutylene-Styrene Triblock Copolymer [Taxus]

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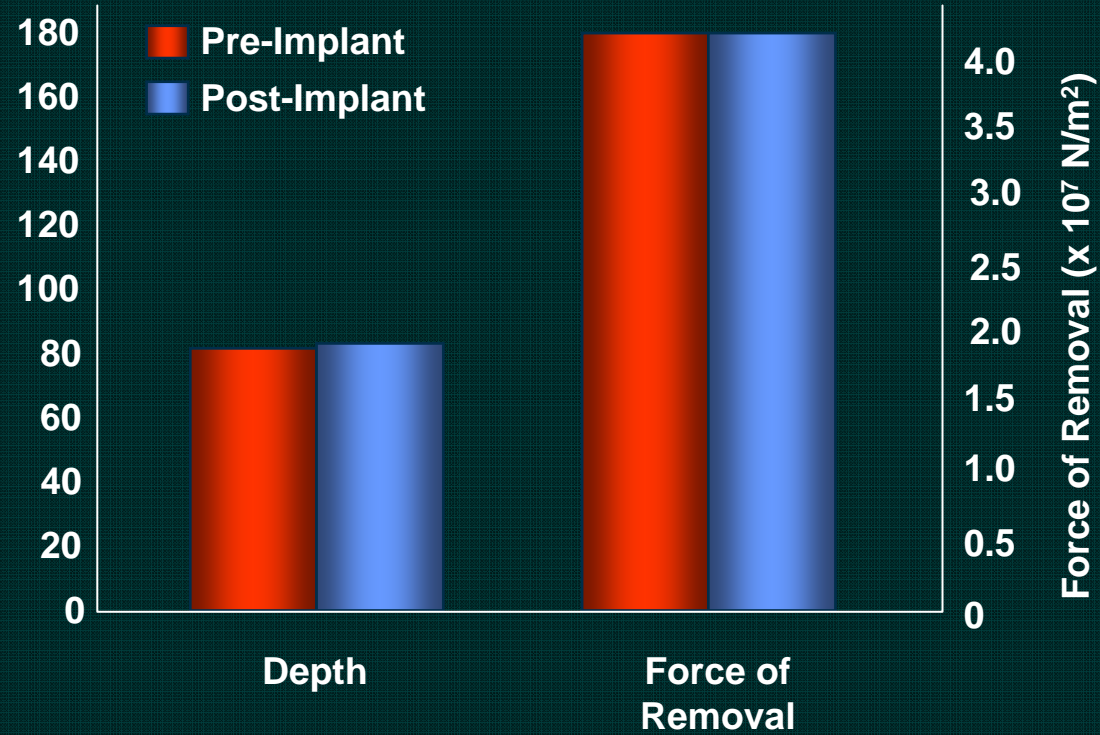
Endeavor Biocompatibility

