*Hot Topic III: Next Generation of DES*

# Next Generation DES: Results from Preclinical Data

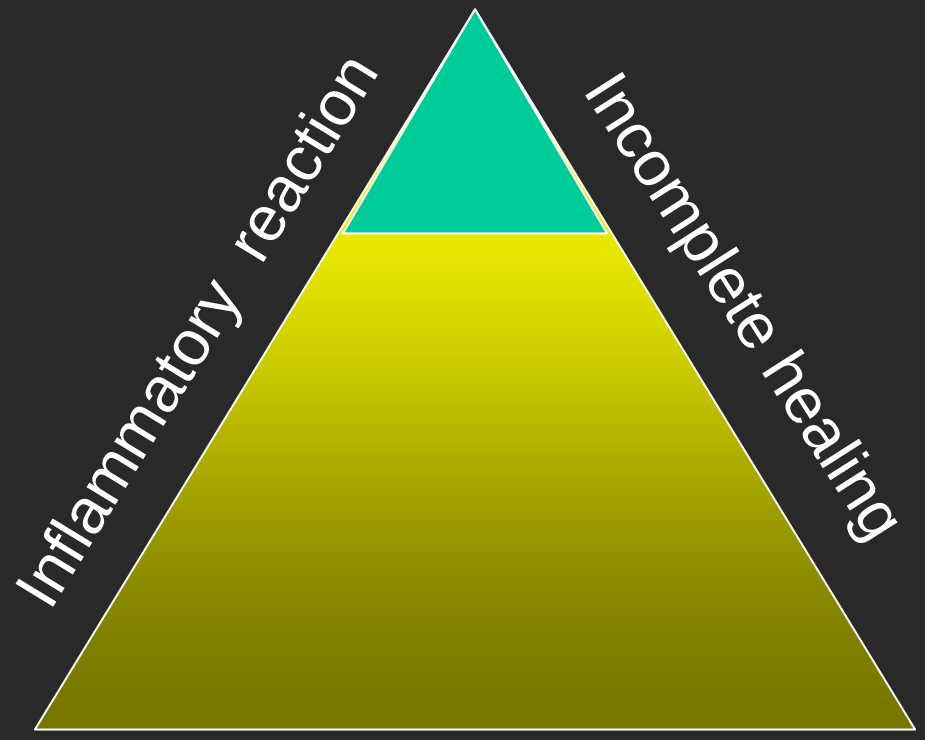
Renu Virmani, MD

*CVPath Institute, Inc.*

*Gaithersburg, Maryland, USA*

# Components of 1st DES (Cypher and Taxus) and Pathology

**Metal/Design** Thick struts >140 microns




**Polymer**

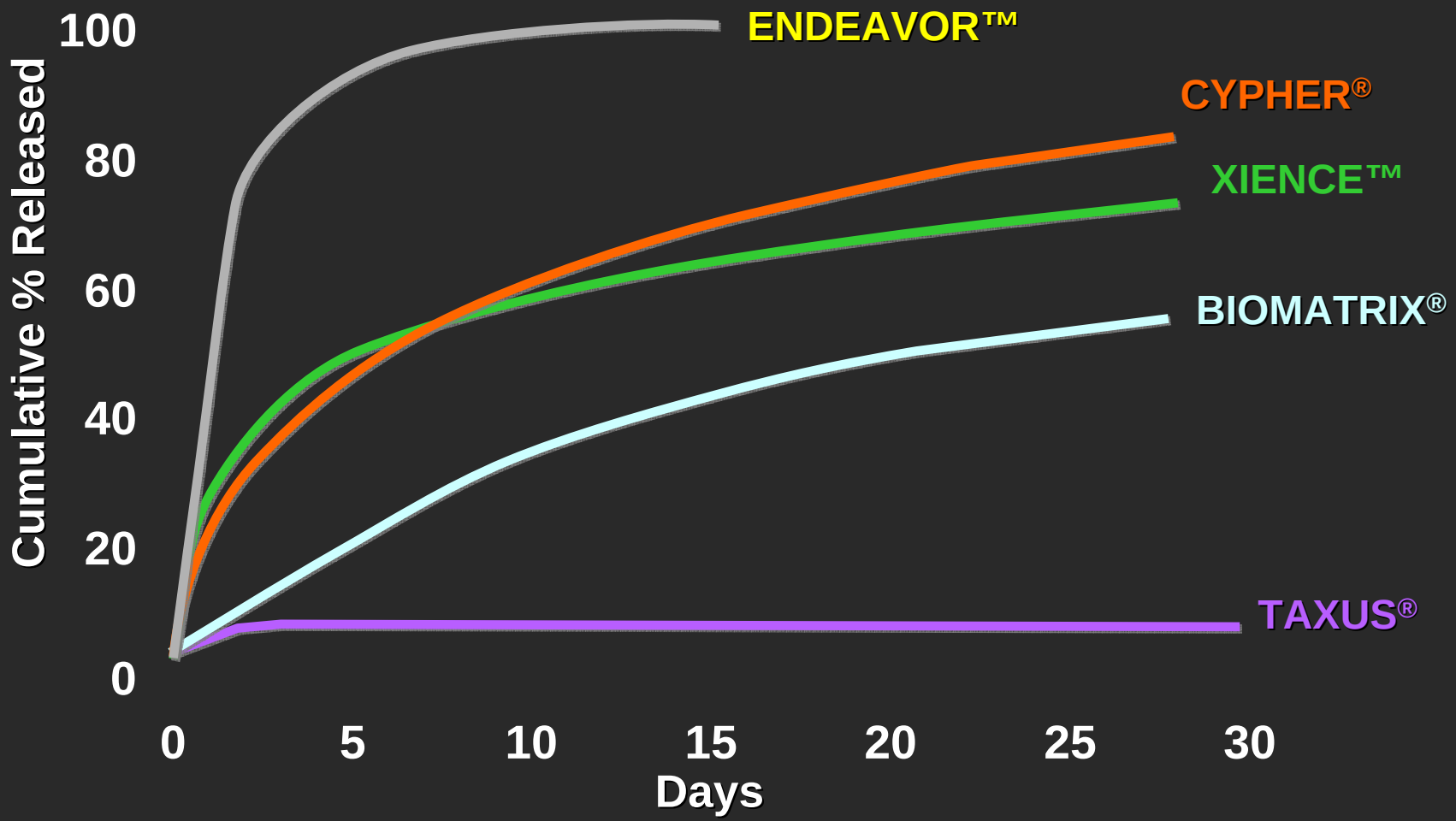
PEVA+PBMA
SIBBS
NON-ERODABLE

Release kinetics

**Drugs**

Sirolimus-90 days
Paclitaxel->90 days

# *Comparative Elution Profiles*




BIOMATRIX®

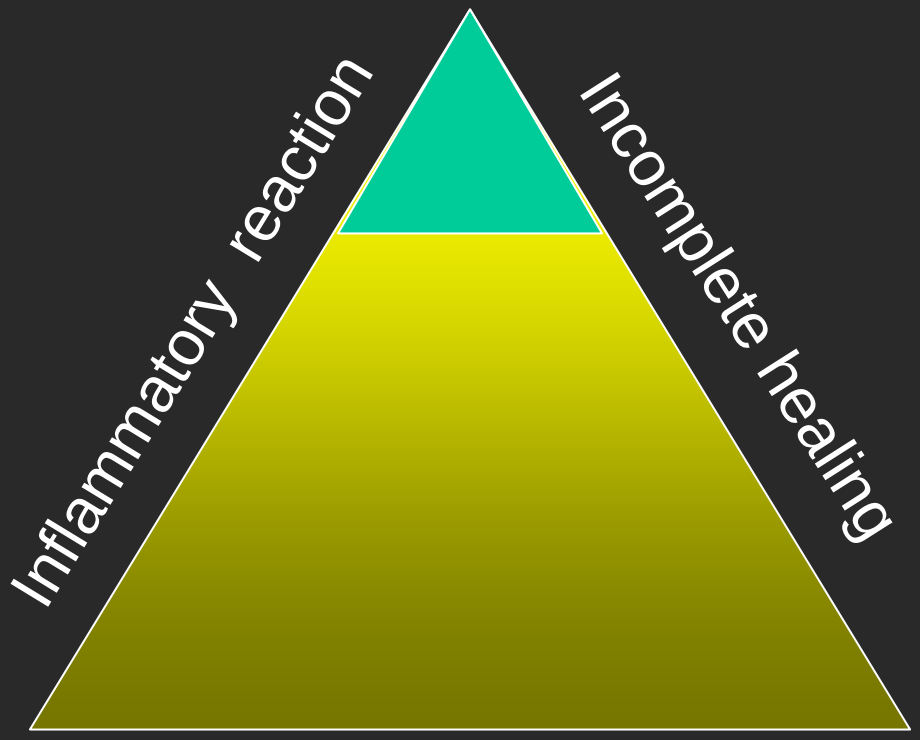
Not available for sale in the United Sates

# What can we expect from next generation DES?

# Components of 2nd DES (Endeavor and Xience)

**Metal/Design**

Cobalt-chromium with thin struts (<90 micron)




**Polymer**

**PC coating (Endeavor)**

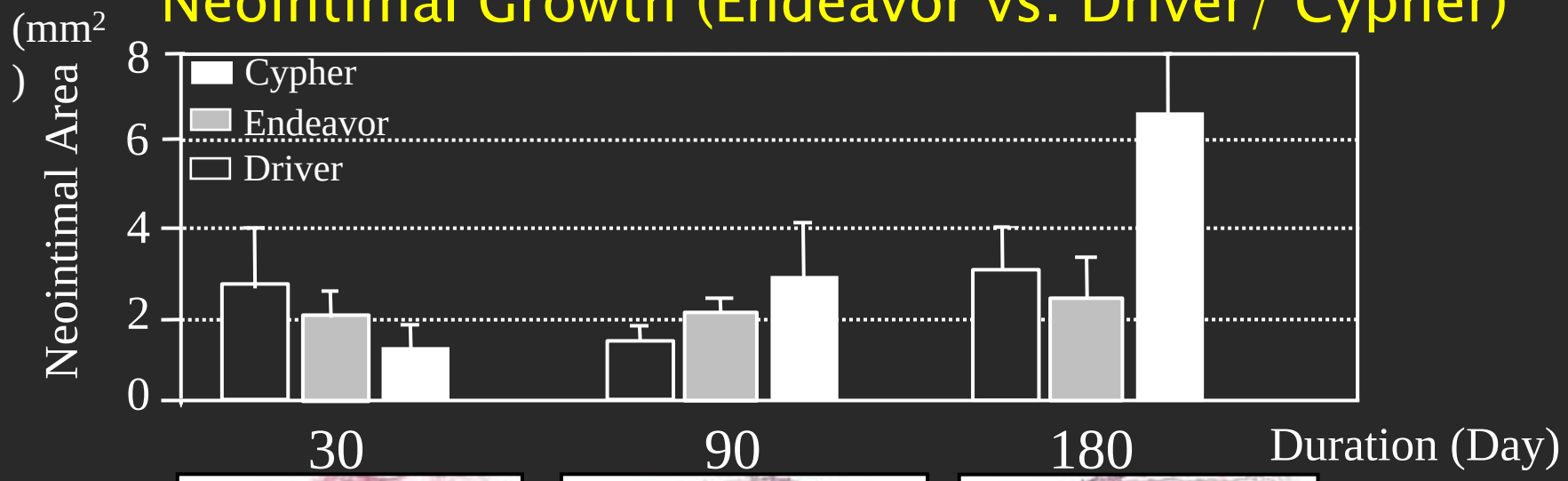
**Fluoropolymer**

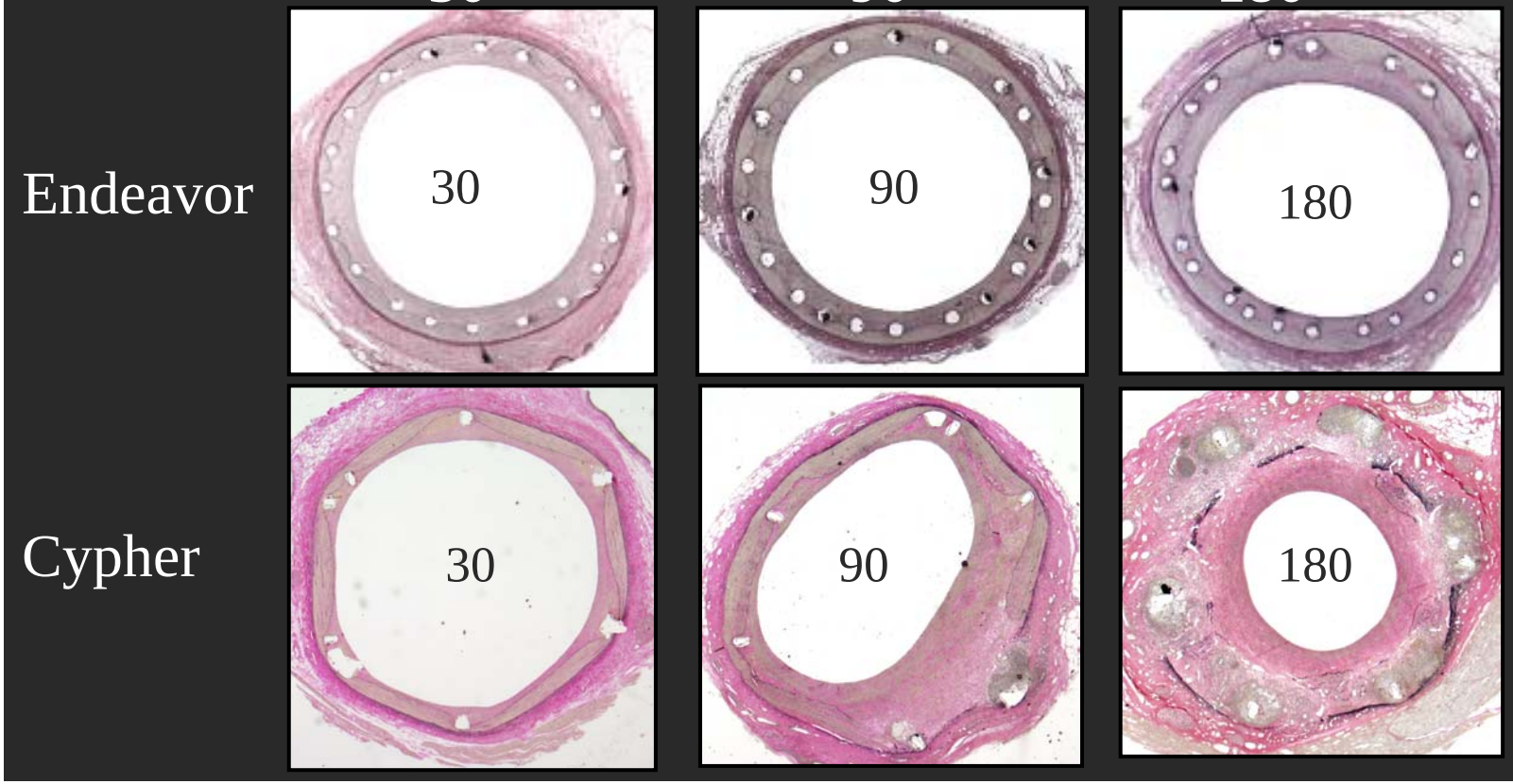
**Drugs**

Zotarolimus (90% at 15 d)

