



Stents coronários. Plataformas, liga. Novos desenhos

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São Paulo, 23 de Julho de 2013

Disclosure Slide

- Clinical Investigator—

CardioMind Stent

GENOUS

ELIXIR

EVOLVE II

DESolve

ABSORB EXTEND

Leaders Free

Global Leaders

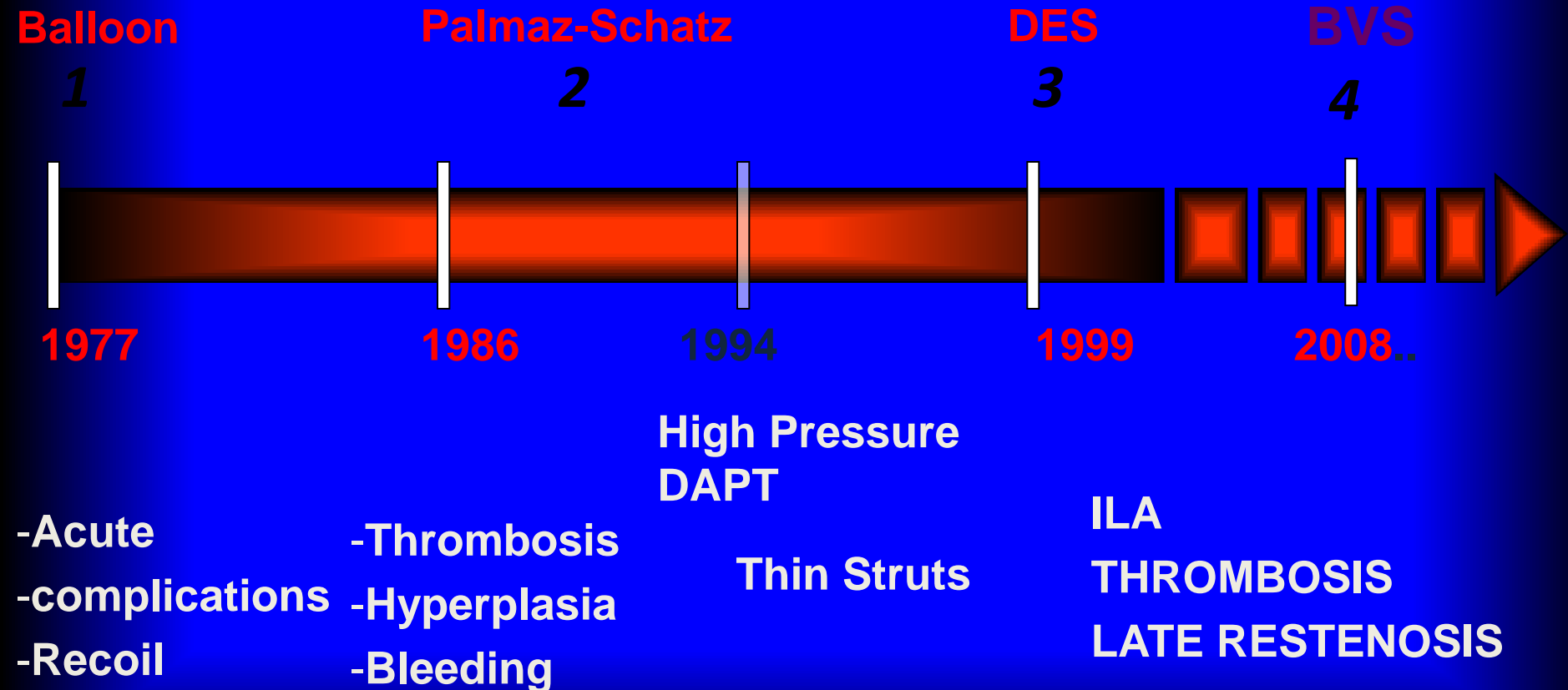


Agenda

- The four evolutions in PCI
- The evolution in metallic stents
- The data about each generation
- The potential benefits of BVS
- Conclusion

PCI

The fourth Evolution



First Generation DES

TAXUS

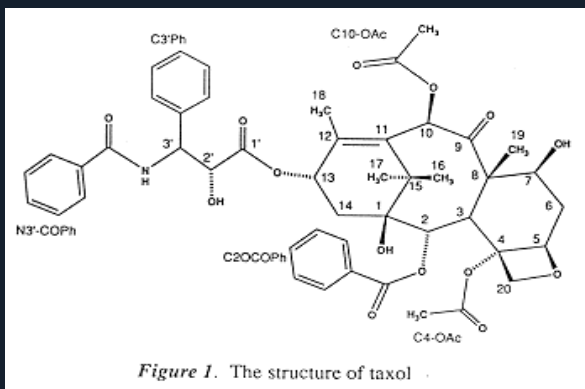
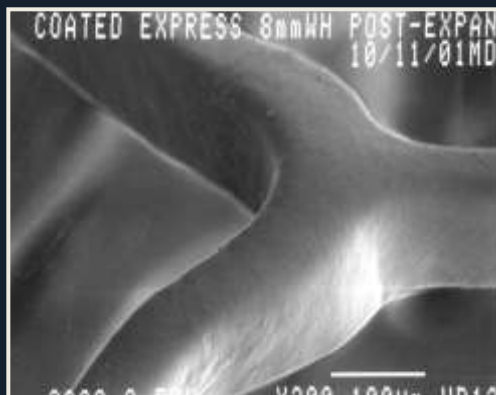


Figure 1. The structure of taxol

Paclitaxel
Drug



Polyolefin derivative
Polymer

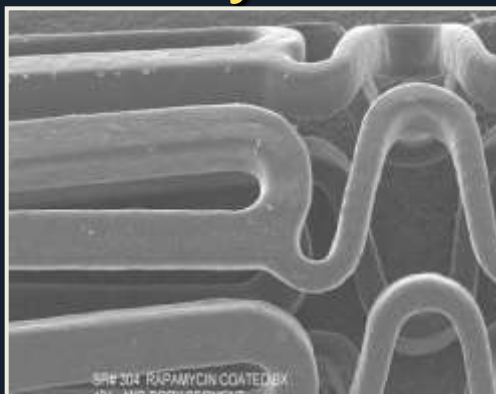


Express²
Stent

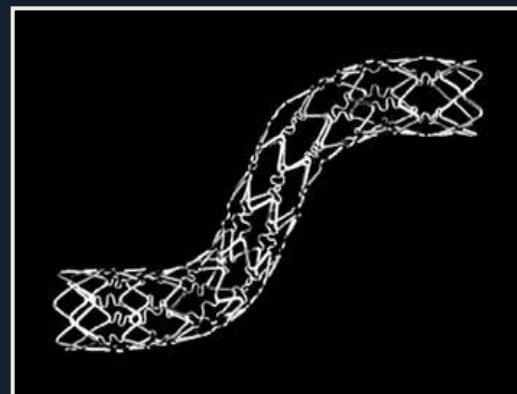
Cypher



Sirolimus

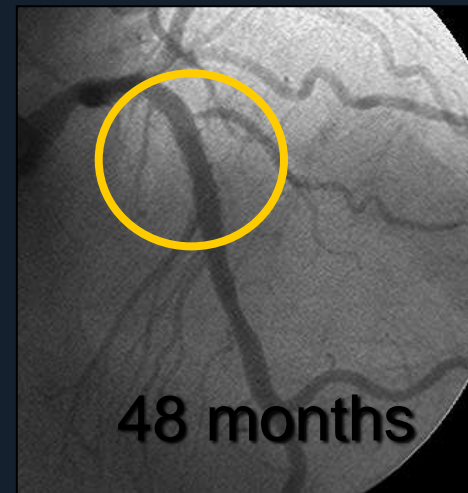
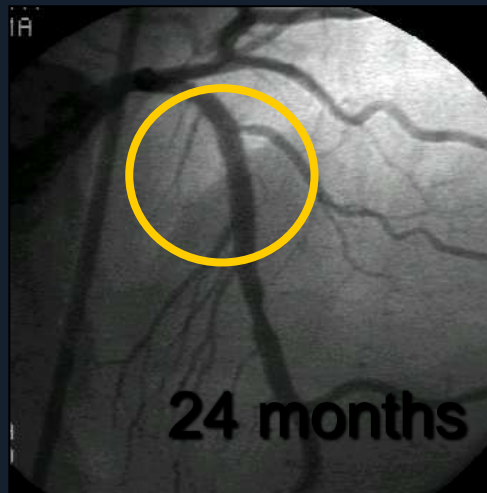
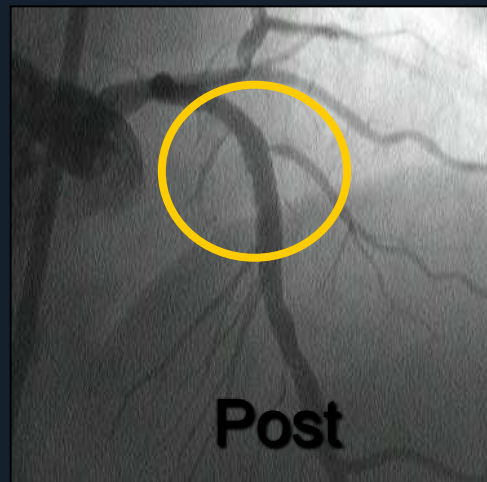
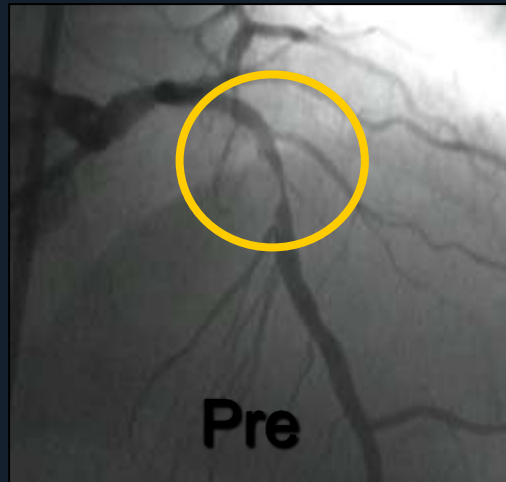


PEVA + PBMA blend



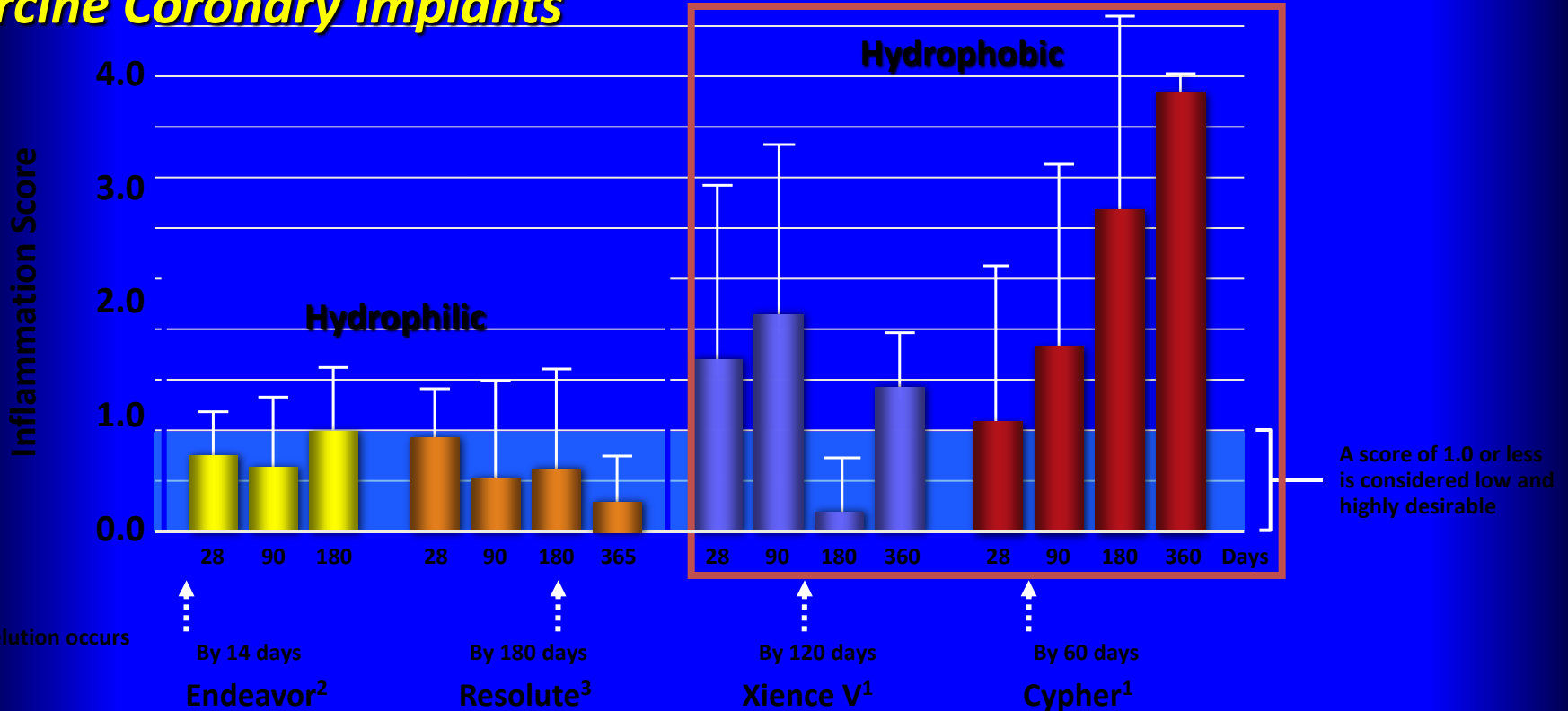
BX Velocity

DES - A Transforming Technology



Inflammation Scores

Porcine Coronary Implants



**Low inflammation scores seen with Endeavor and Resolute ZES
Higher inflammation scores (>1) seen with Xience V and Cypher DES**

