The Science behind XIENCE™ V

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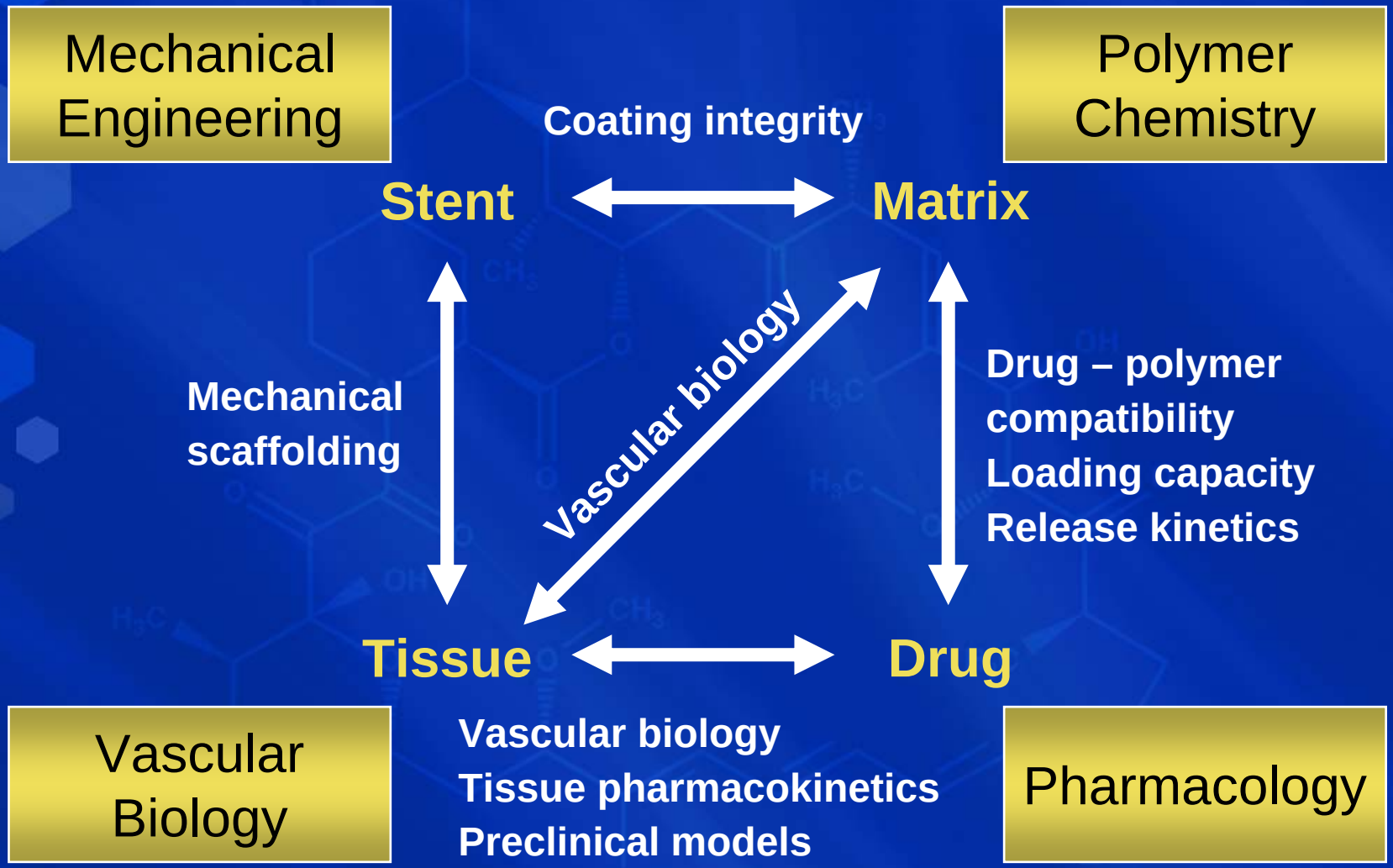
Summit TCT April 25

Drug Eluting Stent System Design

SE2924433D

Drug Eluting Stent System Design



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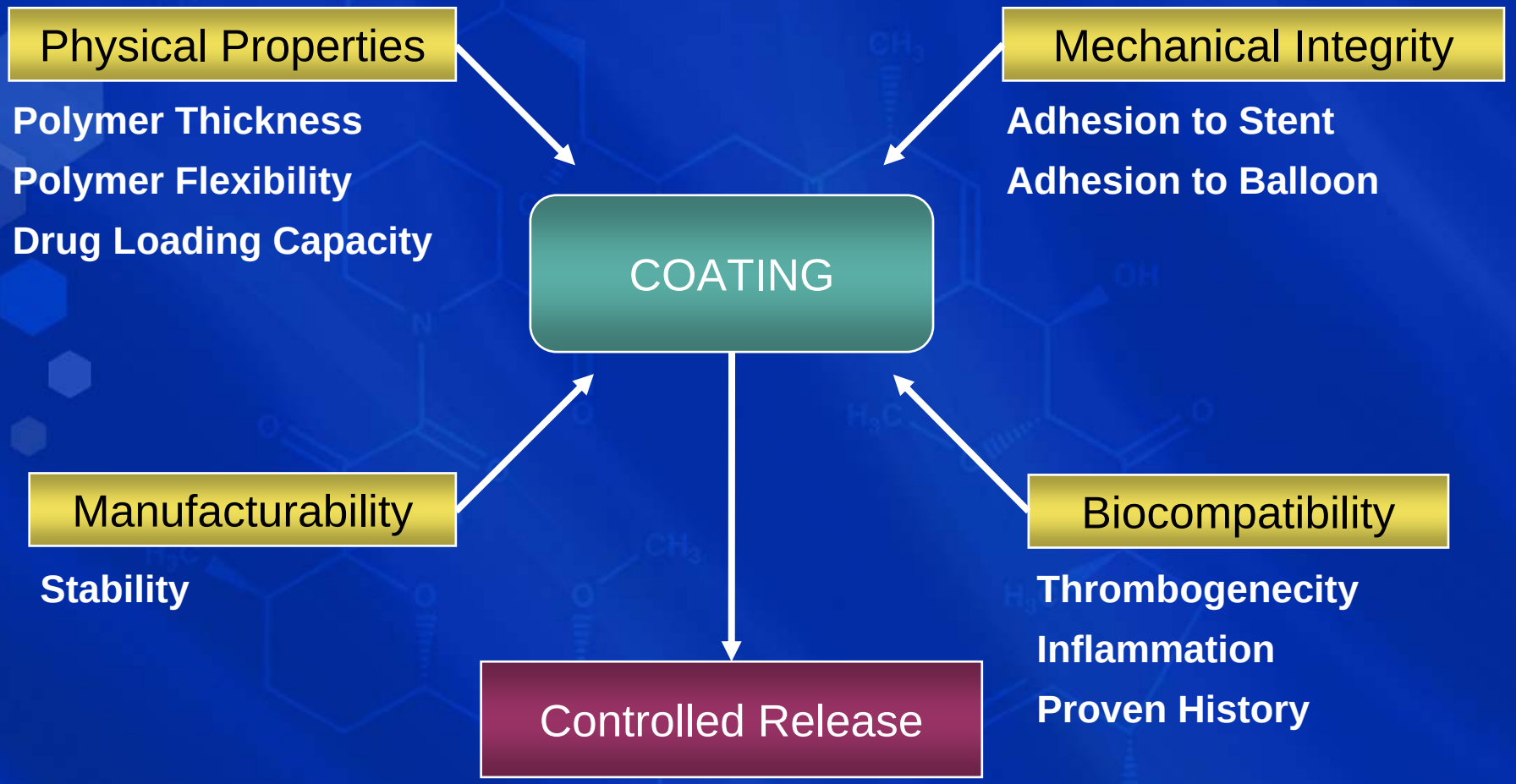
Pharmacology

Preferred Drug

- Mechanism of Action (MOA)
- Functional at μg level
  - Allows for thin drug reservoir coating
- Wide therapeutic window
  - Excellent tissue compatibility
- Drug stability
  - Product yield (manufacturing)
  - Shelf-life
- Proven clinical experience

Polymer Characteristics for Controlled Drug Release



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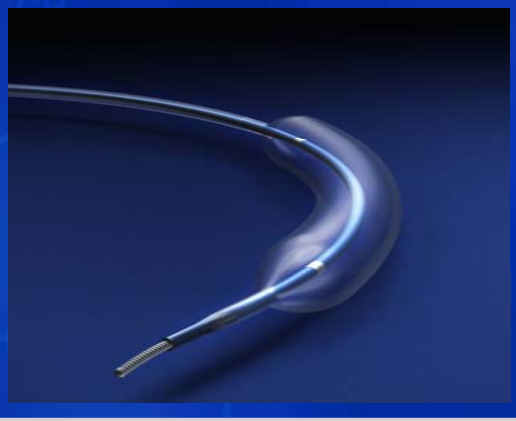
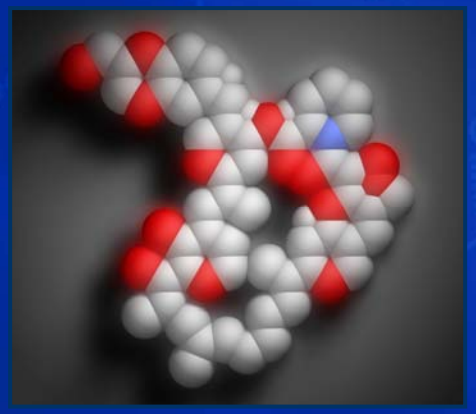
XIENCE V DES Components

MULTI-LINK VISION Stent

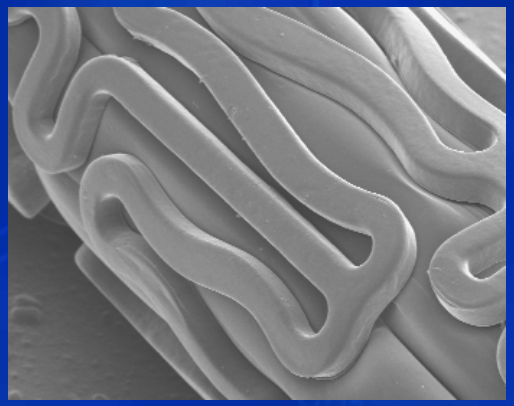
MULTI-LINK VISION Stent Delivery System



Everolimus



Fluoropolymer



CAUTION: XIENCE™ V is an investigational device. Limited by Federal (U.S.) law to investigational use only.

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Key Product Attributes:

Excellent acute success

- Proven Guidant MULTI-LINK VISION Platform
- Coating integrity from delivery to deployment
- Minimal coating thickness

Commitment to sustainable clinical outcomes

- Everolimus is a cytostatic proliferation inhibitor that causes cell cycle arrest in the late G1 phase
- Fluoropolymer technology allows for controlled release of Everolimus without sacrificing biocompatibility
- SPIRIT Family of Trials—over 4,000 XIENCE V patients studied by 2007

Excellent Acute Success

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MULTI-LINK VISION Platform

Cobalt Chromium Technology

- Allows for thinner struts without compromise to radiopacity or radial strength.[1]

Thin Strut Stent Design

- Outstanding flexibility and conformability
- .0032” strut thickness

Low System Profile

- Excellent deliverability

1. As compared to stainless steel. Source: ASTM International.

XIENCE V Stent Design – MULTI-LINK VISION® Stent

6-crest

- For 2.5 mm and 3.0 mm expansion diameters
- Can be post-dilated to 3.5 mm

9-crest

- For 3.5 mm and 4.0 mm expansion diameters
- Can be post-dilated to 4.5 mm

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XIENCE V Delivery System – MULTI-LINK VISION SDS

- Specifically designed for stent delivery
- Soft, highly flexible Pebax balloon material
- Short abrupt tapers
- 5F guide catheter compatible

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XIENCE V Fluoropolymer

- Fluoropolymers are extremely biocompatible with a proven history in blood contacting applications
  - Haemodialysis machines
  - Cardiac sutures
  - Vascular grafts
  - Guide catheters
- High drug loading
  - Minimize coating thickness
- Good physical coating integrity
  - Excellent adhesion to metal
  - Good ductility and flexibility

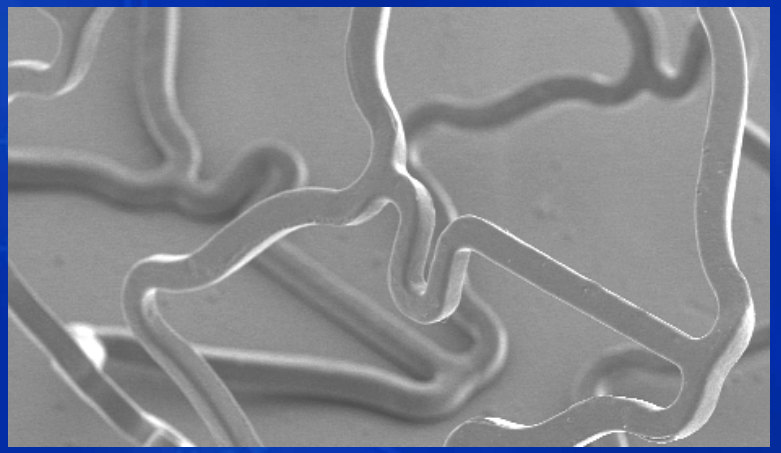

Photo taken by and on file at Abbott Vascular.

