22nd CARDIOVASCULAR SUMMIT
TCTAP 2017
April 25-27, 2017
Coex, Seoul, Korea

April 26, 2017
Presentation Theater, Level 1 - 5:36-5:44pm

DES Technology: Plateau or Innovation Still Needed?

Spencer B. King III, M.D., M.A.C.C.

Emeritus Professor of Medicine
Emory University School of Medicine
The Andreas Gruentzig Cardiovascular Center
Editor-in-Chief: JACC Cardiovascular Interventions

NO ROI

DES Technology:

Favors Plateau

1. Acute Results
2. In-stent Restenosis
3. Stent Thrombosis

Lower risk of stent thrombosis and restenosis with unrestricted use of 'new-generation' drug-eluting stents: a report from the nationwide Swedish Coronary Angiography and Angioplasty Registry (SCAAR)

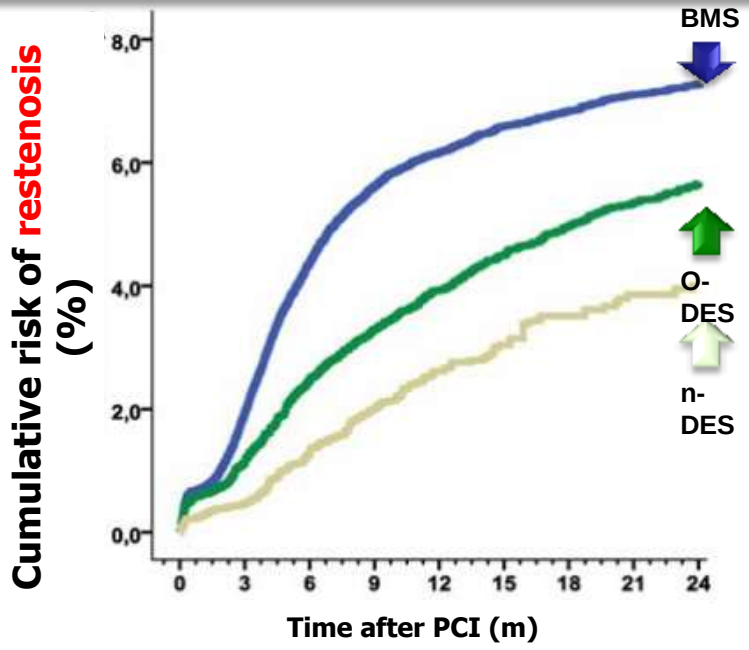
Sarno G. et al. Eur Heart J. 2013;127:e6-e245

EUROPEAN SOCIETY OF CARDIOLOGY

94.384 stent implantations/ BMS: 64.631, o-DES: 19.2012, n-DES: 10.551

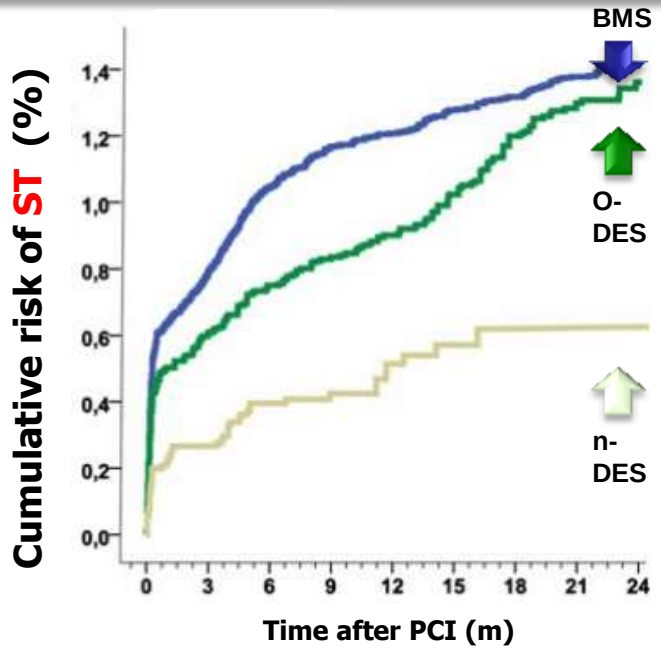
Older generation DES (o-DES):

Cypher and Cypher Select
Taxus Express,Taxus Liberte´ &
Endeavor



Newer generation DES (n-DES):

Endeavor Resolute
Xience V, Xience Prime &
Promus, Promus Element



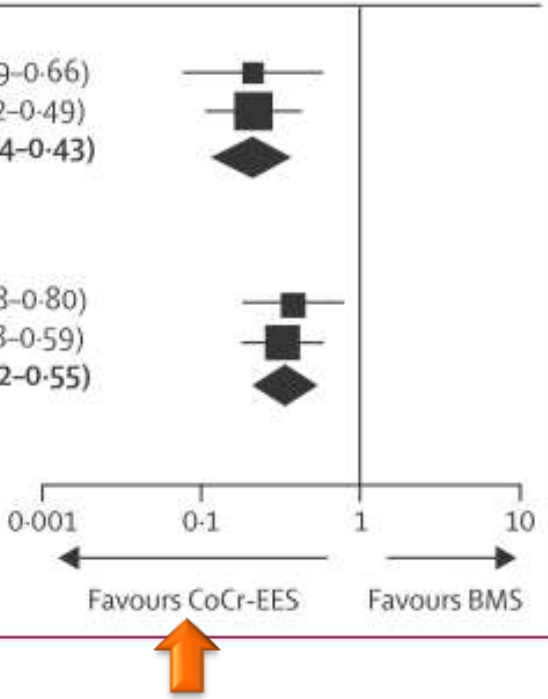
Stent thrombosis with drug-eluting and bare-metal stents: evidence from a comprehensive network meta-analysis

Lancet 2012; 379: 1393–402

Articles

49 RCT with > 50.000 pt.
2nd generation CoCr EES emerged as the device with the lowest rate of ST compared with BMS or other DES

	log (odds ratio)	SE	Weight	Odds ratio IV, random, 95% CI
(A) Definite thrombosis				
Direct estimate	−1·427	0·519	32·4%	0·24 (0·09–0·66)
Indirect estimate	−1·421	0·359	67·6%	0·24 (0·12–0·49)
Total (95% CI)			**100·00%**	**0·24 (0·14–0·43)**
Test for overall effect Z=4·82 (p<0·00001)				
(B) Definite or probable thrombosis				
Direct estimate	−0·968	0·377	39·4%	0·38 (0·18–0·80)
Indirect estimate	−1·122	0·304	60·6%	0·33 (0·18–0·59)
Total (95% CI)			**100·00%**	**0·35 (0·22–0·55)**
Test for overall effect Z=4·48 (p<0·00001)				



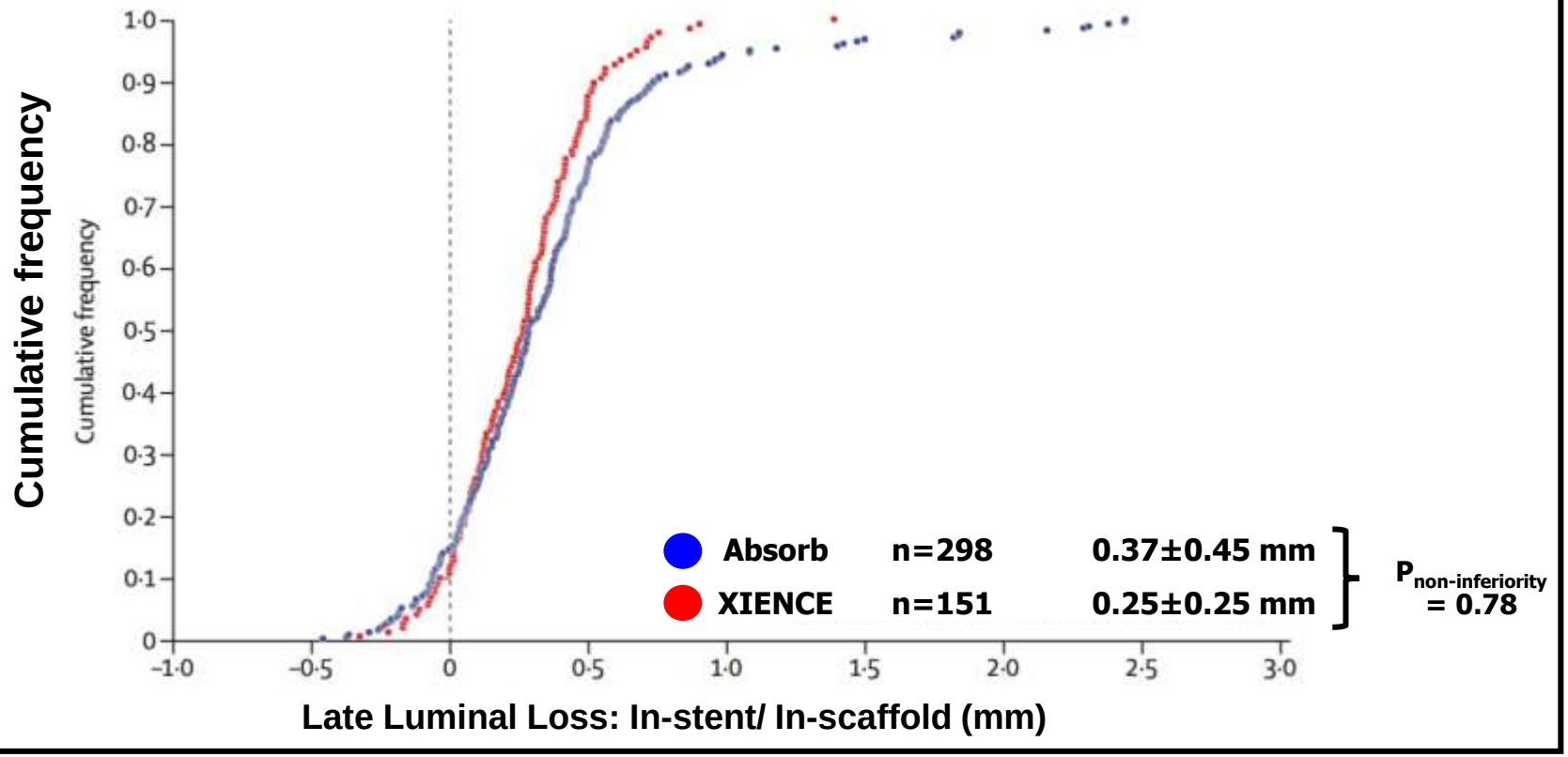
Comparison of an everolimus-eluting bioresorbable scaffold with an everolimus-eluting metallic stent for the treatment of coronary artery stenosis (ABSORB II): a 3 year, randomised, controlled, single-blind, multicentre clinical trial

Patrick W Serruys, Bernard Chevalier, Yohei Sotomi, Angel Cequier, Didier Carrié, Jan J Piek, Ad J Van Boven, Marcello Dominici, Dariusz Dudek, Dougal McClean, Steffen Helqvist, Michael Haude, Sebastian Reith, Manuel de Sousa Almeida, Gianluca Campo, Andrés Iñiguez, Manel Sabaté, Stephan Windecker, Yoshinobu Onuma

ELSEVIER

Lancet. 2016 Nov 19;388(10059):2479-2491

***501* patients were randomly assigned to the Absorb group or the Xience group.**
At *3 year follow-up*, the co-primary endpoint was the *non-inferiority angiographic LLL*.