1. Data from Abbott Xience V US physicians presentation SE2924433D. Taxus testing was not available.

2. Data on file at Medtronic, Inc. Endeavor testing was not performed at 365 days.

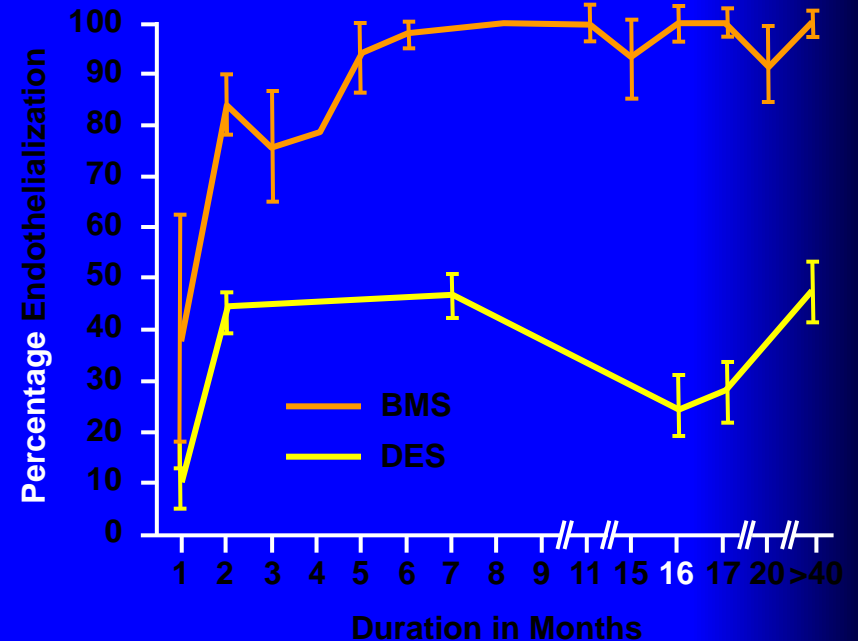
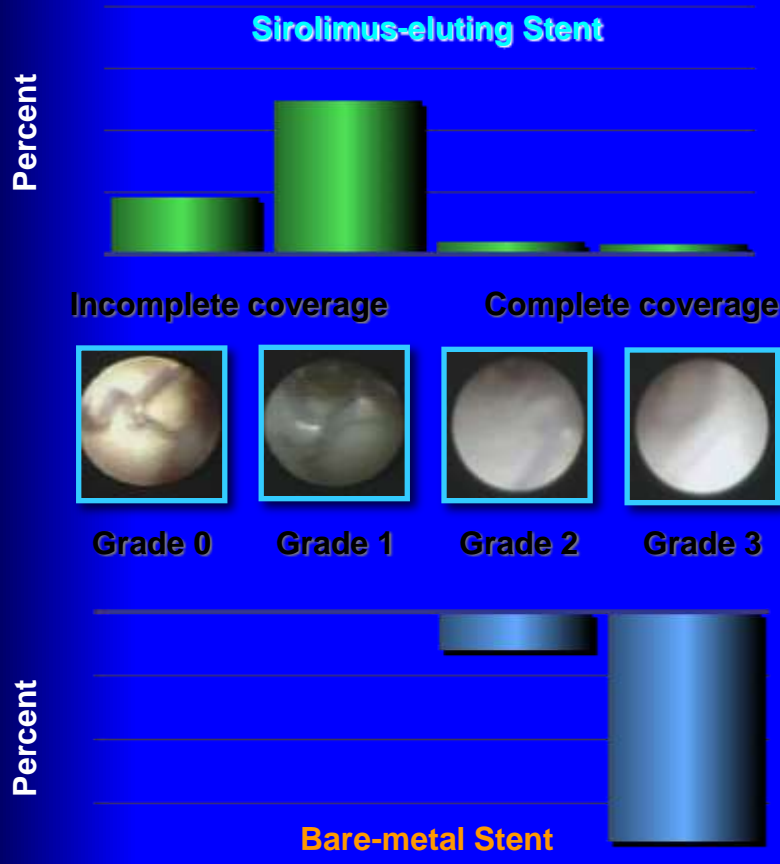
3. Data on file at Medtronic, Inc.

Error bars denote standard deviation. Preclinical results may not be indicative of clinical performance of DES

Incomplete Strut Endothelialization

With DES?

1. Kotani J et al. JACC. 2006;47:2108.
2. Joner M et al. JACC. 2006;48:193.



Angioscopy at 3-6 months post SES implantation¹

Virmani autopsy data²



Longer period of anti-platelet therapy is needed after DES

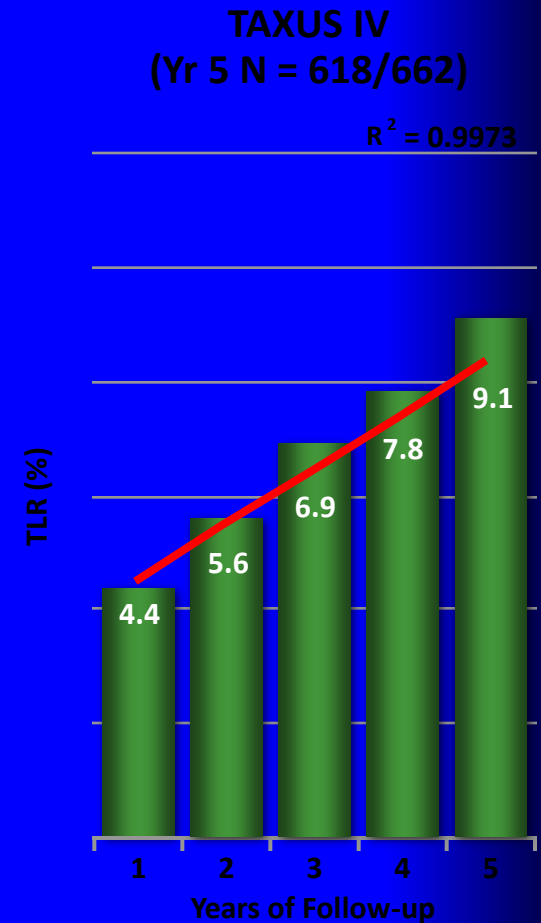
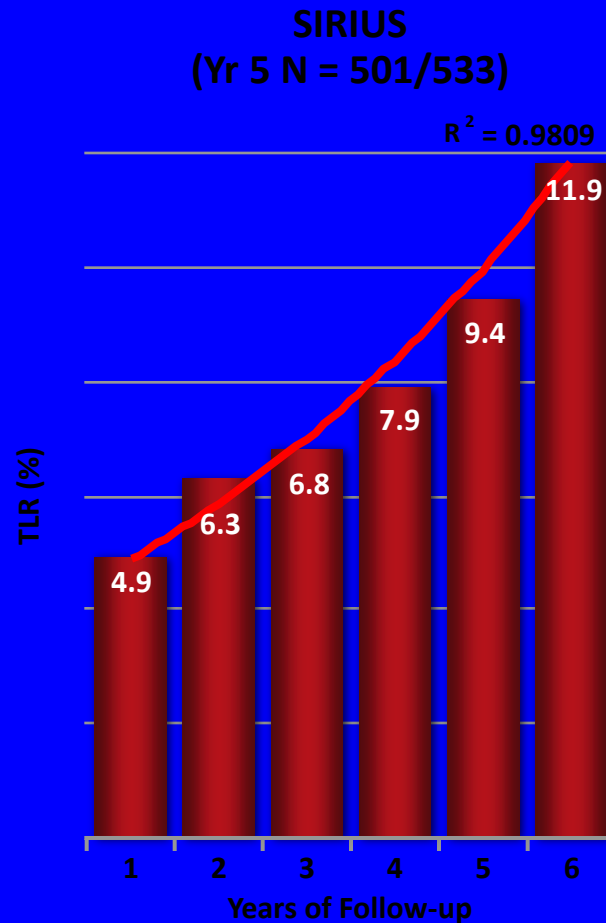
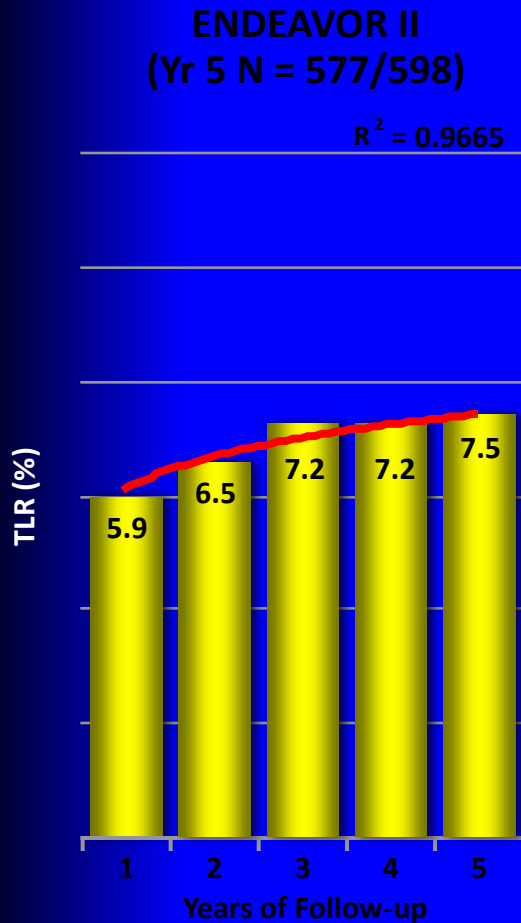
Late and very Late ST

- In patients with complex multivessel disease, the rate of combined definite, probable and possible stent thrombosis was as high as 9.4% at 5 years *Serruys PW J Am Coll Cardiol 2010; 55: 1093 – 1101.*
- Abnormal responses to acetylcholine of the segments distal to the first-generation DES, suggesting that the structure and function of the endo- thelium remained abnormal

Hofma SH Eur Heart J 2006; 27: 166 – 170.

Pivotal Trials TLR: DES Arms

Rates of TLR Over Time



Results come from separate clinical trials. Data may differ in a head-to-head comparison.

*SIRIUS n = 501/533 is at 5 years. 271/533 followed to 6 years. Note, 6 year data unavailable for Endeavor and Taxus.

