Morning Roundtable Forum: Meet the Experts over Breakfast
DES & New BRS

Can Improved Scaffold Technology Reduce Clinical Complications?

-Insights and Speculation-

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Emeritus Professor of Medicine

Erasmus MC
Universitair Medisch Centrum Rotterdam

Dr. Honoris Causa in Biomedical Engineering

THE UNIVERSITY OF
MELBOURNE

CARDIOVASCULAR SUMMIT
TCTAP 2018

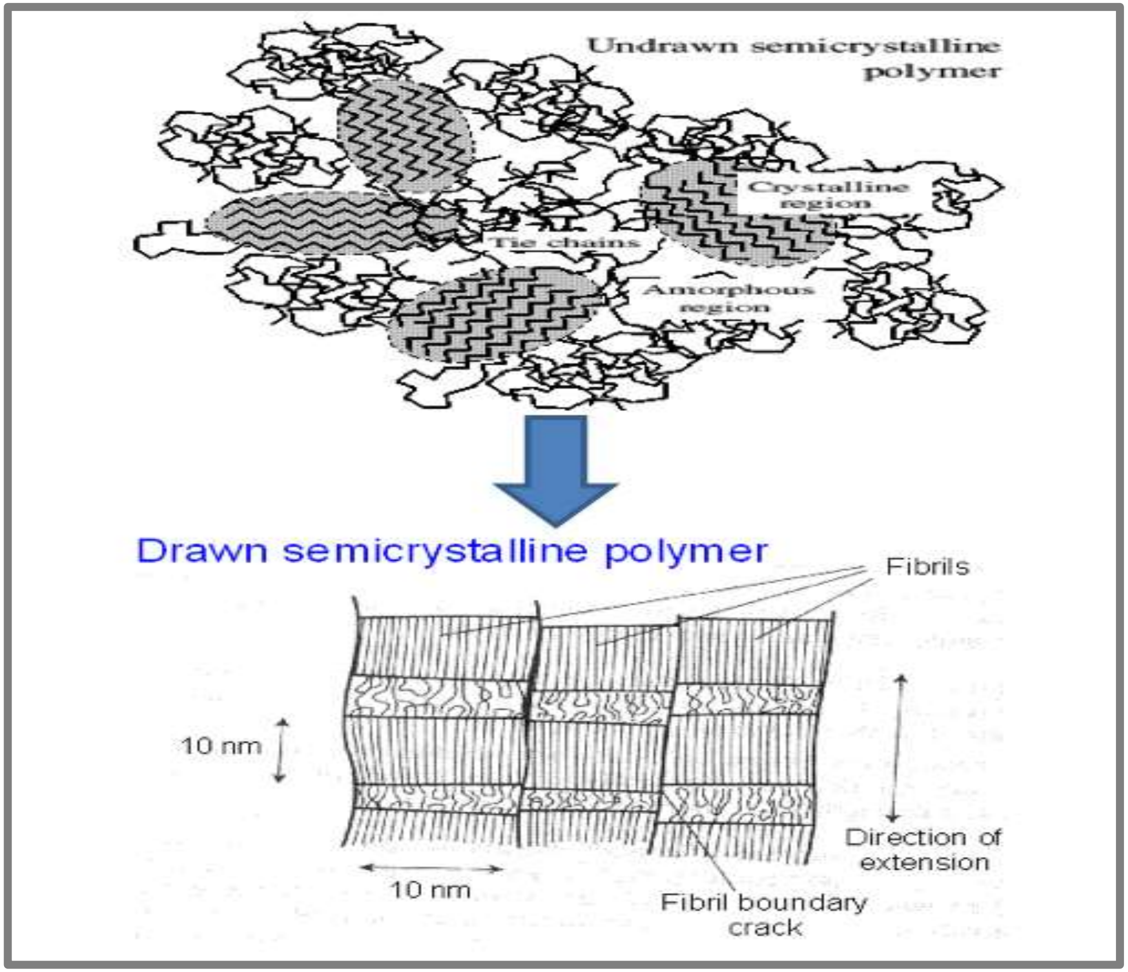
Sunday, April 29, 2018, 7:16 AM – 7:24 AM, Room 104, Level 1

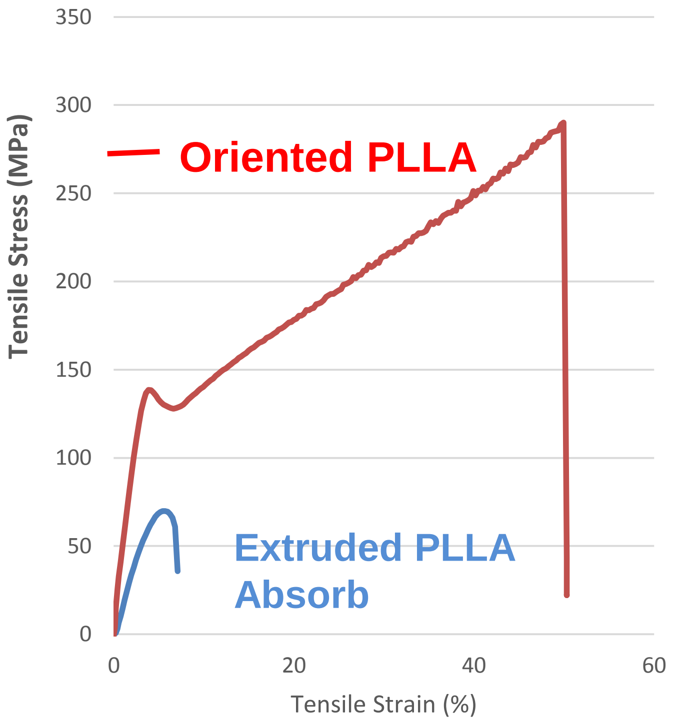
CVRF

How improved scaffold technology can improve safety and efficacy

Shortcomings	Possible solution
○ Low tensile strength, low radial force, recoil <> ○ thick strut, wide footprint	• Increase tensile strength, good radial force -> thin strut (oriented PLLA, cold worked Magnesium)
○ Quadratic strut ○ Difficult to embed ○ Disturb laminar flow	• Circular strut (single monofilament fiber) • Easy to embed • Less disturbance of laminar flow
○ Increase local viscosity and thrombogenicity ○ Main determinant of neointimal thickness and Lumen reduction	• Use of biodegradable material non-thrombogenic: Magnesium WE-43, Proprietary Mg alloy without rare earth elements
○ Slow down the cell coverage	• Circular strut
○ Late structural discontinuity (dismantling)	• Faster bioresorption (single monofilament fiber, Magnesium)

How to increase tensile strength and radial force by altering molecular orientation of PLLA



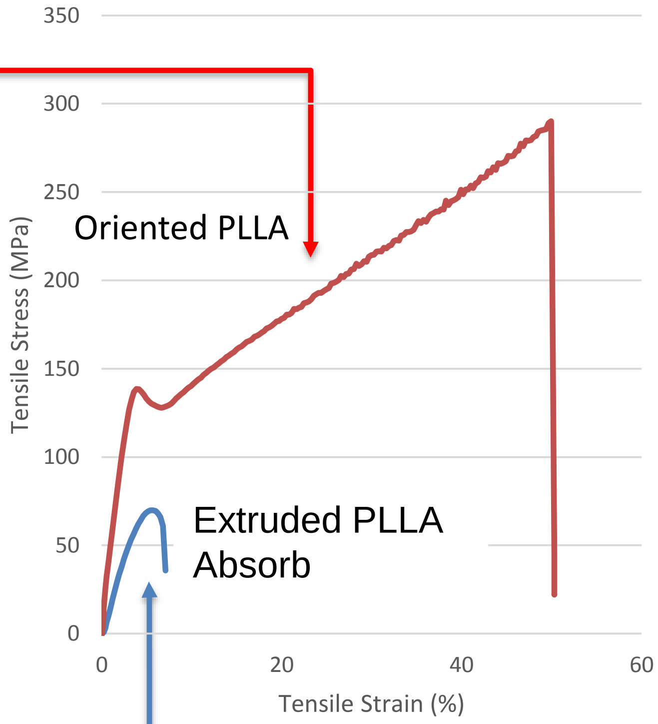


- Tube wall thickness of < 95 µm and even < 75 microns can be achieved
- Scaffold tube thickness comparable to metallic DES

How to increase tensile strength and radial force by altering molecular orientation of PLLA

Material	PLLA	Oriented PLLA	Mg Alloy	Stainless Steel	Cobalt Chrome
Ultimate tensile strength (MPa)	~30-50	220-260	343* 280	670	820-1200
Tensile Modulus (Gpa)	1.2-3.0	5-7	45	193	243
Elongation (%)	2-6	40-70	23	48	35-55

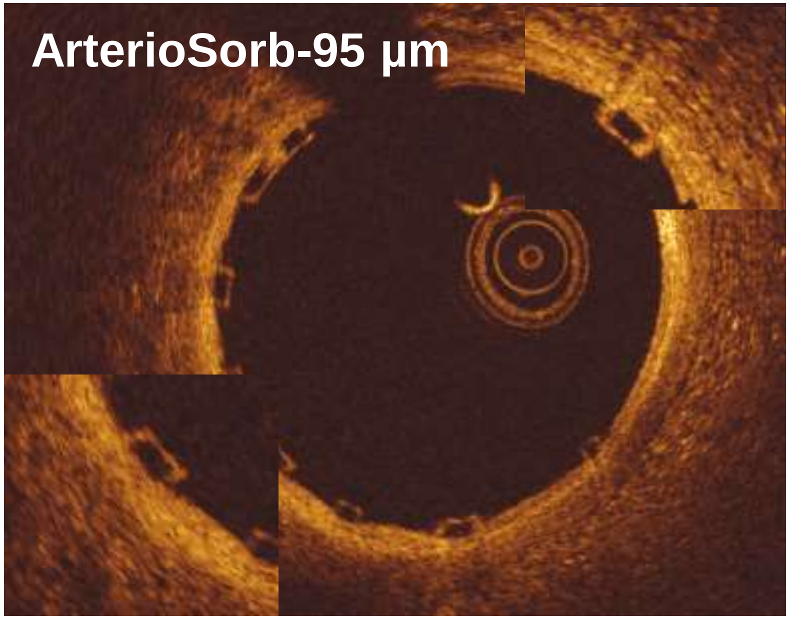
*cold worked



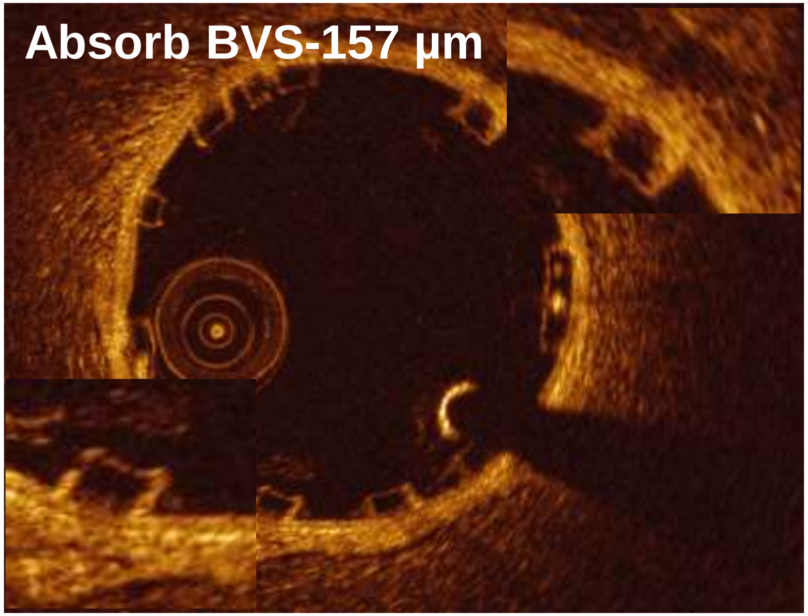
- ➢ **Tube wall thickness of < 95 µm and even < 75 microns can be achieved**
- ➢ **Scaffold tube thickness comparable to metallic DES**

Oriented polylactide, stronger and thinner strut
Reducing the protrusion without increase of recoil

ArterioSorb from Arterius
(Profile: 1.22 mm)
Protrusion distance: 89±7 µm



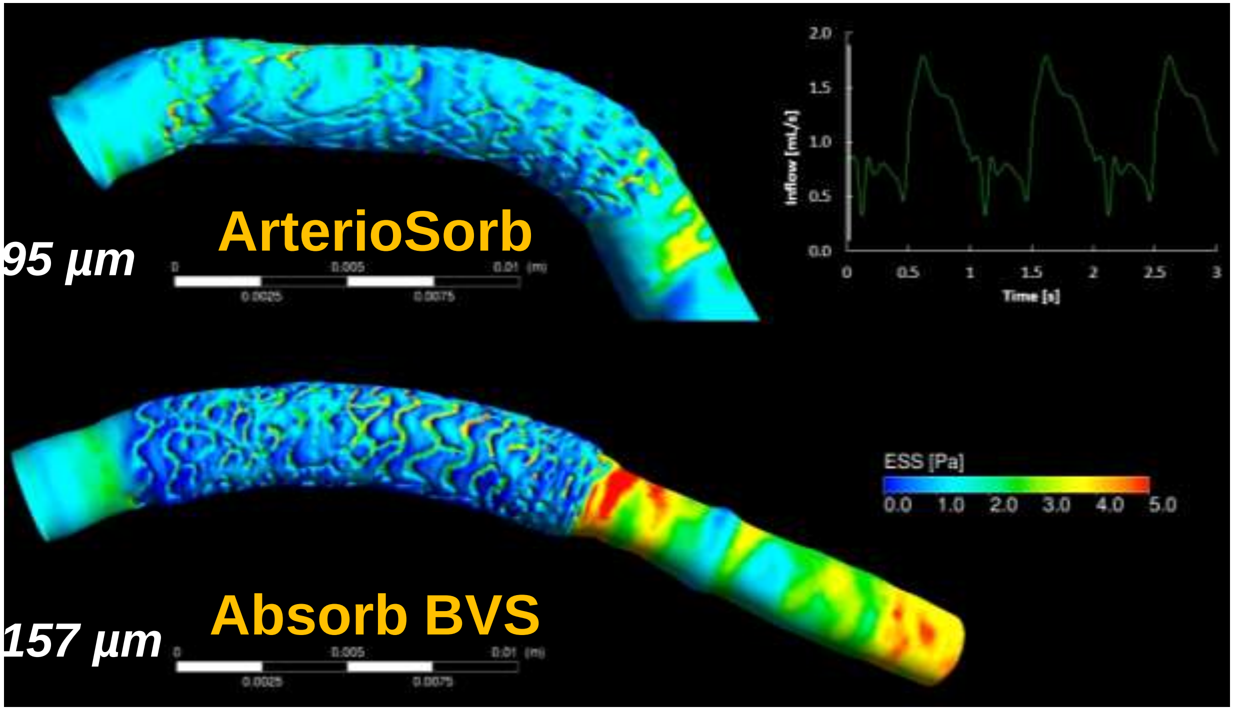
Absorb BVS from Abbott
(Profile: 1.43 mm)
Protrusion distance: 150±9 µm

