# What comes next?
# Newer-generation bioresorbable scaffold: Insights from shear stress simulations

**Patrick W. Serruys MD, PhD Imperial College, London, United Kingdom**

**Yoshi Onuma, MD,PhD Erasmus MC, Rotterdam, The Netherlands**

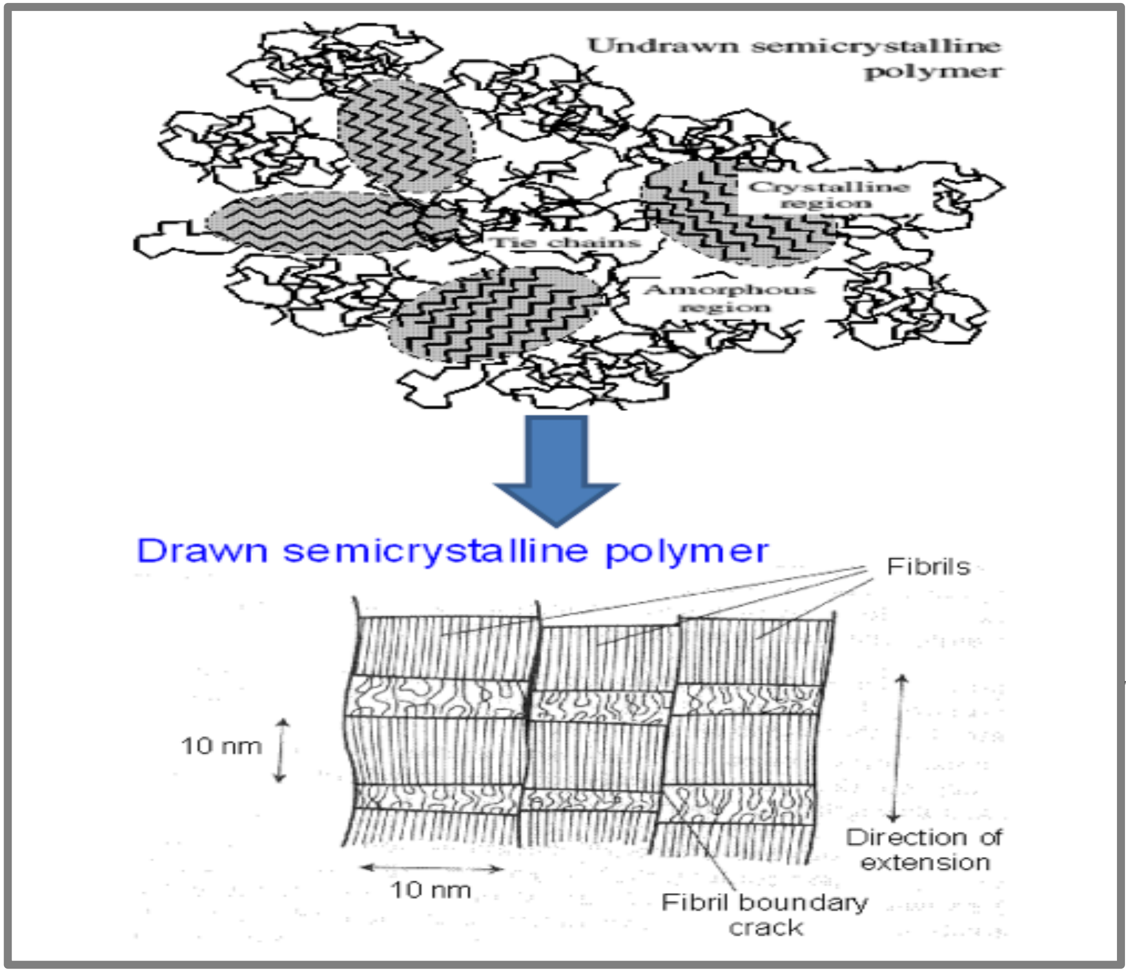
**17:15-18:20**

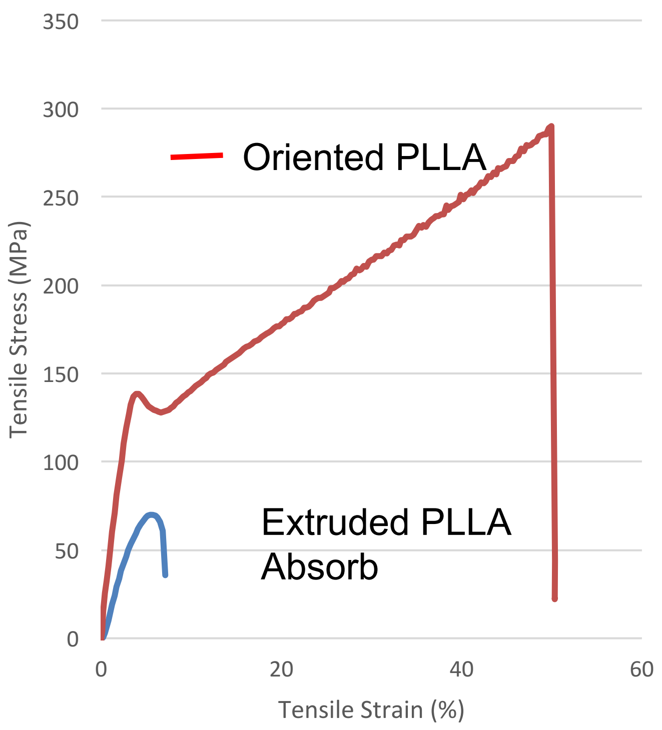
**Friday October 13th**

# How improved scaffold technology can reduce clinical complication?

| Shortcomings | Possible solution |
|---|---|
| ○ Low tensile strength, low radial force, recoil <><br>○ thick strut, wide footprint | • Increase tensile strength, good radial force -> thin strut (oriented PLLA, Arterius technology) |
| ○ Quadratic strut<br>○ Difficult to embed<br>○ Disturb laminar flow | • Circular strut (Manli technology)<br>• Easy to embed<br>• Less disturbance of laminar flow |
| ○ Increase local viscosity and thrombogenicity<br>○ Main determinant of neointimal thickness and LA reduction | • Use of biodegradable material non-thrombogenic: Magnesium |
| ○ Slow down the cell coverage | • Circular strut |
| ○ Late structural discontinuity (dismantling) | • Faster bioresorption (Manli technology) |

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



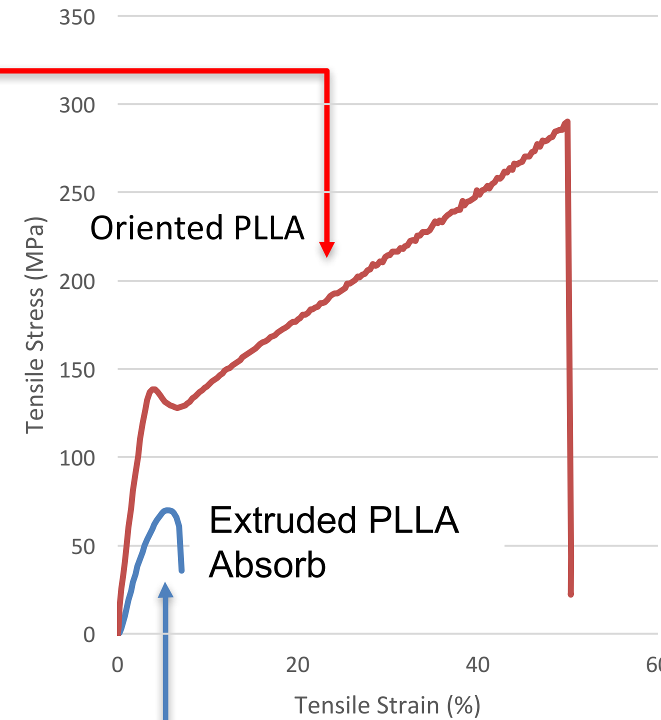

- **Tube wall thickness of < 95 µm and even < 75 microns can be achieved**
- **Scaffold tube thickness comparable to metallic DES**

University of Southampton

ARTERIUS

# 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 | 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 |



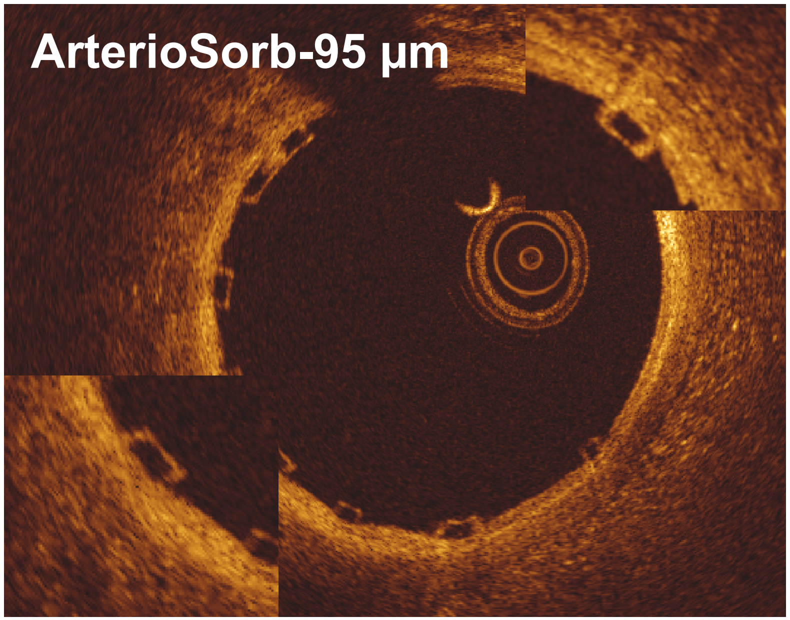

- ➢ Tube wall thickness of < 95 µm and even < 75 microns can be achieved
- ➢ **Scaffold tube thickness comparable to metallic DES**