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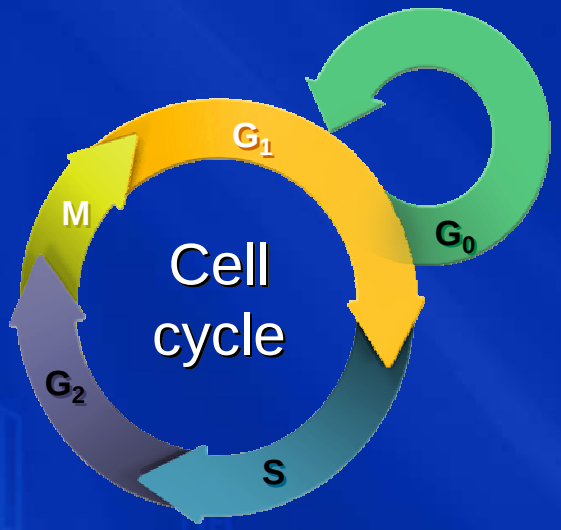
Drug

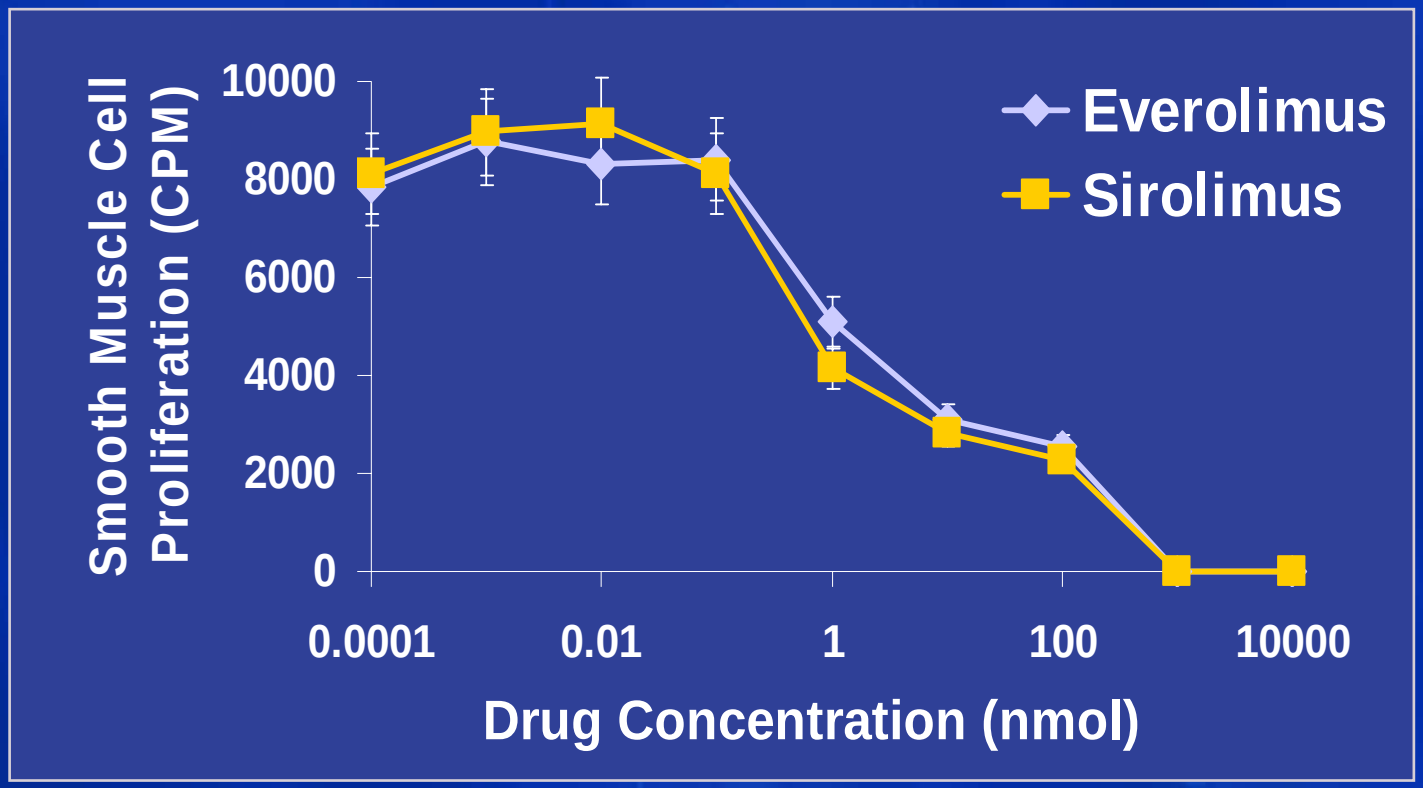
Everolimus

- Developed by Novartis
- Immunosuppressant drug
  - Targets primary causes of chronic rejection in heart, renal, and lung transplant patients
- Proliferation inhibitor
  - Inhibits growth factor-stimulated cell proliferation by causing cell cycle arrest in the late G1 stage
- Active ingredient in CERTICAN® (Novartis)
  - Approved for prevention of rejection of heart and kidney transplant in over 60 countries
  - Investigational drug; Novartis received approvable letter from FDA



Proven Pre-clinical Effectiveness

Everolimus and Sirolimus inhibit vascular smooth muscle cell proliferation



Sources: Novartis Pharma AG; Schuler et al. Transplantation. 1997; 64:36-42

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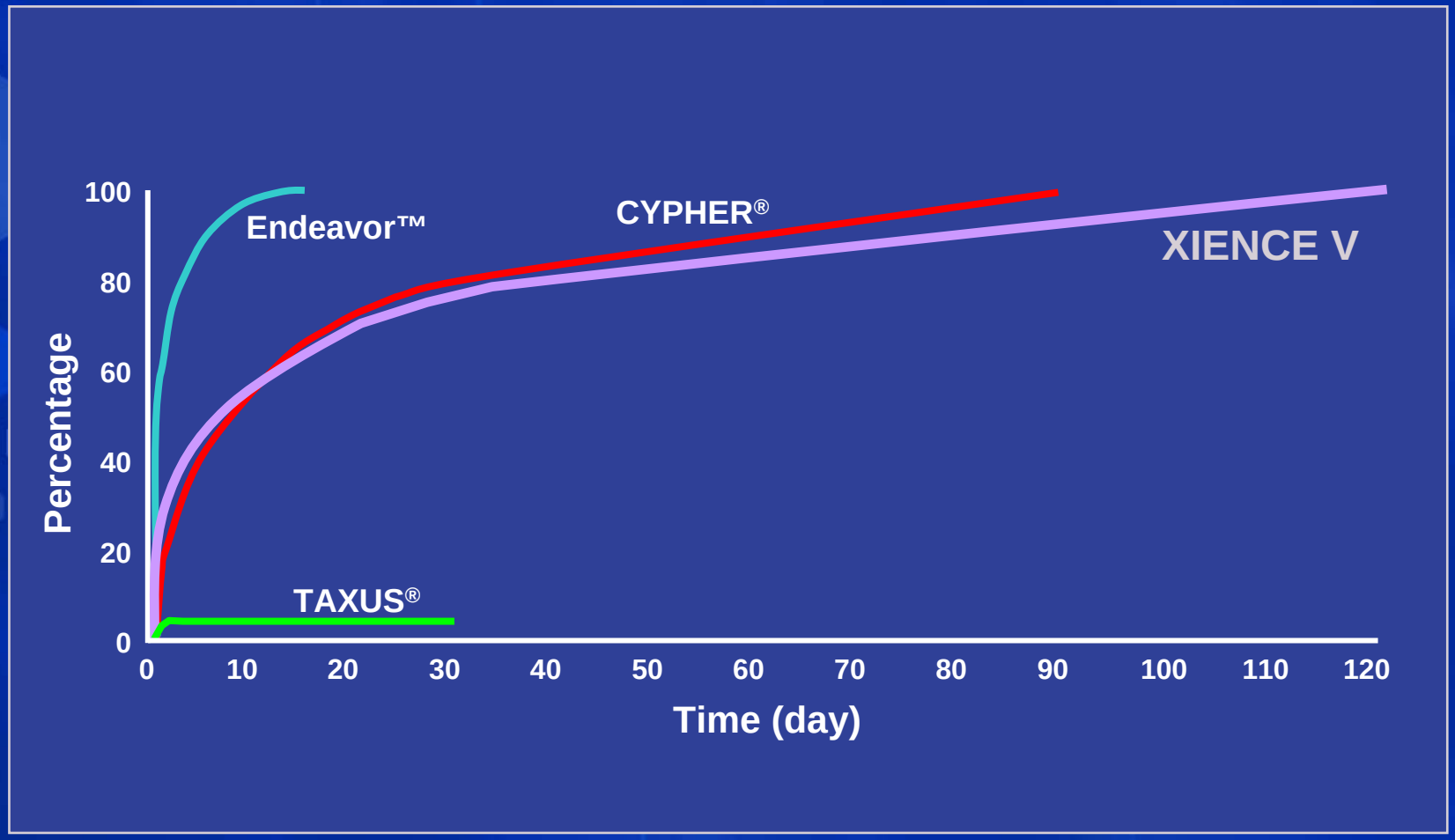
DES Release Profiles *(in vivo)*



Source: Medtronic Vascular Data Presentation, TCTMD; TAXUS IV SR Presentation, TCTMD; Cypher Presentation, TCTMD; Data on file at Abbott Vascular.

XIENCE V
Pre-clinical Studies

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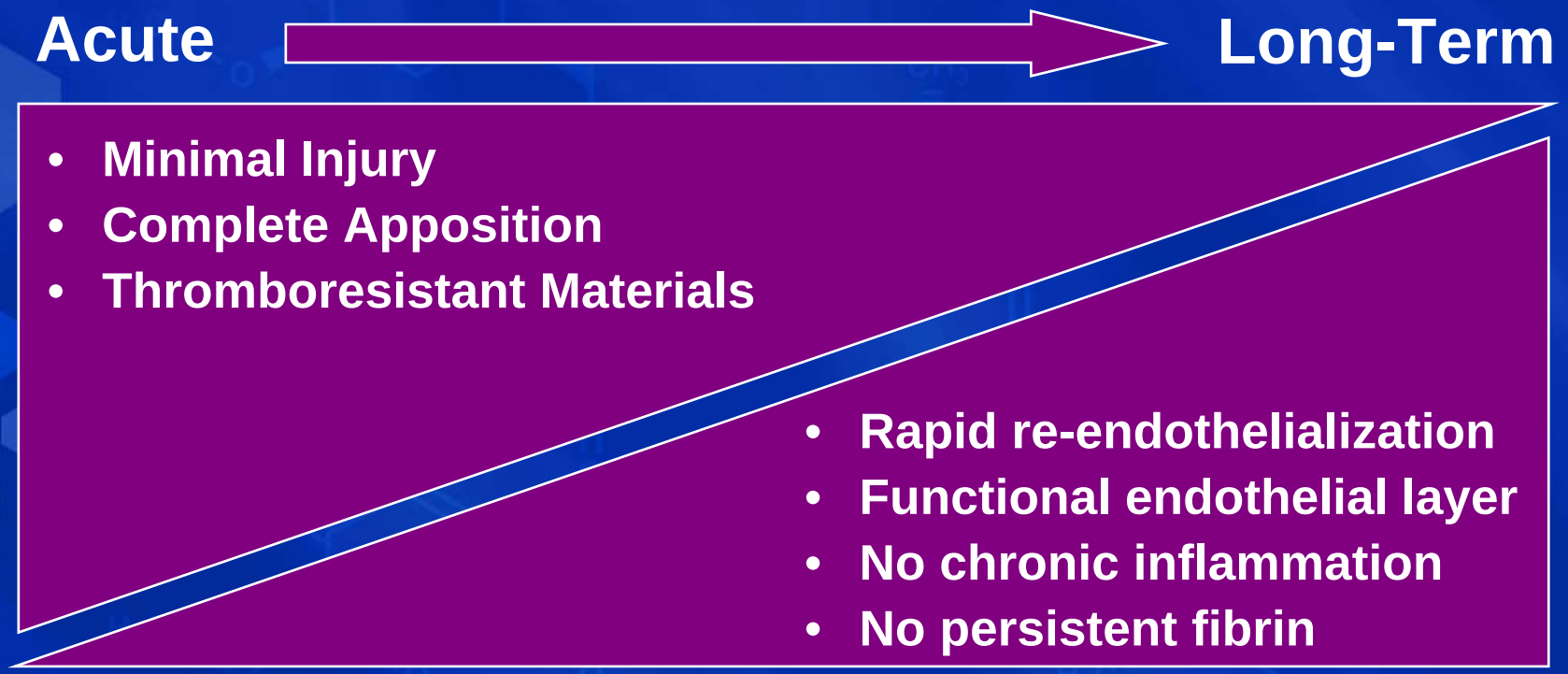
Safety Data