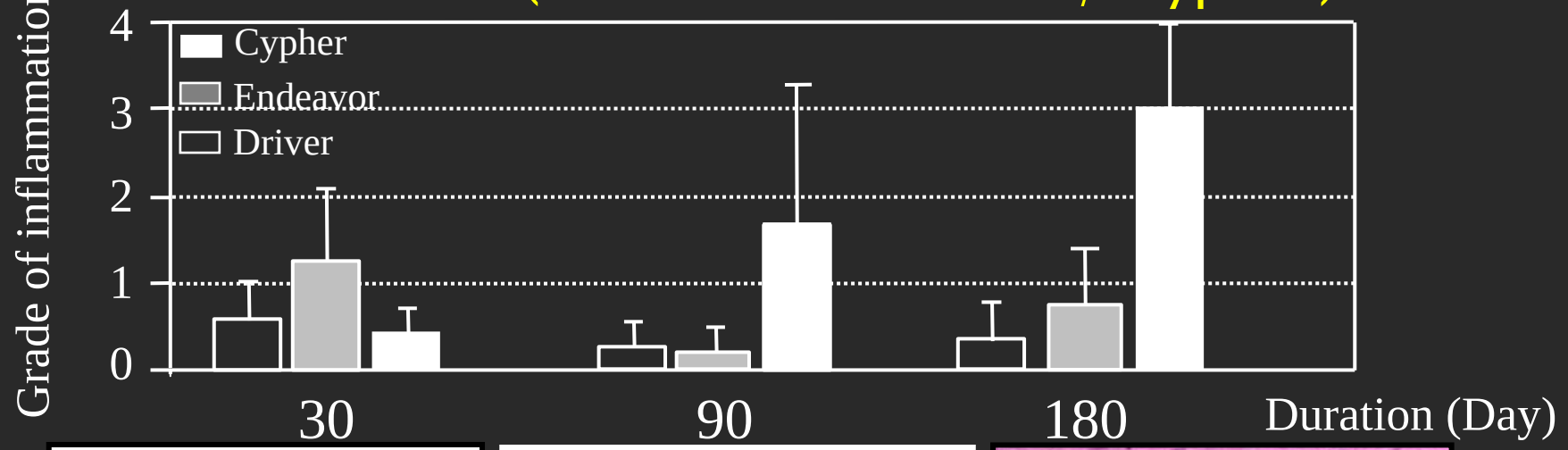
Everolimus (80% at 28 d)

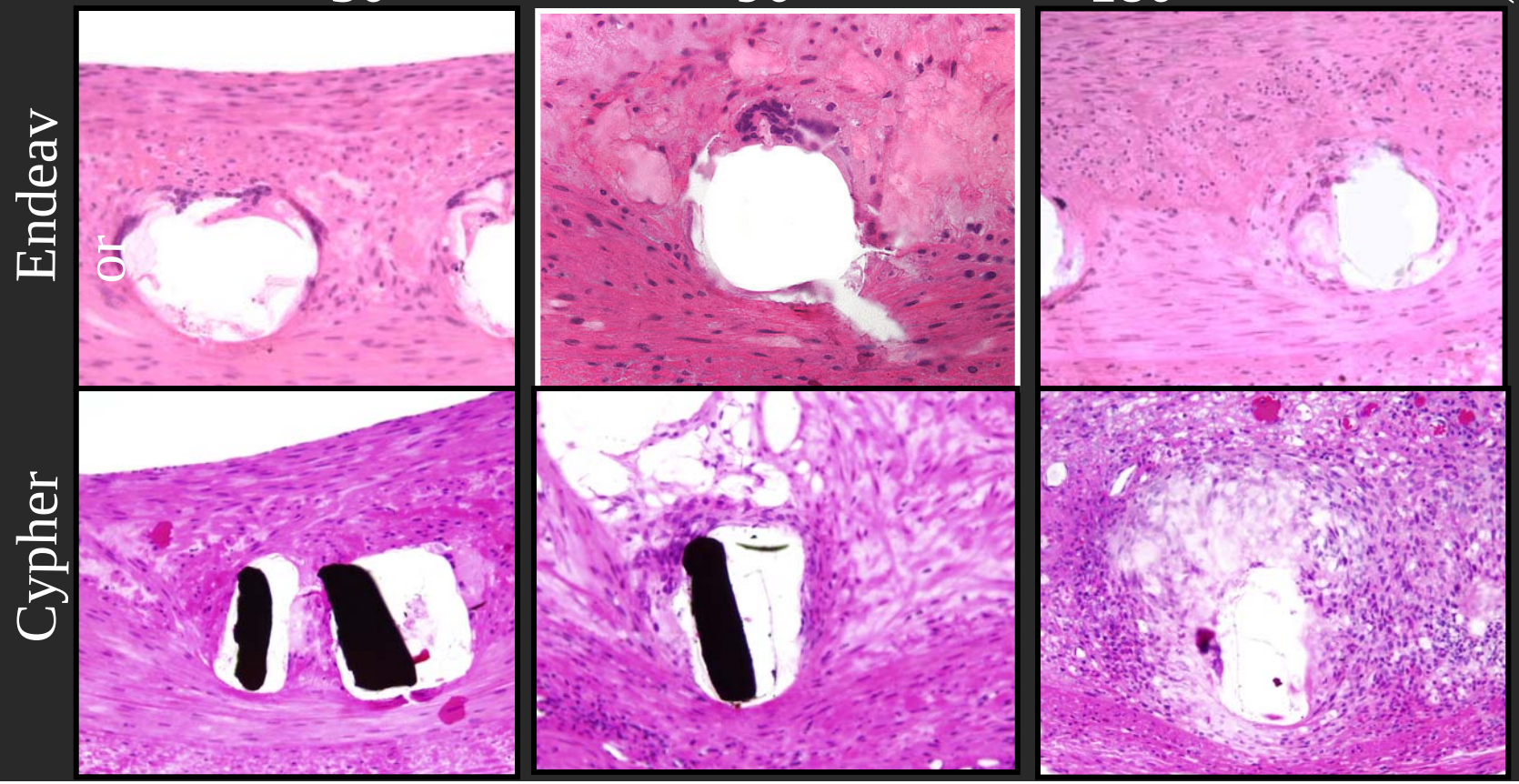
# Neointimal Growth (Endeavor vs. Driver/ Cypher)