DES Technology:

Favors Need for Innovation

1. Neoatherosclerosis
2. Impaired Vasomotion
3. Lesion Preparation

Innovations with Technology?

Drug
- Novel Antiproliferative Drugs

Polymer
- Bioresorbable polymer
- Polymer composition
- No polymer

Selective Drug Delivery
- Abluminal Drug Coating

Alloy
- Metallic, Durable
- Metallic, Bioresorbable
- Polymeric, Bioresorbable

Strut Design and Thickness
- Open/Closed cells
- Hybrid cells
- Thinner struts
- Mesh covered struts

Dedicated Stents
- Bifurcation stenting

Alloy Design
- Longitudinal Integrity
- Strut Cross Linkage

Gene Expression Modification

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DES Technology:

Favors Need for Innovation

Neoatherosclerosis

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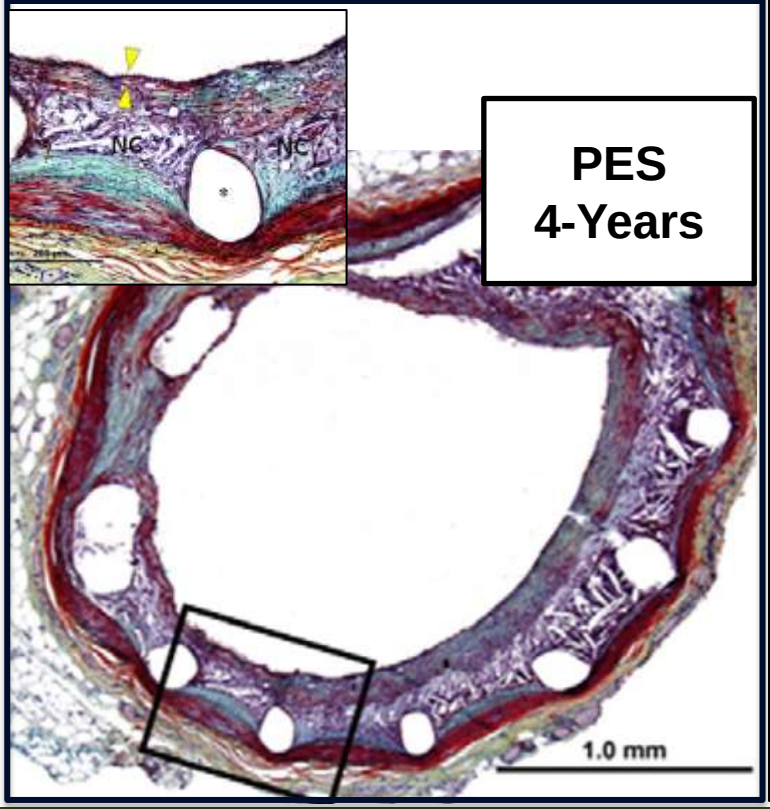
In-Stent Neoatherosclerosis

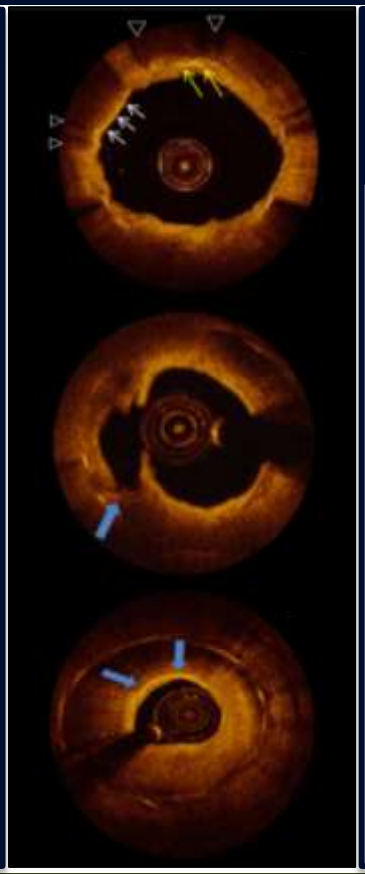
A Final Common Pathway of Late Stent Failure

Seung-Jung Park, MD, PhD,* Soo-Jin Kang, MD, PhD,* Renu Virmani, MD,†
Masataka Nakano, MD,† Yasunori Ueda, MD‡
Seoul, South Korea; Gaithersburg, Maryland; and Osaka, Japan

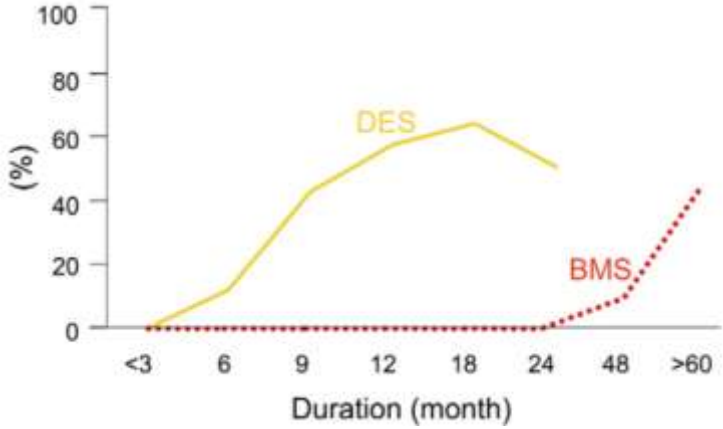
In-stent neoatherosclerosis is an important substrate for both ISR and LST, especially in the extended phase.

Histological findings of neoatherosclerosis





The atherosclerotic change in SES is seen in 40% of cases by 9-m; in the BMS, the atherosclerotic change does not begin to appear until 2-y