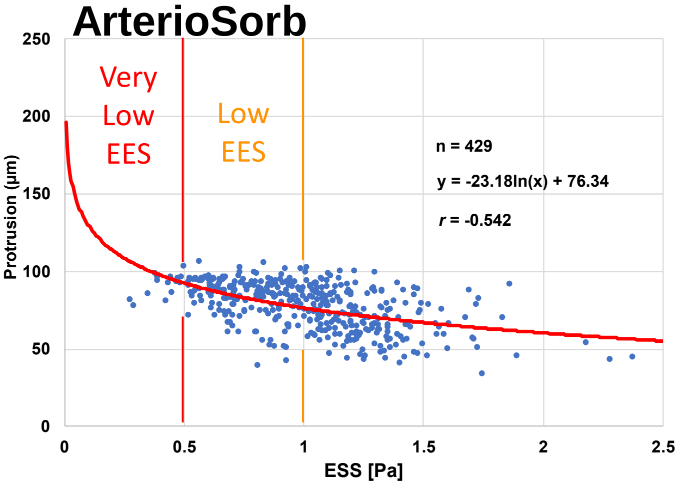


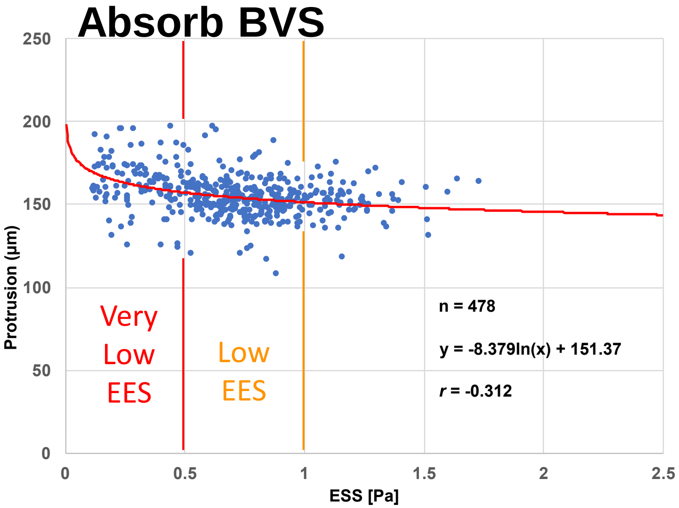
	After device deployment		After post-dilatation (PD) A: **19.24**±4.80 atm X: **18.42**±4.56 atm	
Scaffold	**Device balloon-artery ratio**	**Acute recoil (%)**	**PD balloon-artery ratio**	**Acute recoil (%)**
Arteriosorb-95 (n=25)	1.09±0.11	4.69±7.38	1.11±0.09	2.65±3.81
Xience (n=15)	1.12±0.11	2.70±4.52	1.14±0.10	1.06±4.13

Courtesy of Dr. Onuma, Rasha Al-Lamee, Guy Leclerc (AccelLAB, Montreal)

Thin struts reduce struts protrusion, very low-shear stress (dark-blue color), risk of thrombus peri-strut and neointima

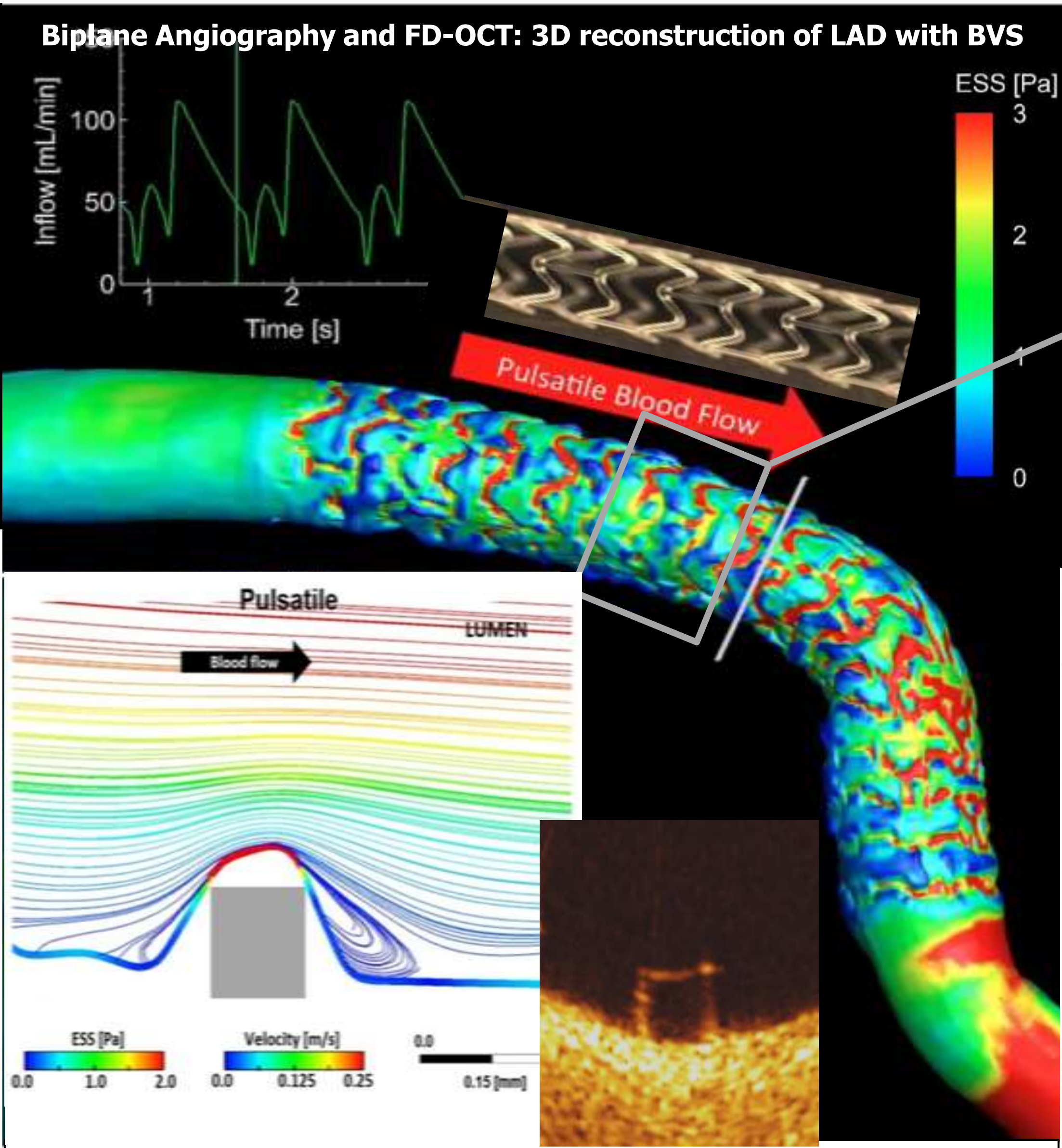




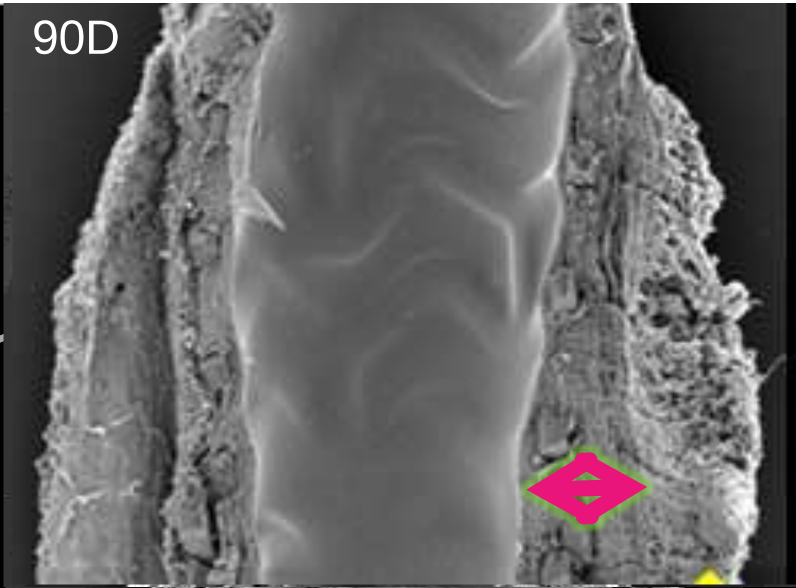


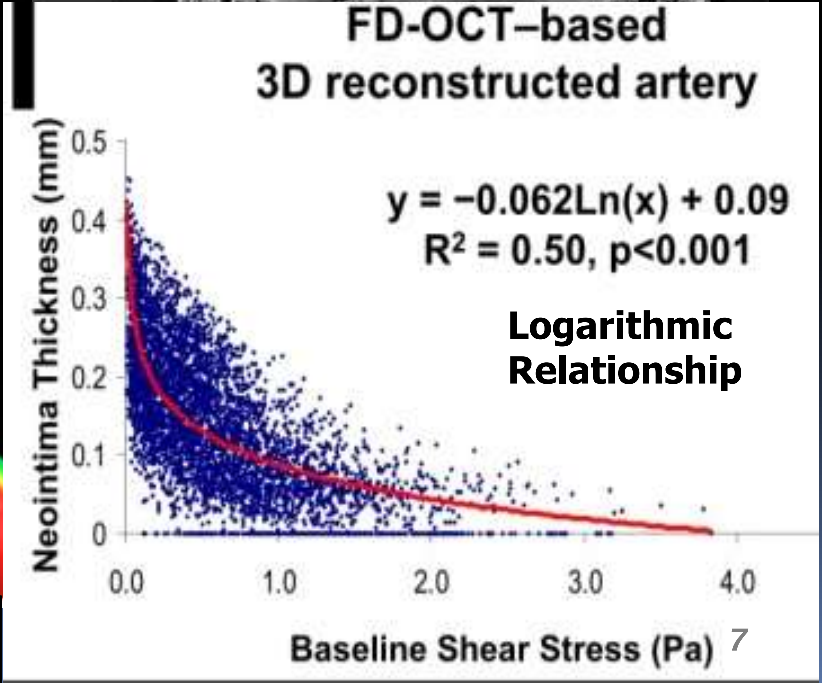
Tenekecioglu E, Torii R, Serruys PW et al. Non-Newtonian pulsatile shear stress assessment: a method to differentiate bioresorbable scaffold platforms. Eur Heart J 2017 Sep 1;38(33):2570.

Low Shear Stress generated by thick protruding strut is the main determinant of neointimal thickness and Lumen Area reduction



Biplane Angiography and FD-OCT: 3D reconstruction of LAD with BVS





Teneckecioglu, Serruys et al. JACC Cardiovasc Interv. 2016;9(20):2167-2168.
Bourantas, Serruys et al. JACC Cardiovasc Interv. 2014;7:100-1.

How improved scaffold technology can improve safety and efficacy

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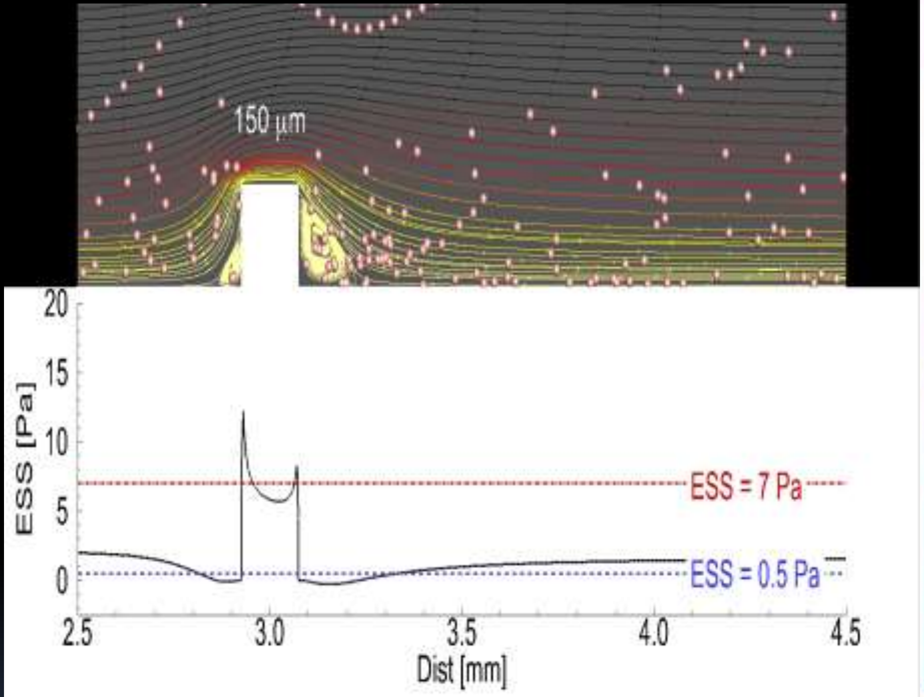
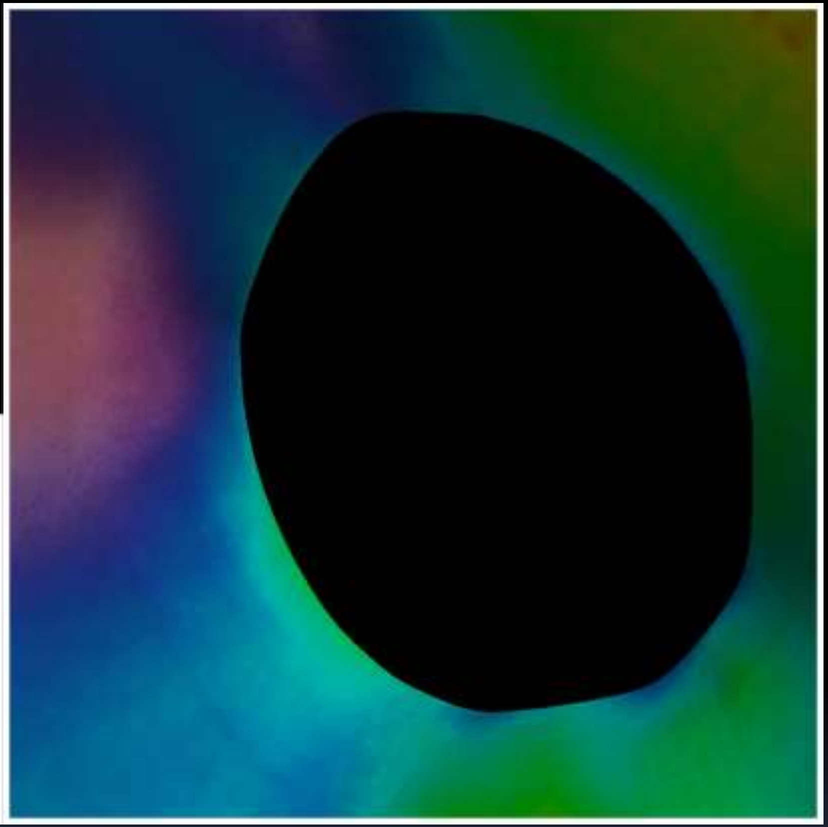
Non-Newtonian (cell tracking) shear stress and viscosity in early systole

