Bench-testing evaluation of a novel fully drug-eluting BRS

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Potential conflicts of interest

Speaker's name: Patrick W. Serruys, MD, PhD

- **I do not have any potential conflict of interest**

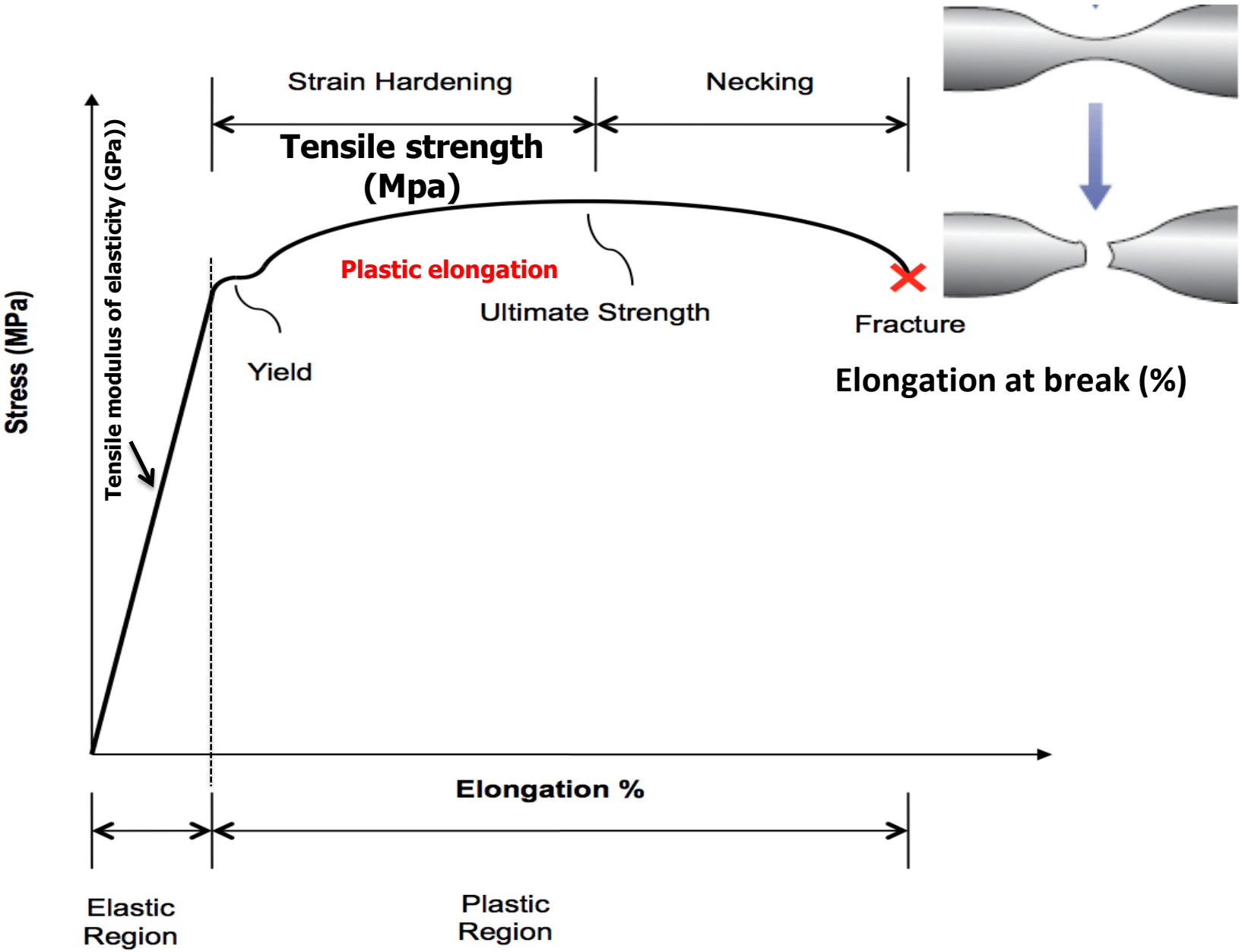
Current limitation of BRS

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.

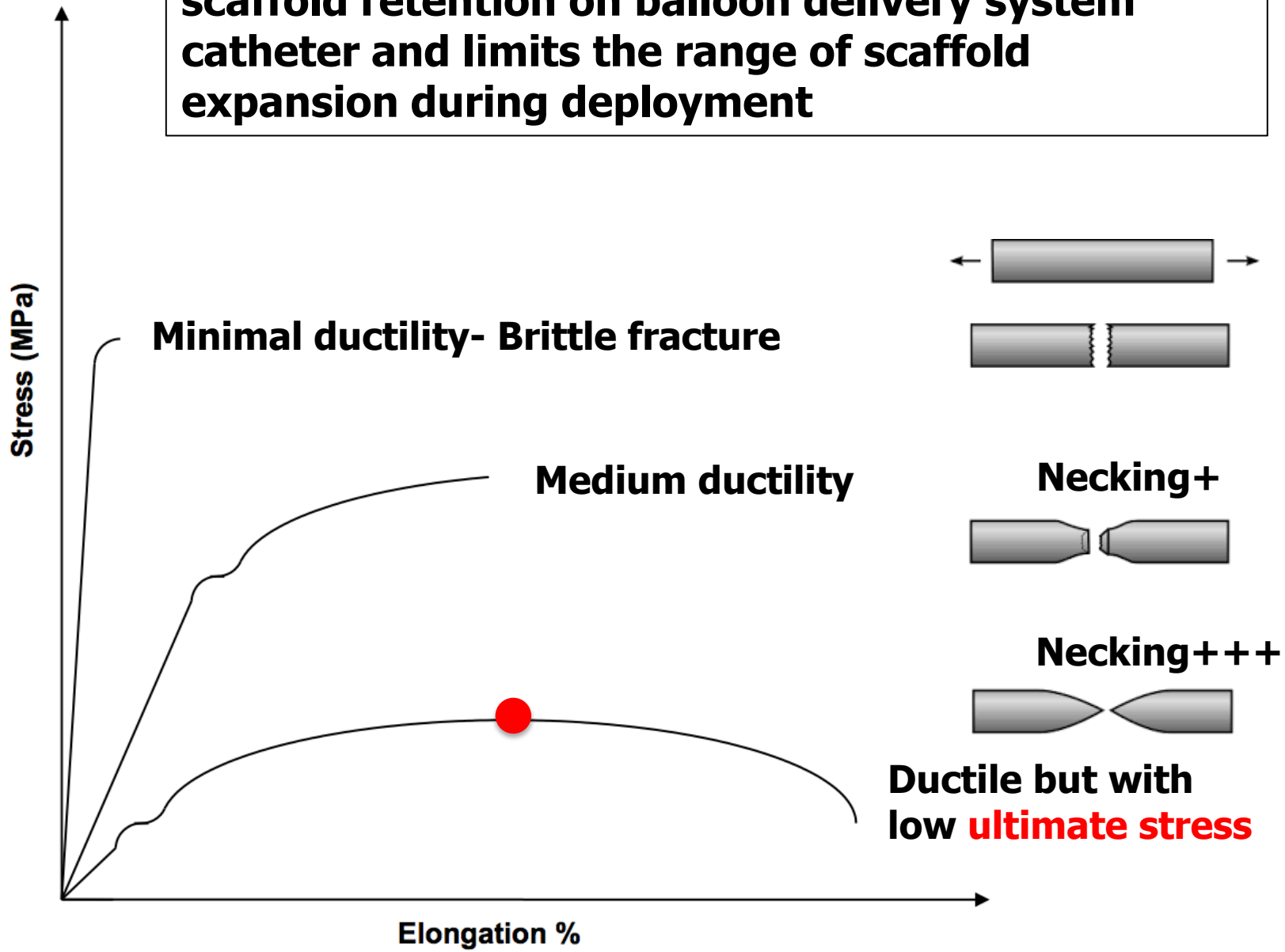
Currently, three primary limitations exist:

- **Low tensile strength and stiffness which require thick struts to prevent acute recoil**
- **Insufficient ductility which impacts scaffold crimping and 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**

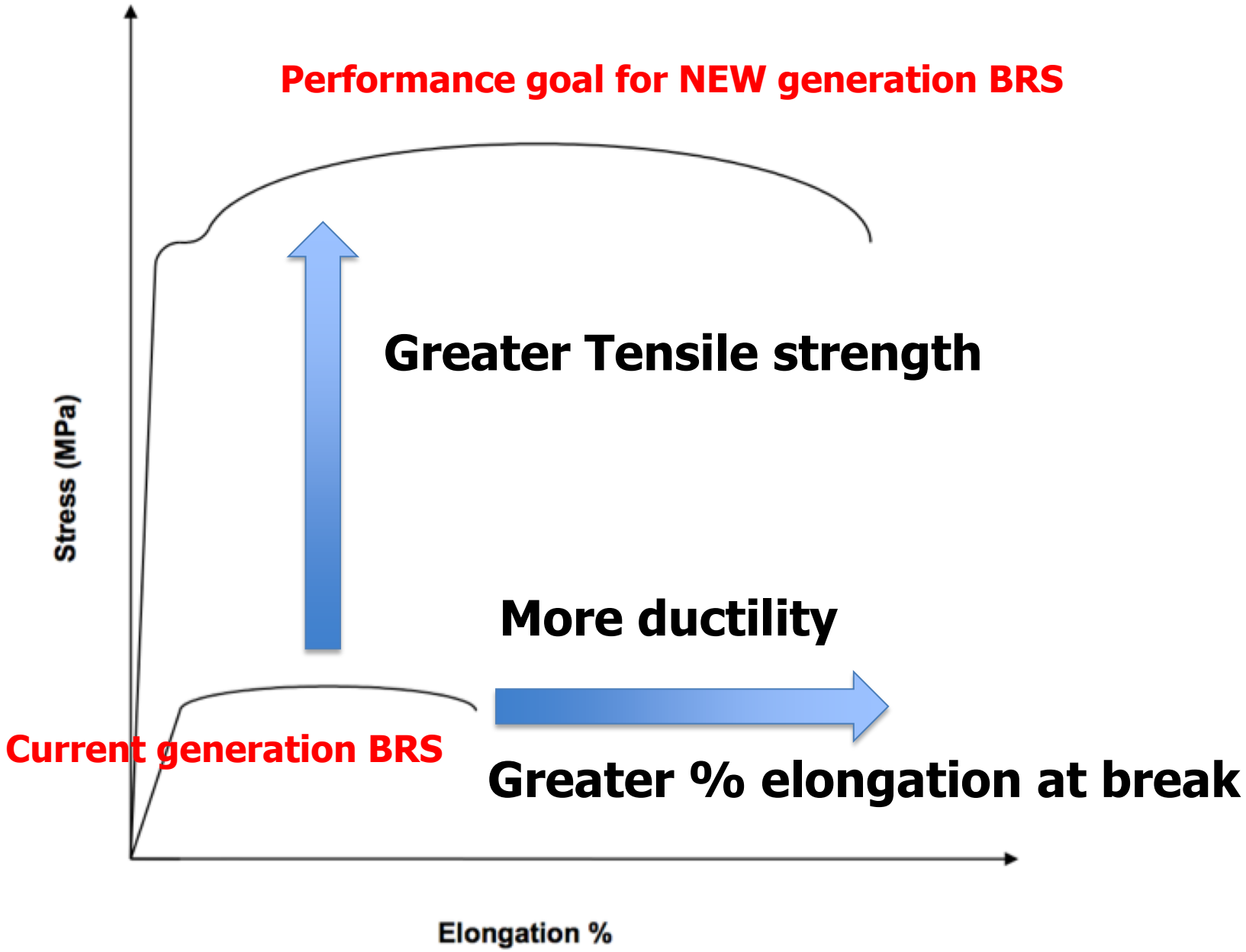
Let's take a "crash course" of material science



DUCTILITY is **a solid material's ability to deform under tensile stress;** Insufficient ductility impacts scaffold retention on balloon delivery system catheter and limits the range of scaffold expansion during deployment