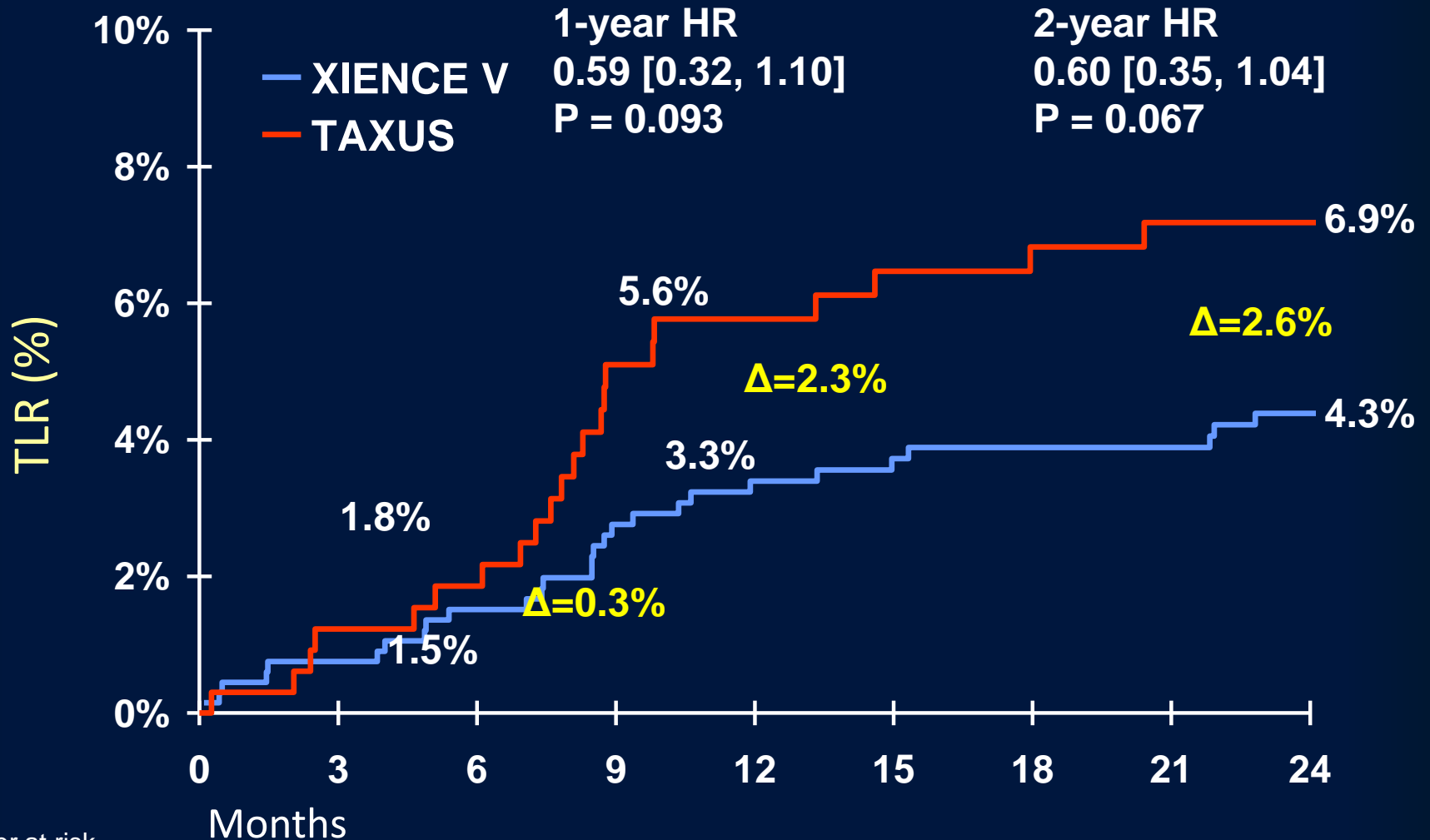
5 year Outcomes in the Sirius Trial, Weisz et al. JACC Vol. 53, No. 17, 2009. 6-Year Outcomes, CRT 2009.

5 Year Clinical Results of TAXUS IV, Stone, ACC 2007

ENDEAVOR II 5 year : Meredith *et al.* PCR. 2009.

R^2 were calculated by Medtronic

SPIRIT III: Ischemia-driven TLR (N=1,002)

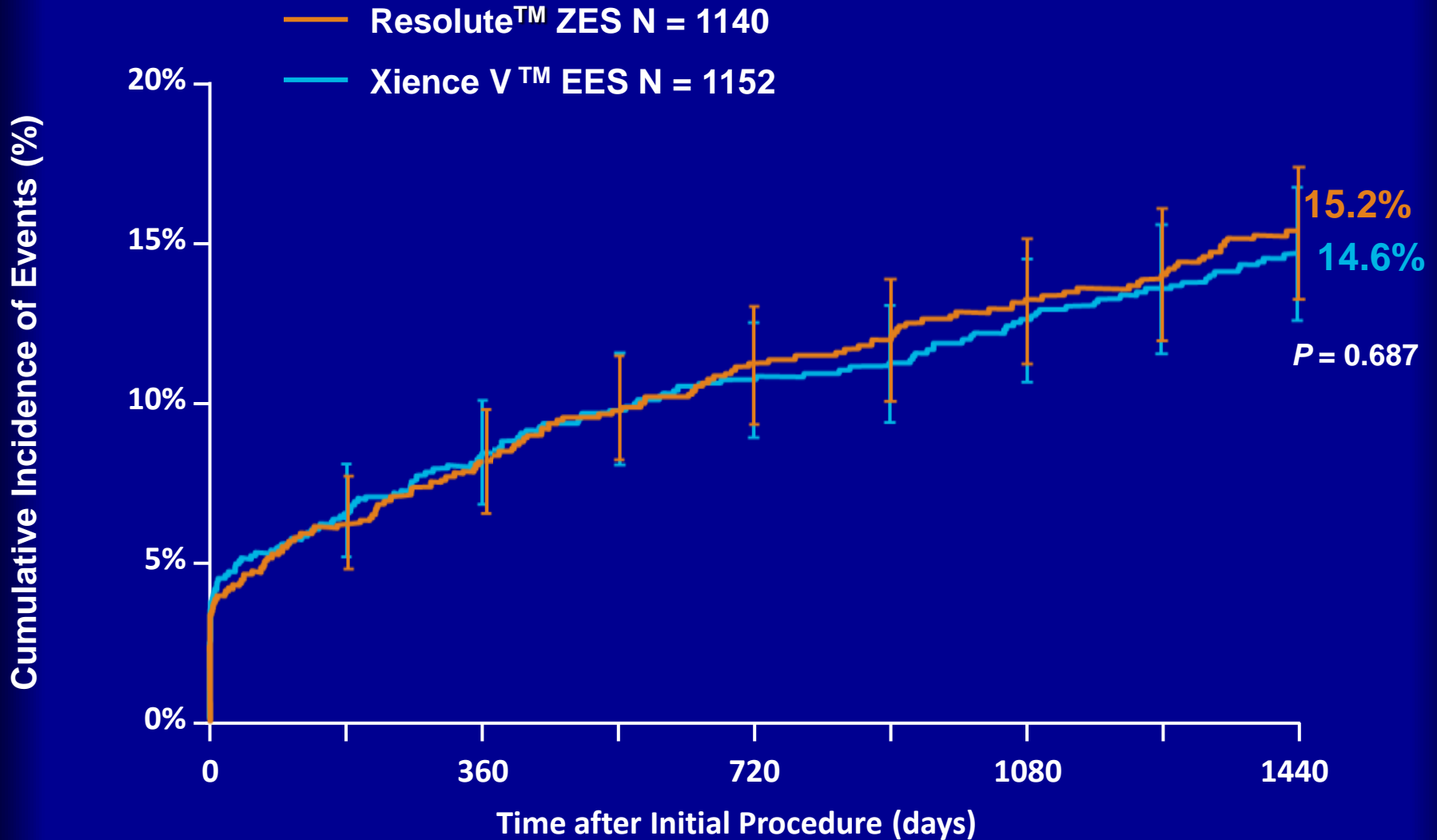


Number at risk

XIENCE V	669	659	650	636	624	610	609	604	599
TAXUS	332	321	317	301	294	284	281	280	278

RESOLUTE All Comers


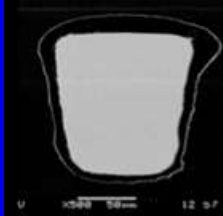
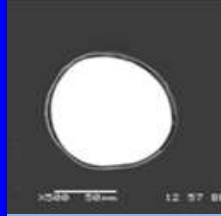

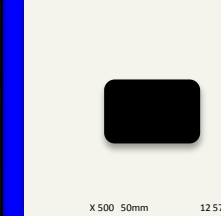
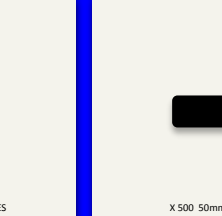
Target Lesion Failure to 4 Years



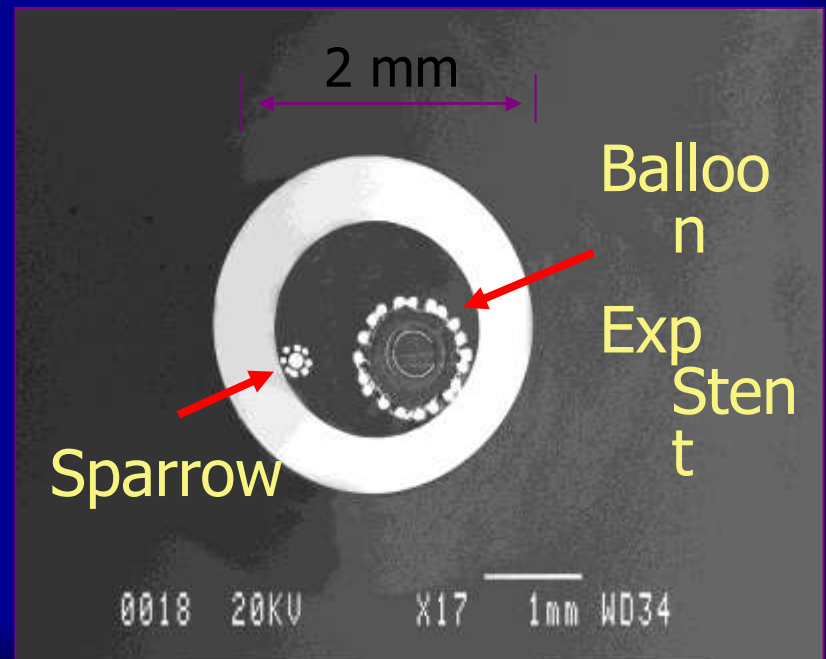
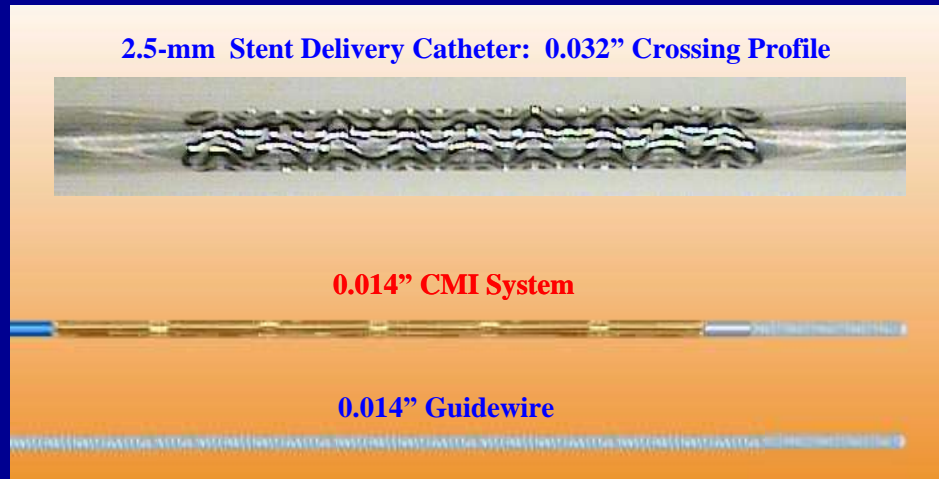
TLF (Target Lesion Failure) is defined as cardiac death, TVMI, or clinically driven TLR.