- *In vivo* animal testing was conducted to demonstrate the safety of the XIENCE V Stent, and the safety of 2 overlapped XIENCE V Stents, in 2 animal models
  - A low injury porcine coronary artery model*
  - A low injury non-atherosclerotic rabbit iliac model**

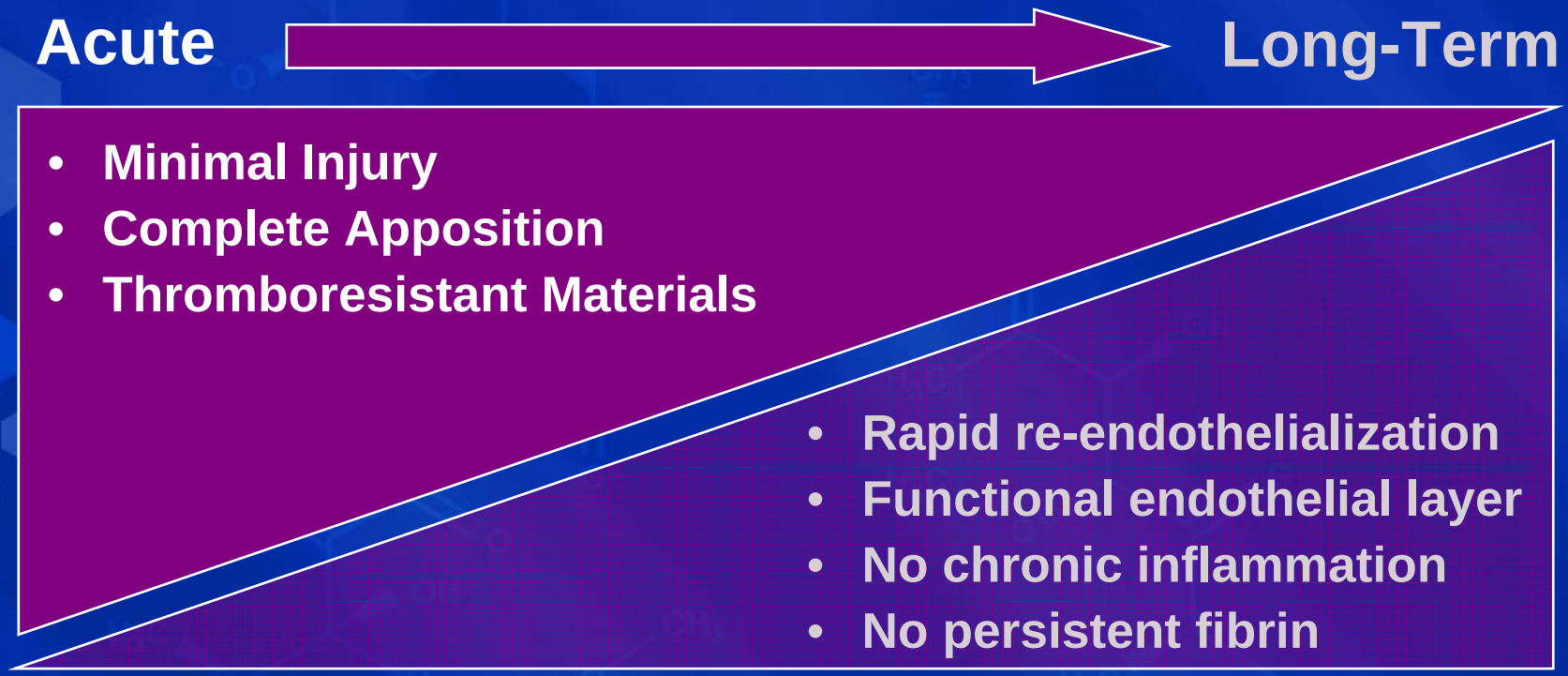
* Studies conducted with 3.0 x12 mm stents containing 56 µg Everolimus

** Studies conducted with 2.5 x 8 mm stents containing 37 µg Everolimus

The Science of Safety

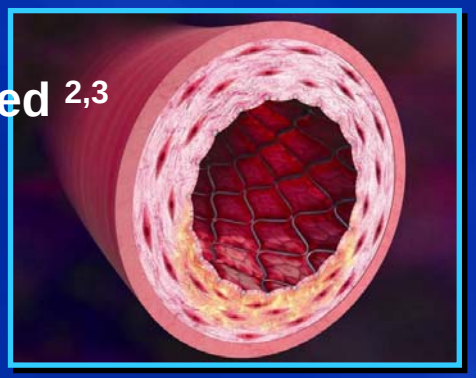


The Science of Safety



ENDOTHELIAL INJURY AND HEALING POST-STENT IMPLANTATION

- ***Endothelial denudation*** [1]
  - **Small area – little to no intimal hyperplasia observed** [2,3]
  - **Large area**
    - **Focal fibrin deposition +** ***thrombus formation***
    - ***Inflammation***
    - ***Activation of SMCs***
  - **Severe and deeper injury results in delayed re-endothelialisation** [4]



- ***Subsequent arterial healing process begins immediately*** [1,5]
  - **Eventually is essential for restoring normal arterial function**
  - **In around 15 - 20 % of patients this normal process is exaggerated resulting in re-stenosis**

The Science of Acute Safety

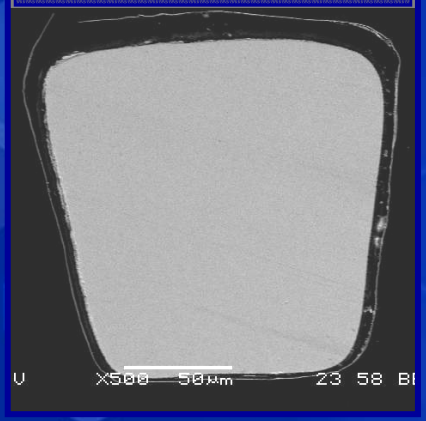
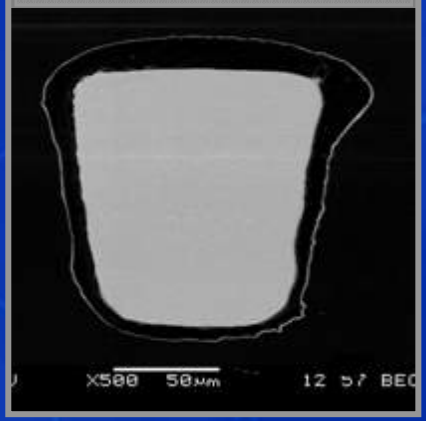
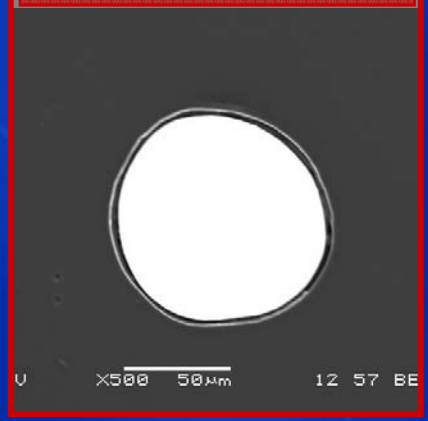
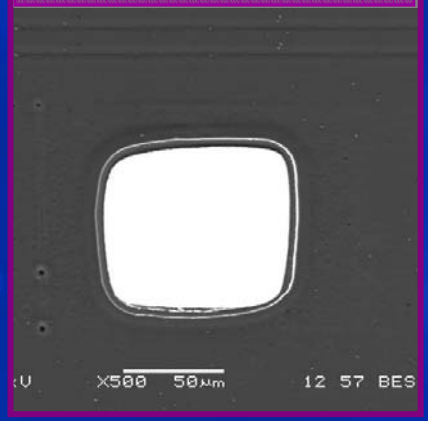
Maximizing Acute Safety	Desired Attributes
• Minimal Injury	• Thin Struts • Low Stent to Shoulder
• Complete Apposition	• Conformable Stent Pattern
• Thromboresistant Materials	• Polymer • Implant

Minimal Injury

Minimizing Strut and Polymer Thickness

Acute

Long-Term

CYPHER®	TAXUS®	ENDEAVOR	XIENCE V
			
Strut Thickness:	Strut Thickness:	Strut Thickness:	Strut Thickness:
140 um	**132 um**	**91 um**	**81 um**
Polymer Thickness:	Polymer Thickness:	Polymer Thickness:	Polymer Thickness:
12.6 um	**16 um**	**5.3 um**	**7.6 um**
Total:	**Total:**	**Total:**	**Total:**
152.6 um	**148 um**	**96.3 um**	**88.6 um**

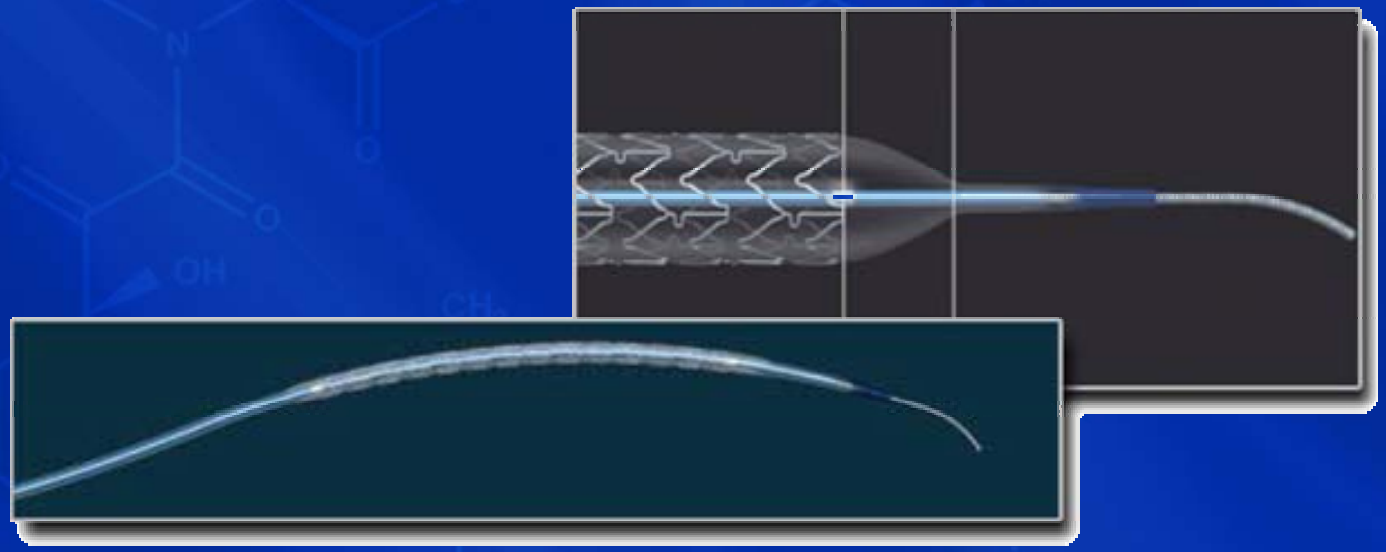
3.0 mm diameter stents, 500x magnification

