

**Evolution of Novel
BioMime™ Sirolimus Eluting Stent
on a Biodegradable Polymer Platform**

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Disclosure Statement of Financial Interest

I, Wojciech Wojakowski DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

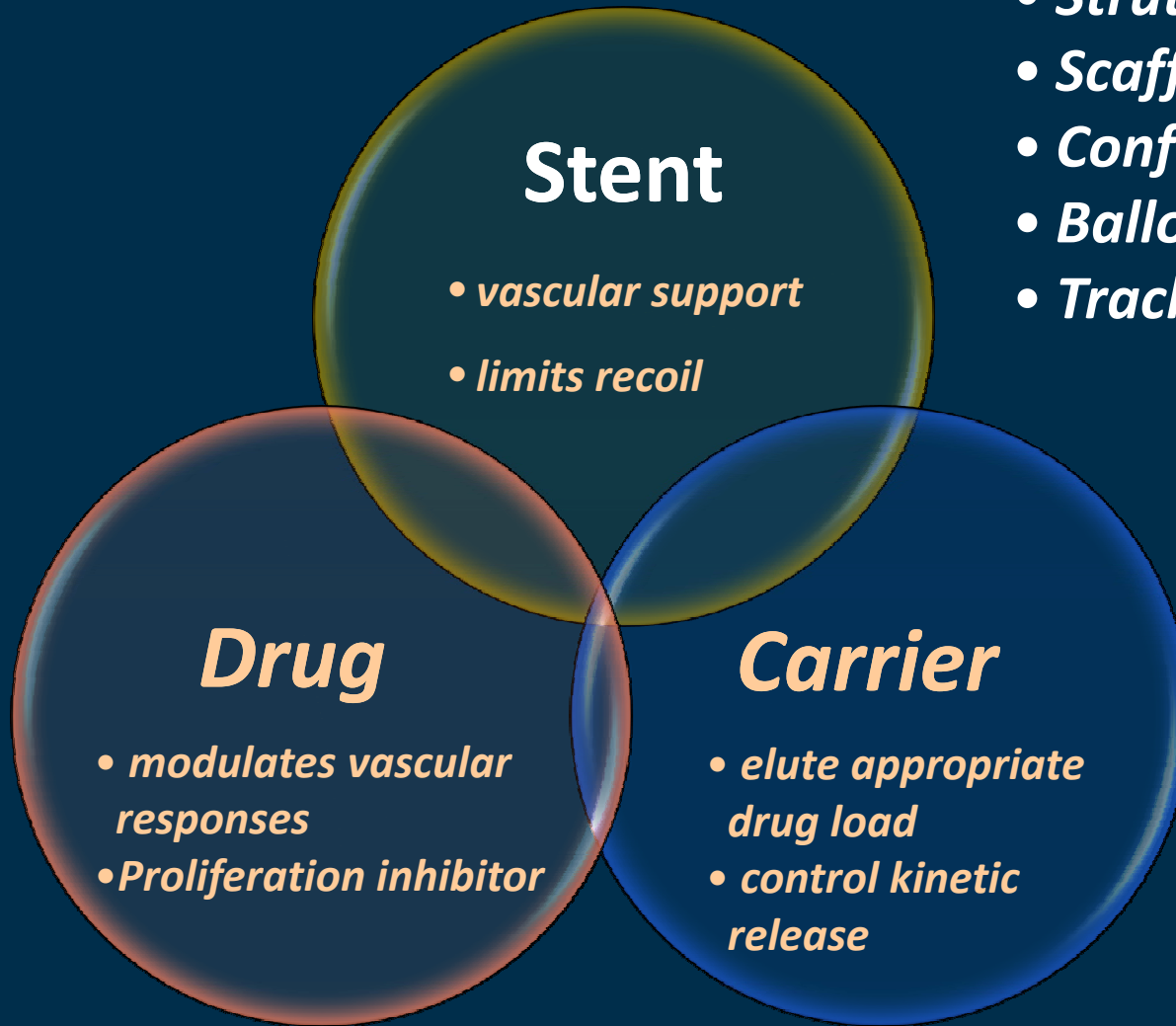
DRUG ELUTING STENTS

*Significant reduction of in-stent restenosis
and TLR vs. BMS, but:*

- *ISR still present (7-15%)*
- *Stent thrombosis is a valid safety concern*
- *Procedure-, patient-, stent-related factors*

STENT-RELATED FACTORS

- ***incomplete endothelialization/neointima coverage***
- ***inflammatory reaction***
- ***polymer/drug hypersensitivity reaction***
- ***late incomplete apposition***
- ***chronic drug toxicity***
- ***endothelial dysfunction***

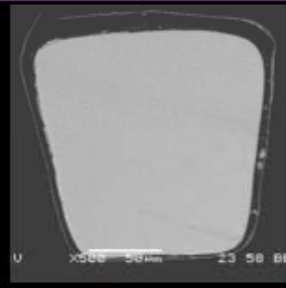
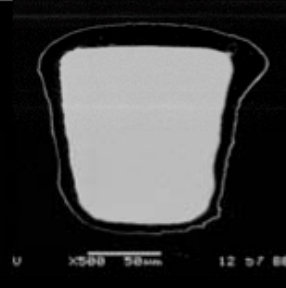

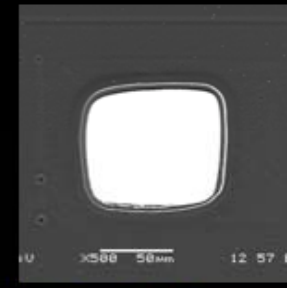


- *Strut Thickness*
- *Scaffolding*
- *Conformability*
- *Balloon Tapers*
- *Trackability*

MINIMIZING STRUT AND POLYMER THICKNESS TO REDUCE INJURY AND IMPROVE HEALING

1st generation DES

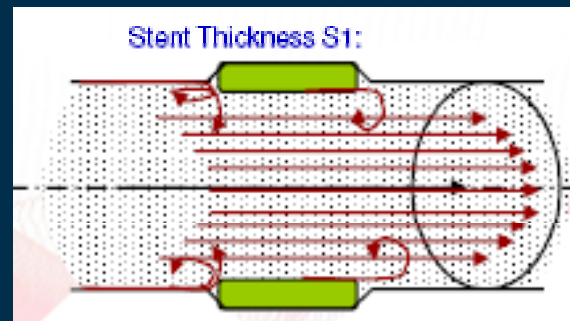
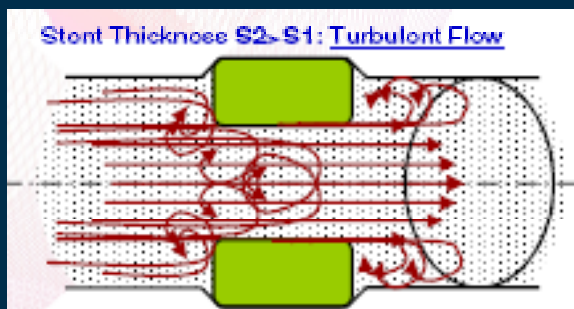
2nd generation DES