Inflammation scores are consistently low up to 180 days



Endeavor DES System

PC Technology

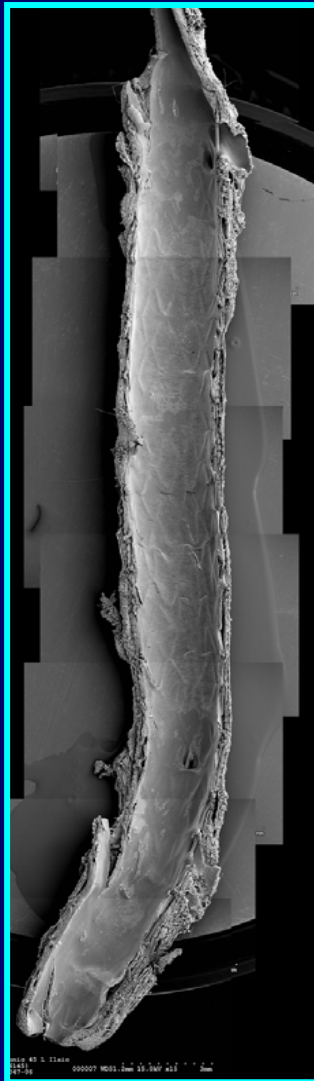


Mechanically Stable

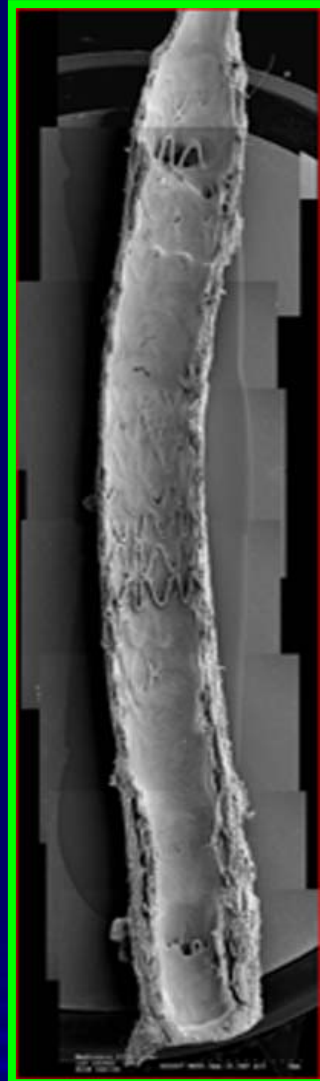
Strut Coverage and Endothelialization

Endeavor vs Driver

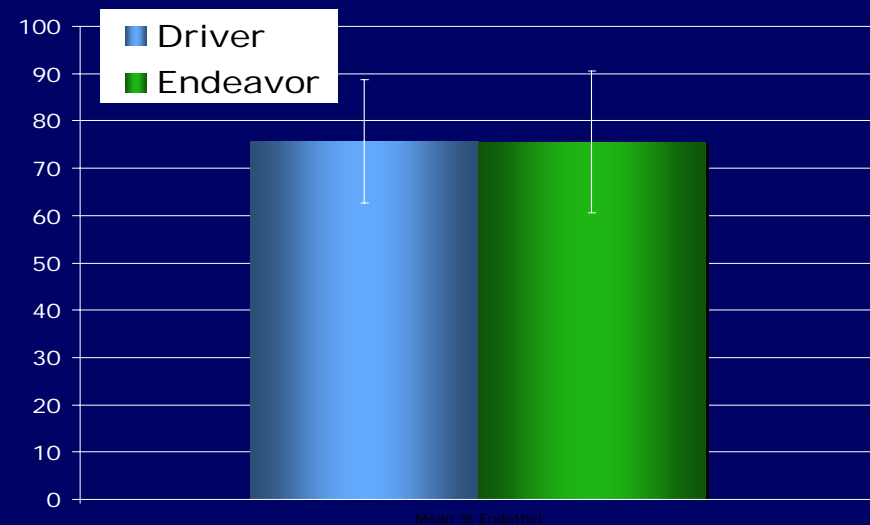
Driver



Endeavor



% of Struts Endothelialized



Strut Coverage and Endothelialization

Endeavor vs Cypher vs Taxus

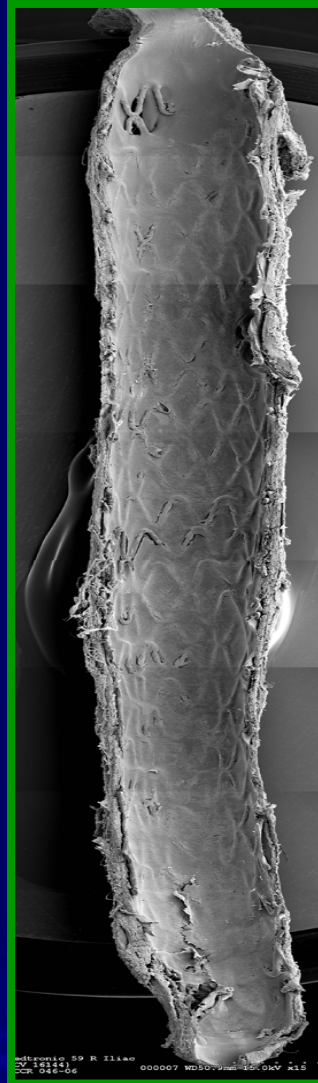
Cypher



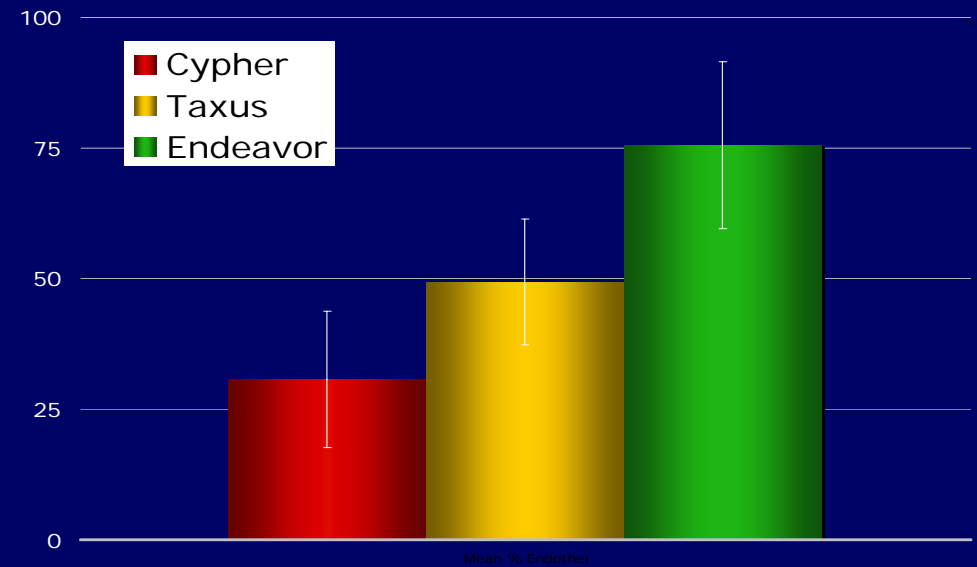
Taxus



Endeavor



% of Struts Endothelialized



Study design

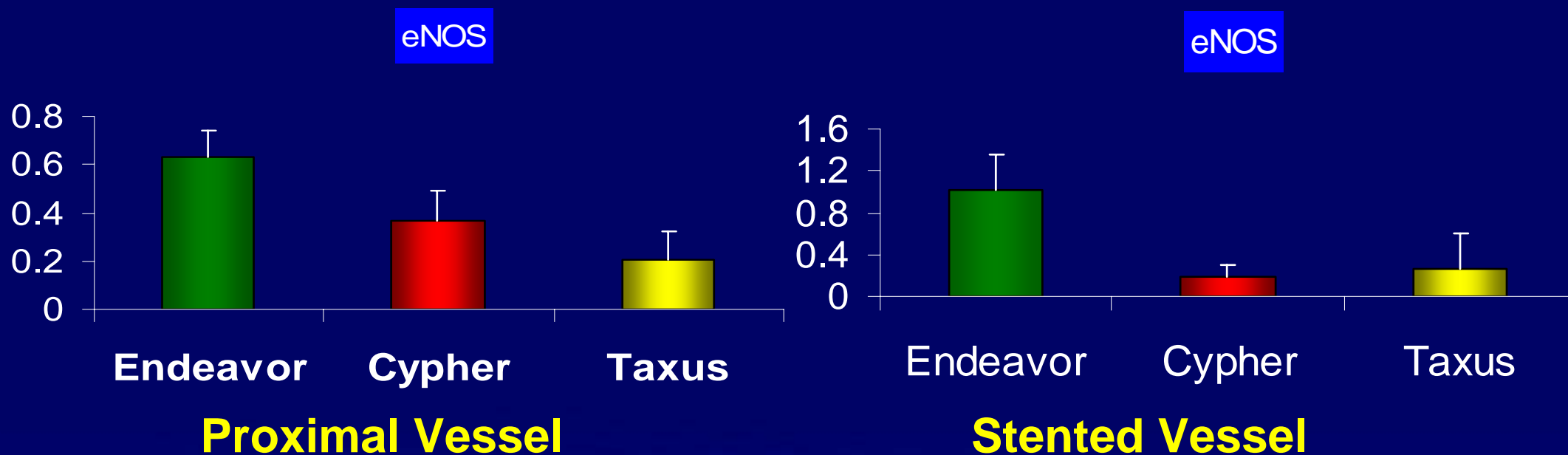
- Cypher, Taxus, Endeavor and Driver stents were implanted in porcine coronary arteries
- Harvest tissues 28 and 90 days after stenting
 - 28 days evaluate polymer with drug present
 - 90 days evaluate polymer after drug depleted
- Evaluate endothelial function
 - Acetylcholine challenge just prior to euthanasia
- Evaluate inflammation and polymer biocompatibility
 - Real Time RT-PCR to evaluate local gene expression
 - Histological with immunohistochemistry for cytokines, NOS, etc.



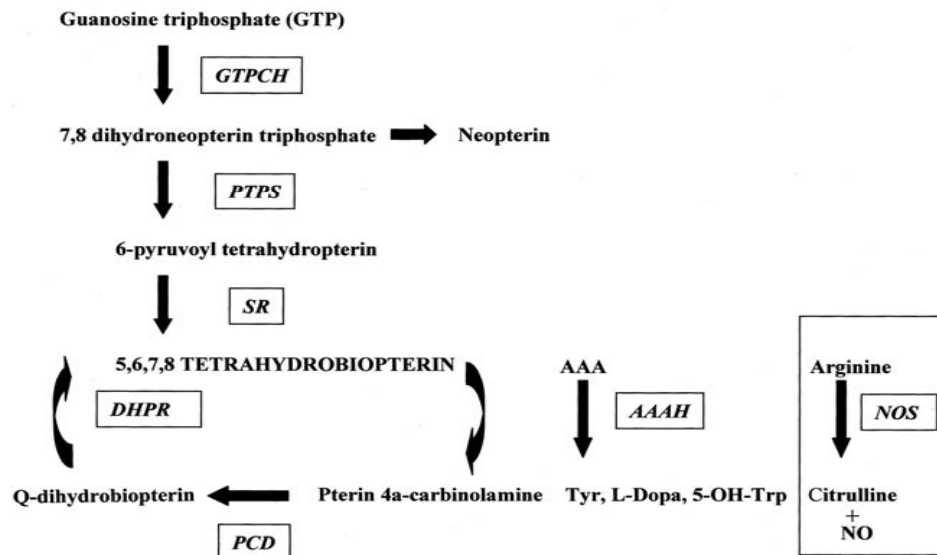
NO and Endothelial Cell Function

Endothelial Nitric Oxide Synthase (eNOS)

