

## **Next BRS : What Are Going to Change?**

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# What are the new BRS going to change?

## **Mechanical, design, and material improvements of new BRS:**

**1. Stronger and ductile scaffold**

**1. Thinner/round struts**

**1. Fast resorption without inflammation**

## **Expected clinical improvements with new BRS:**

**1. More radial strength, flexible sizing, resistance to fracture**

**2. improved deliverability with thinner profile; Improvement in rheology and decreased thrombogenicity**

**3. Early manifestation of anatomic-physiological benefits: late lumen enlargement, restoration of vasomotion, and plaque reduction; Reduction of late events**

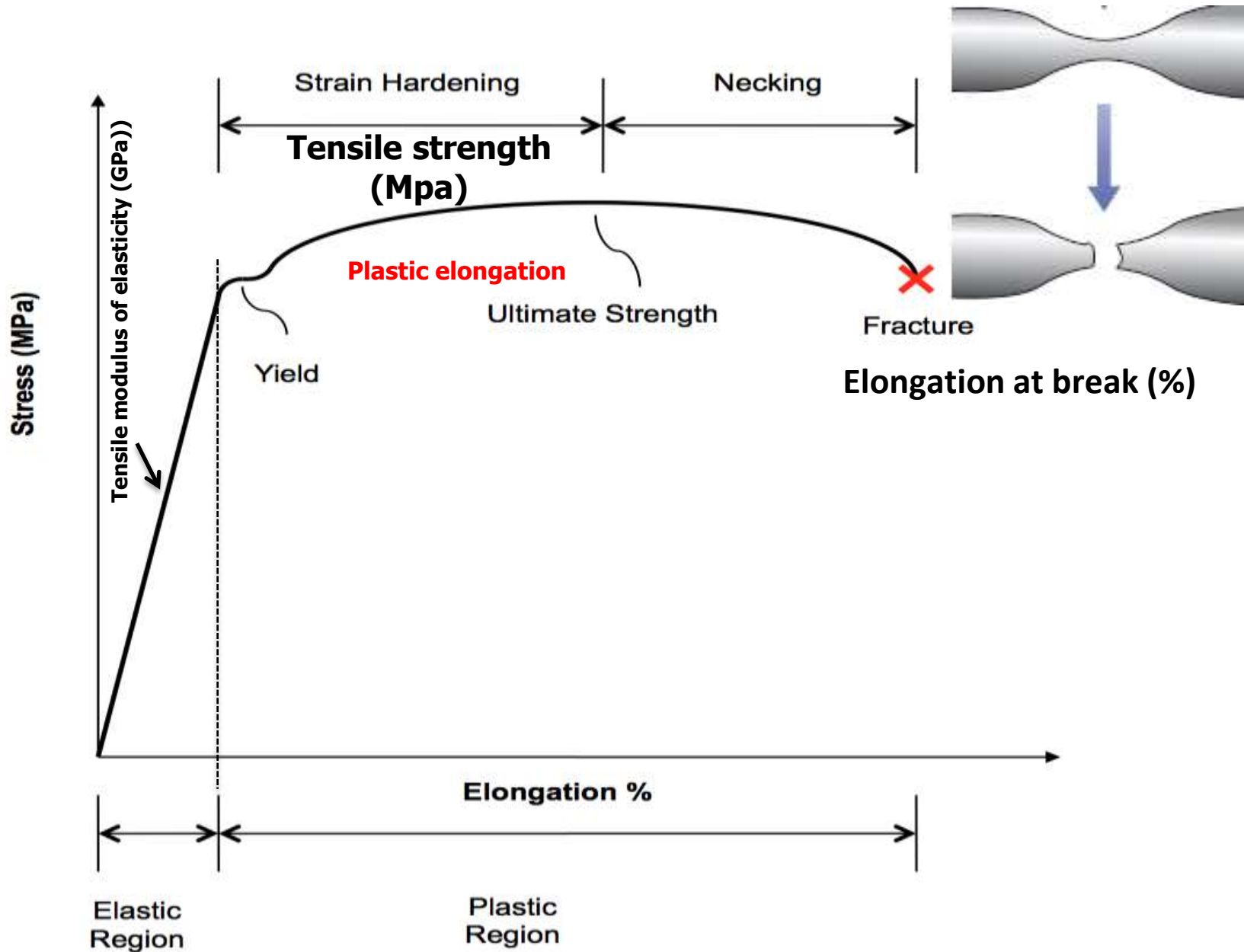
# Current limitation of BRS

If a bioresorbable scaffold is ultimately expected to have the same range of applicability as a durable metal stent, **the gap in mechanical properties** must be reduced.

Currently, three primary limitations exist:

- **Low tensile strength and stiffness** which require thick struts to prevent acute recoil
- **Insufficient ductility** which impacts scaffold retention on balloon catheter and limits the range of scaffold expansion during deployment
- **Instability of mechanical properties** during vessel remodeling if bioresorption is too fast