J Am Coll Cardiol. 2012 Jun 5;59(23):2051-7

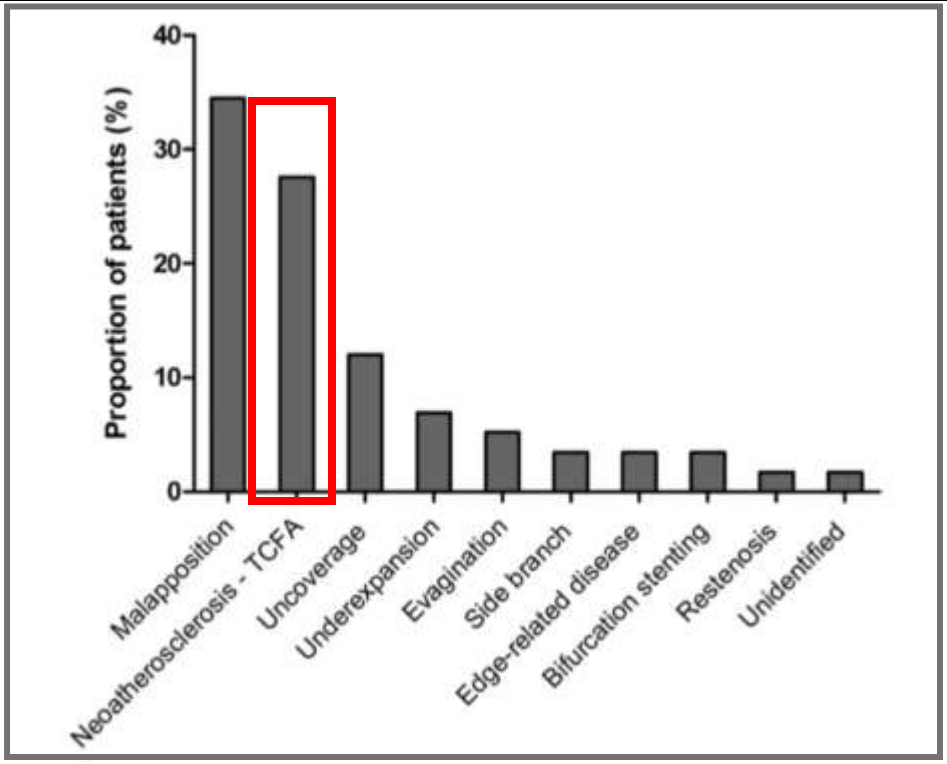
Circulation

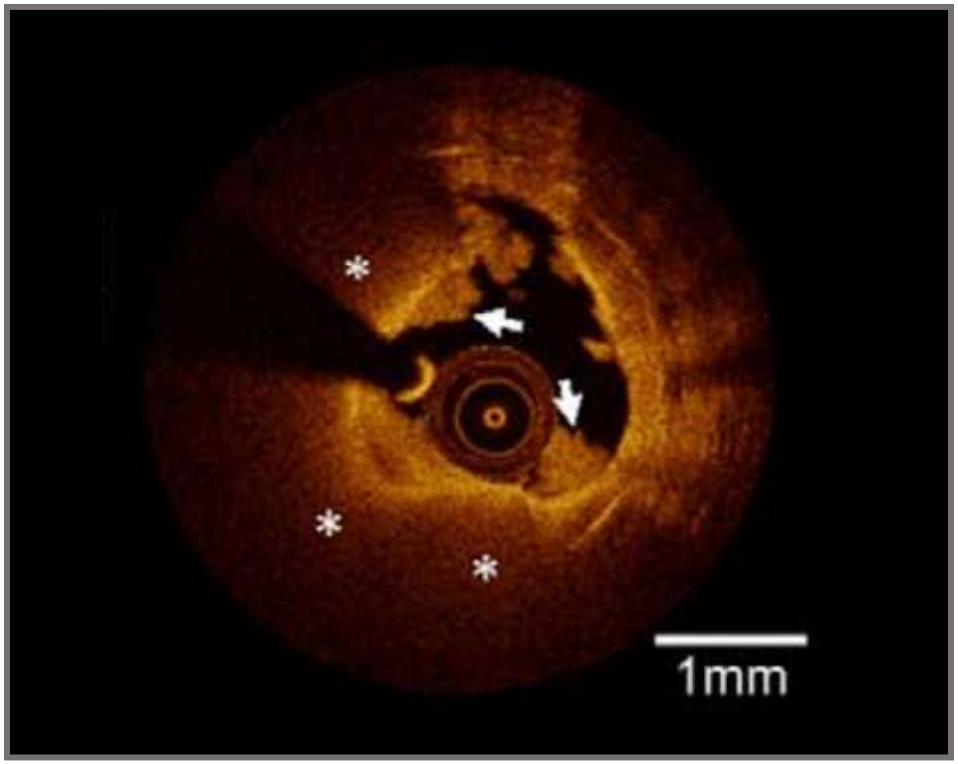
Mechanisms of Very Late Drug-Eluting Stent Thrombosis Assessed by Optical Coherence Tomography

Masanori Taniwaki, MD; Maria D. Radu, MD, PhD; Serge Zaugg, MSc; Nicolas Amabile, MD, PhD; Hector M. Garcia-Garcia, MD, PhD; Kyohei Yamaji, MD, PhD; Erik Jørgensen, MD, DMSc; Henning Kelbæk, MD, DMSc; Thomas Pilgrim, MD; Christophe Caussin, MD; Thomas Zanchin, MD; Aurelie Veugeois, MD; Ulrik Abildgaard, MD, DMSc; Peter Jüni, MD; Stephane Cook, MD; Konstantinos C. Koskinas, MD, MSC; Stephan Windecker, MD; Lorenz Räber, MD, PhD

American Heart Association. Learn and Live

Between 2010 and 2014, 64 patients were investigated at the time point of VLST (>1y) as part of an international optical coherence tomography registry. The most frequent findings were strut malapposition (34.5%), **neoatherosclerosis (27.6%),** uncovered struts (12.1%), and stent underexpansion (6.9%).

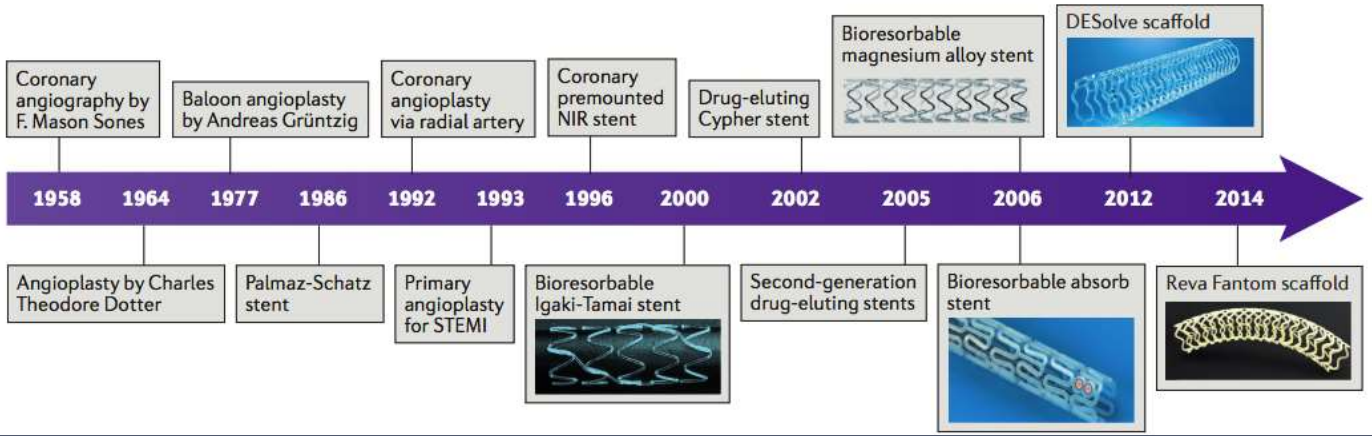


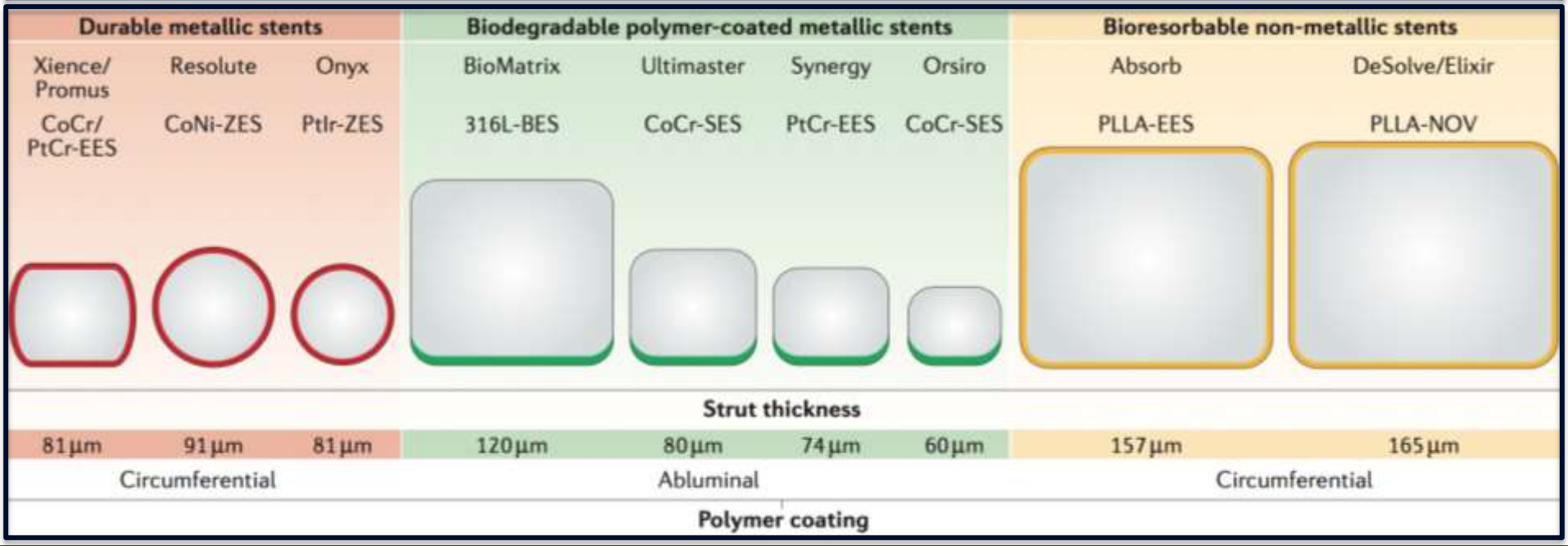


Bioresorbable vascular scaffolds — basic concepts and clinical outcome

Ciro Indolfi[1,2], Salvatore De Rosa[1] and Antonio Colombo[3]

nature REVIEWS CARDIOLOGY





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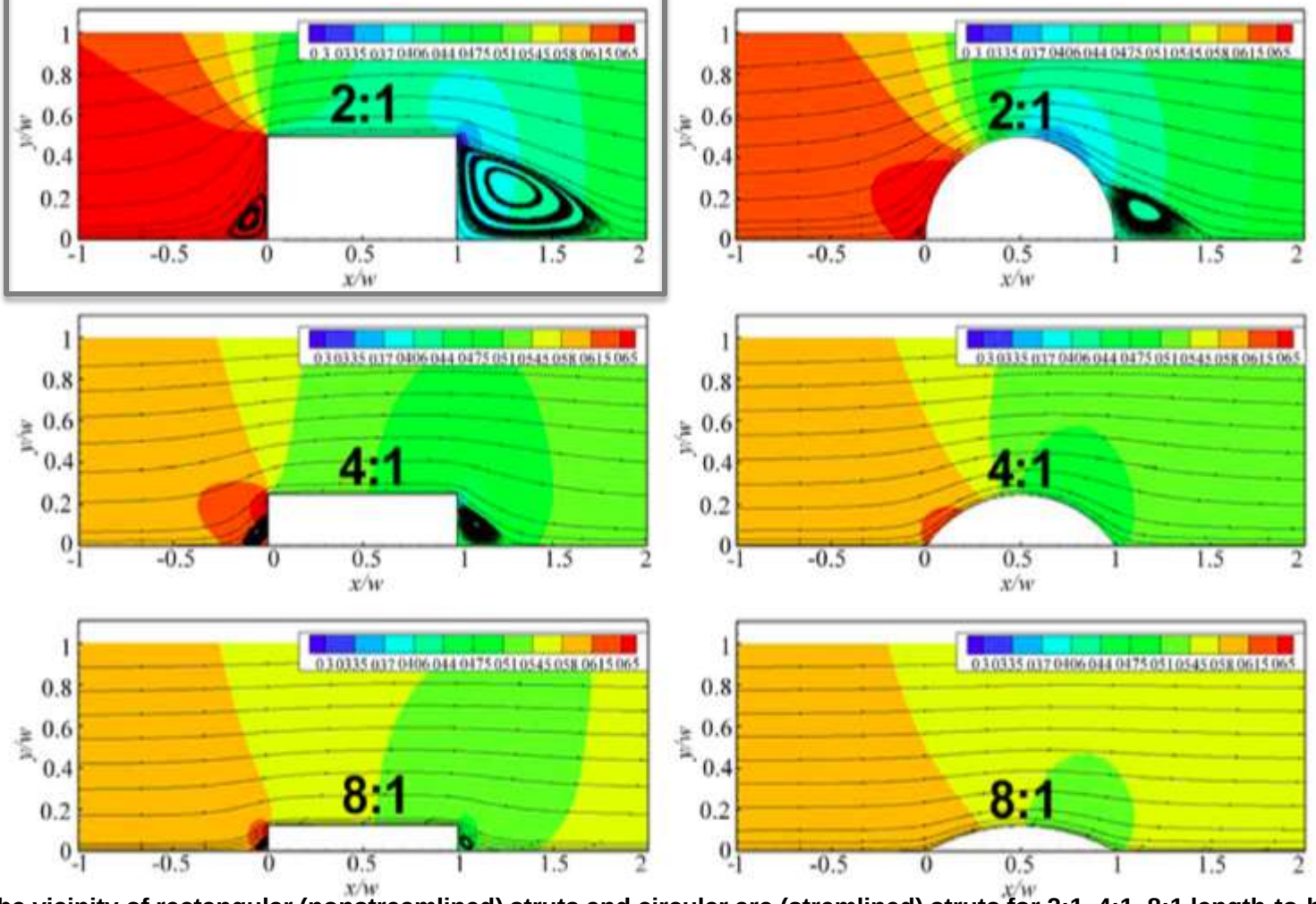
Hemodynamically Driven Stent Strut Design