Navier Stokes (ESS) and Quemada (viscosity) equations

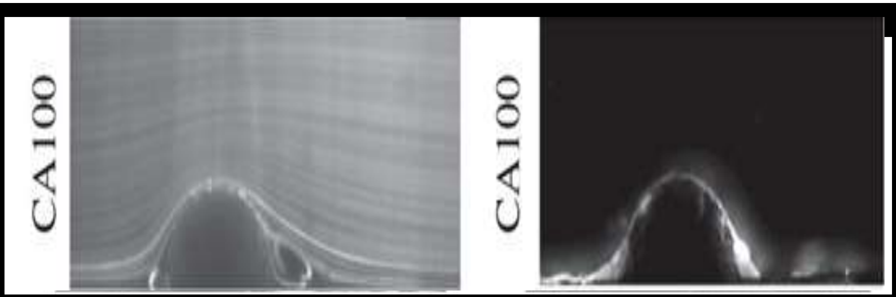




- **Pink fuzzy areas are regions with low shear stress with high viscosity**

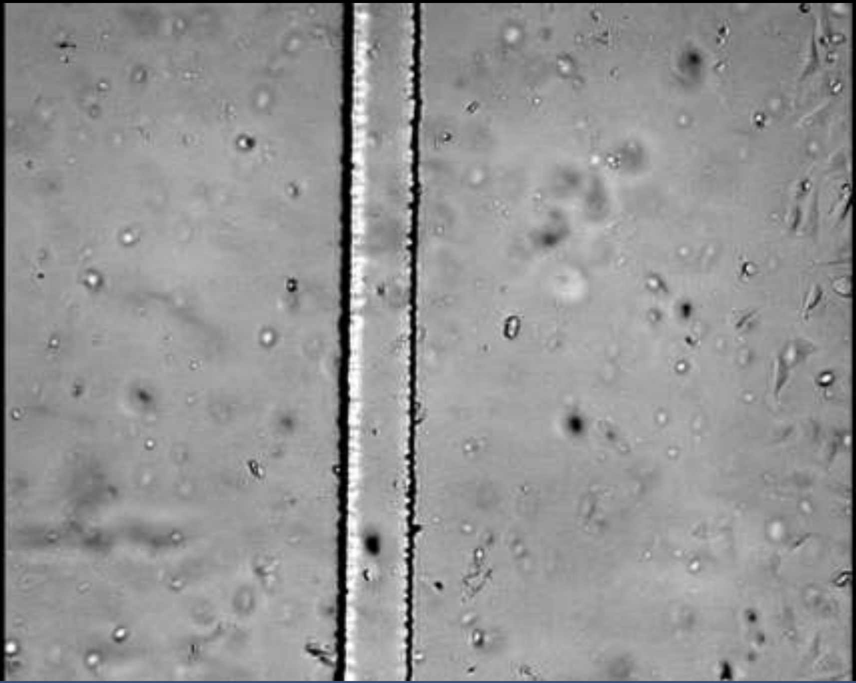
Thondapu V et al, Serruys PW. Endothelial shear stress 5 years after implantation of a coronary bioresorbable scaffold. Eur Heart J. 2018 Feb 2.[Epub ahead of print]

The effect of thick (150 µm), quadratic strut on flow reversal, recirculation, fibrin deposition and endothelial migration and coverage

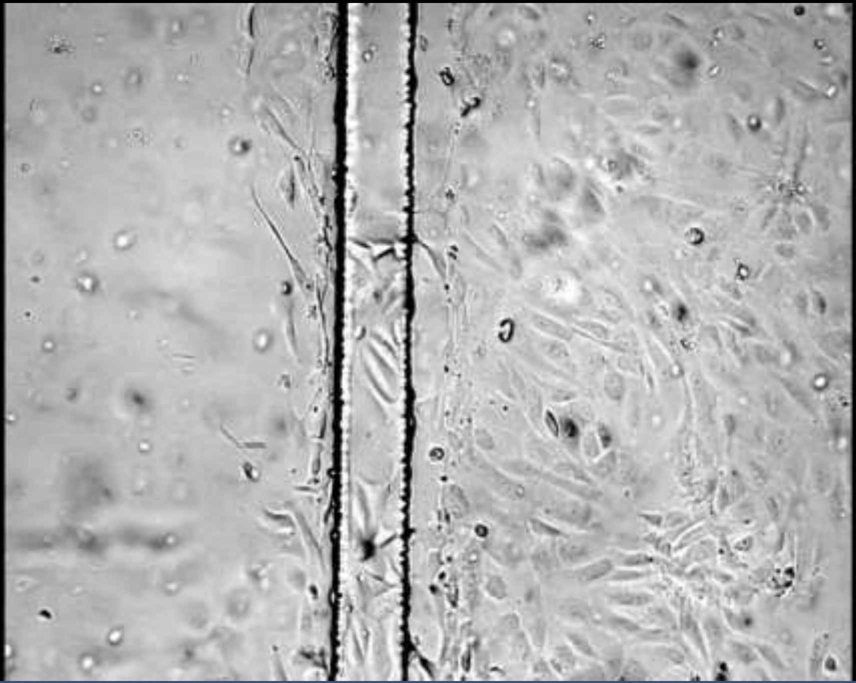


Circular
strut
(next slide)

0-24 hr

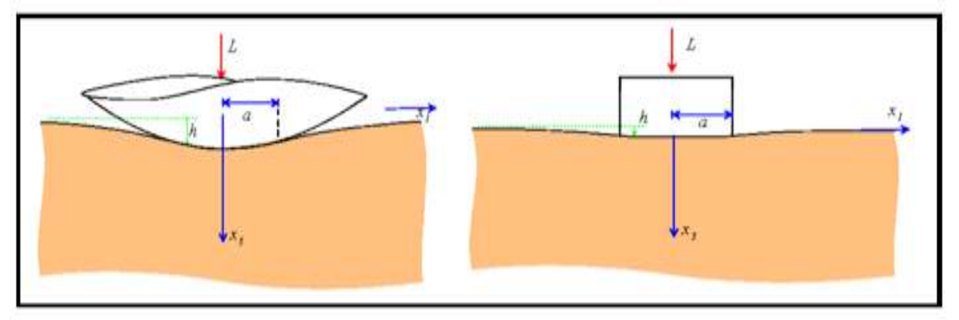


40-72 hr



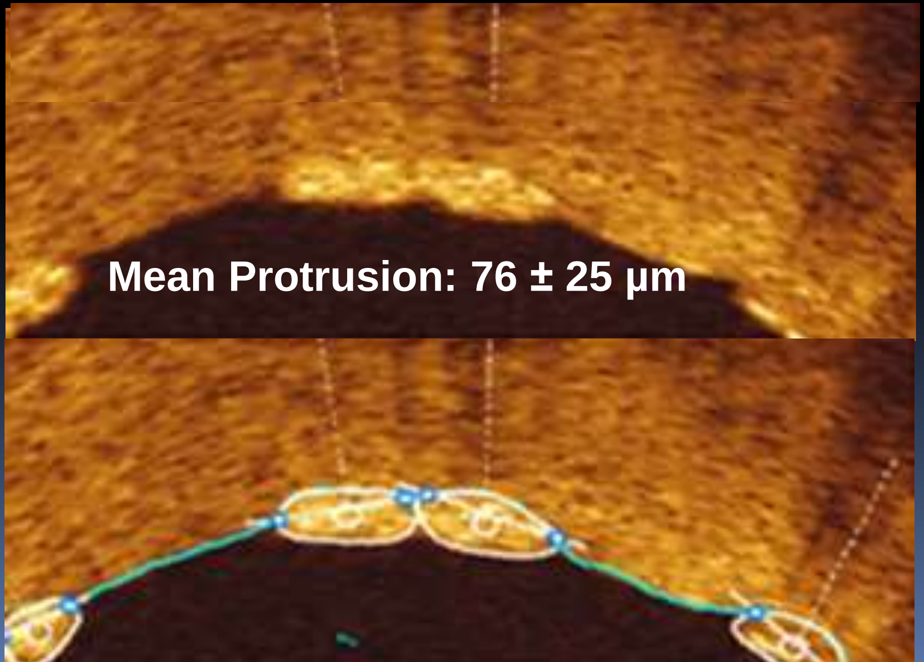
Hsiao ST et al. Endothelial repair in stented arteries is accelerated by inhibition of Rho-associated protein kinase. Cardiovasc Res. 2016 Dec;112(3):689-701

CIRCULAR STRUTS (mono fiber) PENETRATE INTO THE VESSEL WALL BETTER THAN THE *QUADRATIC* STRUTS

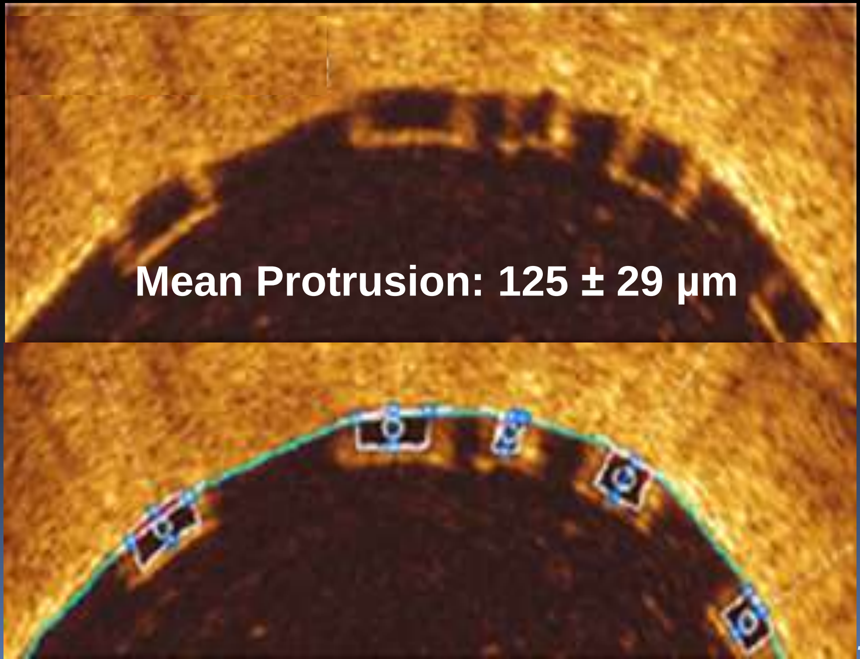


$$p(\rho)=\frac{2\mu h}{\pi(1-\nu)\sqrt{a^2-\rho^2}}$$

Inverse relationship between contact radius and contact pressure

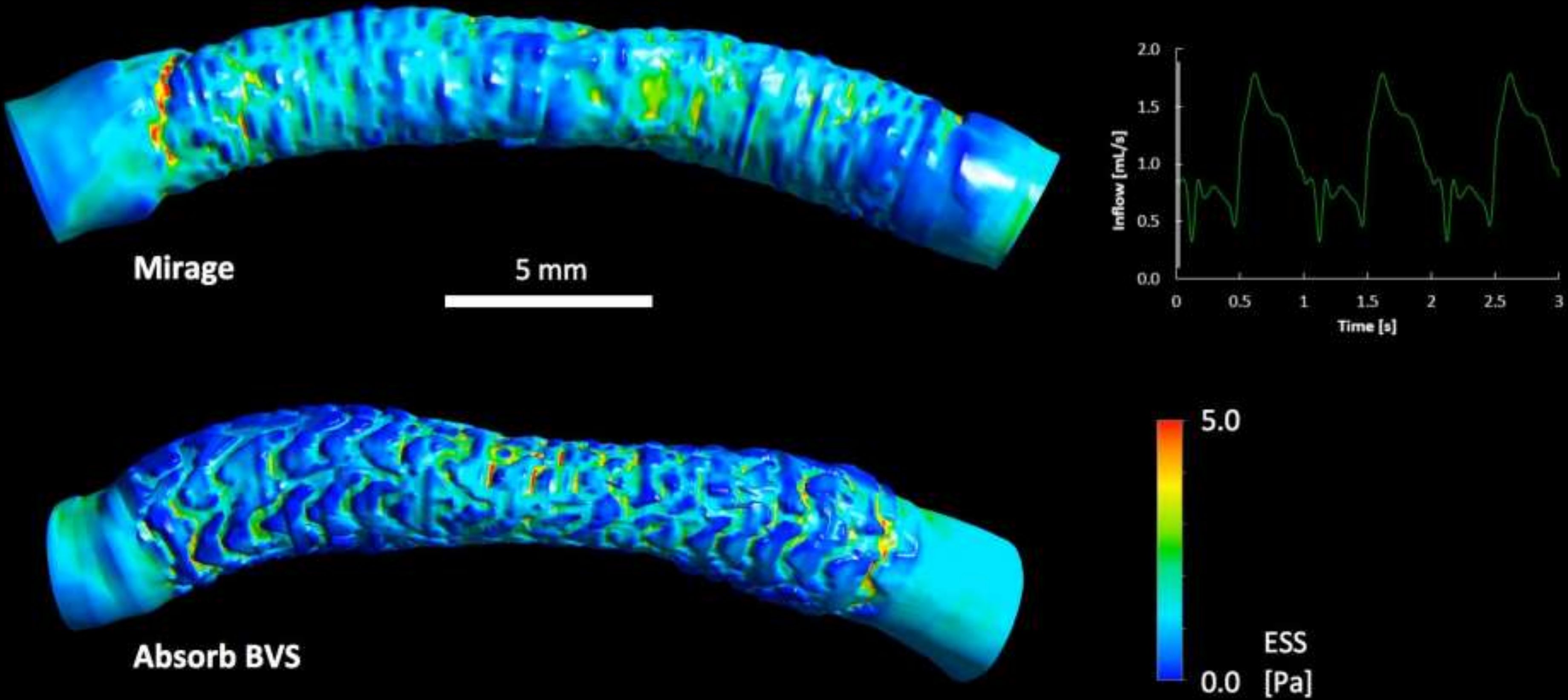


Mean Protrusion: 76 ± 25 µm



Mean Protrusion: 125 ± 29 µm

Circular strut design and reduced strut protrusion reduce low-shear stress (dark blue) in Mirage compared to the Absorb