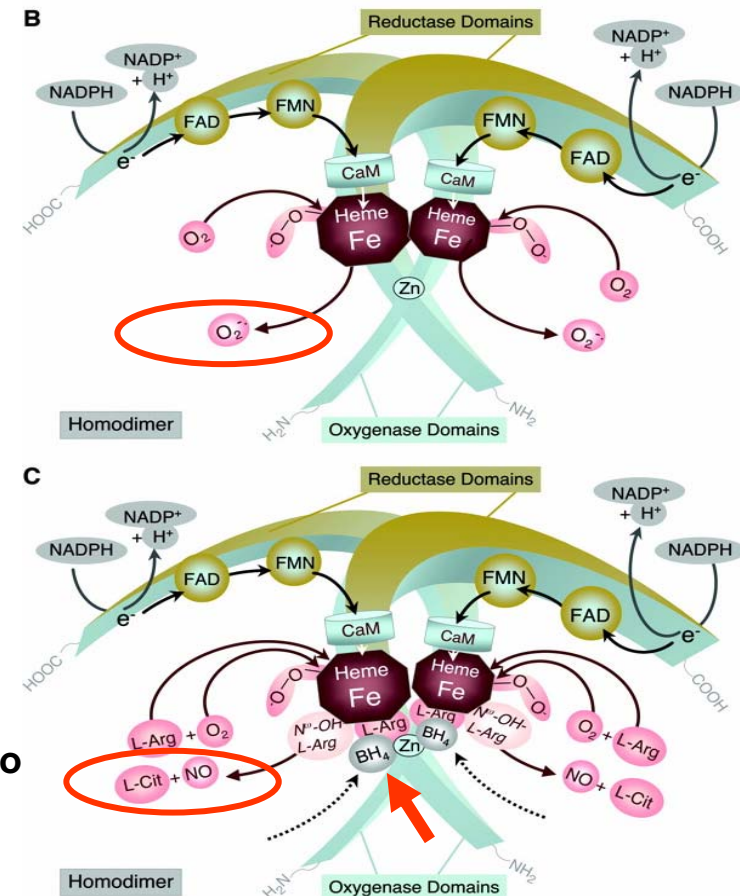
- eNOS is the protein that produces NO and is marker of endothelial cell function
- Both proximal and stent vessels have significantly more eNOS present than either Taxus or Cypher



GTP Cyclohydrolase (GTPCH) is important for eNOS activity



- **GTPCH increases tetrahydrobiopterin (BH4) production**
- **Absence of BH4 may lead to eNOS uncoupling and generation of reactive oxygen species**

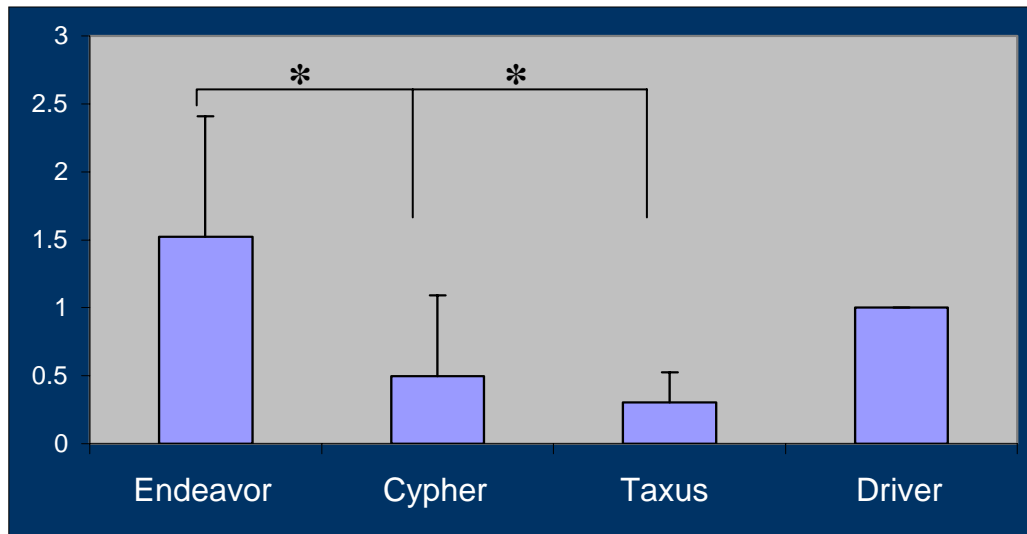


Franscini N et al. Circulation 2004; 110: 186-192.

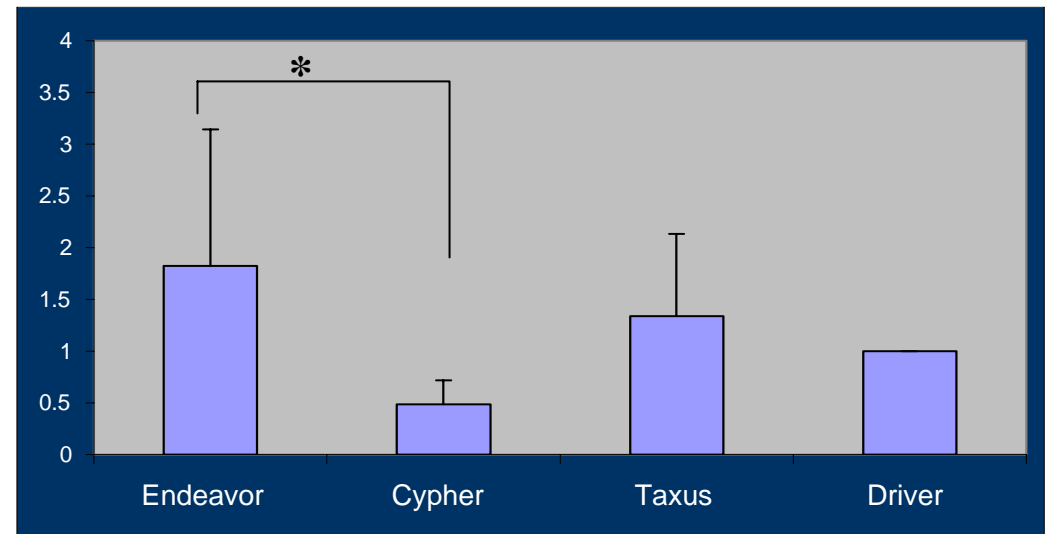
Foerstermann U and Muenzel T. *Circulation* 2006; 113: 1708-1714