JUAN M. JIMÉNEZ[1] and PETER F. DAVIES[1,2,3]

Non streamlined struts

Streamlined struts



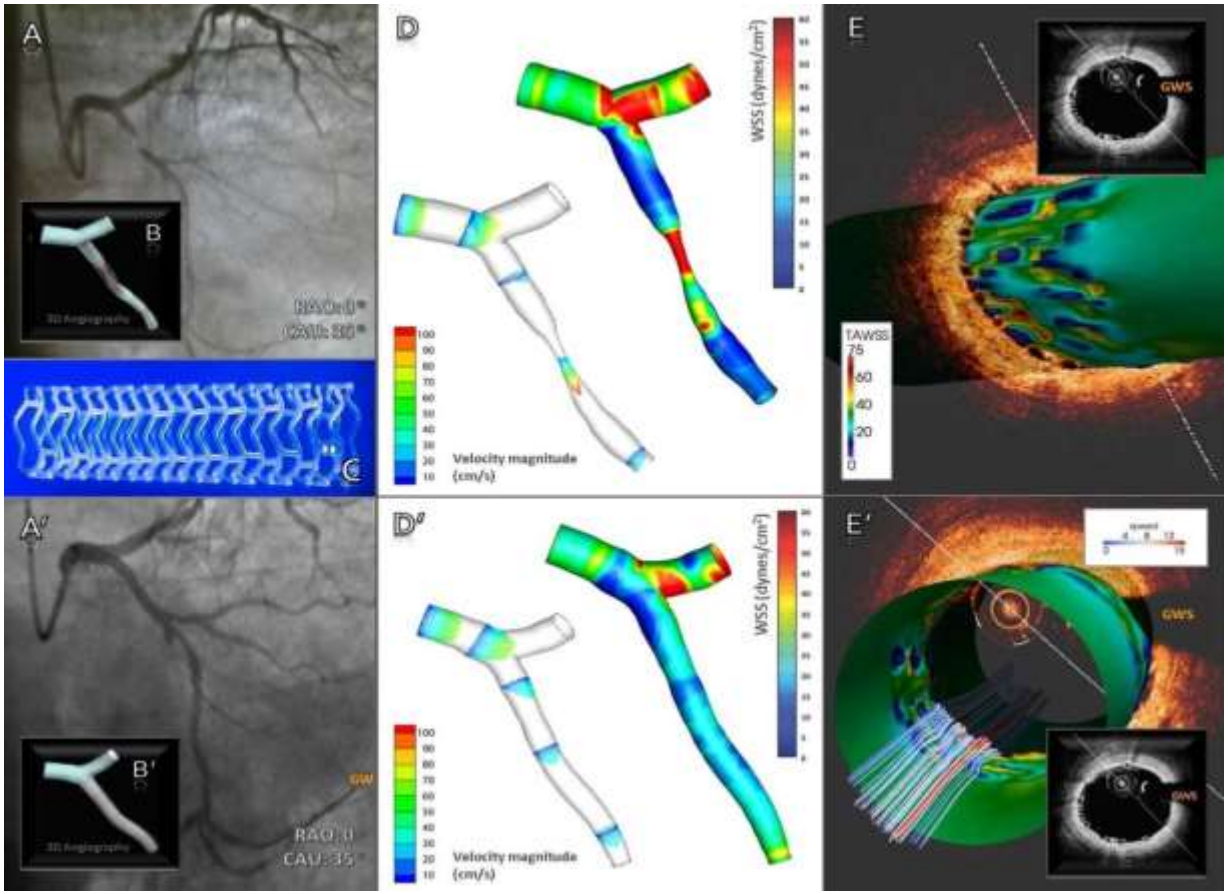
Streamlines at the vicinity of rectangular (nonstreamlined) struts and circular arc (stremlined) struts for 2:1, 4:1, 8:1 length-to-height ratios. Recirculation zones occur in rectangular struts of all aspect ratios but only in thick circular-shaped struts with a 2:1 length-to-height ratio

Biomechanical Assessment of Fully Bioresorbable Devices

Bill D. Gogas, MD,* Spencer B. King III, MD,*† Lucas H. Timmins, PhD,‡ Tiziano Passerini, PhD,§ Marina Piccinelli, PhD,‖ Alessandro Veneziani, PhD,§ Sungho Kim, PhD,‡ David S. Molony, PhD,‡ Don P. Giddens, PhD,‡ Patrick W. Serruys, MD, PhD,¶ Habib Samady, MD*

Atlanta, Georgia; and Rotterdam, the Netherlands

JACC Cardiovasc Interv. 2013 Jul;6(7):760-1



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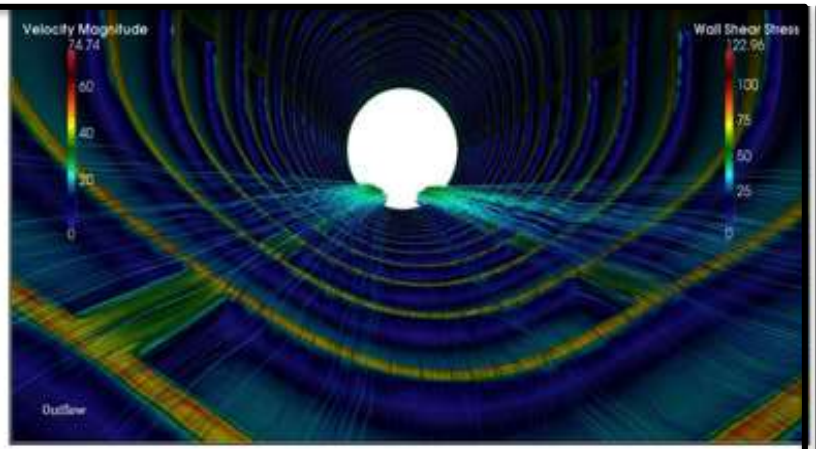
Computational fluid dynamics applied to virtually deployed drug-eluting coronary bioresorbable scaffolds: Clinical translations derived from a proof-of-concept

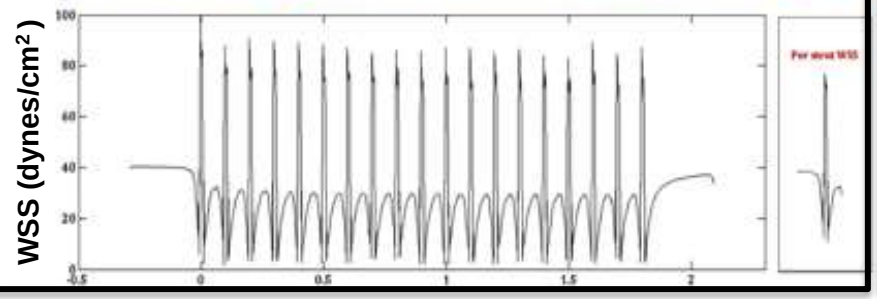
Bill D. Gogas[1,6,†], Boyi Yang[2,6,†], Tiziano Passerini[2], Alessandro Veneziani[2,6], Marina Piccinelli[3,6], Gaetano Esposito[2,6], Emad Rasoul-Arzrumly[1,6], Mosaab Awad[1], Girum Mekonnen[1,6], Olivia Y. Hung[1,6], Beth Holloway[1,6], Michael McDaniel[1,6], Don Giddens[4,6], Spencer B. King III[1,5,6], Habib Samady[1,6,*]

Glob Cardiol Sci Pract.
2014 Dec 31;2014(4):428-36

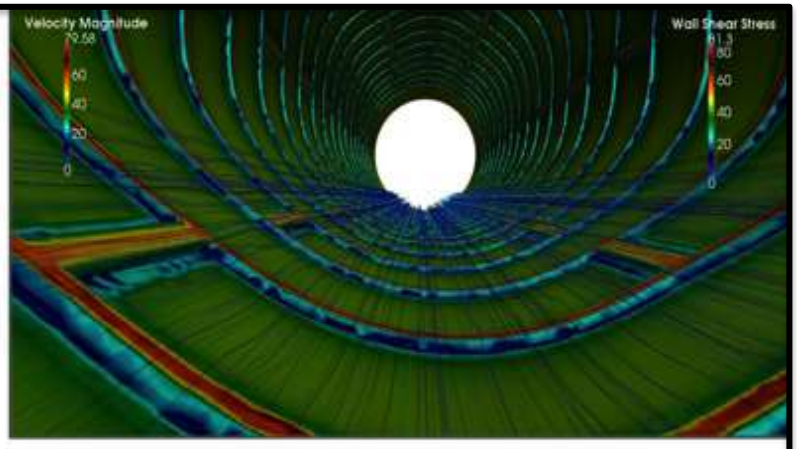
CFD simulations following virtual scaffold deployment were calculated at the inflow, endoluminal surface (top surface of the strut), and outflow of each strut surface post-procedure (stage I) and at a time point when 33% of scaffold resorption has occurred (stage II) [6-9-month]