# Let's take a "crash course" of material science

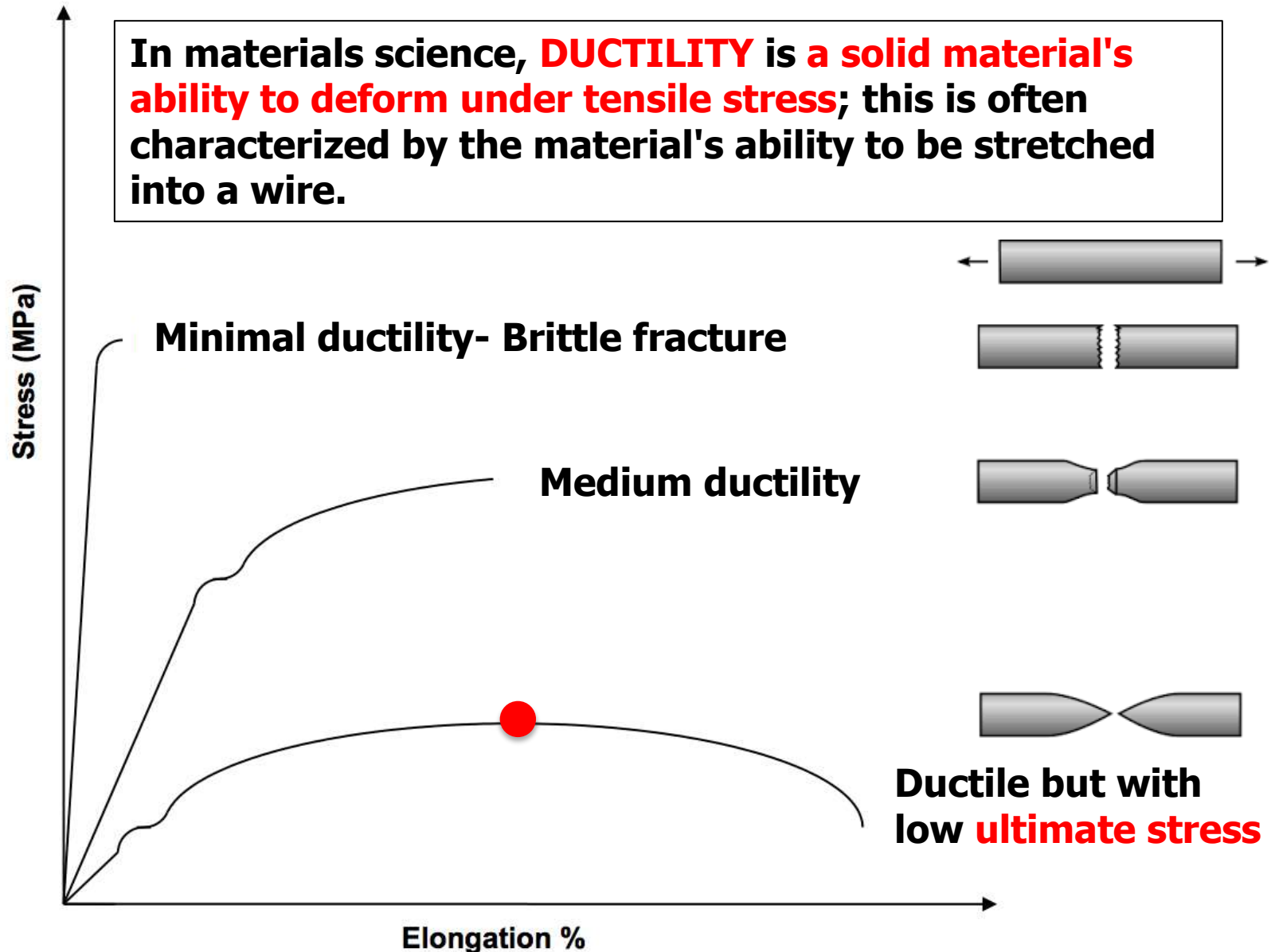


# Mechanical properties of metal vs. PLLA

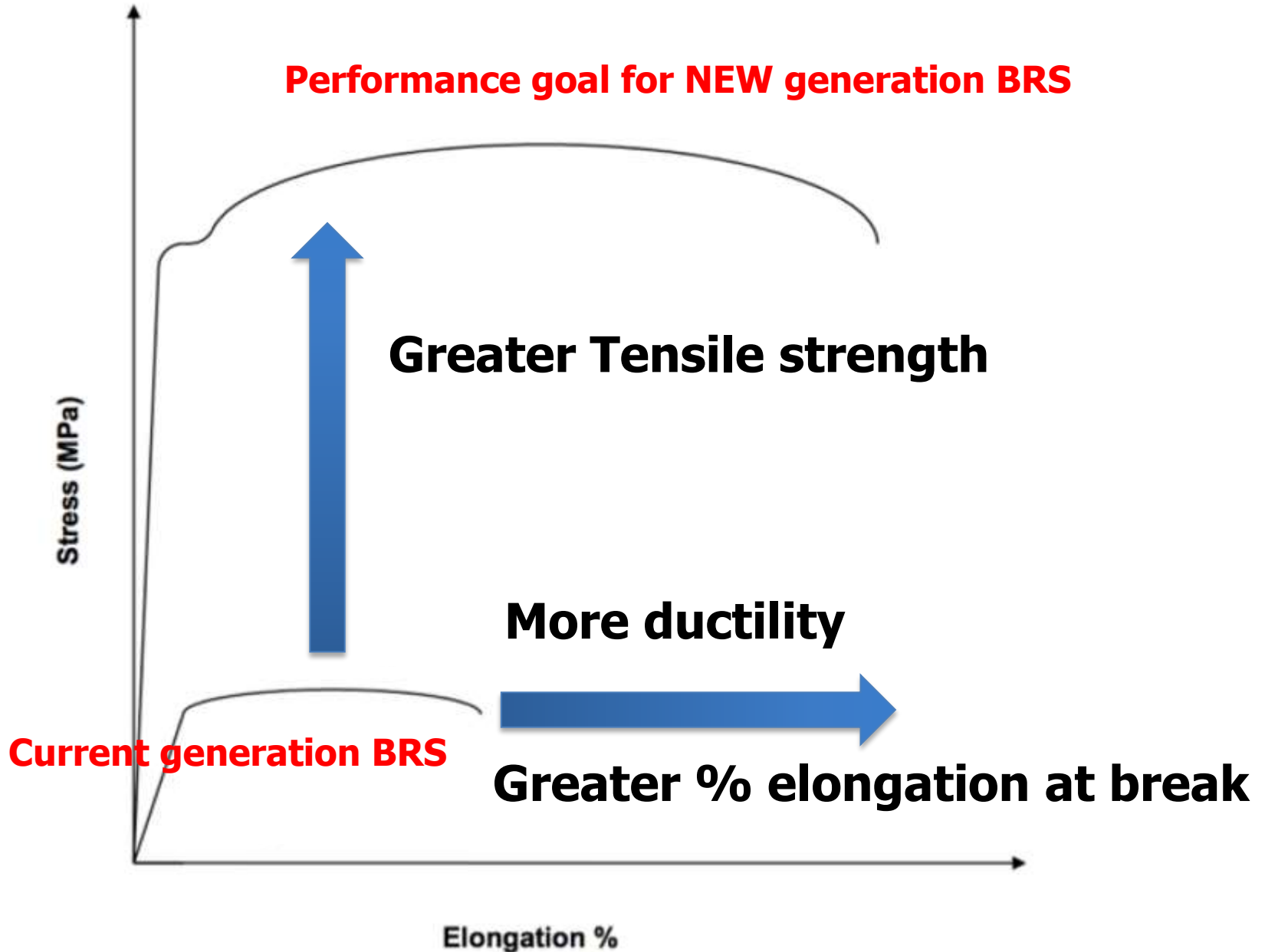
<b>Polymer/ metal</b>	<b>Tensile modulus of elasticity (Gpa)</b>	<b>Tensile strength (Mpa)</b>	<b>Elongation at break (%)</b>
<b>Poly(L-lactide)</b>	<b>3.1-3.7</b>	<b>60-70</b>	<b>2-6</b>
<b>Poly (DL-lactide)</b>	<b>3.1-3.7</b>	<b>45-55</b>	<b>2-6</b>
<b>Cobalt chromium</b>	<b>210-235</b>	<b>1449</b>	<b>~40</b>
<b>Magnesium alloy</b>	<b>40-45</b>	<b>220-330</b>	<b>2-20</b>

# Insufficient ductility impacts scaffold retention on balloon catheter and limits the range of scaffold expansion during deployment

In materials science, **DUCTILITY** is a solid material's ability to deform under tensile stress; this is often characterized by the material's ability to be stretched into a wire.



# Performance goal and mechanical dilemma



# Bioresorbable Scaffolds

From Basic Concept  
to Clinical Applications



Patrick Serruys | Yoshinobu Onuma

SECTION EDITORS:

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**(Pre-CE mark, Pre FDA, pre**  
**PMDA and pre CFDA)**

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**Qualimed**

**Merilife**

**Orbus Neich**

**Abbott: New generation**  
**Absorb scaffold**

**Arterius**

**Manli**

**Boston Scientific**

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**Lepu**



**Use of metal stand alone  
or in combination of polymer**

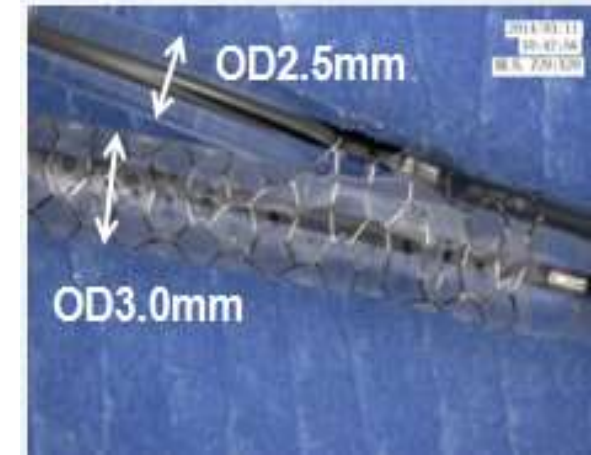
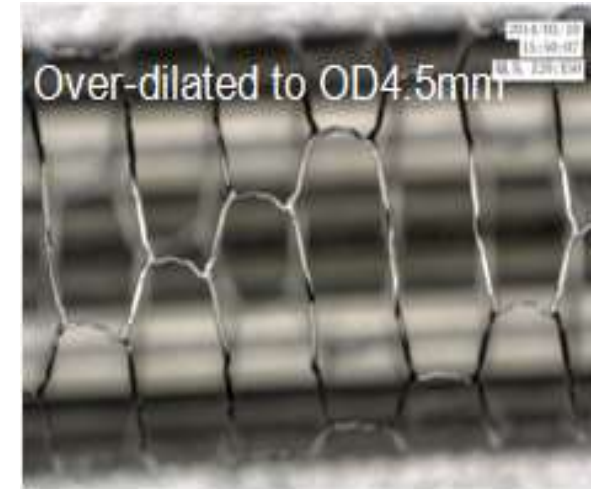
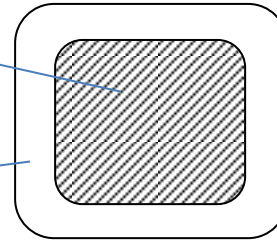
# Use of metal stand alone or in combination of polymer

## e.g. Nitrided iron bioresorbable stent

**BRS:**

Nitrided iron

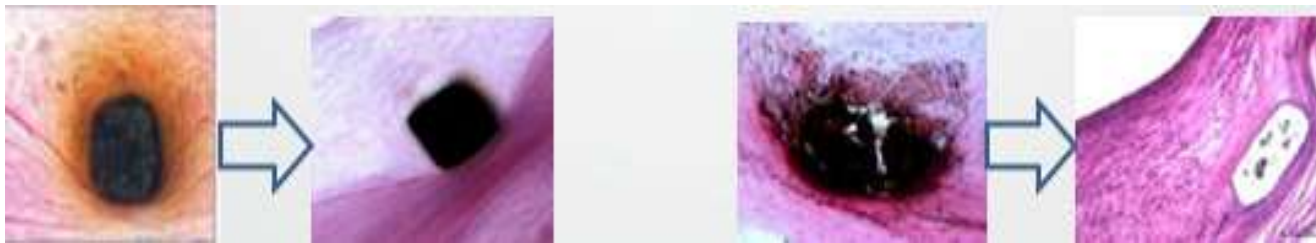
PLA+ Sirolimus



Unique problems of iron stent:

1. Material aspects
  - a) Understand how iron behaves in vivo and in vitro situations
  - b) Expedite in vivo corrosion of iron**
  - c) Eliminate particulates during in vivo corrosion
2. Biological aspects
  - a) Develop extraction methodology for biological tests of iron ions
  - b) Remove rust staining from tissue for subsequent histological observation .....