Data on file at Abbott Vascular

Acute
Long-Term

Minimal Injury
Short, Abrupt Tapers

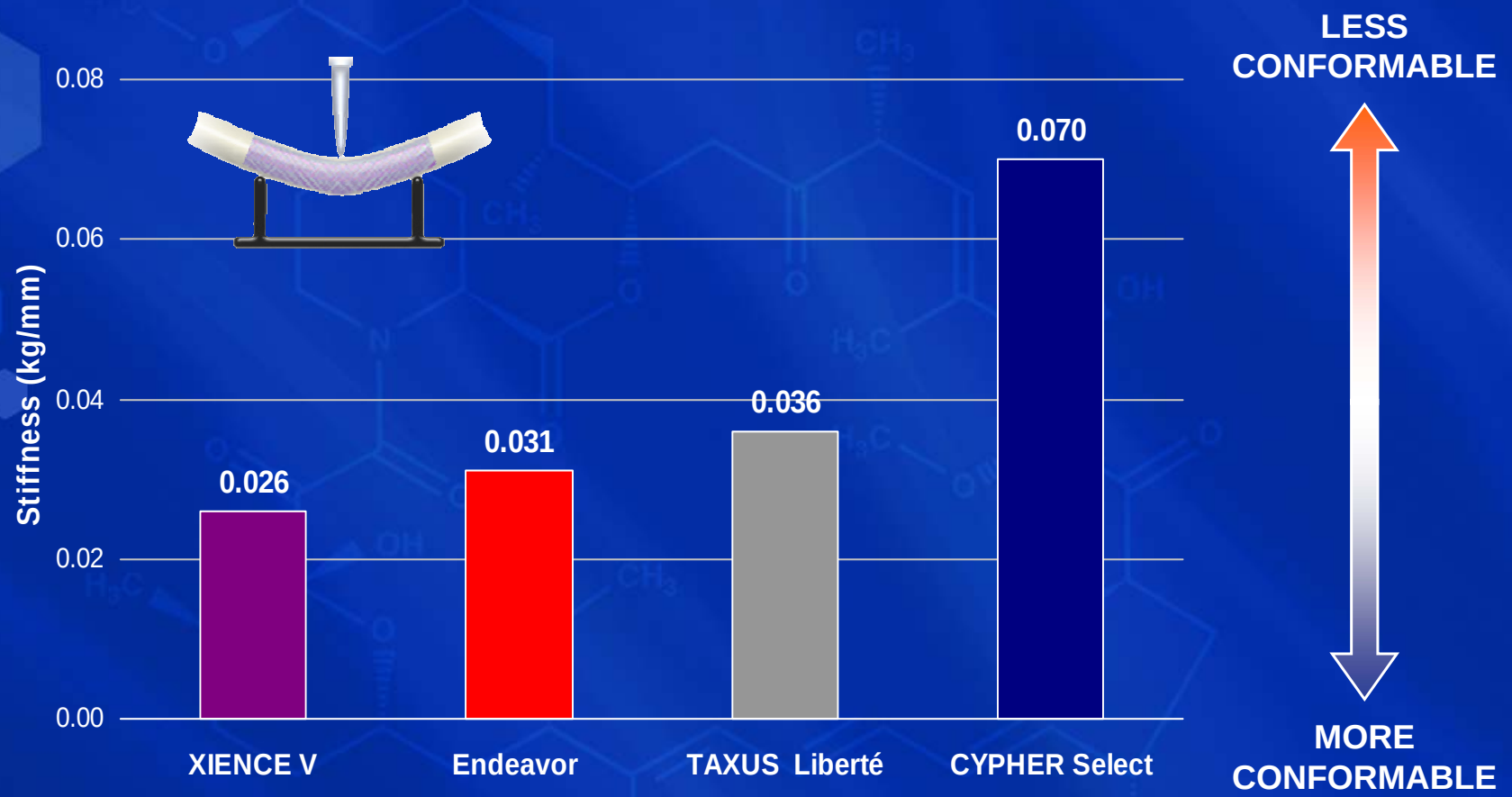
- Specifically designed for stent delivery
- Soft, highly flexible Pebax balloon material
- Short abrupt tapers
- 5F guide catheter compatible



Photos taken by and on file at Abbott Vascular.

Complete Apposition
Flexible, Conformable Stent Design

Acute
Long-Term



Tests performed by and data on file at Abbott Vascular.
3.5 mm x 28 mm XIENCE V , CYPHER Select, and TAXUS® Liberté. 3.5 mm x 30 mm Endeavor

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Thromboresistant Fluoropolymer
Proven Medical Applications

	Fluoro Polymer
Drug Eluting Stent:	• XIENCE V Everolimus Eluting Coronary Stent System
Other Applications:	• Arterial Prostheses • Graft Prostheses • Hemodialysis membrane • Vascular suture • Guiding Catheter • Other blood contacting surfaces

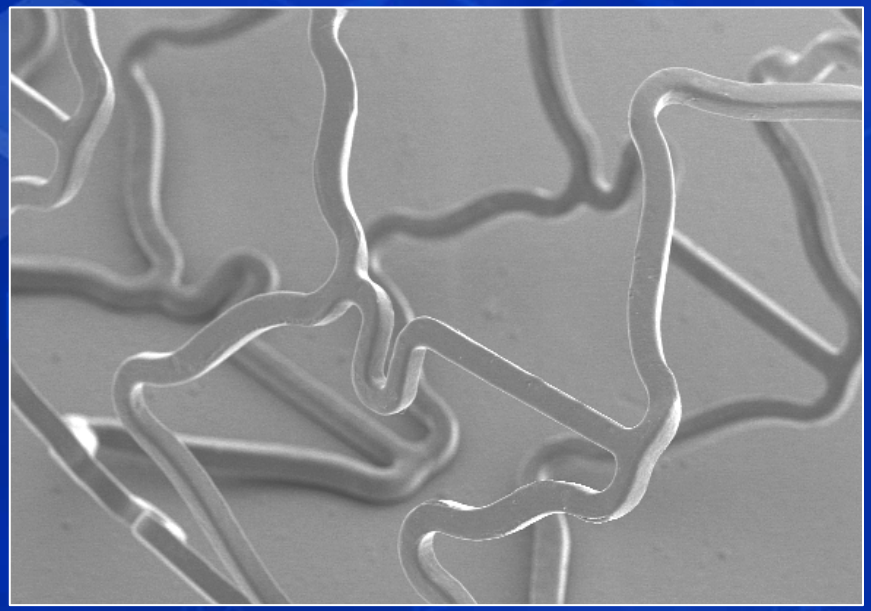
- The inert and hemocompatible properties of fluoropolymers make it an excellent choice for use in a variety of medical applications

Thromboresistant Materials

Coating Integrity - XIENCE V Fluoropolymer

Acute

Long-Term



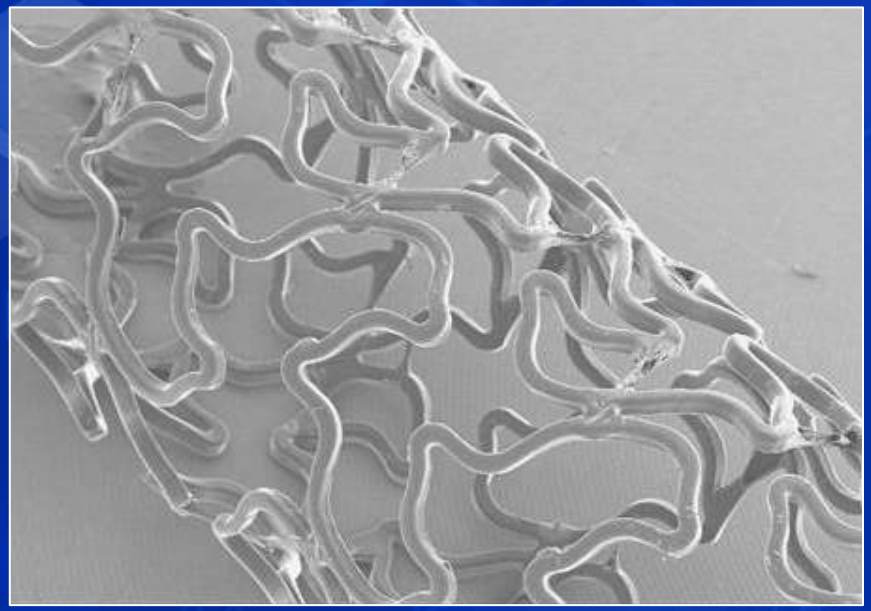
- Consistent coating integrity to minimize platelet aggregation and inflammation

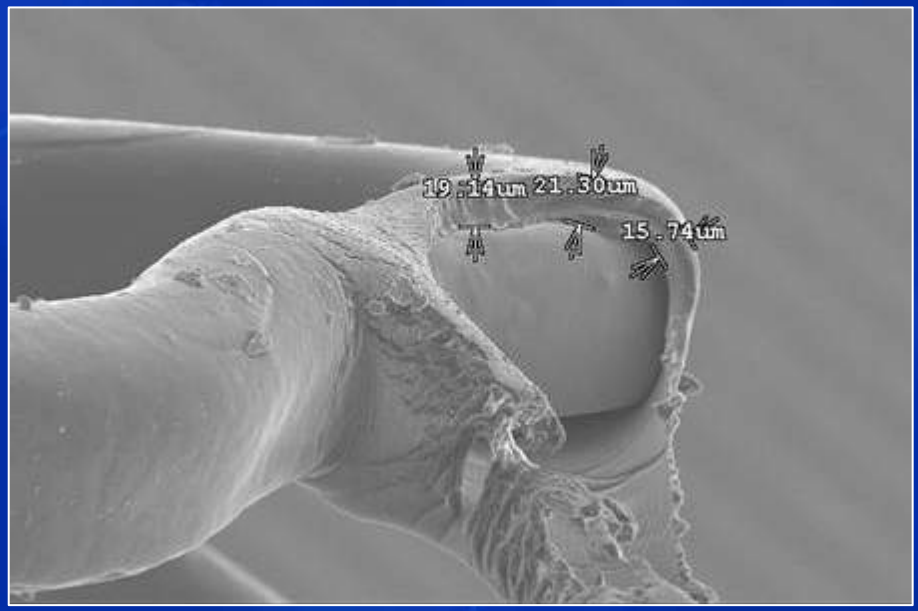
Photos taken by and on file at Abbott Vascular

