CARDIOVASCULAR SUMMIT
TCTAP 2015

Can We Justify the Global Use of BVS?

Yes, It Can Replace Metal Stent.

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27 Companies developing bioresorbable scaffolds (cvpipeline)

Company	Product Name	Biodegradable material used for backbone	Drug elution	Phase of development
Abbott	Absorb	PLLA	Everolimus	CE mark, U.S. clinical trial enrollment complete
Elixir	DESolve	PLLA polymer	Novolimus	CE mark
Elixir	DESolve 100	PLLA polymer	Novolimus	CE mark
Elixir	DESolve AMI	PLLA polymer	Novolimus	Clinical studies underway
BIOTRONIK	DREAMS	Magnesium	Sirolimus	Clinical studies underway
ART	ART18Z	PLLA + PDLLA	None	Clinical studies underway
Amaranth Medical	Sirolimus-eluting Fortitude	PLLA	Sirolimus	Clinical studies underway
Huaan	XINSORB	PLLA	Sirolimus	Clinical studies underway
Lepu	NeoVas	PLLA	Sirollimus	Clinical studies underway
ManLi Cardiology	MIRAGE	PLLA	Sirollimus	Clinical studies underway
Meril	MeRes	PLLA	Sirolimus	Clinical studies underway
MicroPort	Microport Bioabsorbable Scaffold	PLLA	Sirolimus	Clinical studies underway
QualiMed	QualiMed Mg Absorbable Scaffold	Magnesium		Clinical studies underway
REVA	ReZolve	Tyrosine polycarbonate	Sirolimus	Clinical studies underway
Amaranth Medical	Next generation	PLLA	Sirolimus	Preclinical study underway
Amaranth Medical	FORTITUDE	PLLA	None	Preclinical study underway
ART/ TERUMO	ART18Z + sirolimus eluting	PLLA + PDLLA	Sirolimus	Preclinical study underway
Arterius	ArterioSorb	PLLA	Sirolimus	Preclinical study underway
Boston Scientific	FAST	Magnesium		Preclinical study underway
Cardionovum	ReNATURAL	PLLA		Preclinical study underway
LifeTech	Lifetech Iron Stent	Iron	Sirollimus	Preclinical study underway
Medtronic	Mg Spiral	Magnesium	Unknown	Preclinical study underway
OrbusNeich	On-AVS	PLLA copolymer	Sirolimus	Preclinical study underway
REVA	Fantom	Tyrosine polycarbonate	Sirolimus	Preclinical study underway
Xenogenics	Ideal BioStent	Salicylate	Sirolimus	Preclinical study underway
Zorion Medical	ZMED	PLLA	Unknown	Preclinical study underway
Abbott	Next-Gen Absorb	PLLA	Everolimus	Preclinical study underway
S3V	Avatar	PLLA	Unknown	Unknown
Envision Scientific	BIOLUTE	PLLA	Sirolimus	In development
Kyoto Medical	IGAKI-TAMAI	PLLA	None	In development
Sahajanand	Sahajanand Bioabsorbable	PLLA	Unknown	In development

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 "crush course" of material science

