



Development Of DES Technology

HUO Yong ,MD FACC
Peking University First Hospital
President-elect Chinese Society of Cardiology

Drug-eluting Stents in 2004

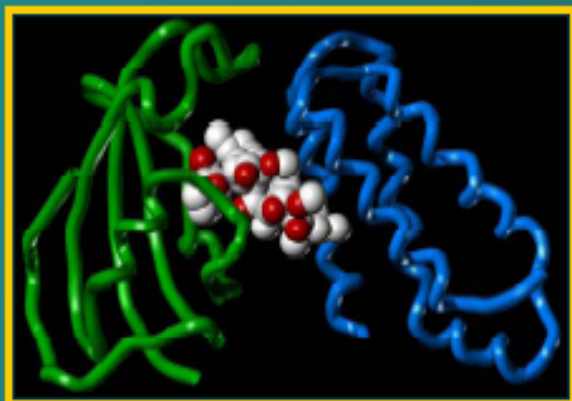
Safety and Efficacy Proven

Drug

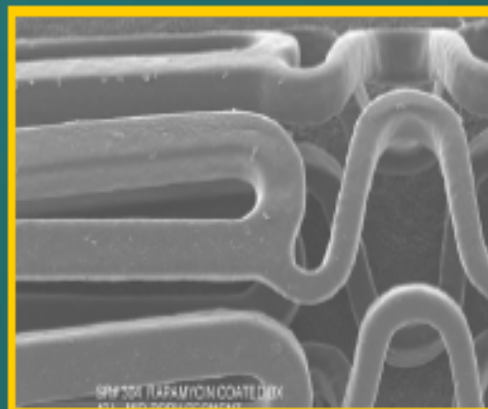
Polymer

Stent

Cypher



Sirolimus

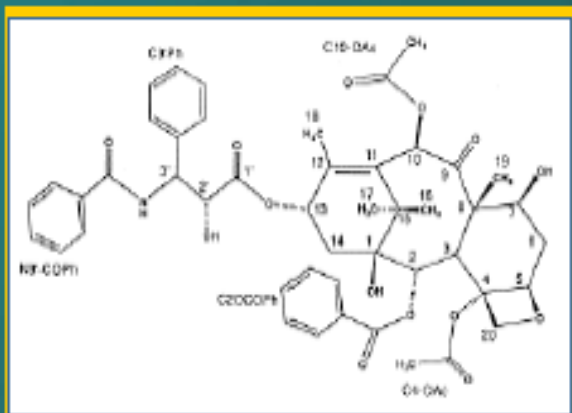


PEVA + PBMA blend

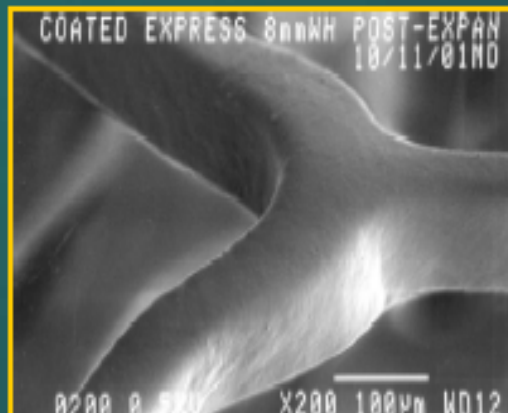


BX Velocity

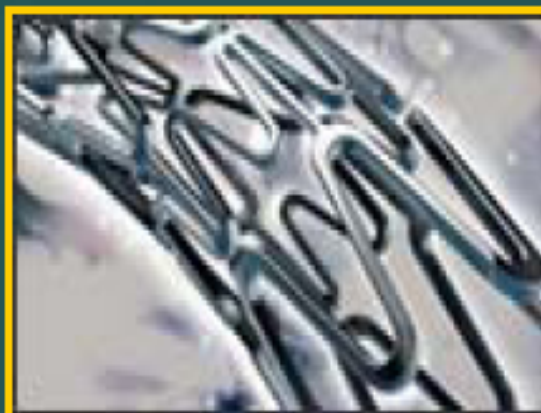
TAXUS



Paclitaxel



Polyolefin derivative



Express²

Drug stents made in China

○ **Microport:**

Firebird

Firebird II

○ **Lepu:**

Partner

Nanoplus

○ **JW:**

Excel

○ **Yinyi :**

Paclitaxel stent

○ **Sinomed**

Buma

○ **Yisheng**

SES, PLGA, Co-ch



The Status Of DES

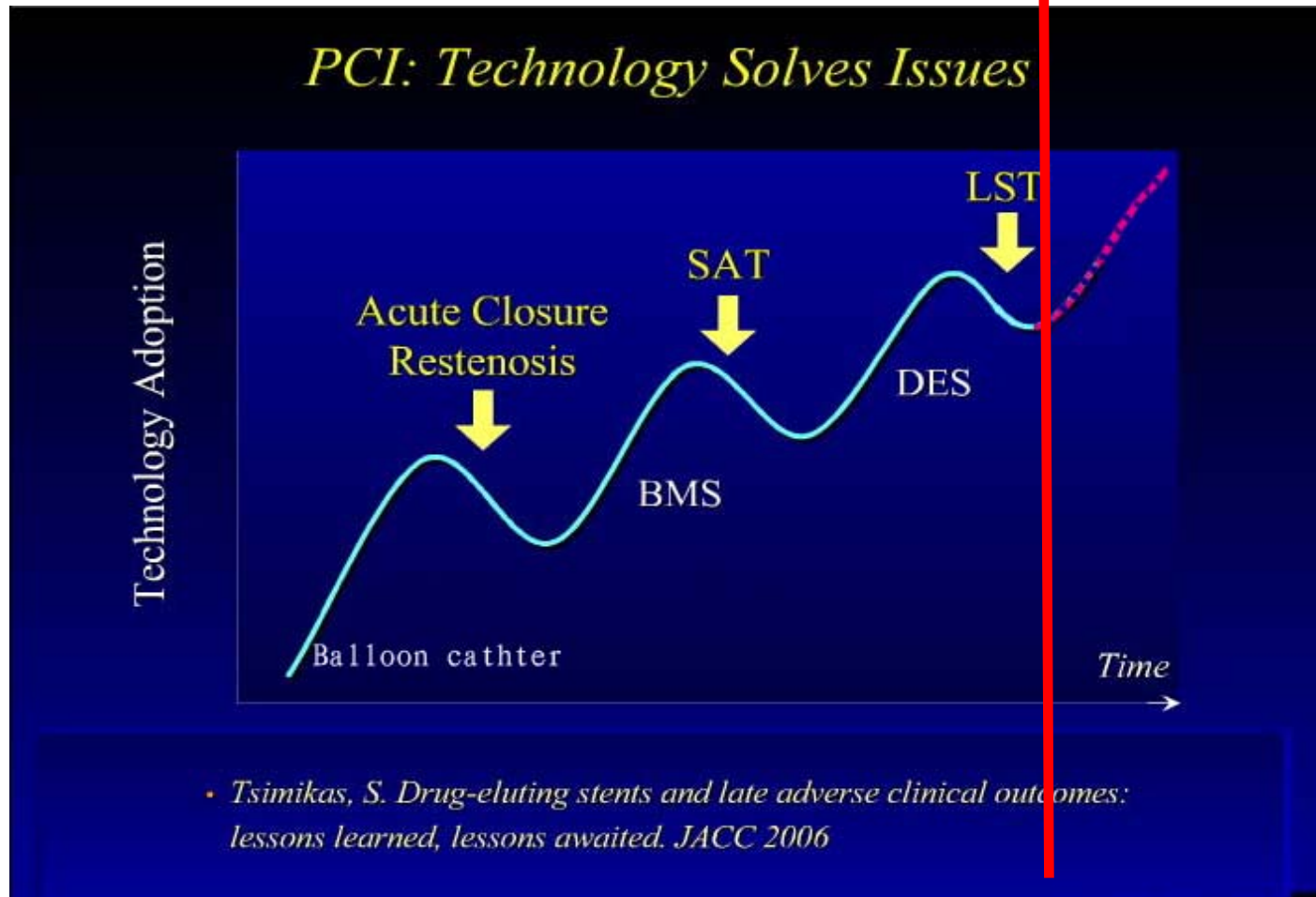
- Basically solved the problem of restenosis
- End the history of interventional devices fighting against restenosis nearly two decades
- Risk of late-thrombosis