CYPHER®	TAXUS® EXPRESS	ENDEAVOR™	XIENCE™ V
			
Strut Thickness: 140 µm	Strut Thickness: 132 µm	Strut Thickness: 91 µm	Strut Thickness: 81 µm
Polymer Thickness: 12.6 µm	Polymer Thickness: 16 µm	Polymer Thickness: 5.3 µm	Polymer Thickness: 7.6 µm
PEVA+PBMA	SIBBS	PC	Fluoropolymer
Sirolimus	Paclitaxel	Zotarolimus	Everolimus

BioMime™



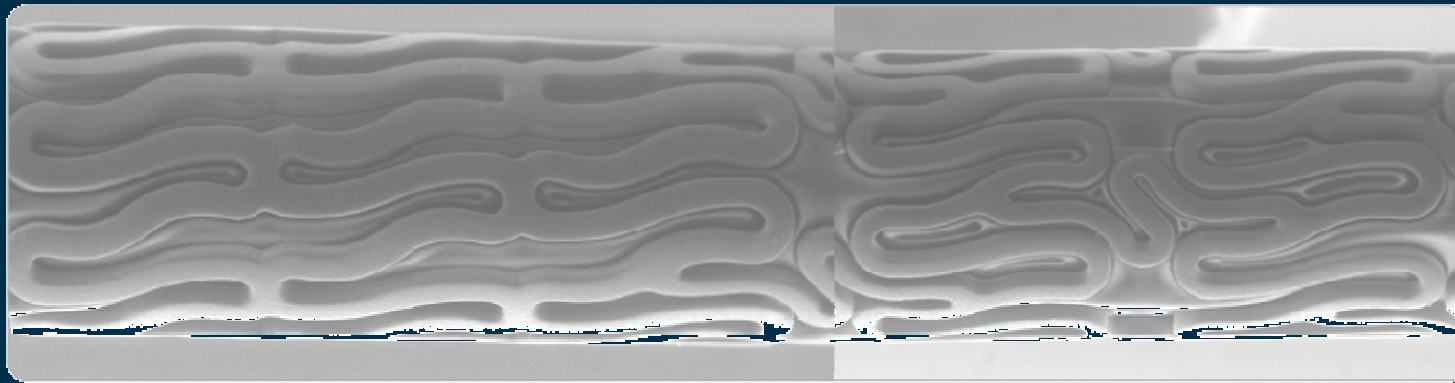
Strut Thickness:
65 µm
Polymer Thickness:
2 µm
PLLA & PLGA
Sirolimus



STENT DESIGN

- BioMime™ stent is built on CE marked NexGen™ – cobalt chromium platform.
- Hybrid cell design

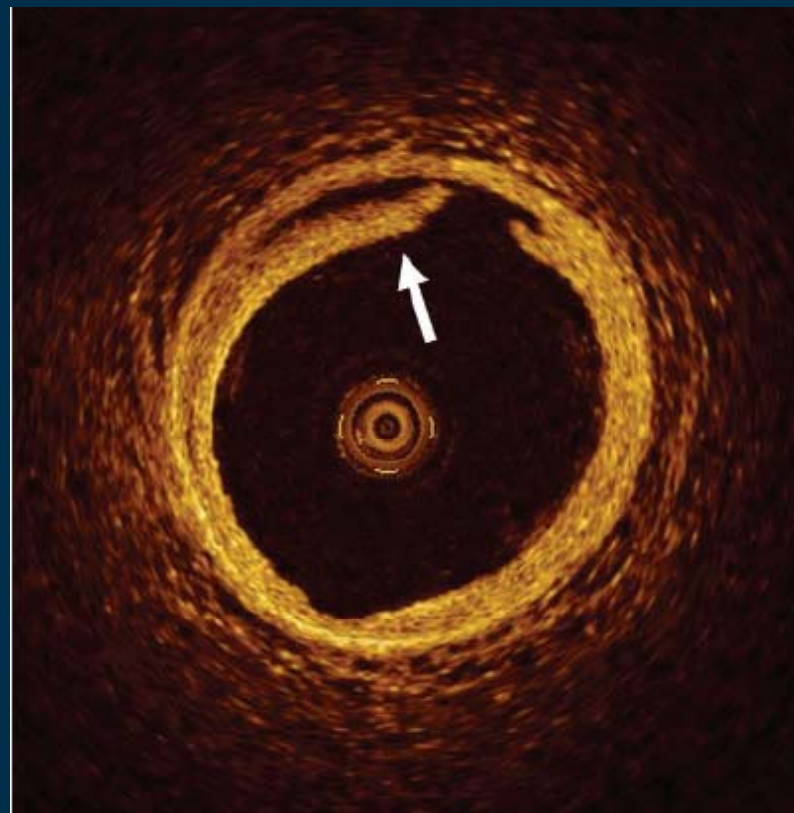
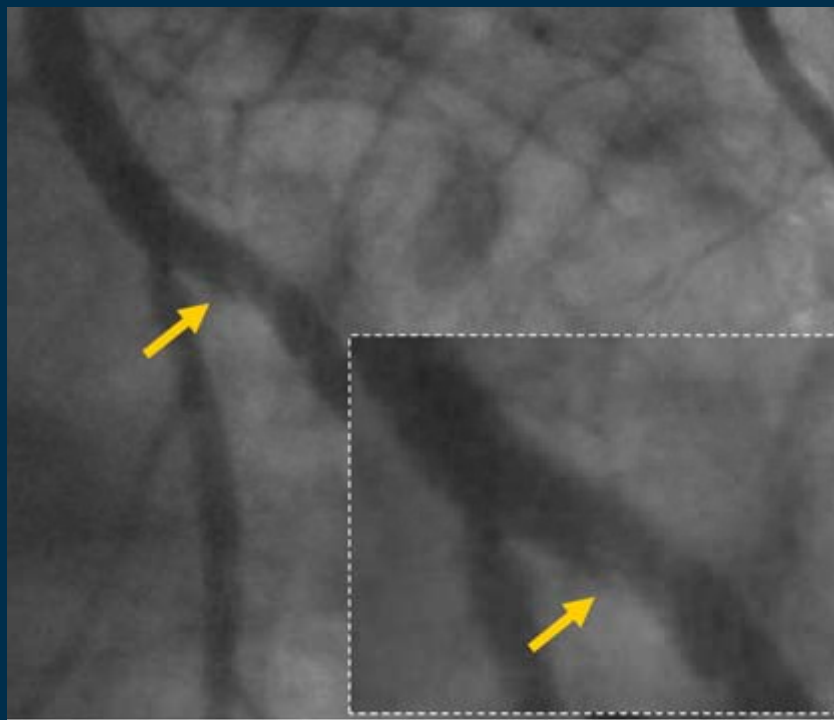
SEM image of crimped BioMime SES at 50x



Closed cell at edges

Open cell in mid - segment

EDGE DISSECTION IN OCT



Edge dissection

Edge dissection visible, n (%)

20/76 (26.3)