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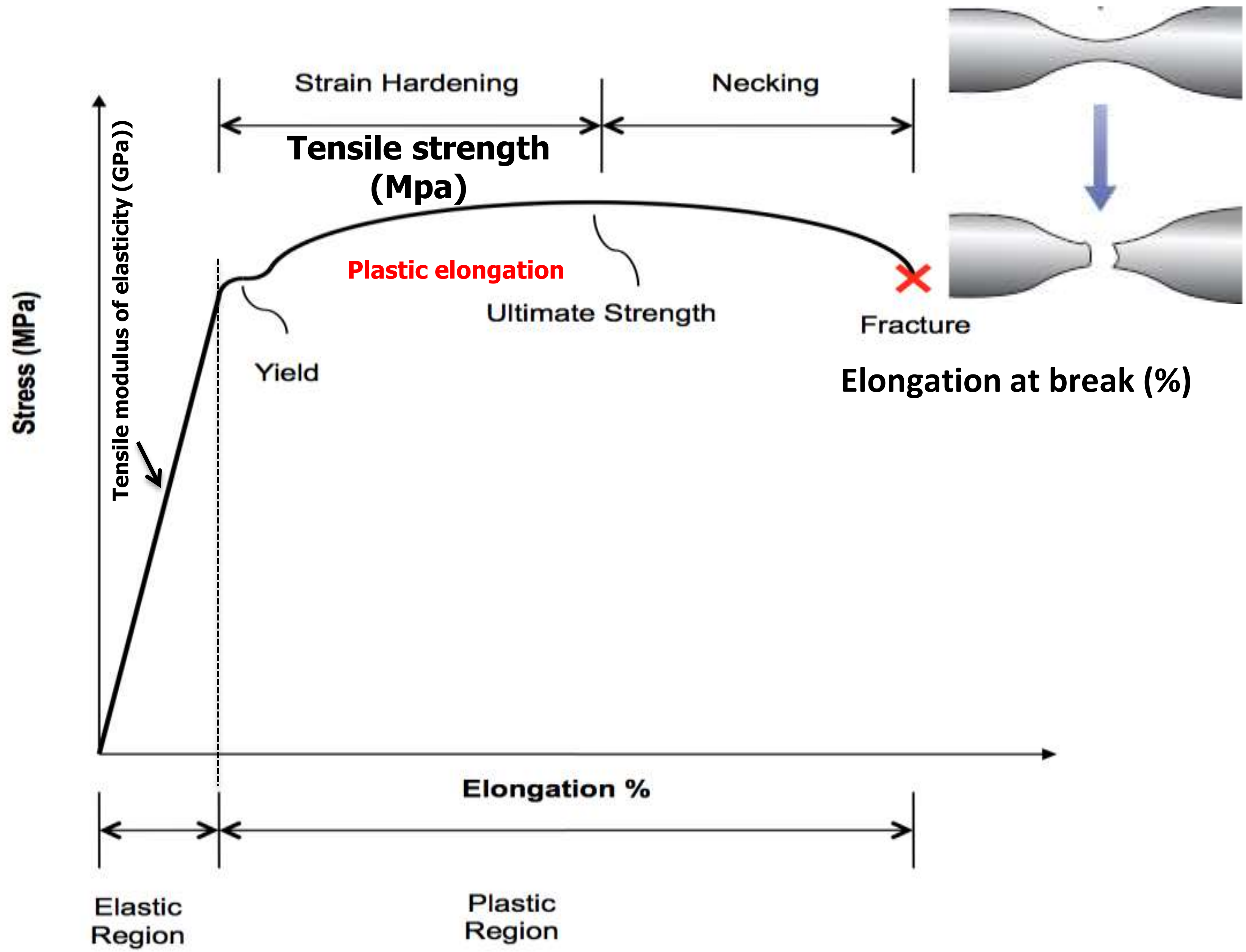