Acute

Long-Term

Coating Integrity - TAXUS® Liberté



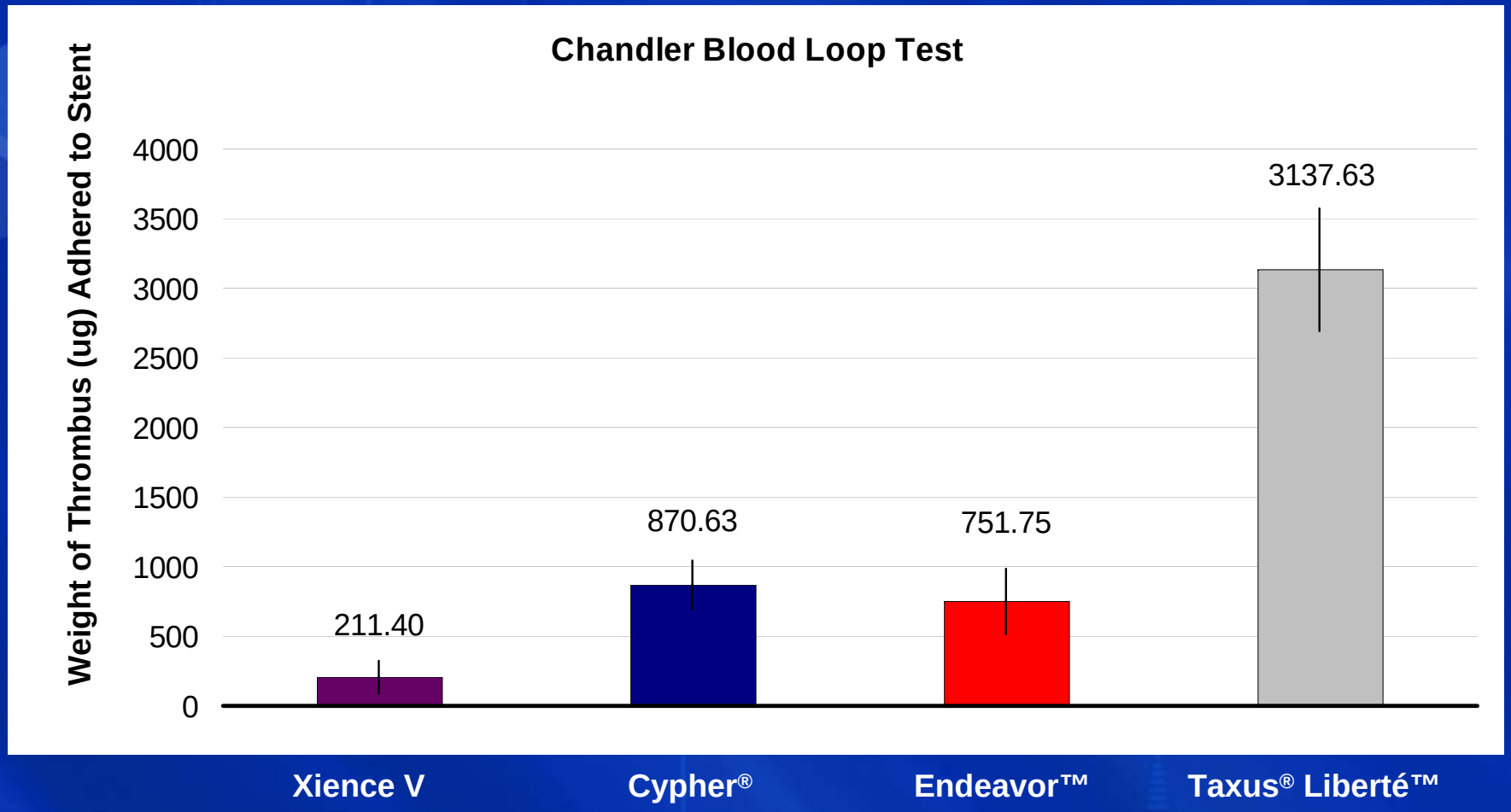


- Intense webbing of polymer
  - Touch points led to webbing of polymer

Photos taken by and on file at Abbott Vascular

Thromboresistant Materials
Minimal Platelet Aggregation

Acute
Long-Term



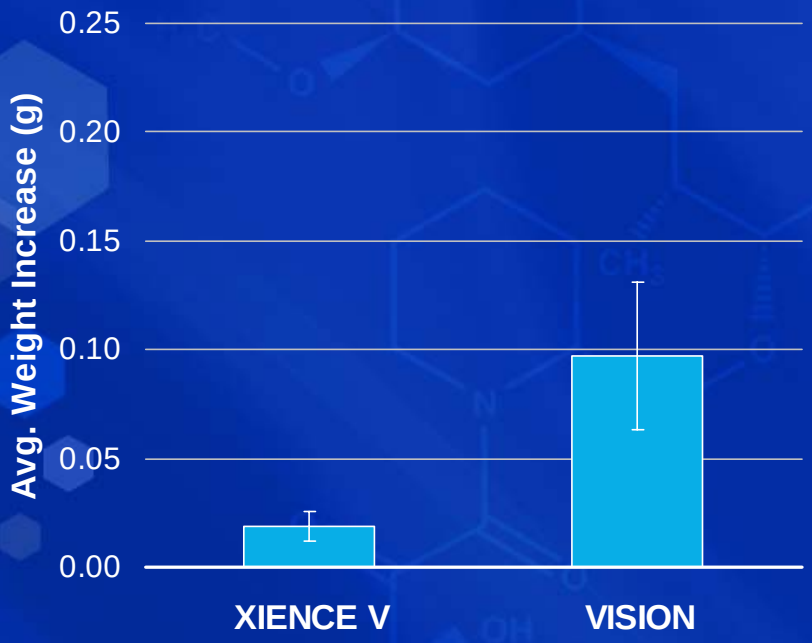
Data on file at Abbott Vascular

Thromboresistant Materials

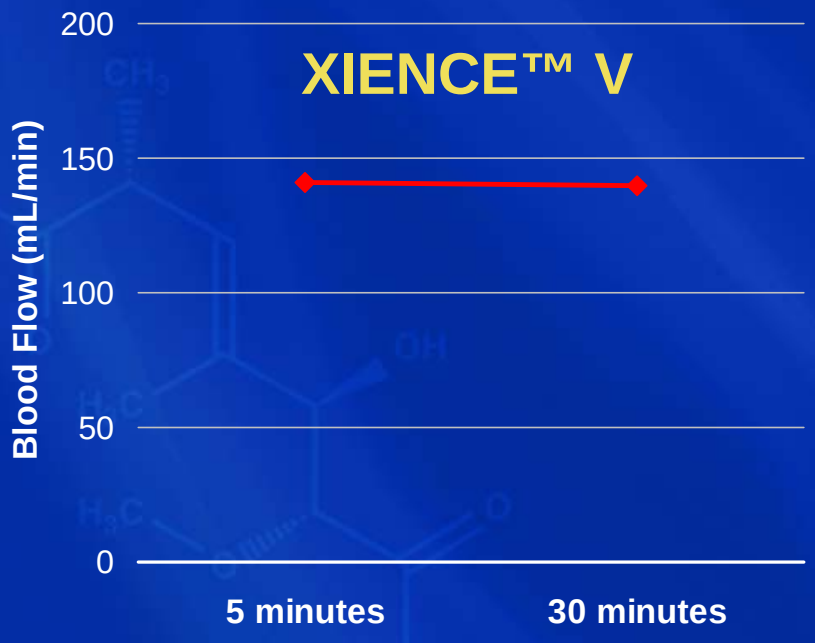
Ex-Vivo Shunt Study

Acute

Long-Term



Low thrombus adherence due to smooth coating integrity and hemocompatibility of the XIENCE V Fluoropolymer.



No reduced flow between 5 minutes and 30 minutes porcine in-vivo.

Data on file at Abbott Vascular

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The Science of Safety

Acute → **Long-Term**

- **Minimal Injury**
- **Complete Apposition**
- **Thromboresistant Materials**

- **Rapid re-endothelialization**
- **Functional endothelial layer**
- **No chronic inflammation**
- **No persistent fibrin**

The Science of Long Term Safety

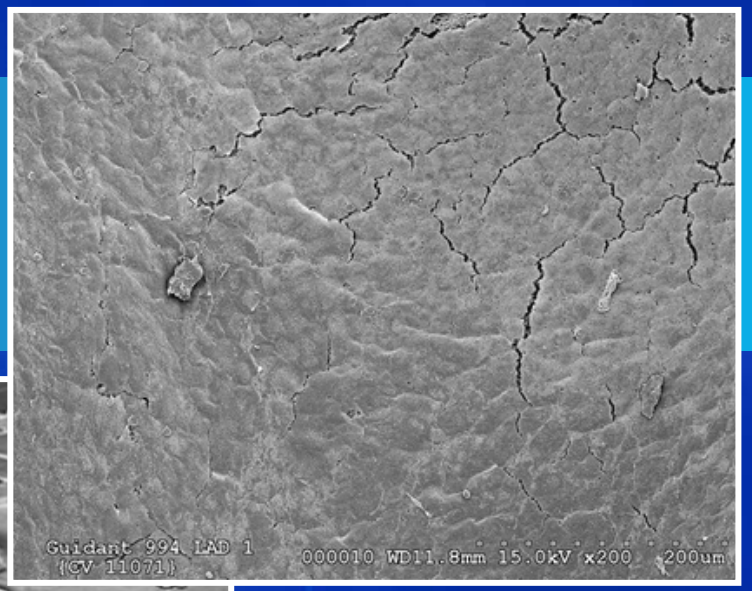
Maximizing Long-term Safety	Desired Attributes
• Rapid Re-endothelialization	• Complete coverage • Decreased VEGF Production
• Functional endothelial layer	• Presence of CD-31
• Minimal inflammation	• No persistent foreign body response • Lack of medial necrosis • No positive remodeling
• No persistent fibrin	

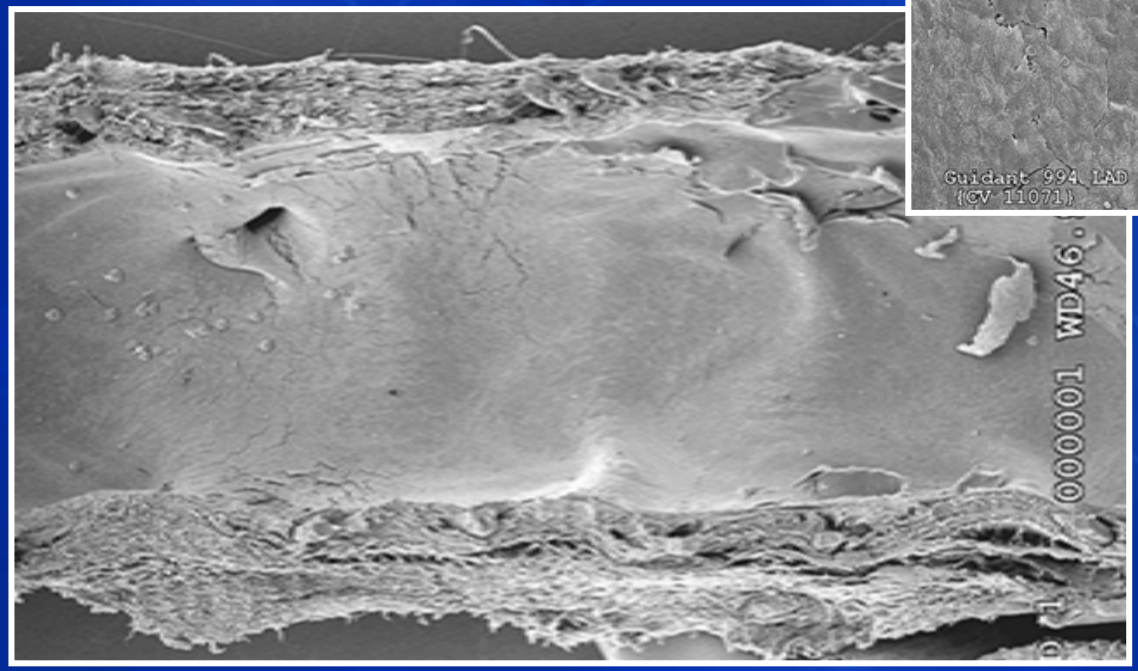
Acute
Long-Term

Rapid Re-endothelialization

Porcine Model, XIENCE™ V Stent at 28 Days

Complete luminal endothelialization observed at low and high magnification (SEM)





Photos on file at Abbott Vascular.

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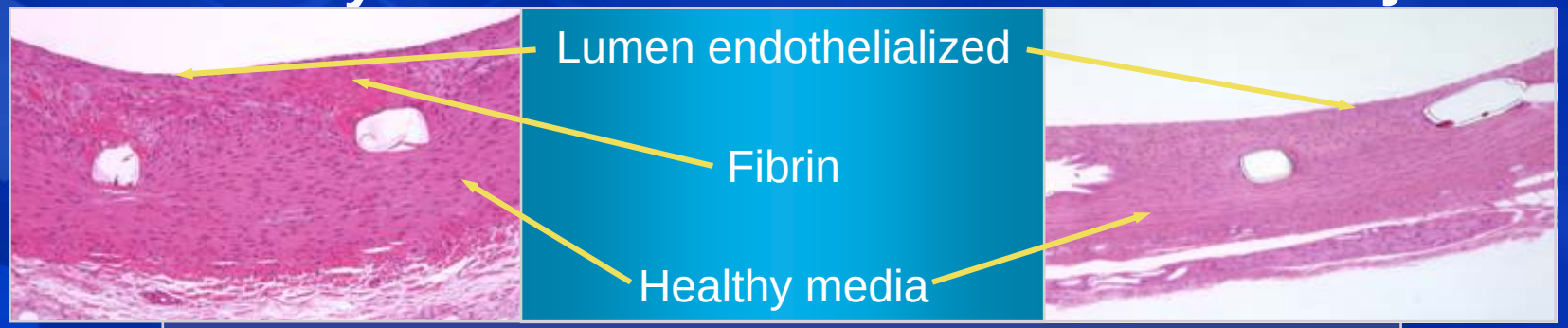
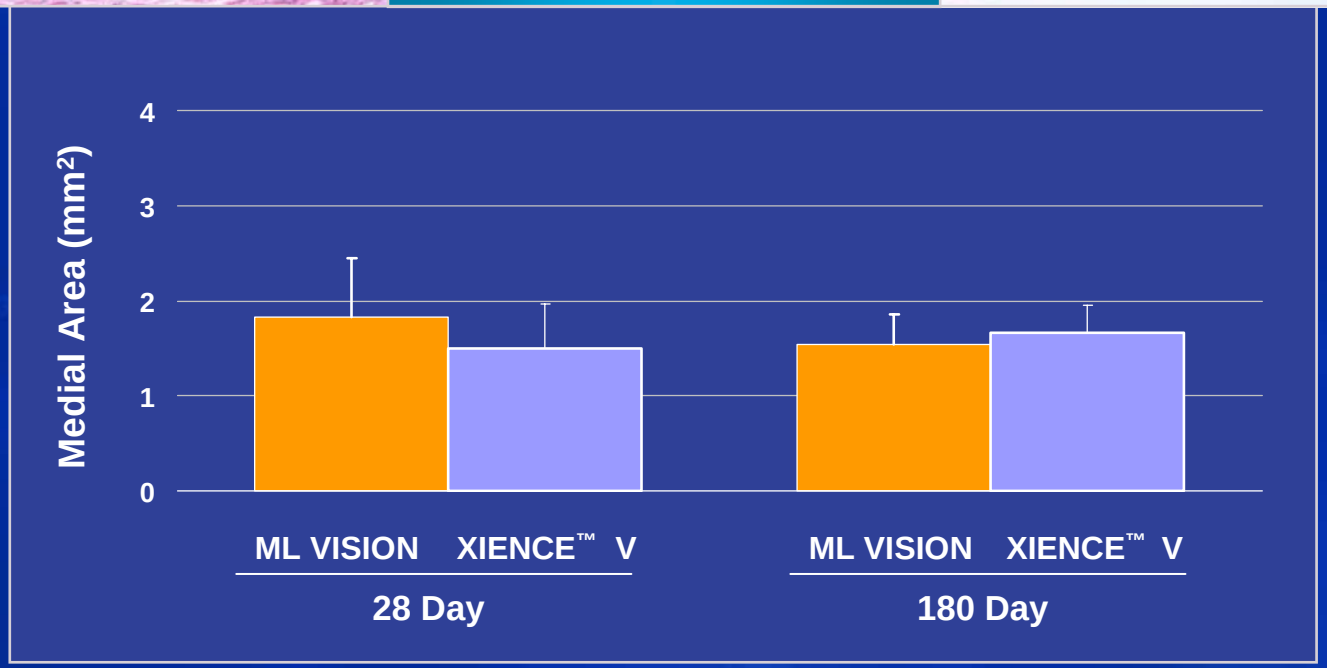
Acute
Long-Term