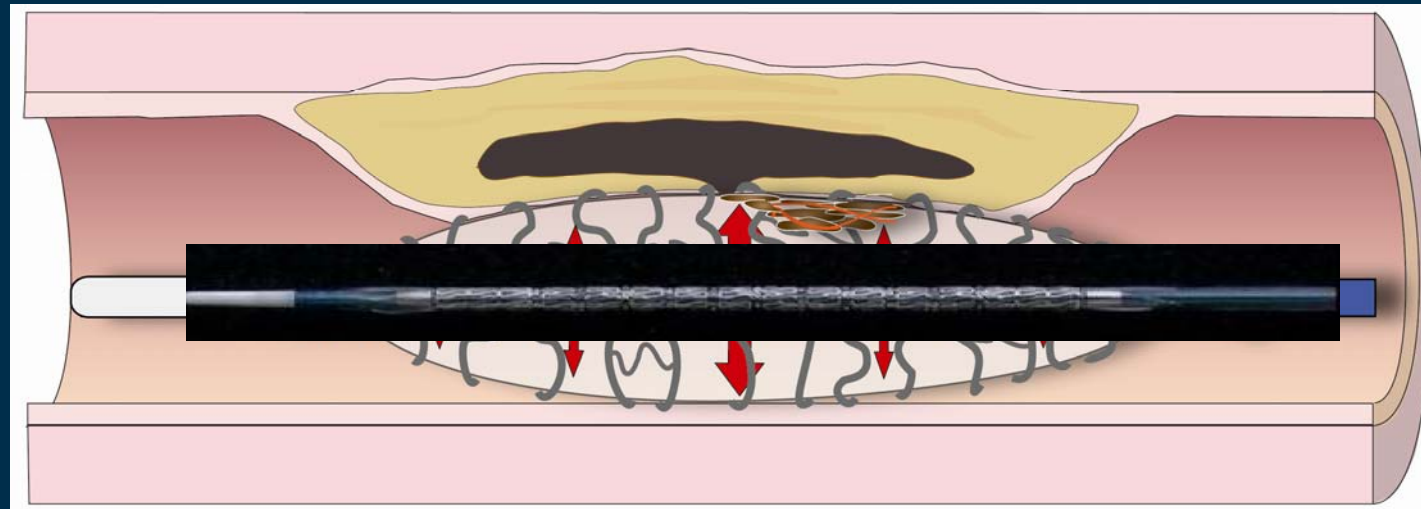
Length edge dissection flap, mean (SD)

744 (439)

Gonzalo et al. International Journal of Cardiology (2010)