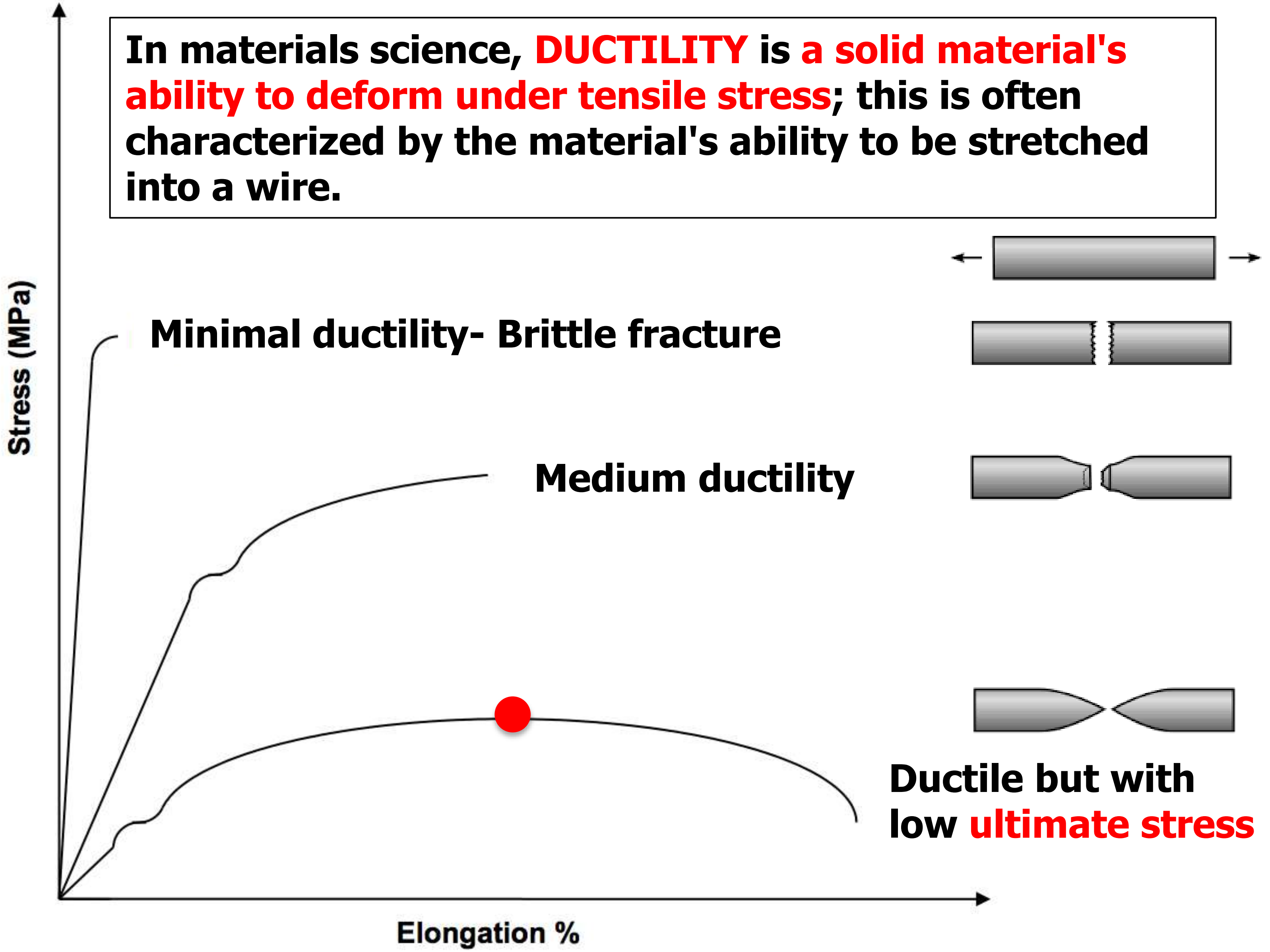
Mechanical properties of metal vs. PLLA

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
Cobalt chromium	210-235	1449	~40
Magnesium alloy	40-45	220-330	2-20