Moving Towards Nanotech

Low Strut Thickness with Potential to minimize vessel injury

	Cypher	Taxus	Endeavor	Xience V	BioMime	Mitsu
						
Strut thickness	140 μm	132 μm	91 μm	81 μm	65 μm	40 μm
Coating thickness	12.6 μm	16 μm	5.3 μm	7.6 μm	2 μm	< 2 μm
Polymer	PEVA-PBMA	SIBBS	PC	Fluoro	PLLA + PLGA	None
Drug	Sirolimus 1.4 $\mu\text{g}/\text{mm}^2$	Paclitaxel 1.0 $\mu\text{g}/\text{mm}^2$	Zotarolimus 10.0 $\mu\text{g}/\text{mm}^2$	Everolimus 1.0 $\mu\text{g}/\text{mm}^2$	Sirolimus 1.25 $\mu\text{g}/\text{mm}^2$	Merilimus 0.45 $\mu\text{g}/\text{mm}^2$
	1 st Gen	1 st Gen	2 nd Gen	2 nd Gen	3 rd Gen	4 th Gen

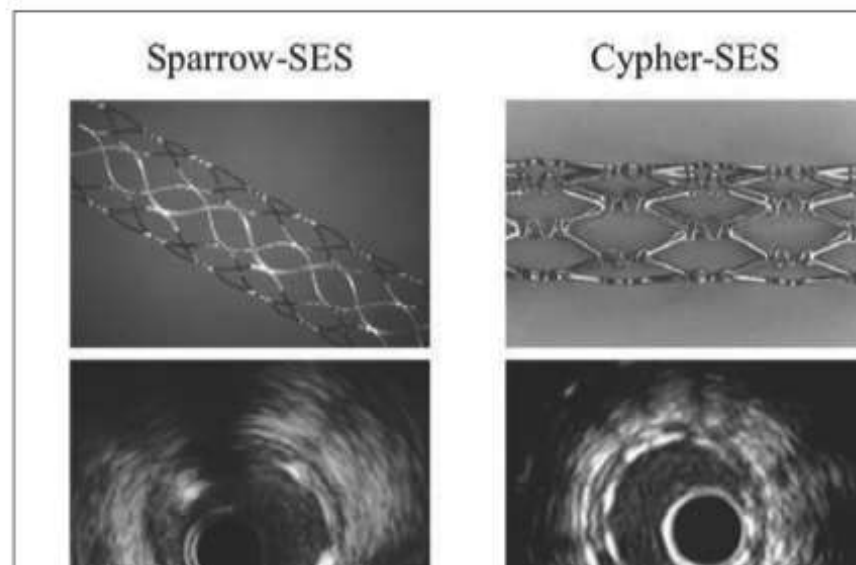
CardioMind® Sparrow® Stent Delivery System: “Stent-in-a-Wire” .014” Guidewire Design



Intravascular Ultrasound Comparison of Small Coronary Lesions Between Novel Guidewire-Based Sirolimus-Eluting Stents and Conventional Sirolimus-Eluting Stents

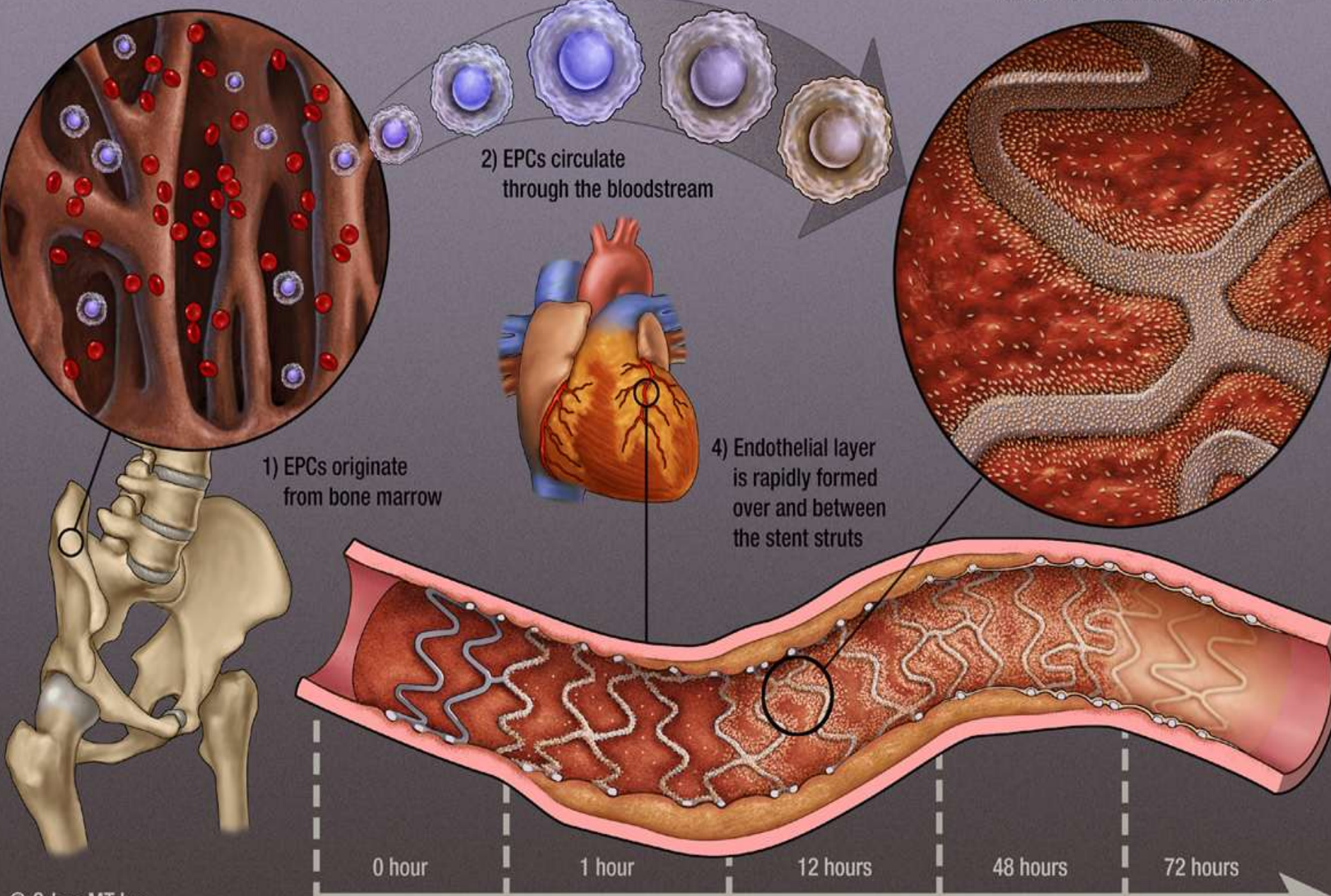
Teruyoshi Kume, MD, PhD¹, Katsuhisa Waseda, MD, PhD¹, Bon-Kwon Koo, MD, PhD¹, Roberto Botelho, MD², Stefan Verheye, MD, PhD³, Robert Whitbourn, MD⁴, Ian Meredith, MD, PhD⁵, Stephen Worthley, MD, PhD⁶, Koh Tian Hai, MD⁷, Paul G. Yock, MD¹, Alexandre Abizaid, MD, PhD⁸, Peter J. Fitzgerald, MD, PhD¹, Yasuhiro Honda, MD¹

ABSTRACT: Background. The Sparrow stent system (Biosensors International) consists of a self-expanding, ultra-thin nitinol stent mounted within a 0.014" guidewire designed for small or tortuous coronary lesions. We compared the intravascular ultrasound (IVUS) findings between the novel self-expanding sirolimus-eluting stent (Sparrow-SES) and a conventional balloon-expandable sirolimus-eluting stent (Cypher-SES) in patients with small coronary disease. **Methods.** We examined 14 lesions treated with the Sparrow-SES from CARE II, compared with 22 small vessel lesions treated with Cypher-SES. IVUS examination was performed post-procedure and 8 months later. Volumetric data were standardized by length as volume index (VI; mm³/mm). **Results.** While baseline stent VI trended smaller in Sparrow-SES, follow-up stent VI became similar between the 2 groups due to a significant increase of stent VI in self-expanding Sparrow-SES



GENOUS: the Role of Endothelial Progenitor Cells (EPCs)

3) EPCs are captured by antibodies immobilized on the stent surface



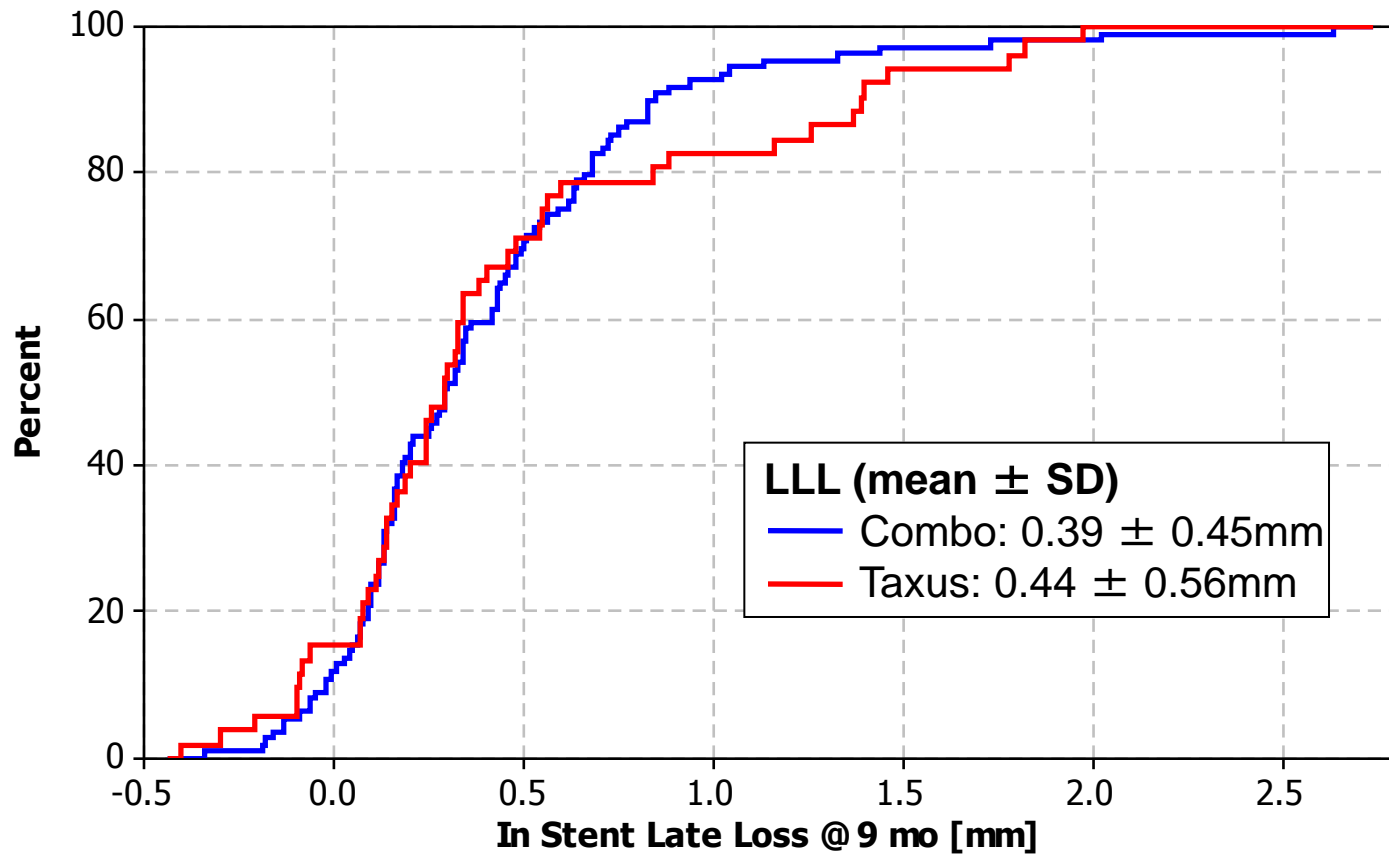
The REMEDEE Trial

A Randomized Comparison of a Combination Sirolimus-Eluting Endothelial Progenitor Cell Capture Stent With a Paclitaxel-Eluting Stent

Michael Haude, MD, PhD,* Stephen W. L. Lee, MD,†
Stephen G. Worthley, MBBS, PhD,‡ Sigmund Silber, MD, PhD,§
Stefan Verheye, MD, PhD,|| Sandra Erbs, MD,¶ Mohd Ali Rosli, MD,#
Roberto Botelho, MD, PhD,** Ian Meredith, MBBS, PhD,†† Kui Hian Sim, MBBS,‡‡
Pieter R. Stella, MD, PhD,§§ Huay-Cheem Tan, MBBS, ||| Robert Whitbourn, MBBS,¶¶
Sukumaran Thambar, MBBS,## Alexandre Abizaid, MD, PhD,*** Tian Hai Koh, MBBS,†††
Peter Den Heijer, MD, PhD,‡‡‡ Helen Parise, ScD,§§§ Ecaterina Cristea, MD,§§§
Akiko Maehara, MD,§§§ Roxana Mehran, MD§§§

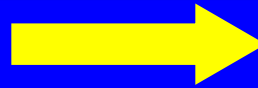
Neuss, Munich, and Leipzig, Germany; Hong Kong, Hong Kong; Adelaide, Melbourne, and Newcastle, Australia; Antwerp, Belgium; Kuala Lumpur and Sarawak, Malaysia; Minas Gerais and São Paulo, Brazil; Utrecht and Breda, the Netherlands; Singapore, Singapore; and New York, New York