Performance goal and mechanical dilemma



Mechanical properties of metal vs. PLLA

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

Onuma and Serruys Circulation 2011

"Playing" with composition of polymers

Polymer composition

Poly(L-lactide)

Poly (DL-lactide)

Poly (glycolide)

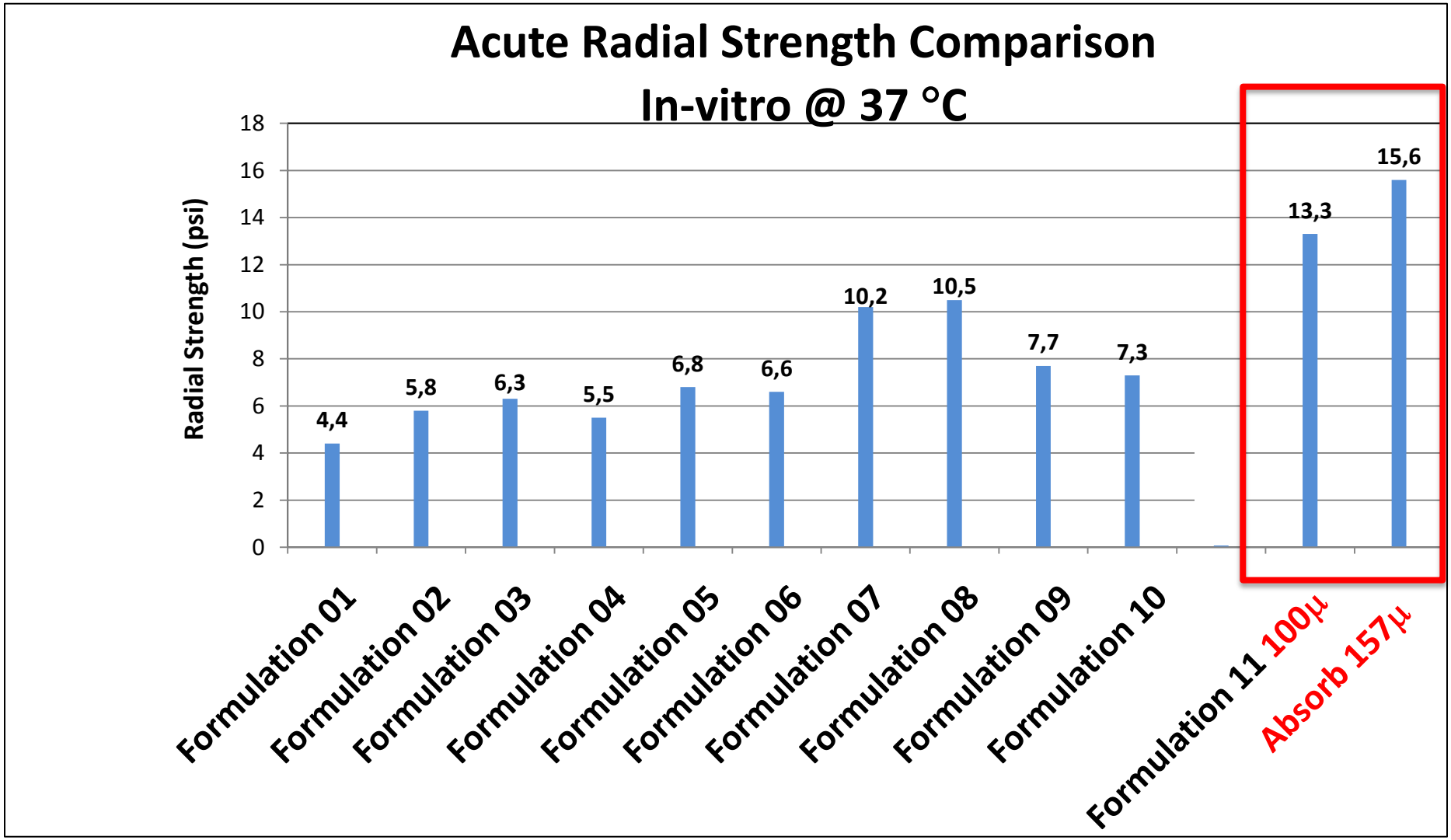
50/50 DL-lactide/glycolide

82/18 L-lactide/glycolide

70/30 L-Lactide/ε-caprolactone etc…

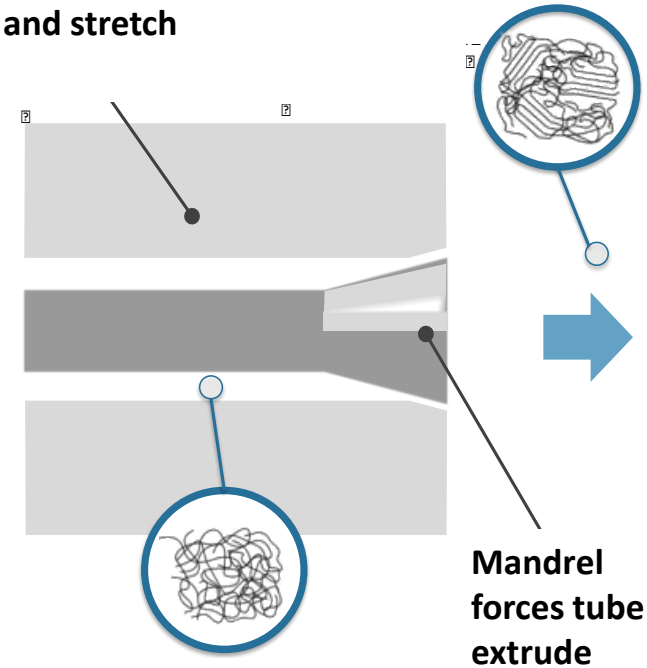
Onuma and Serruys Circulation 2011

#1 "Playing" with composition of polymers



#2 "Playing" with molecular orientation and mechanical property of PLLA: ArterioSorb™ scaffold of ARTERIUS

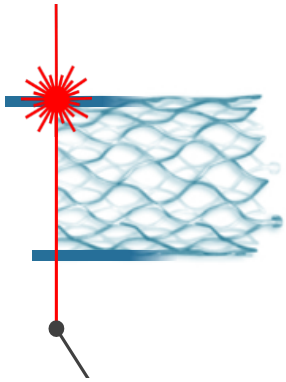
Heated Die helps polymer to become plastic and stretch