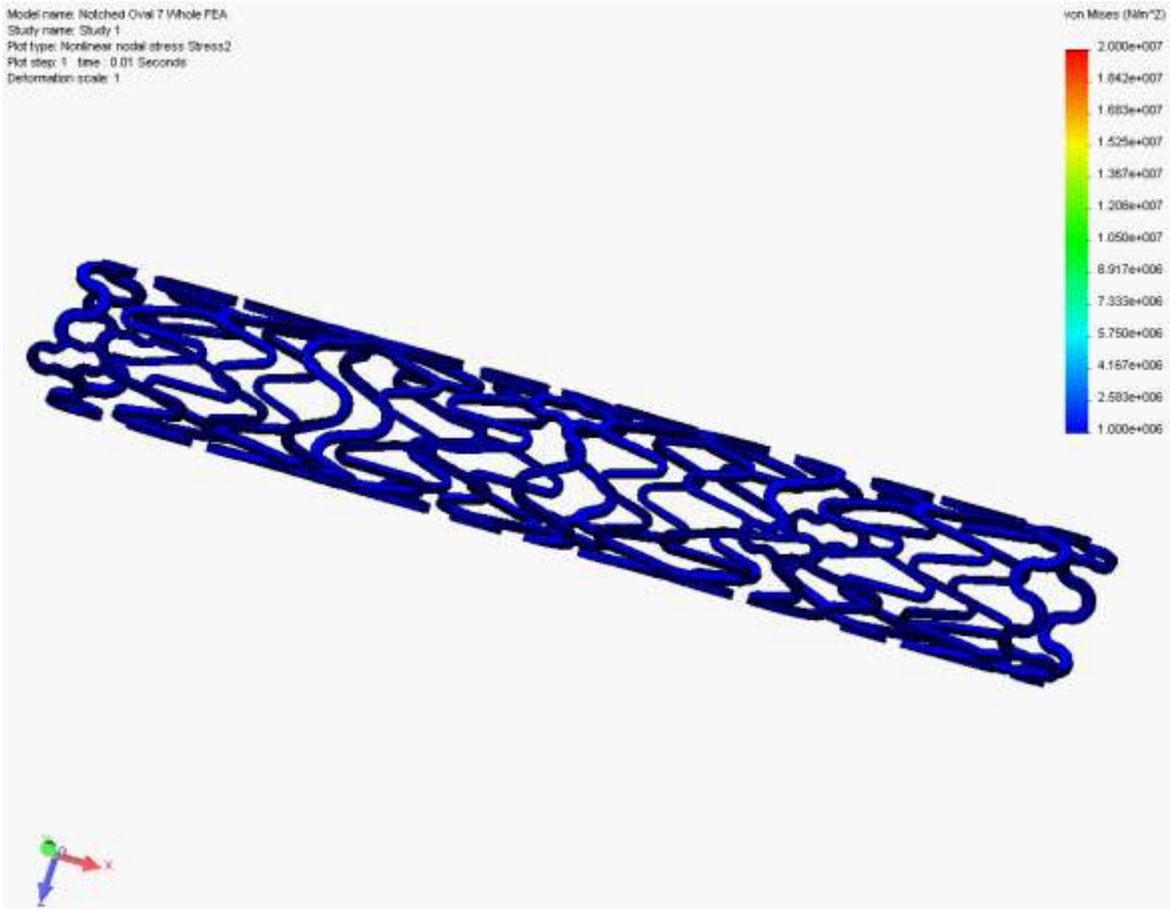
Onuma, Serruys Circulation 2011

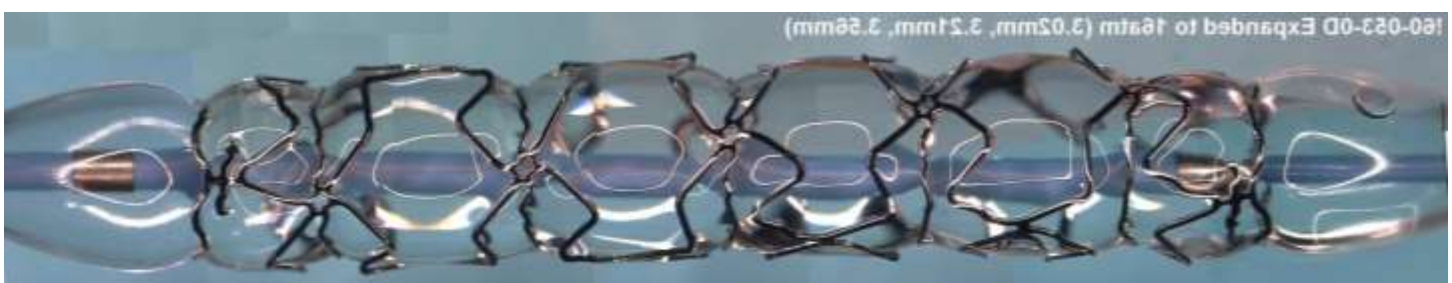
Insufficient ductility impacts scaffold retention on balloon catheter and limits the range of scaffold expansion during deployment

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.