Technological Change To Clinical Problems

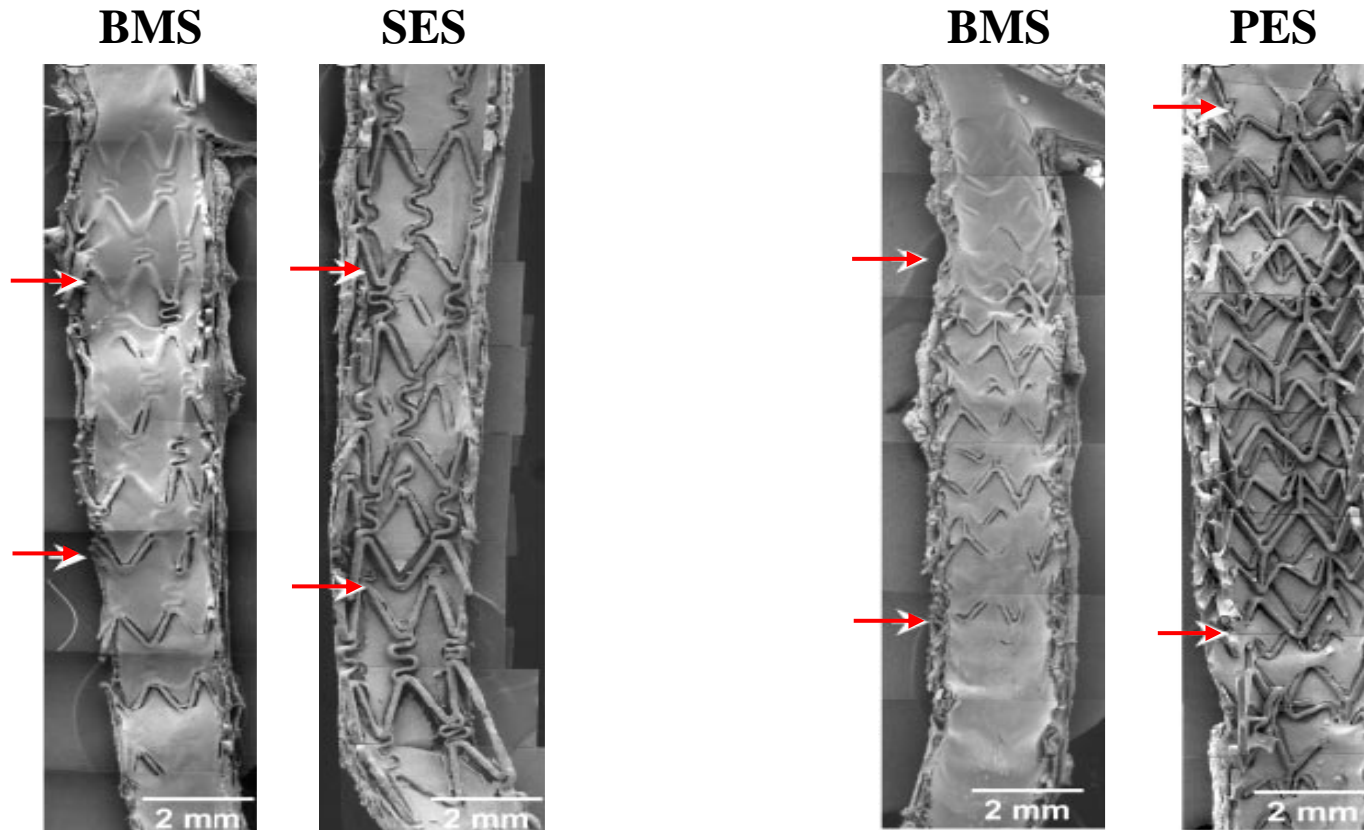
Restenosis

Safety



Delayed Endothelialization

BMS vs DES



Conclusions:

- BMS showed far greater endothelialization than DES
- Lack of coverage highlighted in areas of overlap
- Less surface coverage by endothelial cells in PES than SES

Finn et al. *Circulation*. 2005;112:270-278.

Is Delayed Endothelialization The Crucial Problem?

- **Lack of systematic basic research**

- The crucial factor in delayed endothelialization is not clear

- Possible ways to promote endothelialization

- Combination of Reducing stent-related safety factors and ways to promote endothelialization



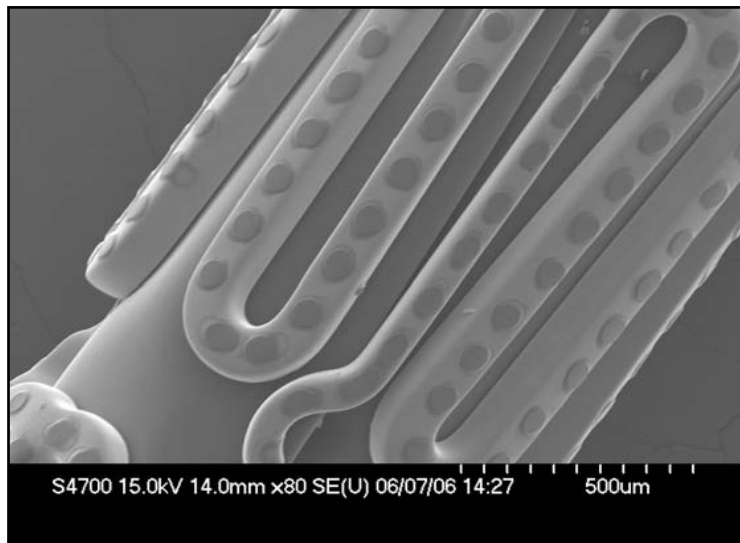
Direction Of Development Of A New Generation Of Drug Stents—longterm safety