UNIVERSITY OF Southampton

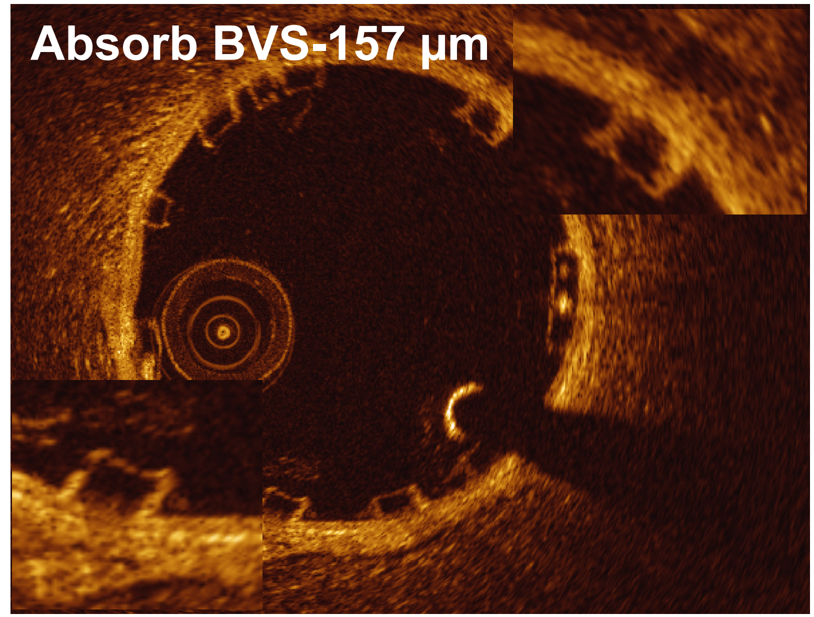
ARTERIUS

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

**ArterioSorb from Arterius**
**Protrusion distance: 89±7 µm**



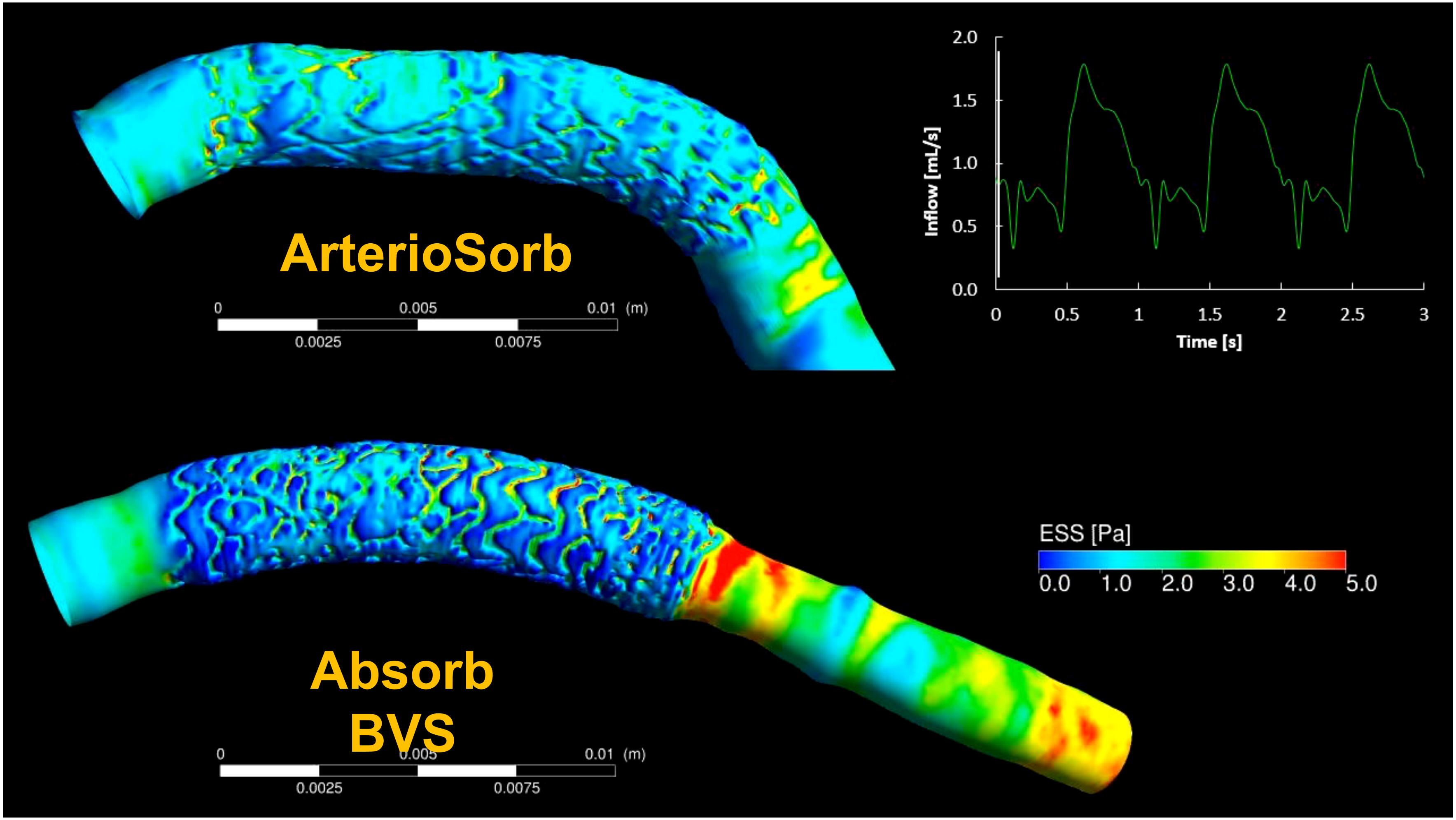

**Absorb BVS from Abbott**
**Protrusion distance: 150±9 µm**




| Scaffold | Lumen diameter (mm) | Balloon-artery ratio | Scaffold-artery ratio | Acute recoil (%) |
|---|---|---|---|---|
| Arteriosorb-95 (n=31) | 2.91±0.17 | 1.10±0.06 | 1.06±0.05 | 3.01±5.06 |

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

# Reduced struts protrusion , reduces low-shear stress (dark-blue color), reduces risk of thrombus peri-strut




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 ehx358. doi: 10.1093/eurheartj/ehx358

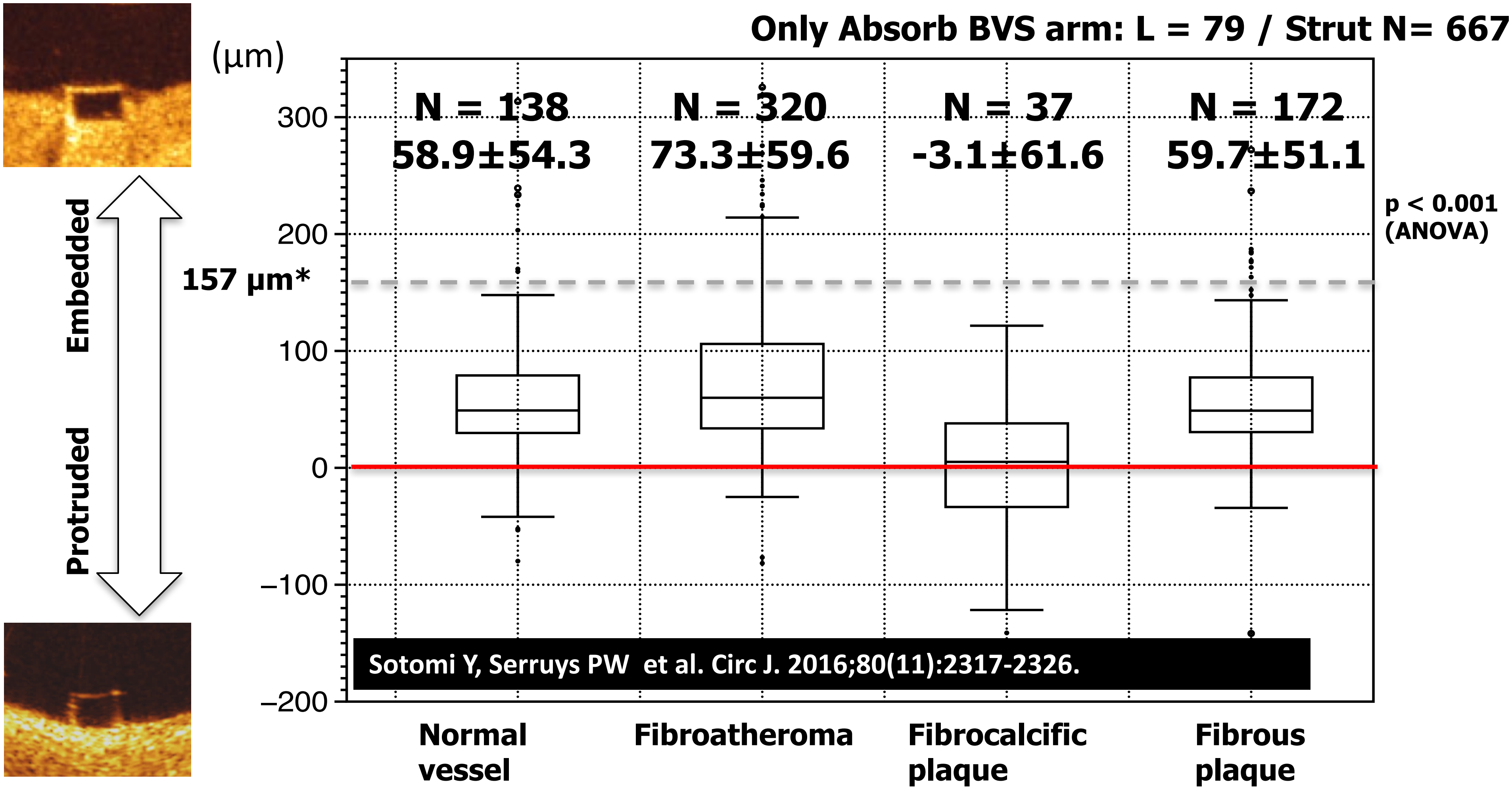
THE UNIVERSITY OF MELBOURNE

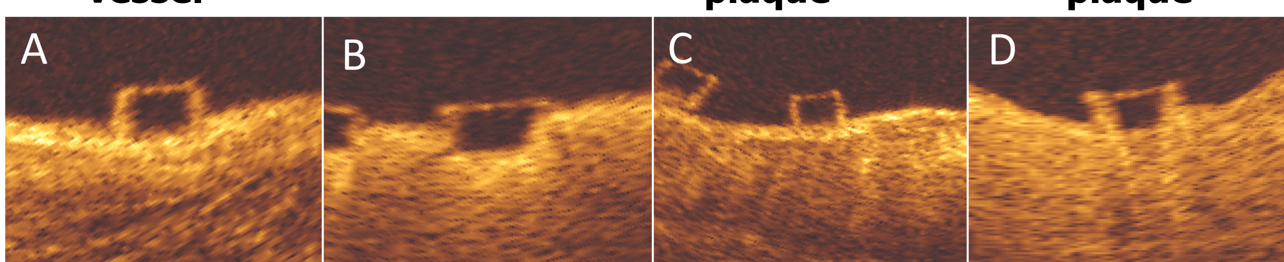
Erasmus MC

# How improved scaffold technology can reduce clinical complication?

| Shortcomings | Possible solution |
|---|---|
| ○ Low tensile strength, low radial force, recoil <><br>○ thick strut, wide footprint | • Increase tensile strength, good radial force -> thin strut (oriented PLLA, Arterius technology) |
| ○ Quadratic strut<br>○ Difficult to embed<br>○ Disturb laminar flow | • Circular strut (Manli technology)<br>• Easy to embed<br>• Less disturbance of laminar flow |
| ○ Increase local viscosity and thrombogenicity<br>○ Main determinant of neointimal thickness and LA reduction | • Use of biodegradable material non-thrombogenic: Magnesium |
| ○ Slow down the cell coverage | • Circular strut |
| ○ Late structural discontinuity (dismantling) | • Faster bioresorption (Manli technology) |