In-stent Late Lumen Loss at 9 Months Cumulative Frequency Distribution

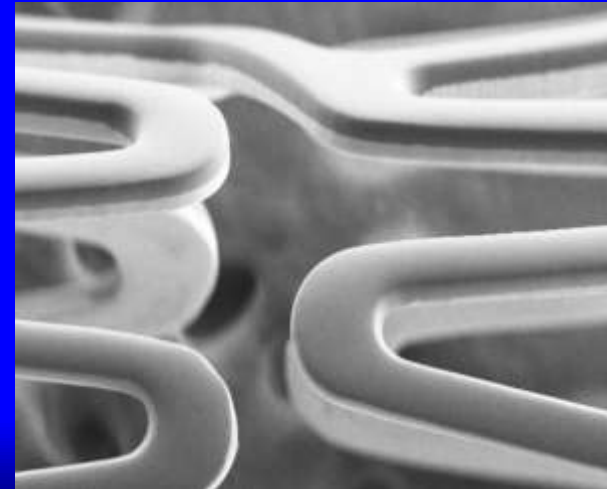
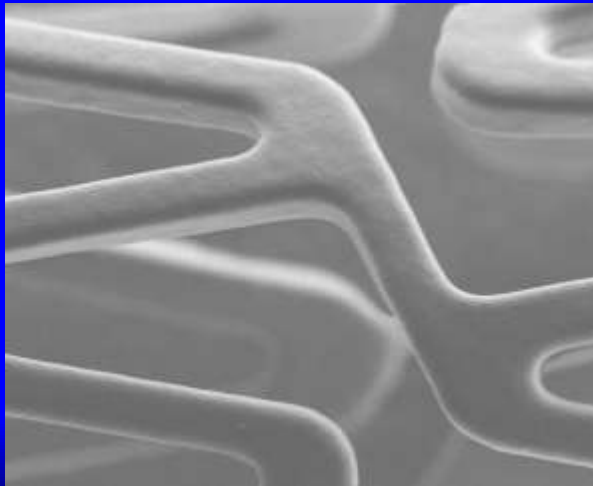
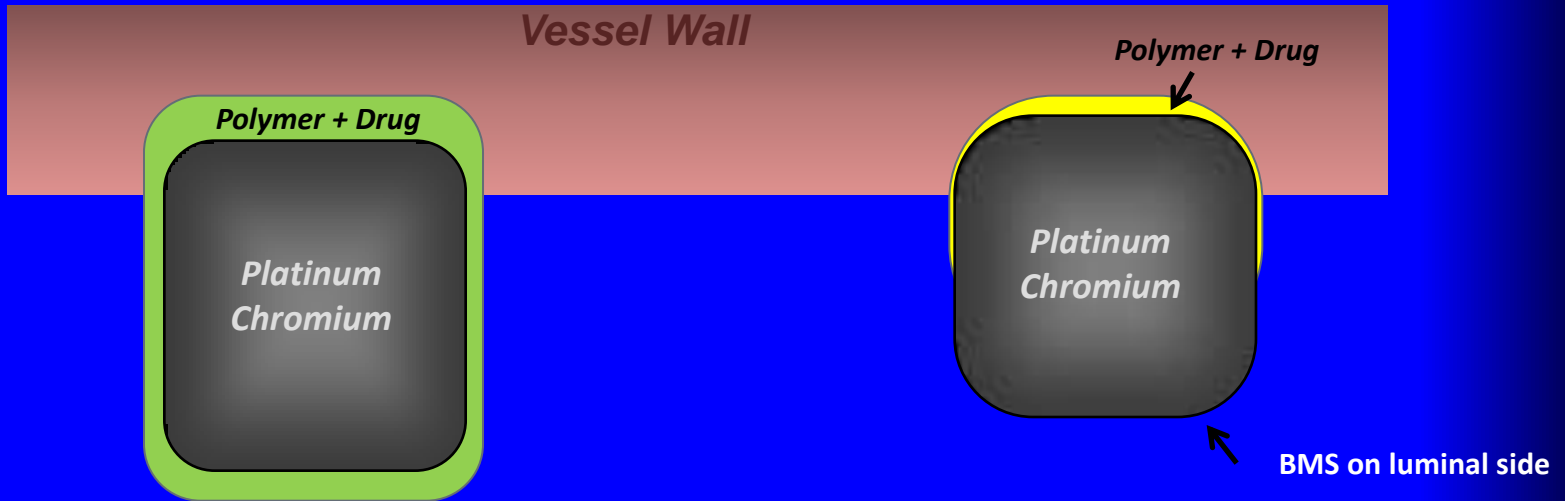


Drug-Eluting Technology Progression

Current DES
Conformal Biostable Polymer



SYNERGY™ DES
Abluminal Bioabsorbable Polymer





Biodegradable Polymer are Better

European Heart Journal

Volume 33, Issue 10, May 2012, Pages 1214-1222

Biodegradable polymer drug-eluting stents reduce the risk of stent thrombosis at 4 years in patients undergoing percutaneous coronary intervention: A pooled analysis of individual patient data from the ISAR-TEST 3, ISAR-TEST 4, and LEADERS randomized trials

Stefanini, G.G.^a, Byrne, R.A.^b, Serruys, P.W.^c, De Waha, A.^b, Meier, B.^a, Massberg, S.^b, Jni, P.^d, Schömig, A.^b, Windecker, S.^{ac}, Kastrati, A.^b  

^a Department of Cardiology, Bern University Hospital, Bern, Switzerland

^b Deutsches Herzzentrum, Technische Universität, Lazarettstraße 36, 80636 Munich, Germany

^c Thoraxcenter, Erasmus University, Rotterdam, Netherlands

^d Clinical Trials Unit, Bern University Hospital, Bern, Switzerland

4062 Randomized Patients

4 Years FU

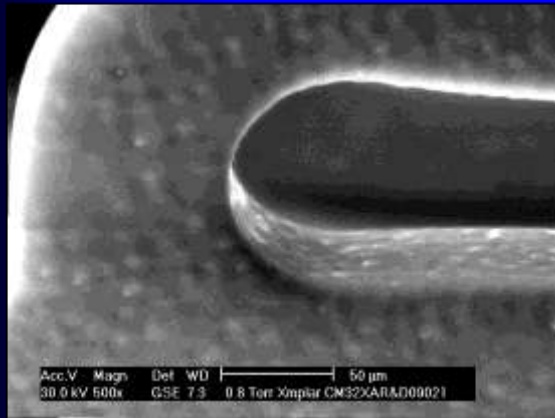
- TVR (HR 0,82, 95% CI 0,680 -0,98 P=0,029)
- ST (HR 0,56, 95% CI 0,35-0,90 P=0,015)
- VLST (HR 0,22, 95% CI 0,80- 0,61 P= 0,004)
- Land Mark 1- 4 years MI
(HR 0,59, 95% CI 0,73-0,95 P = 0,031)



Nanotech

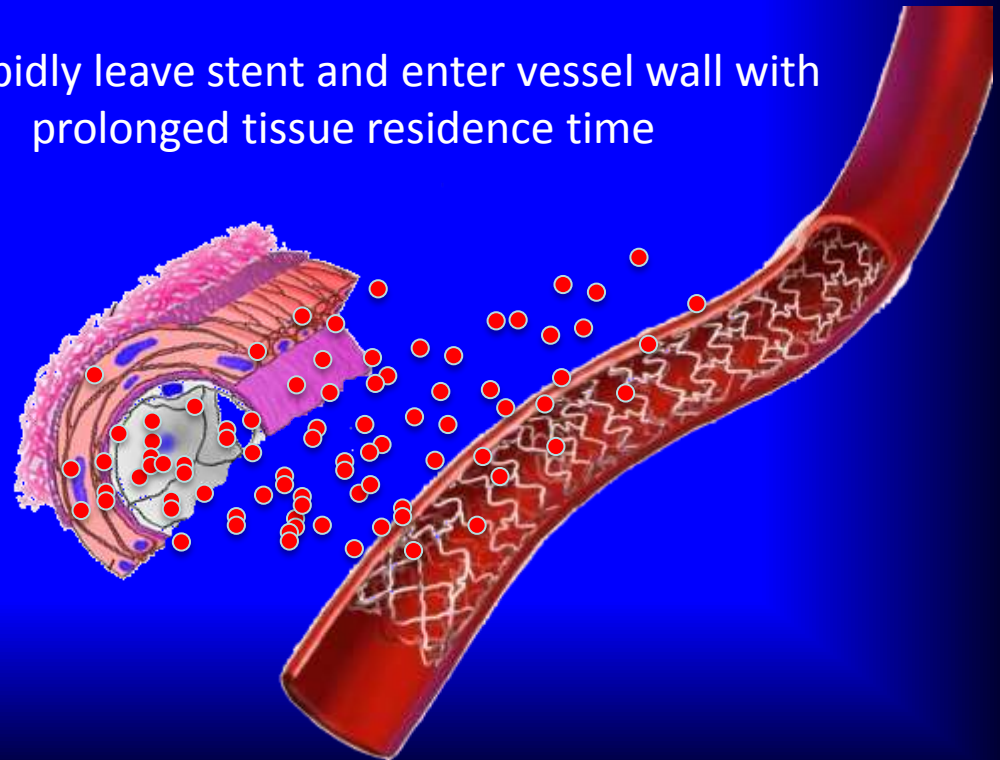
The Polymer-Free Formulation

Unique Formulation - Solid lipid nano-spheres (SLN) consisting of Merilimus + lipid (<300 nm)

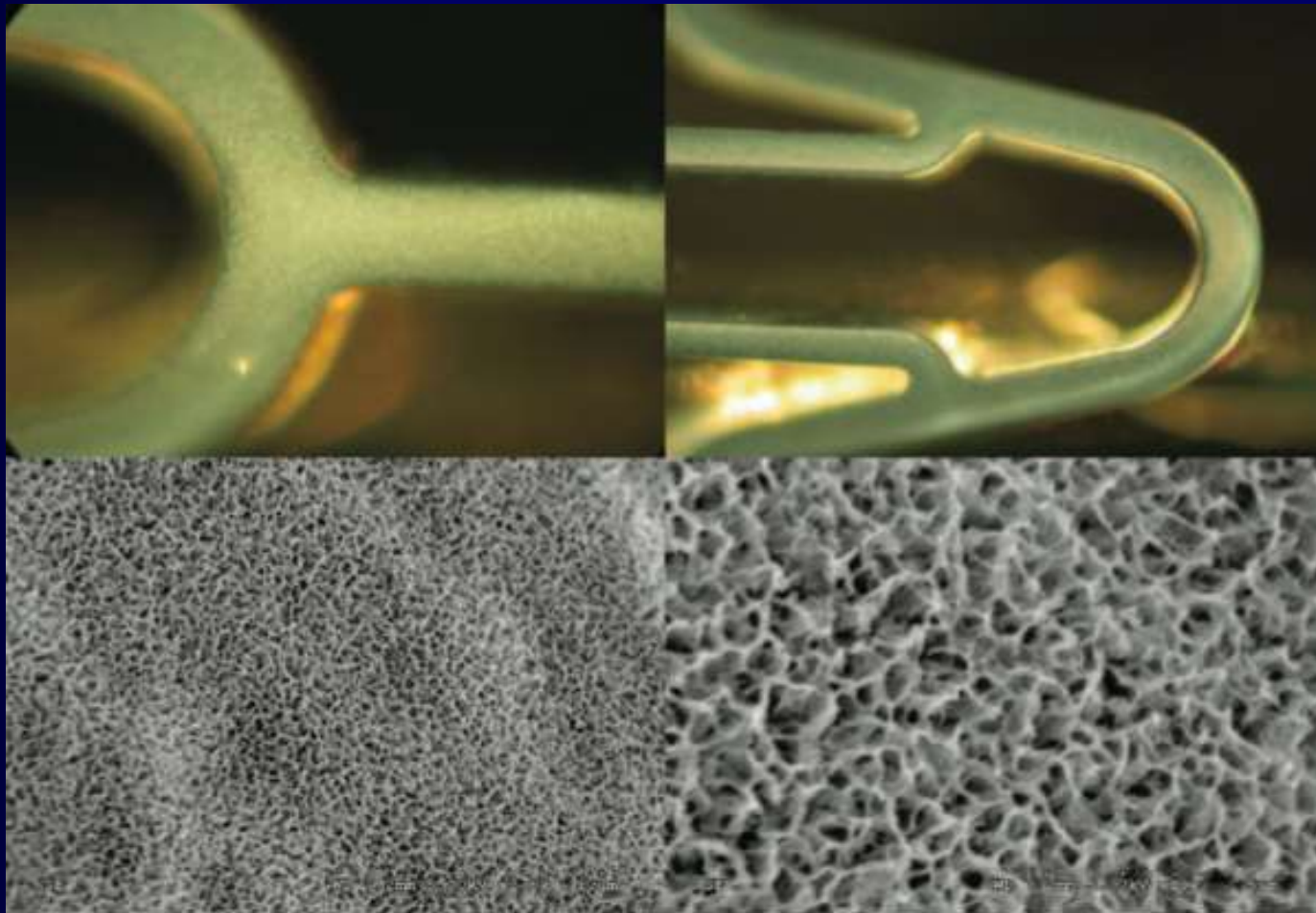


SEM picture of struts coated with nano-formulation

SLN rapidly leave stent and enter vessel wall with prolonged tissue residence time



VESTAsync drug-eluting stent system



Trial record **1 of 39** for: [global leaders](#)

[Previous Study](#) | [Return to List](#) | [Next Study](#) ▶

GLOBAL LEADERS: A Clinical Study Comparing Two Forms of Anti-platelet Therapy After Stent Implantation

This study is currently recruiting participants.