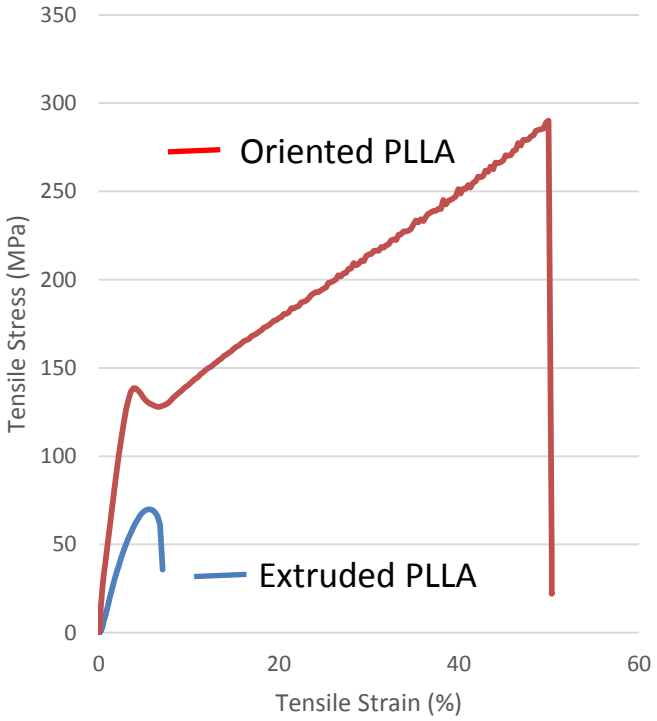
Amorphous polymer tube

Mandrel forces tube to extrude

Semi-crystalline polymer created by stretching or drawing the fibers



Laser cutting of stent (standard technology)

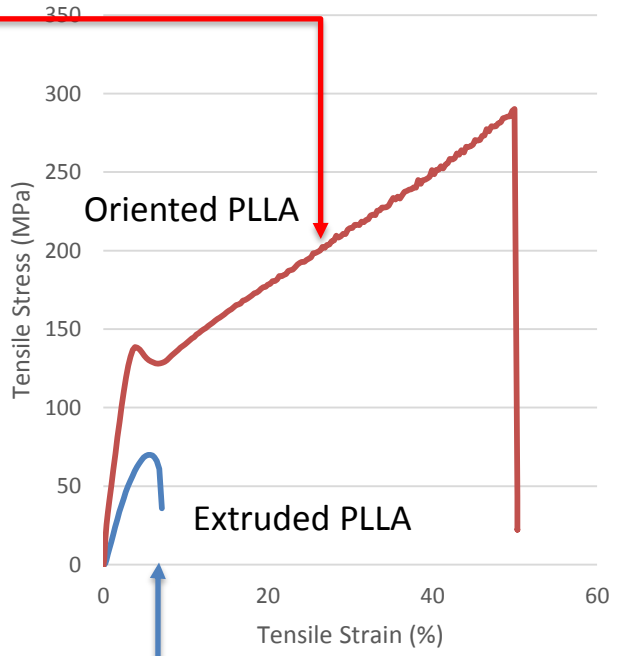


- Tube wall thickness of < 95 µm can be achieved
- Scaffold tube thickness comparable to metallic DES

#2 "Playing" with molecular orientation and mechanical property of PLLA: ArterioSorb™ scaffold of ARTERIUS

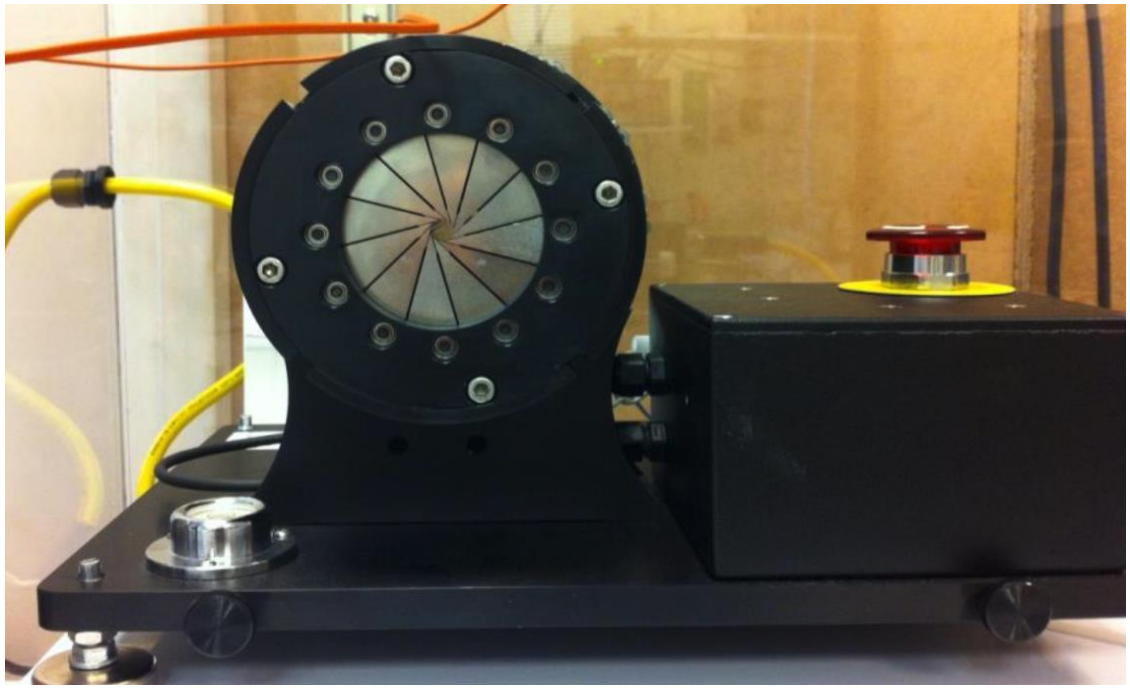
- Oriented material properties significantly higher than un-oriented PLLA
- Favourable comparison to strength of metallic materials used in stent production