Long way to go before CE marking



# Use of metal stand alone or in combination of polymer

## e.g. Unity Hybrid BRS: Magnesium Core with Polymer Outer

- **Stent Expansion**

Uniform expansion of the stent. No cracks or flakes were observed during visual inspection of crimped stents and during expansion to maximum diameter (4.8 mm)

- **Foreshortening**

Measurements of foreshortening resulted to almost zero foreshortening

- **Radial Force (RF)**

Radial force measurements resulted to about 1.500 mN which is comparable to regular stainless steel stents

- **Visibility**

Fluoroscopic visibility can be improved by FePt particle incorporation in the coating of adding markers

- **Acute Recoil Measurement**

Very low acute recoil which ranged between 1.98% and 1.13%

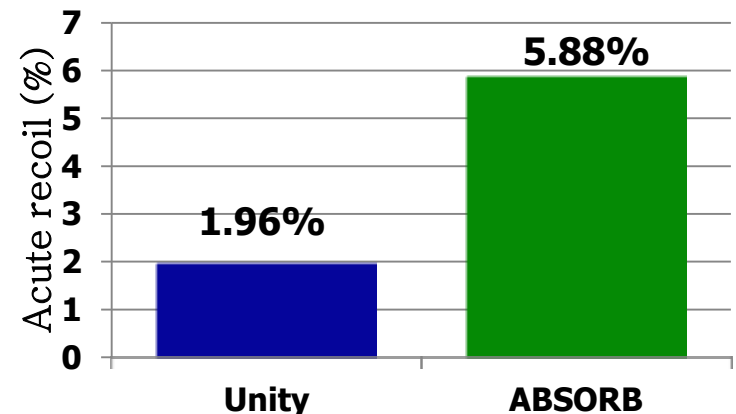
## Backbone (Mg)

The Skeletal portion of the system serves as the main support structure for the body.



## Muscle (polymer)

The Muscles keep bones in place and also play a role in the movement of bones.



# **“Playing” with composition of polymers**

## **Polymer composition**

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**Poly(L-lactide)**

**Poly (DL-lactide)**

**Poly (glycolide)**

**50/50 DL-lactide/glycolide**

**82/18 L-lactide/glycolide**

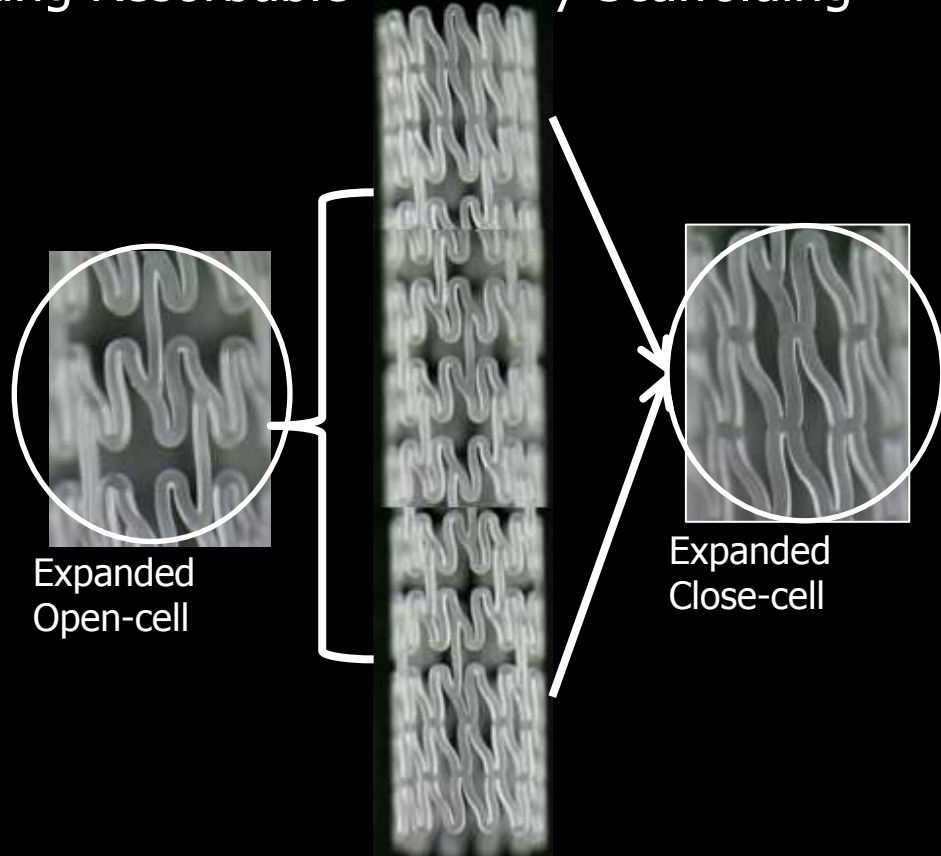
**70/30 L-Lactide/ $\epsilon$ -caprolactone etc...**

# “Playing” with composition of polymers

e.g. MERES: Meril life sciences

MeRes™ - Merilimus Eluting Resorbable Coronary Scaffolding

- New PLA formulation for enhanced radial strength ?
- Hybrid stent geometry
- Strut thickness :  $150 \pm 20 \mu\text{m}$
- Top coat: PDLLA + Sirolimus
- Coating thickness:  $< 5 \mu\text{m}$
- Sirolimus loading:  $1.25 \mu\text{g}/\text{mm}^2$
- RO markers: 3 tri-axial at each end
- Scaffold surface: 28.50%