Verified July 2013 by ECRI bv

Sponsor:

ECRI bv

Collaborators:

Biosensors International

AstraZeneca

The Medicines Company

Information provided by (Responsible Party):

ECRI bv

ClinicalTrials.gov Identifier:

NCT01813435

First received: February 12, 2013

Last updated: July 16, 2013

Last verified: July 2013

[History of Changes](#)

[Full Text View](#)

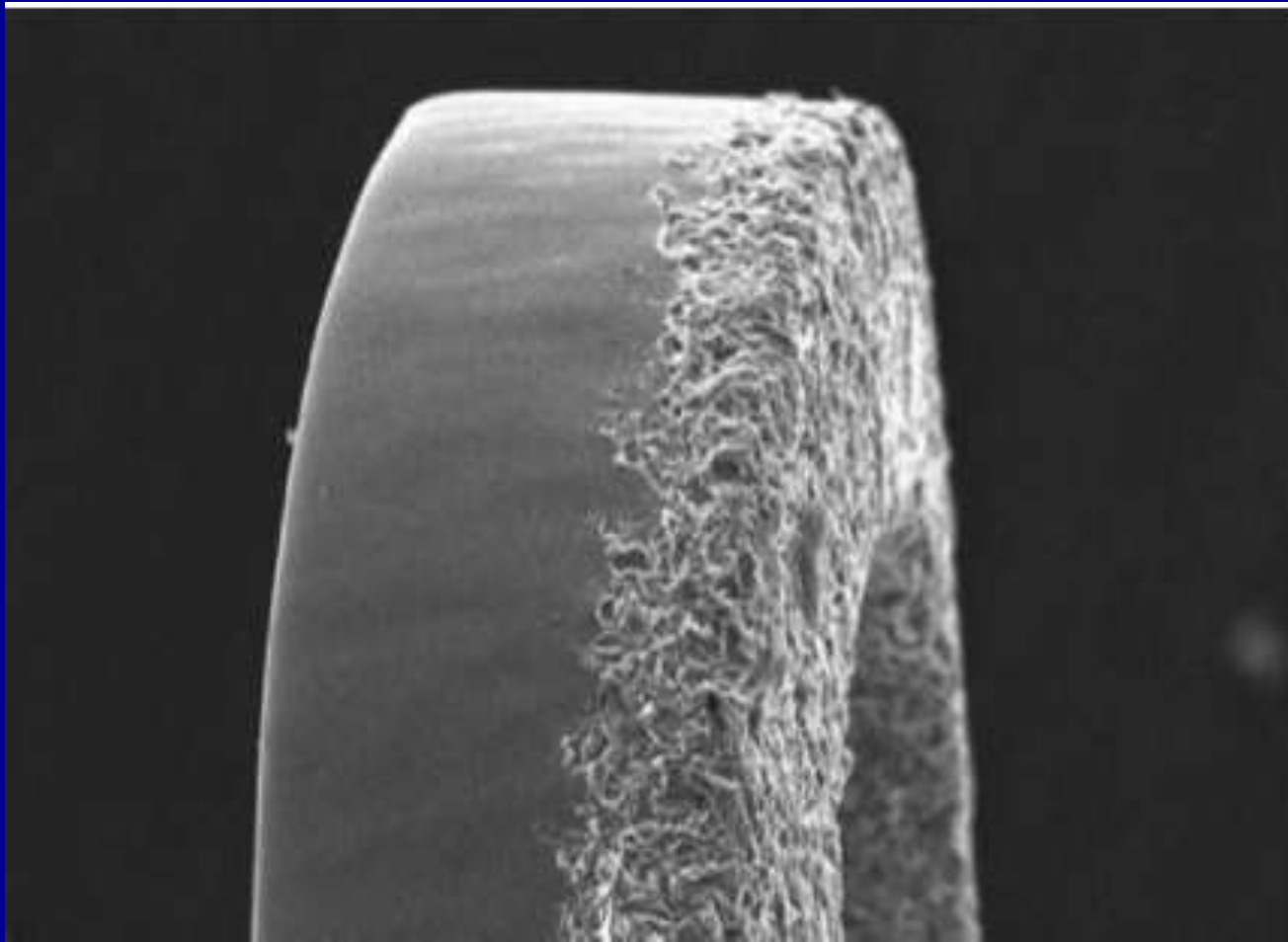
[Tabular View](#)

[No Study Results Posted](#)

[Disclaimer](#)

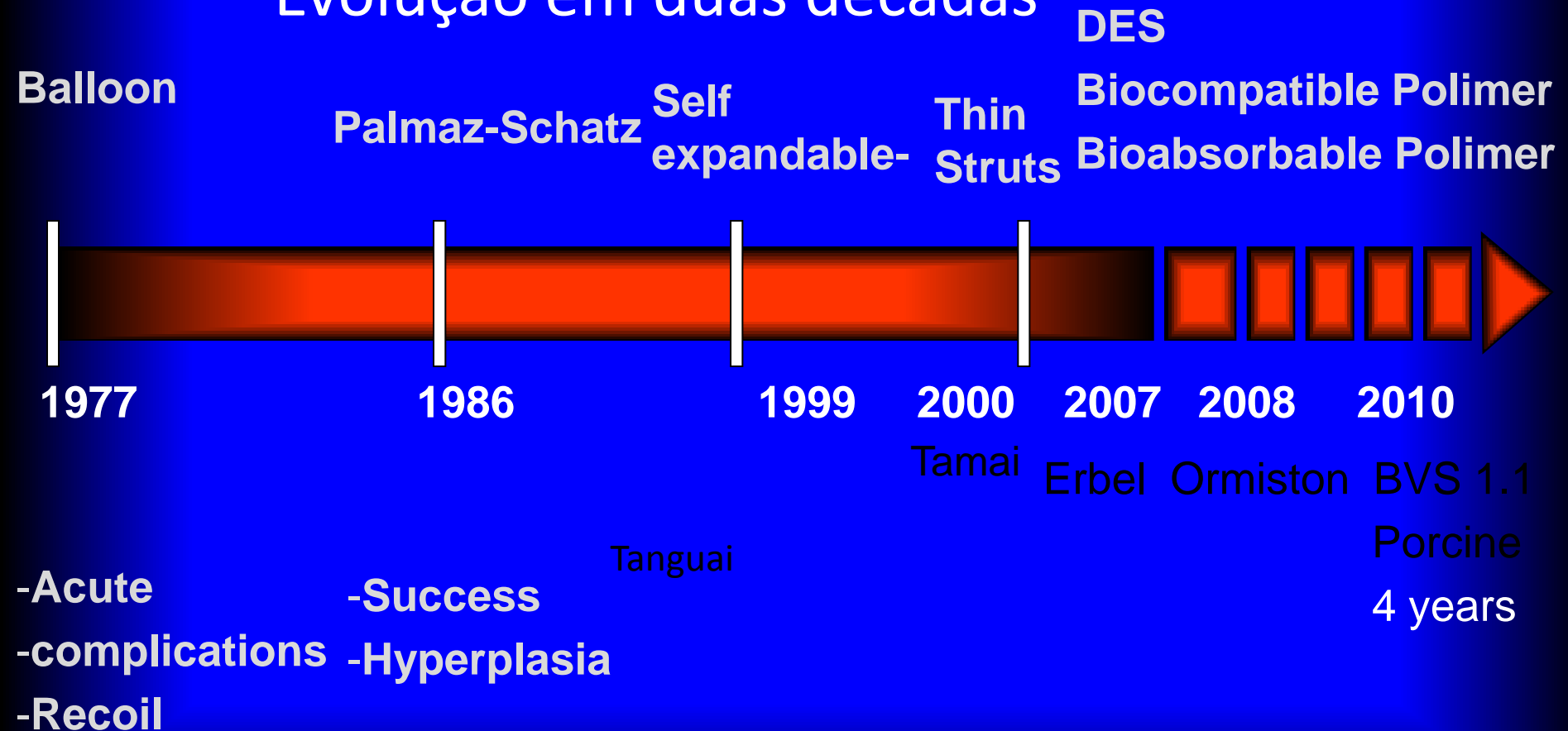
[? How to Read a Study Record](#)

BioFreedom DES system

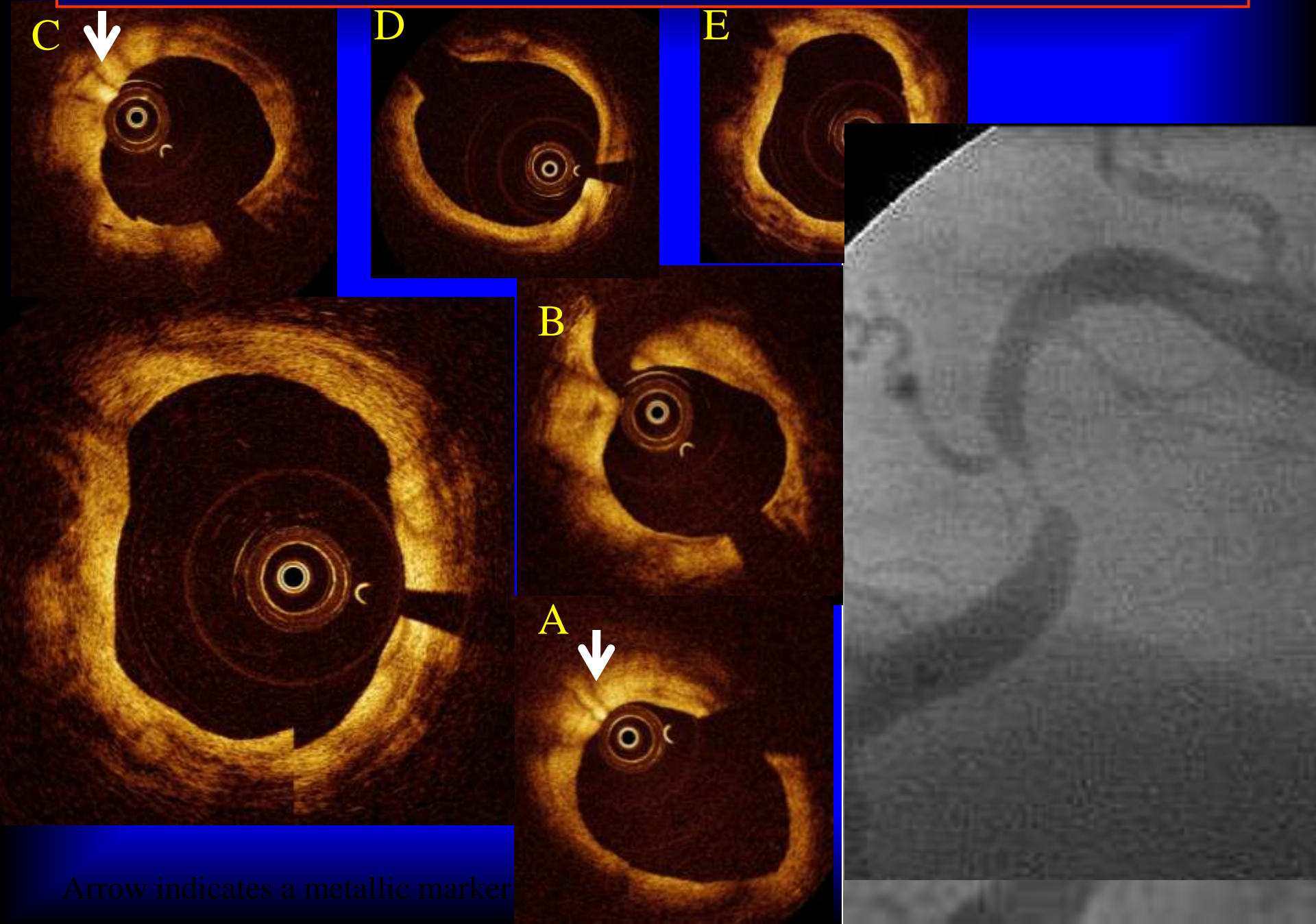


PCI

Evolução em duas décadas



#9 the safety of this technology remains up to 10 years.