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



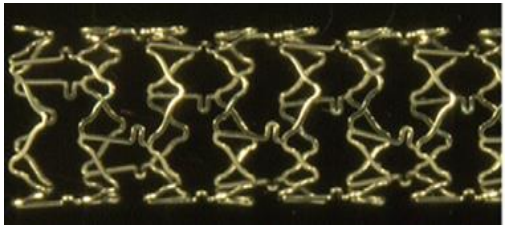
#3 "Playing" with composition of polymers and design of scaffold platform

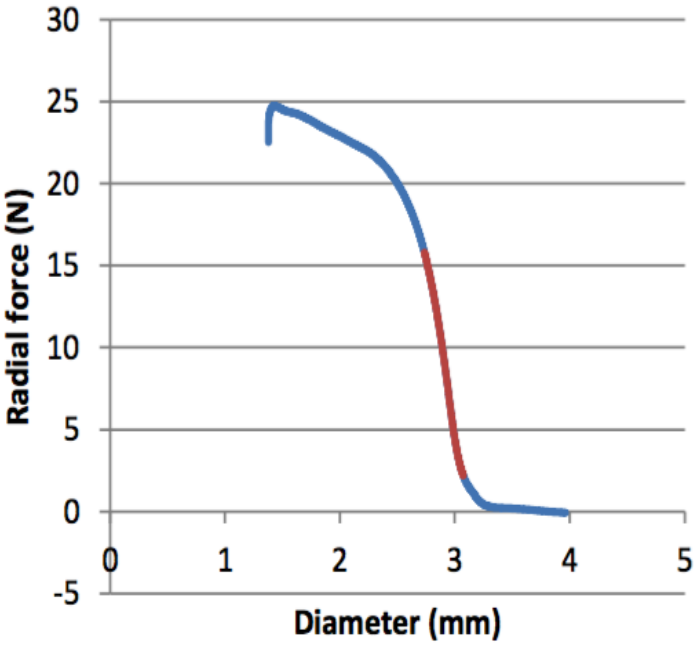
Impact of platform and polymer on radial force compared to metallic stents