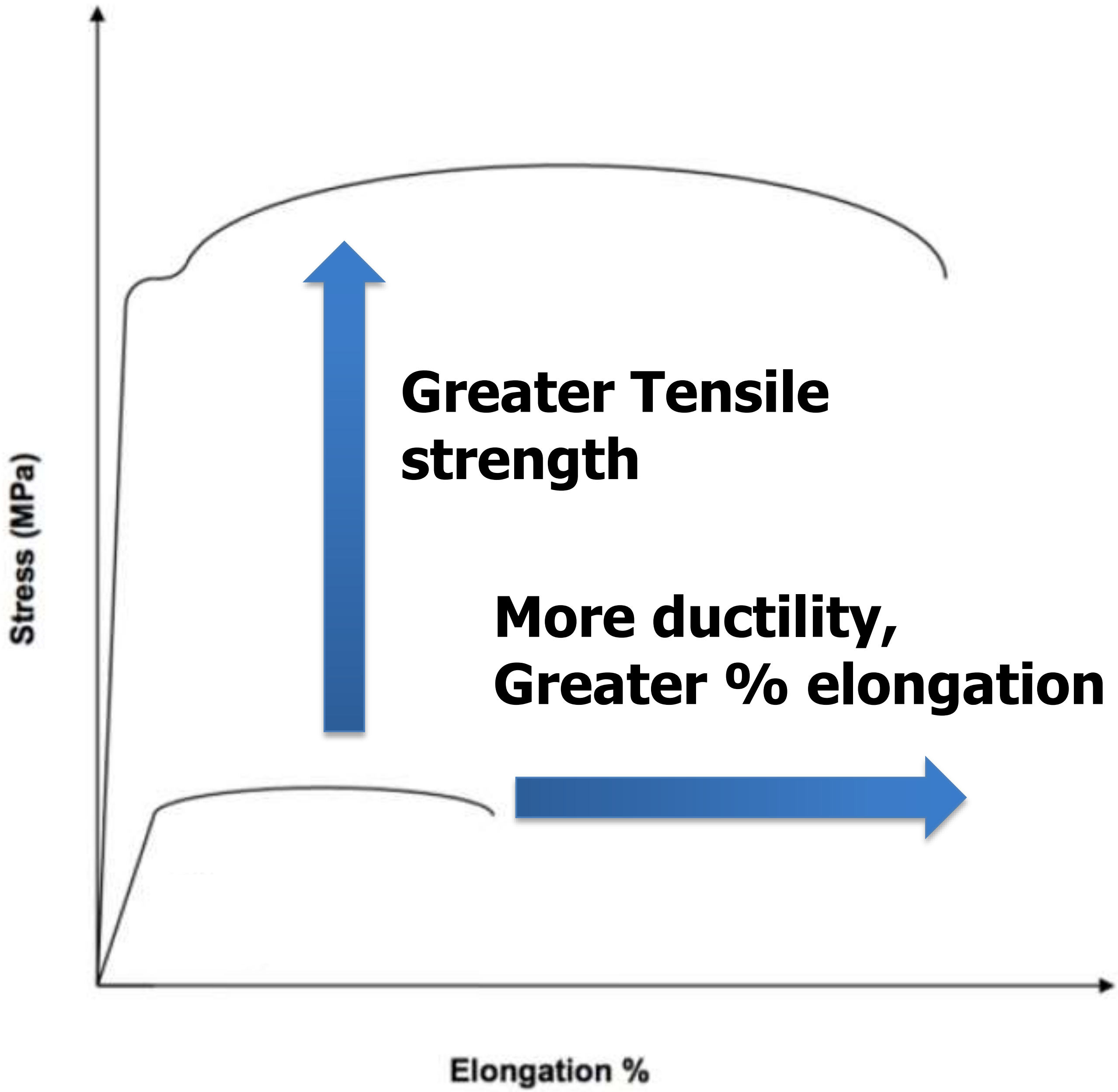


From a single wire to a coronary scaffold/stent
Strain of scaffold during crimping and implantation