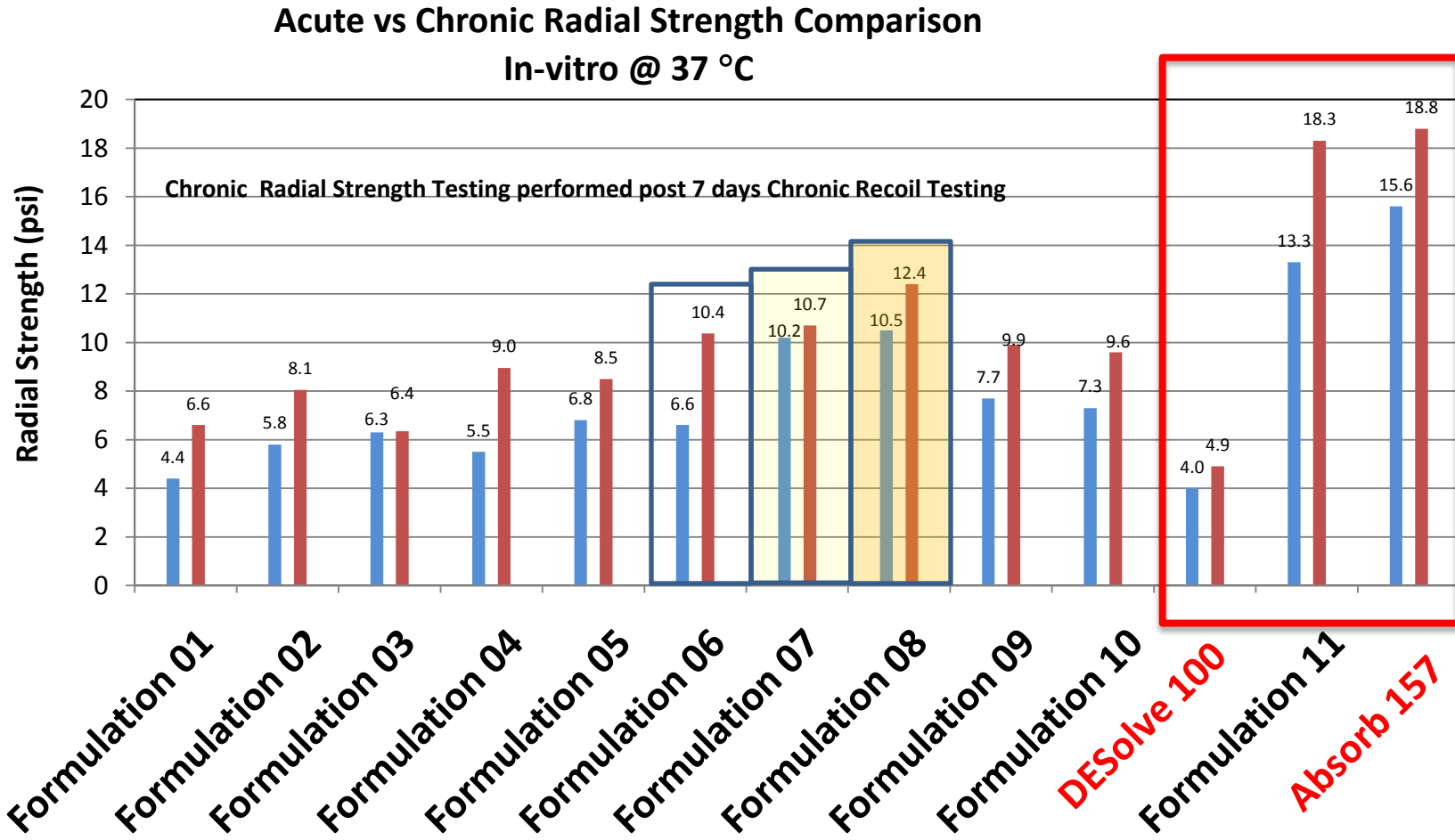


Actual device photographs. Data on file Meril Life Sciences.

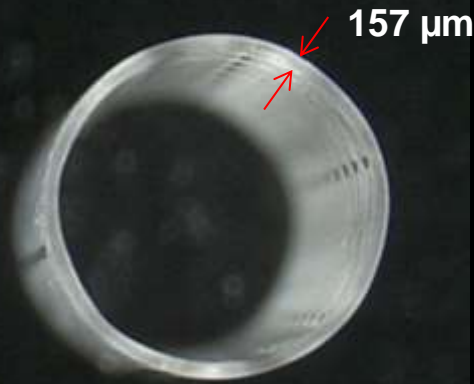
# “Playing” with composition of polymers

## Acute Radial Strength vs Chronic Radial Strength

Chronic radial strength higher than acute radial strength

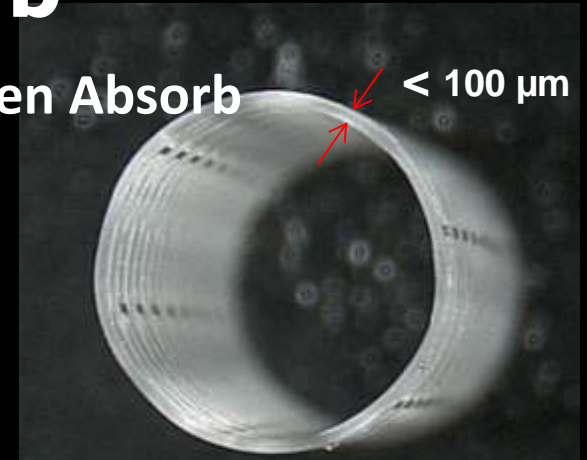


# To the next generation Absorb



Absorb

Next Gen Absorb



## Thinner Struts

- < 100 micron

## Smaller profile

- $\leq 1.245$  mm (3.0x18)
- $\leq 1.270$  mm (3.0x38)

## Larger functional expansion limit

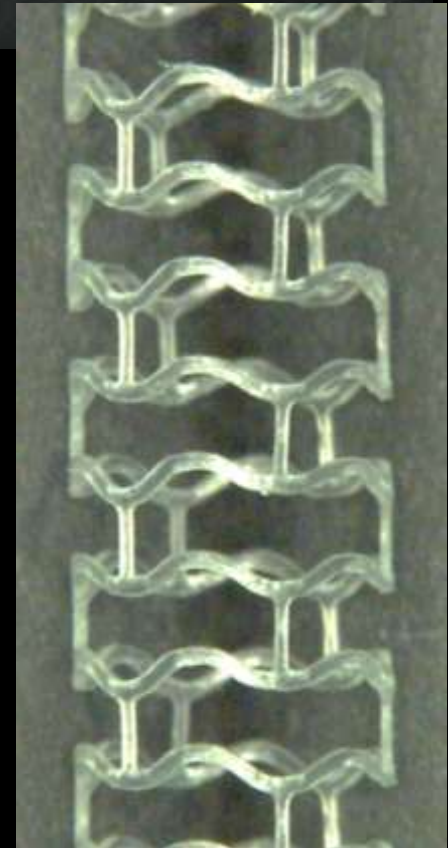
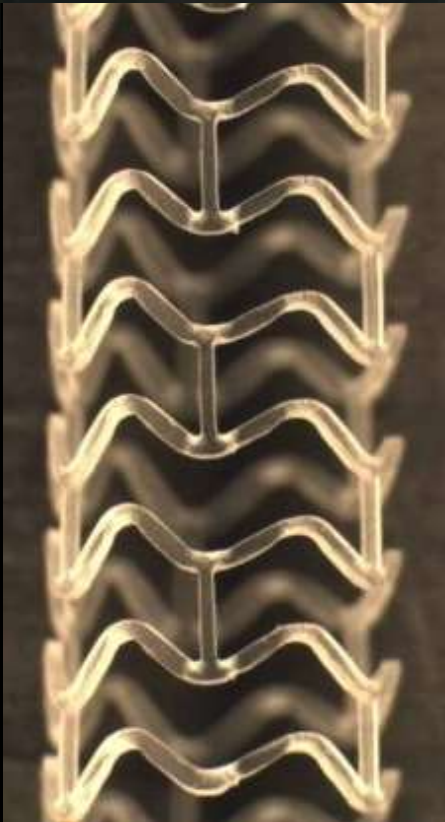
- post-dilatation of **0.75 mm** over nominal of largest diameter scaffold in size family
- $\geq 4.1$  mm at t=aged\* (2.25x28, 3.0x18)

## Broader pressure working range

## Shorter Resorption time

## Unchanged:

- Drug content & elution rate
- Pattern & footprint
- Radial strength
- Scaffold retention