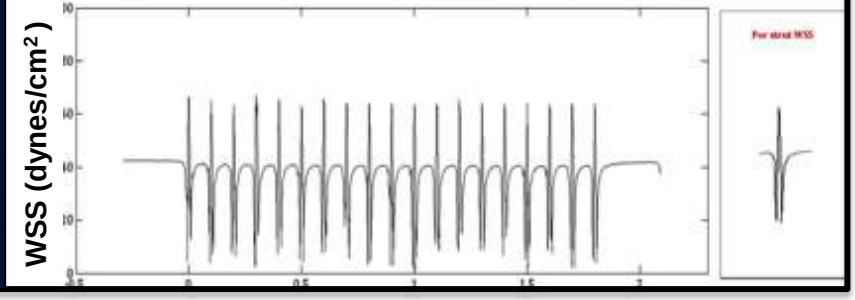
Stage I: Post-procedure



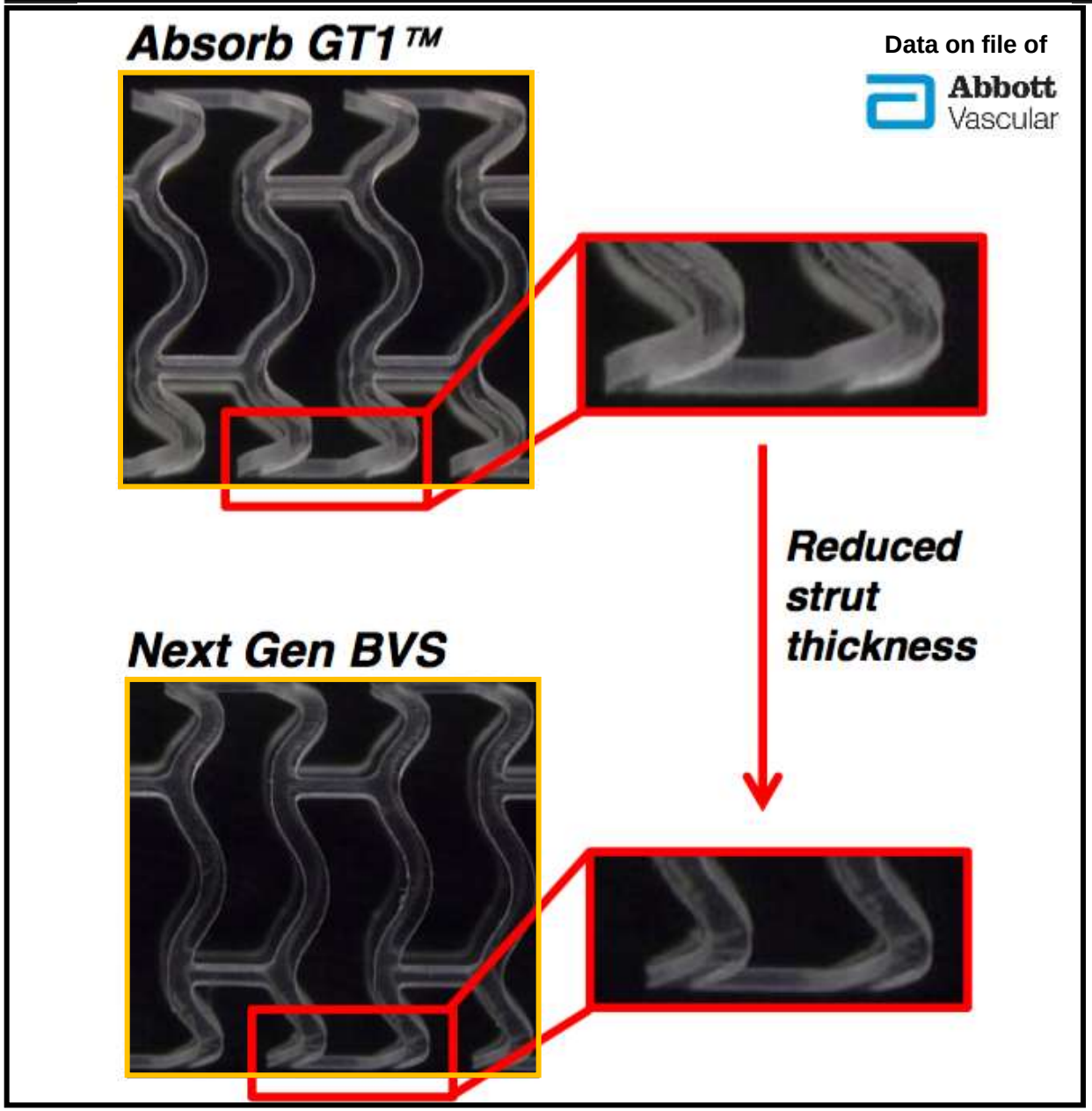


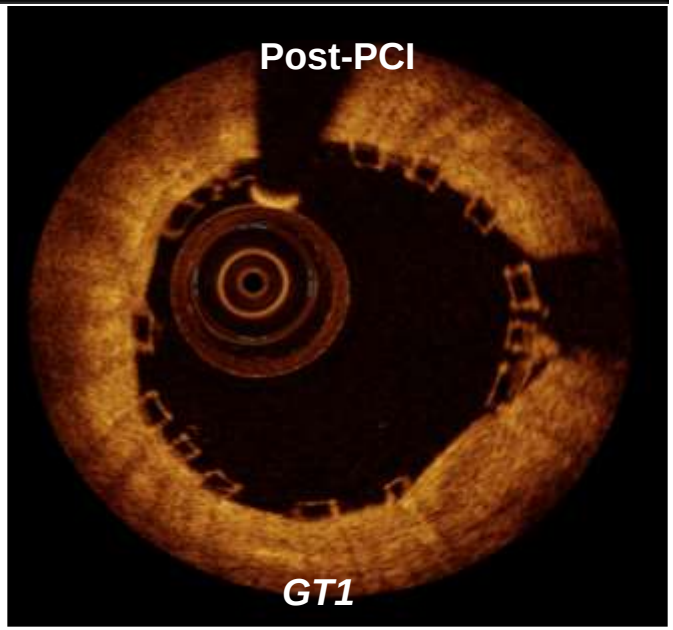
Stage II: 33% Resorption

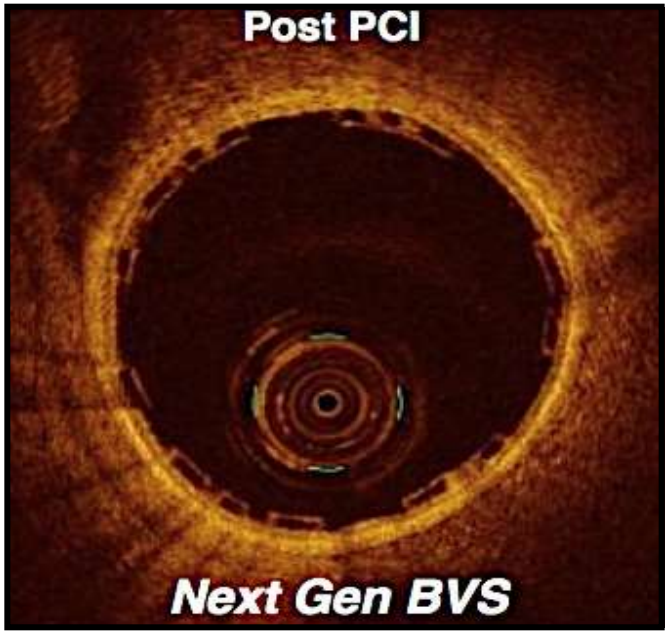




2nd Generation Everolimus-Eluting Absorb BVS







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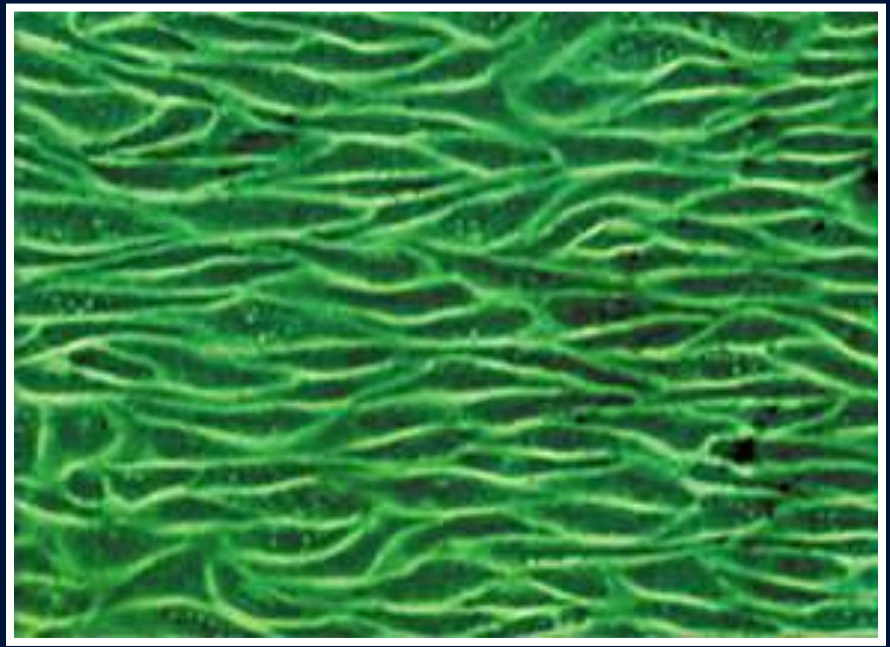
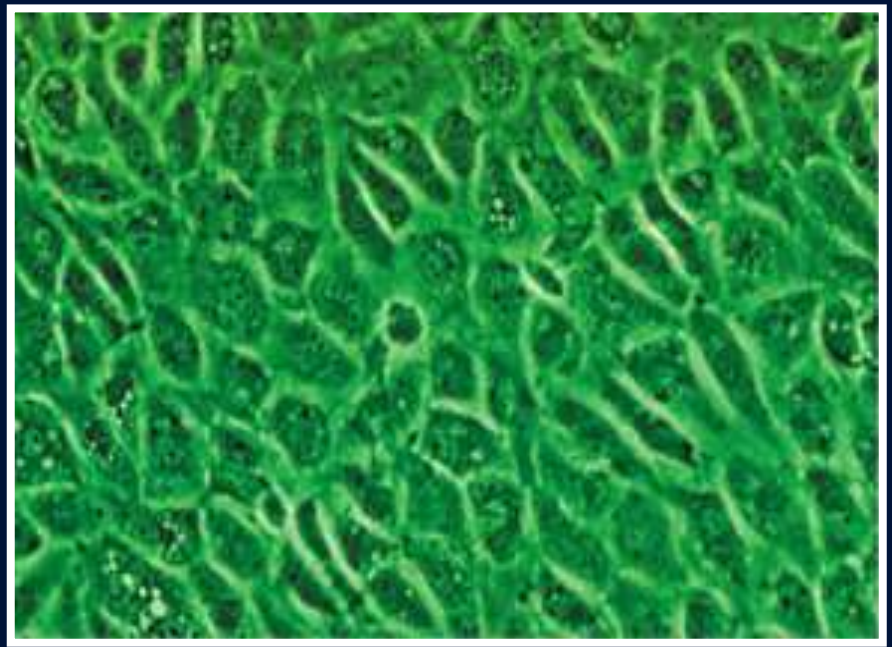
Transformation of Endothelial Cell Morphology by Fluid Shear Stress

Bovine aortic endothelial cells.

Physiologic Arterial Hemodynamic Shear Stress (>15 dynes/cm^2)



Low Arterial Hemodynamic Shear Stress (0-4 dynes/cm^2)



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DES Technology:

Favors Need for Innovation

Impaired Vasomotion

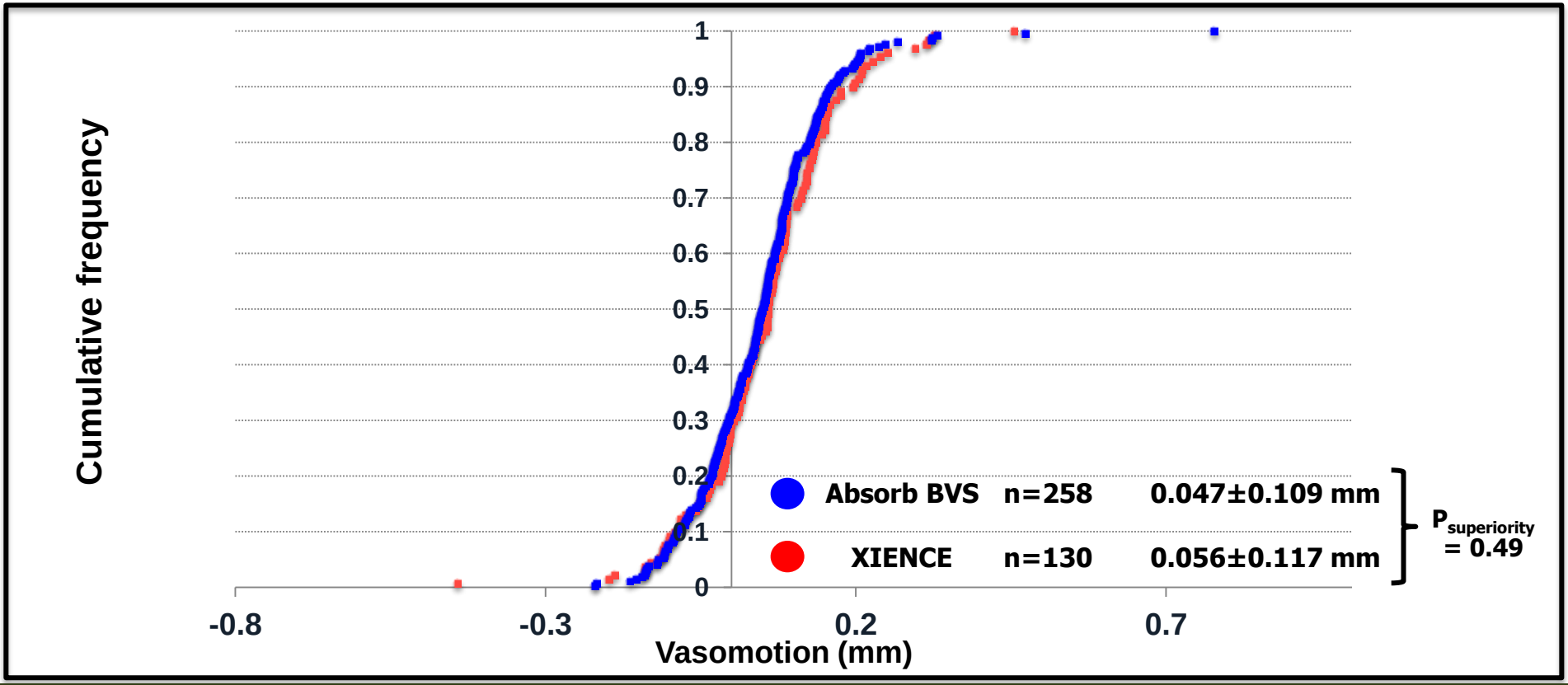