- Reduce the harmful effects of polymer carrier
- The development of fully biodegradable stent
- Different drug or combination

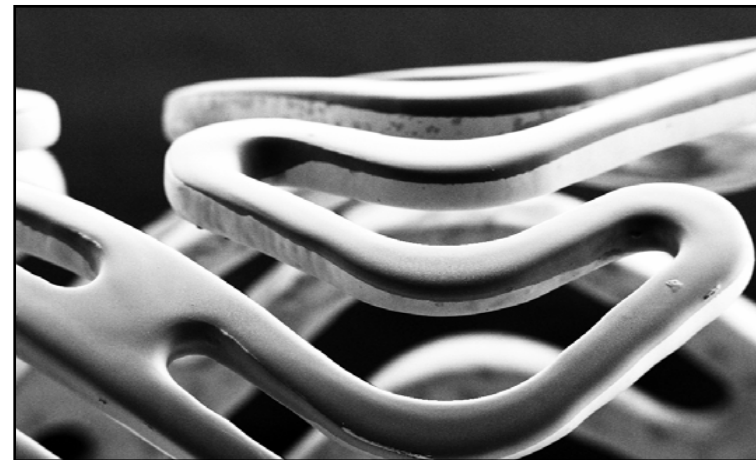


Directional Drug Delivery

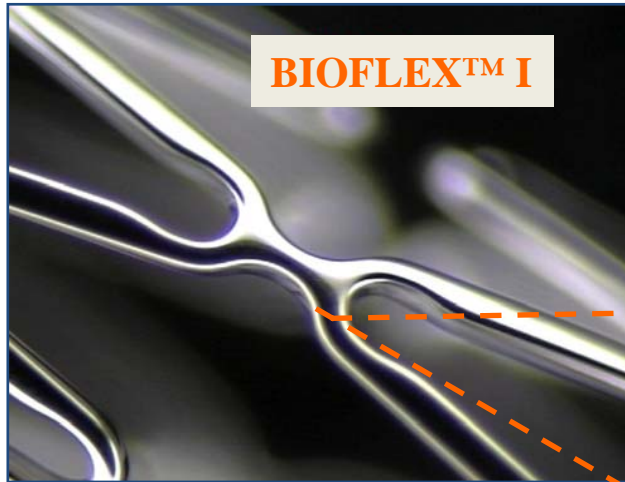
- **Selective coating on the outside surface of the stent**
 - Reduced drug/polymer
 - Luminal surface BMS
 - Drug only where needed



Labcoat JA™ Coating Technology



Directional BioMatrix[®] II Stent Platform

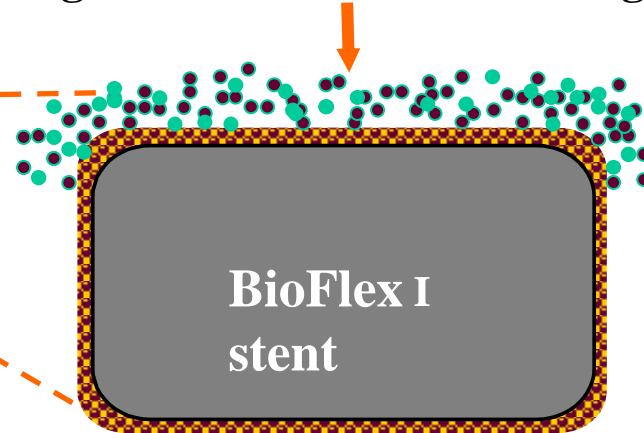


Stent Platform:

- stainless steel (112 μm)
- corrugated ring, quadrature-link[™] design
- radius link enhances axial fatigue life

Biodegradable Drug/Carrier:

- Biolimus A9[®] / Poly (Lactic Acid) 50:50 mix
- abluminal surface only (contacts vessel wall)
- 15 μmeter coating thickness
- degrades in 9 months releasing CO_2 + water



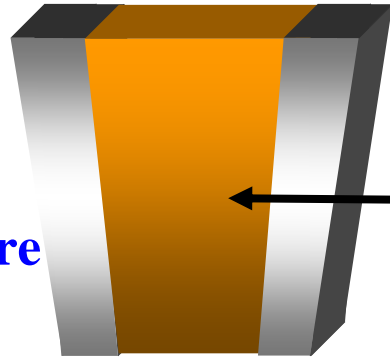
Parylene Durable Primer Coating:

- 5 μmeter thick, encapsulates stent
- prevents surface metal ion migration
- biostable + athrombogenic*

* Data per NHLBI sponsored study, available from BSI

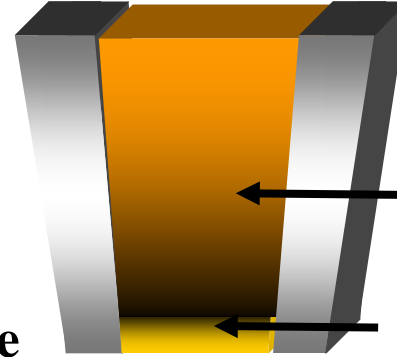
Conor Drug Release Technology

Single Drug Structure



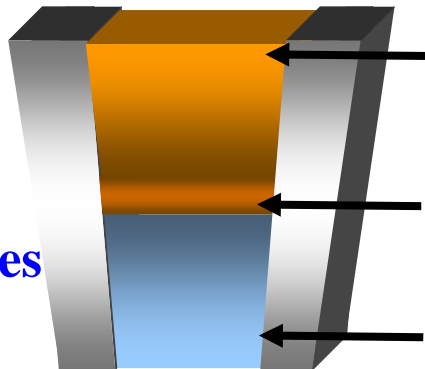
Mural Side

**Simple Drug Reservoir
Uniform Release**



**Drug Reservoir
Luminal Barrier Layer**

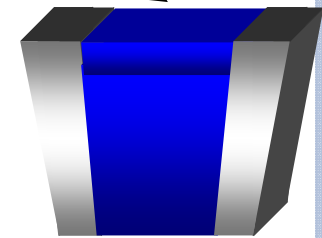
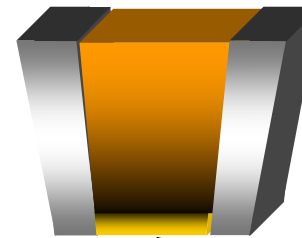
Multiple Drug Structures