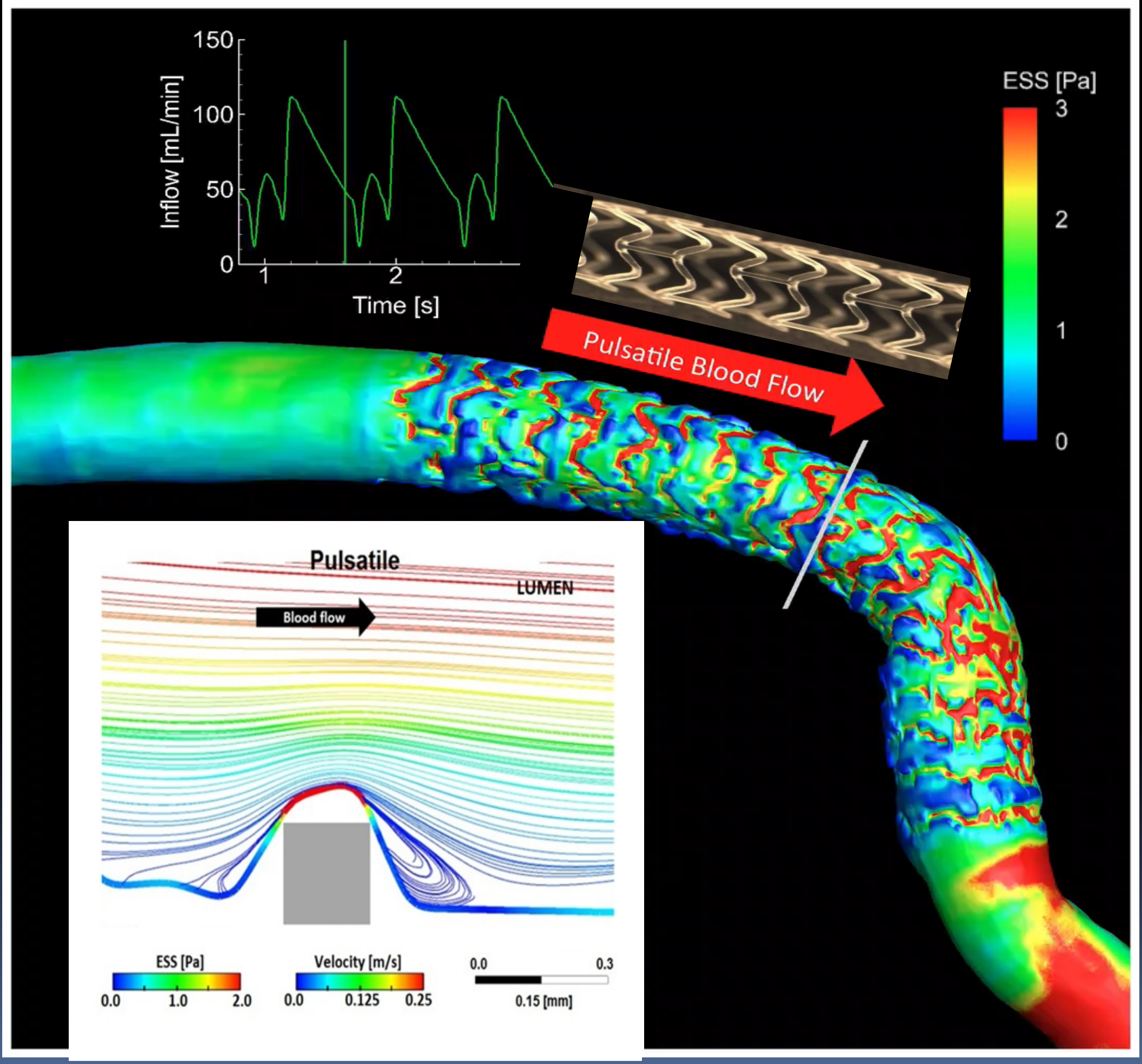
# Embedment depth stratified by underlying plaque type




*strut thickness of BVS

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

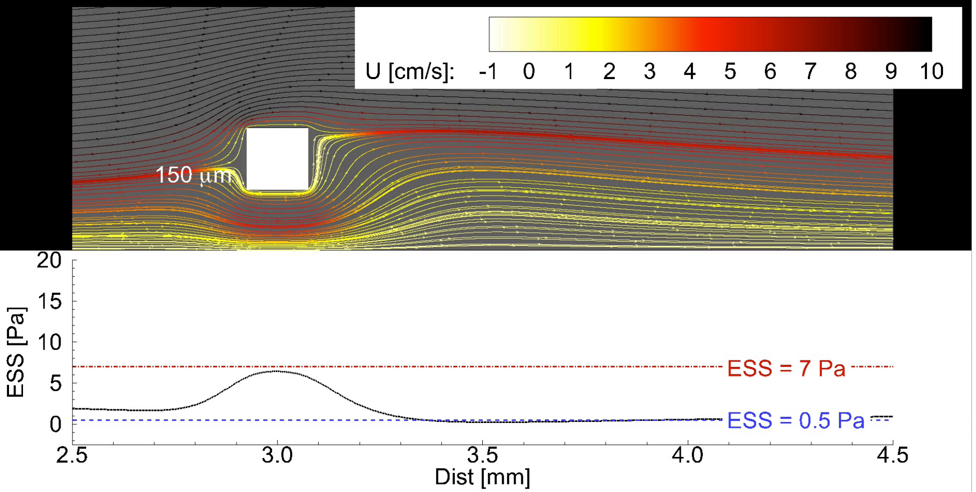


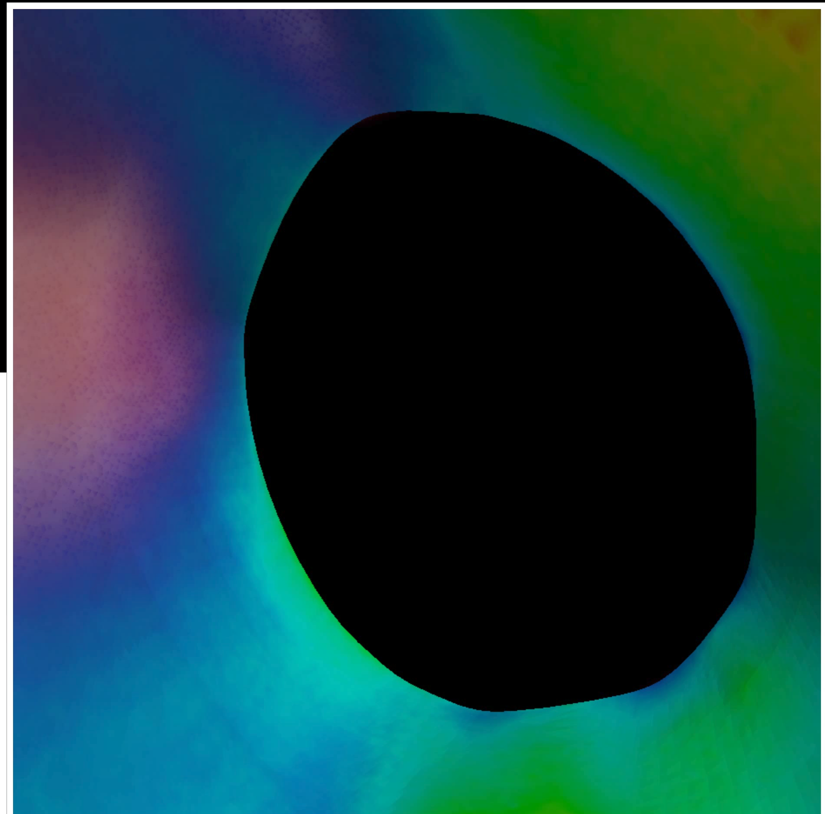

**Tenekecioglu E, Poon E, et al. Serruys PW.**
**The Nidus for Possible Thrombus Formation: Insight From the Microenvironment of Bioresorbable Vascular Scaffold.**
JACC Cardiovasc Interv. 2016 Oct 24;9(20): 2167-2168.

**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.

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

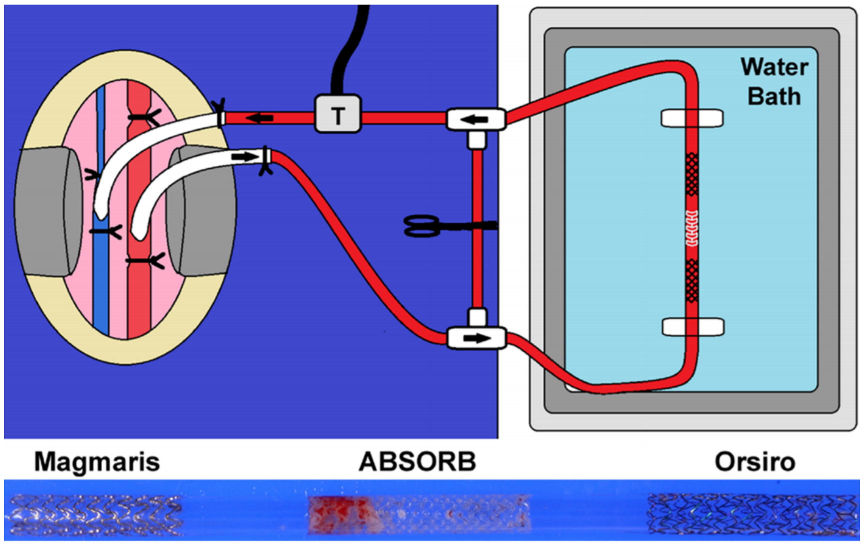
## Navier Stokes (ESS) and Quemada (viscosity) equations