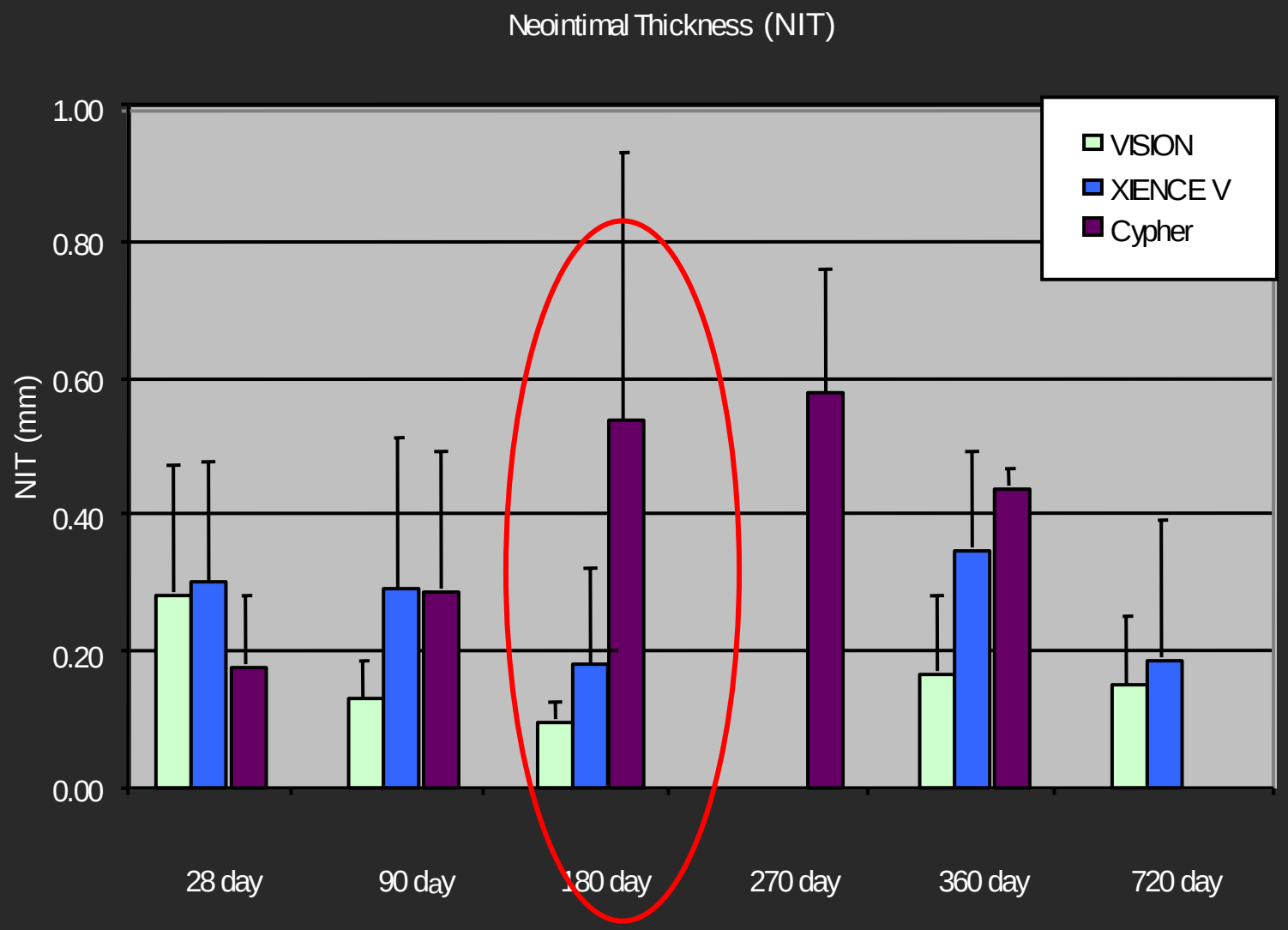



# Inflammation (Endeavor vs. Driver/ Cypher)

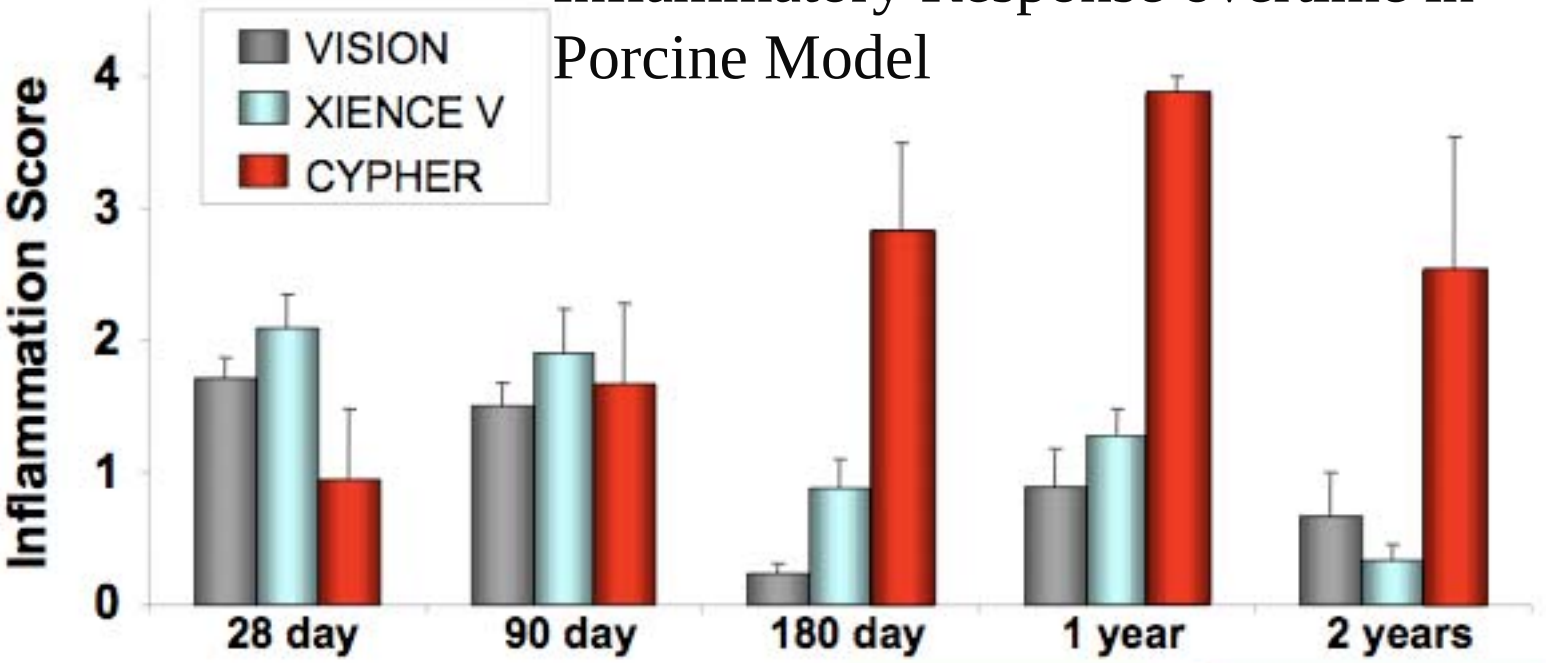


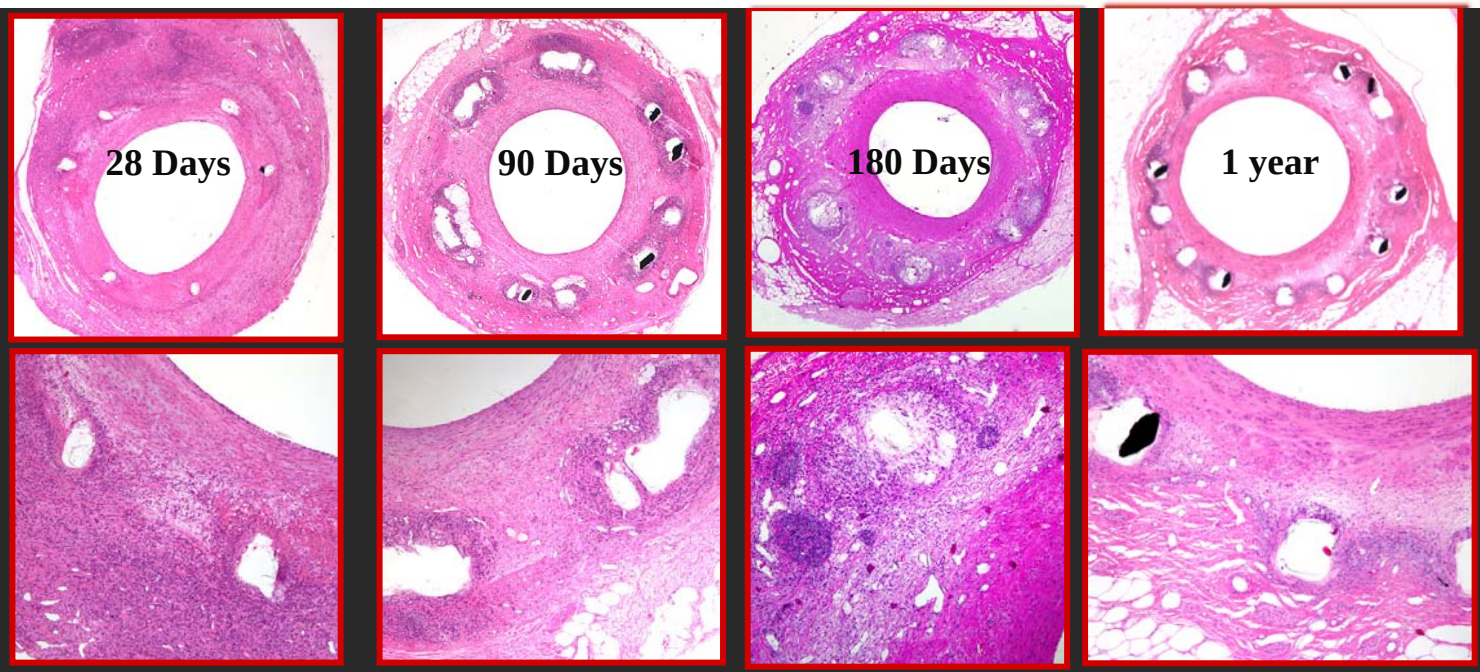
# Long Term Safety Data:Neointimal Thickness over time – Porcine Model



# Inflammatory Response overtime in Porcine Model



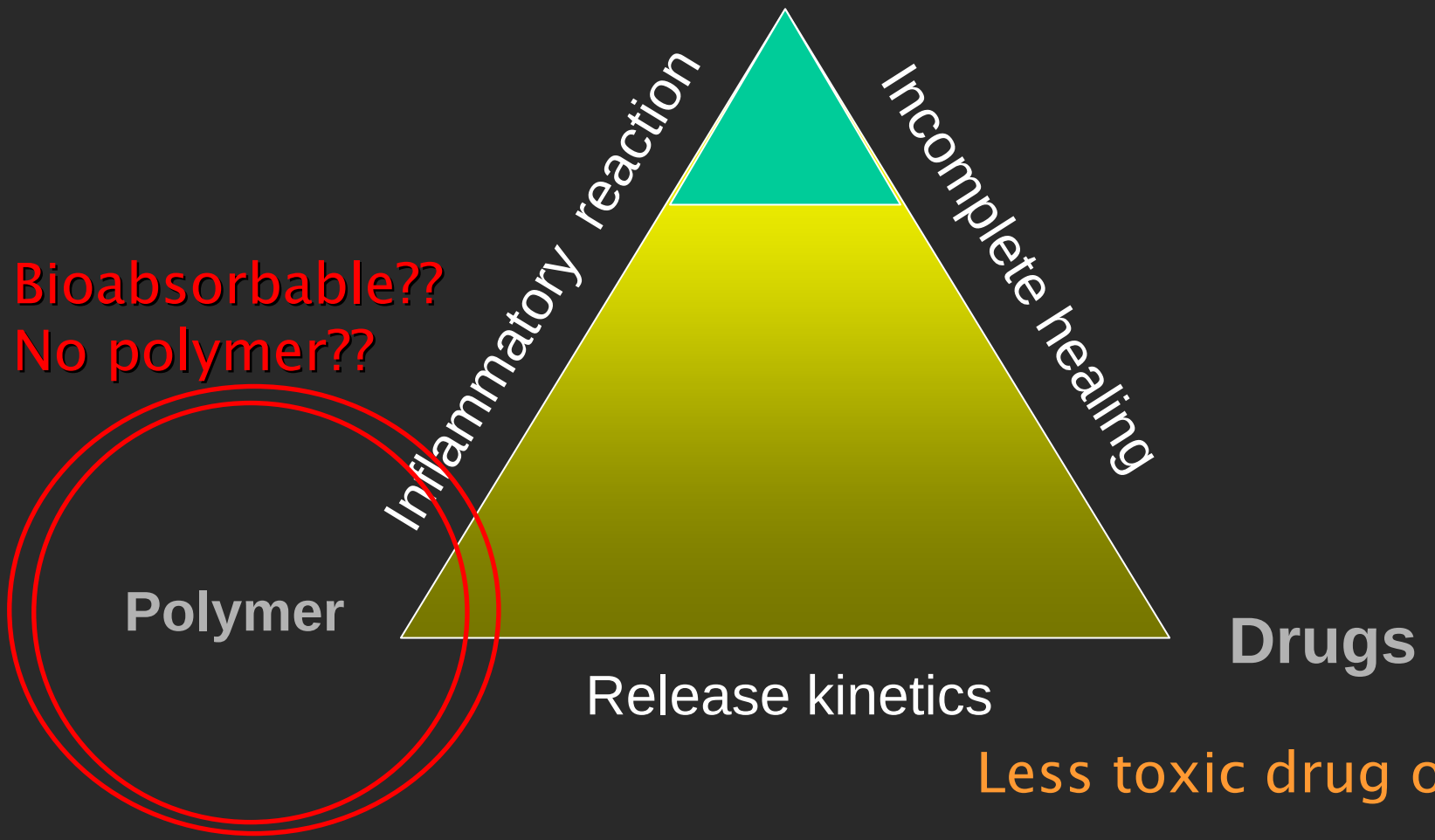

**CYPHER**



Proximal
Polymeric
DES (14-days)
Distal
Cypher
Taxus
Endeavor
Xience V
Vision

# Next Approach ??

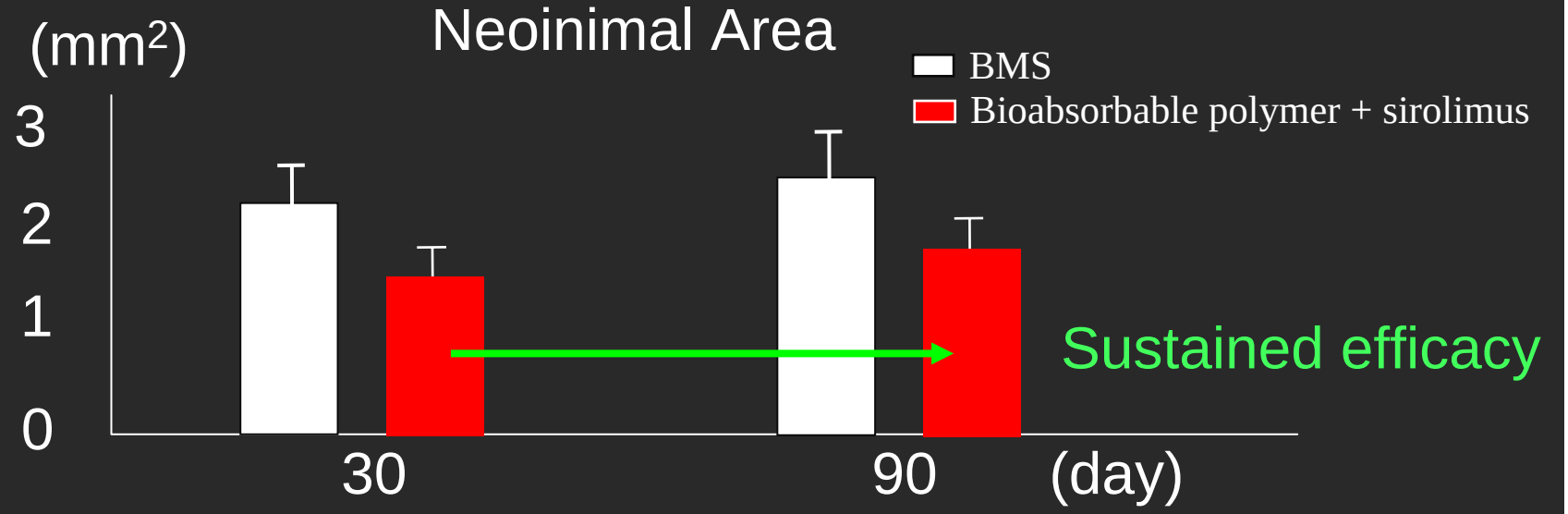
Thin struts with
radial strength




Bioabsorbable??
No polymer??