Comparison of an everolimus-eluting bioresorbable scaffold with an everolimus-eluting metallic stent for the treatment of coronary artery stenosis (ABSORB II): a 3 year, randomised, controlled, single-blind, multicentre clinical trial

Patrick W Serruys, Bernard Chevalier, Yohei Sotomi, Angel Cequier, Didier Carrié, Jan J Piek, Ad J Van Boven, Marcello Dominici, Dariusz Dudek, Dougal McClean, Steffen Helqvist, Michael Haude, Sebastian Reith, Manuel de Sousa Almeida, Gianluca Campo, Andrés Iñiguez, Manel Sabaté, Stephan Windecker, Yoshinobu Onuma

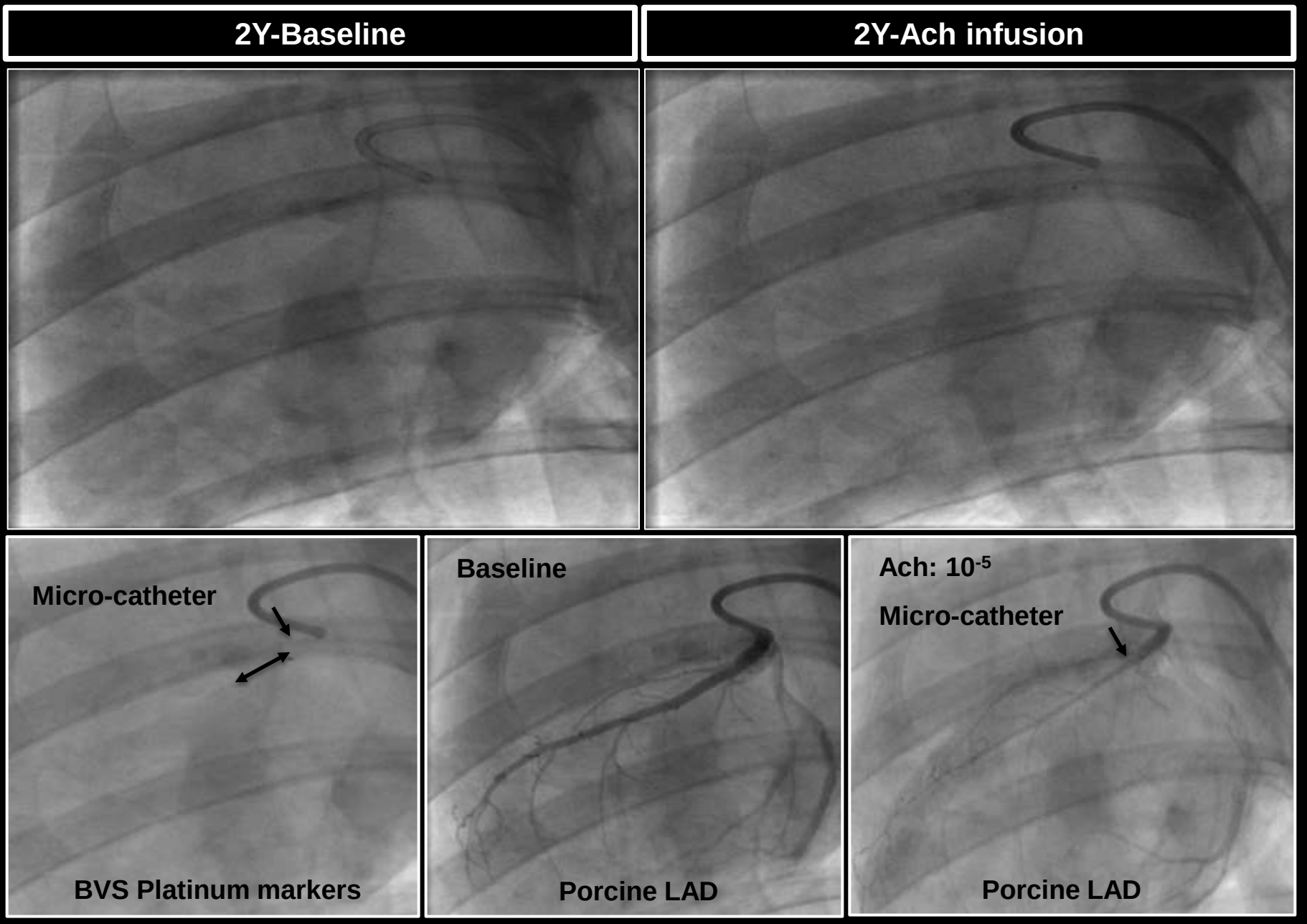
ELSEVIER

Lancet. 2016 Nov 19;388(10059): 2479-2491

***501* patients were randomly assigned to the Absorb group or the Xience group.**
At *3 year follow-up*, *the primary endpoint was superiority of the Absorb BVS vs. the XV stent in angiographic vasomotor reactivity* after administration of intracoronary nitrate.