EuroIntervention

Tenekecioglu E, Serruys PW. EuroIntervention, 2016 Nov 20;12(10):1296

How improved scaffold technology can improve safety and efficacy

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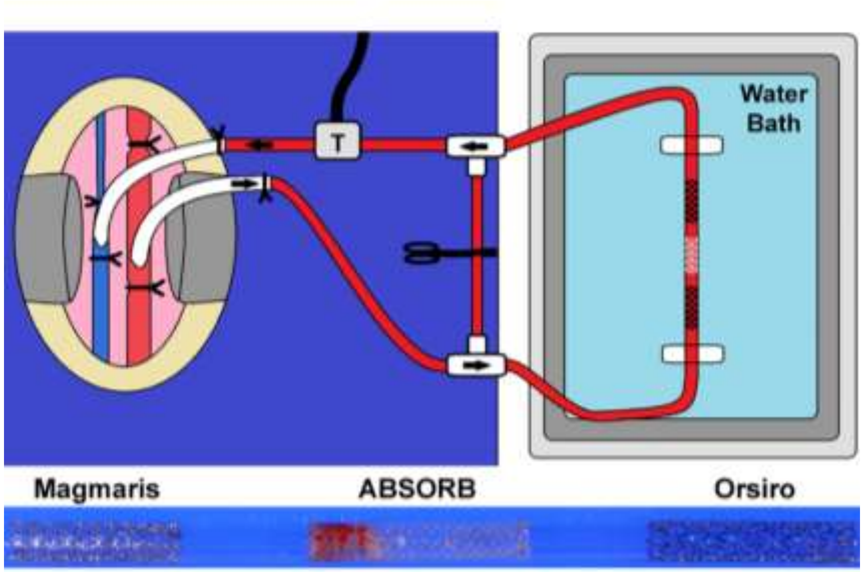
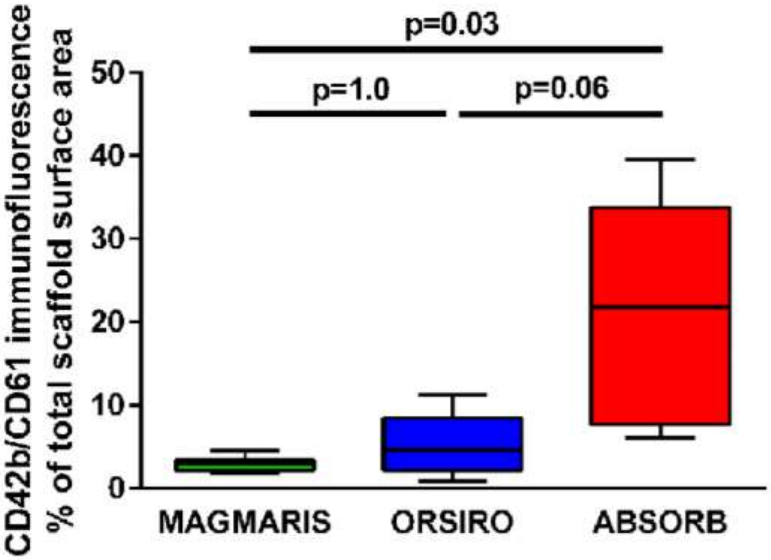
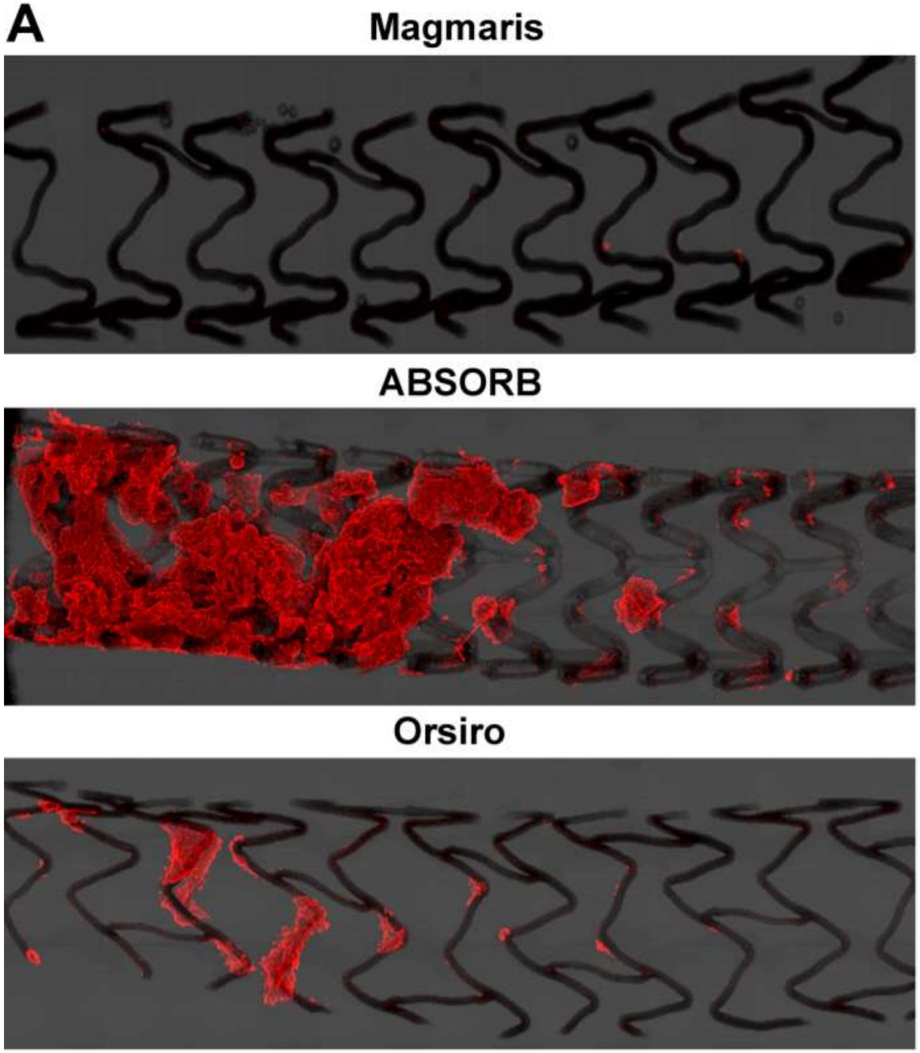
Comparison of Acute Thrombogenicity for Metallic and Polymeric Bioabsorbable Scaffolds: Magmaris vs ABSORB vs Orsiro in a Porcine Arteriovenous Shunt Model

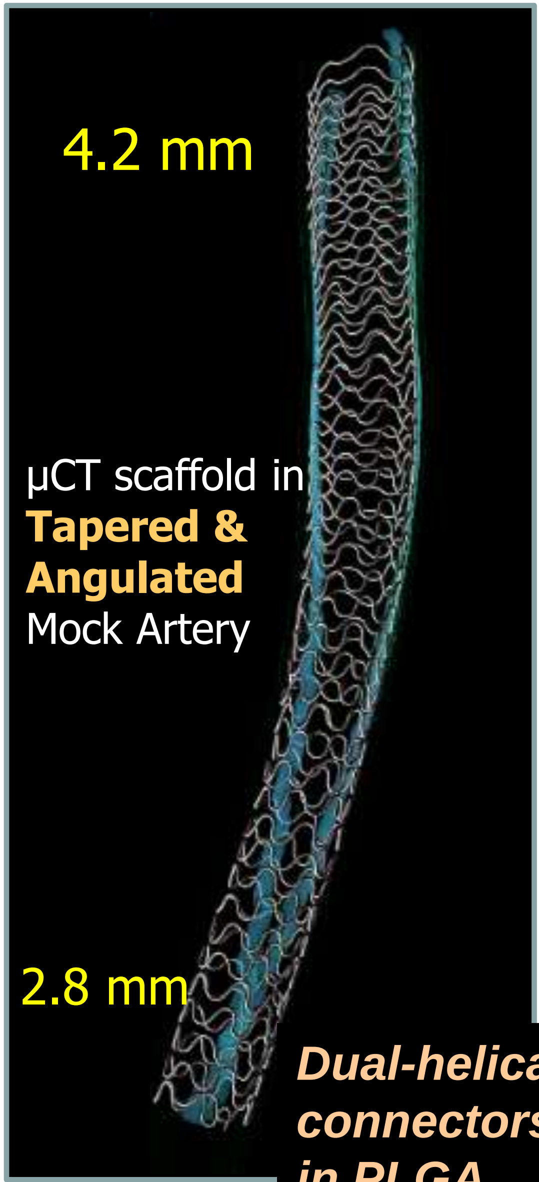






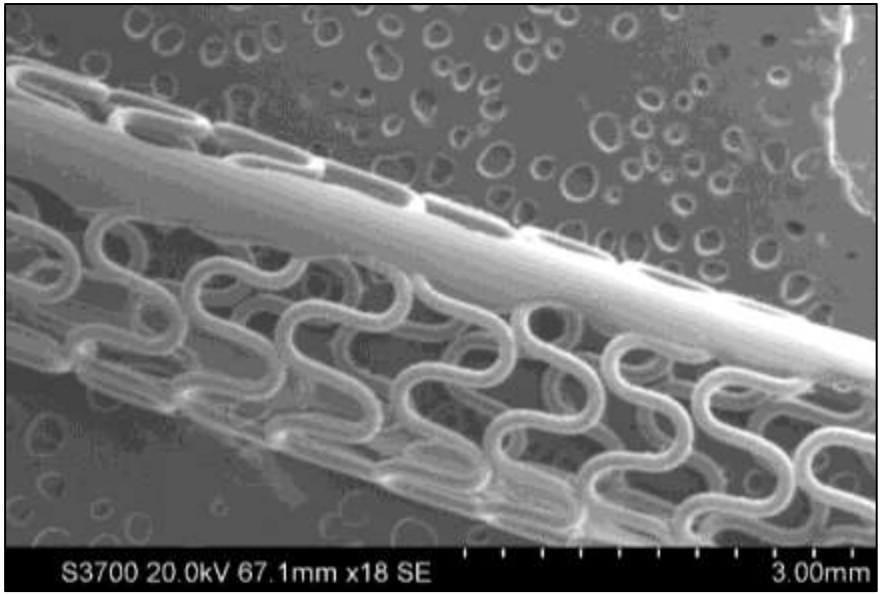
Waksman R et al. Circulation: Cardiovascular Interventions. 2017 Aug;10(8). e004762.

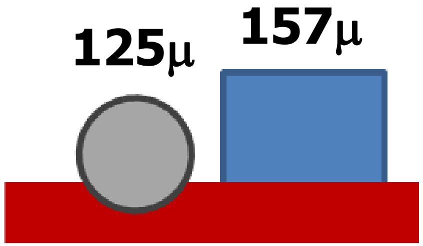
Hybrid Design of Proprietary Cold worked Mg Alloy without rare earth elements and with Dual-Helical connectors in PLGA: 125 µm Round Wire Struts



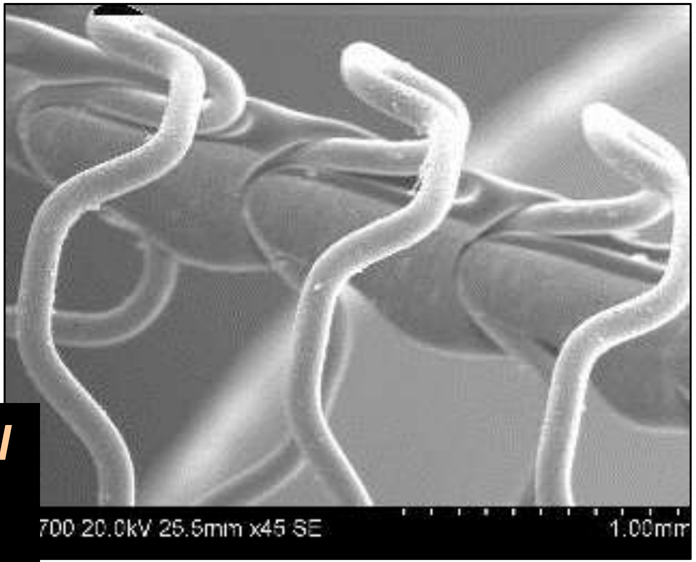
µCT scaffold in **Tapered & Angulated** Mock Artery

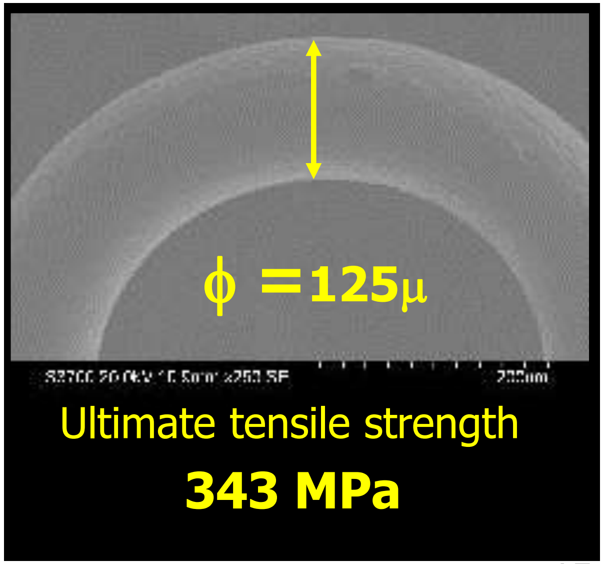
Dual-helical connectors in PLGA





Embedment Mg vs. ABSORB (TO SCALE)