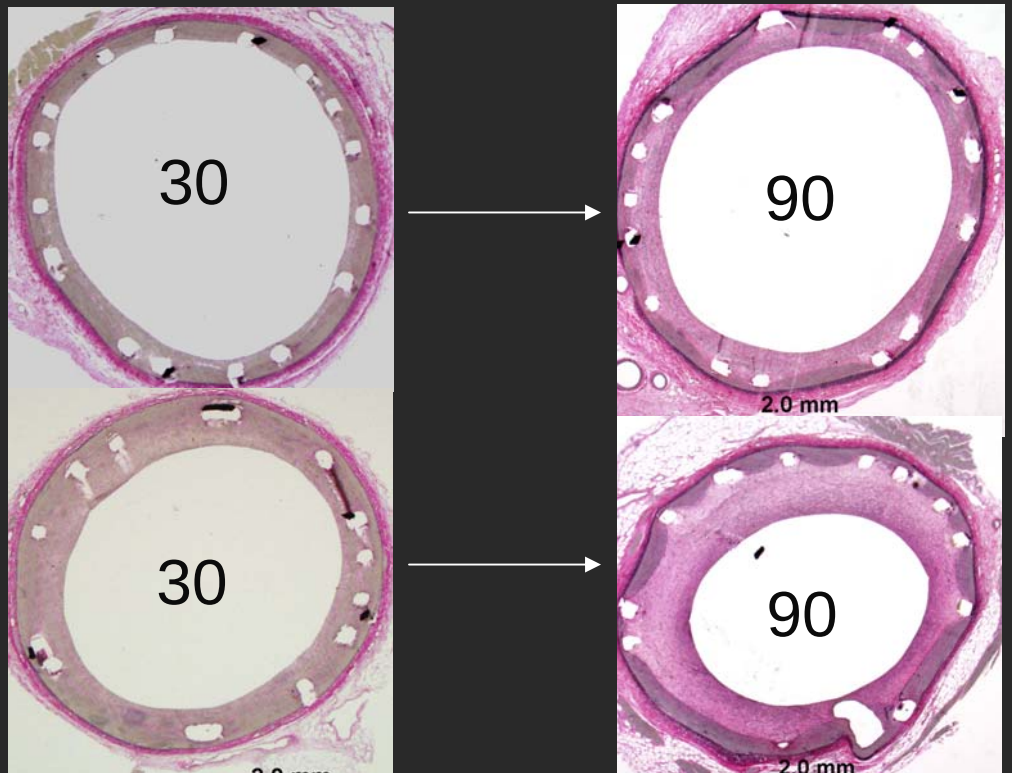
Less toxic drug or dose

# Bioabsorbable Polymer with Sirolimus in the porcine model (SurModics Inc.)

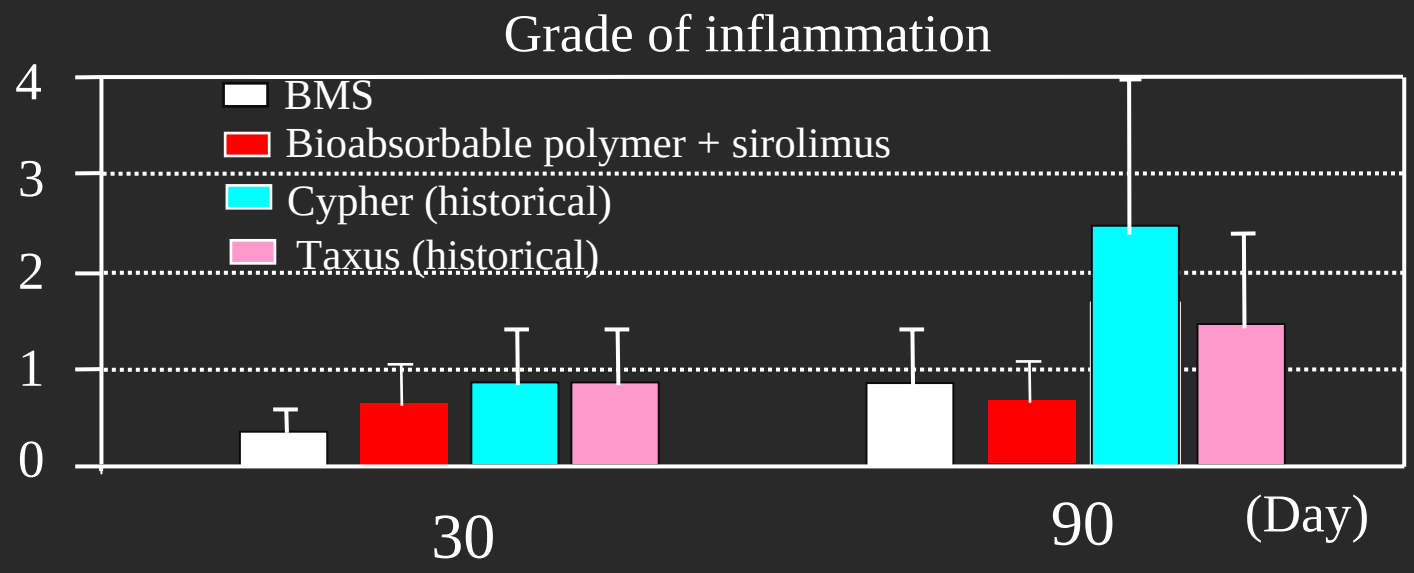


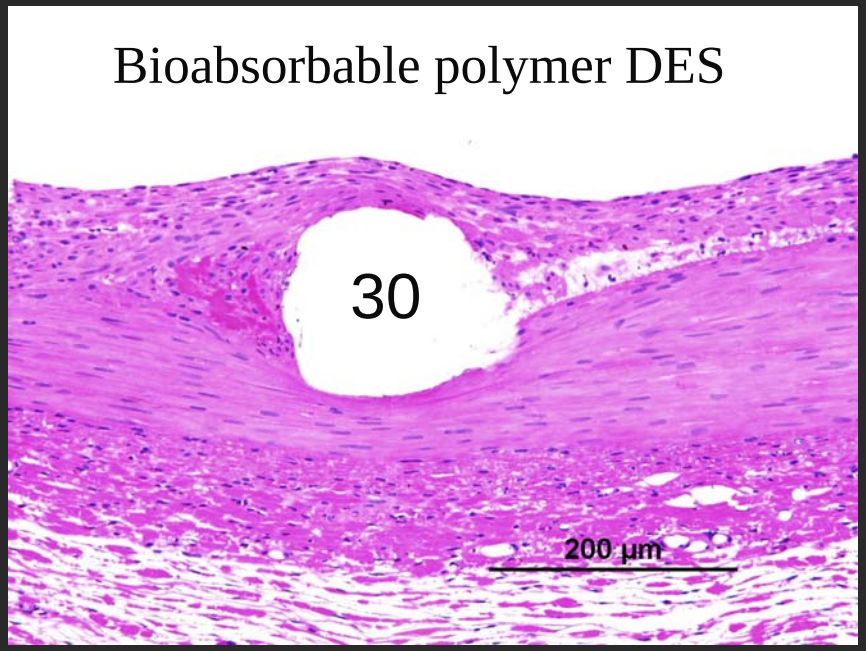

DES
(bioabsorbable polymer)

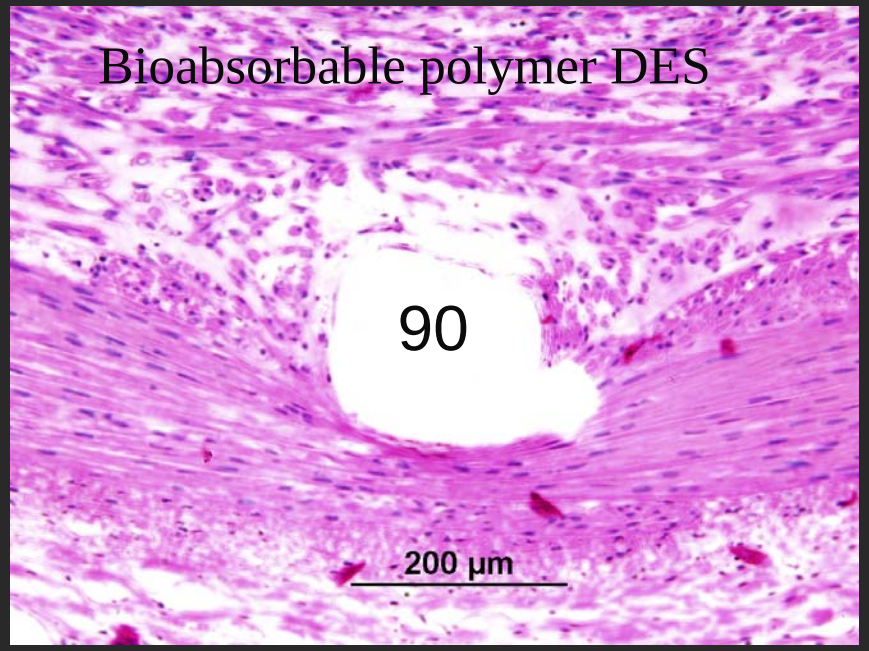
BMS
(bioabsorbable polymer)



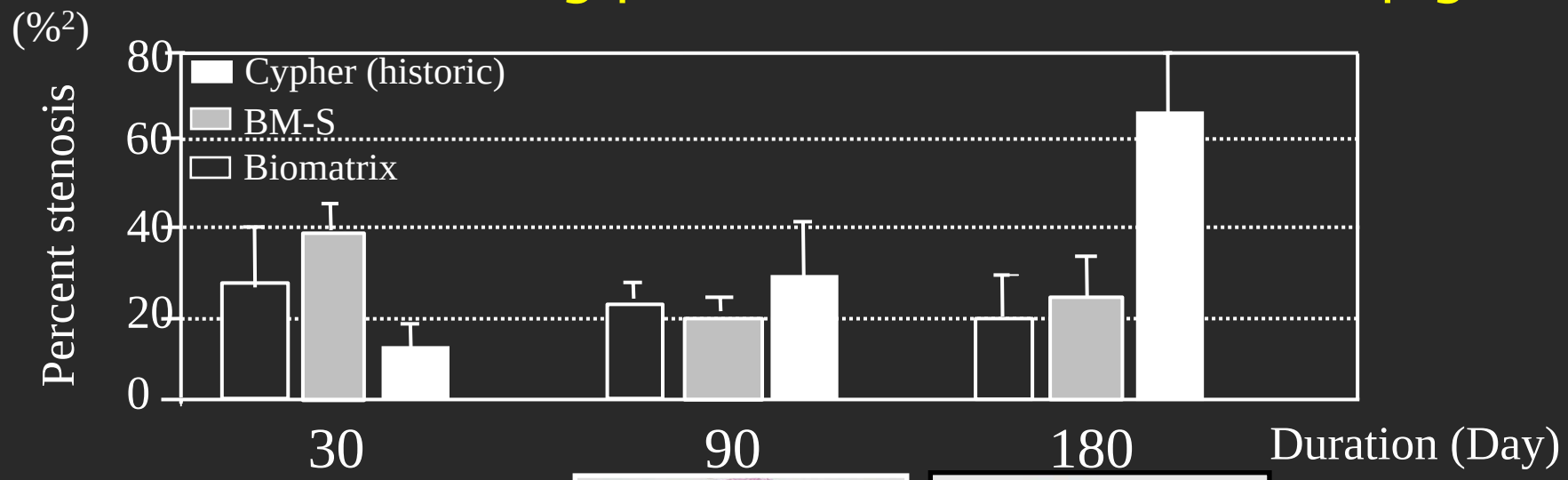
# Bioabsorbable Polymer with sirolimus in the porcine model



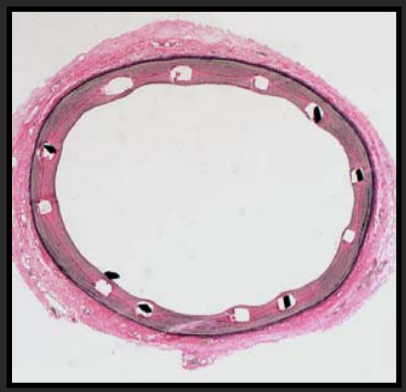
# % stenosis following placement of Biomatrix I in pig CA