Expression of GTPCH mRNA

28 day



90day

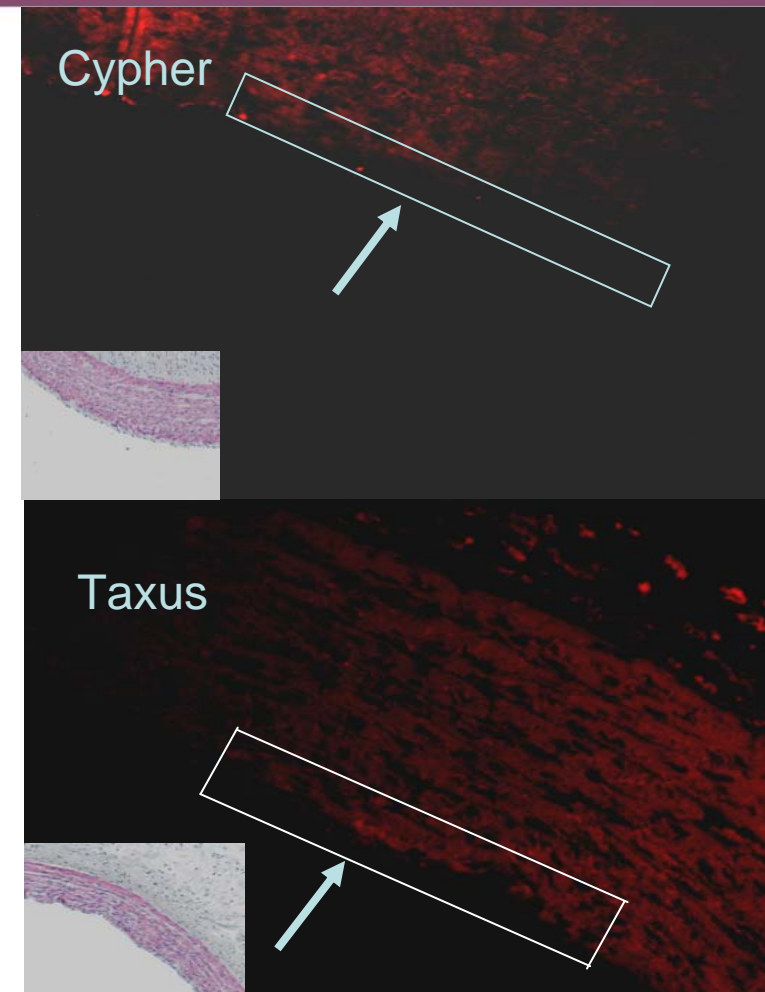
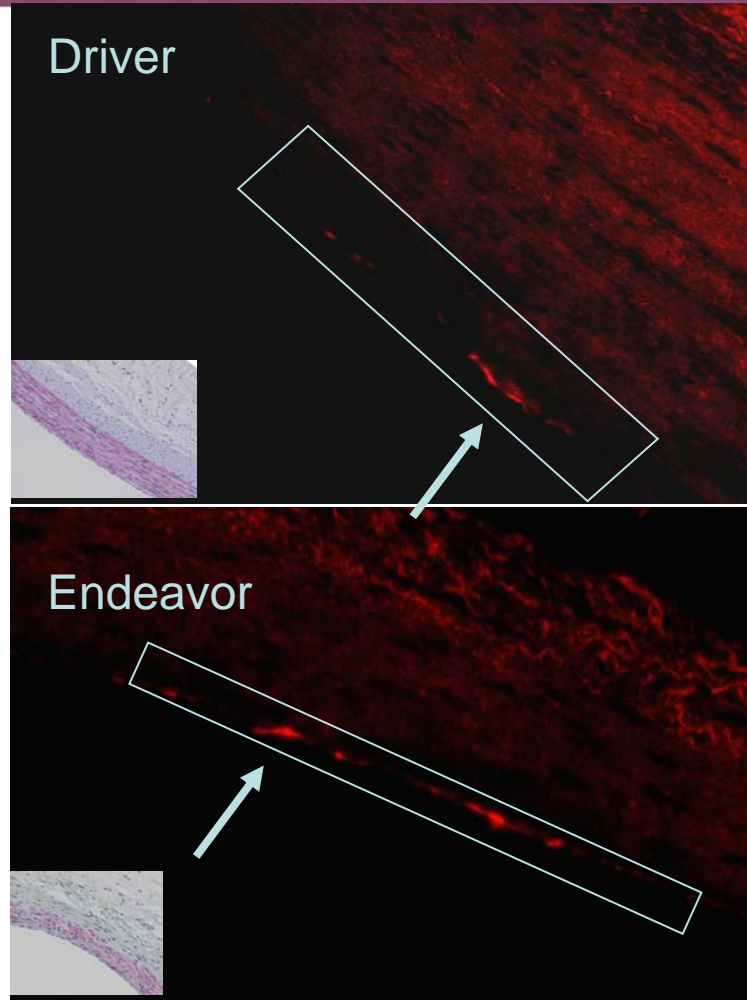


*P<0.05 vs. Endeavor

The expression of GTPCH mRNA was significantly higher in regions proximal to Endeavor stents compared to Cypher and Taxus suggesting functional eNOS and NO generation



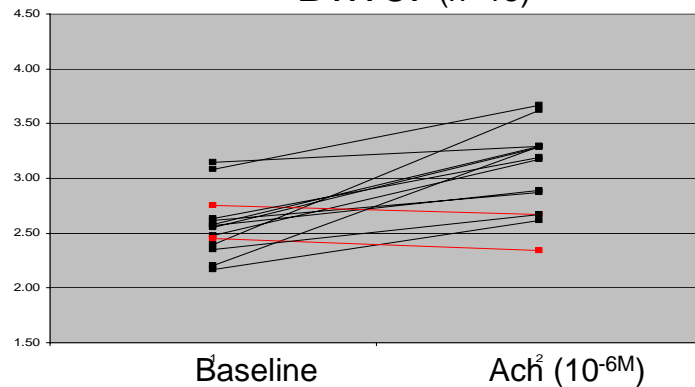
Localization of eNOS by Immunohistochemistry



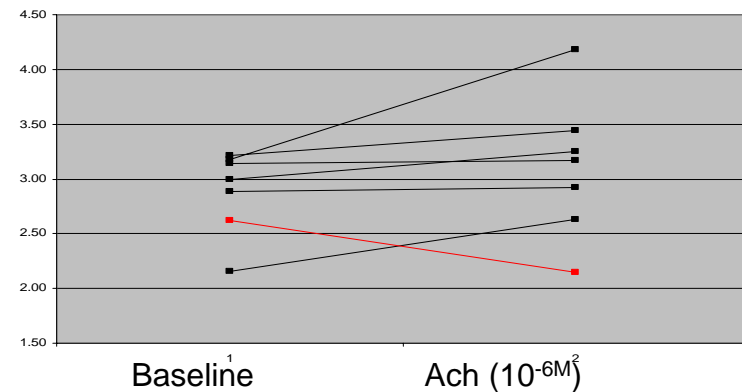
eNOS protein was localized on the luminal surface of vessels proximal to Endeavor and Driver stents

EC Function Was Assessed by ACH Challenge 28 Days After Stenting

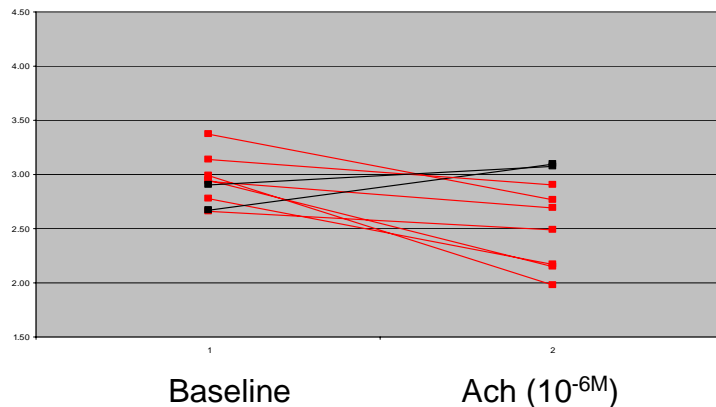
Driver (n=15)



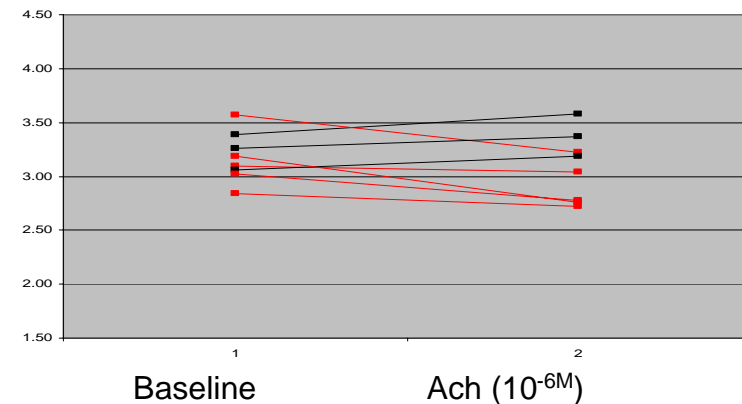
Endeavor (n=7)



Cypher (n=9)



Taxus (n=8)