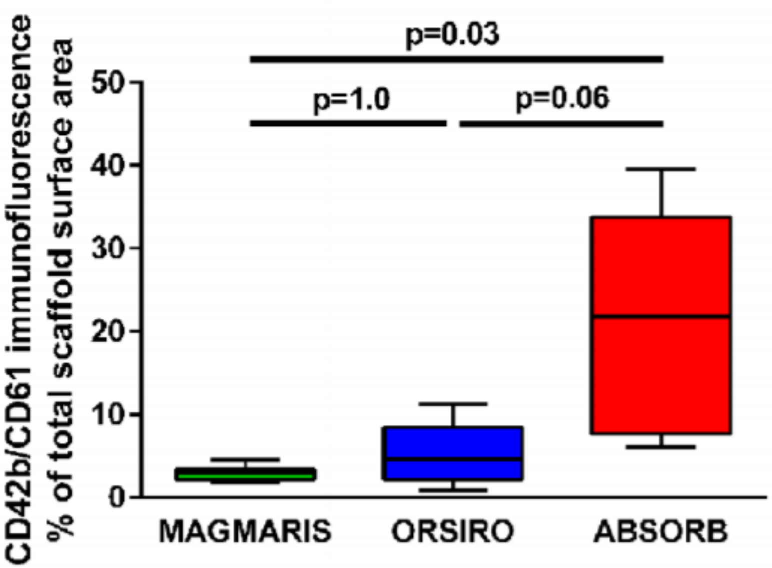


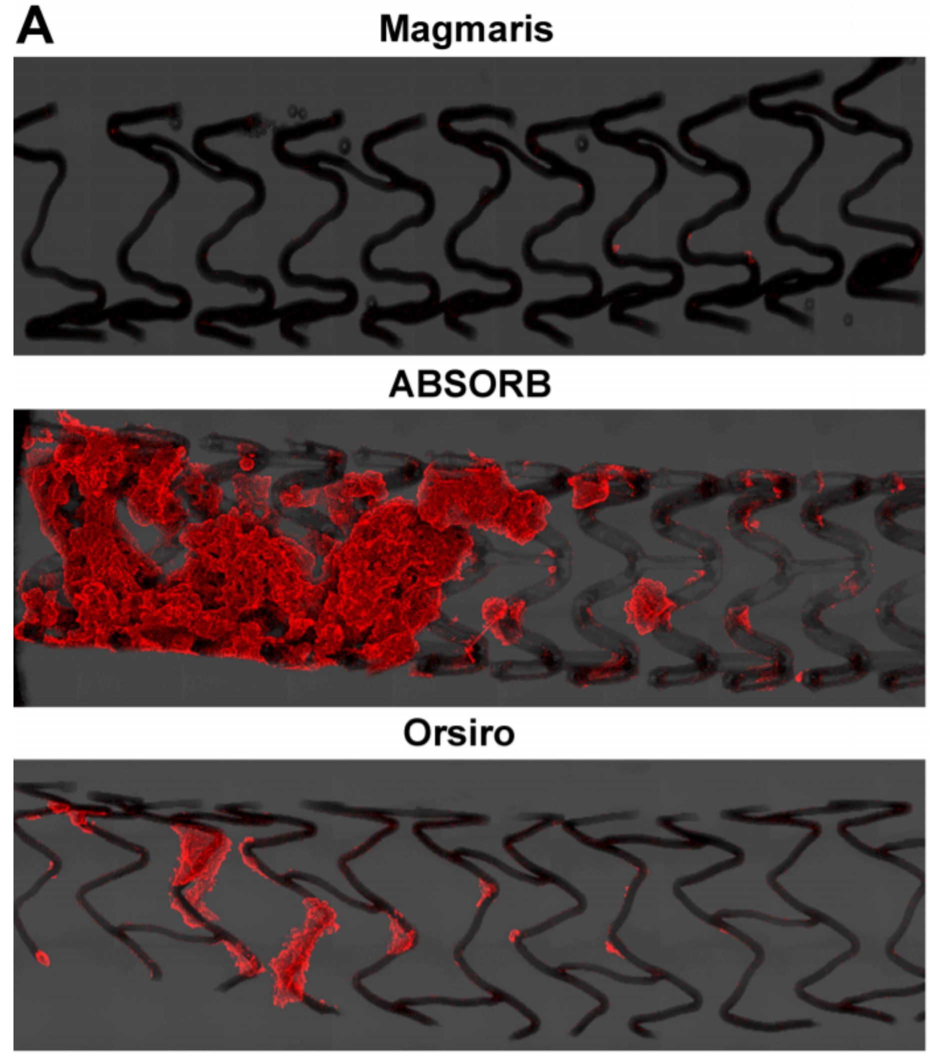



- **Pink fuzzy areas are regions with low shear stress with high viscosity**

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



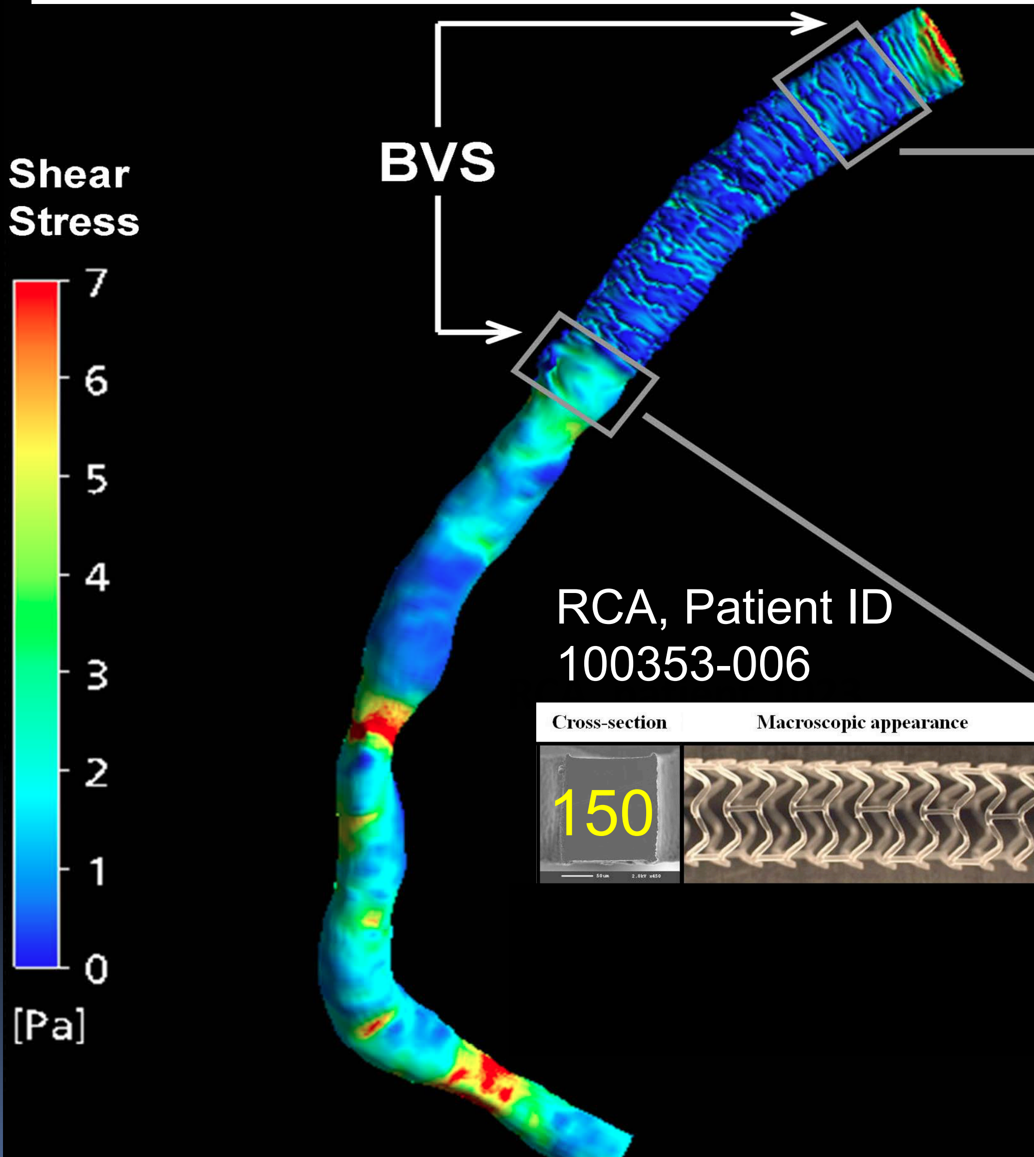



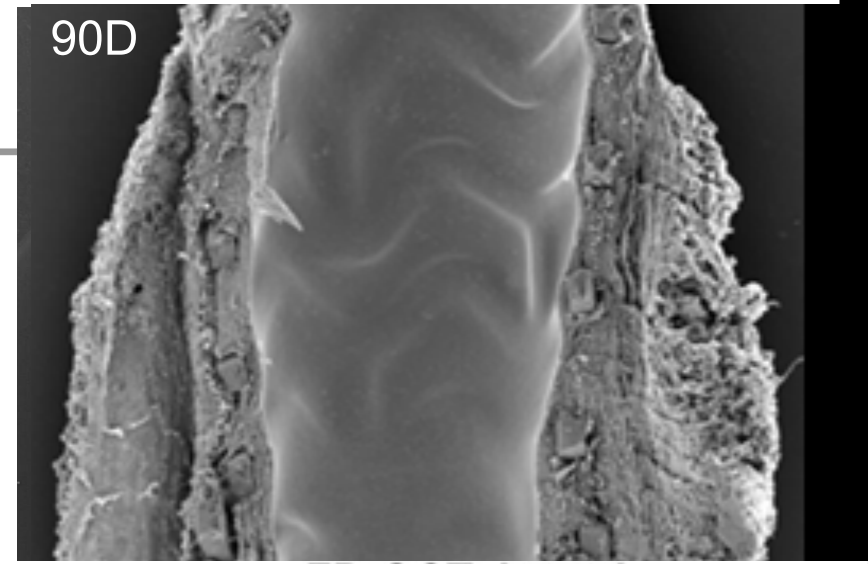



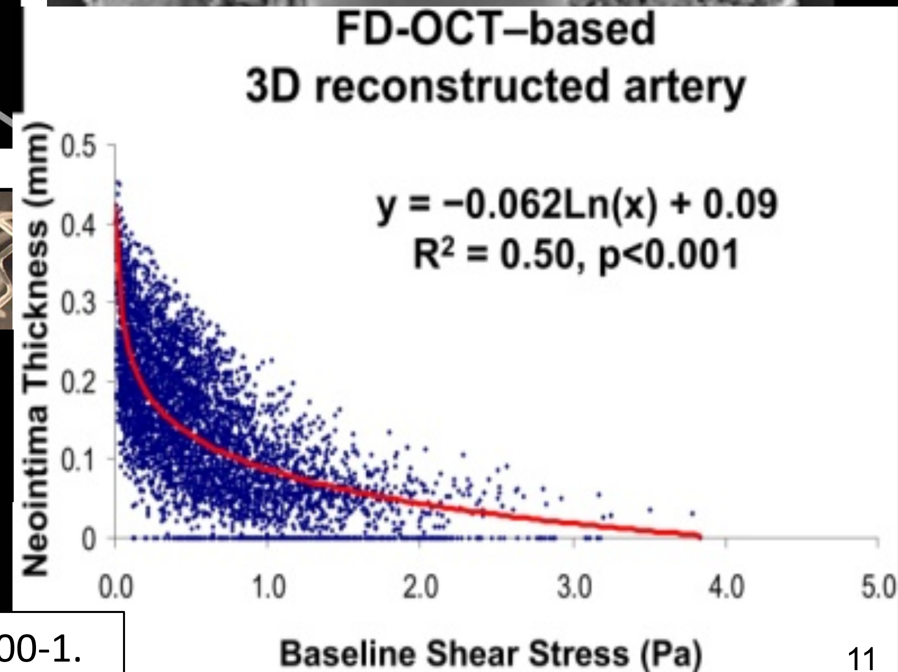

Waksman R et al. Circulation: Cardiovascular Interventions. 2017 Aug;10(8). pii: e004762.