Rapid Re-endothelialization

Porcine Stent Healing at 28 & 180 Days

28 Day **180 Day**





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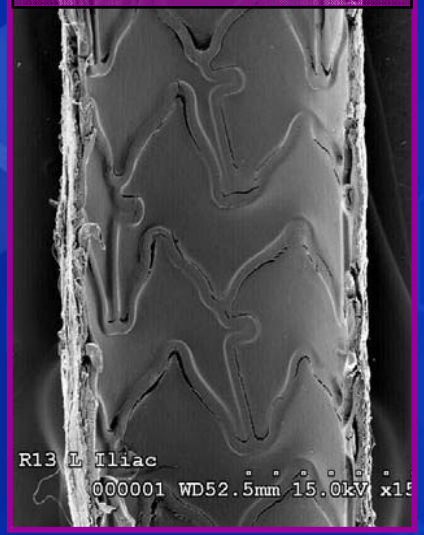
Rapid Re-endothelialization

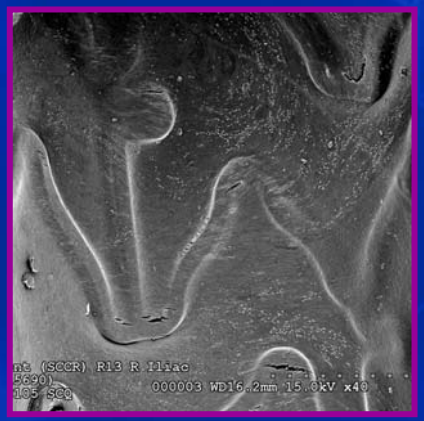
14-Day Rabbit Iliac Study

Acute

Long-Term

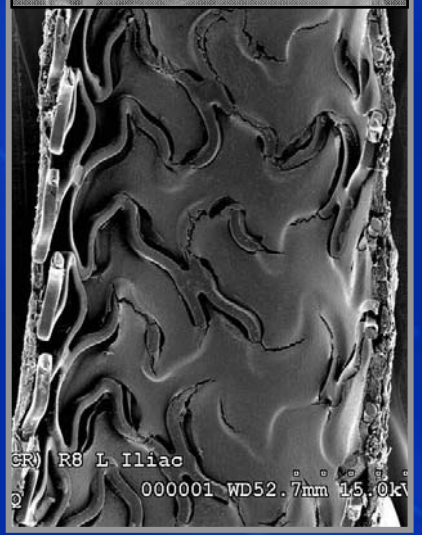
XIENCE V

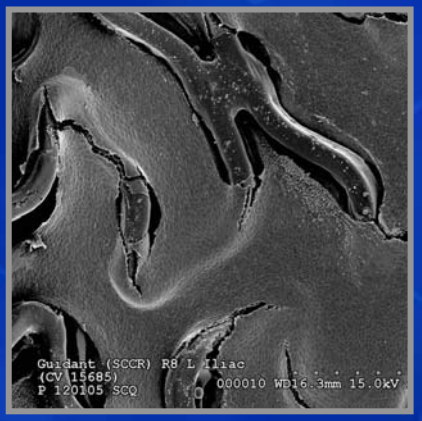




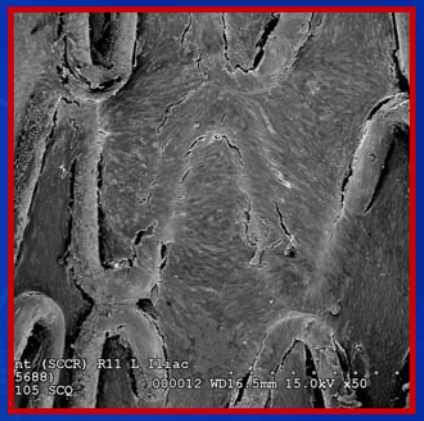
CYPHER®

TAXUS®





ENDEAVOR



Photos on file at Abbott Vascular

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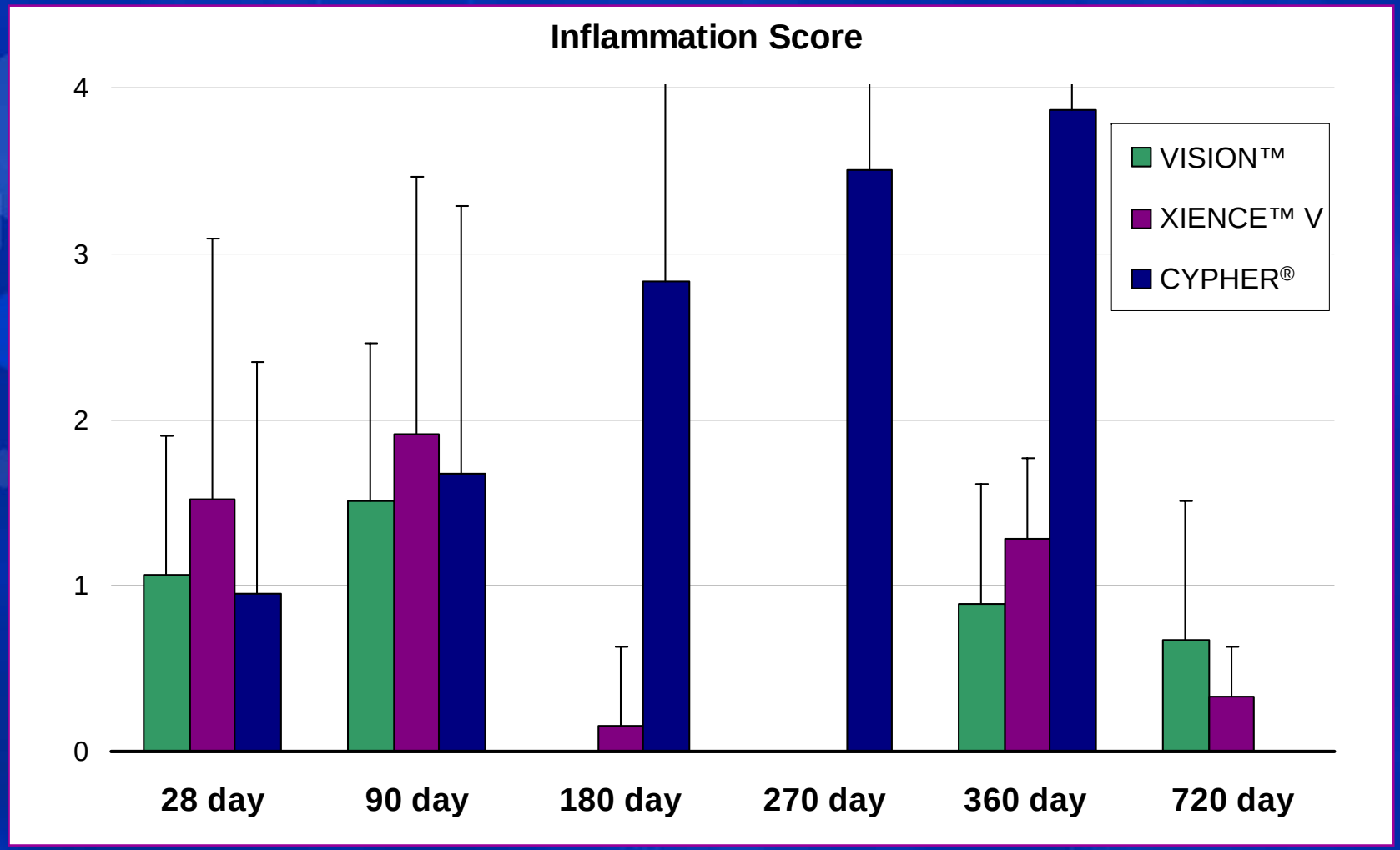
Minimal Inflammation
Porcine Safety Study up to 720 days

Acute
Long-Term

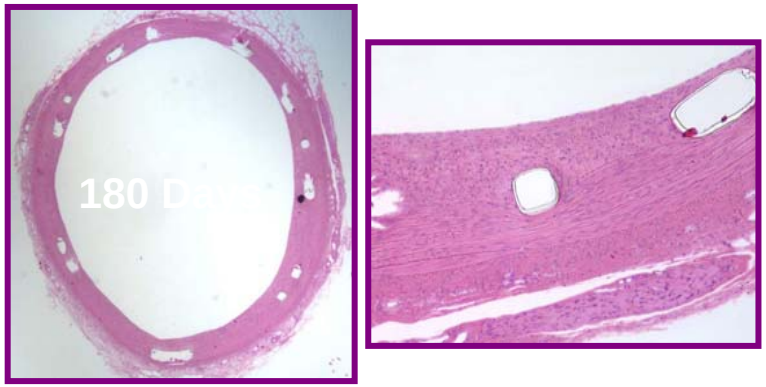


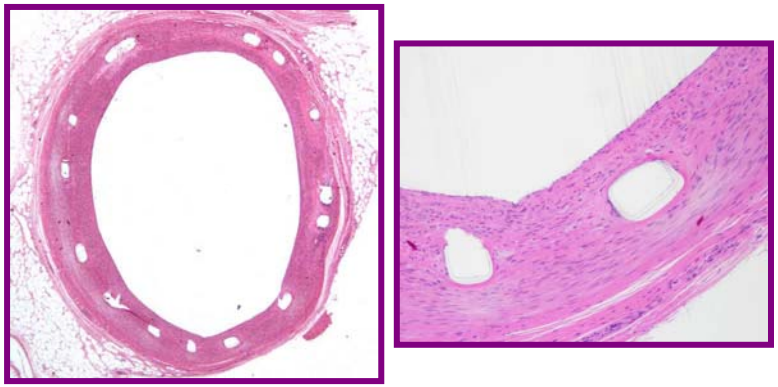
Data on file at Abbott Vascular

Acute
Long-Term

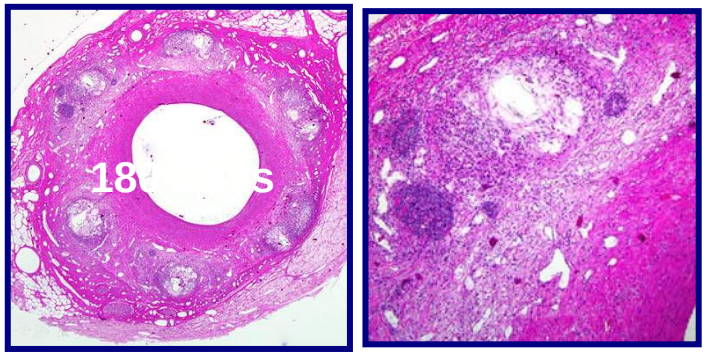
Minimal Inflammation
Porcine Safety Study (representative histology)

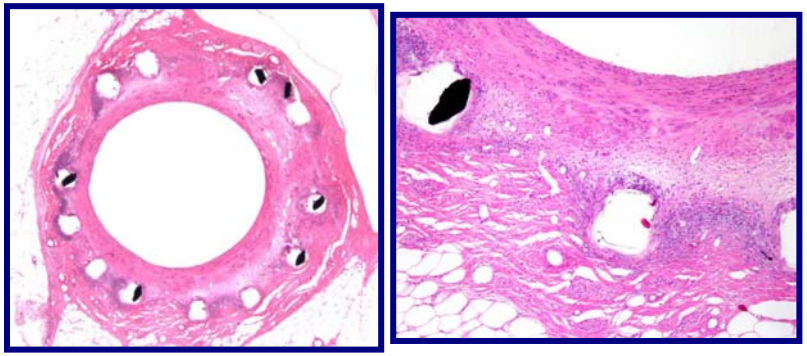
XIENCE V





CYPHER





Photos taken by and on file at Abbott Vascular

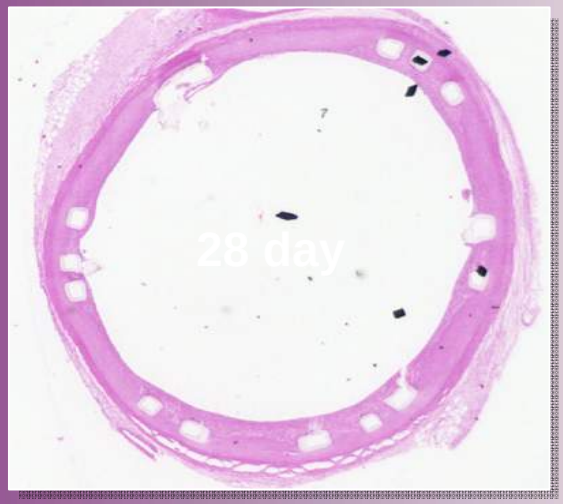
Minimal Inflammation

XIENCE™ V Max Dose Study

Acute

Long-Term

Max Dose



Max Dose study (8x XIENCE V Drug Dose):