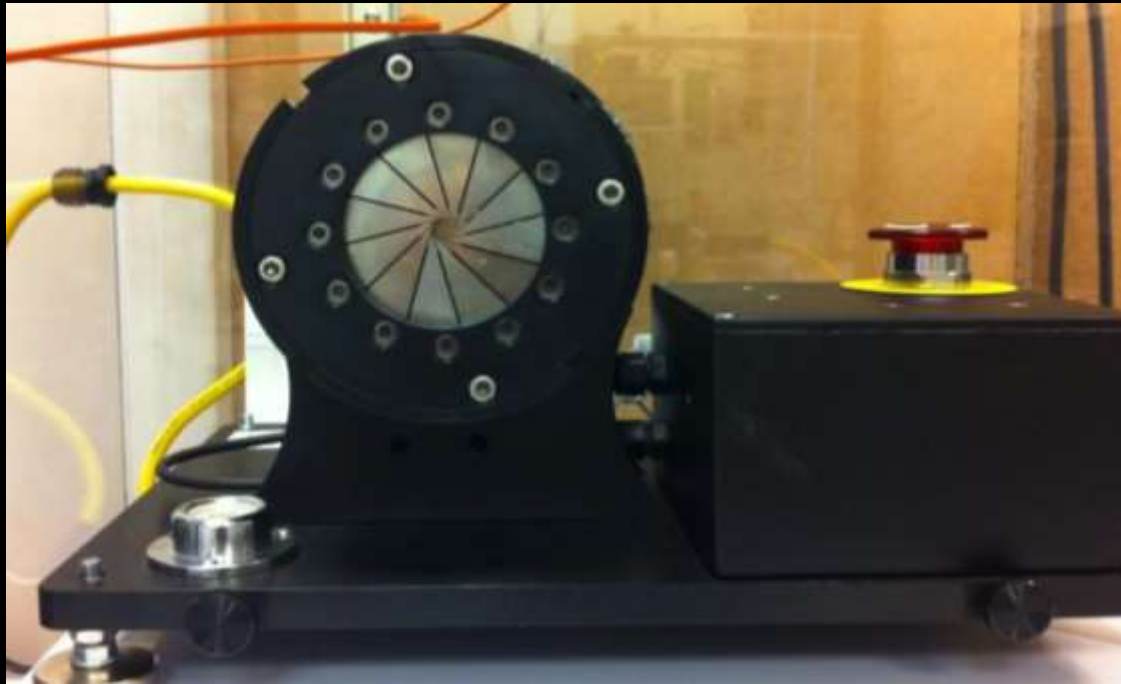


**“Playing” with composition of polymers  
and design of scaffold platform**



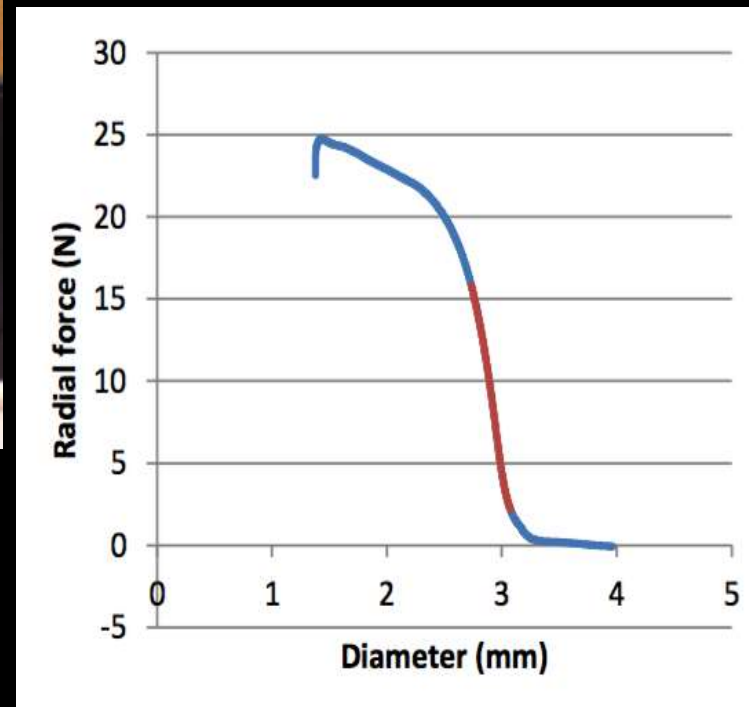
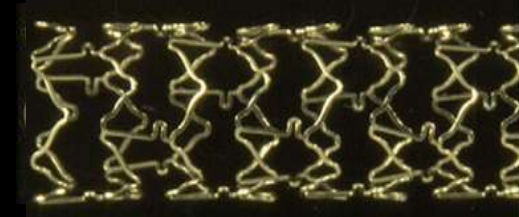
# “Playing” with composition of polymers and design of scaffold platform

## Impact of platform and polymer on radial force compared to metallic stents



**Crush resistance test**

**Metallic  
stent**

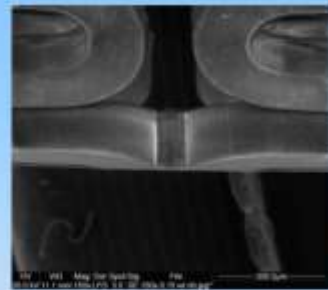
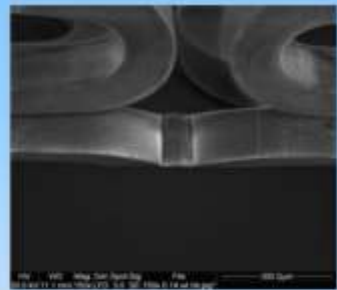
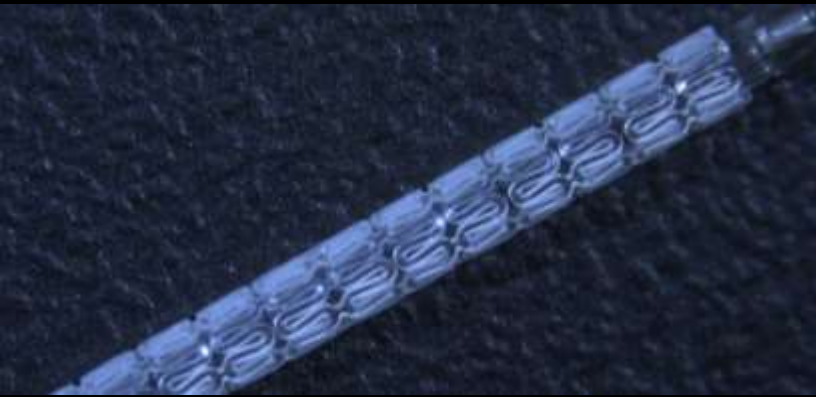