# Thick strut is also the main determinant of neointimal thickness and LA reduction

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

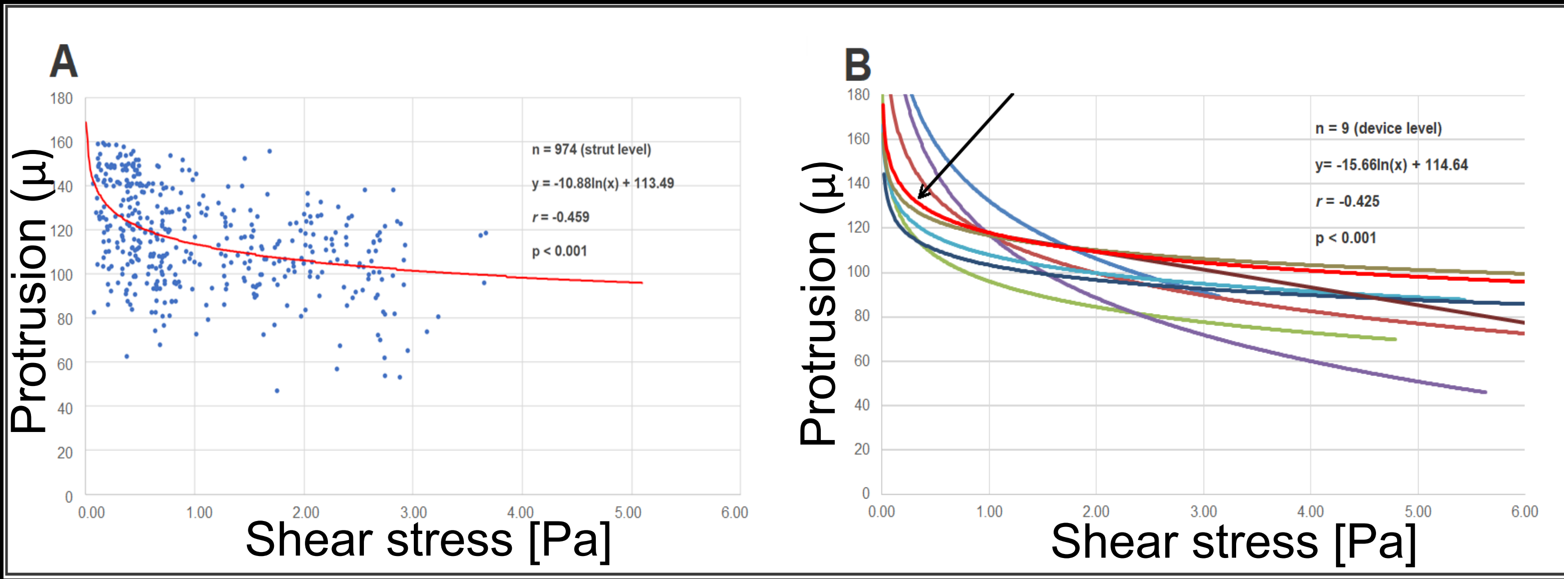


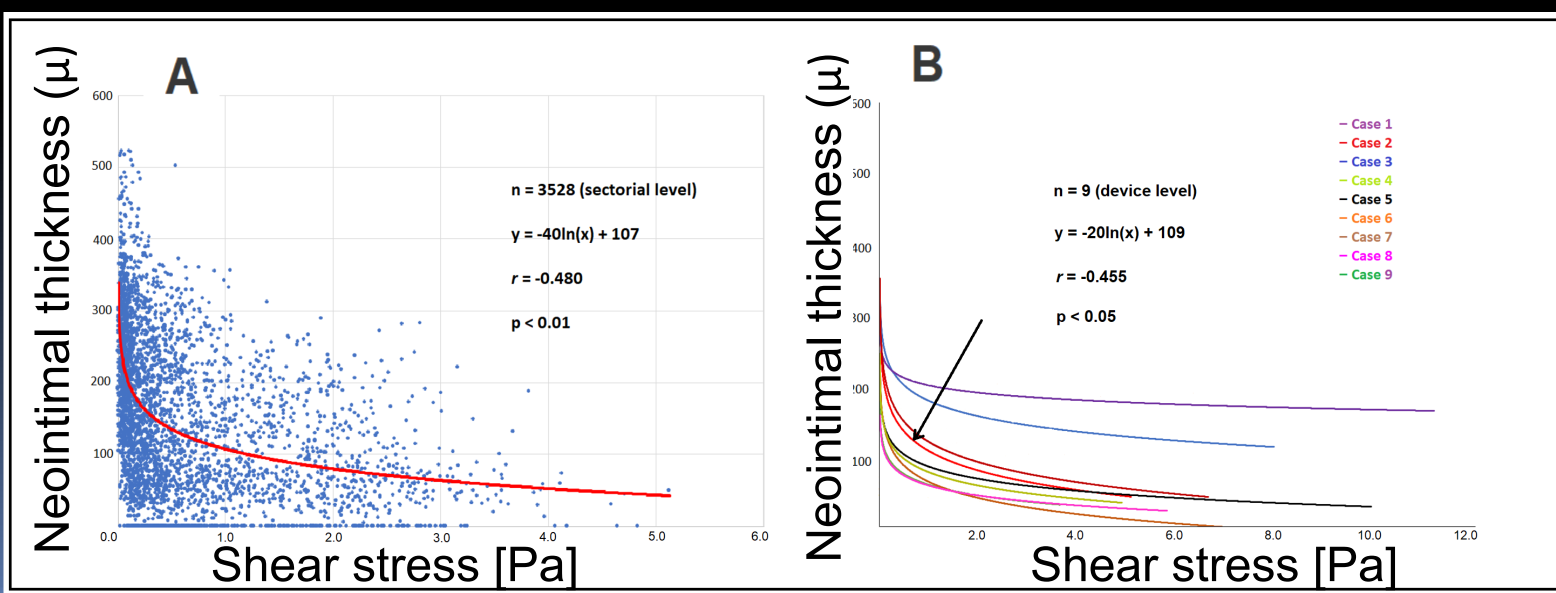




Bourantas, Serruys et al. JACC Cardiovasc Interv. 2014;7:100-1.

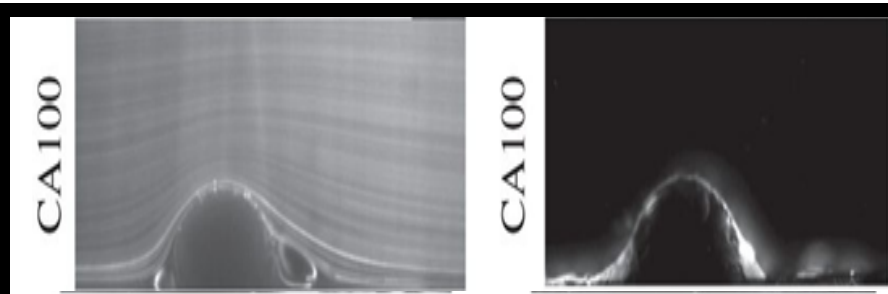
# INVERSE RELATIONSHIP BETWEEN STRUT PROTRUSION AND SHEAR STRESS IN ABSORB BIORESORBABLE SCAFFOLD




# INVERSE RELATIONSHIP SHEAR STRESS AND NEOINTIMAL THICKNESS IN ABSORB BIORESORBABLE SCAFFOLD

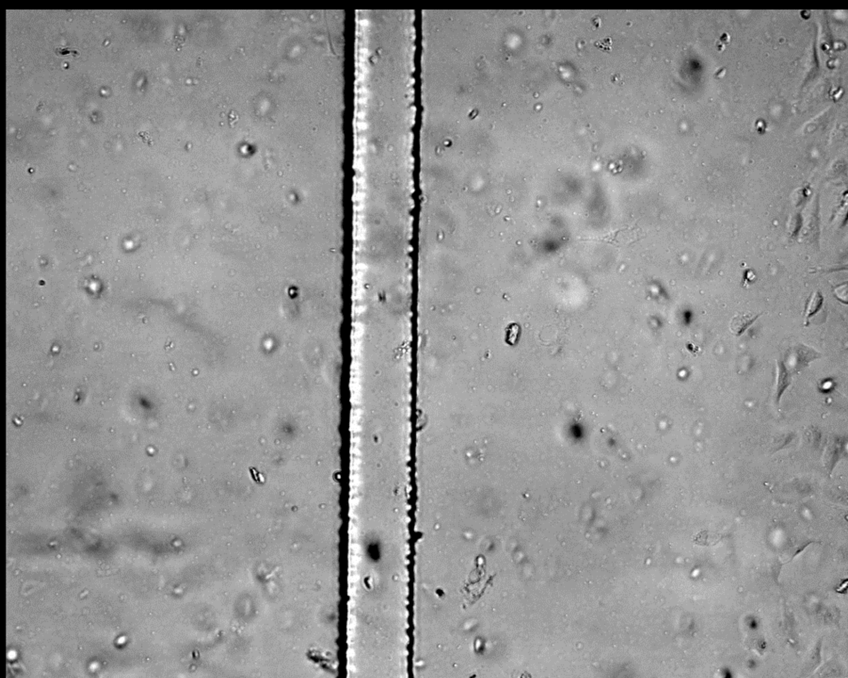


# The effect of thick (150 µm), quadratic strut on flow reversal, recirculation, fibrin deposition and endothelial migration and coverage

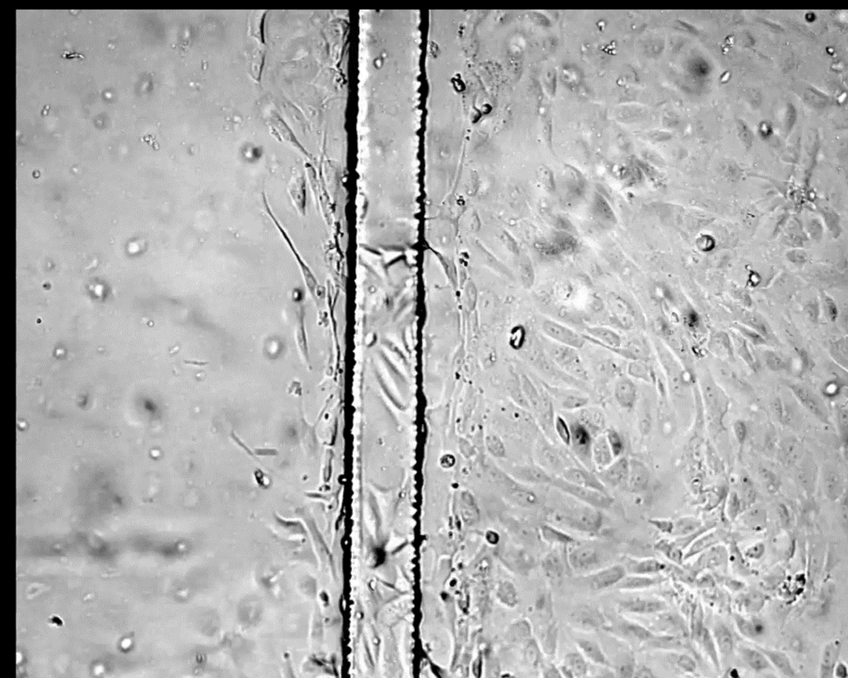



Circular strut (next slide)