Crush resistance test

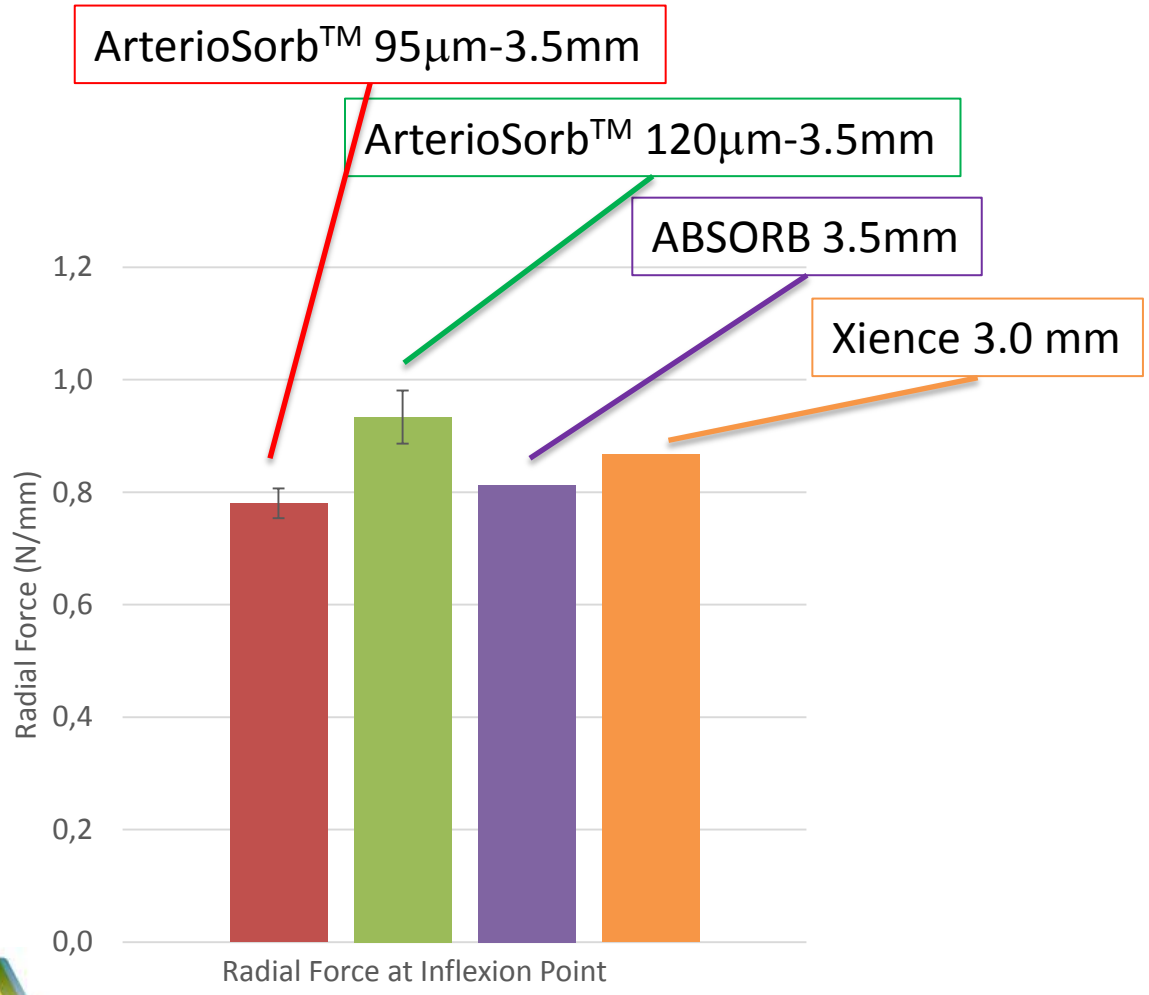
Metallic stent





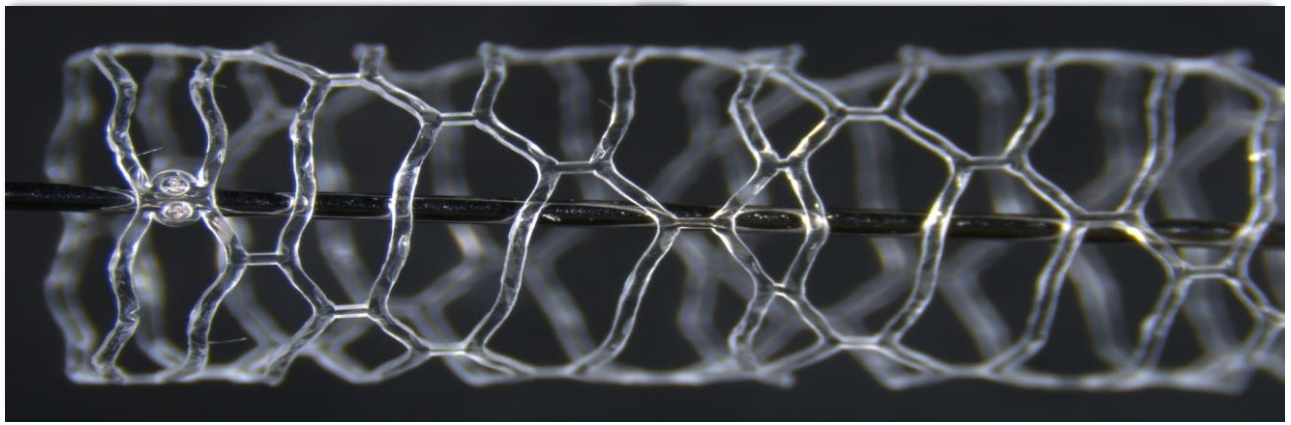
15.8 N

- Crush resistance with radially applied load
- ISO 25539-2 test performed by ProtomedLabs
- ArterioSorb™ has comparable radial strength to ABSORB despite a 95 µ wall thickness



Scaffold	Wall Thickness (µm)
ArterioSorb™ 95 µm-3.5mm	95
ArterioSorb™ 120 µm-3.5mm	120
ABSORB 3.5mm	157
Xience 3.0mm	81