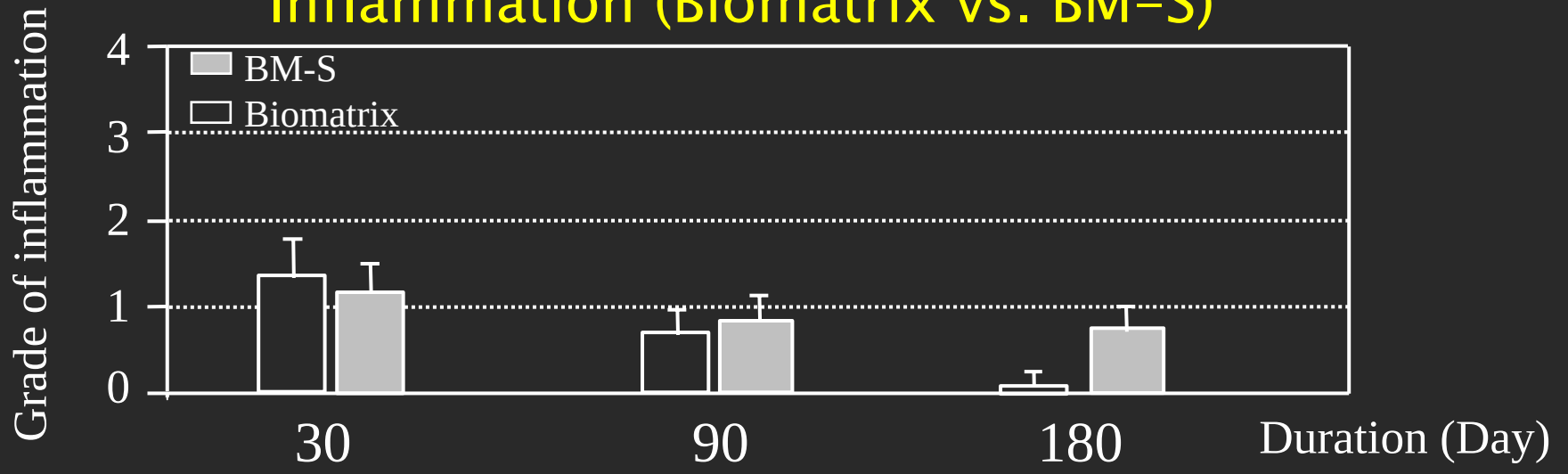

Biomatrix



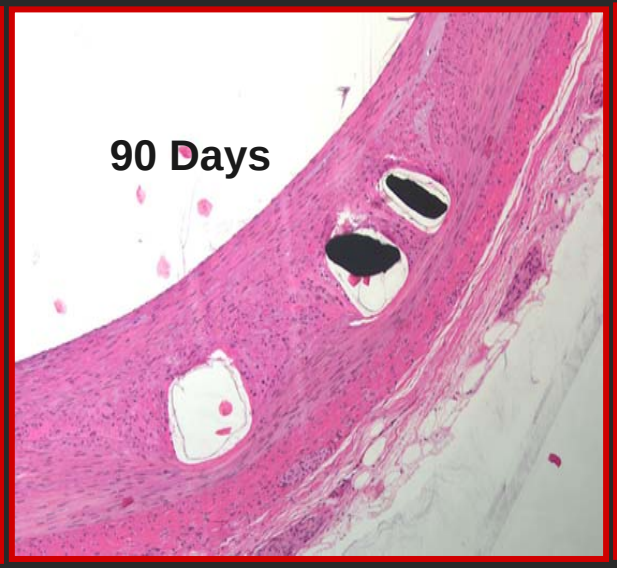

BM-S

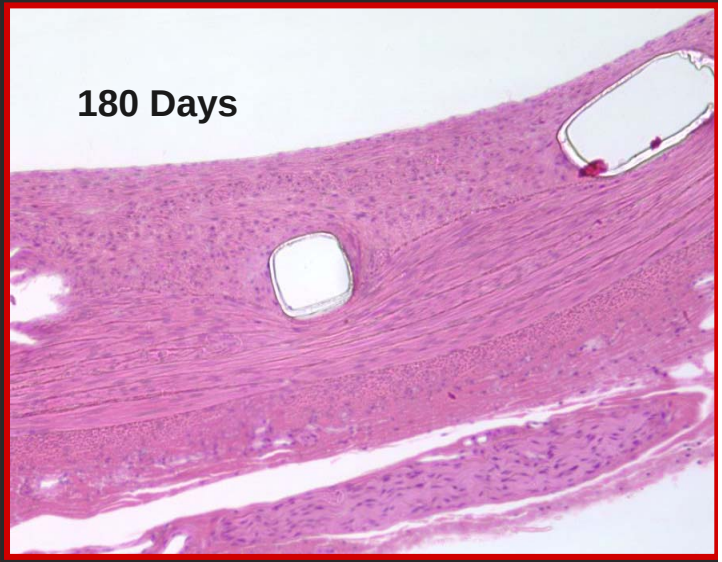


## Inflammation (Biomatrix vs. BM-S)




Xience

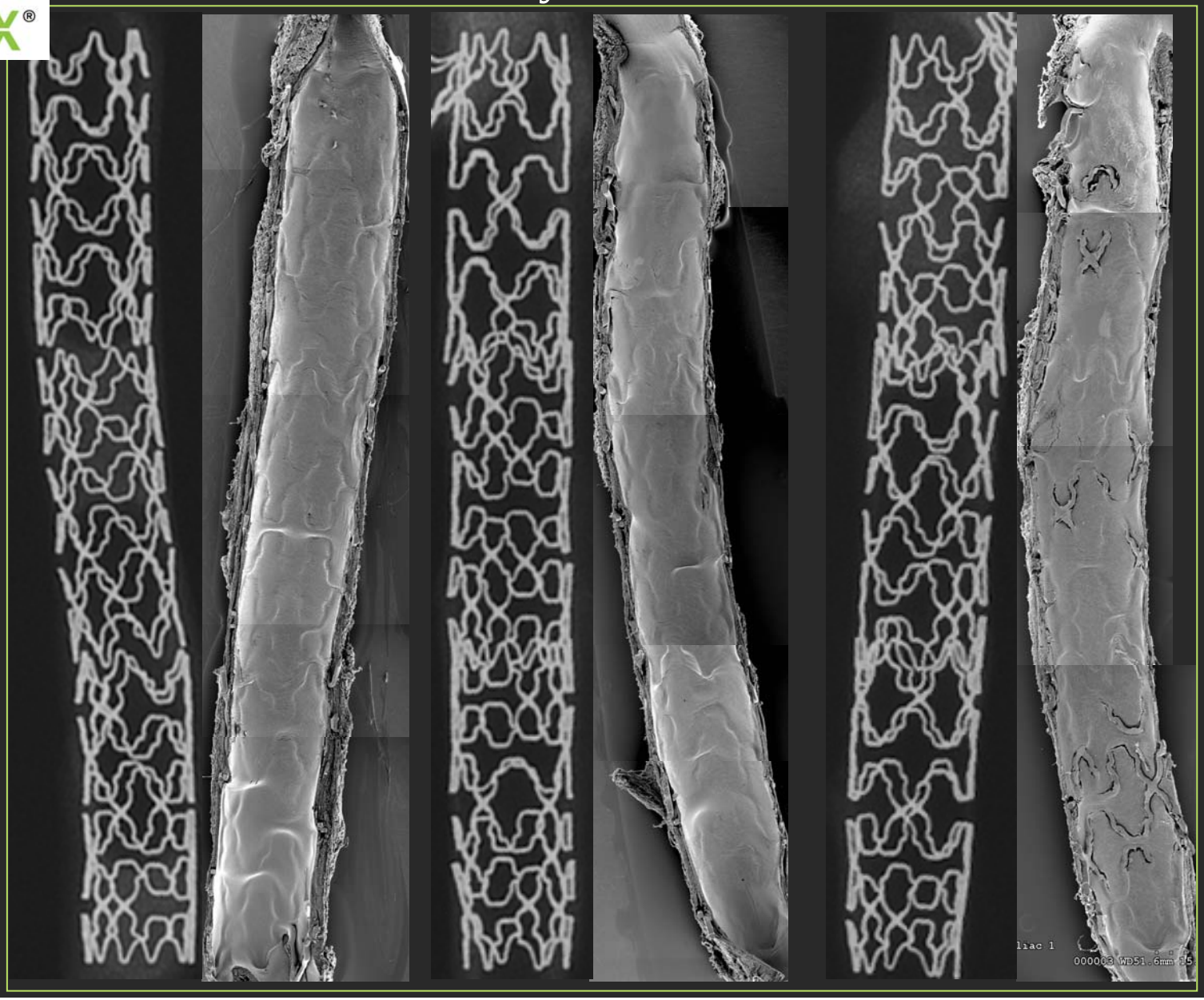
XTENT®

Custom NX®

B A9

# SEM at 28 days in Rabbit Iliac Arteries

BMS Parylene C DES



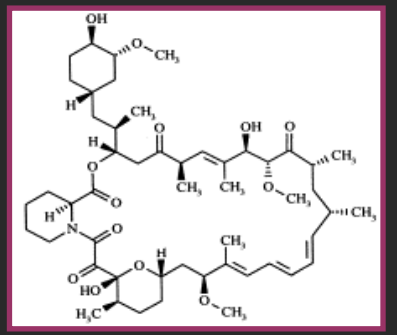
# Novel technology of Synchronnium Plus™

## Hepamer

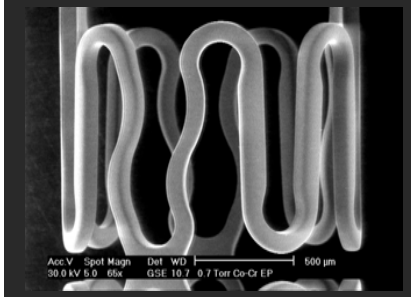
- Covalently bonded Heparinized biodegradable polymers
- Prolonged anti-platelet actions due to chemical linkage
- Improved biocompatibility and hemocompatibility due to presence of heparin molecule
- Sustained Sirolimus delivery upto 48 days

## Sirolimus

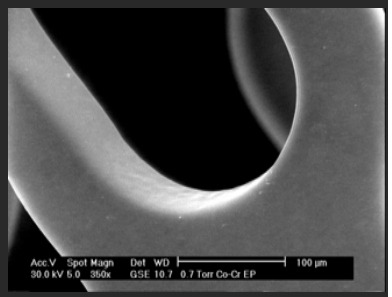
- Sirolimus is a naturally occurring Antibiotic drug.
- Wyeth-Ayerst Laboratories discovered its potent Immunosuppressive activity.
- Approved by FDA for renal and kidney transplantation (1999).



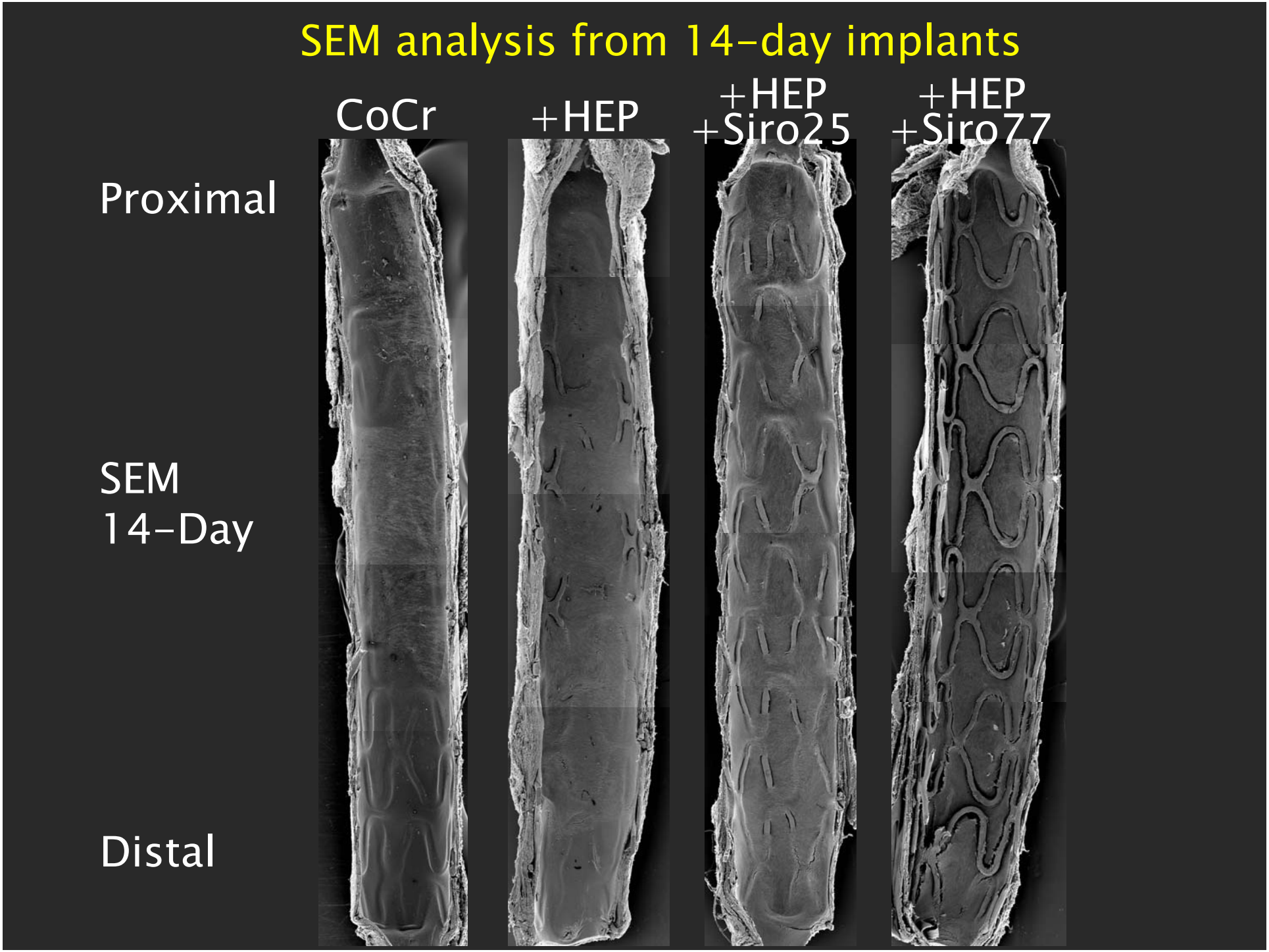
## Coronnium™ Stent

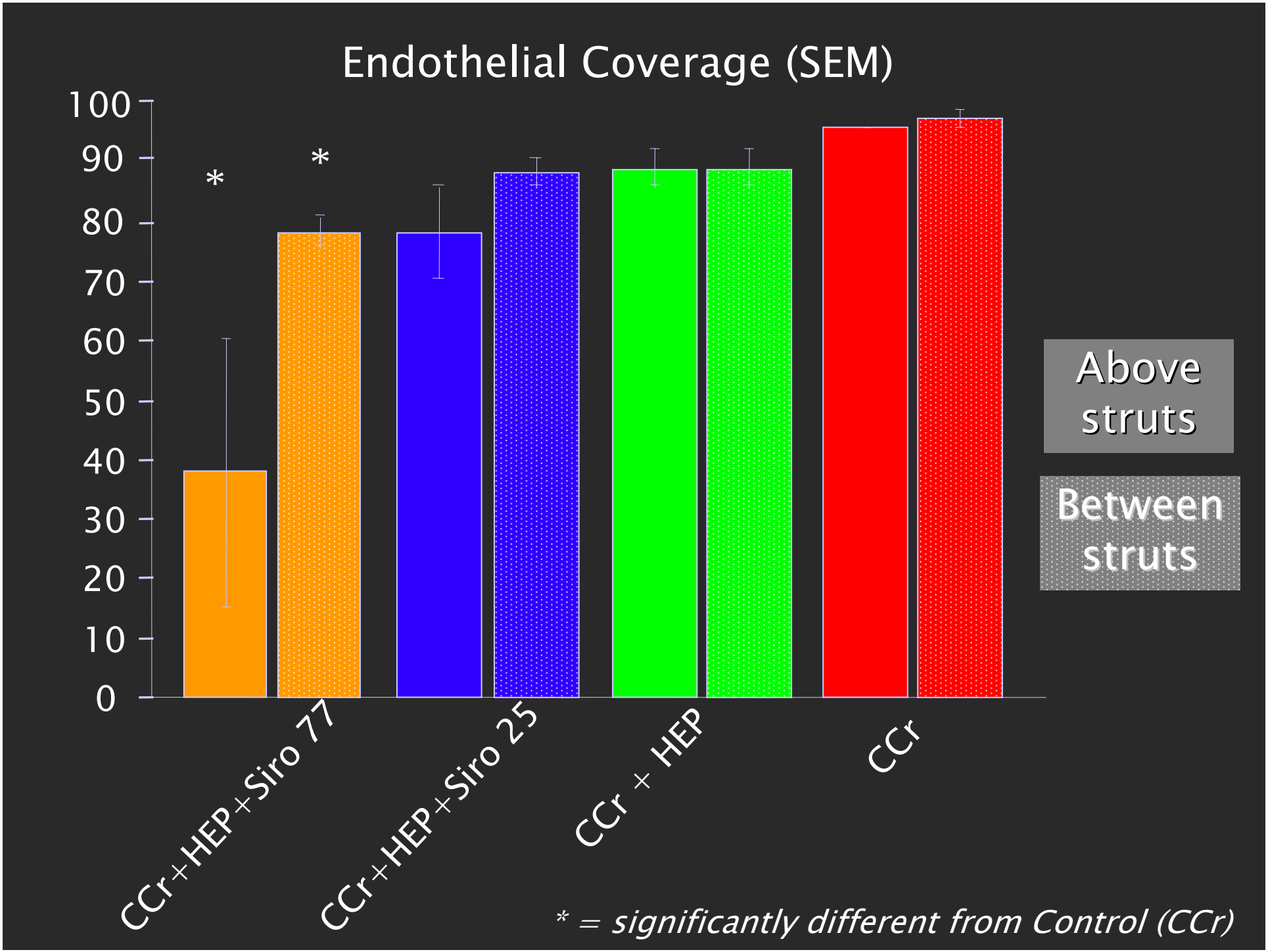



- Cobalt-chromium with round edge and thin-strut (60 µm) minimizes vessel injury
- Smooth surface of Coronnium™ stent with good biocompatible and hemocompatibility reducing incidence of thrombus formation