Ultimate tensile strength

343 MPa

How improved scaffold technology can improve safety and efficacy

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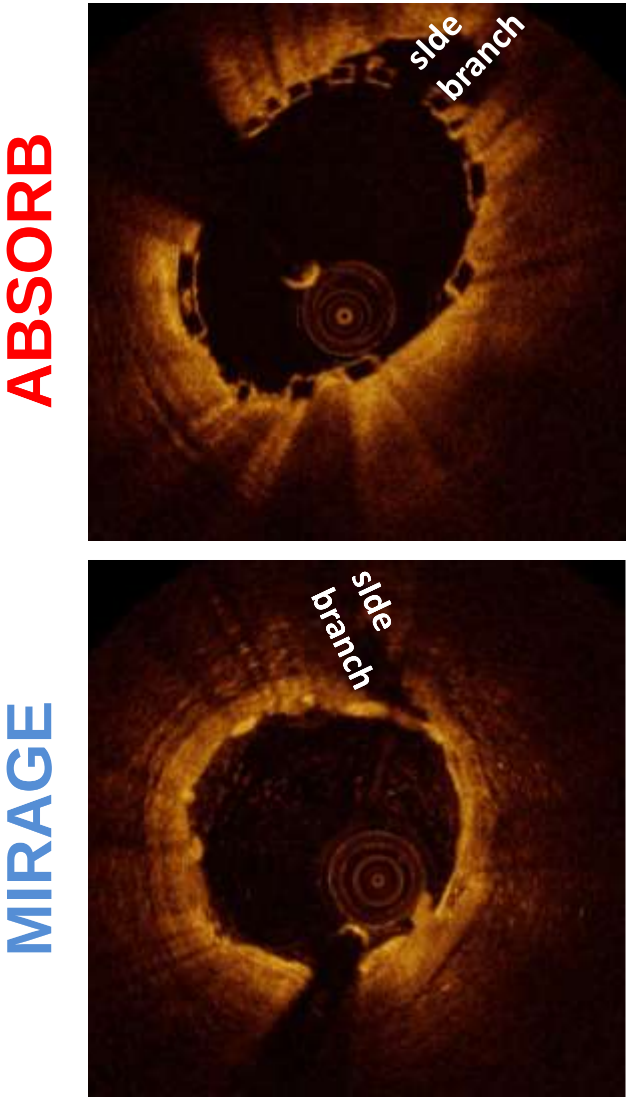
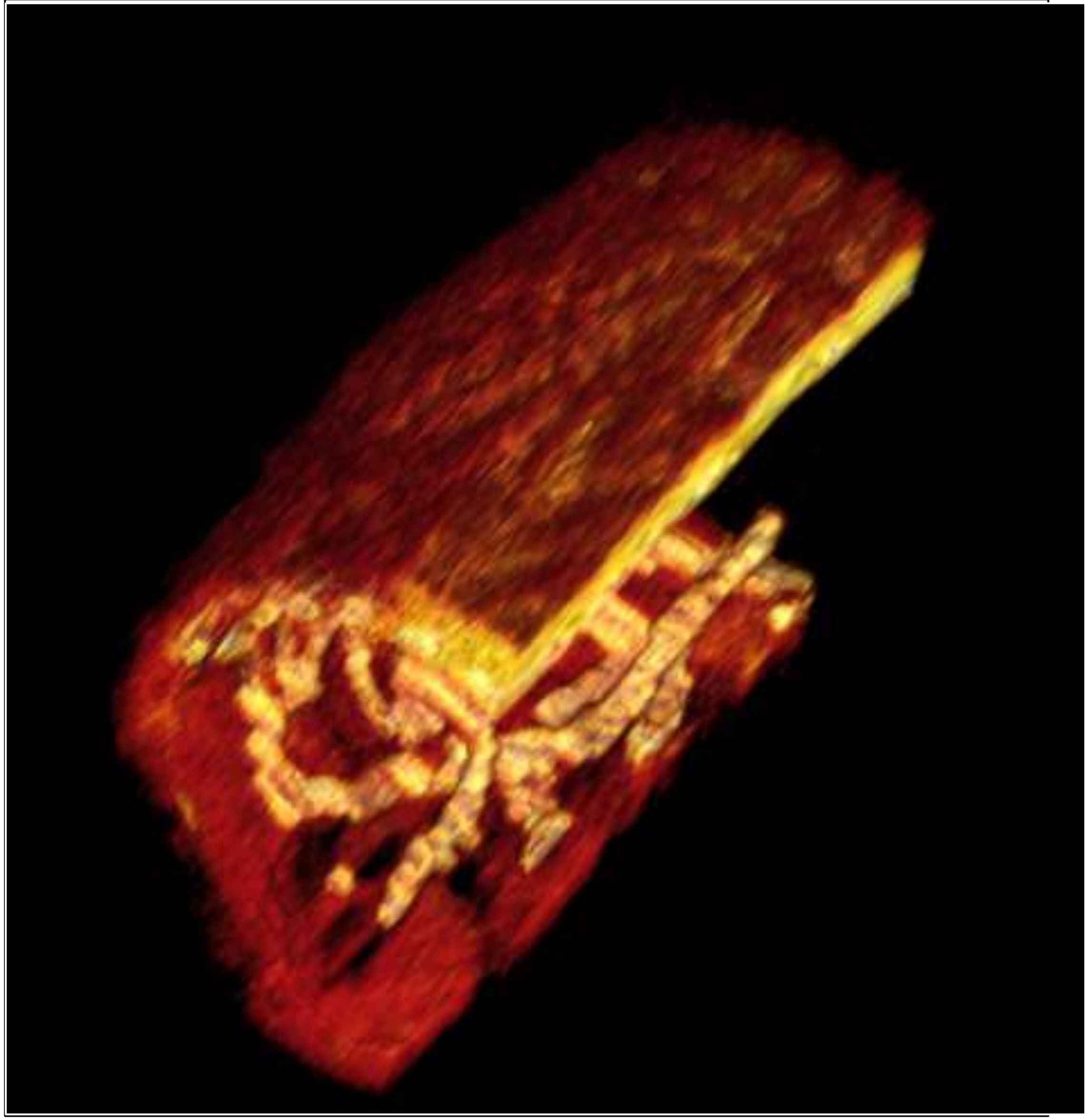
The rate of biodegradation has important impact on bioresorption and dismantling

Post-Procedure





JACC Cardiovascular Interventions

Tenekecioglu E, Serruys PW. JACC Cardiovasc Interv. 2017 Jun 12;10(11):1115-1130.

How to accelerate strut encapsulation in vessel wall and avoid the transient consequence of discontinuity???

- ✓ **Reducing the protrusion of the strut (stronger and thinner strut) -done-**

- ✓ **Better embedment of the struts -done-**

- ✓ **Changing the quadratic shape of the strut into a circular one -done-**

- ✓ **Faster Bioresorption without inducing an inflammatory vasculitis -major dilemma-**

… will result in fast tissue coverage and firm encapsulation of the struts into the vessel wall.

There is room for progress!

THANKS...

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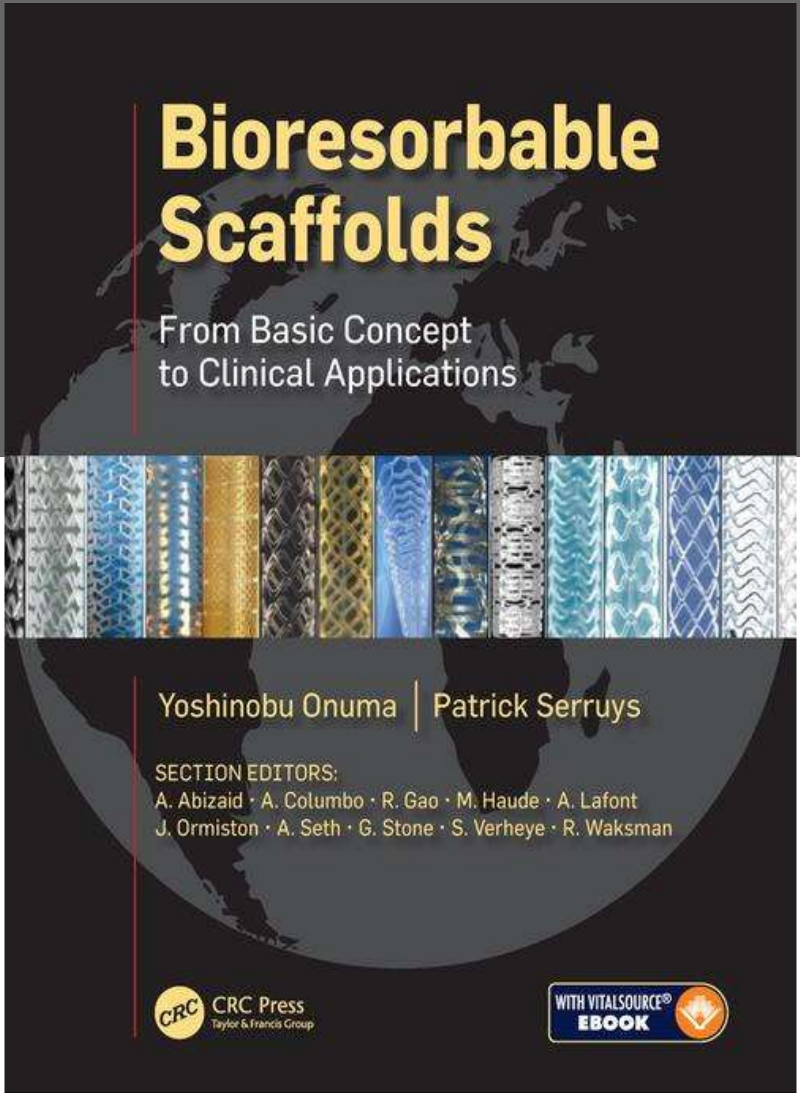
SCIENTIA
SCIENTIA IMPERII DECUS ET TUTAMEN



456pp, 750 illustrations, eBook: 978-1-498-77977-7

Bioresorbable Scaffolds

Edited by:

Patrick W.J.C. Serruys, Imperial College, Erasmus University
Yoshinobu Onuma, Erasmus University

TABLE OF CONTENTS:

- Introduction
- Principles of bioresorption, vascular application
- From bench test to preclinical assessment
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- Clinical evidence of randomised and non randomised trials
- Clinical evidence in specific patient subsets - personal perspective
- Complications (incidence, diagnosis, potential mechanisms and treatment)
- Tips and tricks to implant BRS
- Emerging technologies (Pre-CE mark, Pre FDA, pre PMDA and pre CFDA)

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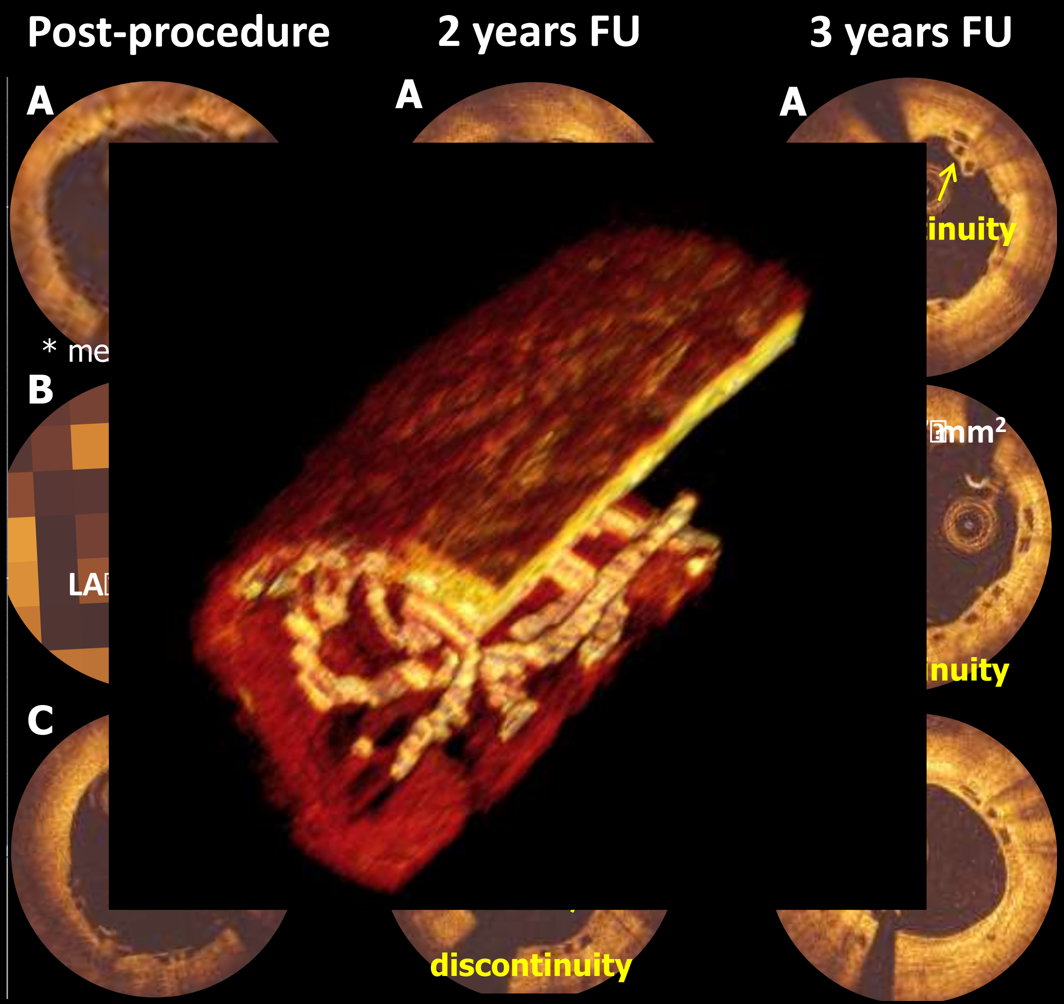
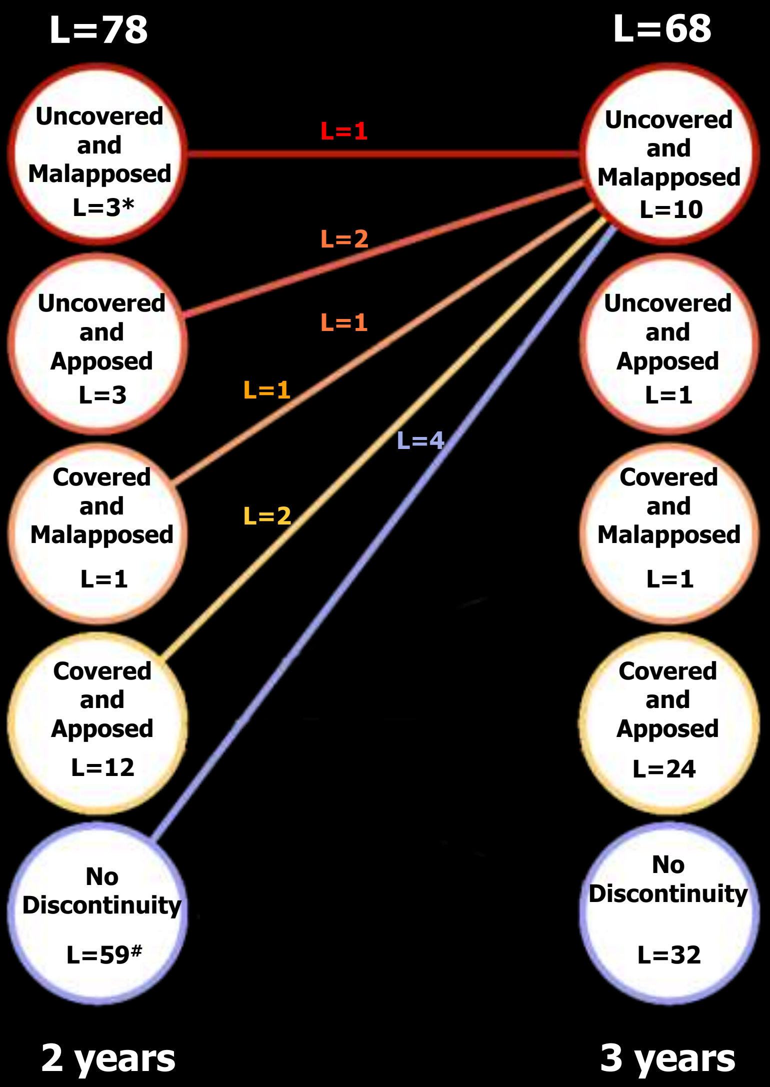
www.crcpress.com/9781498779746

Frequency of late discontinuities between 2 and 3 years (truly serial analysis at lesion level)

-by courtesy of Prof. Kimura





L=78

Uncovered and Malapposed
L=3*

Uncovered and Apposed
L=3

Covered and Malapposed
L=1

Covered and Apposed
L=12

No Discontinuity
L=59#

2 years

L=68

Uncovered and Malapposed
L=10

Uncovered and Apposed
L=1

Covered and Malapposed
L=1

Covered and Apposed
L=24

No Discontinuity
L=32

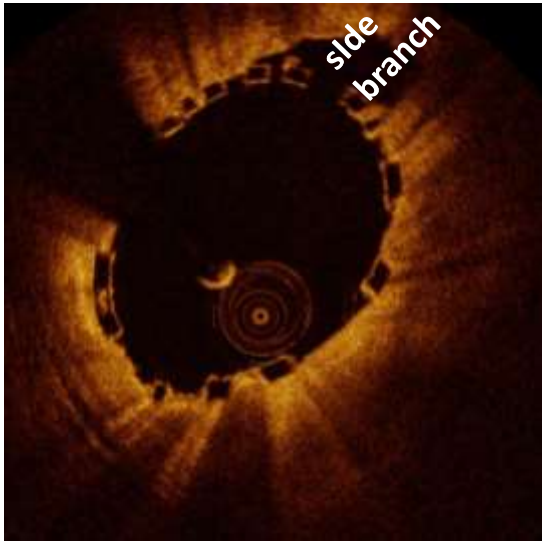
3 years

* Two lesions were not analyzable at 3 years. # Eight lesions were not analyzable at 3 years.