**Drug A released to arterial wall
Barrier layer
Drug B released into bloodstream**

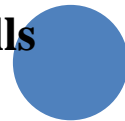
Two Drugs, One Well

Mural Barrier



Luminal Barrier

**Two Drugs, Two Wells
Two Directions**



A Completely Polymer-Free Strategy

Translumina Yukon Choice[®] DES

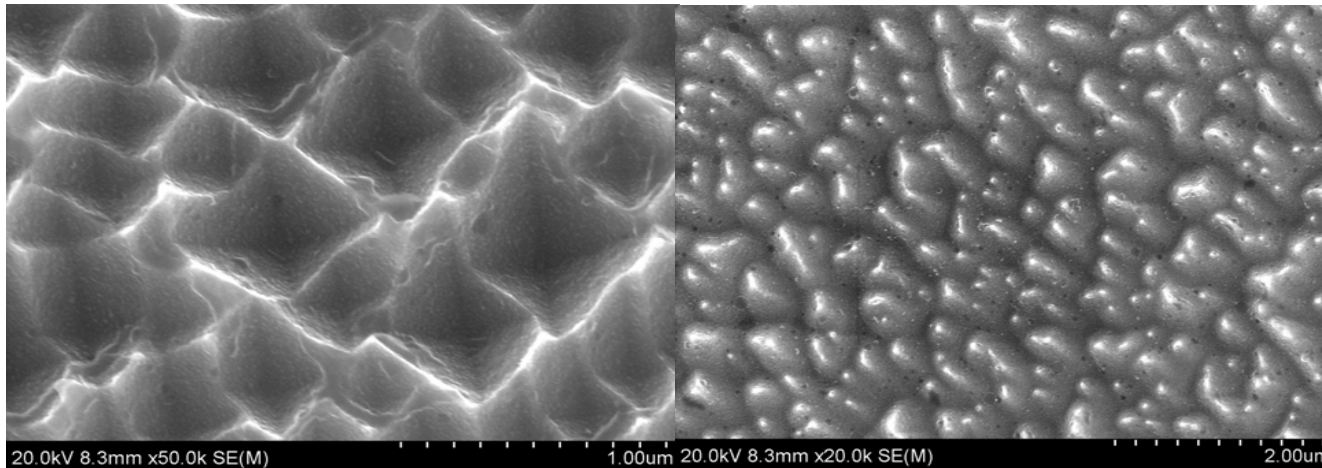
- Polymer-free coating
- Unique roughened surface
- Adjustable dosage for individualized treatment