Arrow indicates a metallic marker

Bioreabsorbable Stents

Igaki-Tamai



PLA

BVS



PLA

REVA



**Tyrosine-
Policarbonate**

BTI



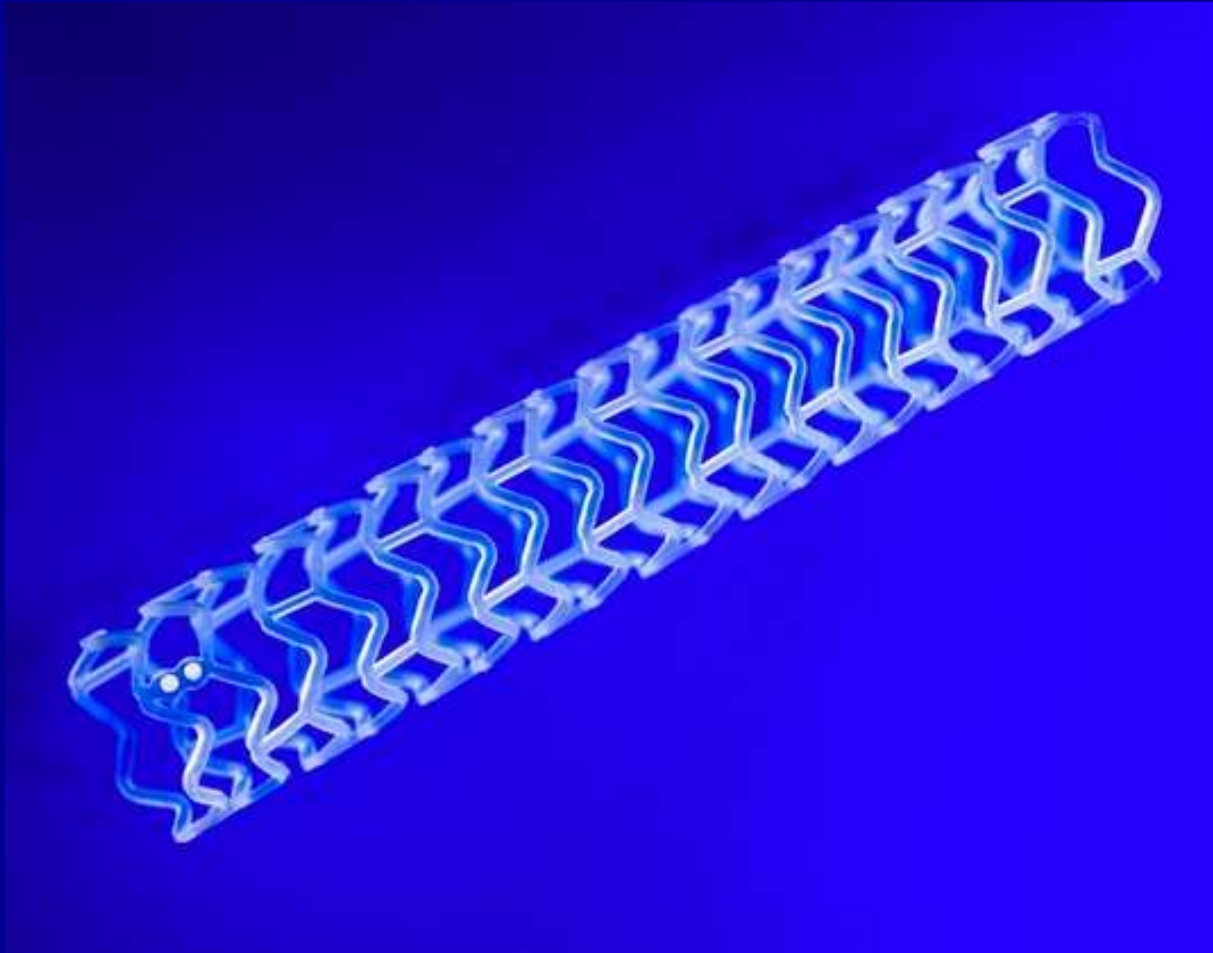
PAE-Salicylate

Biotronik

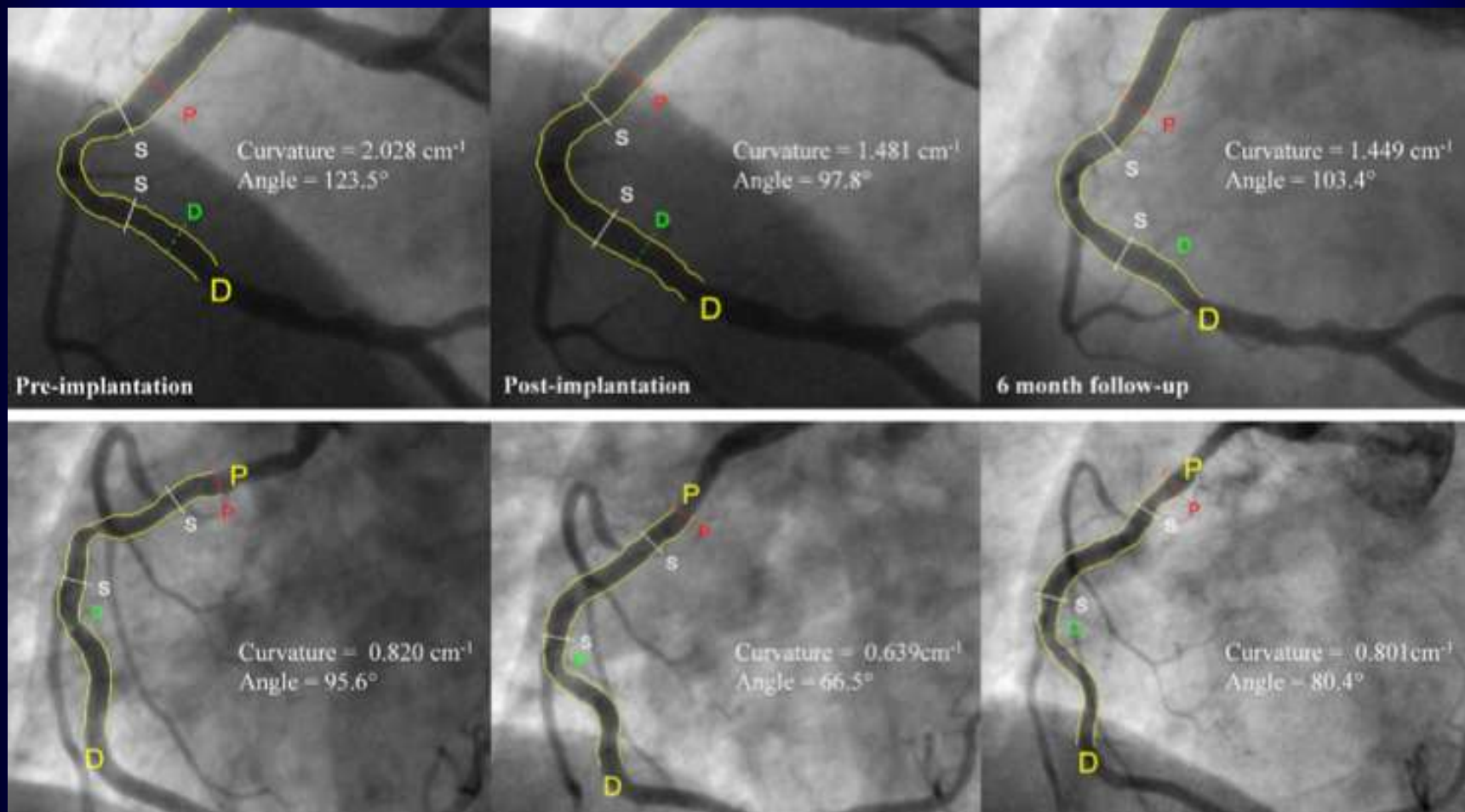


Magnesium

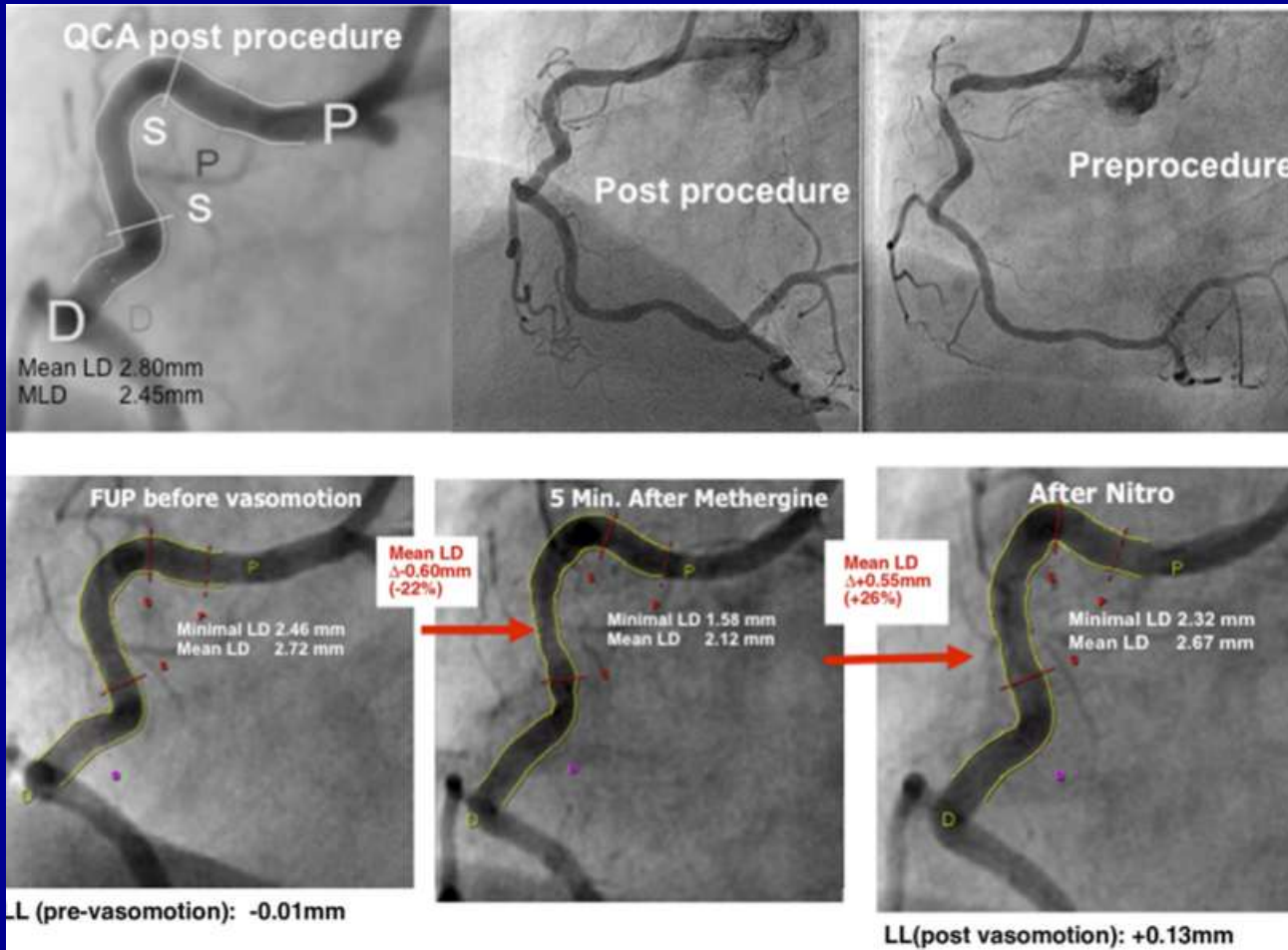
BVS 1.1



Geometric Changes of the Lumen Arterial Wall



Vasomotion



Serruys P J Am Coll Cardiol 2011;58:1578-88

ABSORB Coorte A (Intent-To-Treat Population, ITT)

Hierarquia	6 Meses 30 Pacientes	1 ano 29 Pacientes**	2 anos 29 Pacientes**	5 anos 29 Pacientes**
Fatores isquêmicos				
MACE***	1 (3.3%)*	1 (3.4%)*	1 (3.4%)*	1 (3.4%)*
Morte cardíaca	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
IM	1 (3.3%)*	1 (3.4%)*	1 (3.4%)*	1 (3.4%)*
IM com onda Q	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
IM sem onda Q	1 (3.3%)*	1 (3.4%)*	1 (3.4%)*	1 (3.4%)*
Fator isquêmico TLR	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
por PCI	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
por CABG	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Trombose do stent Def/Prob	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