Performance goal and mechanical dilemma



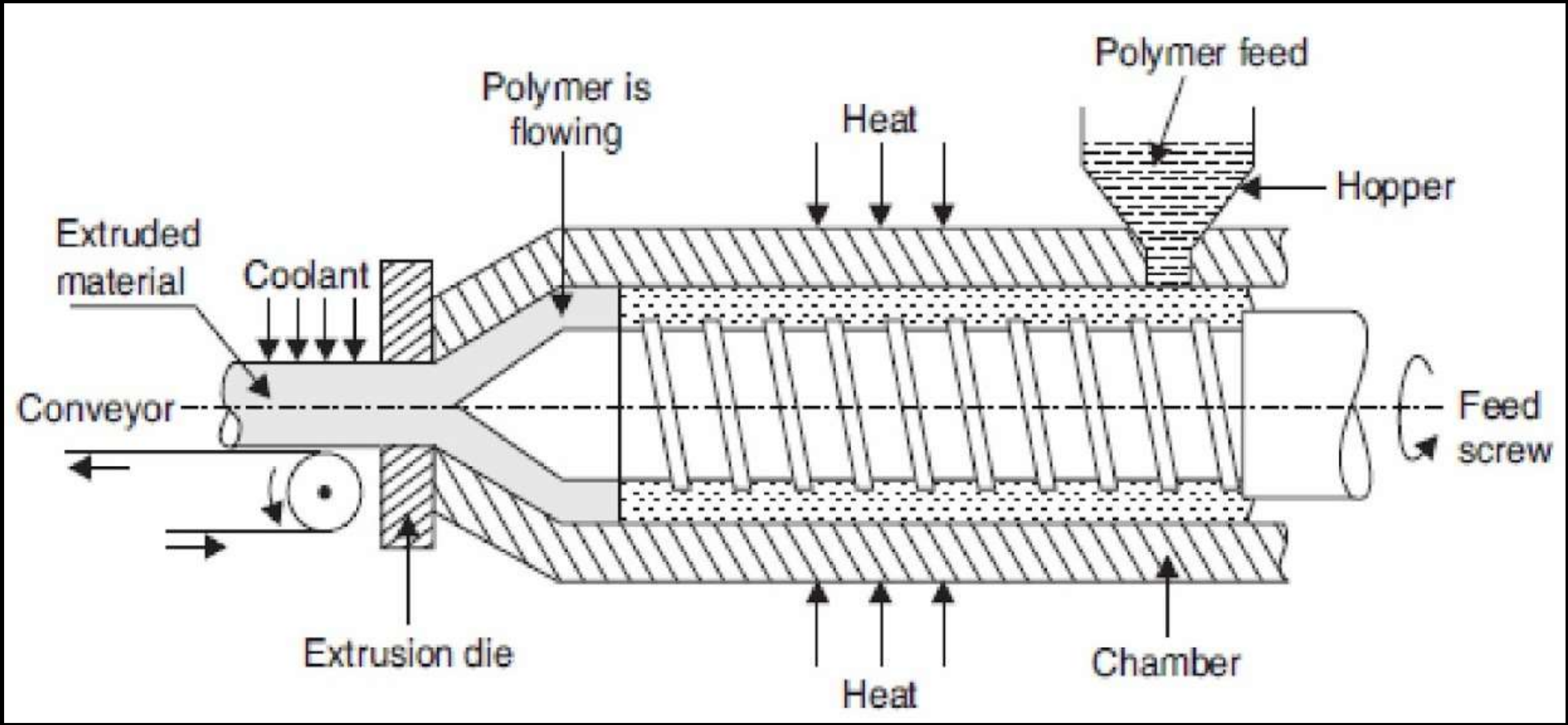
Processing methods of PLLA

	Processing method	Materials form
Zeus Inc	Extrusion tubing	PLLA
Arterius	Solid orientation by die-drawing of extruded tubing	PLLA
Abbott Vascular	Blow-moulding of extruded tubing	PLLA
Elixir	Spraying PLLAD dissolved in a solvent onto a mandrel to form a tube. The tube has to be subjected to **annealing** process up to 72 hrs. The device might also require **heat annealing**	PLLA (dissolved in an organic solvent)
ART	**Annealing** of the scaffold made from a tube	PLLA (specifically synthesised)

Annealing is a heating of a polymeric part to below it's glass transition temperature in order to relieve the internal stresses introduced into the part during its fabrication (molding, cooling after molding, machining, welding)