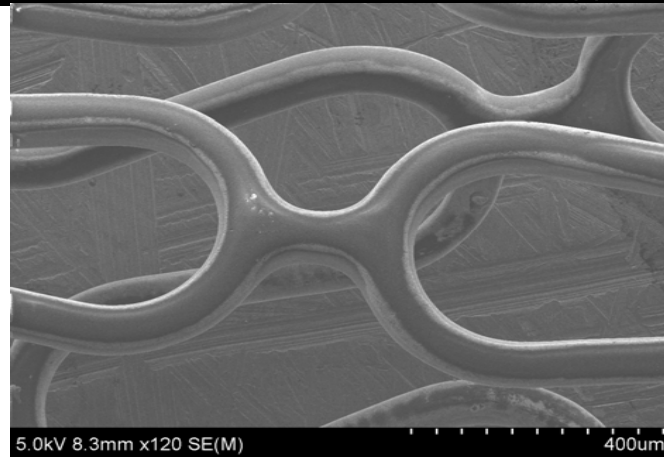
**Some New DESs in China
(from Lepu)**



Nano Polymer-Free Drug Eluting Stent Of Lepu Medical



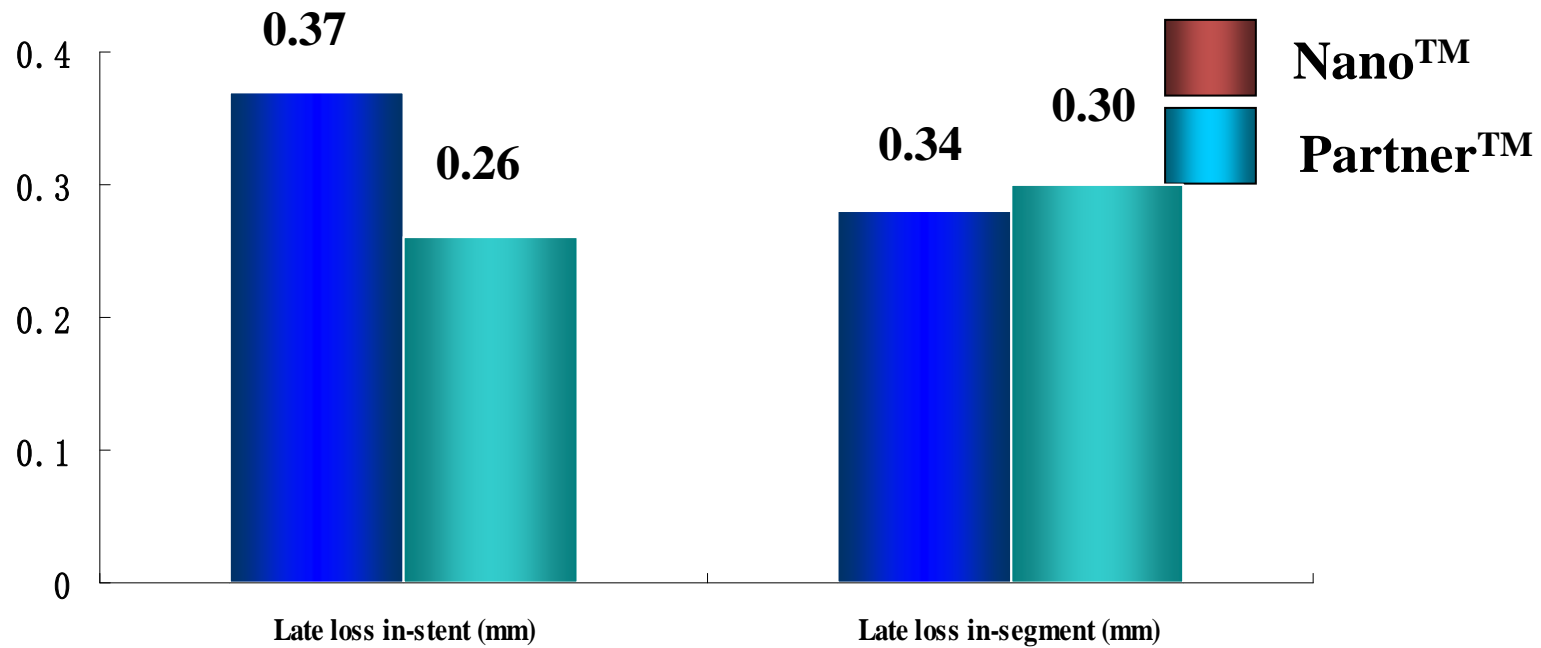
**Nano-porous
drug-loading**



**The stent surface
uniform after drug-
loading**



Results From Nano FIM Clinical Study: LL at 6 ~ 8 Months



• Same safety as BMS, same effectiveness as DES

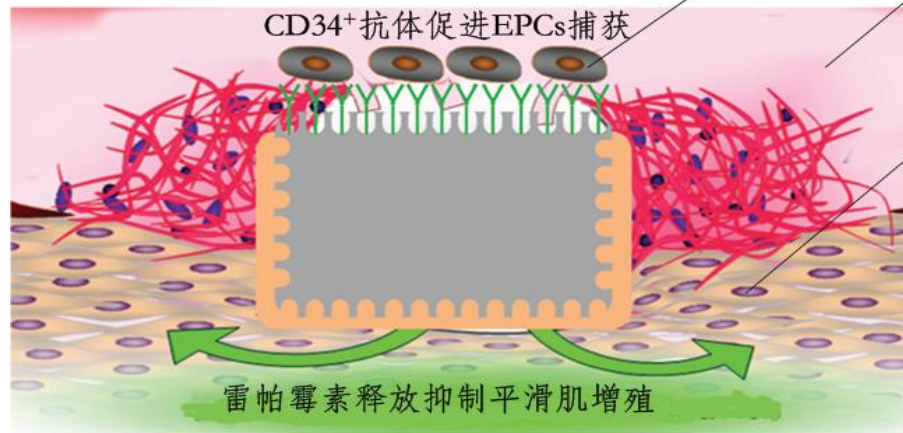
Design Principle Of EPC Capturing And Drug Eluting Combination Stent

CD34 antibody Facilitates EPC Capturing

内皮祖细胞 Progenitor cells

血管腔 Lumen

血管壁平滑肌层
Vascular smooth muscle layer



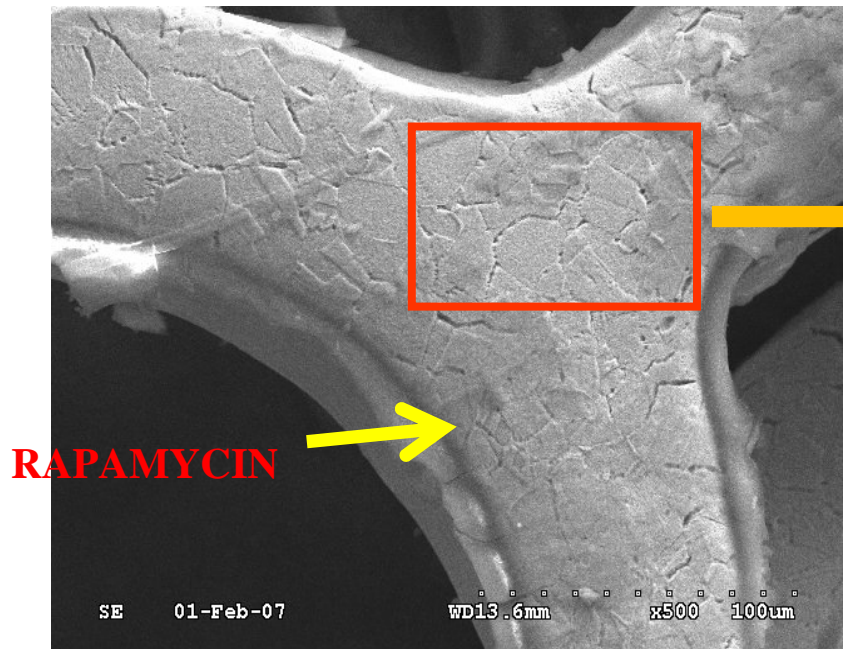
联合支架在冠状动脉内
支架杆局部示意图

The releasing of Rapamycin
Inhibits smooth muscle cell
proliferation

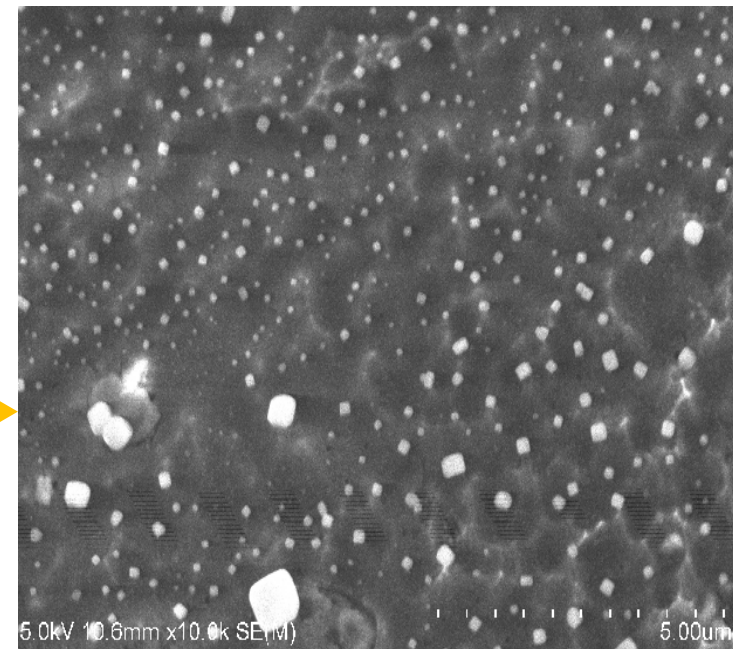
Strut Partial Schematic of Drug
Eluting Combination Stent in the
Coronary