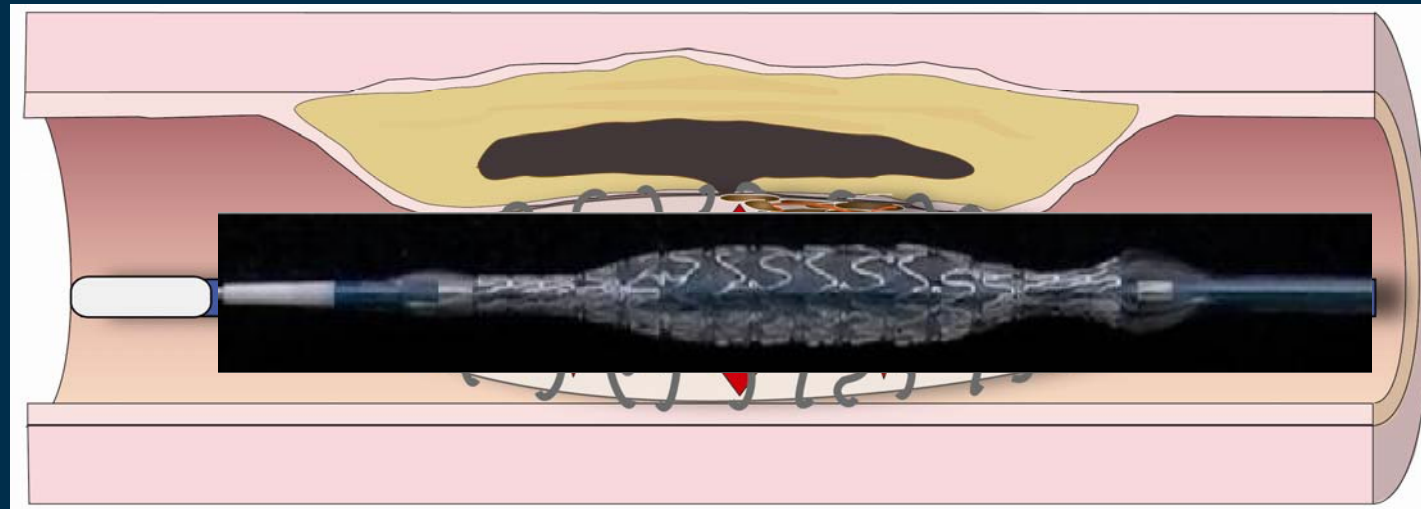
PREVENTION OF EDGE DISSECTION

Staged expansion



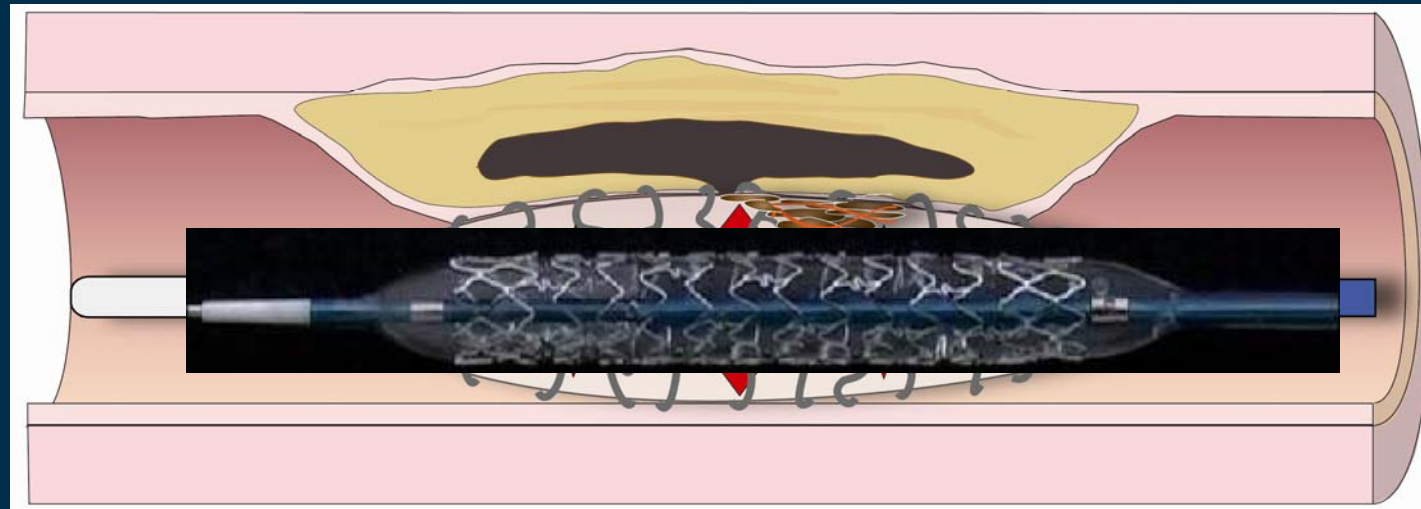
PREVENTION OF EDGE DISSECTION

Staged expansion

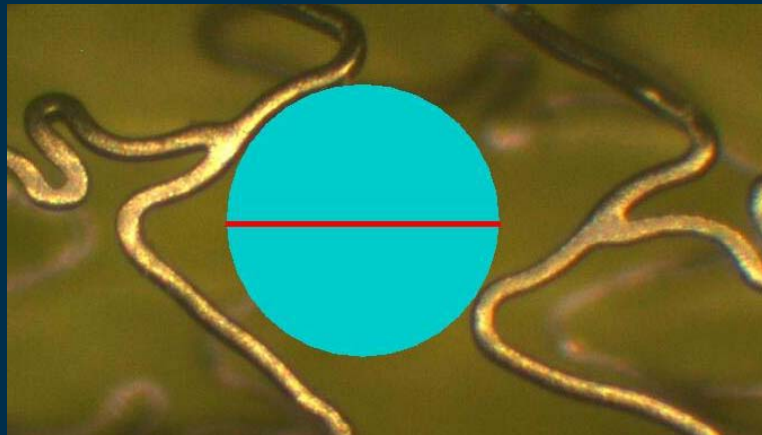


PREVENTION OF EDGE DISSECTION

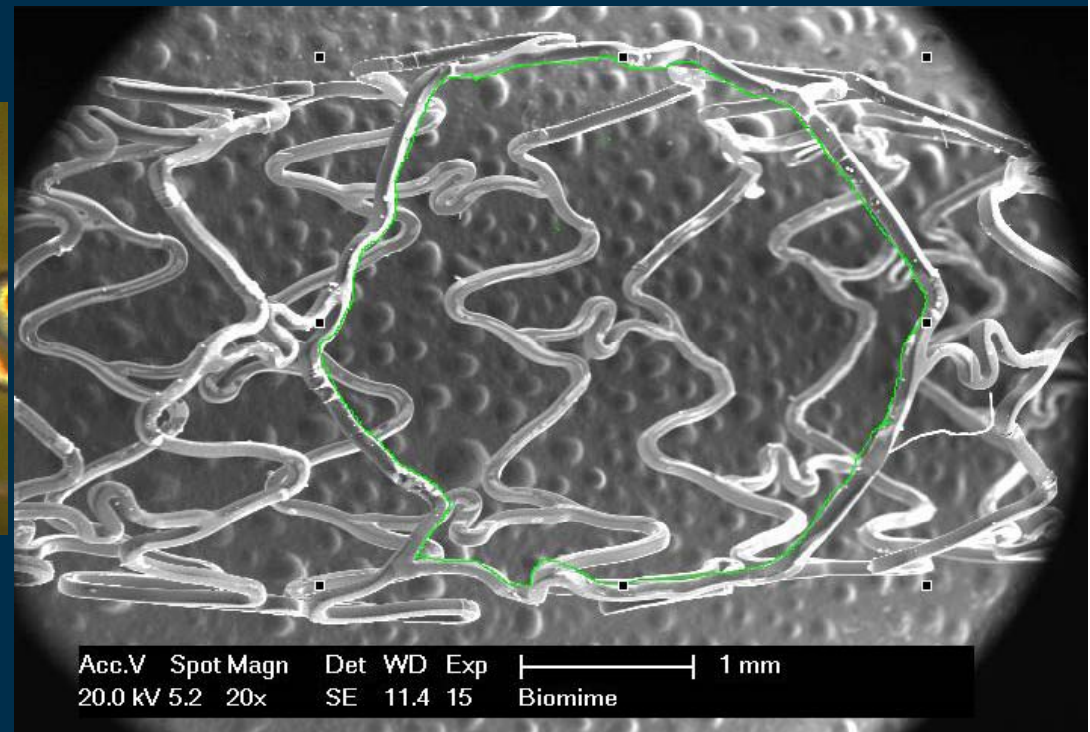
Staged expansion



SIDE BRANCH ACCESS



The area of the largest circle circumscribable in the cell of the stent expanded to the nominal diameter:
 $T_c = 0.71 \text{ mm}^2$



The expanded BIOMIME 3.0 x 16 mm stent after side branch expansion

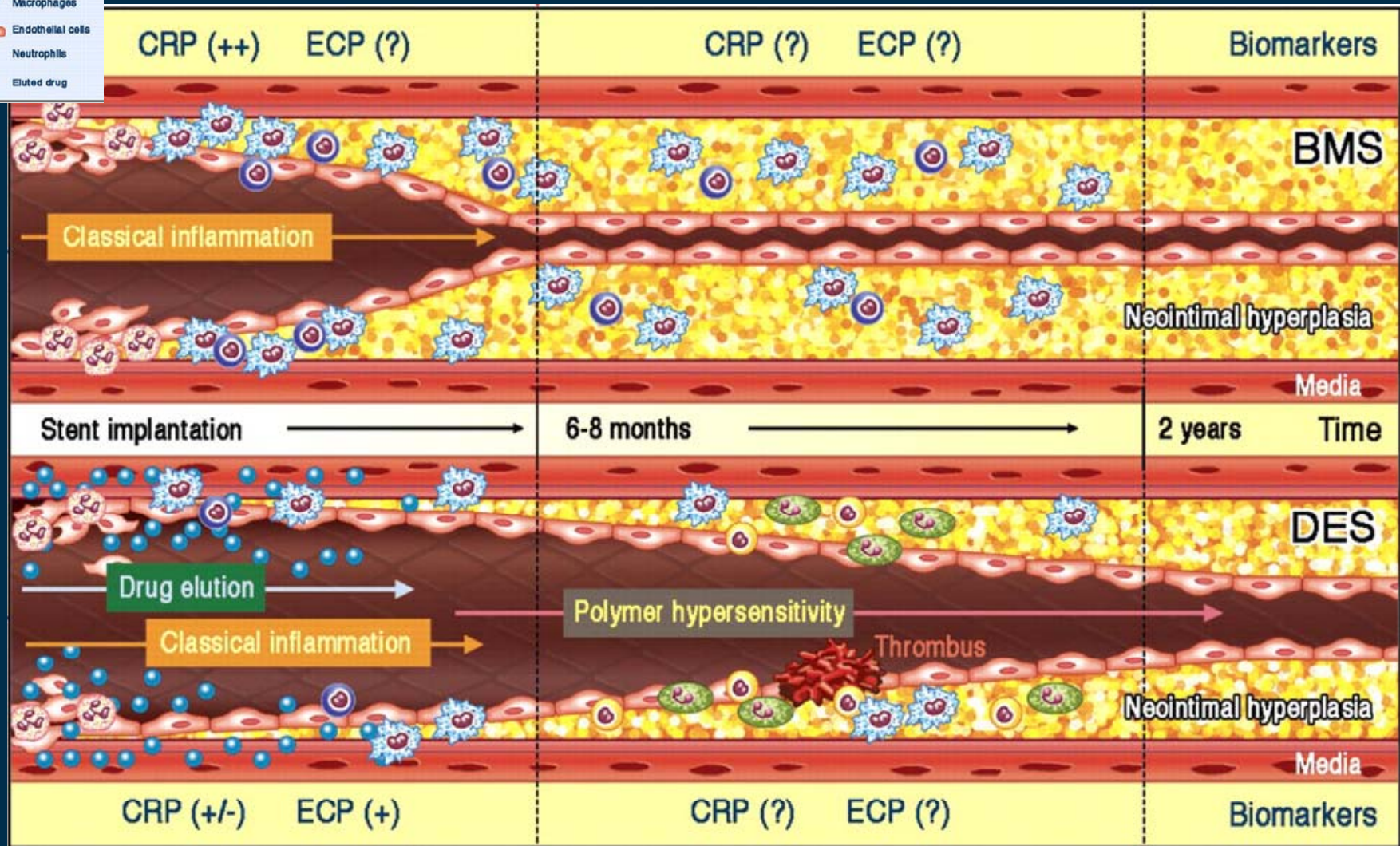
Expanded cell perimeter that ensures side branch access: $K_{\text{SBA}} = 11.29 \text{ mm}$