**15.8 N**

**“Playing” with molecular orientation  
and mechanical property of PLLA**

# “Playing” with molecular orientation and mechanical property of PLLA

## e.g. ARTERIUS: ArterioSorb scaffold



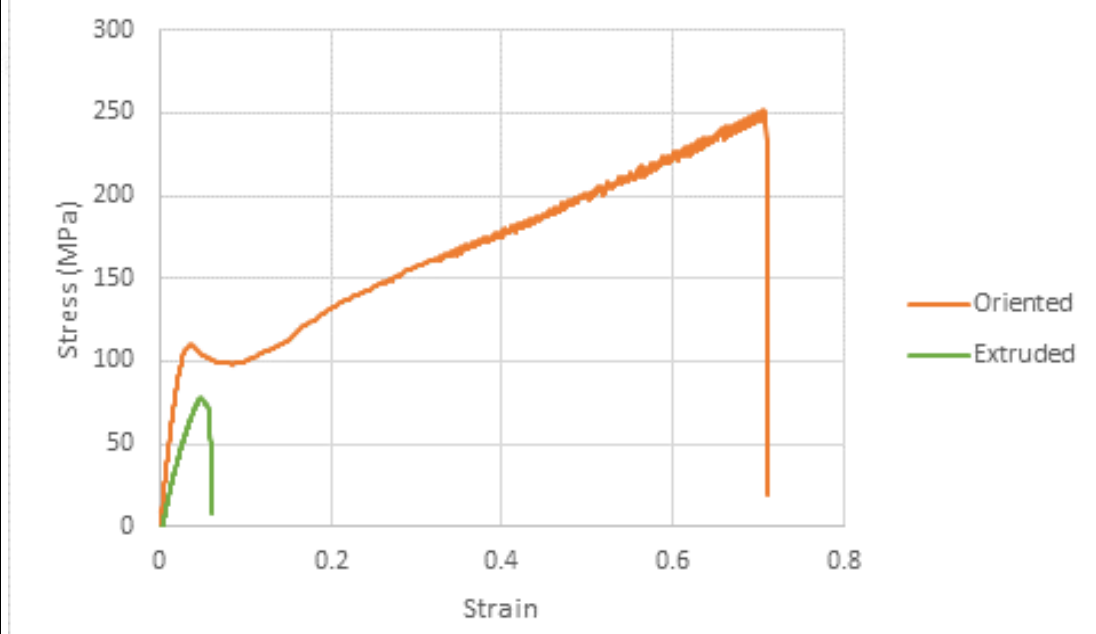
(a) Wall thickness = 110micron

(b) Wall thickness = 140micron

(c) Wall thickness = 150micron

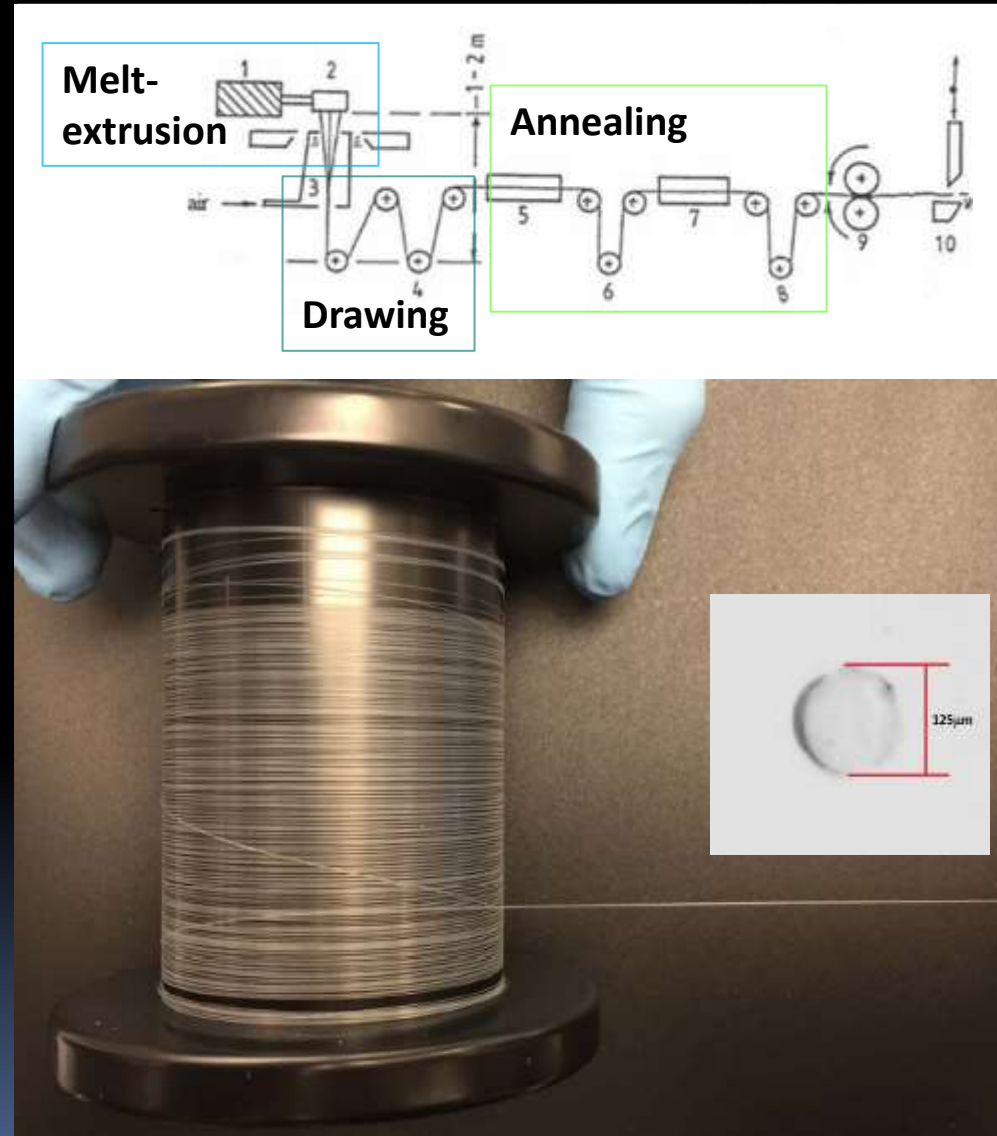
Strut wall thickness (micron)	Target size (mm)
110	2.5 - 3.00
140	3.00 - 3.50
150	3.5 - 4.00

- PLLA based
- Melt processing (EXTRUSION) and DIE-DRAWING (solid phase orientation)
- Solid-Phase Oriented tube with very high mechanical properties
- Thinner strut ( $\leq 150\mu\text{m}$  wall thickness, including  $140\mu\text{m}$  and  $110\mu\text{m}$ ) to be manufactured with enhanced physical performance similar to that of metal alloy stents.

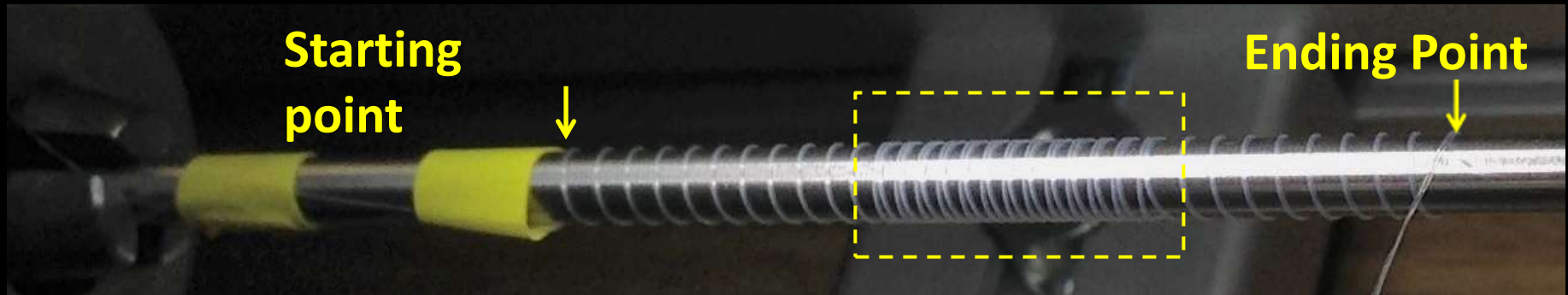


# Manli Cardiology's Microfiber Technology

1. **Highly oriented polylactide constituting a circular monofilament with preferred directional mechanical properties.**
2. **Convert monofilament's directional mechanical properties into scaffold's radial mechanical properties.**
3. **Transform circular monofilament into a scaffold with circular strut geometry.**



# Manli Cardiology's Microfiber Technology



**Coil design enables scaffold to**

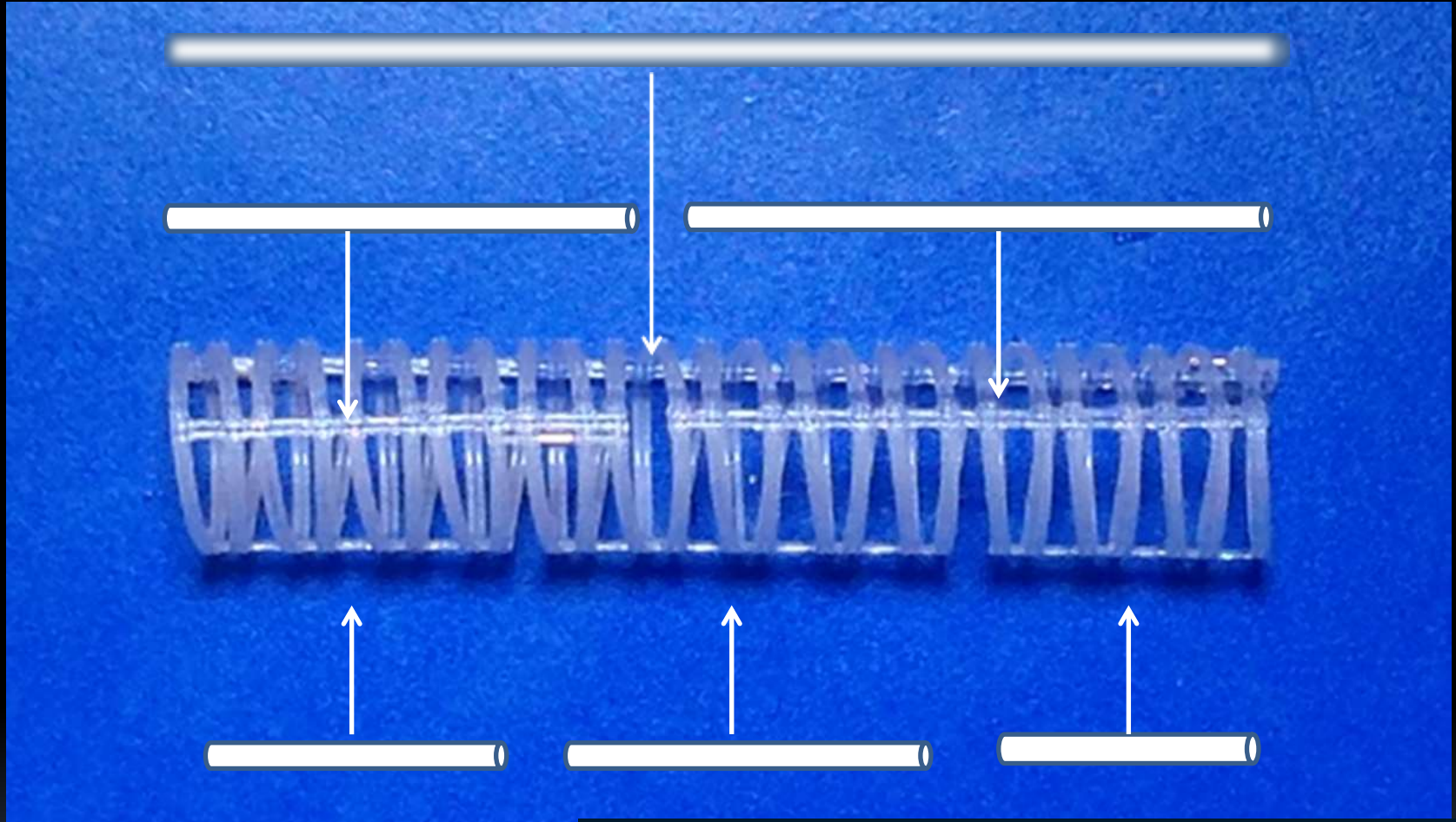
- **Inherit monofilament's directional mechanical properties.**
- **Inherit monofilament's circular geometry**