**0-24 hr**



**40-72 hr**

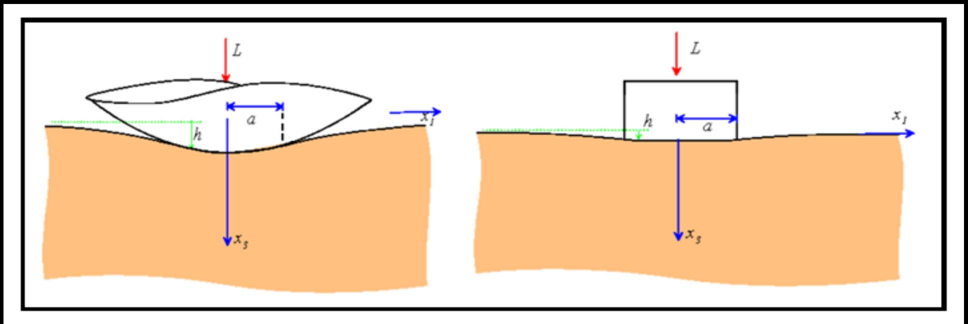


Hsiao ST et al. Endothelial repair in stented arteries is accelerated by inhibition of Rho-associated protein kinase. Cardiovasc Res. 2016 Dec;112(3):689-701

# How improved scaffold technology can reduce clinical complication?

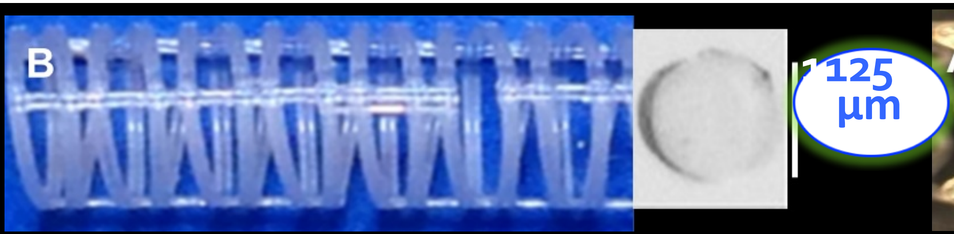
| Shortcomings | Possible solution |
|---|---|
| ○ Low tensile strength, low radial force, recoil <><br>○ thick strut, wide footprint | • Increase tensile strength, good radial force -> thin strut (oriented PLLA, Arterius technology) |
| ○ Quadratic strut<br>○ Difficult to embed<br>○ Disturb laminar flow | • Circular strut (Manli technology)<br>• Easy to embed<br>• Less disturbance of laminar flow |
| ○ Increase local viscosity and thrombogenicity<br>○ Main determinant of neointimal thickness and LA reduction | • Use of biodegradable material non-thrombogenic: Magnesium |
| ○ Slow down the cell coverage | • Circular strut |
| ○ Late structural discontinuity (dismantling) | • Faster bioresorption (Manli technology) |

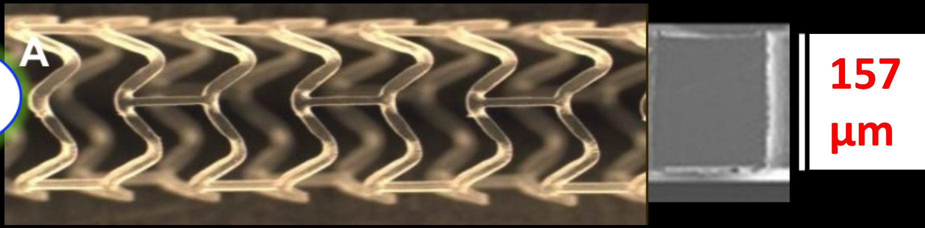
# *CIRCULAR* STRUTS (mono fiber) PENETRATE INTO THE VESSEL WALL BETTER THAN THE *QUADRATIC* STRUTS

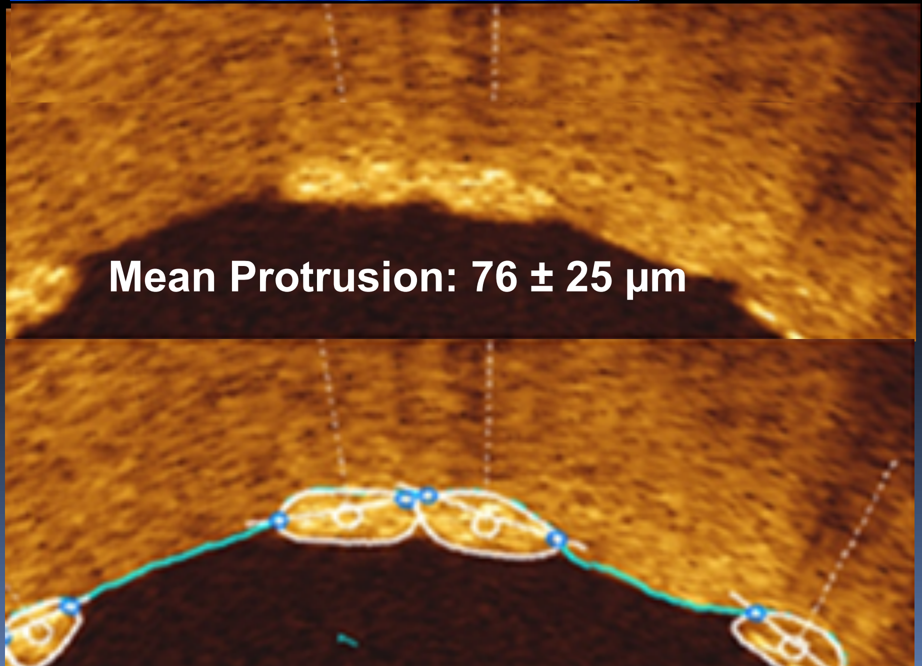


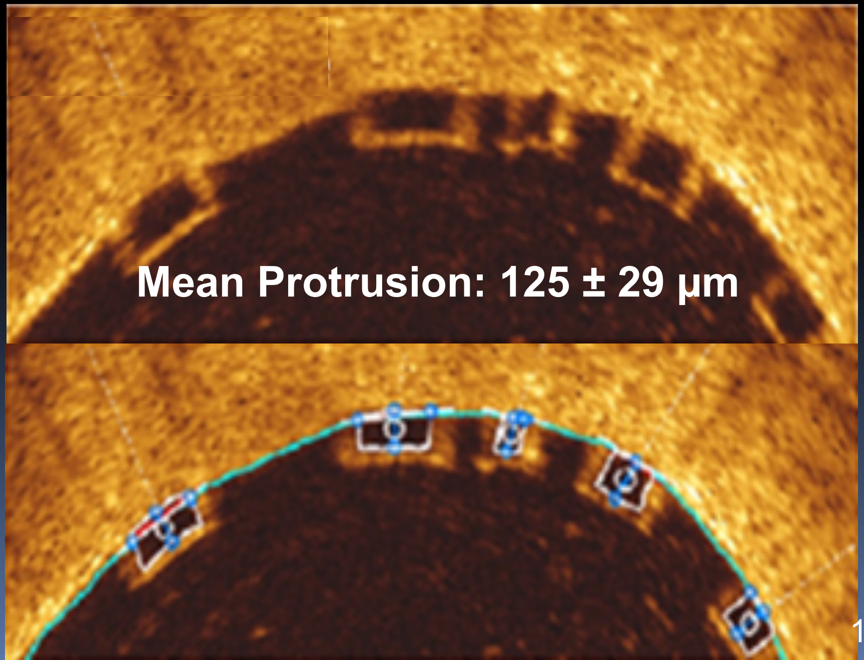

$$p(\rho) = \frac{2\mu h}{\pi(1-\nu)\sqrt{a^2-\rho^2}}$$

**Inverse relationship between contact radius and contact pressure**



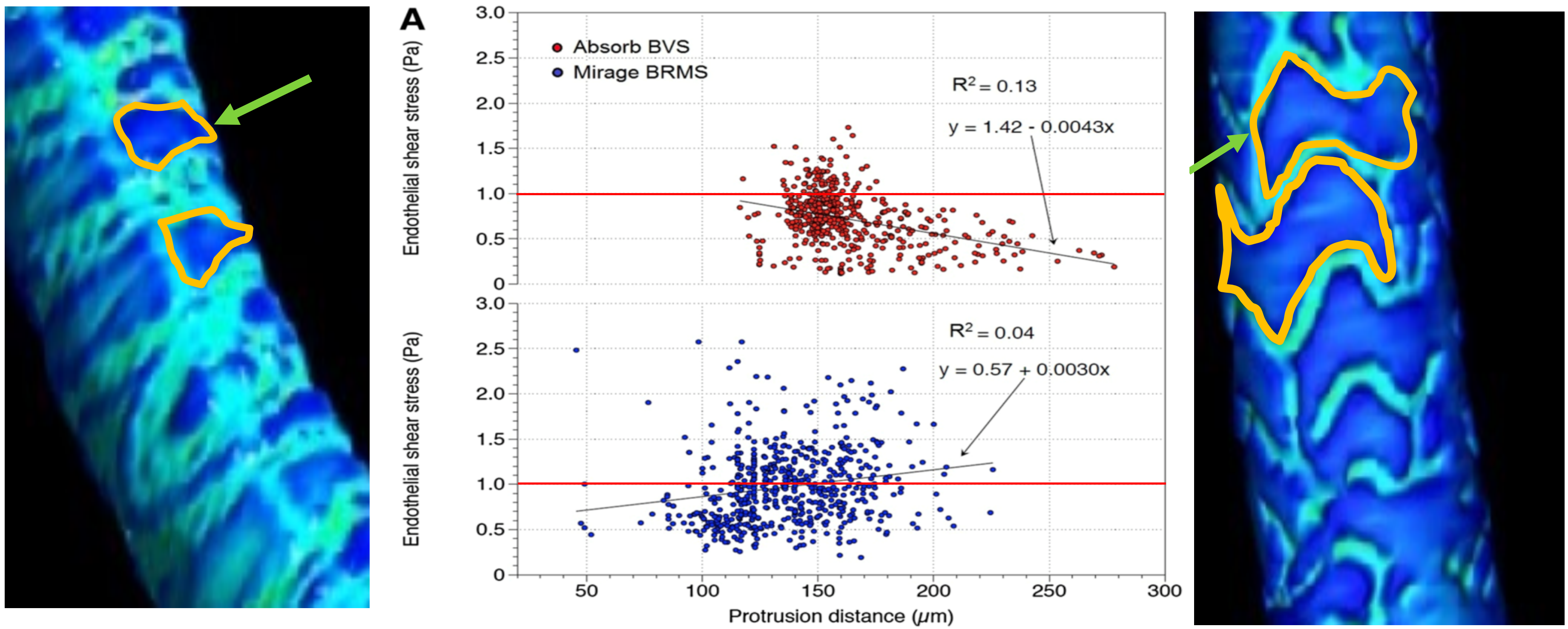



**In a porcine model (n=8) and human randomized trial (n=20), strut protrusion and shear stress differentiated the two devices**