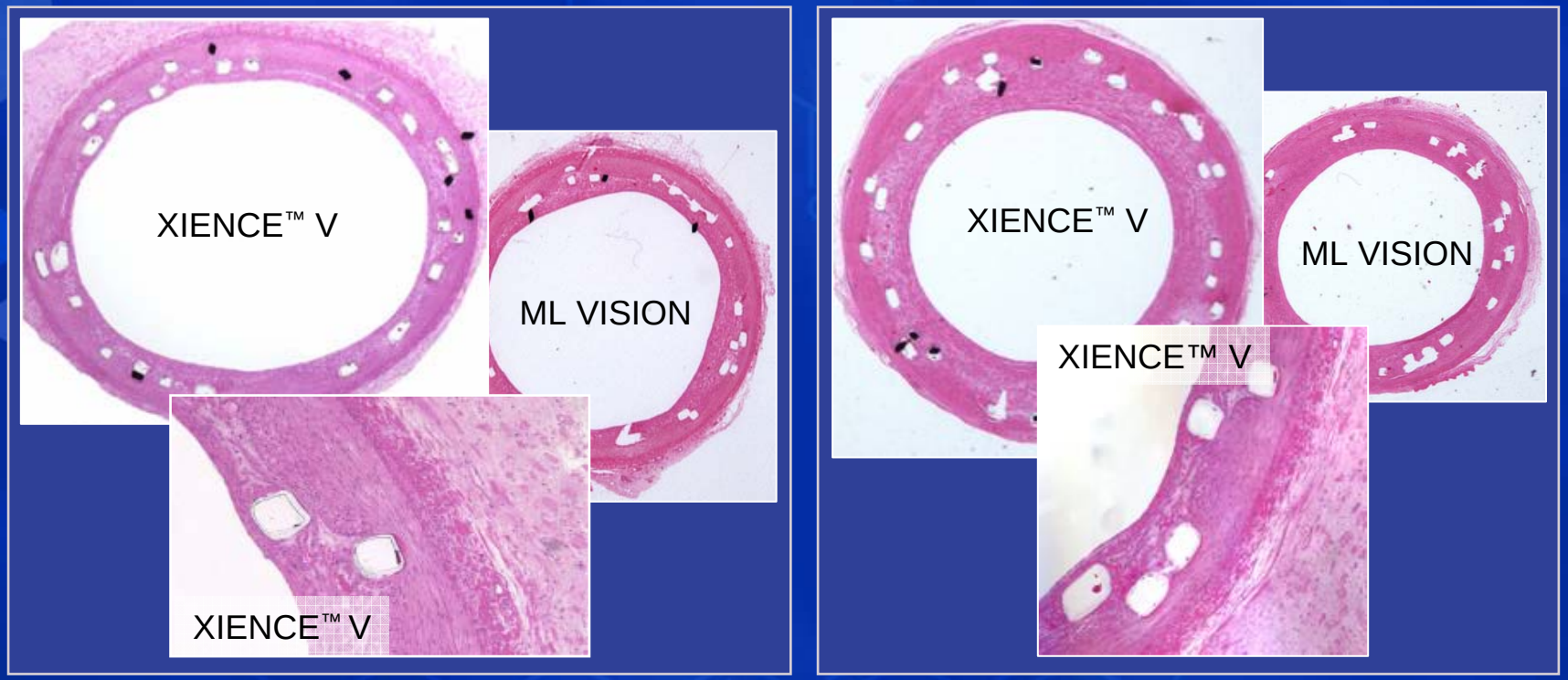
Patent lumens with stent struts completely covered by a well organized, smooth muscle cell-rich neointima.

Photos taken by and on file at Abbott Vascular

Minimal Inflammation
XIENCE™ V Overlapping Stents

Acute
Long-Term

28 Day	180 Day



All vessels are widely patent with a smooth muscle cell rich neointima incorporating all stent struts

Photos on file at Abbott Vascular.

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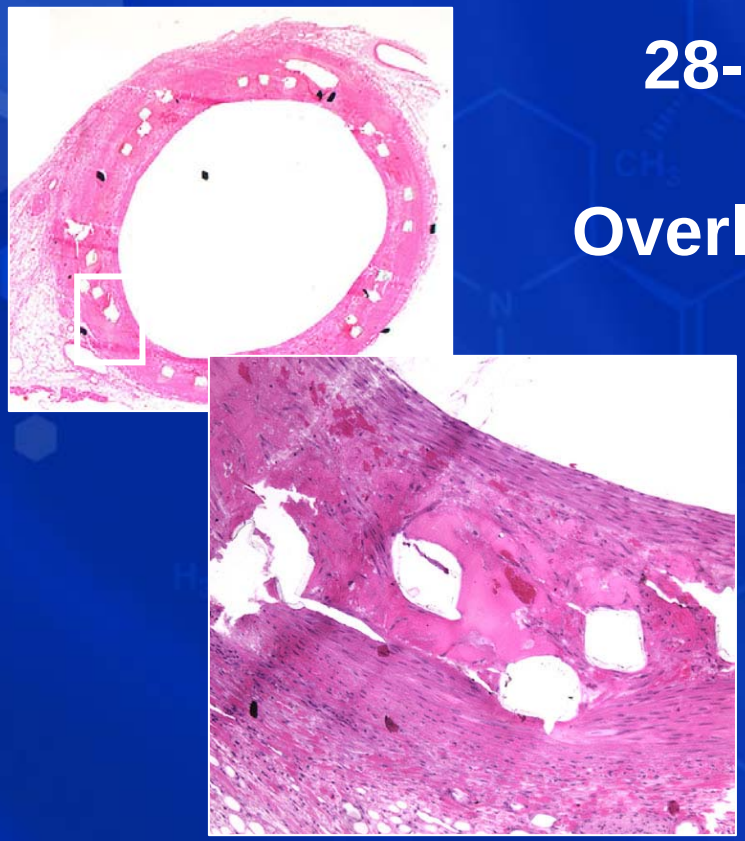
SE2924433D

Minimal Inflammation & Fibrin
No Medial Necrosis with XIENCE V

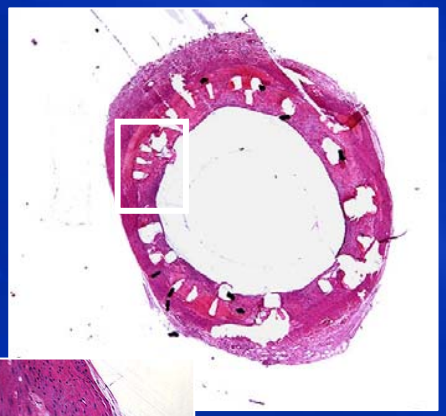
Acute
Long-Term

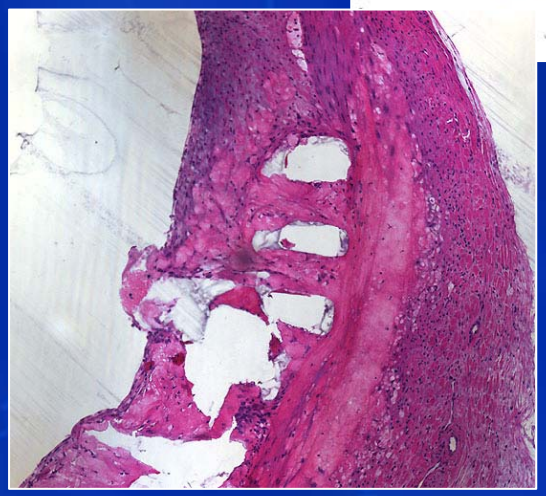
XIENCE™ V



28-day Porcine Model: Overlapping Stents

TAXUS®





Photos taken by and on file at Abbott Vascular

The Science of Long Term Safety

Maximizing Long-term Safety	Desired Attributes
• Rapid Re-endothelialization	✓Complete coverage ✓Decreased VEGF Production
• Functional endothelial layer	✓Presence of CD-31
• Minimal inflammation	✓No persistent foreign body response ✓Lack of medial necrosis ✓No positive remodeling
• No persistent fibrin	

Summary of Pre-clinical Studies Data

The pre-clinical data supports the safety of the XIENCE™ V Stent in the animal model

- Neointima characterized by compact smooth muscle cells in proteoglycan / collagen matrix at 28, 90, 180 days
- Completely endothelialized lumens by 28 days
- Widely patent lumens
- No luminal thrombus
- Inflammation within acceptable range in porcine and rabbit models

XIENCE V
Clinical Studies

Family of Trials

SPIRIT FIRST	SPIRIT II	SPIRIT III	SPIRIT IV	SPIRIT V
Safety and Performance	**Clinical Support for CE Launch**	**U.S. and Japan Approval**	**U.S. Peri-approval**	**Post-CE Mark Approval**
Europe N = 60	International N = 300	U.S./Japan N = 1,380 (1,292/88)	U.S. N = 1,125	International N = 3,021 (Approximate) Diabetic study N = 321 Registry N = 2,700

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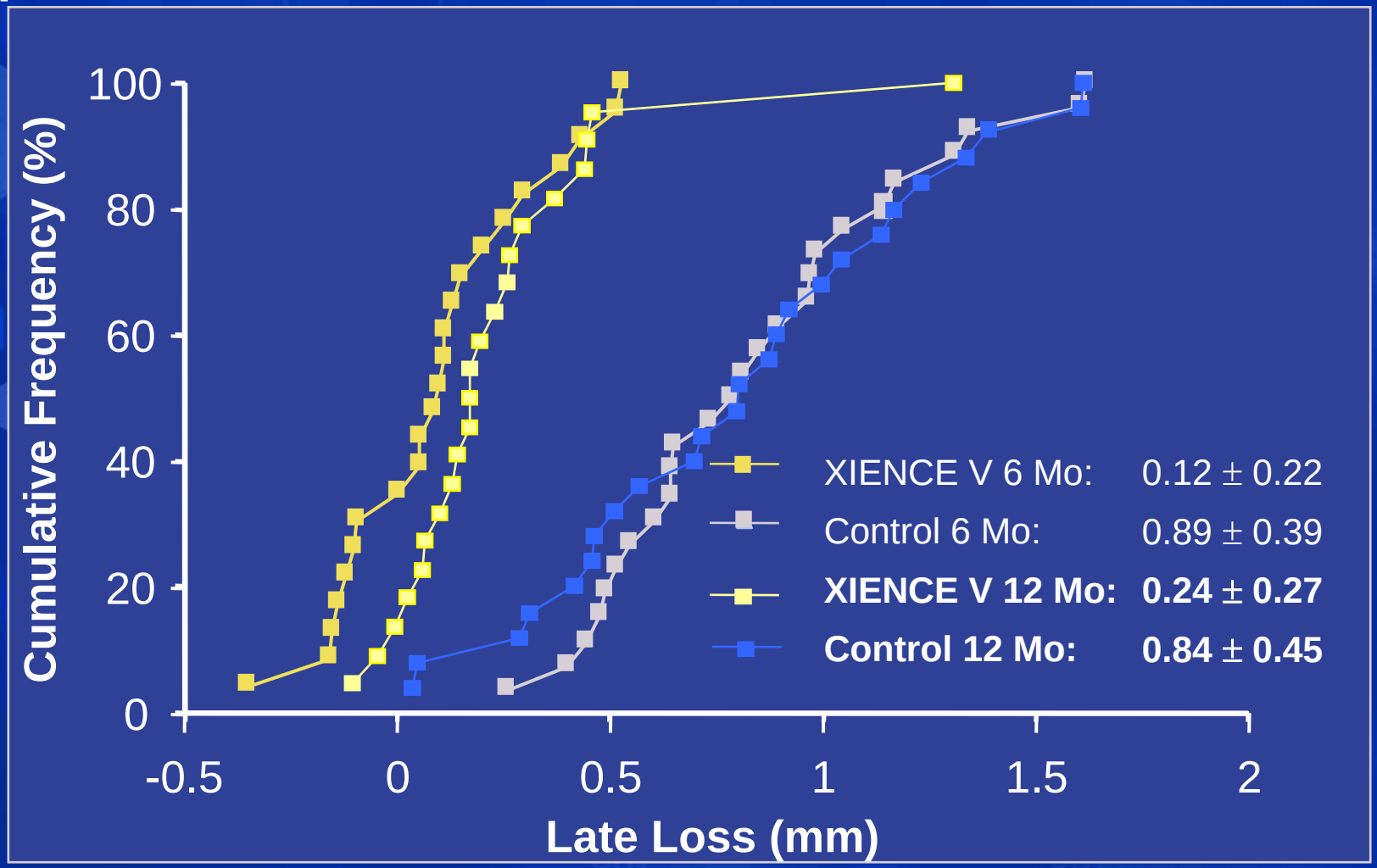
SPIRIT FIRST: In-Stent Late Loss (mm) per QCA to 12 Months



SOURCE: Tsuchida et al. "One-year results of a durable polymer everolimus-eluting stent in de novo coronary narrowings (The SPIRIT FIRST Trial)," *EuroIntervention 2005* 1:266-272.