Crush resistance data on file at Arterius



- Second design iterations are ArterioSorb™ 95 µm and ArterioSorb™ 120 µm strut thickness design leading to lower disruption of arterial flow and less likelihood of thrombosis
- 8 crowns, Smaller cells at the centre provide increased structural support where the stenosis is most severe and a larger dose of drug
- Wider crowns redistributes stresses during expansion
- Dual Platinum markers
- Sirolimus eluting scaffold with different size (PDLA coating)
- Spiral connectors, design provides high radial strength and yet appropriate flexibility for ease of implantation
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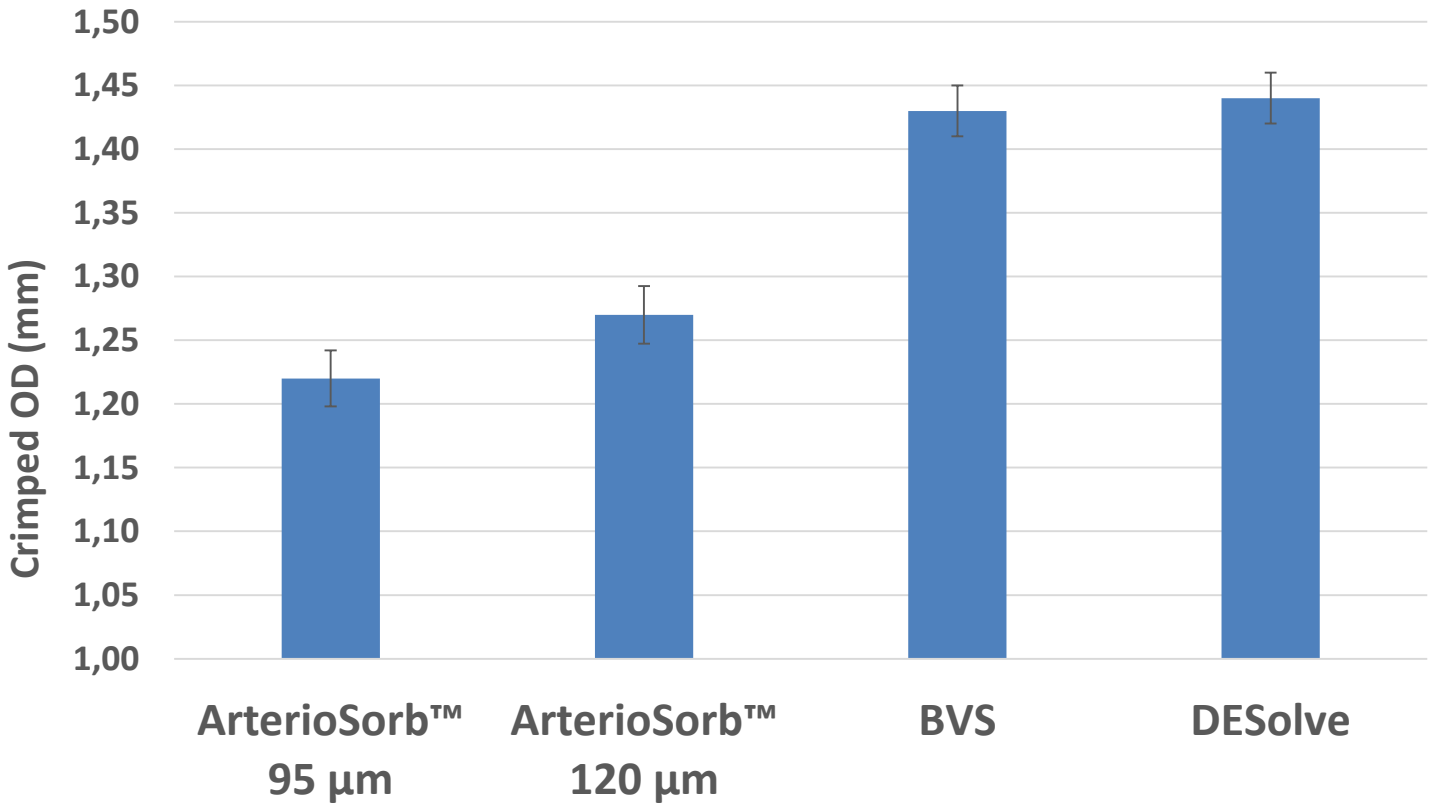
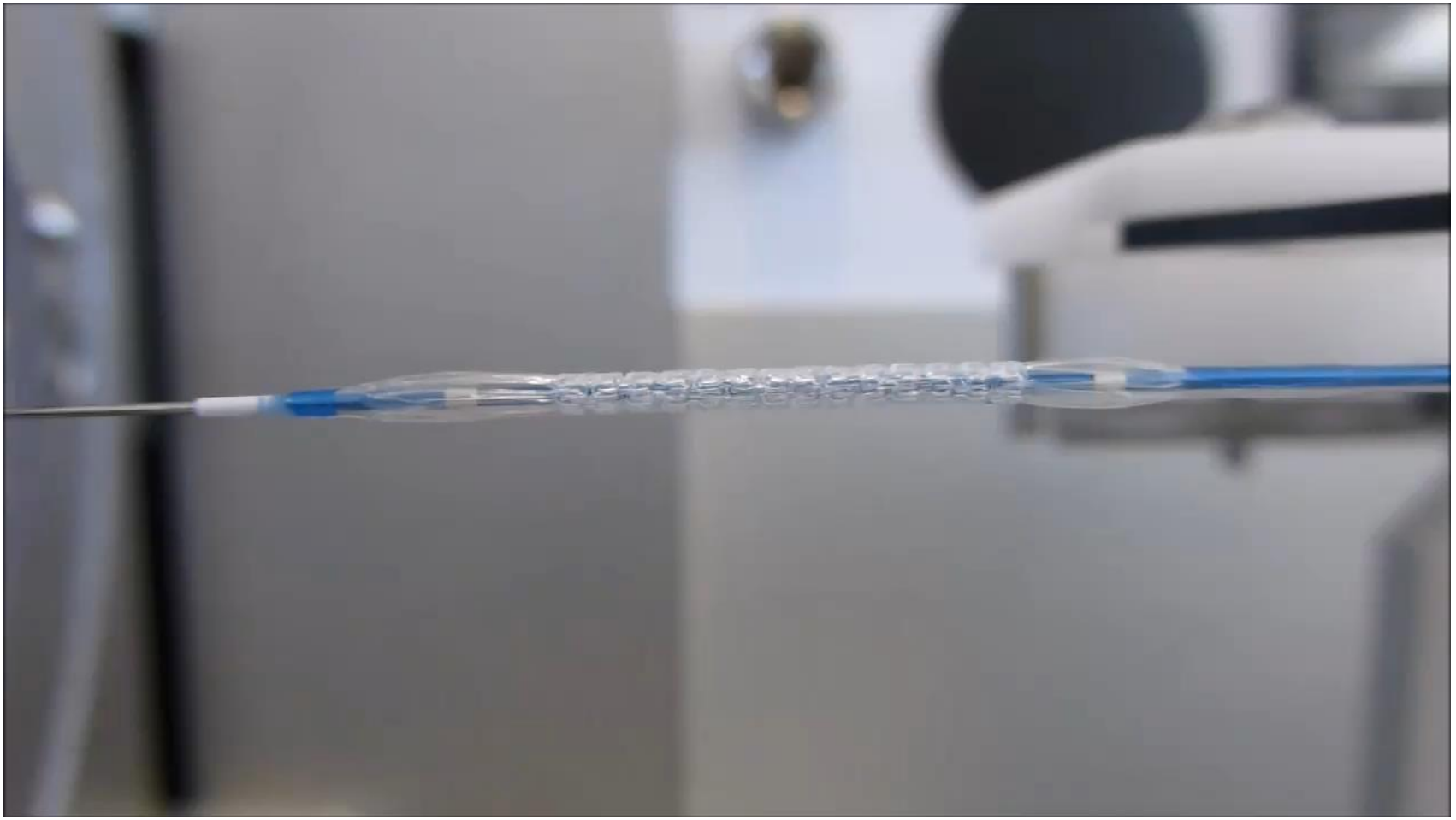
Bench Testing – Scaffold Crimping and Expansion

- **Low crimp profiles for ArterioSorb™ compared to other bioresorbable scaffolds**



BVS and DESolve crossing profiles from Ormiston; EuroIntervention February 2015

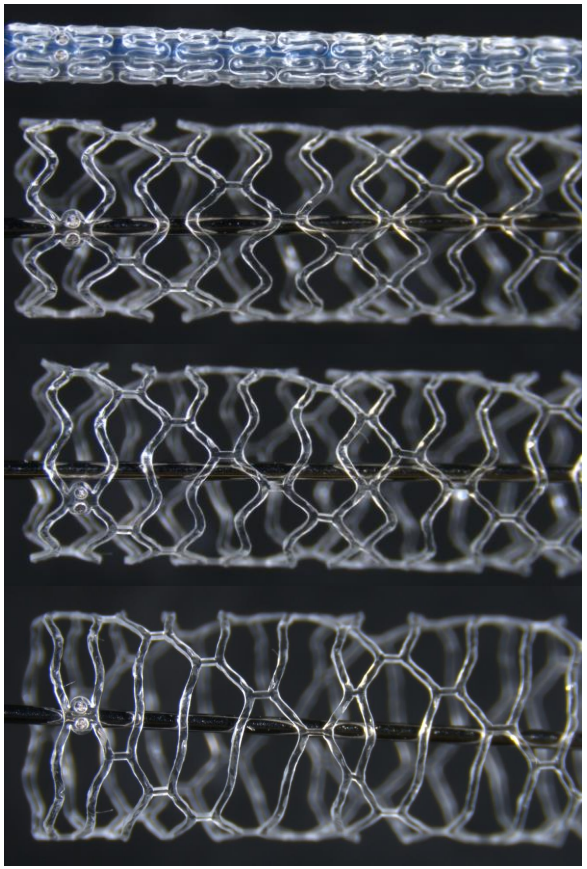
Bench Testing – Scaffold Crimping and Expansion