**3. Make monofilament's circular geometry into scaffold strut's circular geometry.**

**4. Ambient temperature assembly process**



# Manli Cardiology's Microfiber Technology

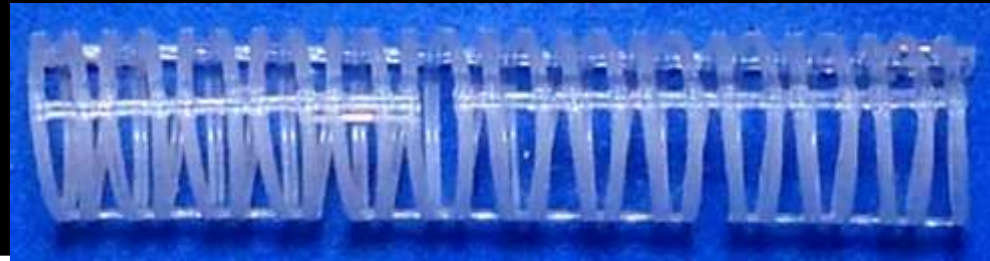


4. Ambient temperature assembly process

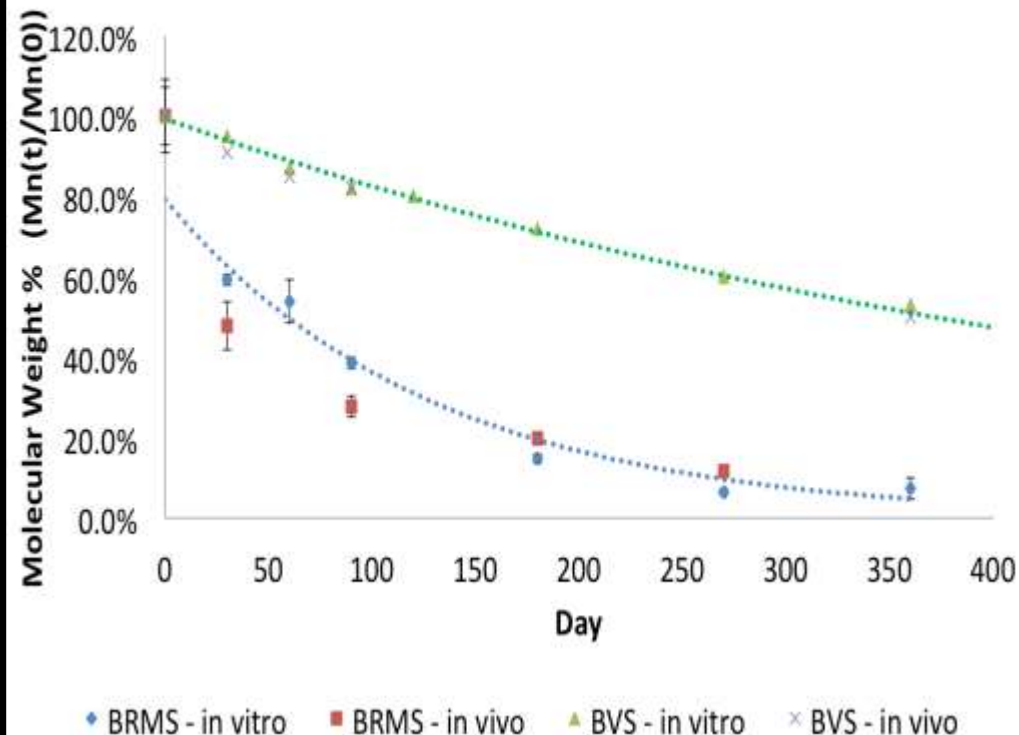
Multiple axial microfibers and radiopaque markers are attached at ambient temperature in the final subassembly process.

# Manli Cardiology's Microfiber Technology

1. Start with highly oriented circular polylactide monofilament with preferred directional mechanical properties.
2. Convert monofilament's directional mechanical properties into scaffold's radial mechanical properties.
3. Make monofilament's circular geometry into scaffold strut's circular geometry.
4. Ambient temperature assembly process



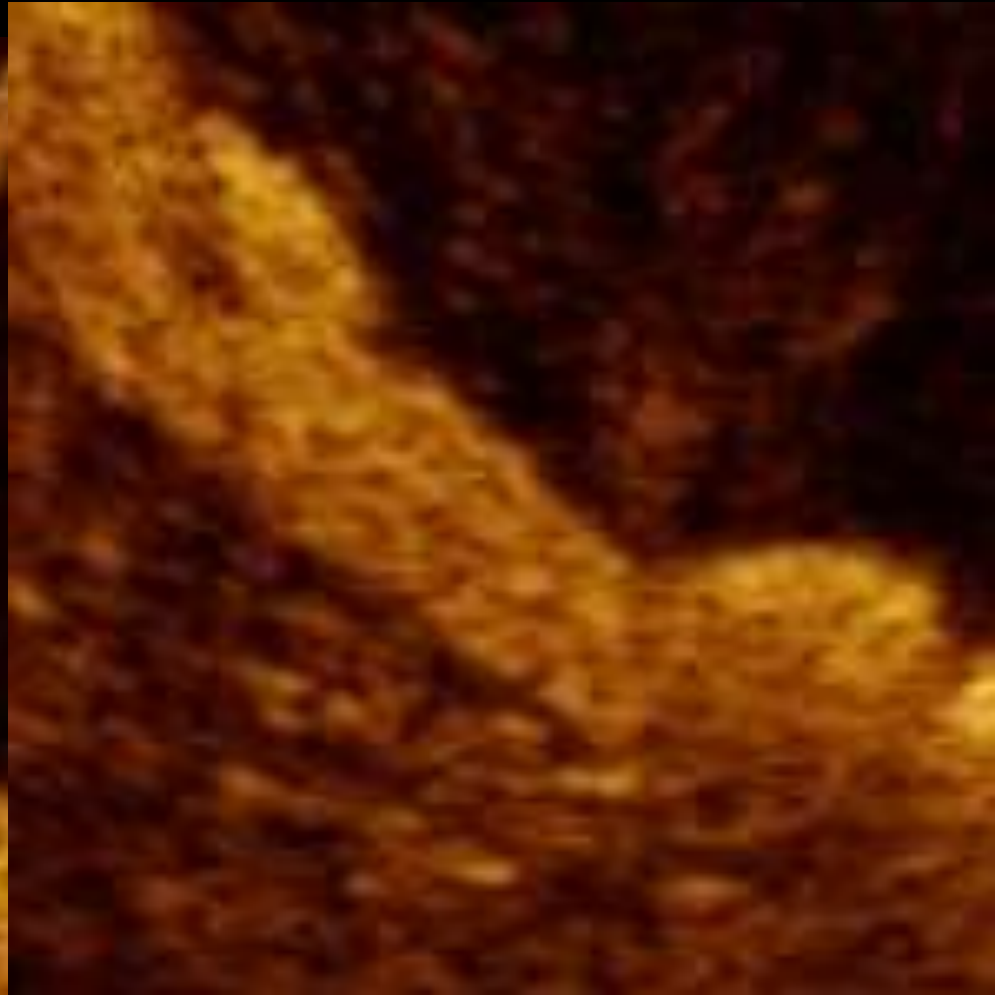
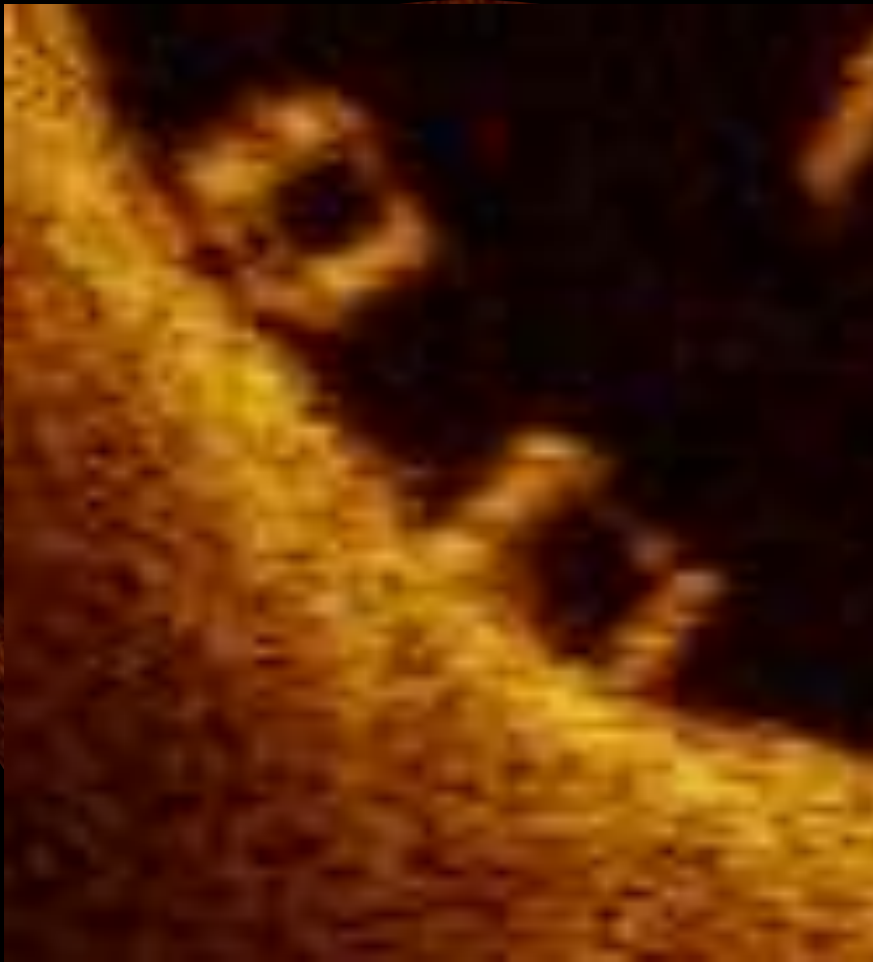
**BRMS MW Degradation Profile**  
*in vitro* and *in vivo*