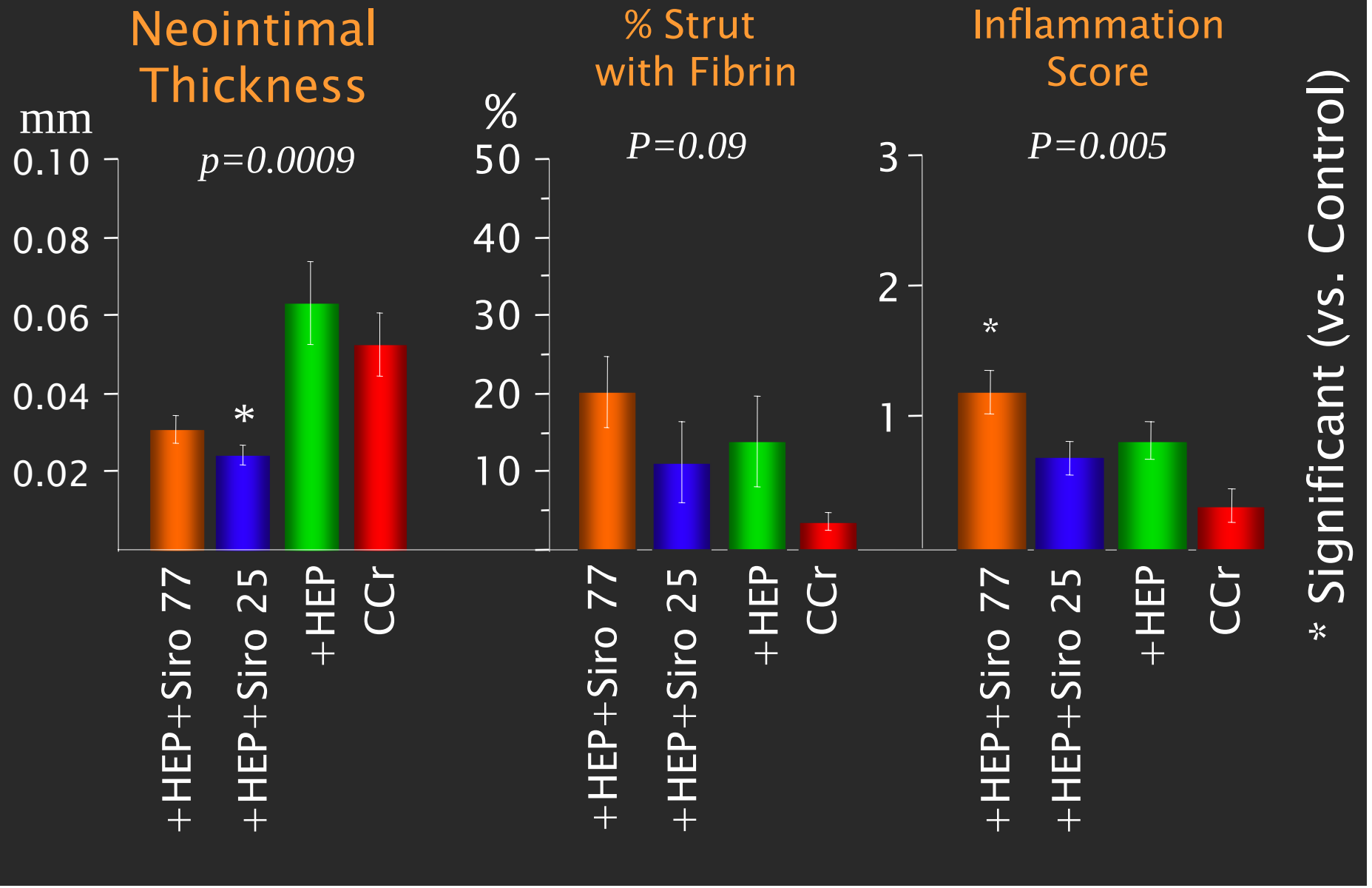


# SEM analysis from 14-day implants

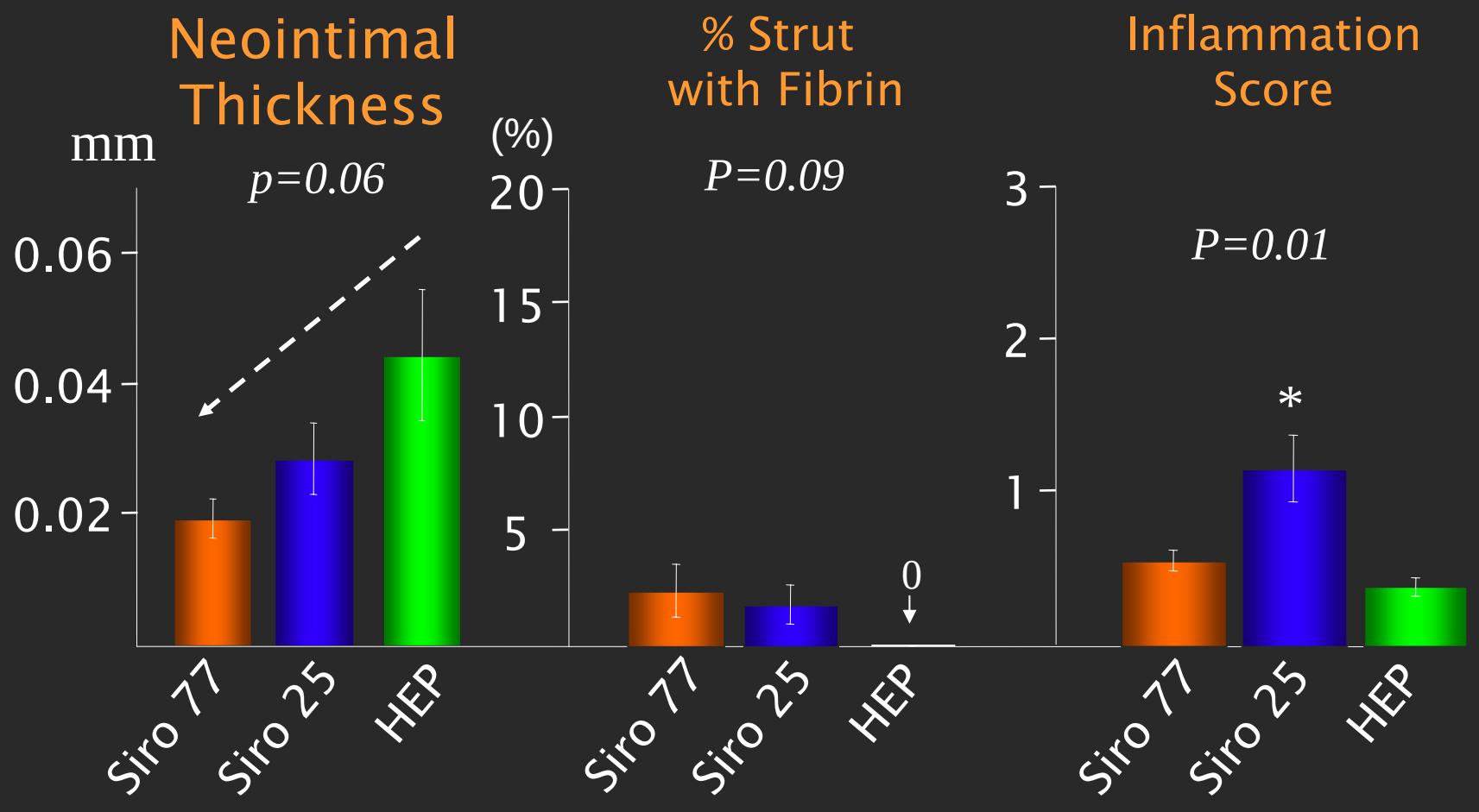



Endothelial Coverage (SEM)
100
90
80
70
60
50
40
30
20
10
0
*
*
CCr+HEP+Siro 77
CCr+HEP+Siro 25
CCr + HEP
CCr
Above struts
Between struts
* = significantly different from Control (CCr)