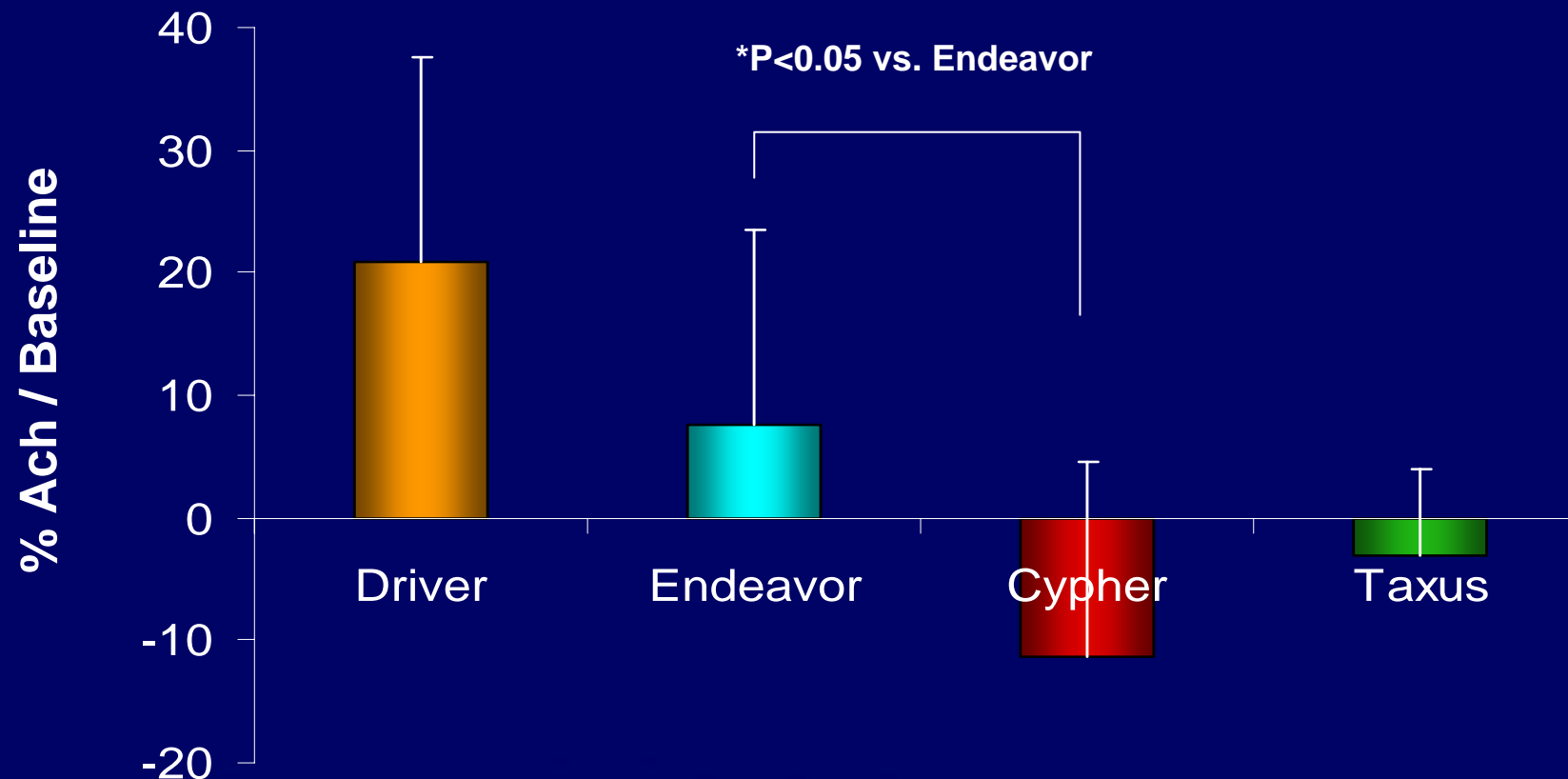


Cypher and Taxus constrict in response to acetylcholine (ACH) suggesting EC dysfunction
Endeavor and Driver show normal vasodilation in response to ACH suggesting normal EC function