Expanded cell area that ensures side branch access: $T_{\text{SBA}} = 8.00 \text{ mm}^2$

Data on file with Meril Life Sciences.

ADVERSE REACTION TO DRUG ELUTING STENTS

-  Th1 lymphocytes
-  Th2 lymphocytes
-  Eosinophils
-  Macrophages
-  Endothelial cells
-  Neutrophils
-  Eluted drug



Stent

- *vascular support*
- *limits recoil*

Drug

- *modulates vascular responses*
- *Proliferation inhibitor*

Carrier

- *elute appropriate drug load*
- *control kinetic release*

Biocompatible
durable polymers

Polymer-free

Bioabsorbable

BIOABSORBABLE POLYMERS

- *Reduced chronic polymer toxicity*
- *Safety and efficacy of biodegradable polymer DES is not inferior to first generation durable polymer based DES*
- *Benefits need to be confirmed in larger populations over longer FU to assess the risk of VLST*

MECHANICAL INTEGRITY

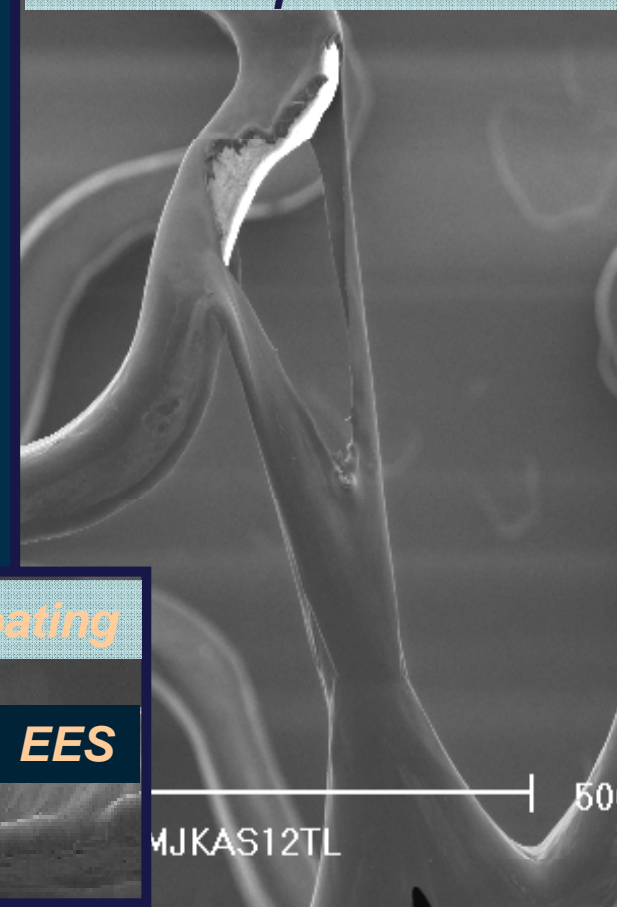
Displacement of Coating

Webbing Without Metal Exposure

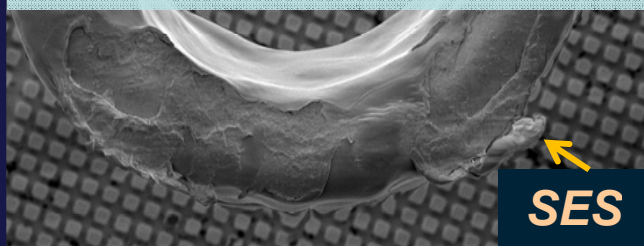


PES

Webbing With Metal Exposure



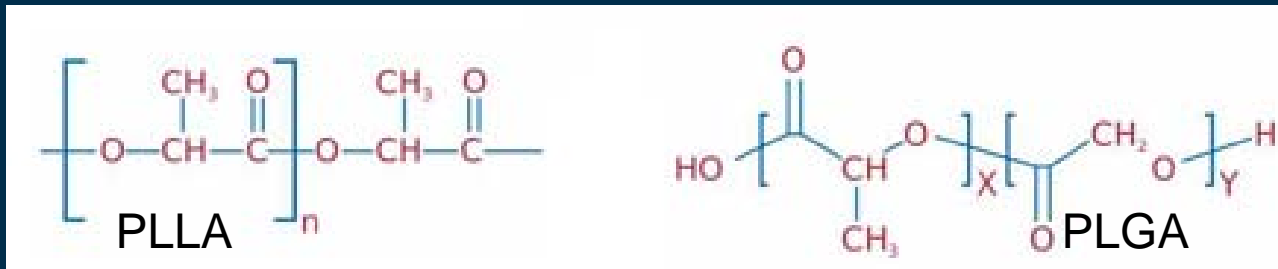
Peeling of Coating



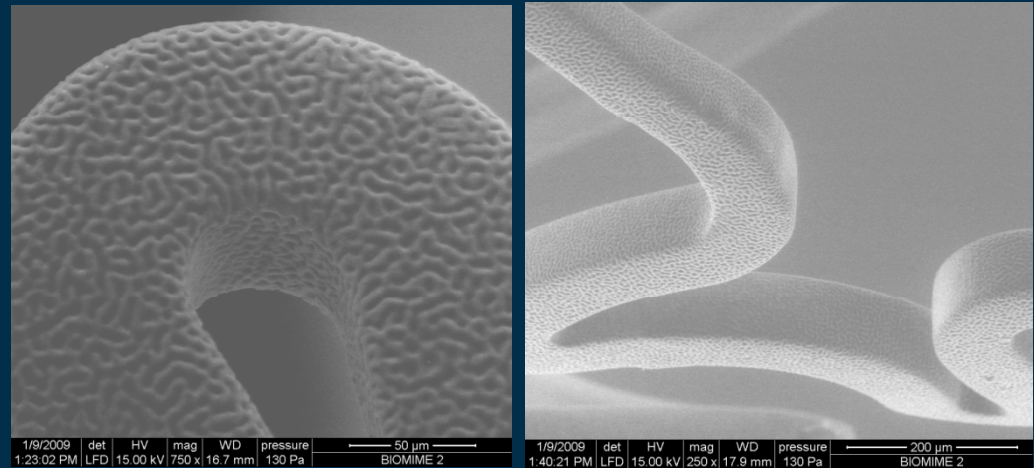
Fragment of Coating



ABOUT BIOPOLY™