Extrusion

Extrusion

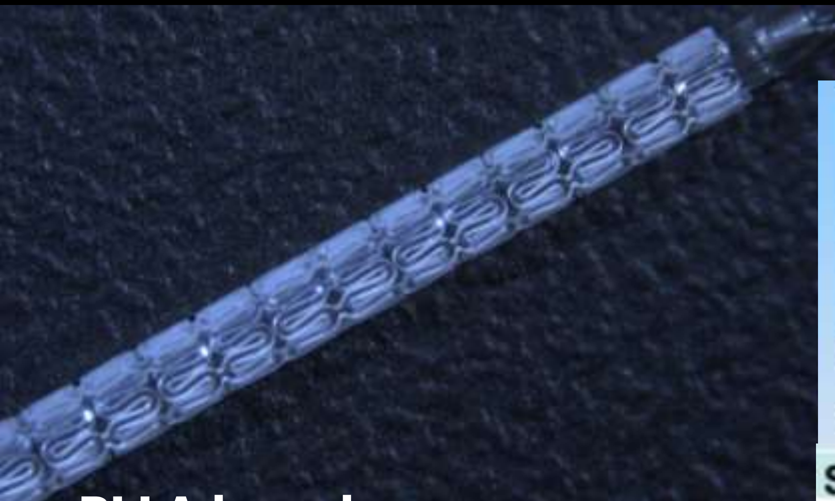


- **Melt polymer resin and shape it into a tubular geometry.**
- **Select a screw based upon the material of interest.**
- **Select process conditions leading to:**

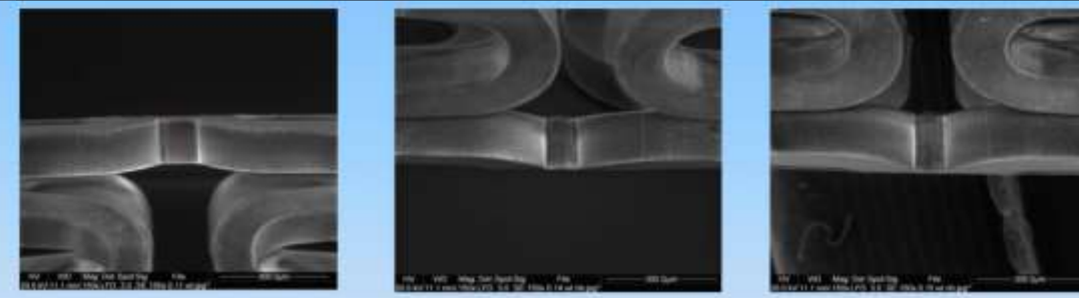
  Predictable and acceptable decrease in polymer molecular weight.

  High concentricity and tight dimensional control.

ARTERIUS: ArterioSorb scaffold

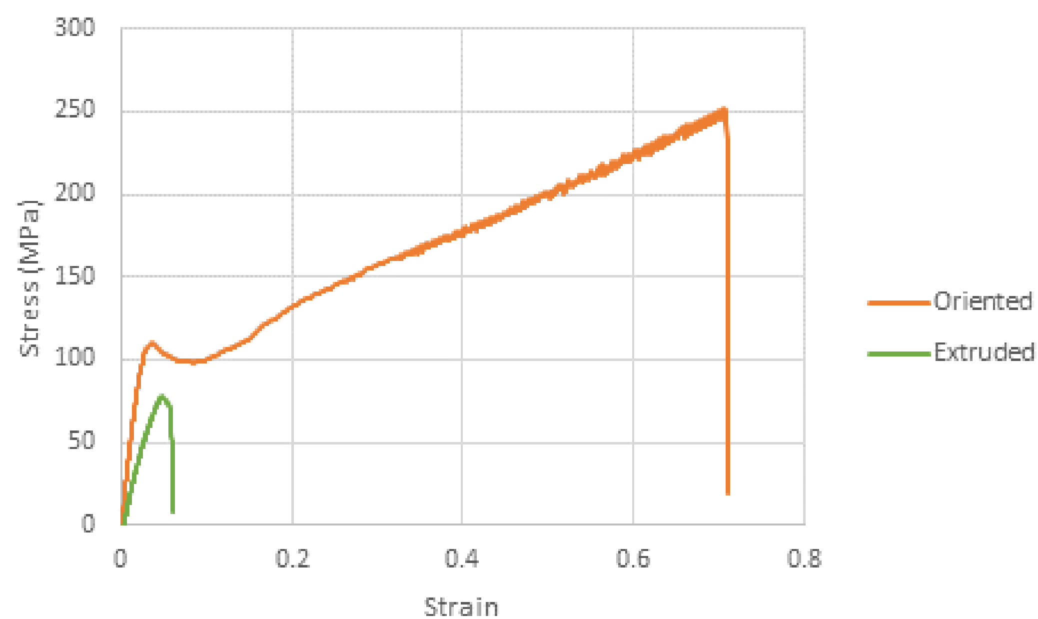


- PLLA based
- Melt processing (EXTRUSION) and DIE-DRAWING (solid phase orientation)
- Solid-Phase Oriented tube with very high mechanical properties
- Thinner strut (≤ 150µm wall thickness, including 140µm and 110µm) to be manufactured with enhanced physical performance similar to that of metal alloy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



(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



Can We Justify the Global Use of BVS?