Endeavor: Rapid recovery of EC function

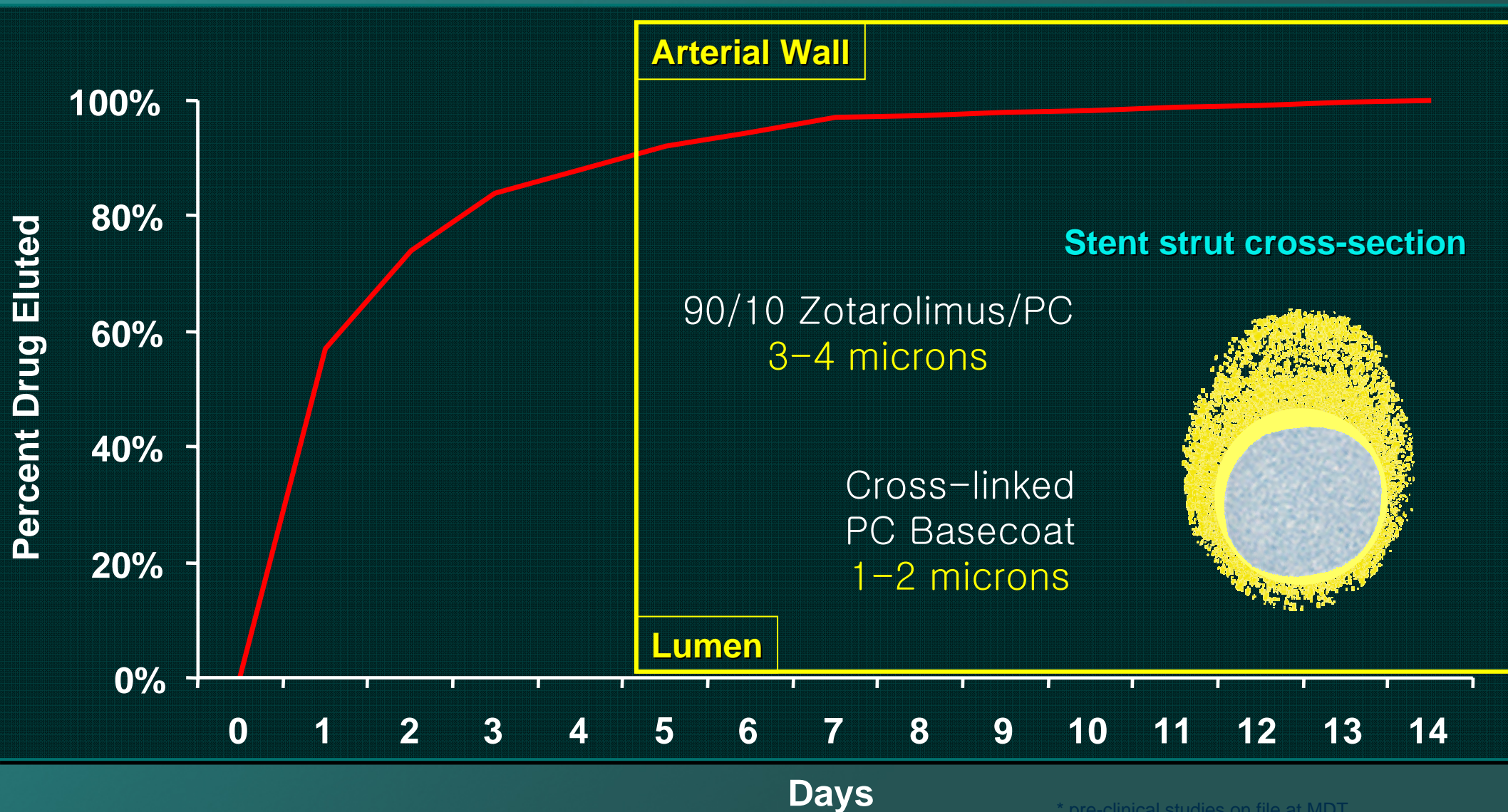
ACH Challenge 28 Days After Stenting

ACH Responses Compared to Baseline



Endeavor Zotarolimus-PC Interaction

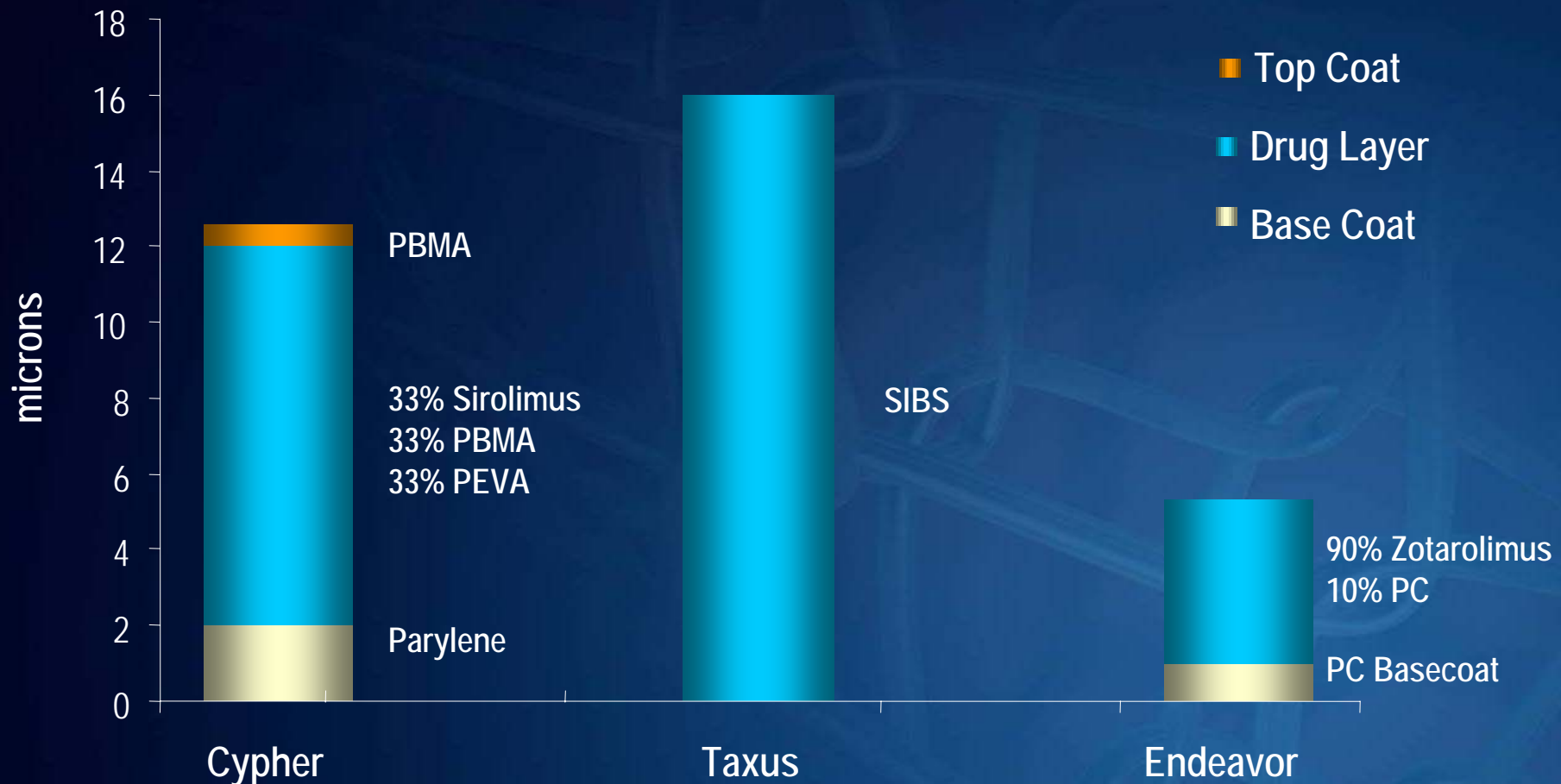
***Drug Eluted by 14 days;
Only PC Basecoat Left Behind***



* pre-clinical studies on file at MDT

Comparison of Polymer Thickness

Drug Eluted by 14 days only PC Basecoat Left Behind



At 15 days there is only a .5 micron thick layer of PC basecoat on Endeavor

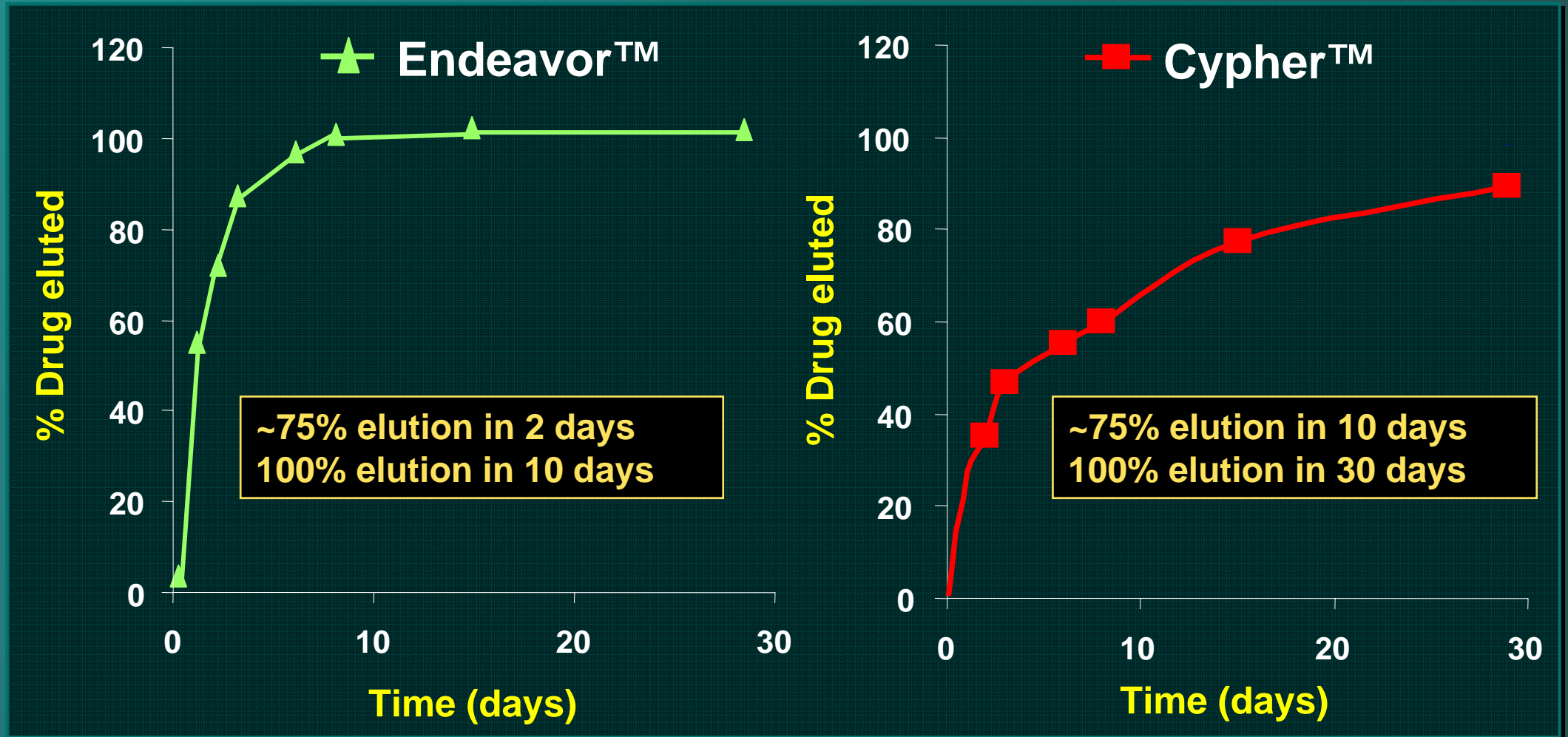
PC Disadvantage

- **Medtronic PC coating: polymer dissolution in 14 days**
- **Elution characteristics set by dissolution**
- **Polymer to drug formulation is difficult to modify**



Comparison of *in vivo* Elution Rates

Rabbit iliac models



Cypher data from B. Chevalier, EuroPCR 2004
Endeavor data from G. Laarman, EuroPCR 2004