* Mesmo paciente – esse paciente também apresentou um TLR, não qualificado como ID-TLR (DS = 42%)

** Um paciente retirou o consentimento e perdeu as visitas de 9, 12, 18 meses e 2, 3, 4 anos; dois pacientes morreram de causas não cardíacas, um em 706 dias e outro em 888 dias pós procedimento

*** MACE (Major Advanced Coronary Events) - Composto por morte cardíaca, infarto do miocárdio (IM), revascularização de lesão alvo (TLR) por PCI or CABG (Coronary artery bypass grafting)

ABSORB Coorte B (ITT)

	30 Dias n = 101	6 Meses n = 101	1 ano n = 101	2 anos n = 100*	3 anos n = 100*
Morte Cardíaca (%)	0	0	0	0	0
Infarto do Miocárdio n (%)	2 (2.0)	3 (3.0)	3 (3.0)	3 (3.0)	3 (3.0)
IM com onda Q	0	0	0	0	0
IM sem onda Q	2 (2.0)	3 (3.0)	3 (3.0)	3 (3.0)	3 (3.0)
Fator isquêmico TLR n (%)	0	2 (2.0)	4 (4.0)	6 (6.0)	7 (7.0)
PCI	0	2 (2.0)	4 (4.0)	6 (6.0)	7 (7.0)
CABG	0	0	0	0	0
MACE n (%)	2 (2.0)	5 (5.0)	7 (6.9)	9 (9.0)	10 (10.0)
TLF n (%)	2 (2.0)	5 (5.0)	7 (6.9)	9 (9.0)	10 (10.0)
TVF n (%)	2 (2.0)	5 (5.0)	7 (6.9)	11 (11.0)	13 (13.0)
Trombose de stent Def/Prob n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

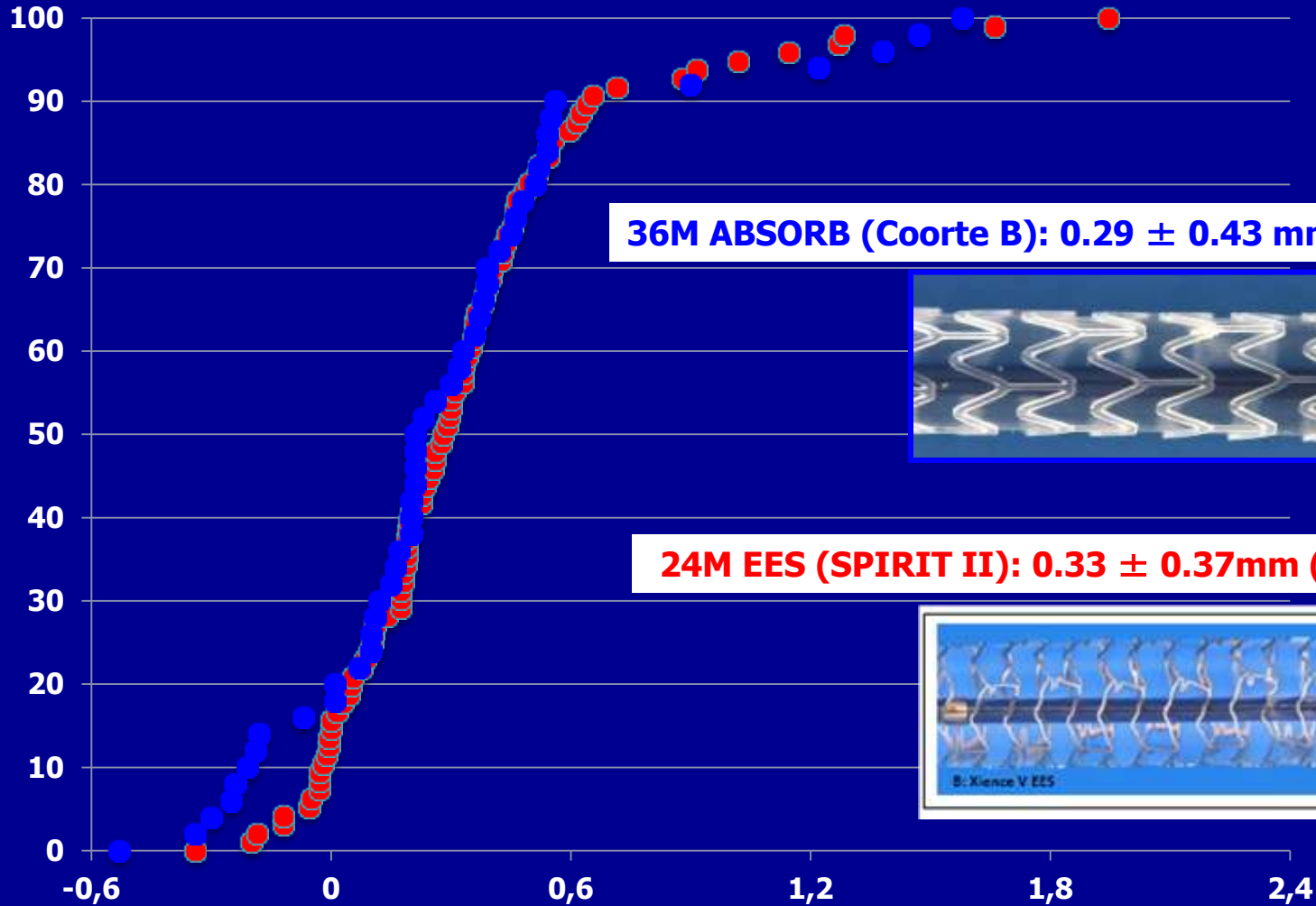
*Um paciente perdeu o acompanhamento

MACE: morte cardíaca, IM, fator isquêmico TLR

TVF (target vessel failure): morte cardíaca, IM, fator isquêmico TLR, fator isquêmico TVR

Dudek, D., ACC 2012. TLF: morte cardíaca, IM em TV, fator isquêmico TLR

Absorb at 3 Y vs. XIENCE V at 2 Y



1 year adjusted propensity score

Resultados clínicos	Absorb (N=503)	XIENCE V (N=635)	P- value*
Infarto do Miocárdio, IM (%)	3.5	2.1	0.16
Ischemic-Driven Target Lesion Revascularization, ID-TLR (%)	1.6	3.1	0.089
MACE (%)	4.7	5.4	0.58
Target Vessel Failure, TVF (%)	4.9	8.5	0.017
Definite/Probable Scaffold/Stent Thrombosis, ST (%)	0.6	0.4	0.65

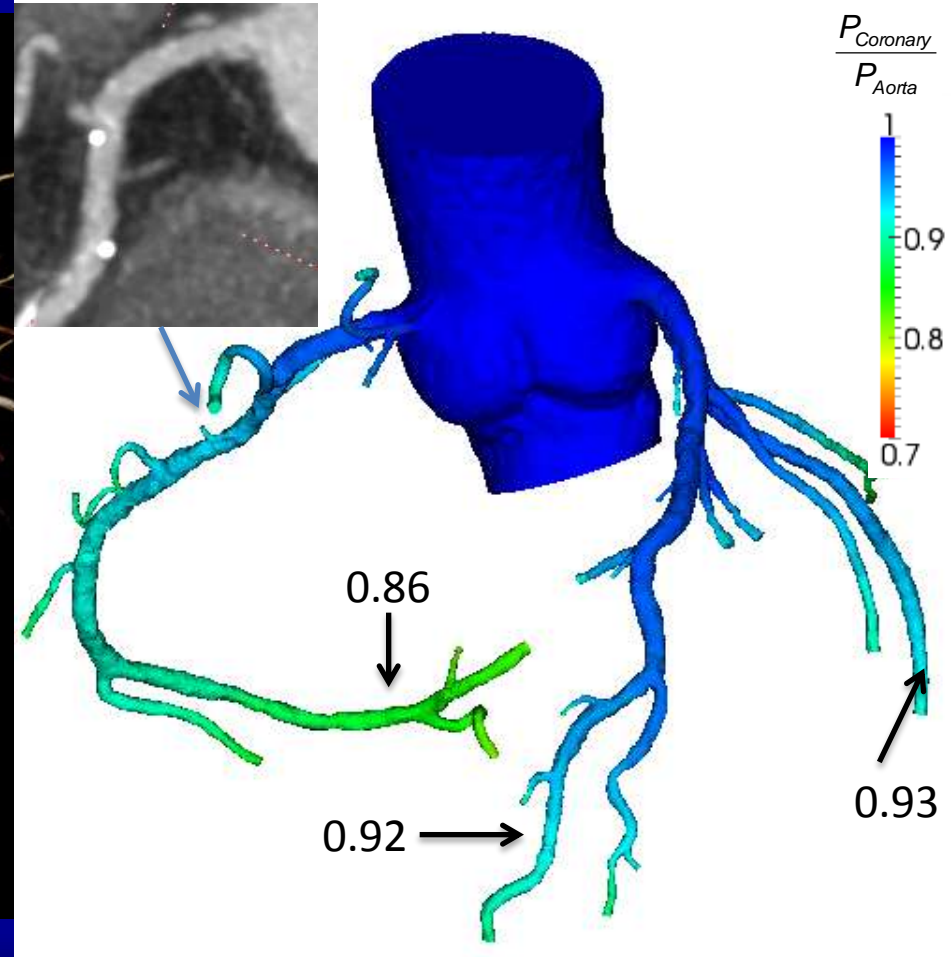
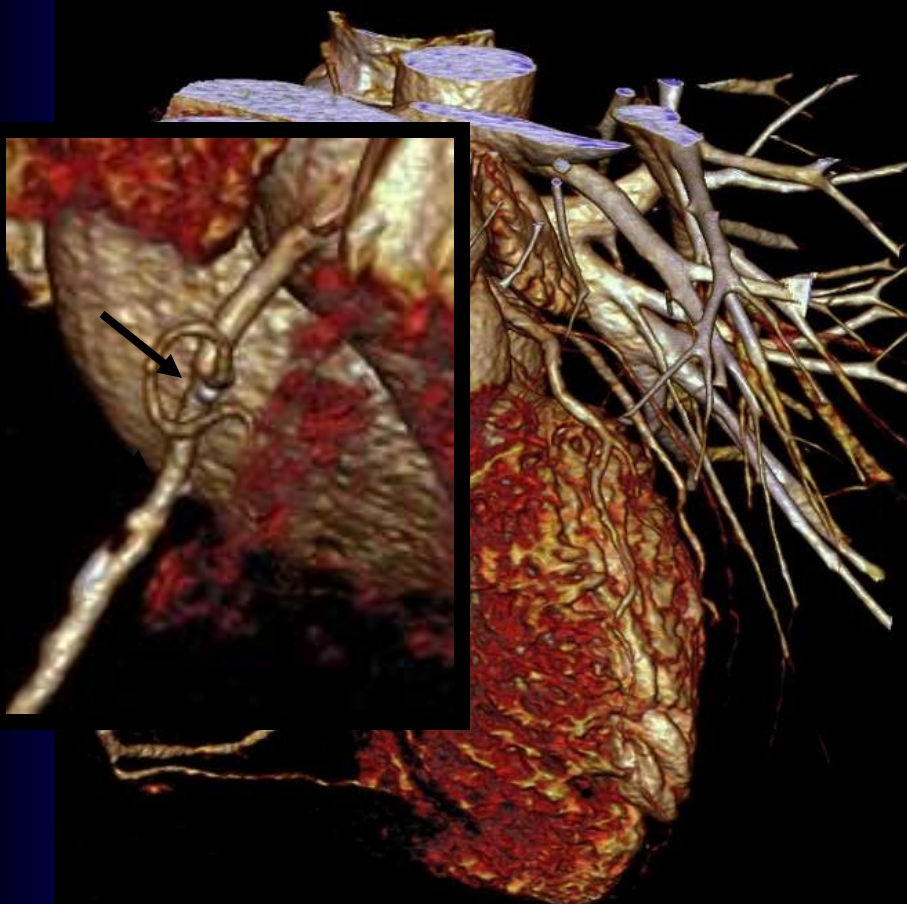
* Valor de P: teste Chi-square ajustado para variáveis dicotômicas.

Absorb BVS Coorte: Pool de ABSORB EXTEND e estudos ABSORB Coorte B

XIENCE V Coorte: Pool de XIENCE V braços dos estudos SPIRIT FIRST, II, and III

Avaliação não invasiva da função e morfometria do vaso

Non Invasive FFR – 5 year FU



Conclusion

- DES significantly reduce repeat PCI
- No impact on Mortality or MI
- Similar ST at any time
- Second generation better than first
- Third generation significantly reduces ST and MI
- BVS may provide further Clinical benefit