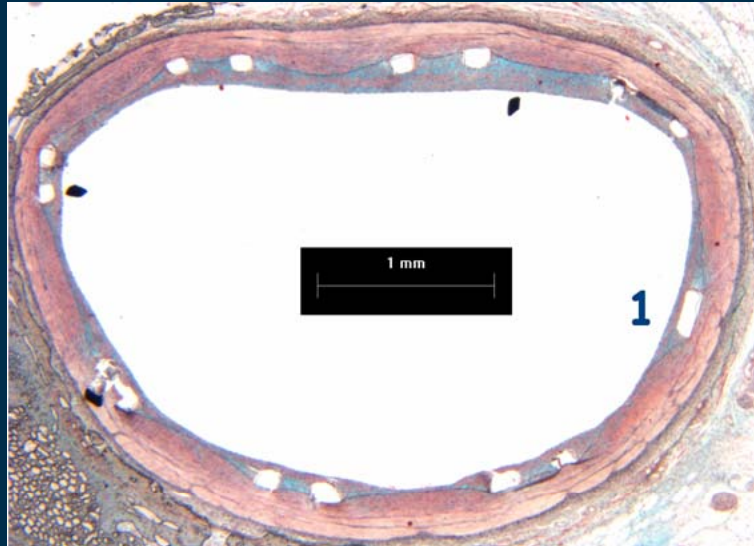


- Biodegradable co-polymer formulation
- Degradation by hydrolysis to carbon dioxide CO₂ and water (H₂O)
- Degradation time of 40-50 days
- Uniformity in stent coating
- Coating thickness of <2 μm



28-DAY POLYMER RESULTS

28-day results – Biodegradable Polymer coated 3.5 x13 in porcine LCx¹



*Absence of Fibrin, Hemorrhage
Necrosis, Fibrinoid or
Inflammation*

No significant differences were found in terms of anatomopathologic features or morphometric measurements, including in-stent endothelialization or neointimal inflammation score versus BMS (all $p > 0.05$)

Stent

- *vascular support*
- *limits recoil*

Drug

- *modulates vascular responses*
- *Proliferation inhibitor*

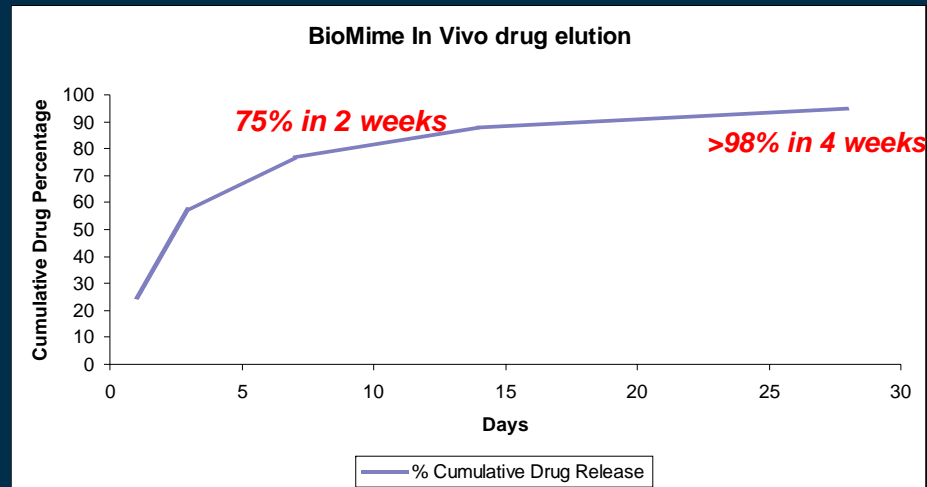
Carrier

- *elute appropriate drug load*
- *control kinetic release*

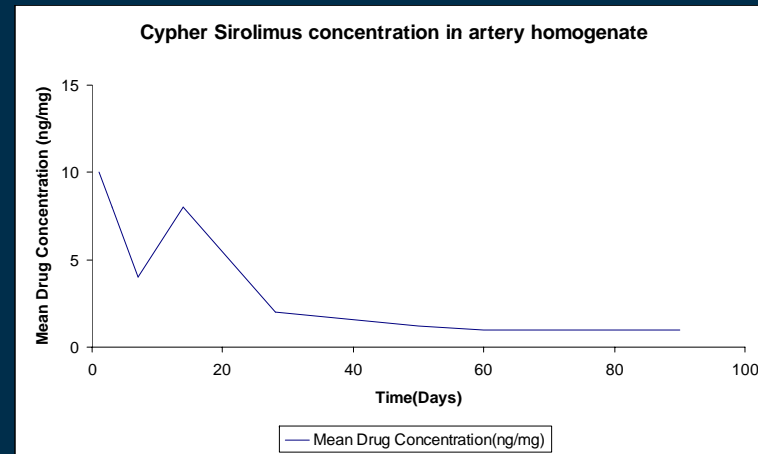
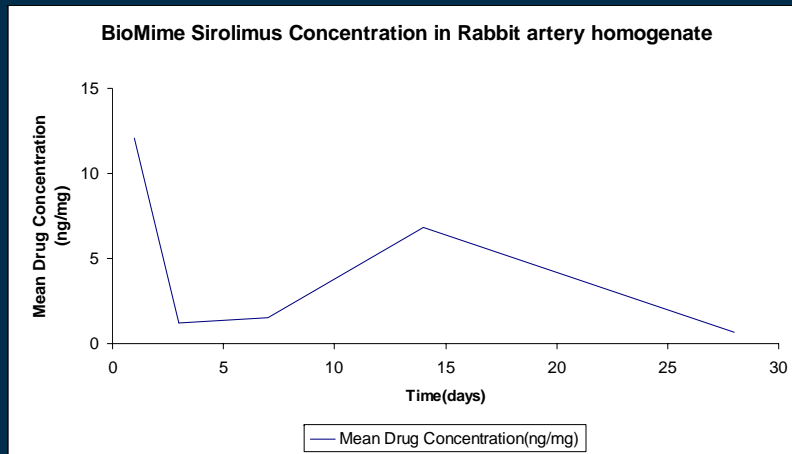
- *Therapeutic Window*
- *Drug Load*
- *Stability*

PK/PD OF BIOMIME

RABBIT ILIAC ARTERY MODEL



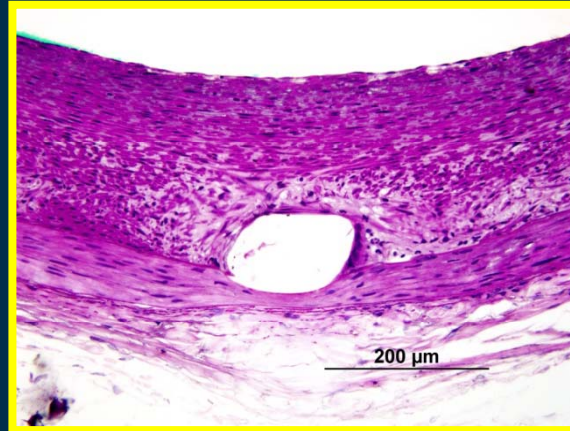
Similar tissue concentrations as Cypher



Data on file with Meril Life Sciences. Rabbit iliac model.