# Morphometric Analysis (Light microscopy) – 28 days

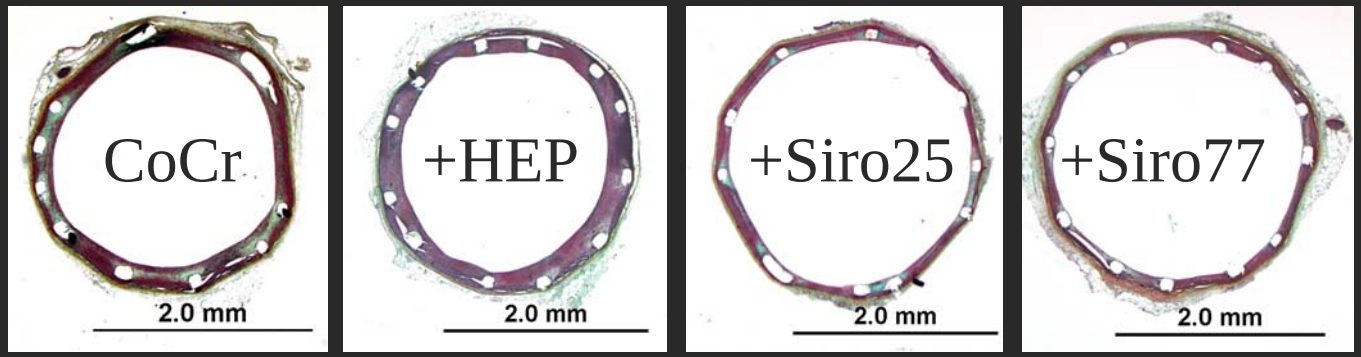


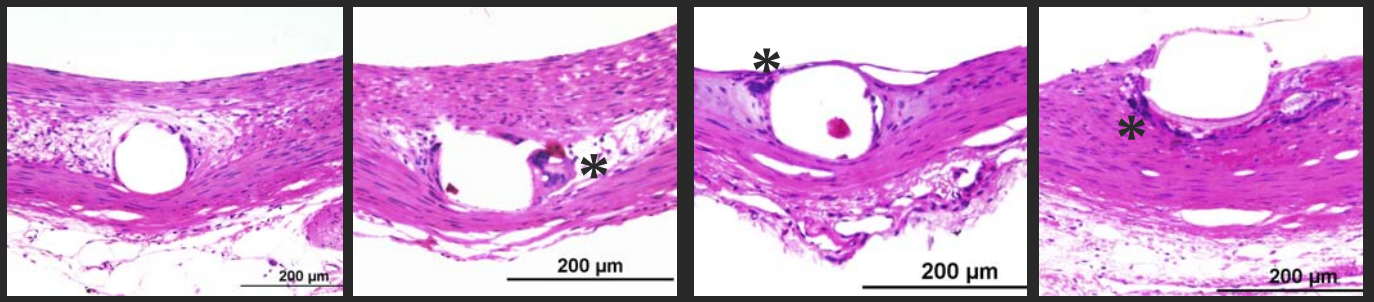
# Morphometric Analysis – 90 days



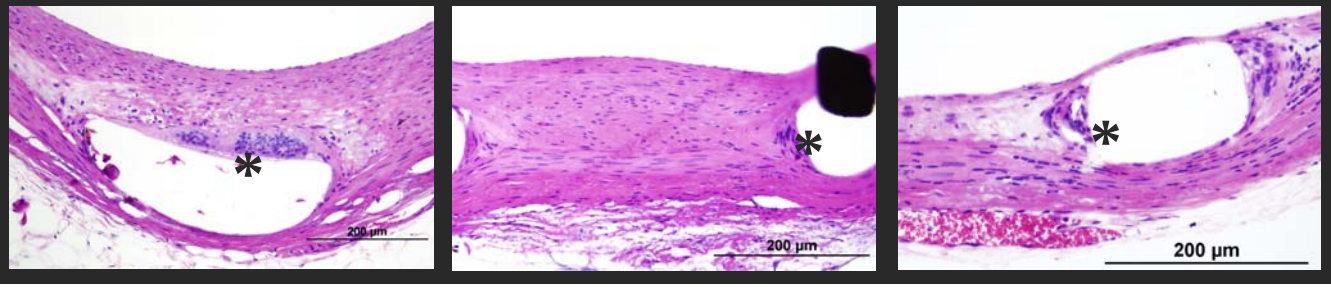
# Histologic Sections

28 days




90 days

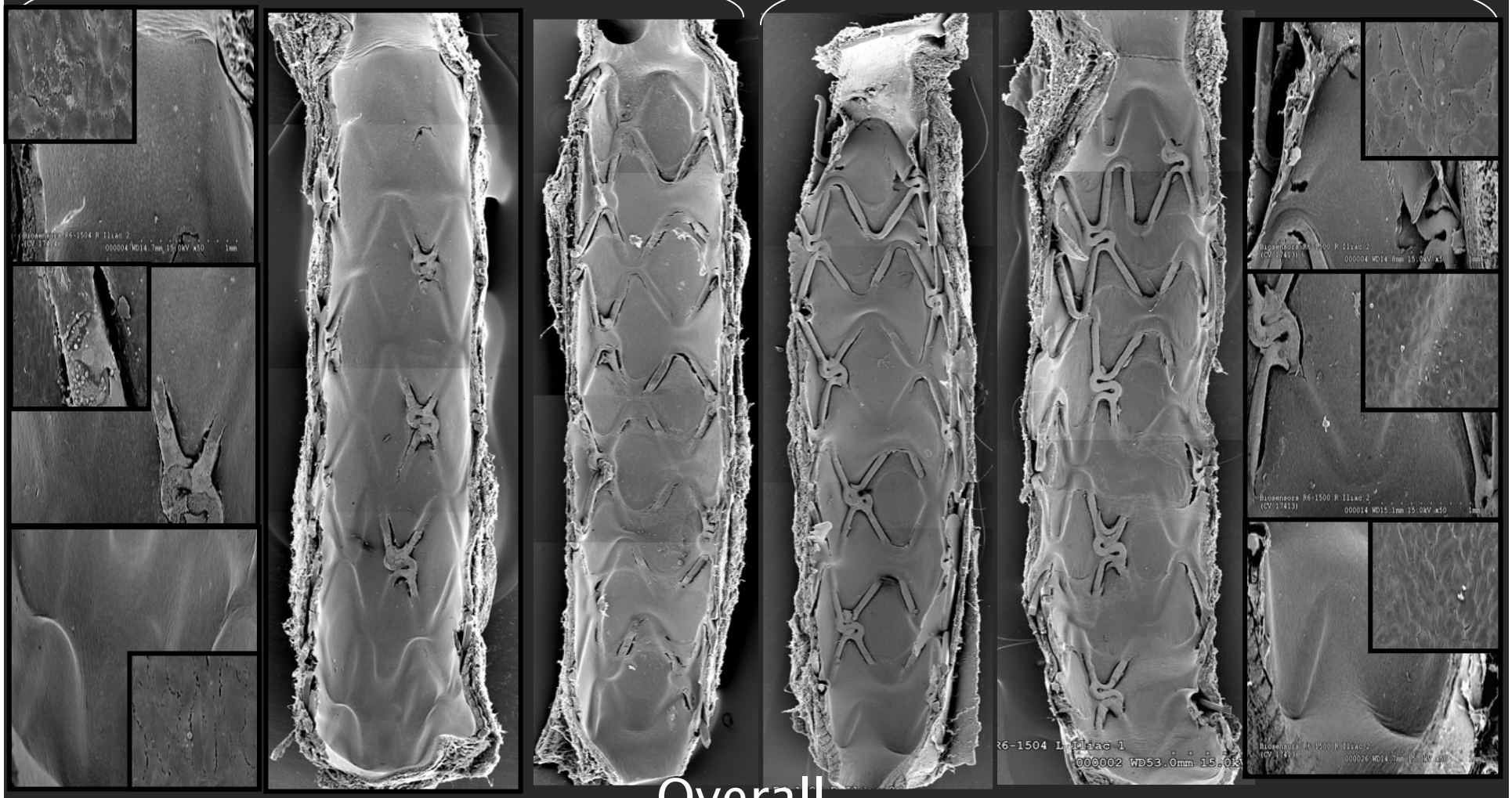

* Giant Cell

# Polymer-Free with textured surface (Freedom Stent) Biosenso

## Endothelialization at 14 days (SEM; Rabbit iliac model)

BMS

Polymer-free DES

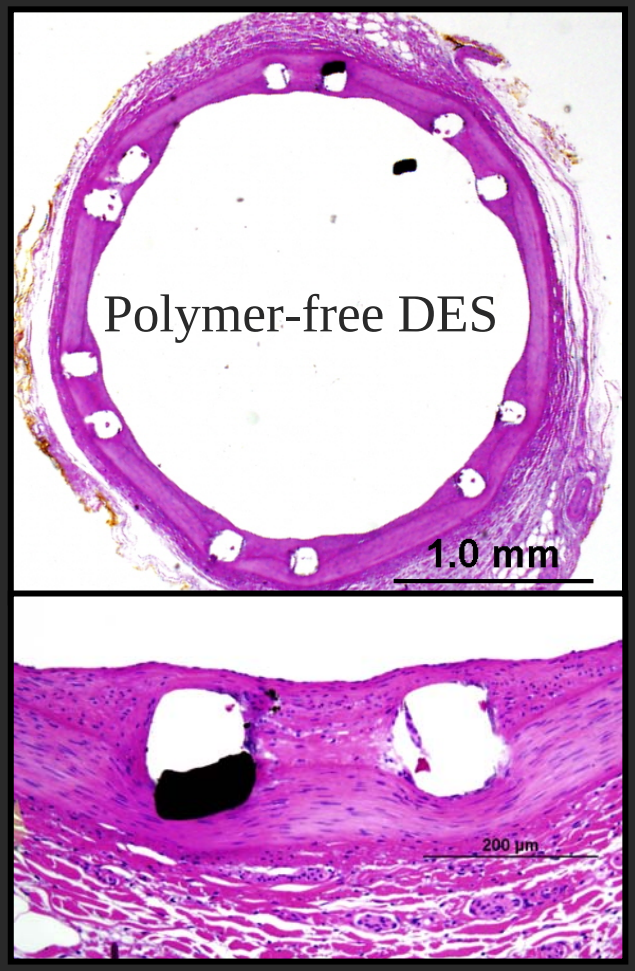


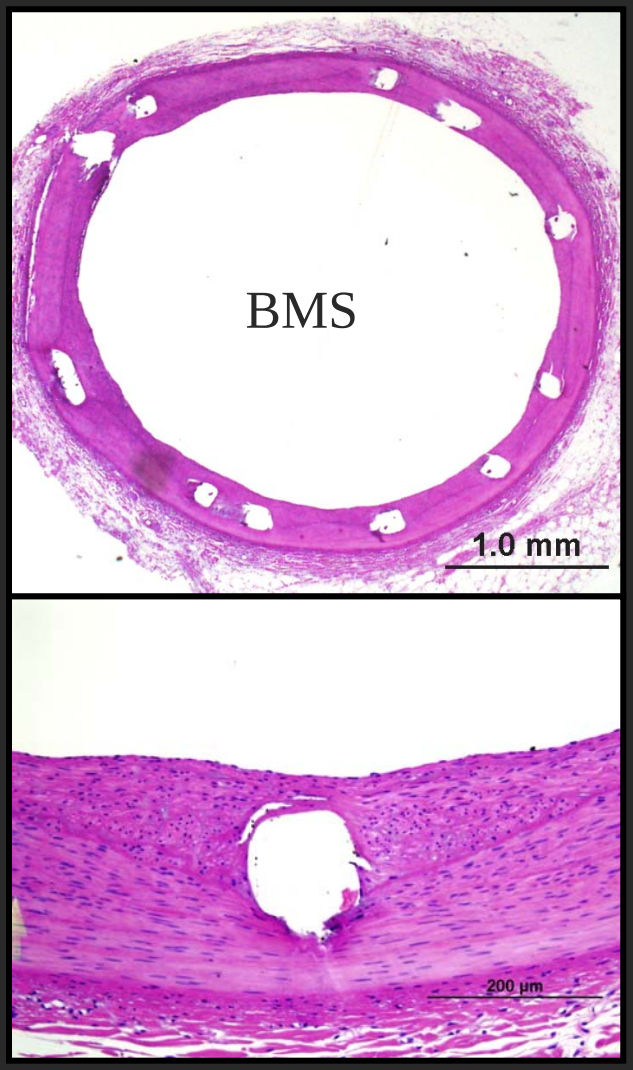
89.9±9.9%

Overall Coverage

78.4±10.7%

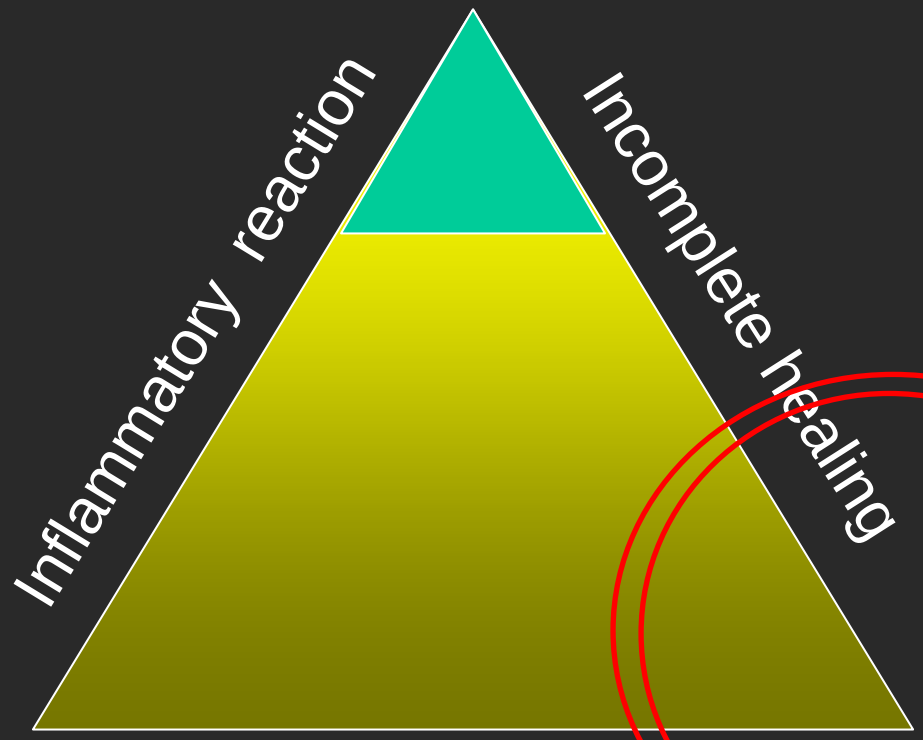
# Light microscopy at 180 days (Porcine coronary model)



# Next Approach ??

Thin struts with
radial strength



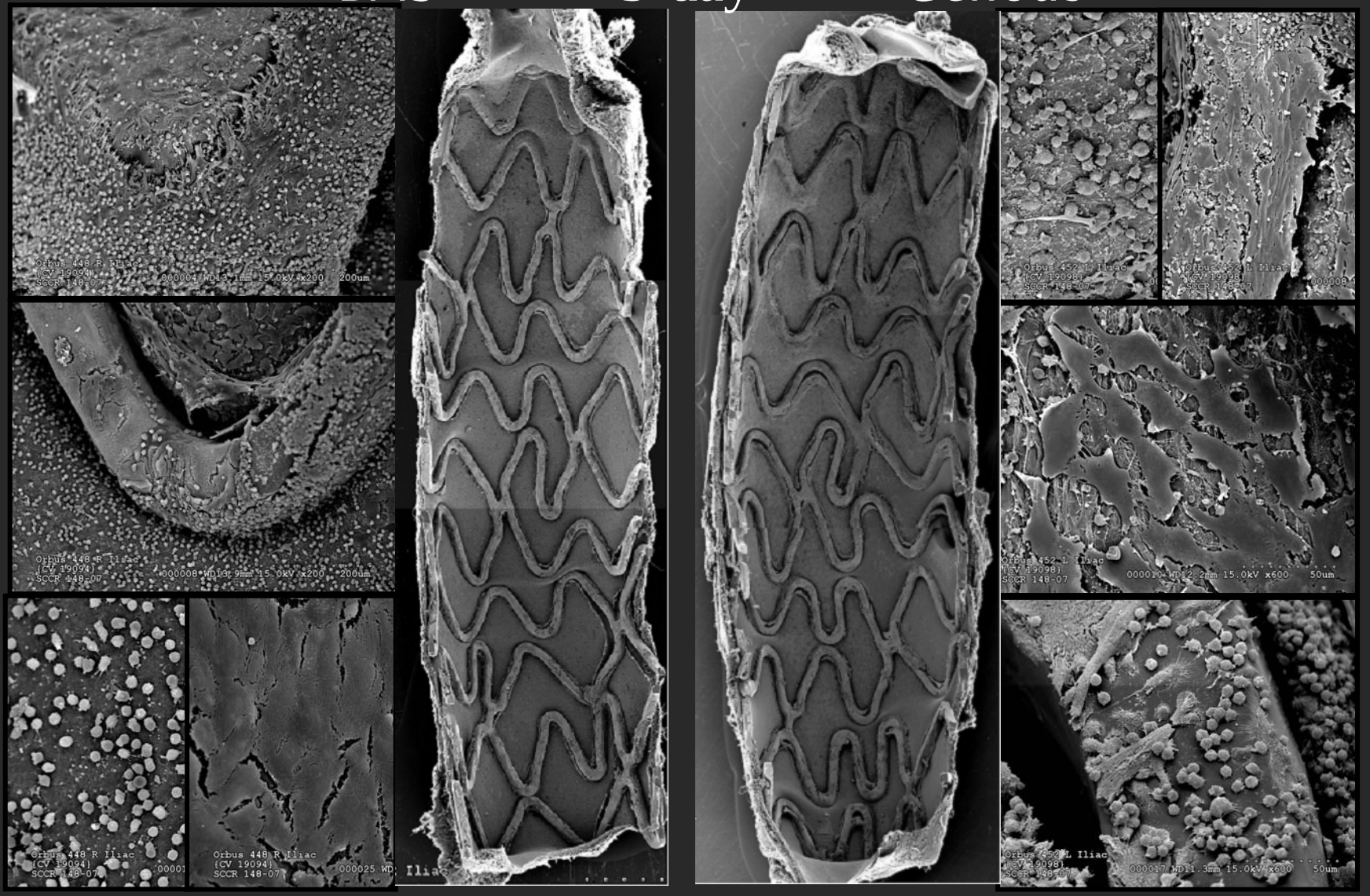

Pro-healing??