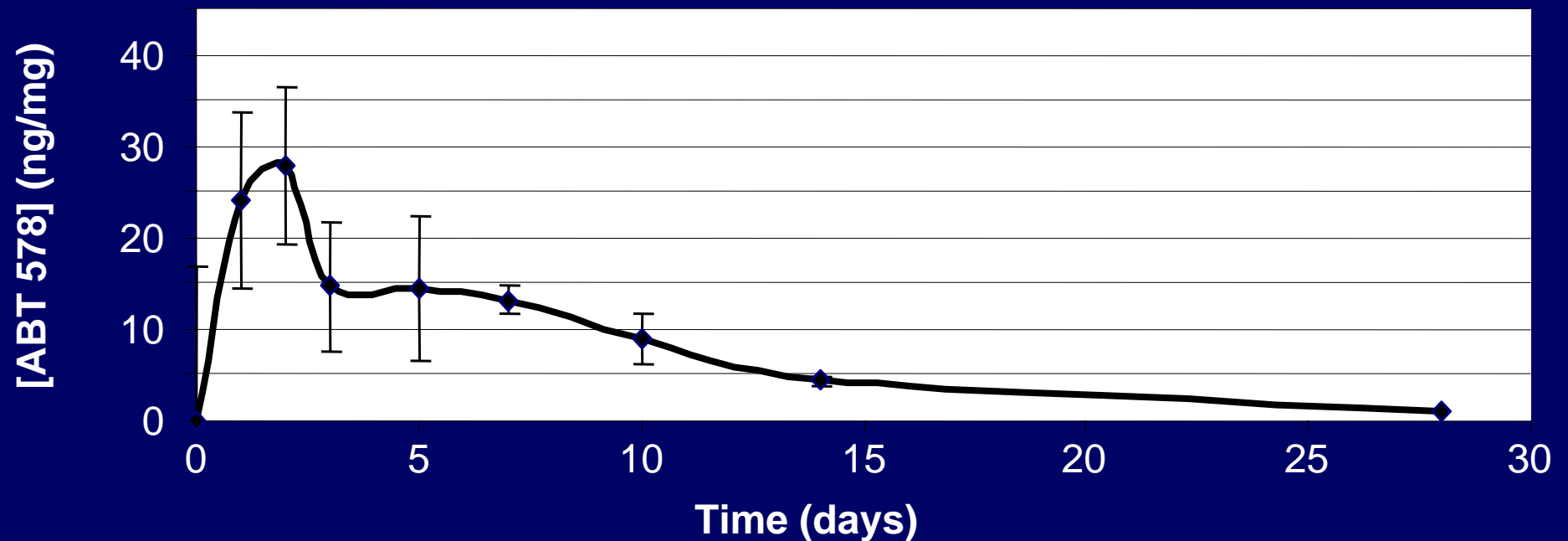
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Zotarolimus Tissue Concentration

Pig Coronary Arteries

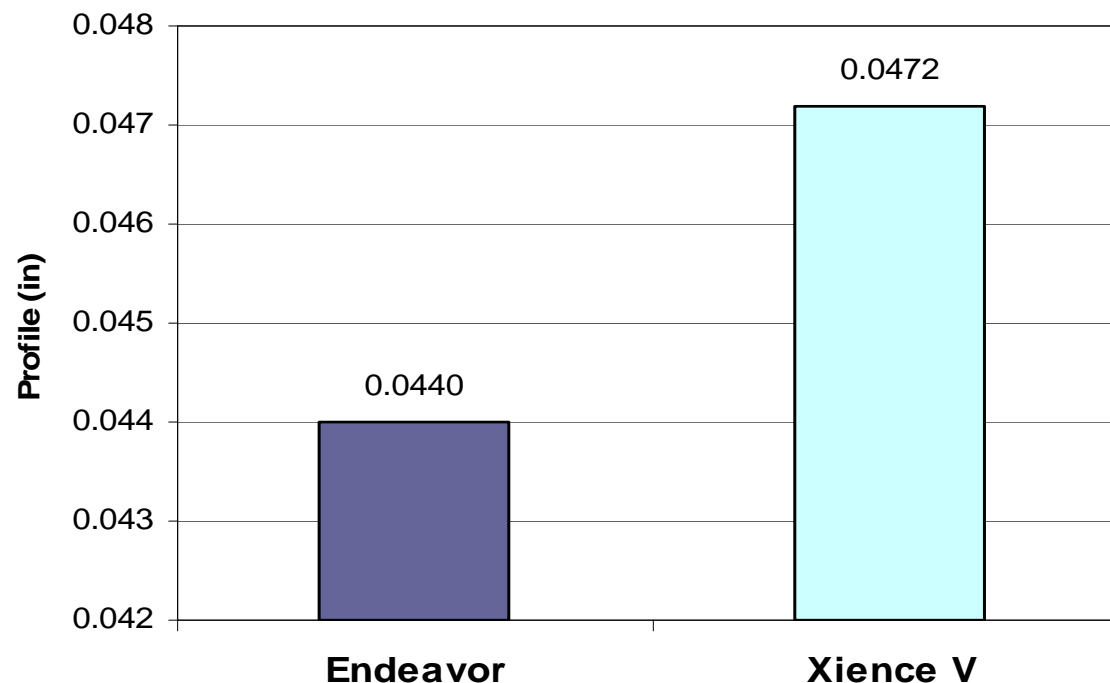
Concentration of Zotarolimus in
Tissue Surrounding the Stent (ng/mg)



Zotarolimus is retained in the tissue for up to 28 days at effective concentrations to control human arterial SMC proliferation.

How does the crossing profile of Xience V/ Promus compare with Endeavor?