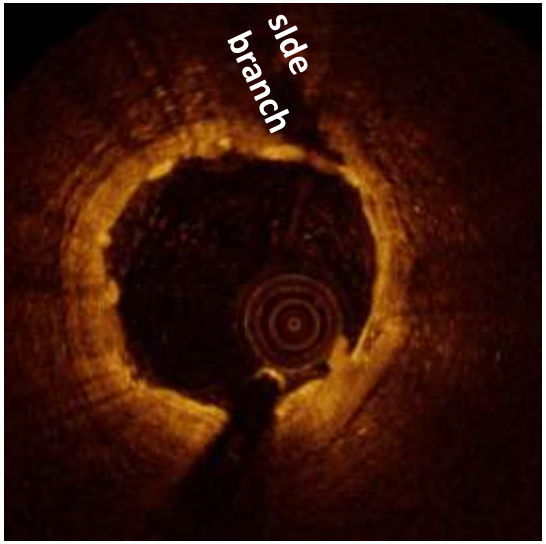
The rate of biodegradation has important impact on bioresorption and dismantling

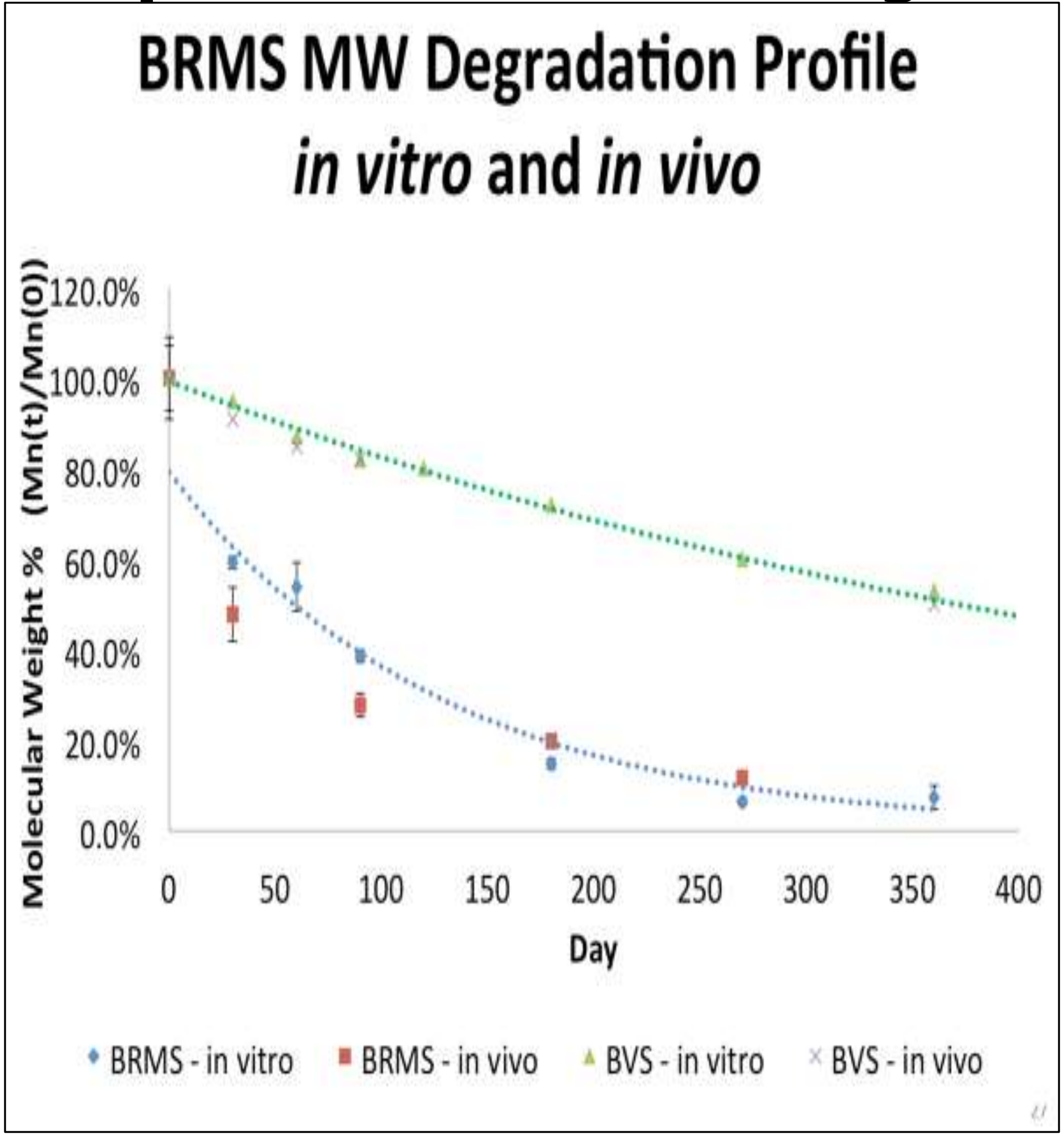
Post-Procedure

ABSORB



MIRAGE





Tenekecioglu E, Serruys PW. JACC Cardiovasc Interv. 2017 Jun 12;10(11):1115-1130.

Back up slides

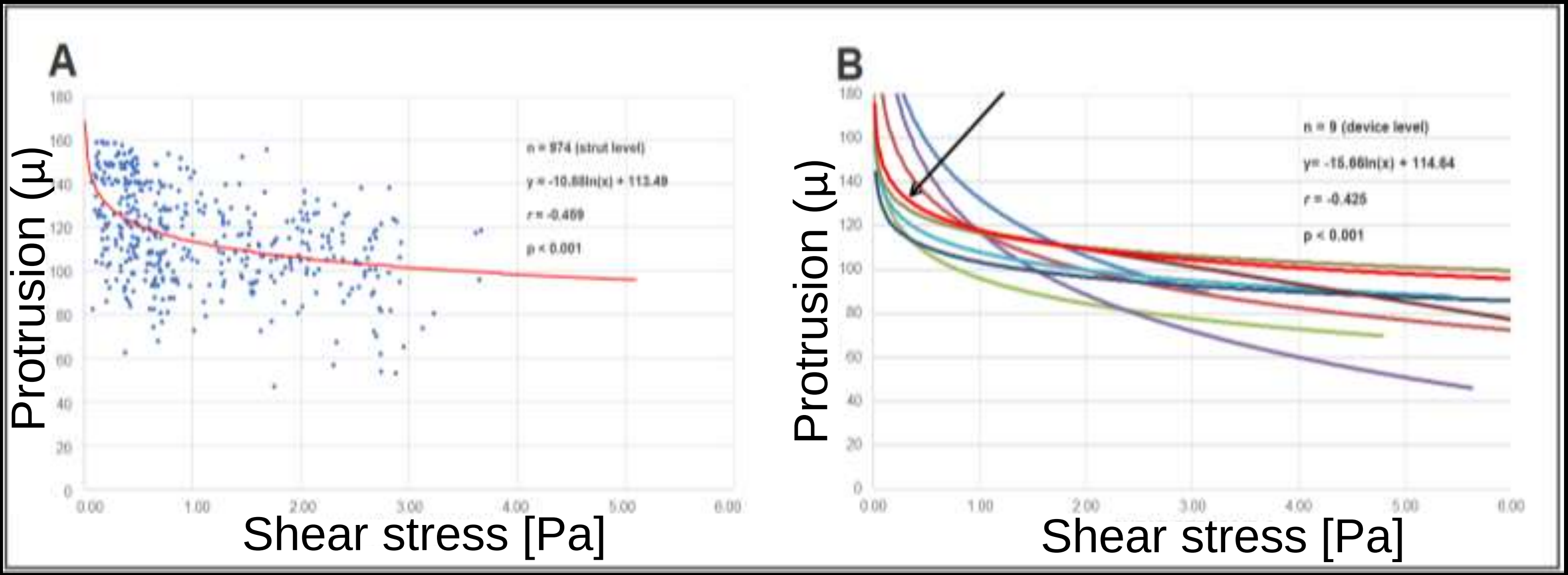
Disclosure Statement of Financial Interest

Patrick W. Serruys, MD. PhD.

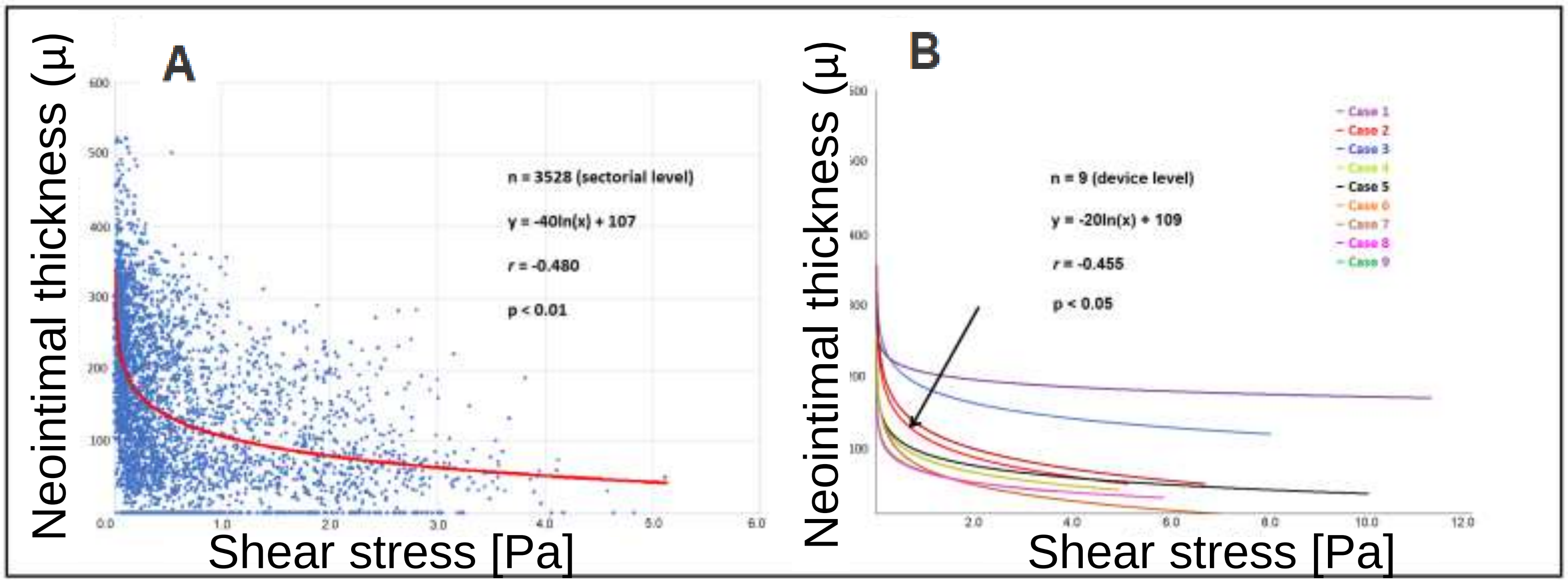
Consulting fees and honoraria from:

- Arterius, Biosensors, Medtronic, Micell Technologies, Sinomed, Philips/Volcano and Xeltis.

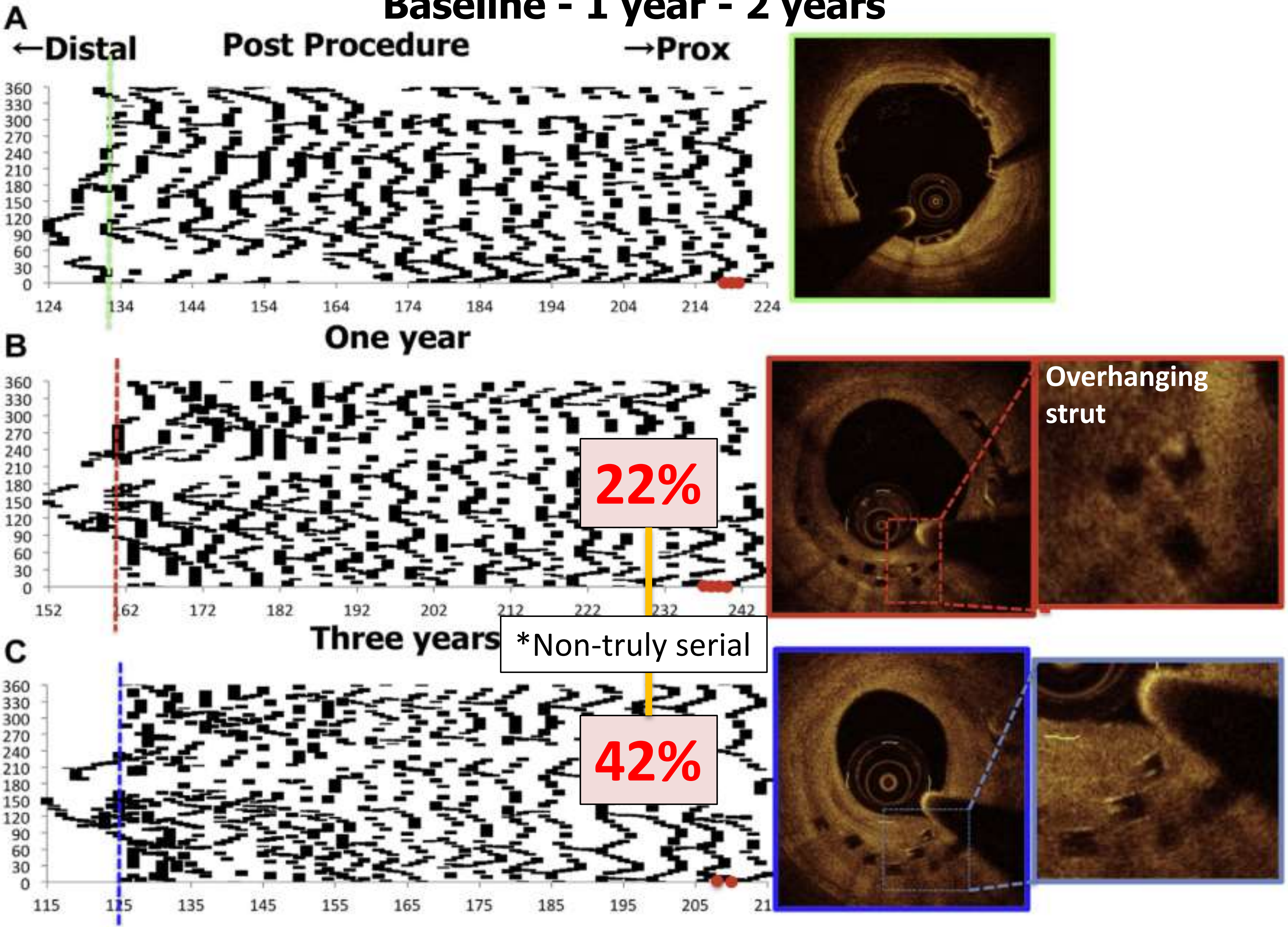
INVERSE RELATIONSHIP BETWEEN STRUT PROTRUSION AND SHEAR STRESS IN ABSORB BIORESORBABLE SCAFFOLD



INVERSE RELATIONSHIP SHEAR STRESS AND NEOINTIMAL THICKNESS IN ABSORB BIORESORBABLE SCAFFOLD



Late discontinuities of a scaffold in human on OCT 2D-3D
Baseline - 1 year - 2 years