EPC Capturing And Drug Eluting Combination Stent



Outer surface-Rapamycin

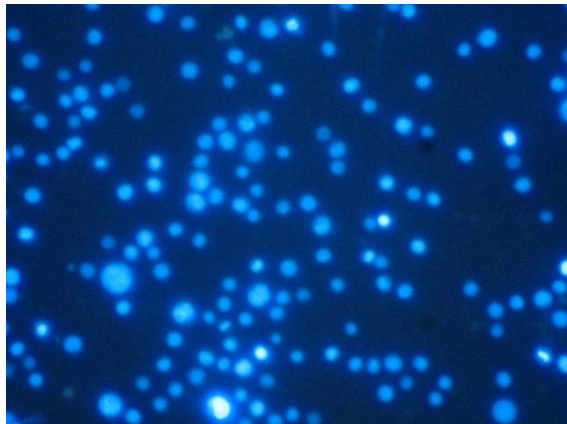


Inner surface-CD34 antibody

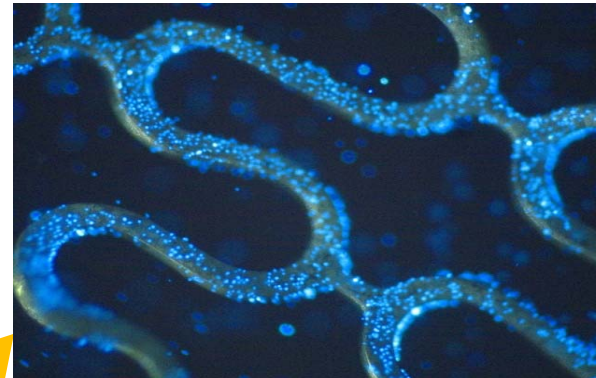


The Activity Of CD34 Antibody Of The Inner Surface

BMS **Combination stent**



**Photo by
microscope**



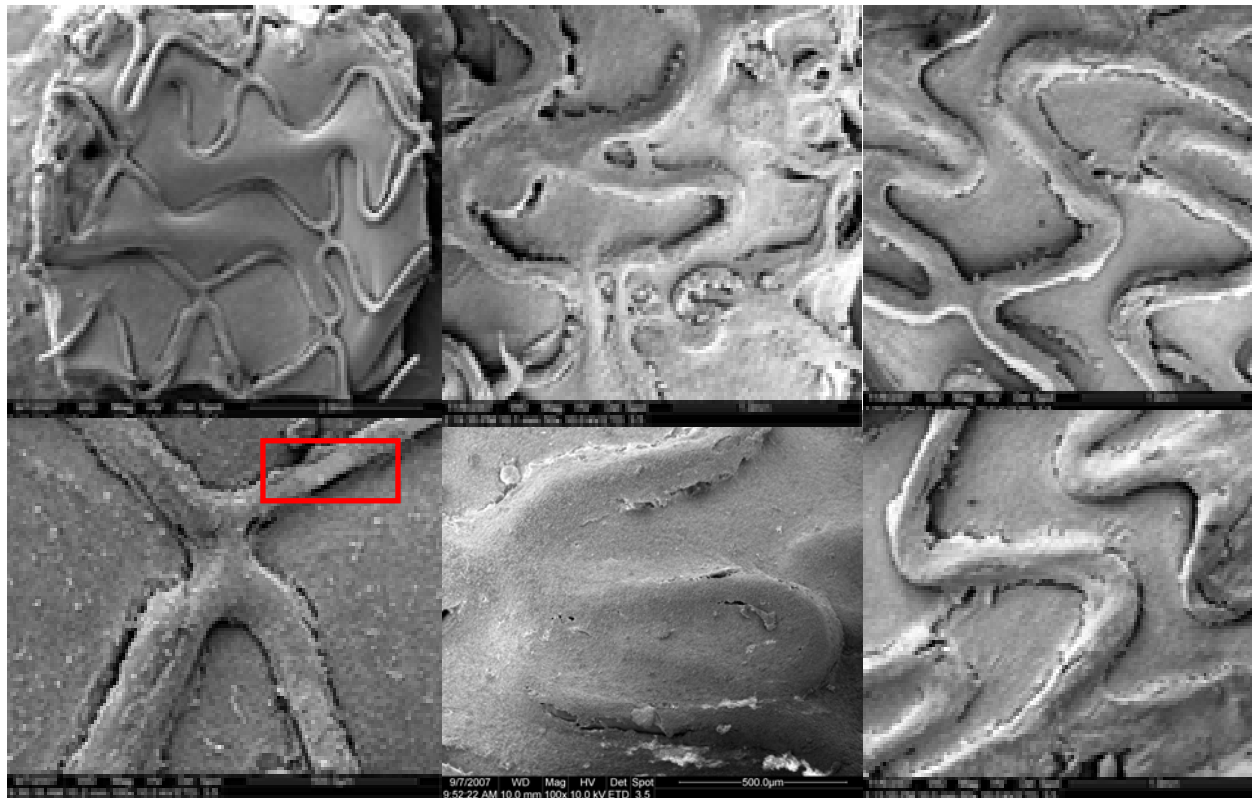
**The inner surface of Combination
stent**