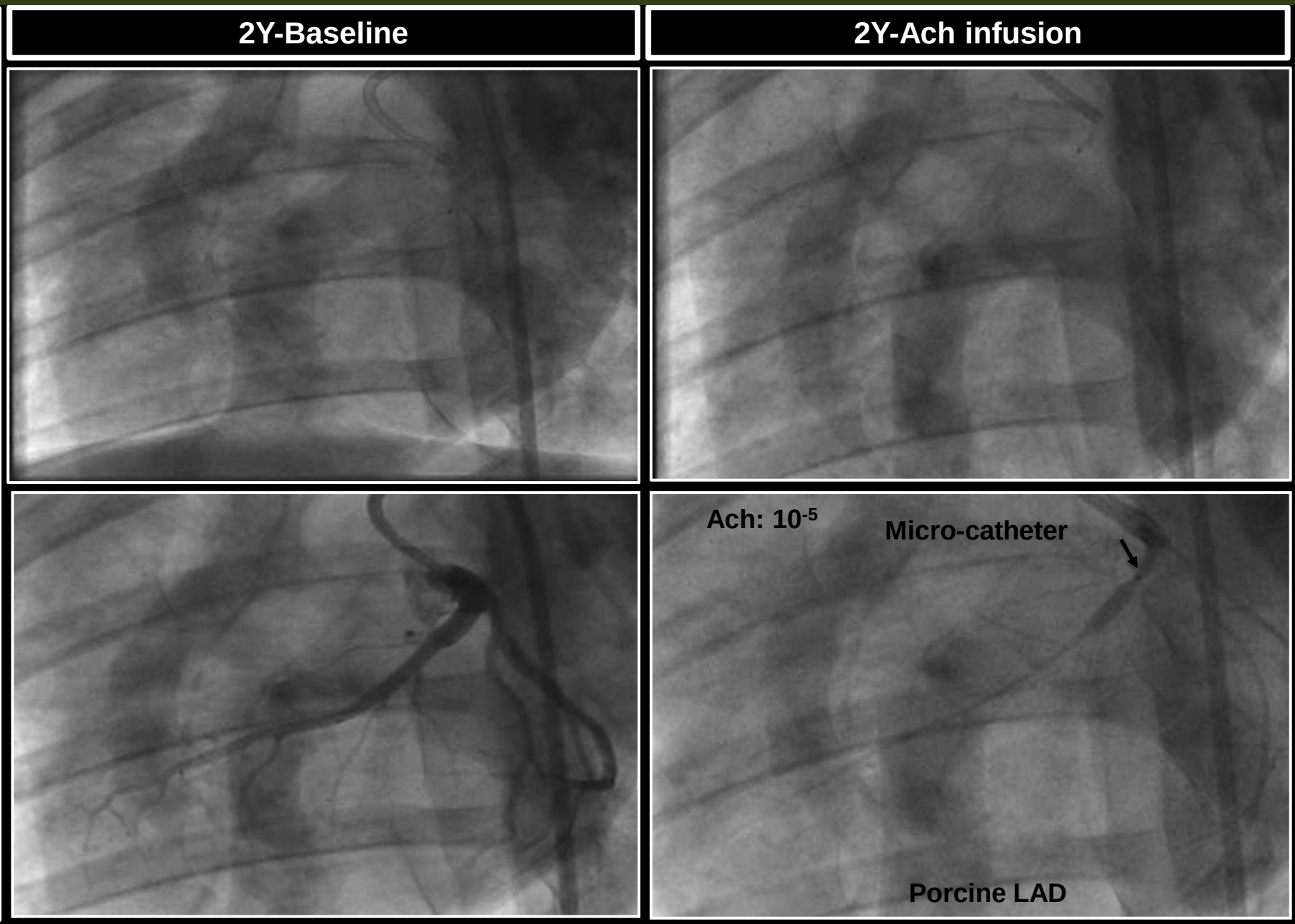


ID: 5512 / 2y follow-up/ Absorb BVS



Gogas BD, Benham J, Hsu S, et al. JACC Cardiovasc Interv. 2016 Apr 11;9(7):728-41

ID: 5487 / 2y follow-up/ Xience V



Gogas BD, Benham J, Hsu S, et al. JACC Cardiovasc Interv. 2016 Apr 11;9(7):728-41

DES Technology:

Favors Need for Innovation

Lesion Preparation

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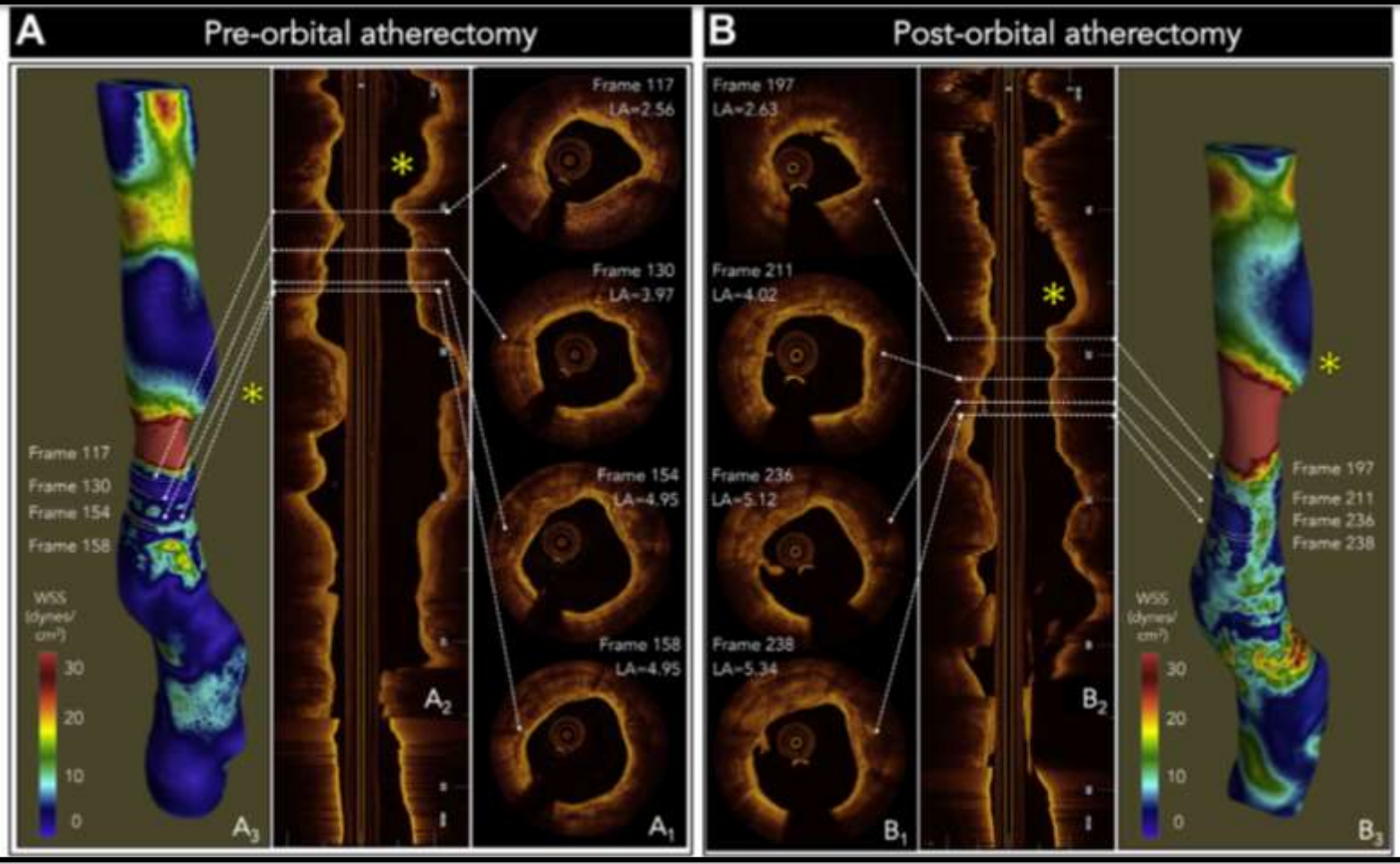
Feasibility of Optical Coherence Tomography–Derived Computational Fluid Dynamics in Calcified Vessels to Assess Treatment With Orbital Atherectomy

JACC Cardiovasc Interv. 2016
Apr 11;9(7):e65-6

Bill D. Gogas, MD, PhD,[a,d] Boyi Yang, PhD,[b,d] Marina Piccinelli, PhD,[c,d] Yasir H. Bouchi, BS,[d] Spencer B. King III, MD,[a,d,e] Nabil Dib, MD, MS,[f] Don P. Giddens, PhD,[d,g] Alessandro Veneziani, PhD,[b,d] Habib Samady, MD[a,d]