22%

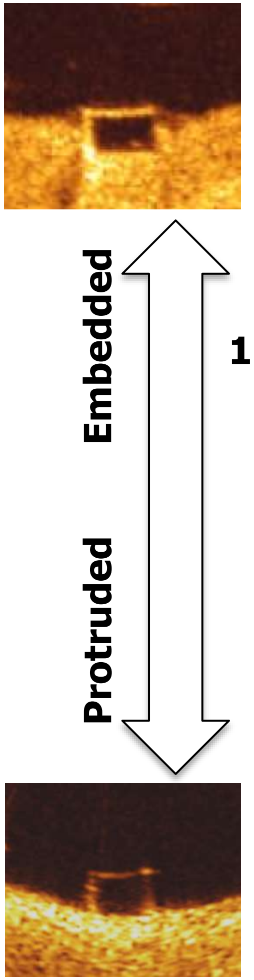
*Non-truly serial

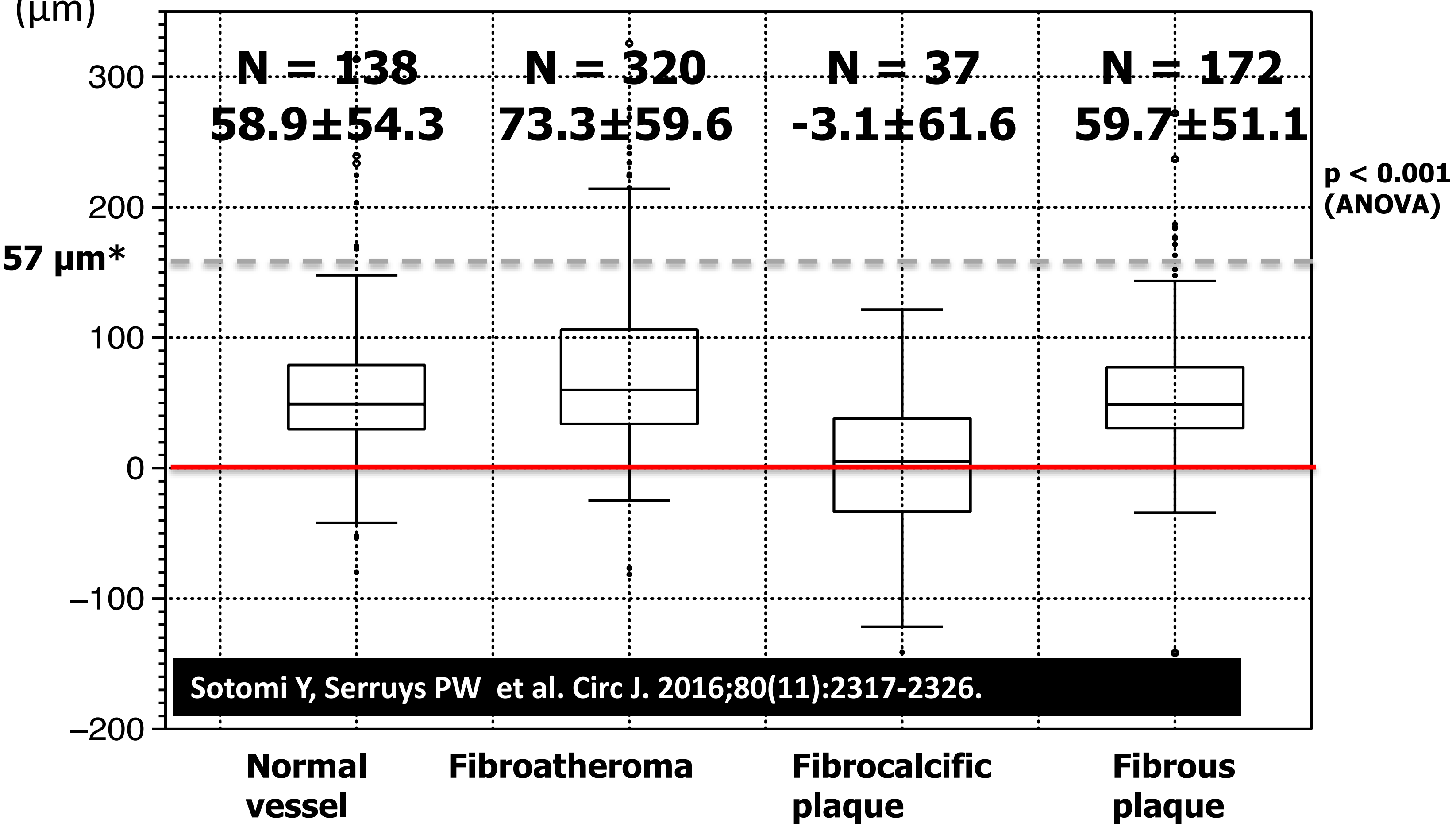
42%

Onuma, Serruys, et al. JACC Cardiovasc Interv. 2014;7(12):1400-11.

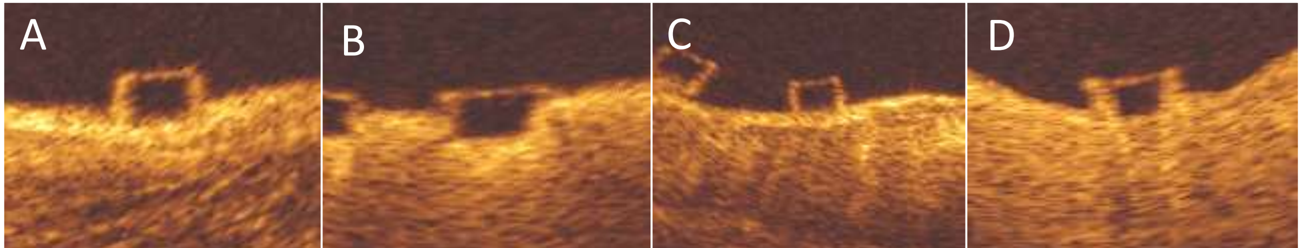
Embedment depth stratified by underlying plaque type in Absorb Japan

Only Absorb BVS arm: L = 79 / Strut N= 667





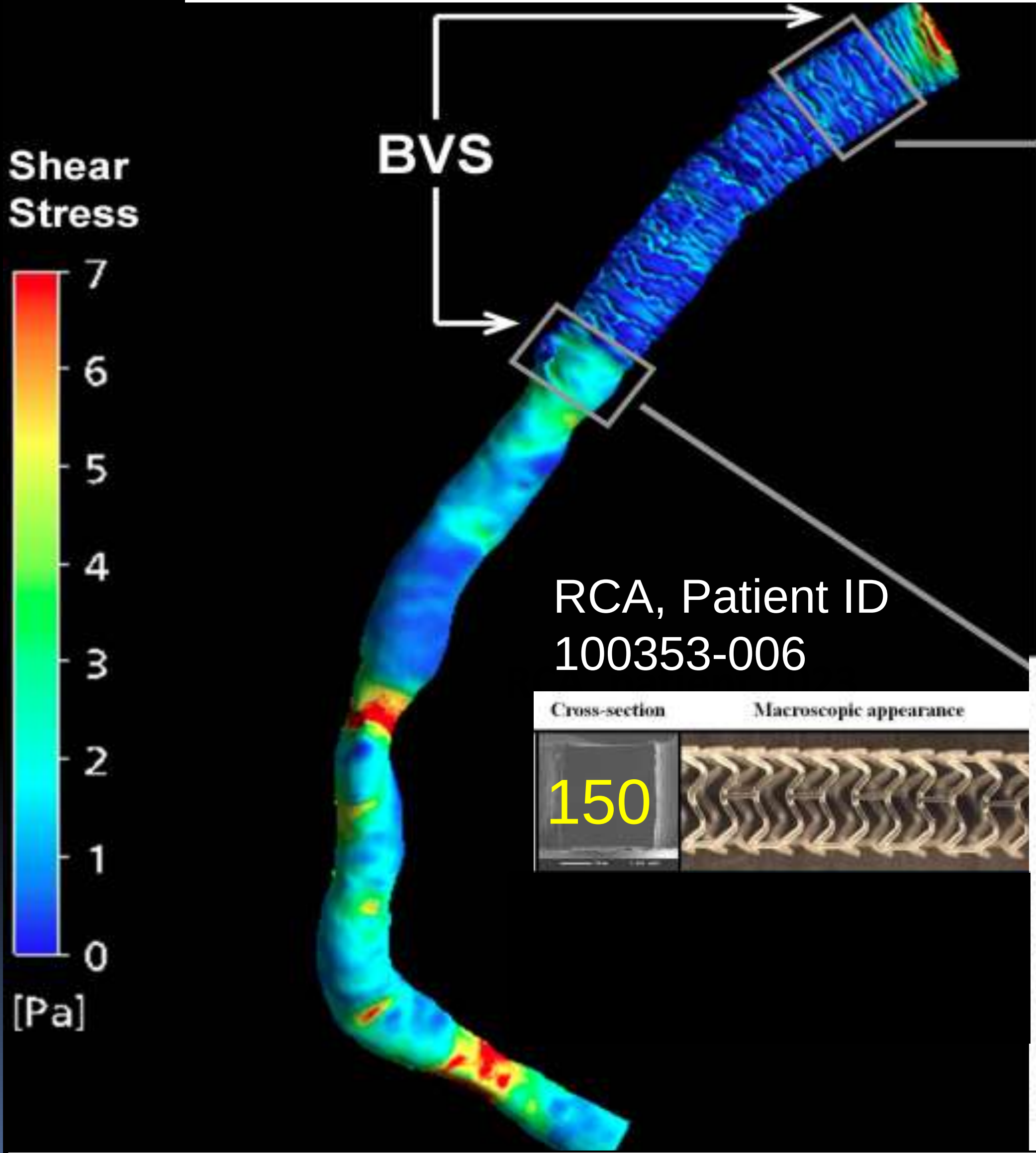
Sotomi Y, Serruys PW et al. Circ J. 2016;80(11):2317-2326.



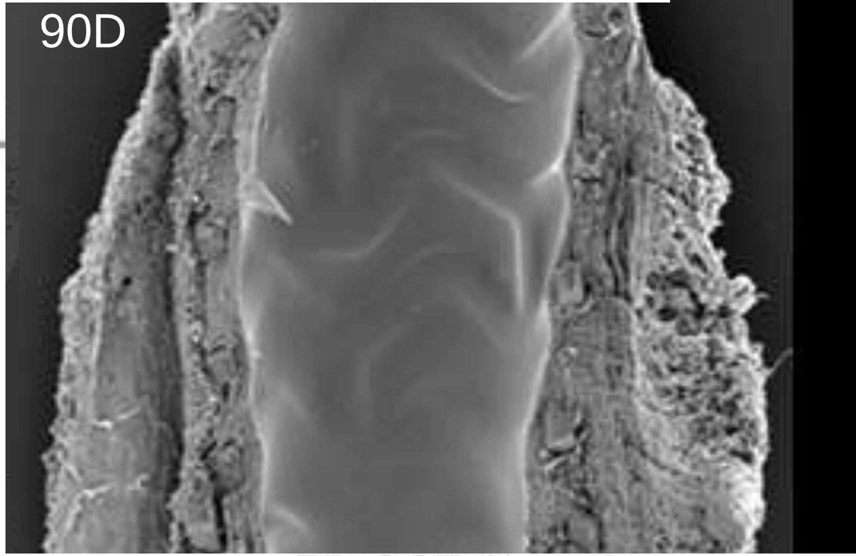
*strut thickness of BVS

Thick strut shear stress determinant of neointimal thickness and LA reduction

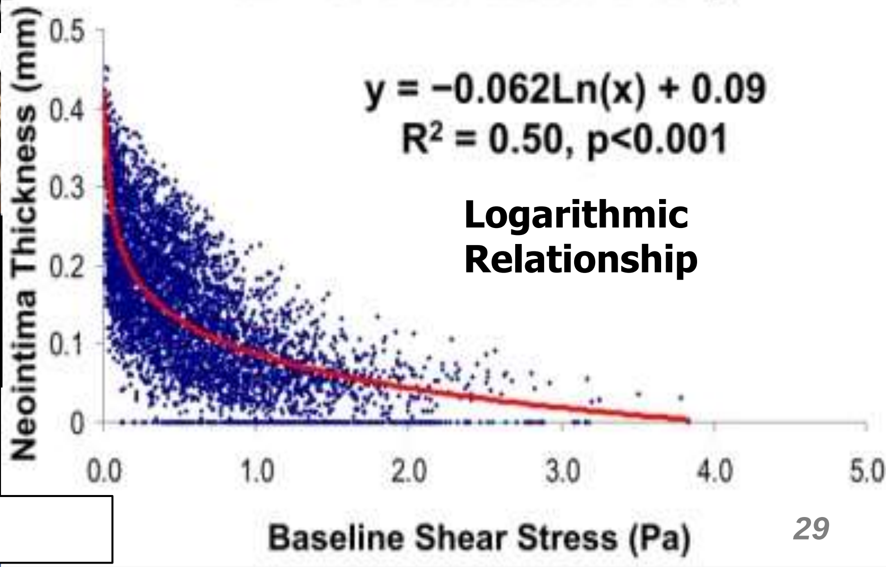
Biplane Angiography and FD-OCT (Terumo): 3D reconstruction of RCA with BVS



RCA, Patient ID 100353-006



FD-OCT–based 3D reconstructed artery



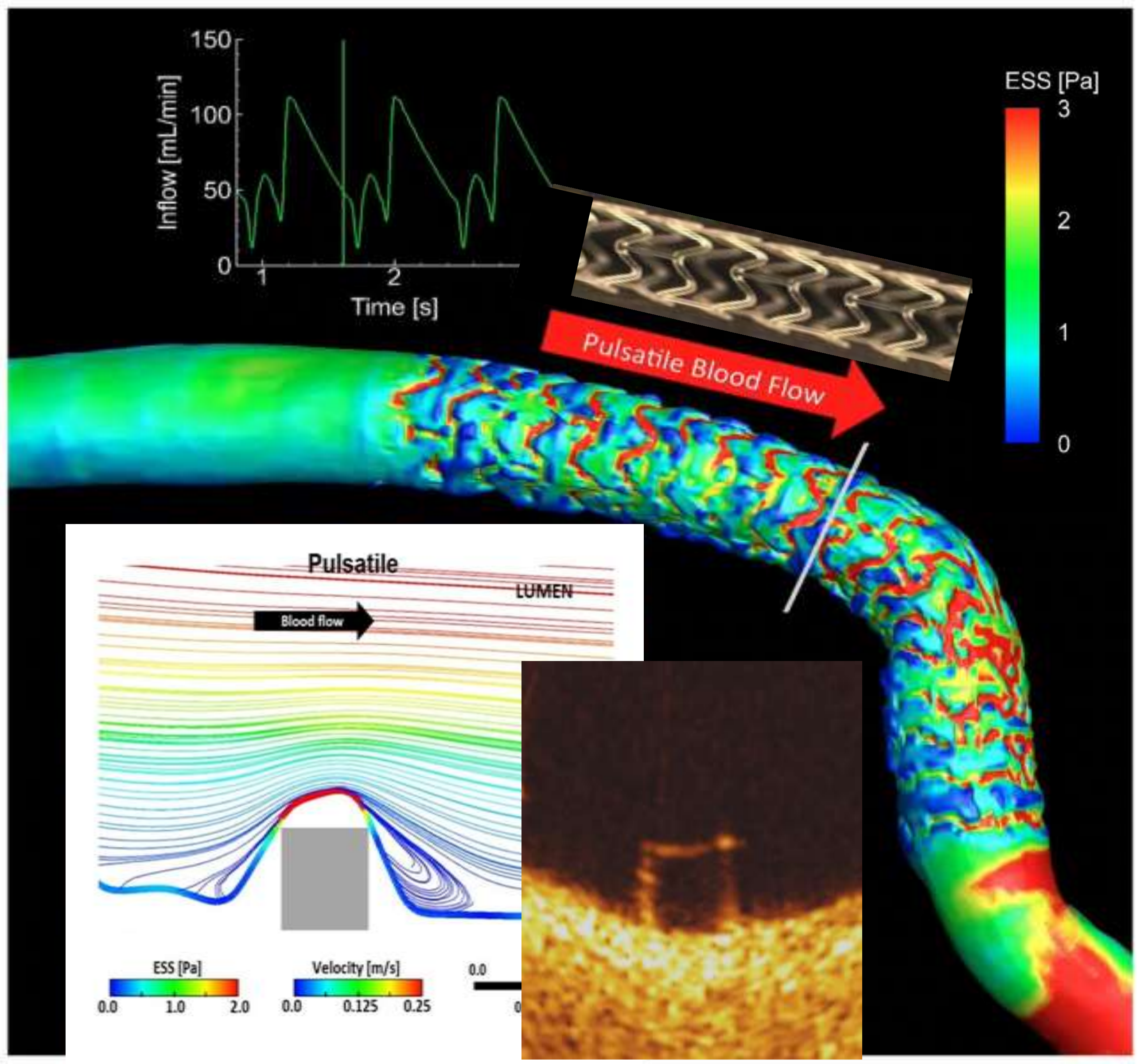
$y = -0.062\mathrm{Ln}(x) + 0.09$

$R^2 = 0.50$, $p<0.001$

Logarithmic Relationship

Bourantas, Serruys et al. JACC Cardiovasc Interv. 2014;7:100-1.