**MIRAGE BRMS** **ABSORB BVS**



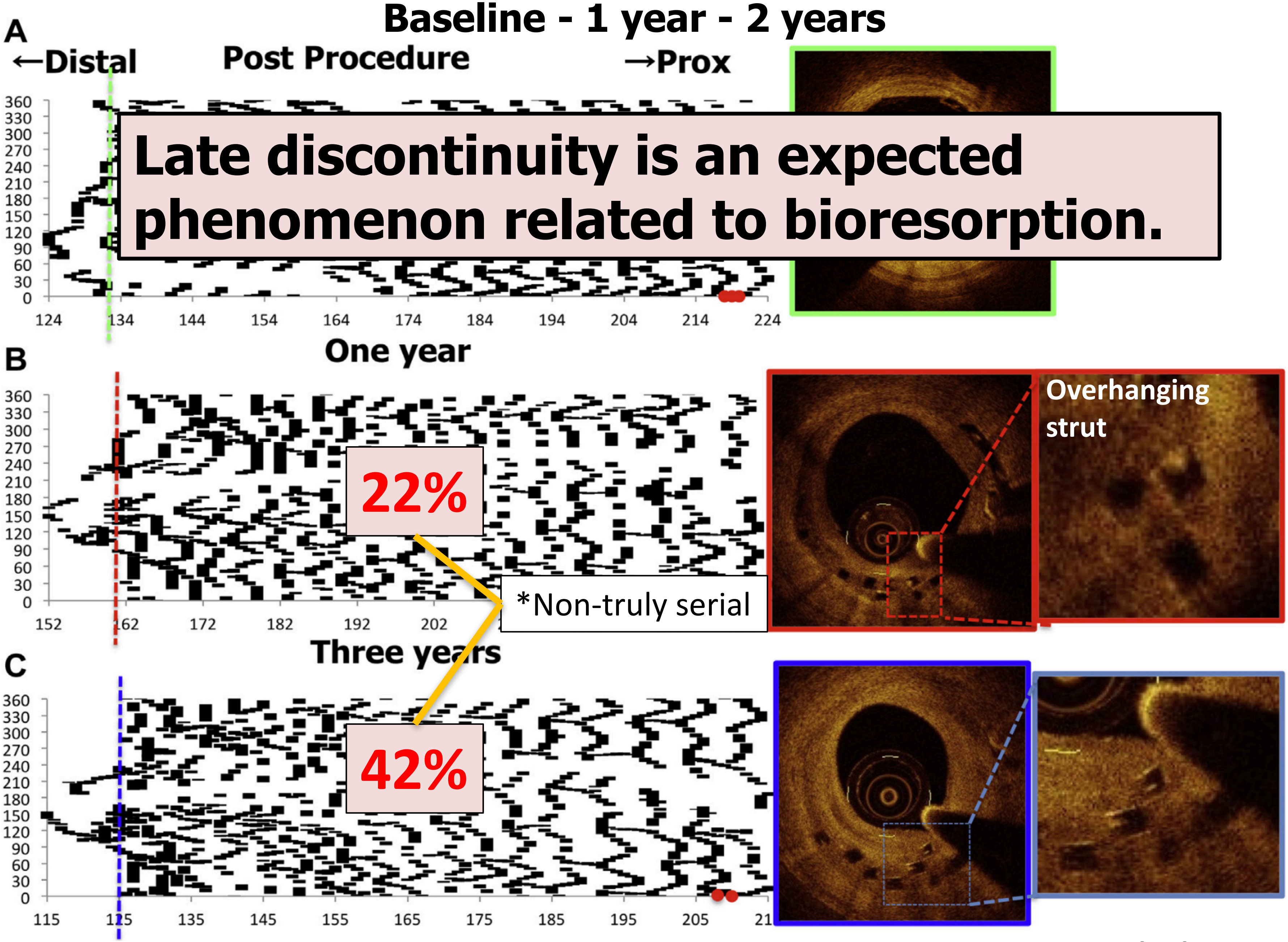

**Note the intense recirculation area behind the quadratic strut in flow model**

Tenekecioglu E, Serruys PW, et al. Int J Cardiol. 2017;227:467-473.
Tenekecioglu E, Serruys PW, et al. Int J Cardiovasc Imaging. 2017;33:1313-13
Tenekecioglu E, Serruys PW et al. JACC: Card Interventions, July 2017

# How improved scaffold technology can reduce clinical complication?

| Shortcomings | Possible solution |
|---|---|
| ○ Low tensile strength, low radial force, recoil <><br>○ thick strut, wide footprint | • Increase tensile strength, good radial force -> thin strut (oriented PLLA, Arterius technology) |
| ○ Quadratic strut<br>  ○ Difficult to embed<br>  ○ Disturb laminar flow | • Circular strut (Manli technology)<br>  • Easy to embed<br>  • Less disturbance of laminar flow |
| ○ Increase local viscosity and thrombogenicity<br>○ Main determinant of neointimal thickness and LA reduction | • Use of biodegradable material non-thrombogenic: Magnesium |
| ○ Slow down the cell coverage | • Circular strut |
| ○ Late structural discontinuity (dismantling) | • Faster bioresorption (Manli technology) |

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



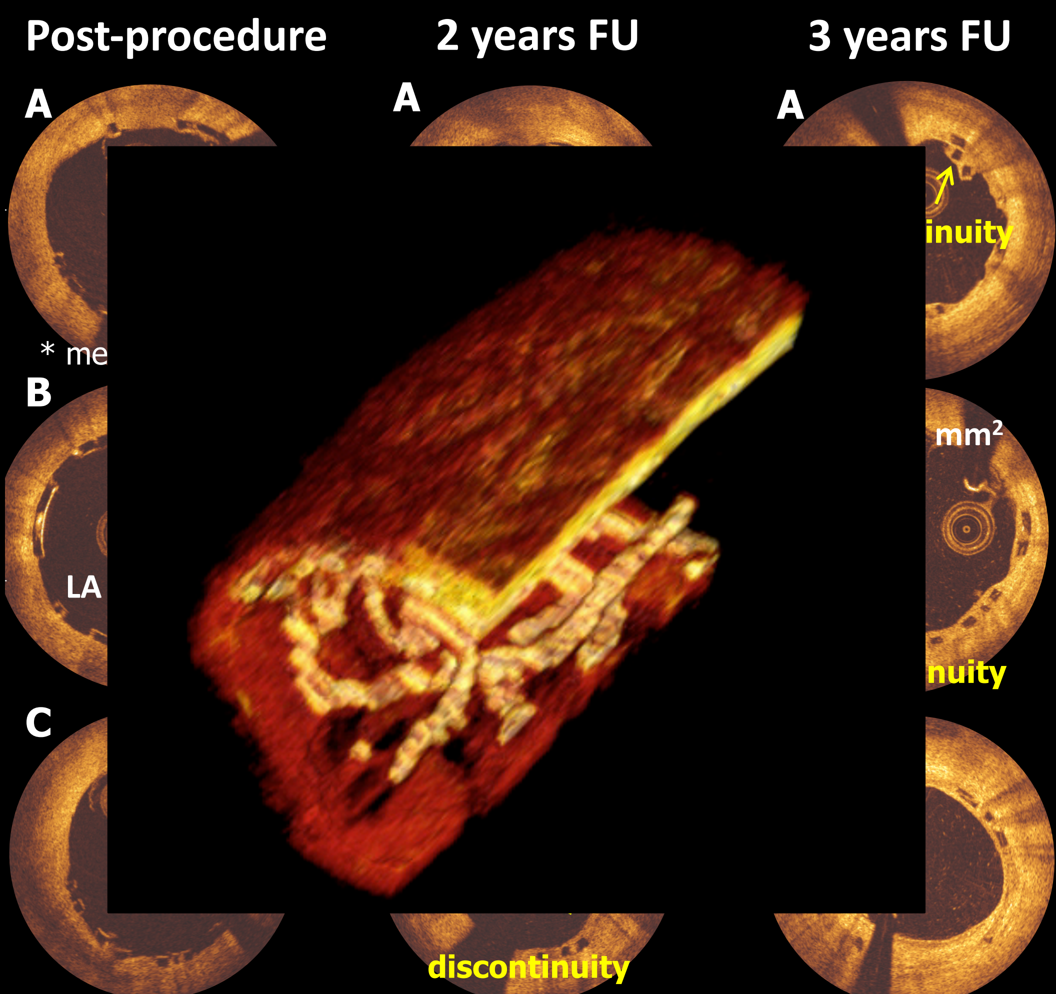

**Late discontinuity is an expected phenomenon related to bioresorption.**

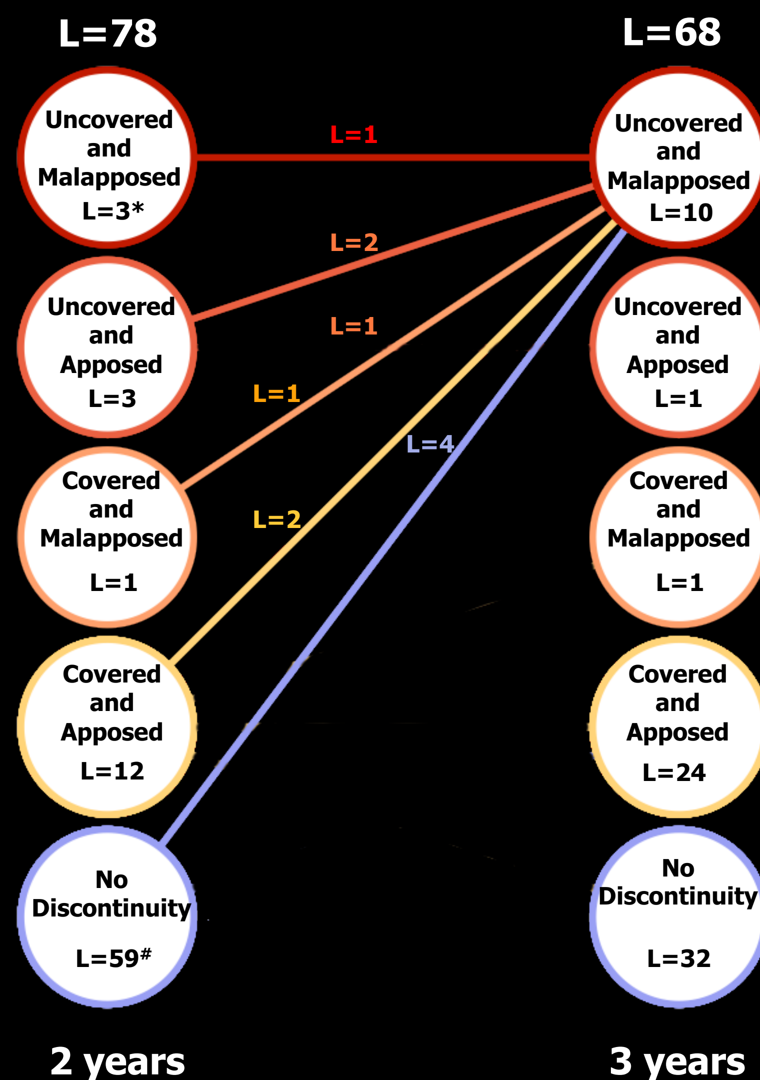


Onuma, Serruys, et al. JACC Cardiovasc Interv. 2014;7(12):1400-11.