RABBIT ILIAC ARTERY IMPLANTS (28-DAYS)

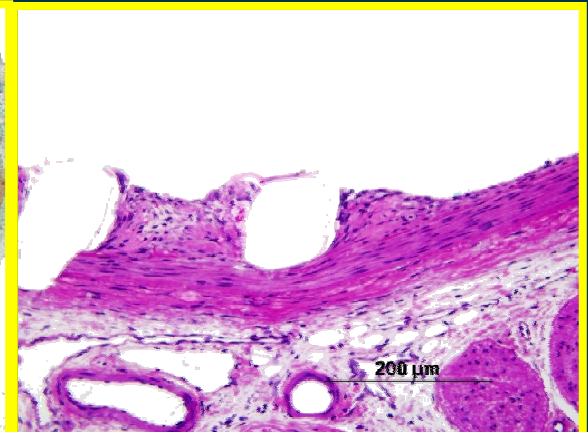
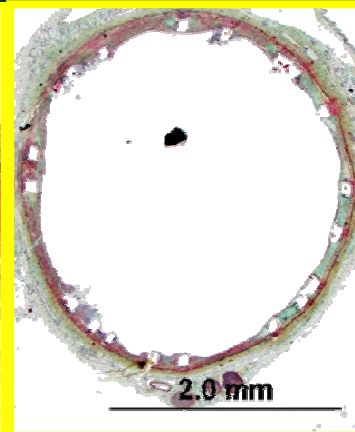
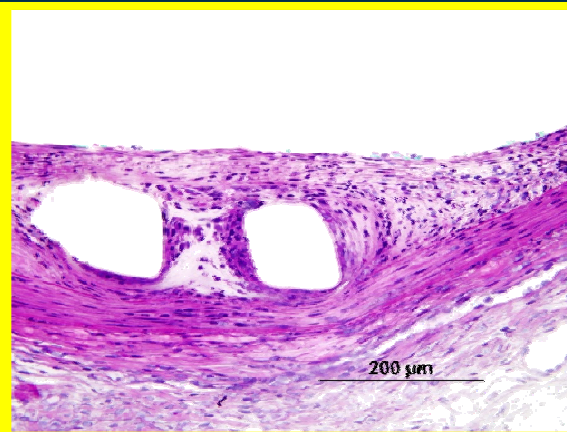
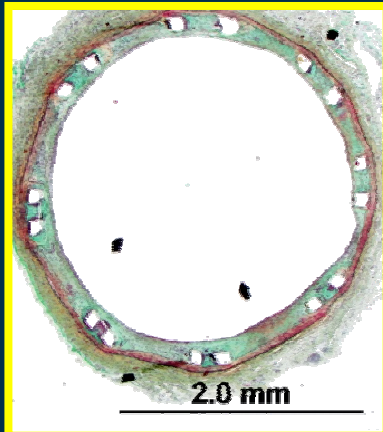
NexGen BMS



BioMime™

Decreased neointimal thickness

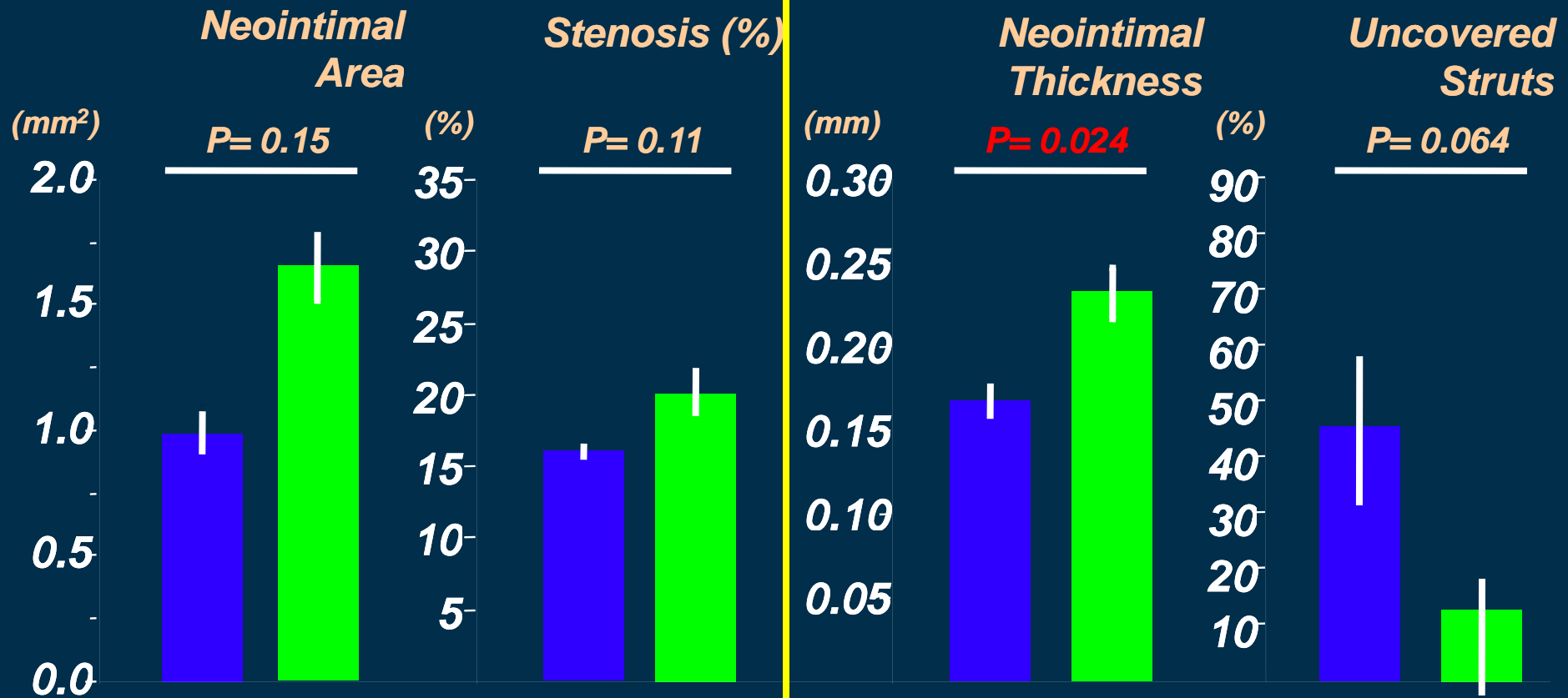
Delayed healing with evidence of uncovered struts