The inner surface of BMS

**Immerse in KG-1a cell suspension
stained by DAPI (CD34+ Cell,ATCC)**

Endothelium Appraisalment EM Morphology On The 7th Day



BMS

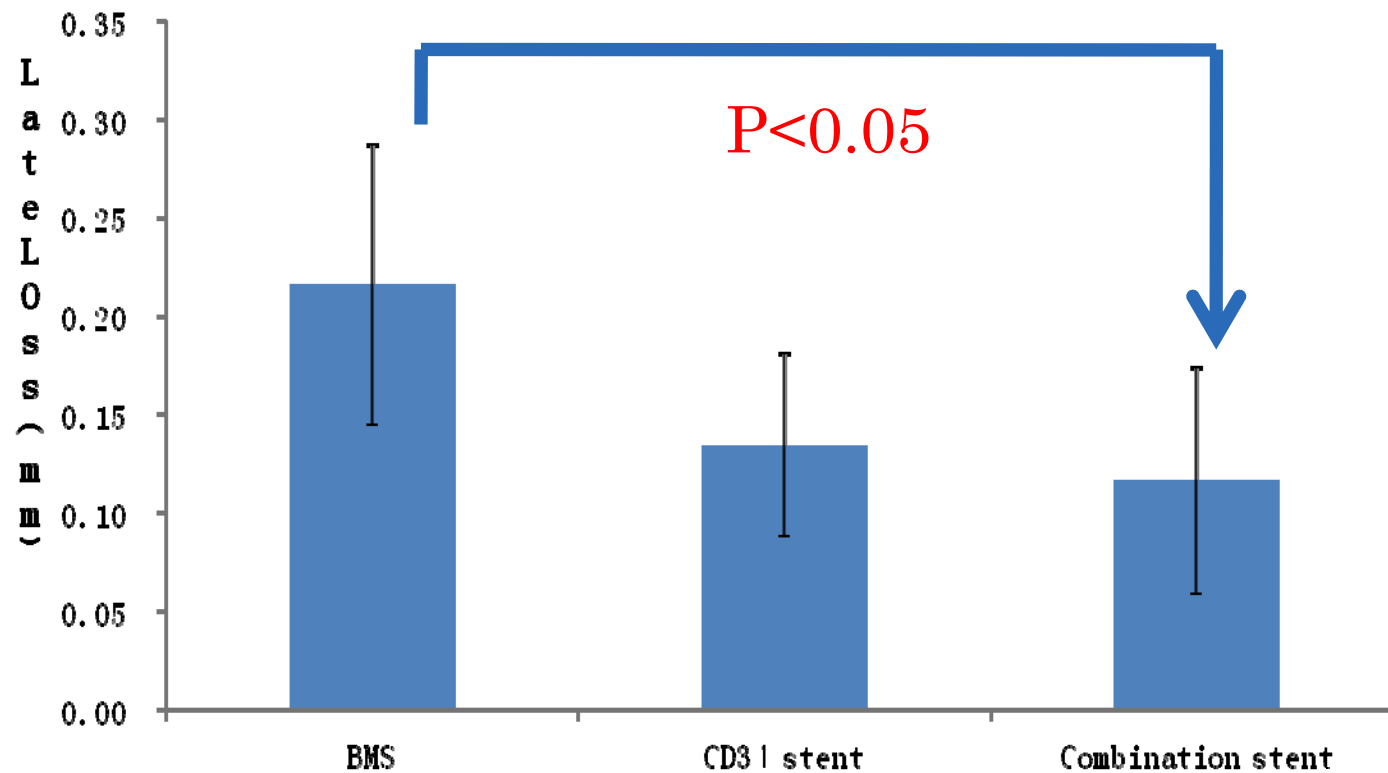
CD34 stent

Combination stent



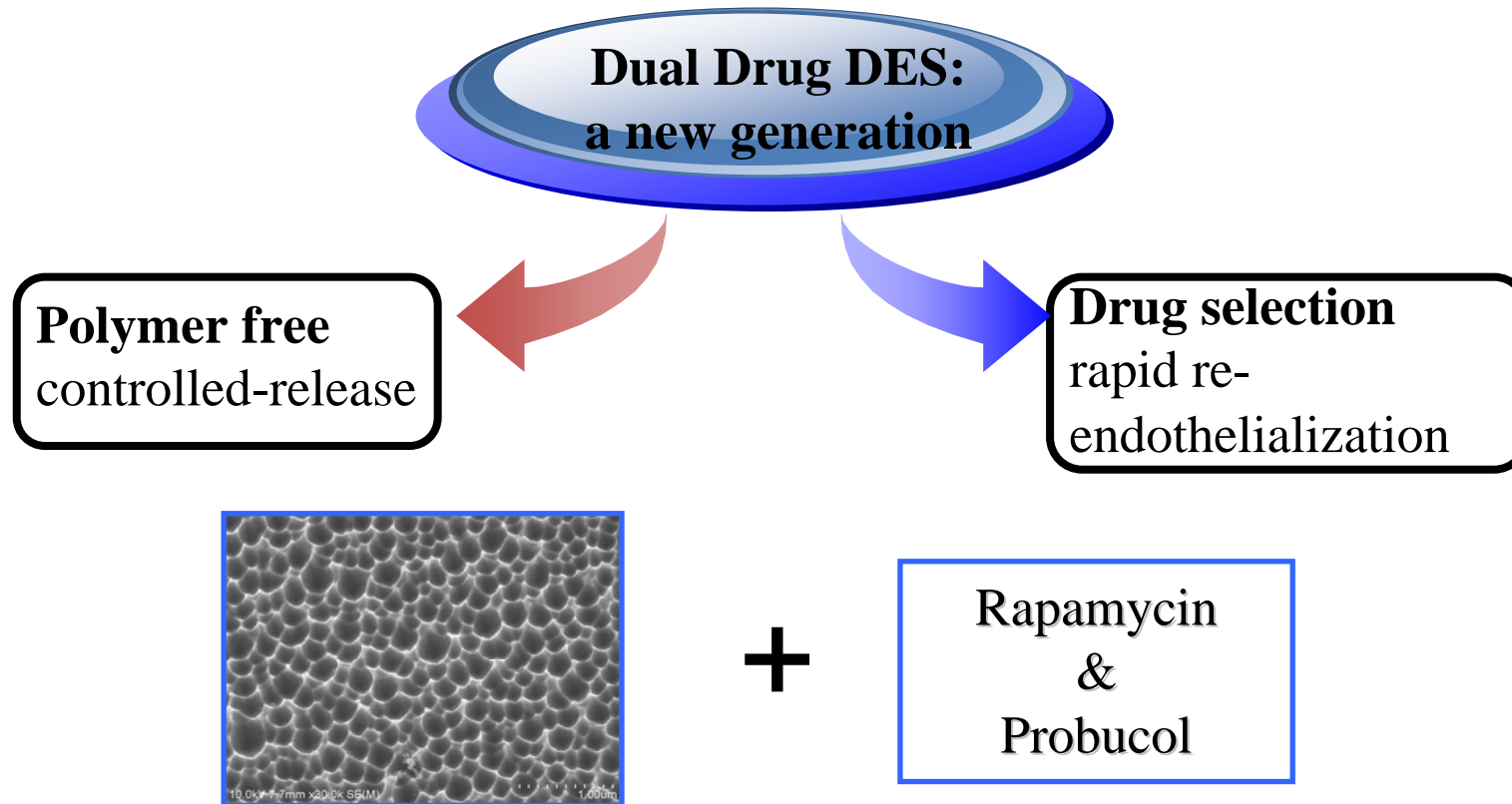
Animal Experimental Results In Porcine-QCA

Late Loss at 28 Day

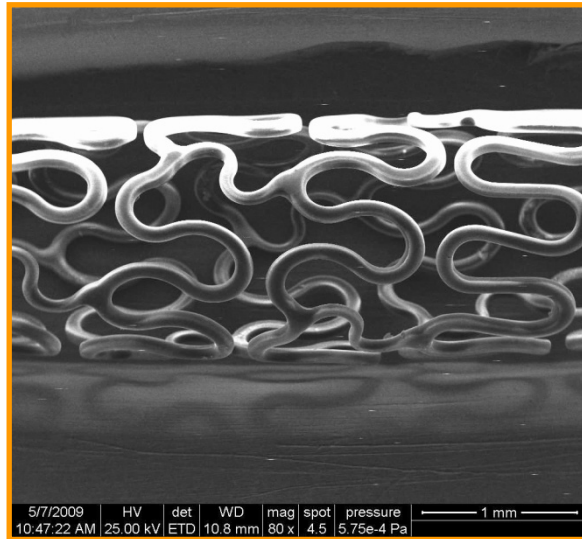


Rapa-probucol polymer-free stent (Dual Drug DES)

Dual Drug DES is our innovative product, originally developed in China and in a leading position in the world; Currently undergoing clinical trials