**From the rectangular shape of the struts  
into the ovoid shape**

**Absorb**

**Mirage**

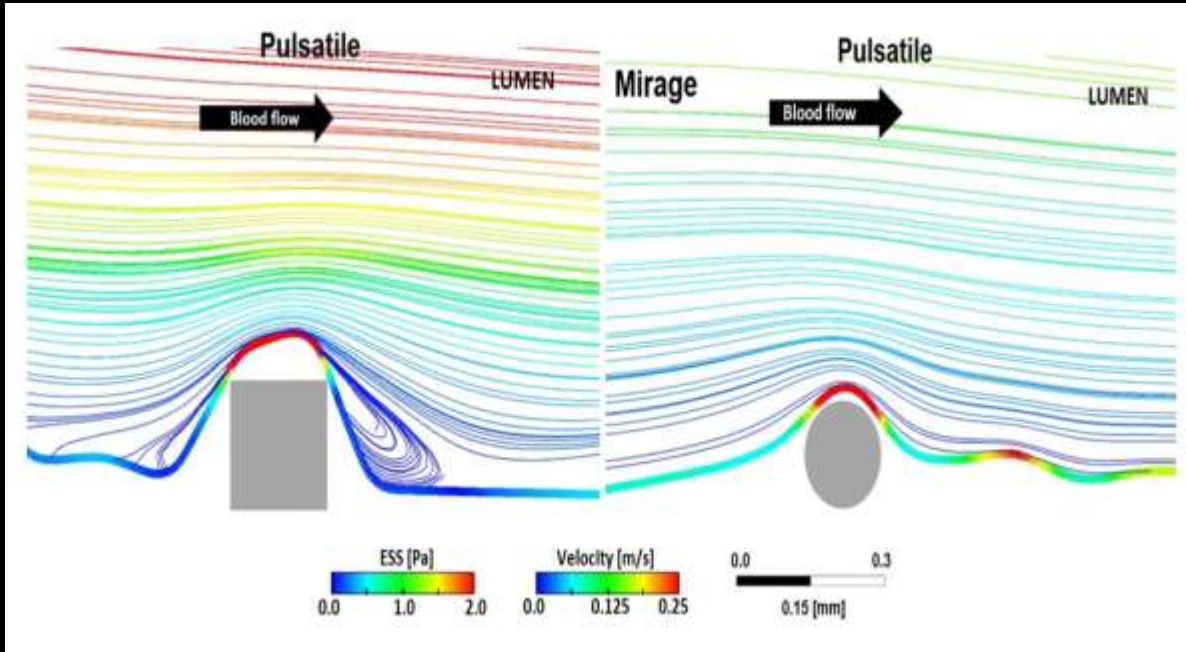




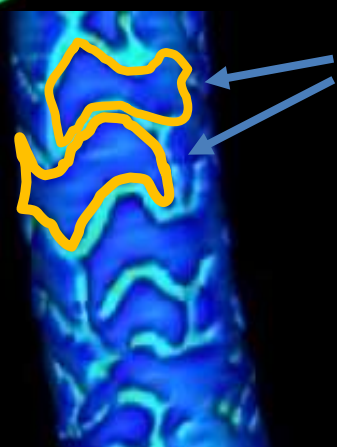
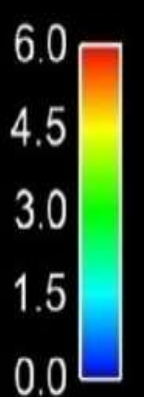
# Shear stress and flow analysis in ABSORB and MIRAGE

ABSORB  
BVS

MIRAGE  
BRMS

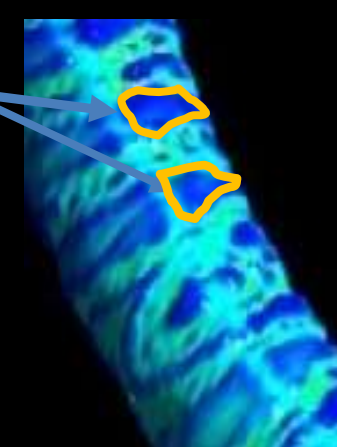
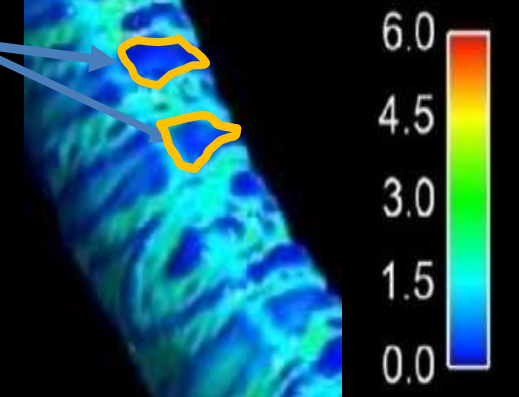


ESS (Pa)



The lower ESS (**dark blue area**) had a wider distribution in the Absorb BVS compared to the Mirage BRMS

ESS (Pa)



# Conclusions

**Future struts of BRS are to be:**

- Stronger and ductile**
- Thinner and round**
- Potentially quickly resorbable but without inducing inflammatory reaction**

**... Yes, we can!**

# Thank You!



Volume 11 - Number 13 - April 2016 - ISSN: 1774-024X

## EuroIntervention

### CORONARY INTERVENTIONS

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- 1468** Significance of prior percutaneous revascularisation in patients with acute coronary syndromes: insights from the prospective PROSPECT registry  
*A. Itiguez, G.W. Stone, et al*
- 1475** Clinical outcomes following "off-label" versus "established" indications of bioresorbable scaffolds for the treatment of coronary artery disease in a real-world population  
*T. Miyazaki, A. Colombo, et al*
- 1479** A novel approach to treat in-stent stenosis: 6- and 12-month results using the everolimus-eluting bioresorbable vascular scaffold  
*P. Janshidi, F. Cuculi, et al*
- 1487** Patient preference regarding assessment of clinical follow-up after percutaneous coronary intervention: the PAPAAYA study  
*M.M. Kok, M.J. Uerman, et al*
- 1495** Does access to invasive examination and treatment influence socioeconomic differences in case fatality for patients admitted for the first time with non-ST-elevation myocardial infarction or unstable angina?  
*S. Mårtensson, M. Osler, et al*
- 1503** Virtual reality training in coronary angiography and its transfer effect to real-life catheterisation lab  
*U.J. Jensen, P. Tornvall, et al*

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*P. Rodrigues, S. Torres, et al*

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- 1522** The prognostic value of acute and chronic troponin elevation after transcatheter aortic valve implantation  
*J.M. Sinning, N. Werner, et al*
- 1530** Emergency transcatheter aortic valve replacement in patients with cardiogenic shock due to acutely decompensated aortic stenosis  
*C. Frerker, K.H. Kuck, et al*
- 1537** First-in-man report of residual "intra-clip" regurgitation between two MitraClips treated by AMPLATZER Vascular Plug II  
*M. Taramasso, F. Maisano, et al*
- 1541** First transfemoral percutaneous edge-to-edge repair of the tricuspid valve using the MitraClip system  
*T. Wengenmayer, S. Grundmann, et al*
- 1545** First Lotus aortic valve-in-valve implantation to treat degenerated Mitroflow bioprostheses  
*F. Castriota, A. Cremonesi, et al*
- 1549** Direct Flow valve-in-valve implantation in a degenerated mitral bioprosthesis  
*G. Bruschi, F. De Marco, et al*

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