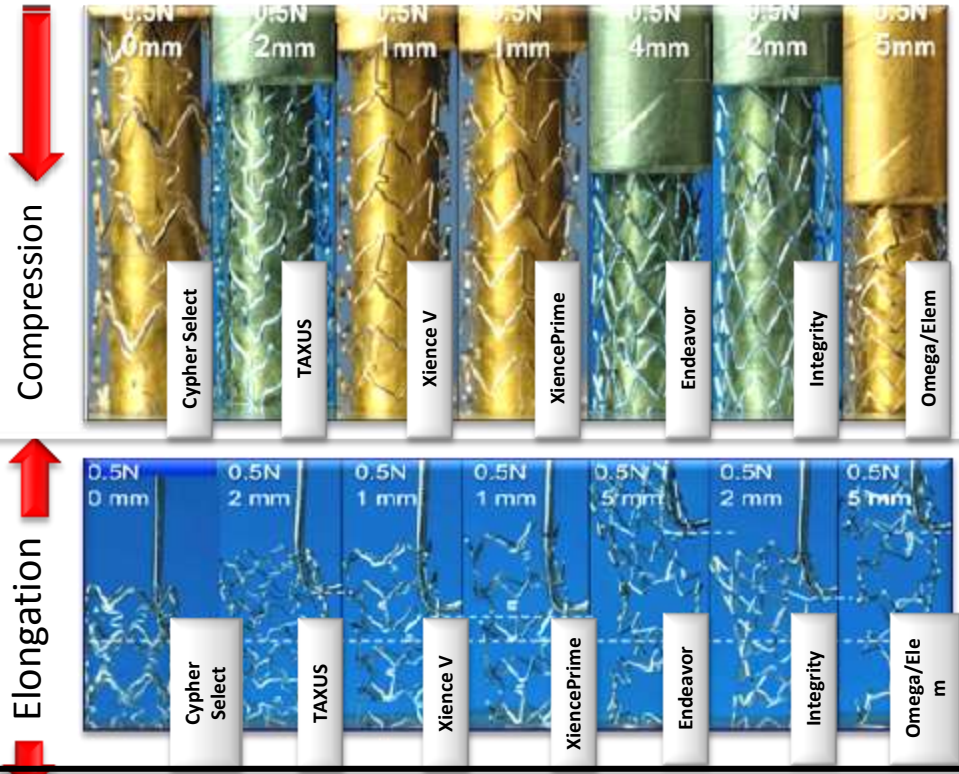
Alloy Design,
Importance of Strut Cross Linkage

Stent Longitudinal Integrity

Ormiston J. et al. JACC Cardiovasc Interv. 2011; 4(12):1310-7

Stents with **2 connectors** between hoops have **less longitudinal strength** when exposed to **compressing or elongating forces** than those with more connectors

Cypher Select was not compressed and appeared to have the greatest longitudinal stability

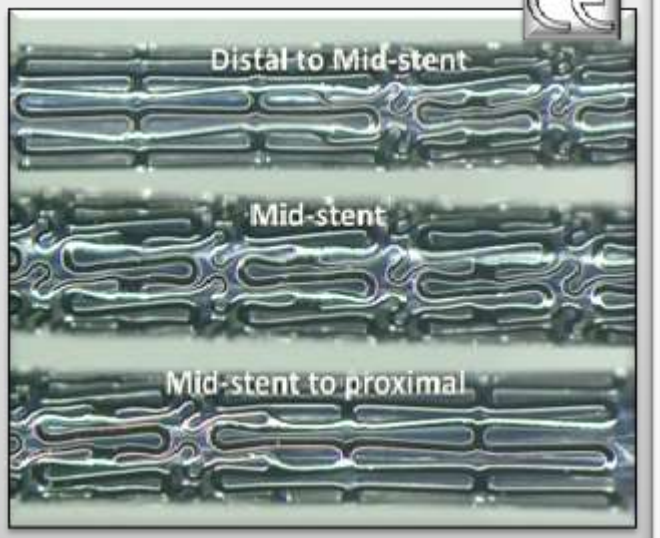


Alloy Design,
Thinner Struts

Closed cells at the edges

Open cells in the middle parts of the stent

Hybrid Design



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DES Technology: Plateau or Innovation Still Needed?

Gene expression modification **may hold promise for changing the natural history of** ***stent thrombosis*** **due to** ***neoatherosclerosis***

Very Late Vasomotor Responses and Gene Expression Profiles of Porcine Coronary Arteries 4 Years after Deployment of the Everolimus-eluting Bioresorbable Vascular Scaffold and the Everolimus-eluting Metallic Xience V stent.

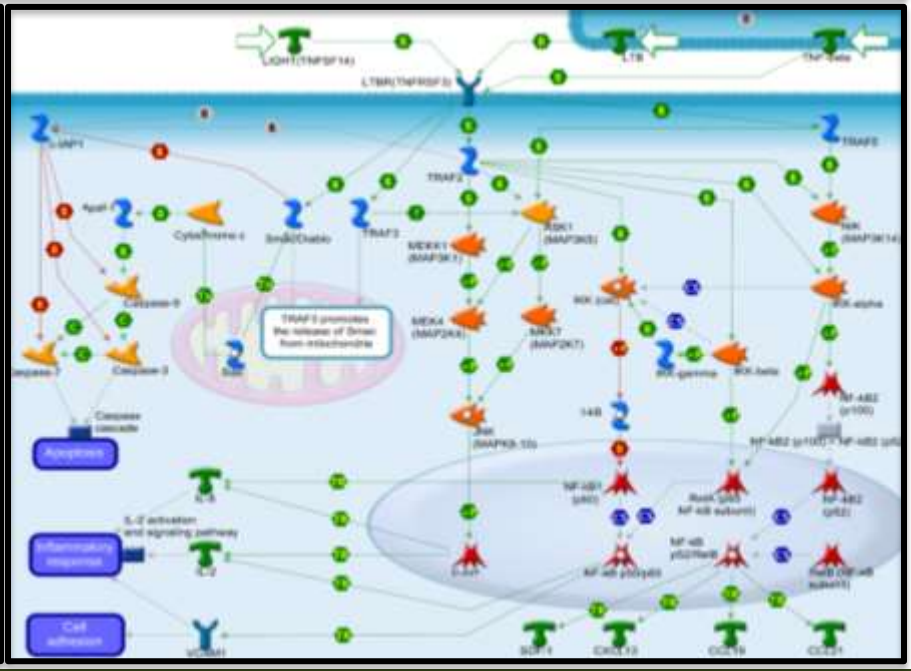
Bill D. Gogas, M.D., Ph.D., F.A.C.C.,[1,2] Sandeep Kumar, Ph.D.,[3] James J. Benham, B.S.,[4] Deepal Panchal, M.S,[5] Yasir Bouchi, B.S.,[2] Olivia Y. Hung, M.D., Ph.D.,[1,2] Rounak Gandhi, M.B.B.S., [2] Nikolaos Spilias, M.D.,[1] Esha Singhal, B. S.,[2] Don P. Giddens, Ph.D.,[3] Alessandro Veneziani, Ph.D.,[6] Richard Rapoza, Ph.D.,[4] Spencer B. King, III, M.D., M.A.C.C.[1,2] Hanjoong Jo, Ph.D.,[3] Habib Samady

J Am Coll Cardiol. 2016 Nov 1;68(18S):B334-B335

Ten Absorb BVS (BVS) and 6 Xience V (XV) DES were randomly implanted in the coronaries of 6 non-atherosclerotic juvenile Yucatan mini swine, followed-up at 4y.

Gene analysis was performed in explanted coronary arterial segments at 4 years. Out of 12.000 genes only 499 showed differential expression (>1.5 fold change with statistical significance of p<0.05). Those differentially expressed genes were used in a pathway analysis using the MetaCore™ Key Pathway Advisor (KPA).

Lymphotoxin-β-receptor (LTβR) signaling pathway expression in XV treated arteries



Molecular Medicine

Deficiency in Lymphotoxin β Receptor Protects From Atherosclerosis in apoE-Deficient Mice

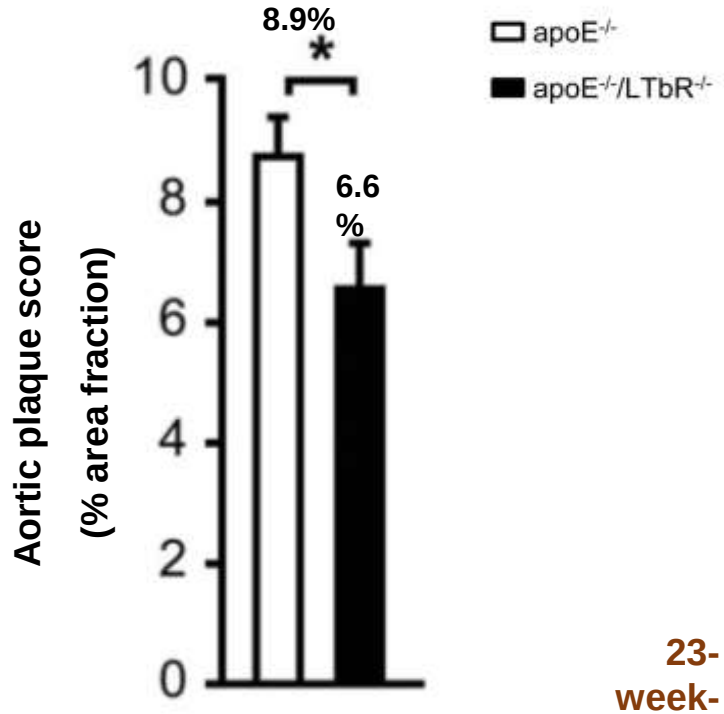
Maria Grandoch, Kathrin Feldmann, Joachim R. Göthert, Lena S. Dick, Susanne Homann, Christina Klatt, Julia K. Bayer, Jan N. Waldheim, Berit Rabausch, Nadine Nagy, Alexander Oberhuber, René Deenen, Karl Köhrer, Stefan Lehr, Bernhard Homey, Klaus Pfeffer, Jens W. Fischer

The extent of atherosclerosis was quantified in en face preparations of the aorta. The atherosclerotic plaque score was significantly lower for apoE-/-mice deficient in LTbR than for their littermate controls area fraction: apoE-/-, 8.9% ± 0.6%; apoE-/-/LTbR-/-, 6.6% ± 0.7%; n = 6-8) as determined by lipid staining with Oil Red O

ApoE−/−

ApoE−/−
LTβR−/−

23-week-old



23-week-old

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DES Technology: Plateau or Innovation Still Needed?

Despite a fairly flat plateau resulting in excellent intermediate term results of DES technology, improved synergy between biomechanics and vascular biology is clearly needed for optimal long-term results.

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Thank you