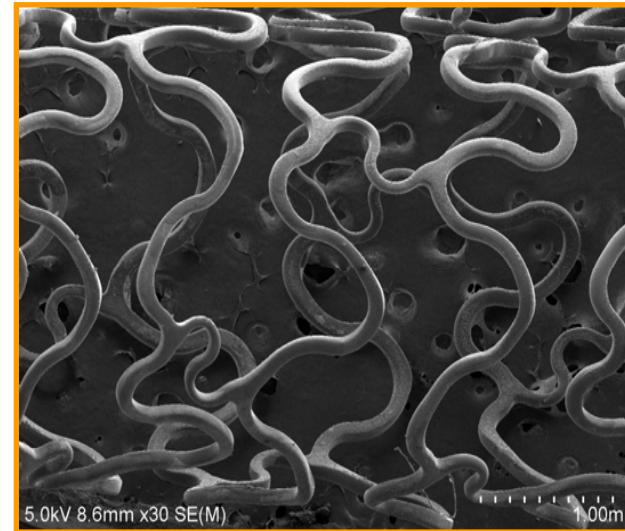


Dual Drug DES——Coating Technology



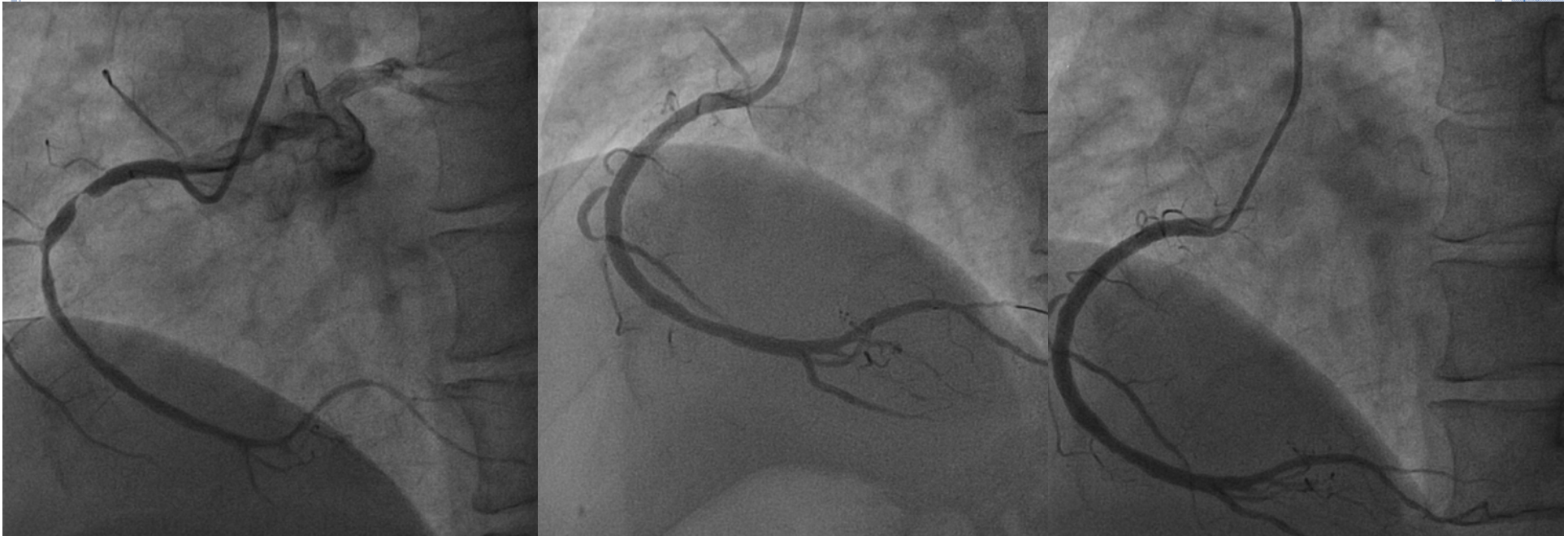
Before expansion

Unique technology for
the metal surface
treatment, and advanced
spraying procedure



After expansion

Great anti-deformability
Coating uniform
No collapse



Base line

Bicare Stent (3.5/24)

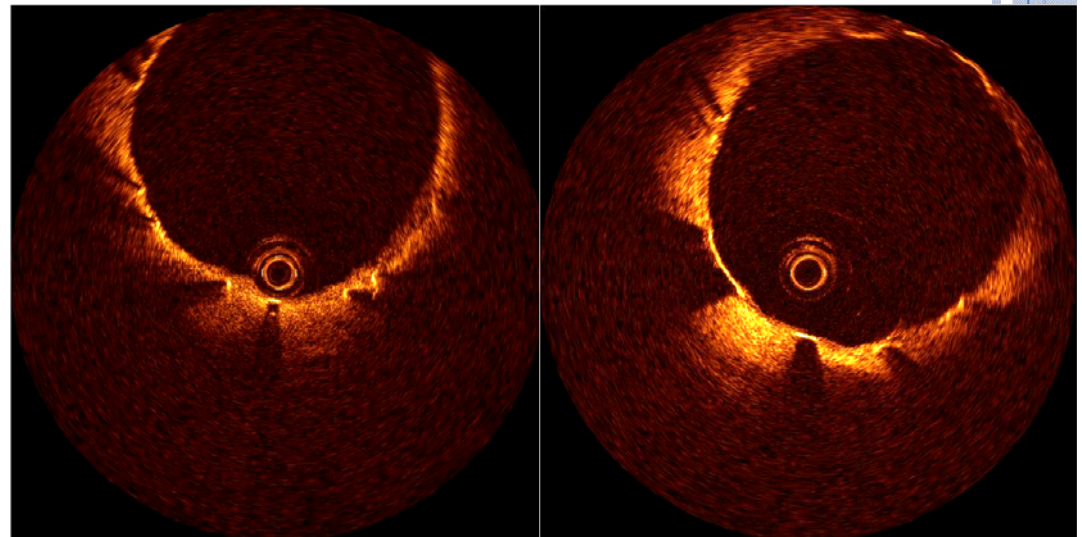
4m F/U

56ys, Male

Unstable AP

3.5/24 Bicore stent in RCA

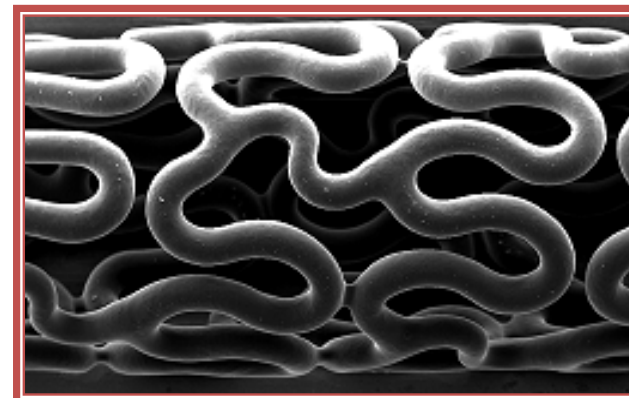
4mo Angio and OCT F/U



Bio-absorbable Stents May Lead Way In Interventional Therapy Revolution

Magnesium alloy bio-absorbable stent

- Chemical anti-corrosion treatment on surface to reduce corrosion rate of magnesium alloy
- Based on formula of magnesium alloy, with method of deformation to improve plasticity and corrosion resistance of magnesium alloy
- Animal trial to begin this year



Bio-absorbable Polymer Stent(Lepu Medical)

1. Special processing to improve physical properties of polymer material to increase strength of stents
2. Experiments of drug and carrier coating with variety of solvents to obtain an even, uniform and smooth drug-carrier coating
3. Meet requirements of keeping physical and chemical performance in expected active time
4. Optimization of stent structure and determination of final design drawing
5. Currently preparing stent samples and carrying out experimental studies



Trends

- A new generation of DES will be focused on safety based on the Effectiveness
- Reduce the harmful effects of polymer is the researching direction
- Polymer-free DES completely eliminate the harmful effects of polymers, with the best safety
- Fully biodegradable stent is the future direction of development