Bioabsorbable??
No polymer??

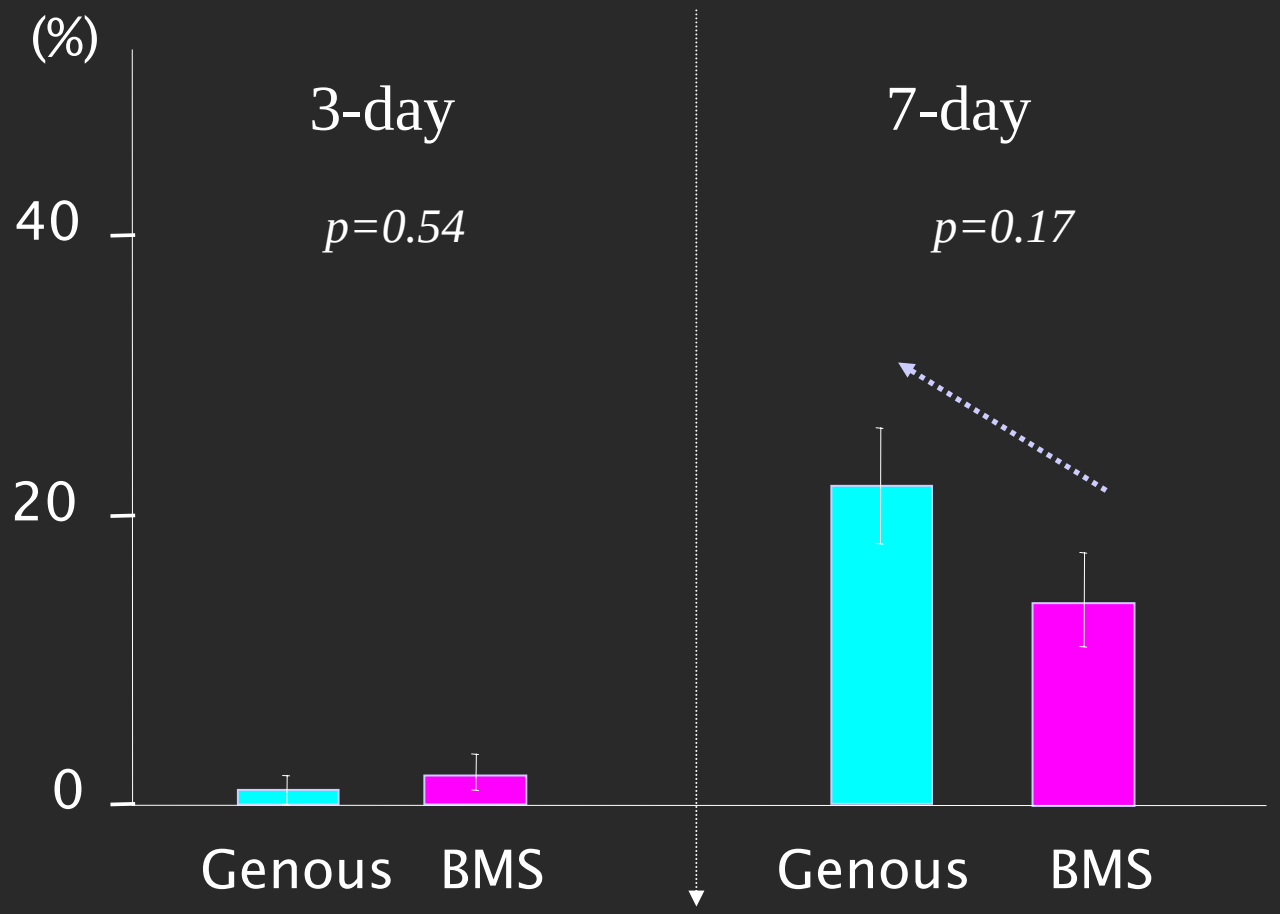
Less toxic drug or dose

# Early endothelialization of Endothelial Progenitor Cell capture stents (Genous) In the rabbit iliac model

BMS 3-day Genous

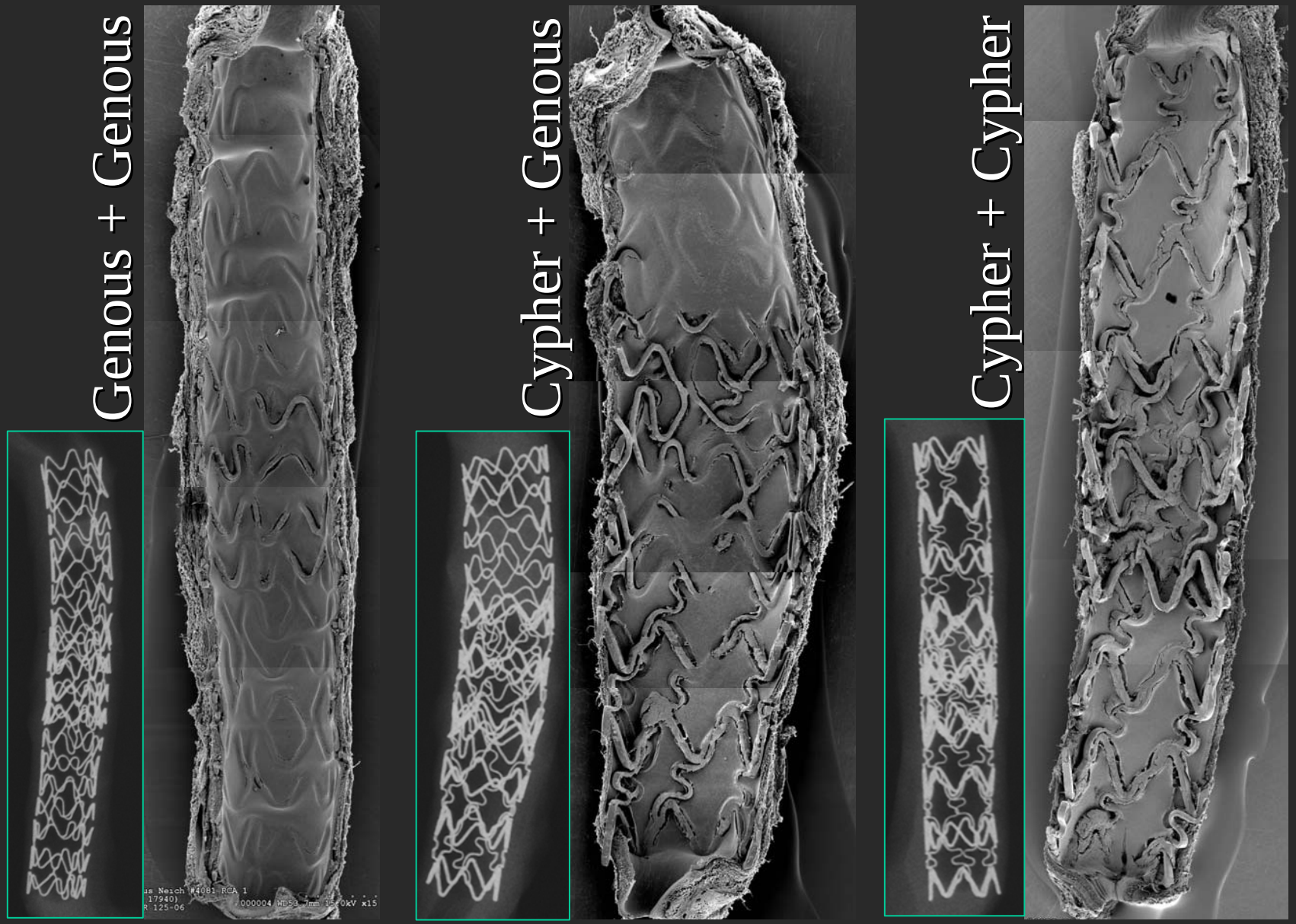


# Early endothelialization of Endothelial Progenitor Cell capture stents (Genous) In the rabbit iliac model (SEM)



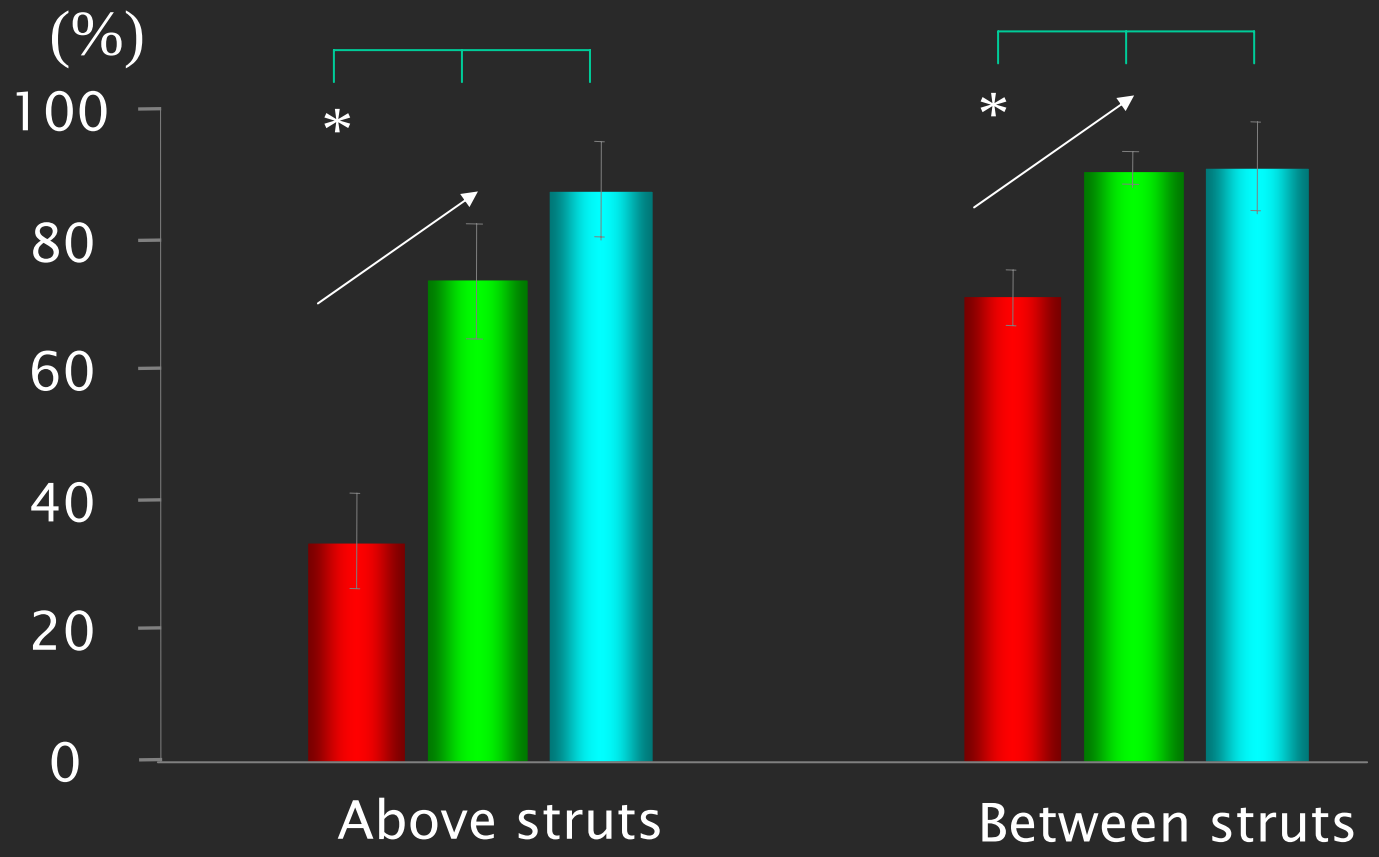
# Overlapping stent in the porcine coronary model

## DES (Cypher) + Genous



# Endothelialization at Overlapped Segment at 14 days


## Overlapped Segment




* significant

# Promising Results in Preclinical Studies

- ✓ New stent designs and materials are beginning to show early good results in animal models, inducing less inflammation and early endothelialization.
- ✓ Next generation of DES with permanent but mostly bioerodable polymers and some without polymers are promising technologies that will soon or are already undergone clinical trials and indeed show early good results.