Fusion of Angio and OCT, pulsatile flow, non-Newtonian shear stress immediately after Absorb implantation in a human being

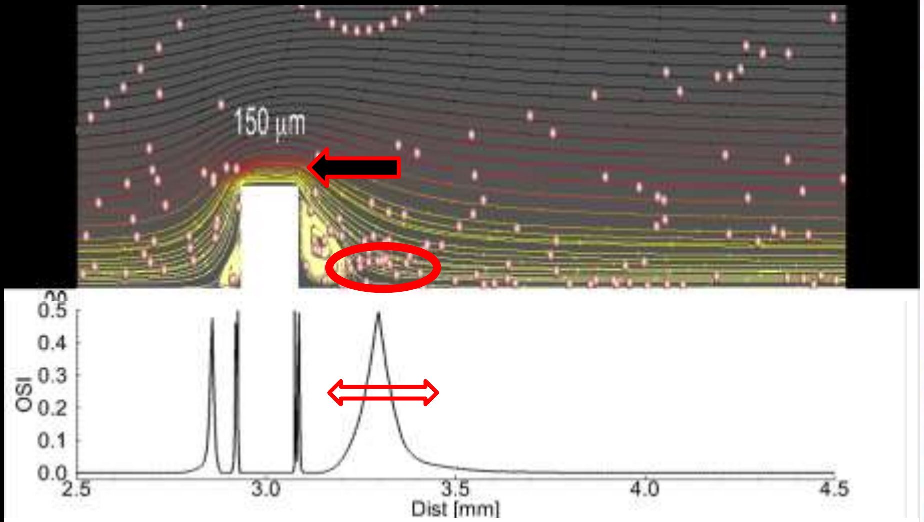


Tenekecioglu E, Poon E, et al. Serruys PW.
The Nidus for Possible Thrombus Formation: Insight From the Microenvironment of Bioresorbable Vascular Scaffold.
JACC Cardiovasc Interv. 2016 Oct 24;9(20): 2167-2168.

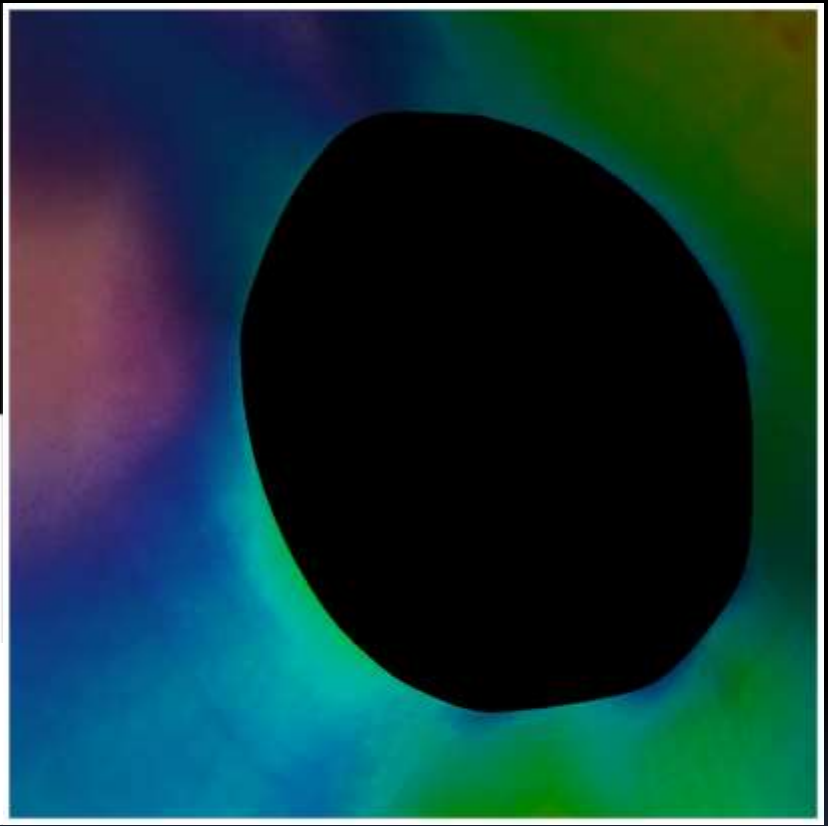
Tenekecioglu E, Serruys PW et al.
Assessment of the hemodynamic characteristics of Absorb BVS in a porcine coronary artery model.
Int J Cardiol. 2017 Jan 15; 227:467-473.

Pulsaltile Non-Newtonian (cell tracking)
Shear stress and Viscosity in early systole

Navier Stokes (ESS) and Quemada (viscosity) equations



High Oscillatory Shear Index (OSI)

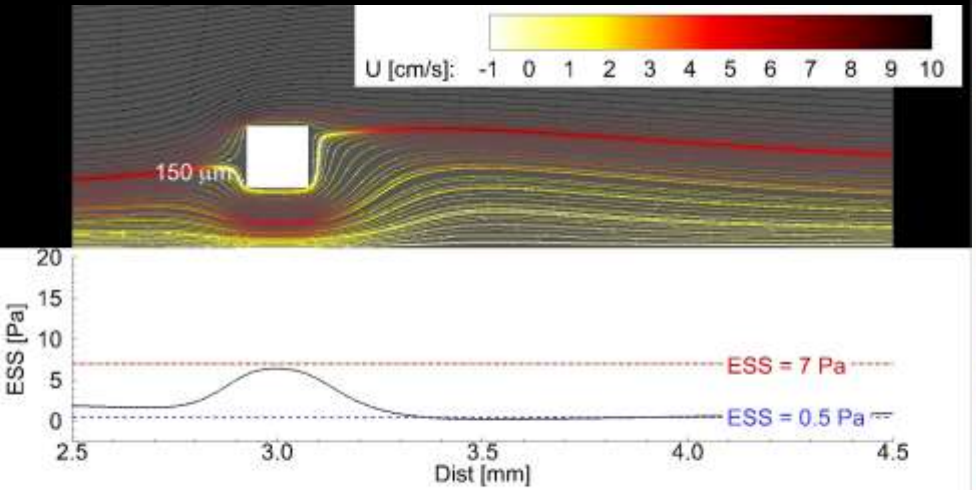


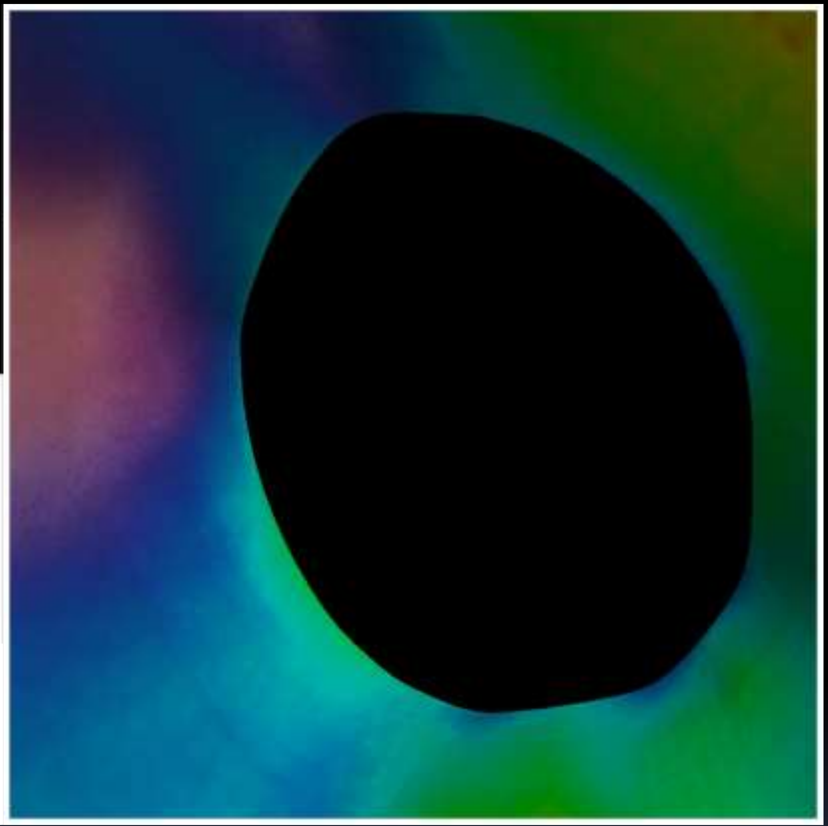
- **Pink fuzzy areas are regions with low shear stress and high viscosity**

Thondapu V et al, Serruys PW. Endothelial shear stress 5 years after implantation of a coronary bioresorbable scaffold. Eur Heart J. 2018 Feb 2.[Epub ahead of print]

Non-Newtonian (cell tracking) shear stress and viscosity in early systole

Navier Stokes (ESS) and Quemada (viscosity) equations





- **Pink fuzzy areas are regions with low shear stress with high viscosity**

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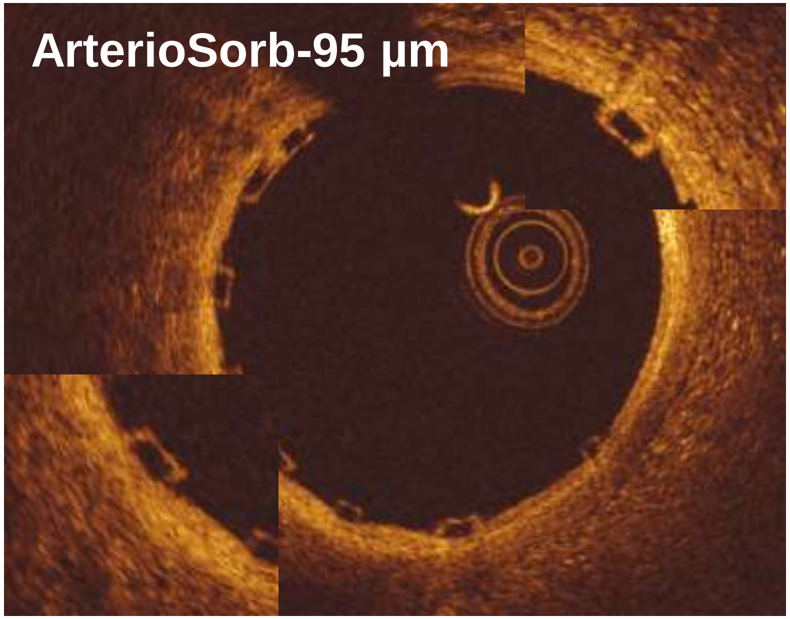
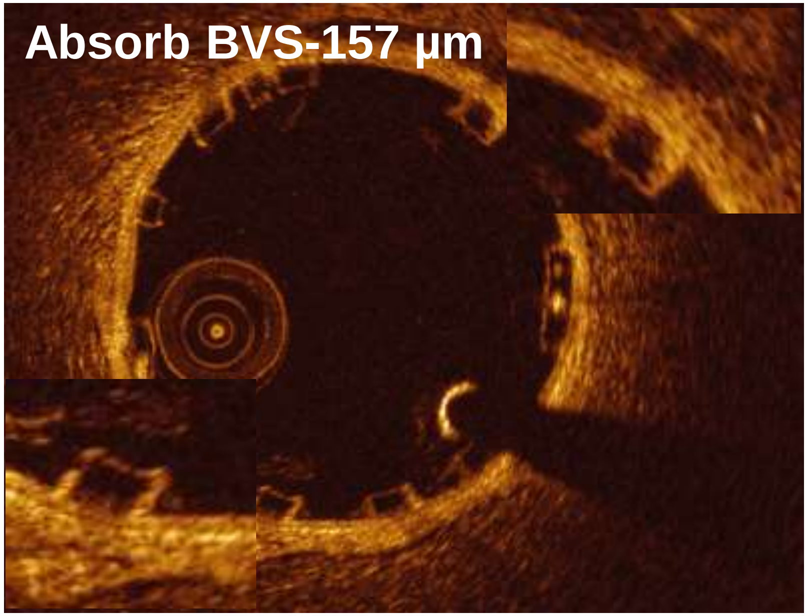
Oriented polylactide, stronger and thinner strut Reducing the protrusion without increase of recoil

ArterioSorb from Arterius
(Profile: 1.22 mm)
Protrusion distance: 89±7 µm



Absorb BVS from Abbott
(Profile: 1.43 mm)
Protrusion distance: 150±9 µm



	After device deployment			After post-dilatation (PD) A: **19.24**±4.80 atm X: **18.42**±4.56 atm		
Scaffold	Device balloon-artery ratio	Mean lumen diameter (mm)	Acute recoil (%)	PD balloon-artery ratio	Mean lumen diameter (mm)	Acute recoil (%)
Arteriosorb-95 (n=25)	1.09±0.11	2.87±0.30	4.69±7.38	1.11±0.09	2.99±0.16	2.65±3.81
Xience (n=15)	1.12±0.11	2.94±0.17	2.70±4.52	1.14±0.10	3.06±0.13	1.06±4.13

Courtesy of Dr. Onuma, Rasha Al-Lamee, Guy Leclerc (AccelLAB, Montreal)