BIOMIME™ LIGHT MICROSCOPY ANALYSIS

28-DAY RABBIT ILIAC

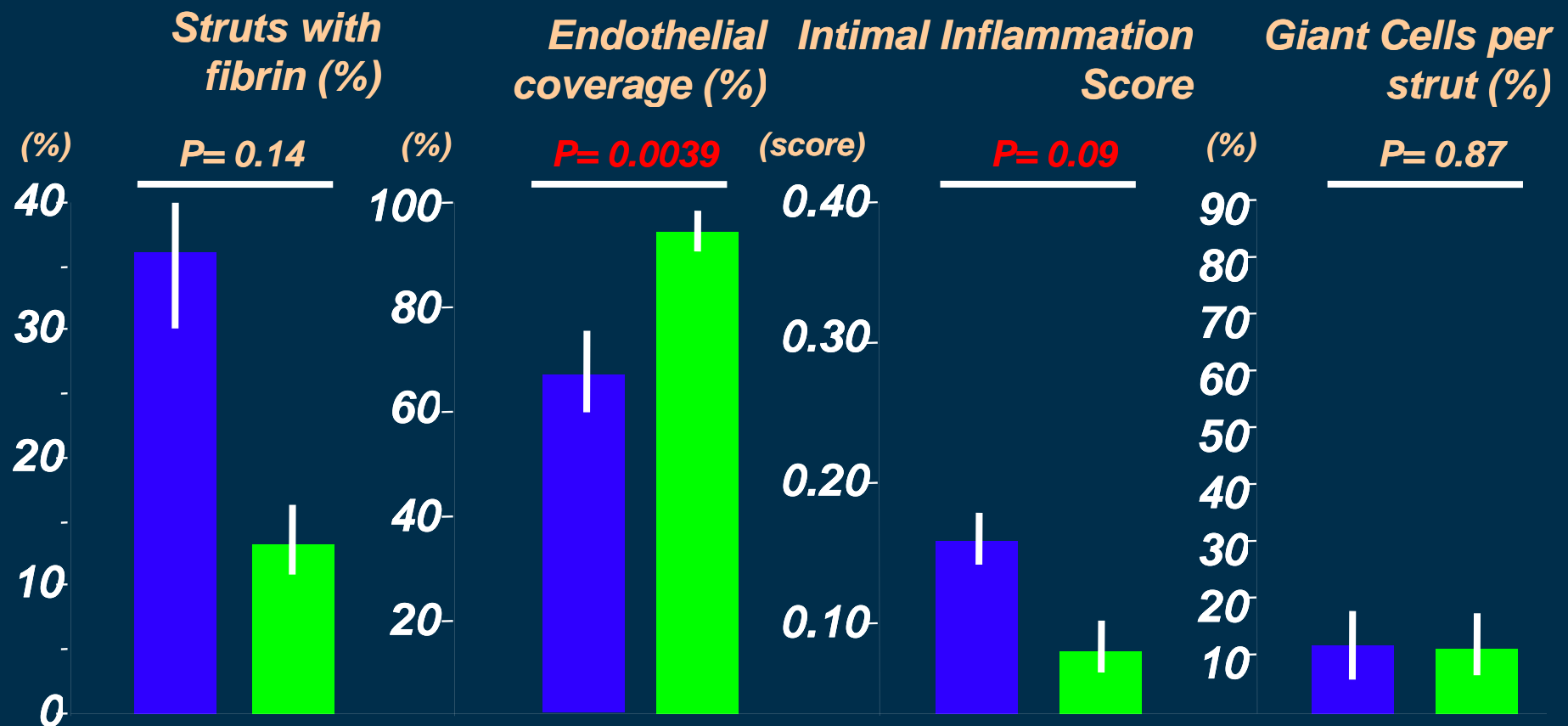
 BioMime™  NexGen BMS



BIOMIME™ LIGHT MICROSCOPY ANALYSIS

28-DAY RABBIT ILIAC (CONT)

 BioMime™  NexGen BMS



meriT-1 Study

Design: prospective, single center primary safety and efficacy trial for BioMime™ Sirolimus Eluting Coronary Stent System.

Principal Investigator – Dr. Sameer Dani, India

Follow-up Time Points	Total Patients Followed up		Death		Myocardial Infarction		Target Lesion / Vessel Revascularization	
			Cardiac	Non-Cardiac	Q-wave	Non-Q-wave	Repeat PCI	CABG
30-Days	All 30 patients	100%	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
6-Months	All 30 patients	100%	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
8-Months	All 30 patients	100%	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
1-Year	All 26patients	87%	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Follow-up Time Points	Total Patients Followed up		Stent Thrombosis				Any Other Complications
			Acute (0D – 1D)	Sub-Acute (>1D – 1M)	Late (>1M – 1Y)	Very Late (>1Y)	
30-Days	All 30 patients	100%	0 (0%)	0 (0%)	N.A.	N.A.	0 (0%)
6-Months	All 30 patients	100%	N.A.	N.A.	0 (0%)	N.A.	0 (0%)
8-Months	All 30 patients	100%	N.A.	N.A.	0 (0%)	N.A.	0 (0%)
1-Year	All 26 patients	87%	N.A.	N.A.	0 (0%)	N.A.	0 (0%)

***4 patients refused Angiographic follow-up. NA = Not Applicable**

meriT-1 Study

QCA Analysis – Follow up

Follow-up QCA – 8 months		(N=26)
Reference Vessel Diameter, mm		2.97 [2.80, 3.28]
In-Segment		
	MLD, mm	2.32 [2.18, 2.62]
	% DS	21.1 [14.9, 26.2]
	Late Lumen Loss, mm	0.18 [0.06, 0.35]
	Binary Restenosis, %	0 (0)
In-Stent		
	MLD, mm	2.67 [2.32, 2.83]
	% DS	10.9 [8.2, 15.6]
	Late Lumen Loss, mm	0.15 [0.09, 0.33]
	Binary Restenosis, %	0 (0)

Preliminary QCA analysis. Median values

meriT-2 Study Design

Prospective, Non-Randomized, Multi- Centre, Real world study involving 250 patients. **Principal Investigator – Dr. Ashok Seth, India**

Baseline Characteristics	Details
Number of patients enrolled	217
Mean age, years	57.5 ± 10.2
Gender, Males	171 (84%)
Body Mass Index (BMI)	25 ± 3.6
Previous MI	75 (37%)
Acute Coronary Syndromes	177 (87%)
Prior PCI	14 (7%)
Prior CABG	4 (2%)
Diabetes	82 (40%)
Hyperlipidemia	27 (13%)
Hypertension	116 (57%)
Smokers	65 (32%)
Family History	18 (9%)

Ongoing study

MACE & ST

- On going study
- 217 patients have been treated
 - 0% MACE at 30days
 - 1 non-cardiac death at 4 months
 - 2 (0.9%) patients had ischemia driven TLR at 4 months
 - 4 (1.8%) patients had TLR at 8 months Angio follow-up
 - 1 (0.5%) SAT

SUMMARY

- *Drug release and tissue concentration is similar to Cypher*
- *Due to its low injury score, BioMime™ demonstrates equivalent neo-intimal scores to Cypher despite having low drug loading*
- *BioPoly™ has demonstrable non-inflammatory behavior in pre-clinicals*
- *Neointimal thickness with BioMime™ is 34% less than its bare metal platform NexGen™ ($p=0.024$)*
- *Optimal scaffolding and wall apposition (hybrid closed and open cell format), highly flexible and deliverable stent system, low balloon overhang, low foreshortening and recoil.*
- *Excellent polymer structural integrity*

Thank you for your attention !