Endeavor has
a 7% lower
crossing profile
than Xience V

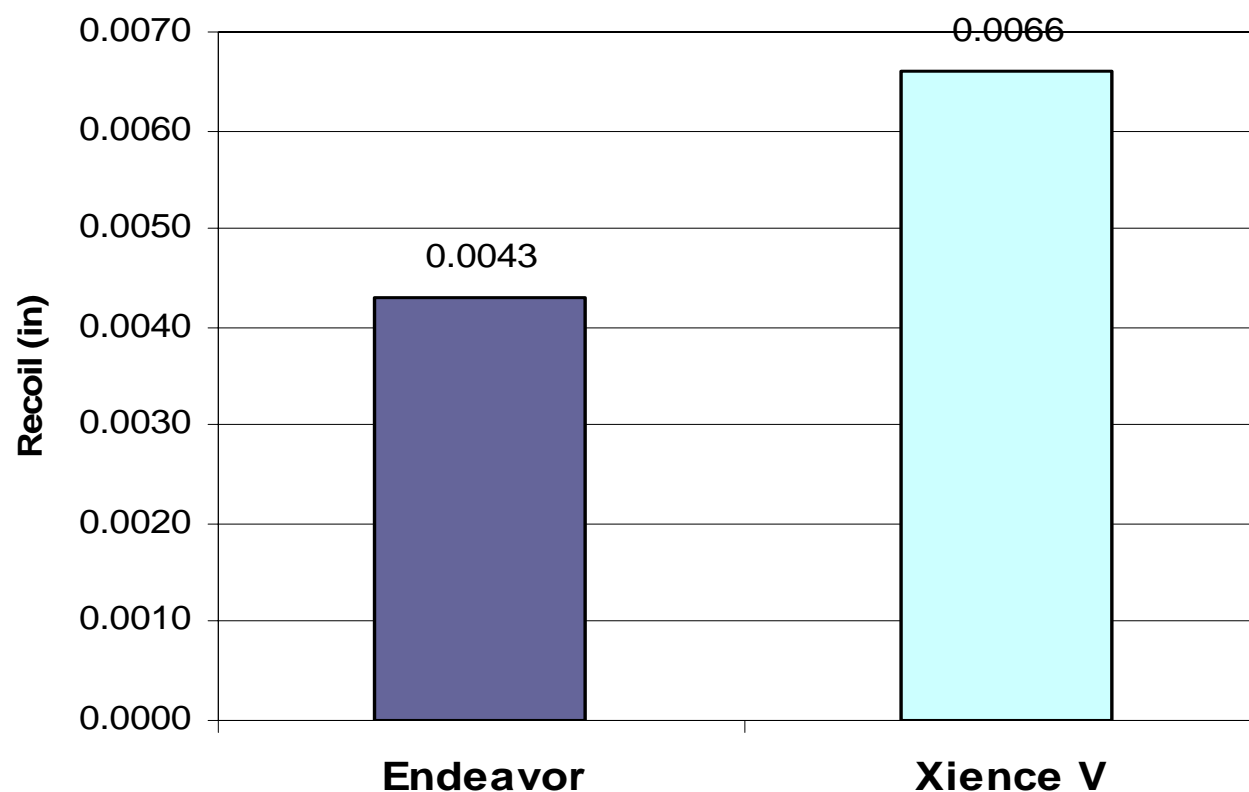


- Lower crossing profile for better access to challenging lesions.
- Xience claims thinner struts, but still has a higher crossing profile.

Ref: Test data on file at Medtronic, Inc. 3.5 x 18mm stents

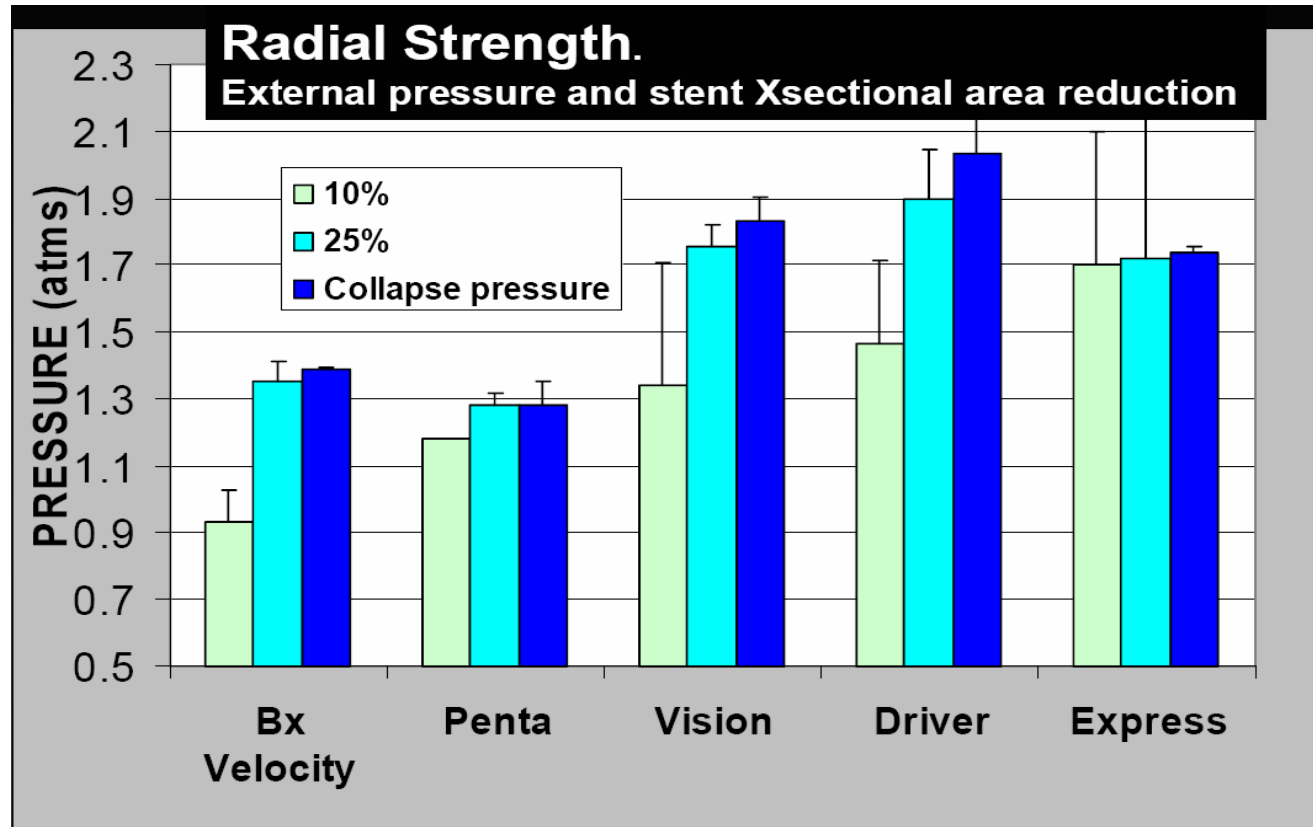
How does the Stent Recoil of Xience V/Promus compare?

Endeavor has
35% less
stent recoil
than Xience



- Endeavor's cobalt alloy and modular design minimizes stent recoil.

How does the Radial Strength of Xience V/Promus platform compare?

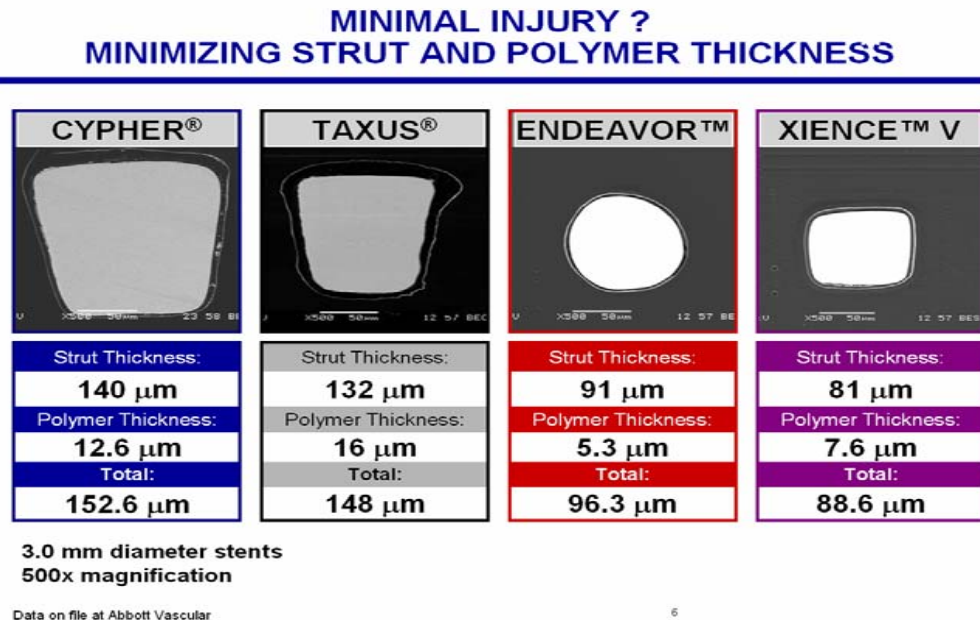


Endeavor's platform presents more Radial Strength in all pressure levels compared with Xience V/ Promus platform.

Ref: Independent study by John Ormiston presentation, Auckland New-Zealand

Does the thickness of Xience/Promus strut mean better clinical results?

ABT Vascular presented:



Buller, Tremblant, February 2007

What is the relationship between polymer thickness and minimal damage?

The Vision of Xience / Promus show:

- Higher crossing profile!
- Higher stent recoil!
- Lower radial strength!

Compared to the Driver of Endeavor

So how does Xience / Promus claim minimal injury? Is this claim clinically meaningful?

DES Safety Fire Storm



Endeavor's safety is well proven

HCRI CEC & ARC ST –
2 Year Kaplan Meier Estimates