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

**-by courtesy of Prof. Kimura**



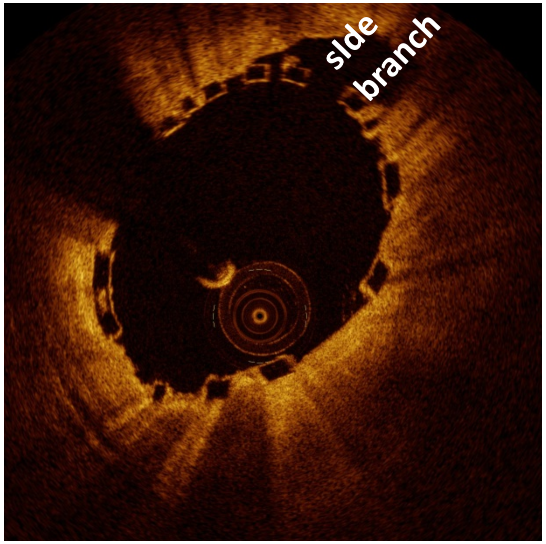




* Two lesions were not analyzable at 3 years. # Eight lesions were not analyzable at 3 years.

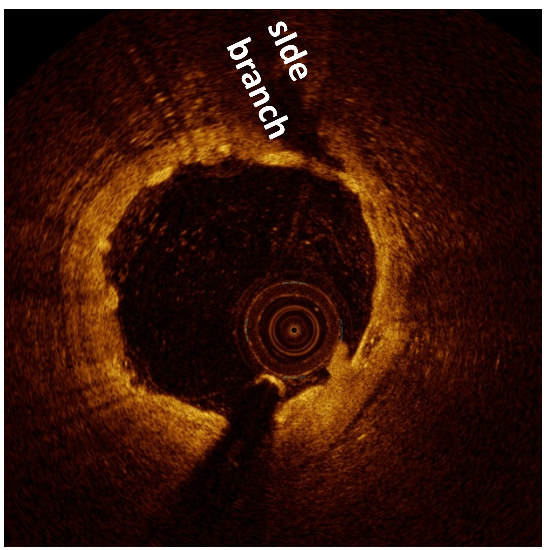
# The rate of biodegradation has important impact on bioresorption and dismantling

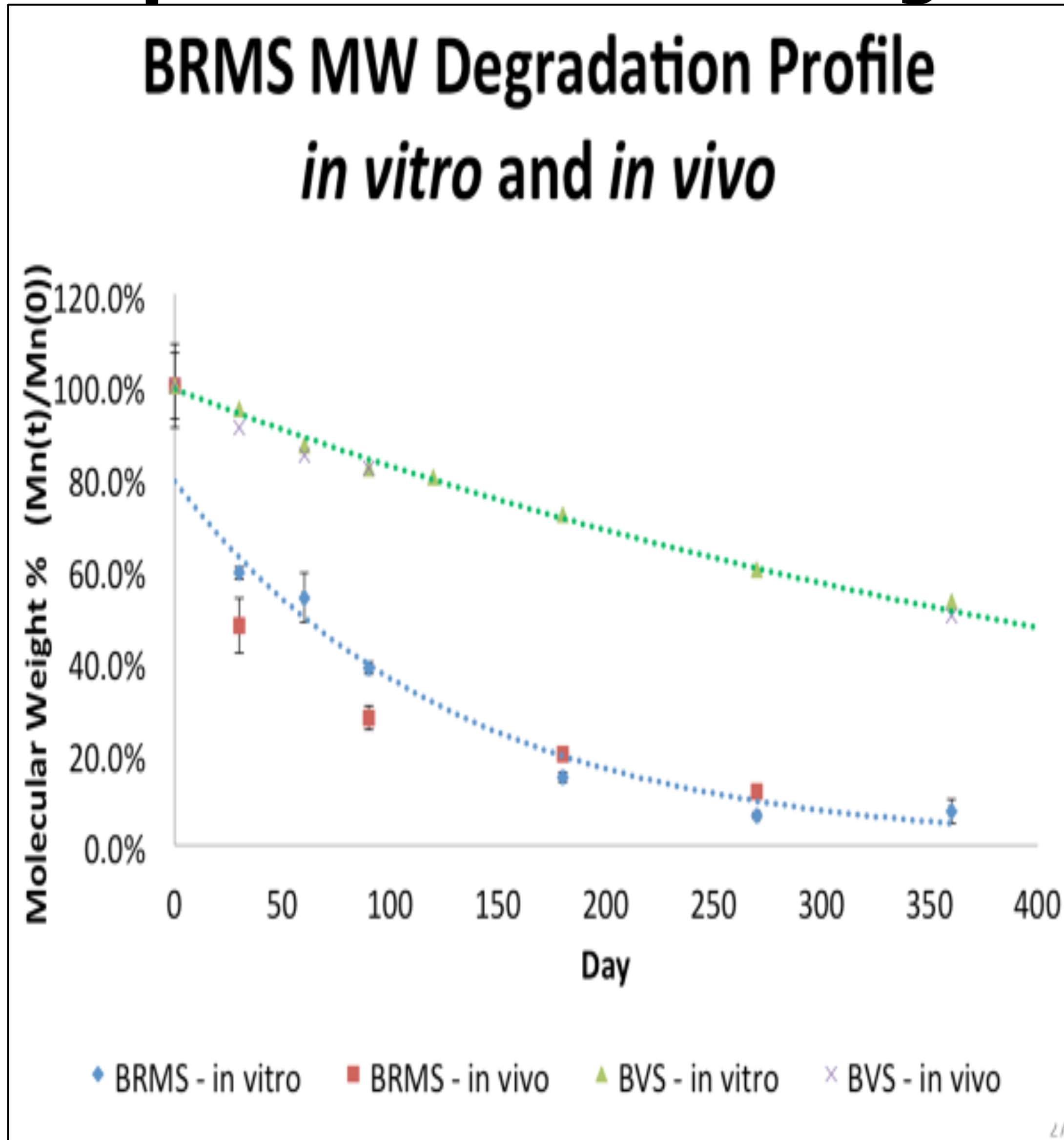
**Post-Procedure**

**ABSORB**




**MIRAGE**



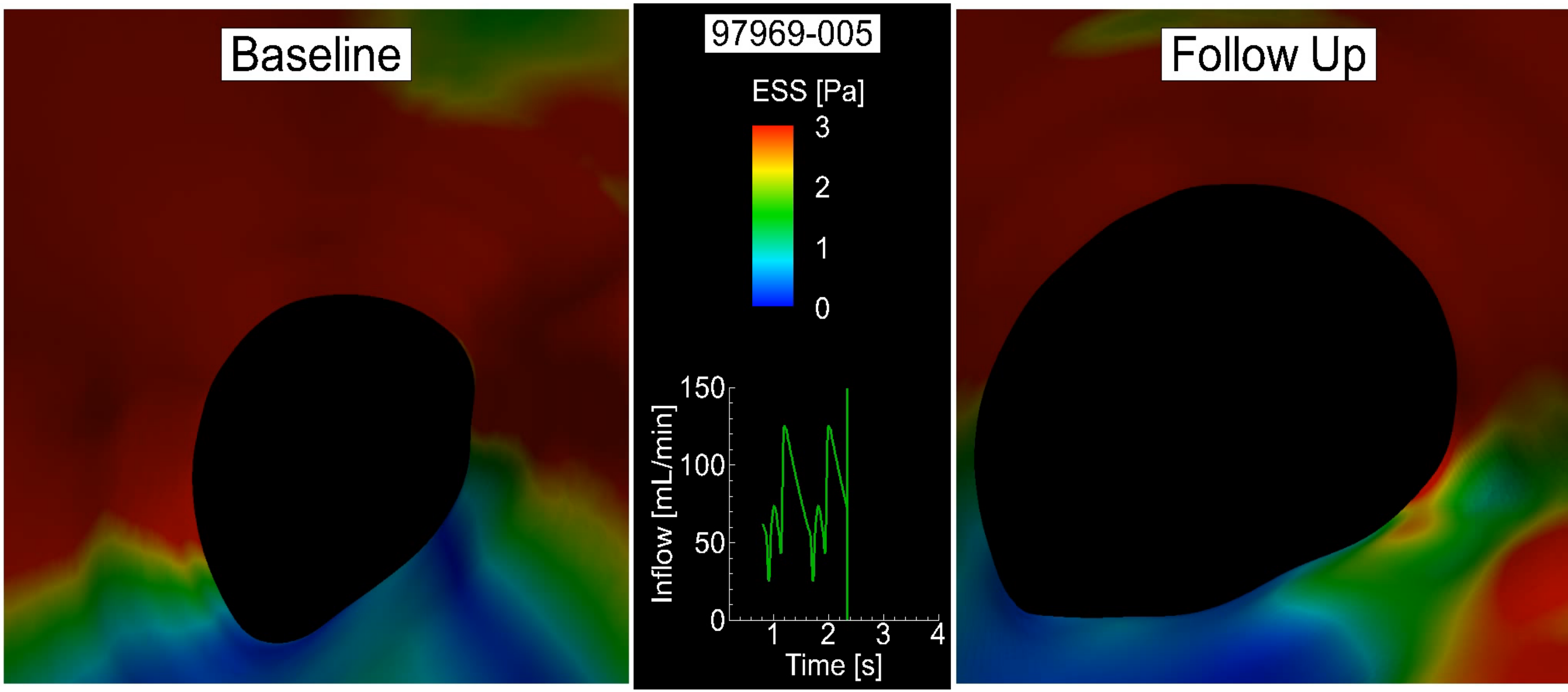
# THE GOOD NEWS…

- **Long-term (5 years) remodeling***
  - **Homogenizes shear stress towards physiological value of shear stress (>1 Pa)**
  - **Eliminates the corrugate appearance of the scaffold (smooth surface at 5 years) ****
  - **Self-corrects the procedural overexpansion or underexpansion created by the operator ****

- **Serruys et al. Glagovian Appraisal of Arterial Remodeling in Absorb Bioresorbable Scaffolds and Xience Metallic Stents. J Am Coll Cardiol. 2017;70:60-74.**

**** Serruys et al. Dmax for sizing, PSP-1, PSP-2, PSP-3 or OCT guidance: interventionalist's jargon or indispensable implantation techniques for short- and long-term outcomes of Absorb BRS?. EuroIntervention. 2017;12:2047-2056.**

# FLYING THROUGH VIEW OF THE SHEAR STRESS DISTRIBUTION AT END SYSTOLE IN THE LUMINAL SURFACE OF CASE 97969-005 POST-IMPLANTATION AND AT 5-YEAR FOLLOW UP




- **Homogenizes shear stress towards physiological value of shear stress (>1 Pa)**
- **Eliminates the corrugate appearance of the scaffold (smooth surface at 5 years)**

**Serruys, Onuma. EuroIntervention. 2017;12(17):2047-2056.**
**Thondapu V, Tenekecioglu E, Serruys PW et al. Eur Heart J Cardiovasc Imaging. 2017 Jul.**

## 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.

-The future is bright!-
There is room for progress!

# THANKS…