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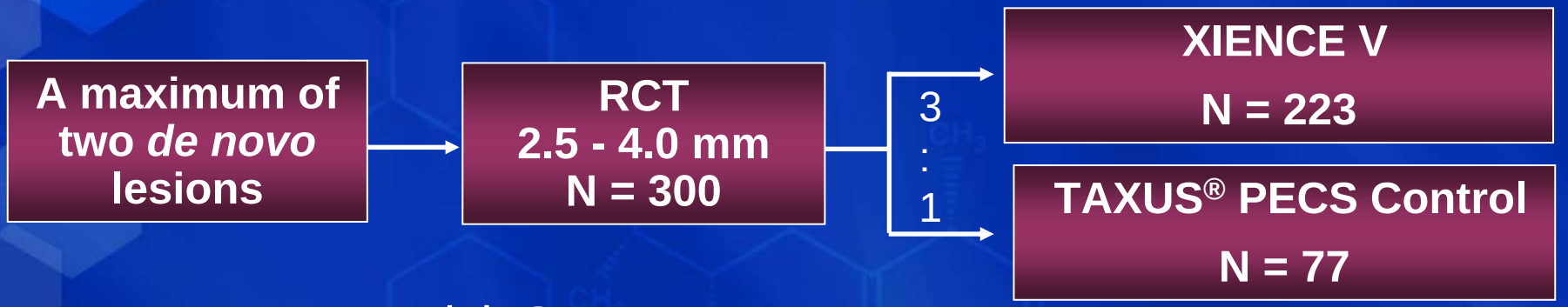
SPIRIT FIRST Key Takeaways

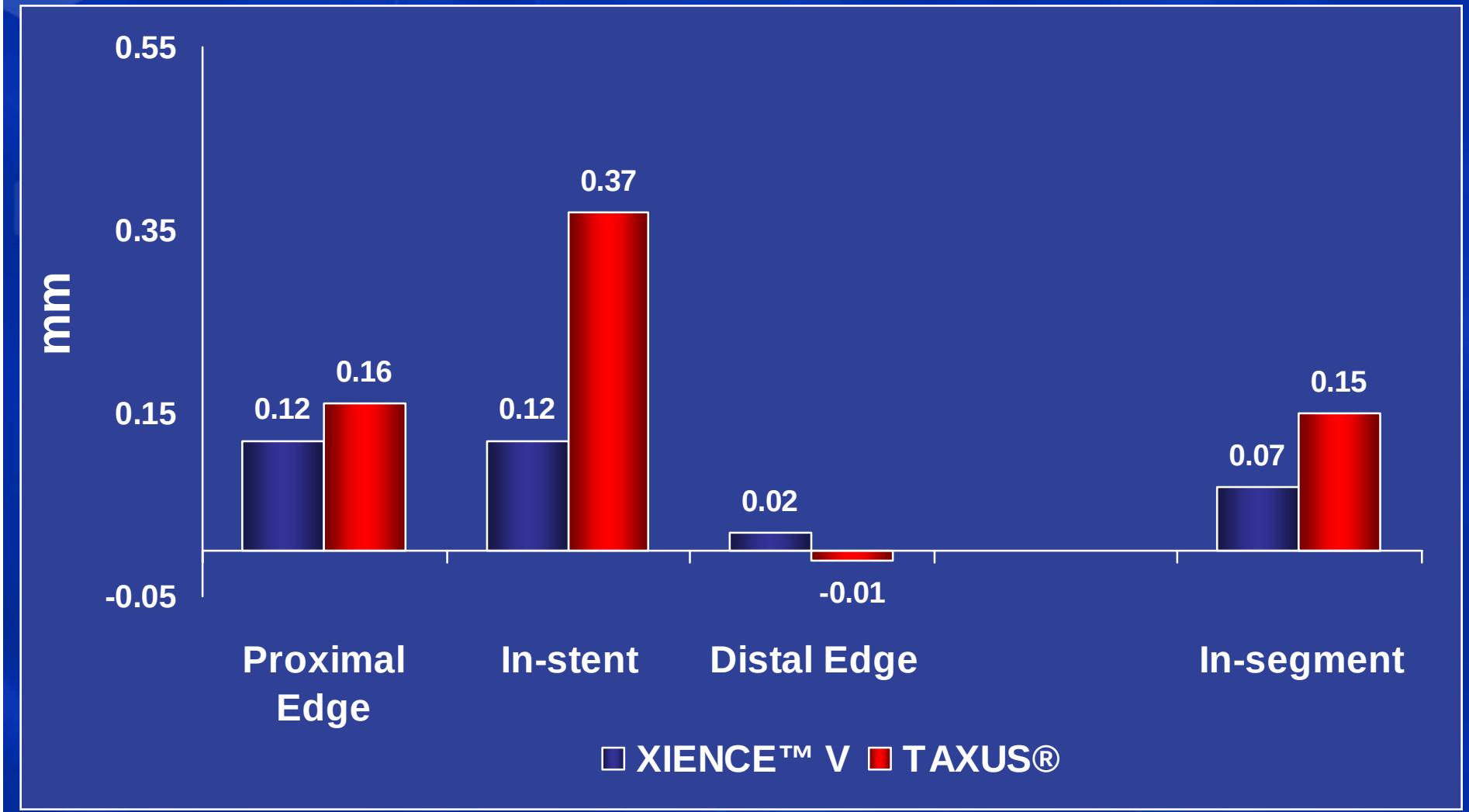
- SPIRIT FIRST met its primary endpoint of in-stent late loss
- Strong 6 month results were sustained to 12 months
- XIENCE V shows promise
  - Late Loss of 0.24 & 0.14 mm (in-stent & in segment)
  - One device-related MACE event (TLR)
  - No acute or late stent thrombosis
  - No late malapposition

Spirit II International



- PI: Dr Patrick Serruys
- RCT: Prospective, single blind
- Primary end point: in-stent late loss at 6 months
- Stent Size: 2.5 – 4.0 mm; Stent lengths: 8, 18, 28 mm
- Angiographic and IVUS follow-up at 6 months for all patients, and at 2 years for subset of 152 patients at selected sites
- Clinical follow-up at 1, 6, 9 months, 1 and 2 years
- 6 months clopidogrel for all arms

Late Loss (mm) –All Lesions



Source: P. Serruys, M.D., WCC 2006

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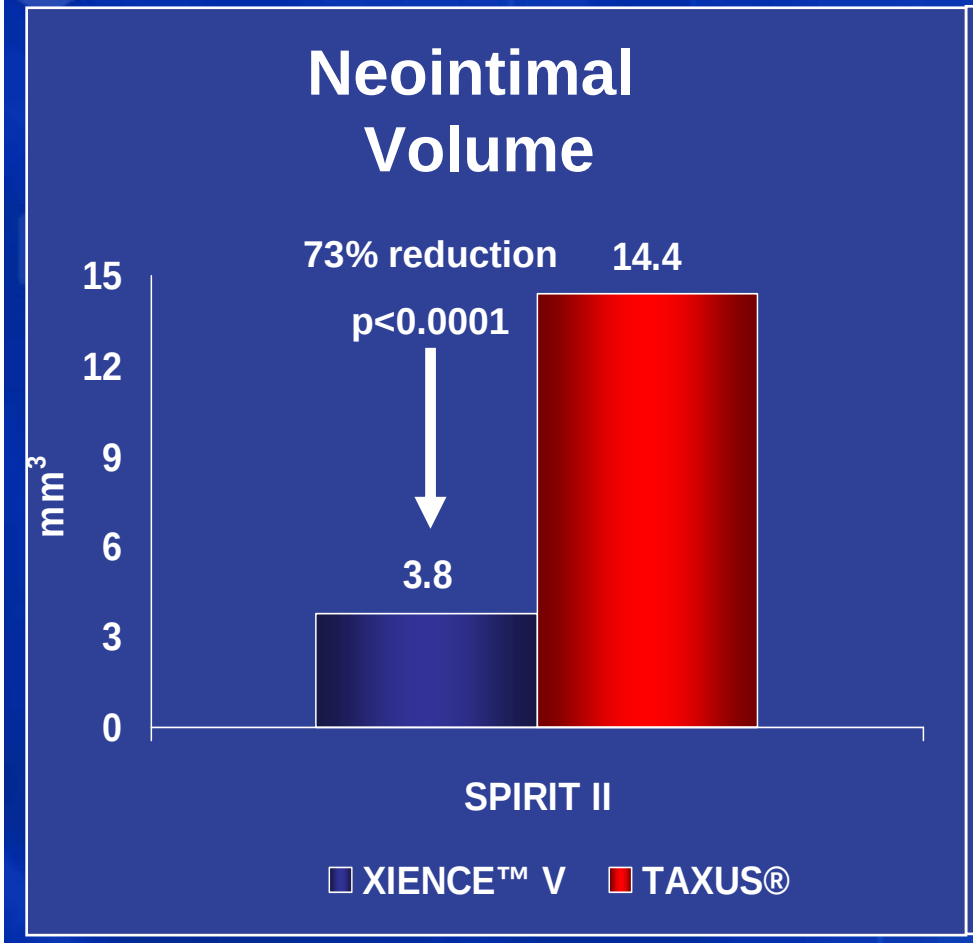
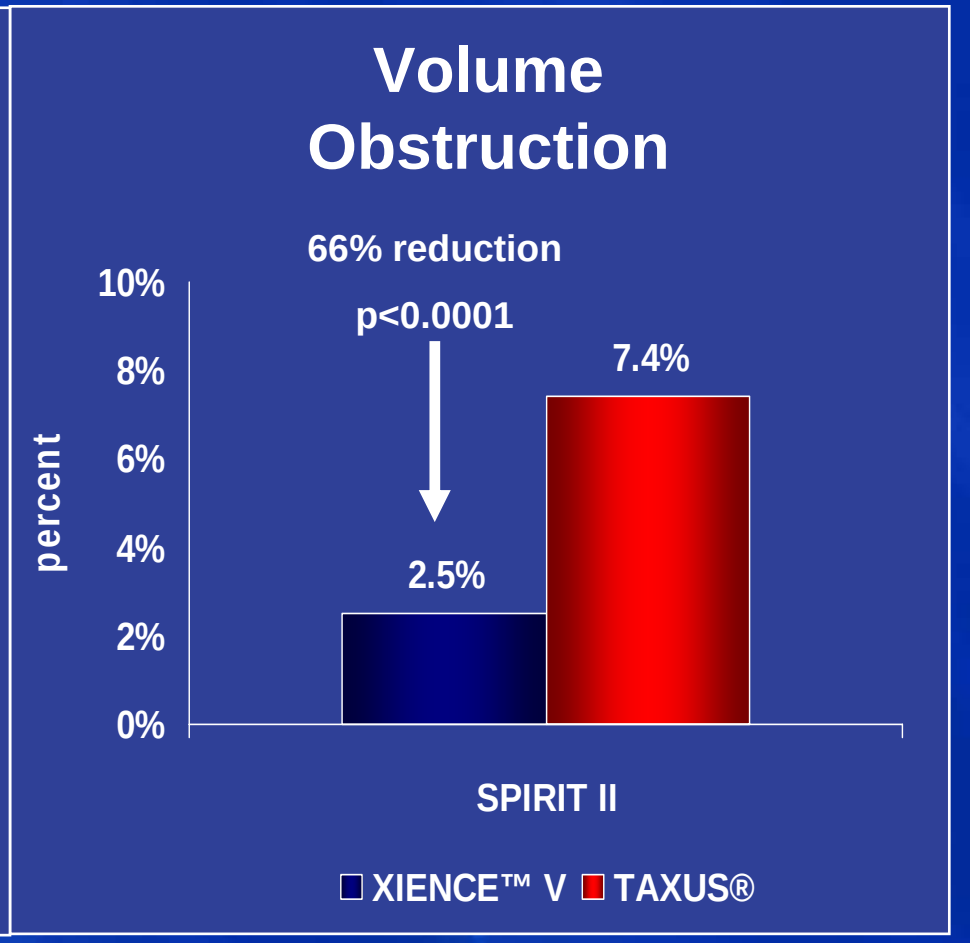
SPIRIT II In-Stent IVUS Results





NOTE: 124 Patients; 140 lesions

Source: P. Serruys, M.D., WCC 2006

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SPIRIT II Conclusions

- SPIRIT II met its Primary Endpoint :
  - XIENCE V was non-inferior to TAXUS® (in-stent late loss 0.11 mm vs 0.36 mm; p<0.0001)
  - XIENCE V proved superior to TAXUS® (in-stent late loss 0.11 mm vs. 0.36 mm; p<0.0001)
- XIENCE V had a statistically significant reduction in volume obstruction and neointimal volume when compared to TAXUS®
- XIENCE V 6M MACE and Stent Thrombosis rates were 2.7% 0.5%, respectively
- SPIRIT II clinical, angiographic and IVUS results confirm the results of SPIRIT FIRST
- US Pivotal Trial Results are pending