Bench Testing – Scaffold Crimping and Expansion

- **Expansion and post-dilatation**

ArterioSorb™ -95µm



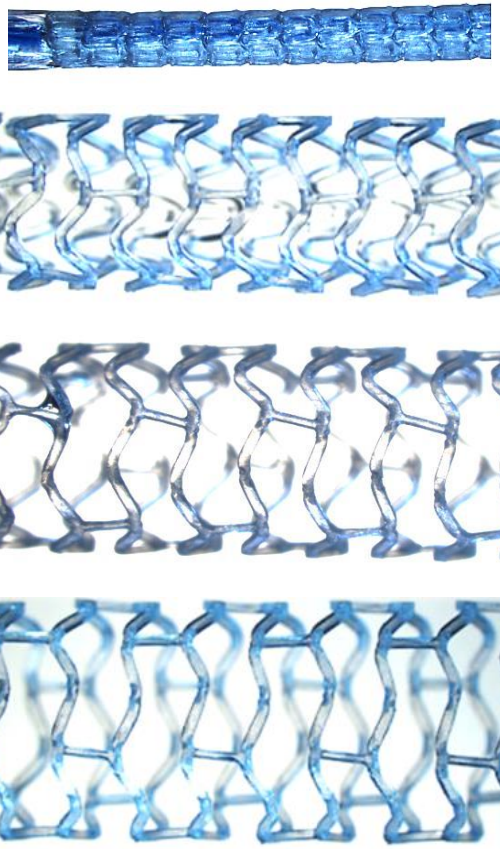
Crimped

3.5mm (nominal)

4.0mm (post-dilatation)

4.5mm (post-dilatation)

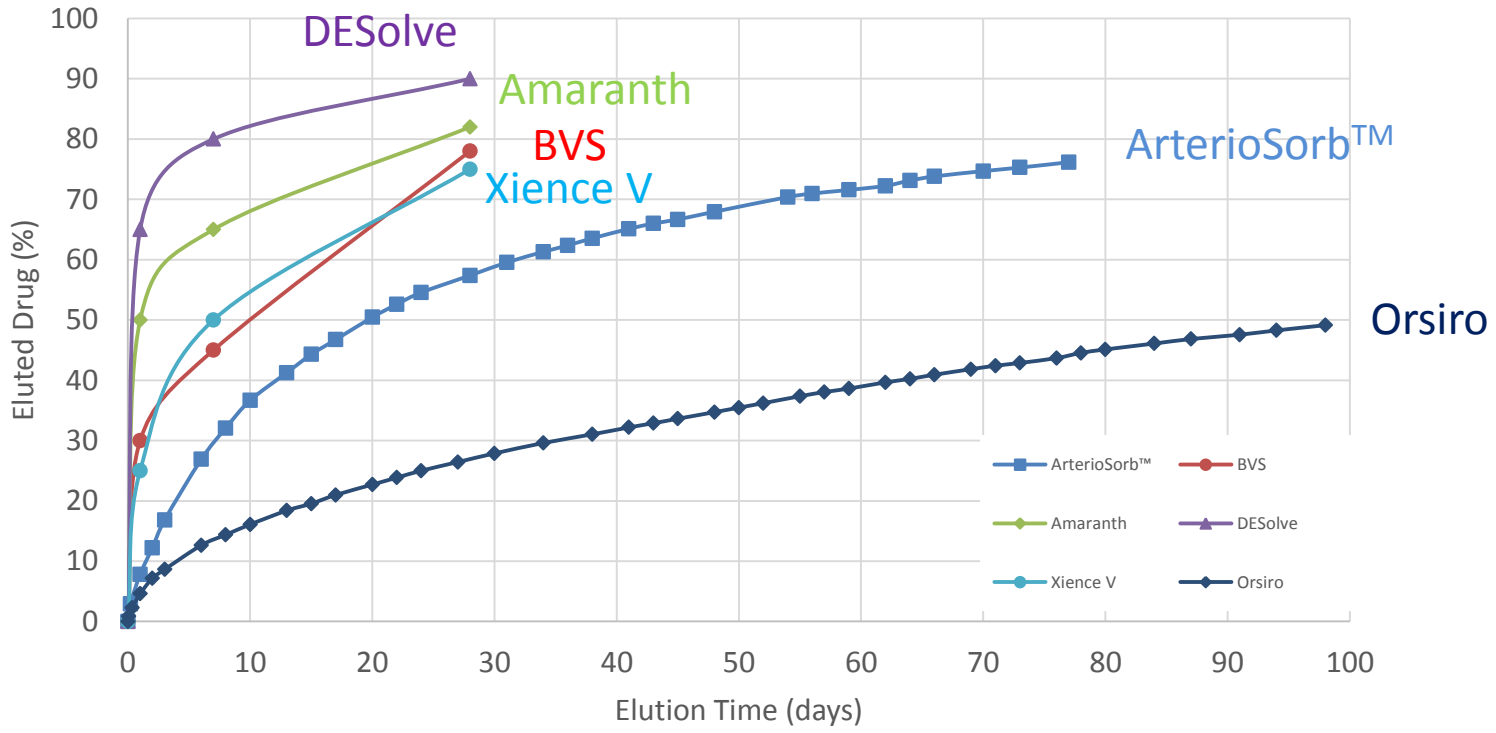
BVS -157µm



BVS images from Foin; EuroIntervention July 2015

Bench Testing – Drug Release

- Sirolimus / PDLA coating
- 1 µg / mm² drug loading



ArterioSorb™ and Orsiro: Data on file at Arterius
Amaranth, Xience V, BVS, DESolve: Data from literature sources

Future directions

- Thinner strut thickness samples
  - Extensive bench-testing of a 95-120 µm strut thickness scaffold has been undertaken
  - Further pre-clinical trials of this thinner strut thickness scaffold

- Clinical Trials
  - FIM: 30 patients - 6 months follow-up
    Start Q2-2017
  - CE Mark: 100 patients - 6 months and 1 year follow up
    Start Q2-2018

Thank you for your attention

Acknowledgements…

- Southampton University (UK) – Stent Design
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- Innovate UK for financial support