Can it replace Metal Stent?

From extrusion
to Spinning and MicroBraiding

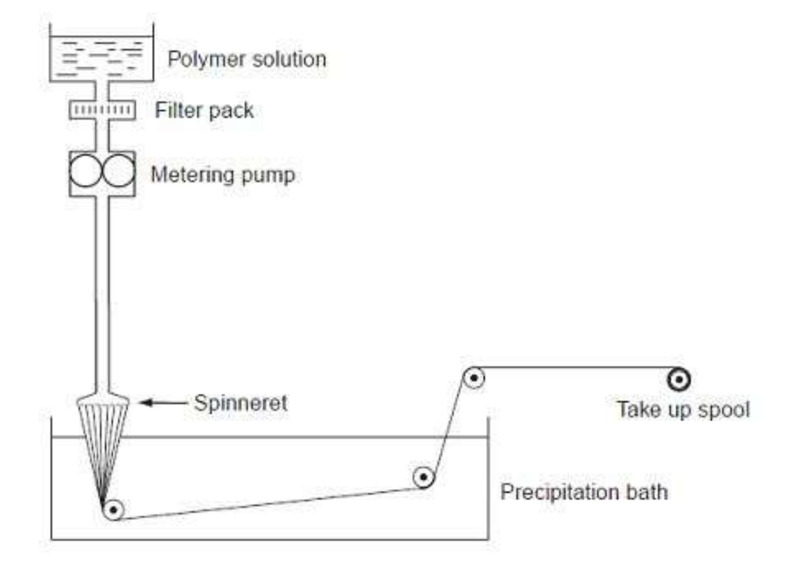
Spinning

- **Solution spinning vs. Melt spinning**

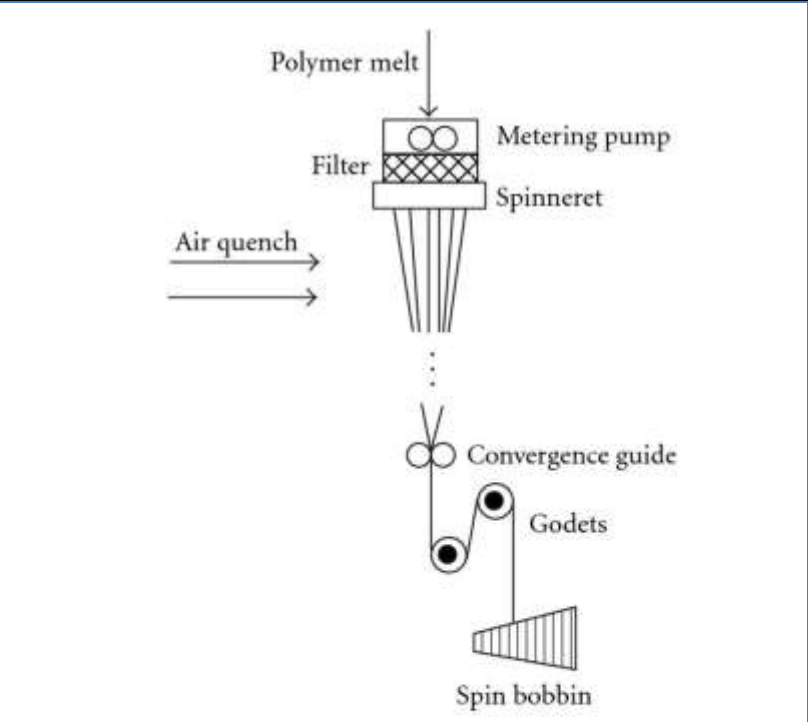
- **In solution spinning, the polymer is dissolved in a solvent whereas in melt spinning the material is melted to form the liquid prior to fiber formation.**

- **Fibers prepared by solution spinning are generally superior to melt spun fibers with respect to mechanical properties** (higher drawability, less thermal degradation, less mechanical degradation, and less hydrolytic degradation)

Solution spinning

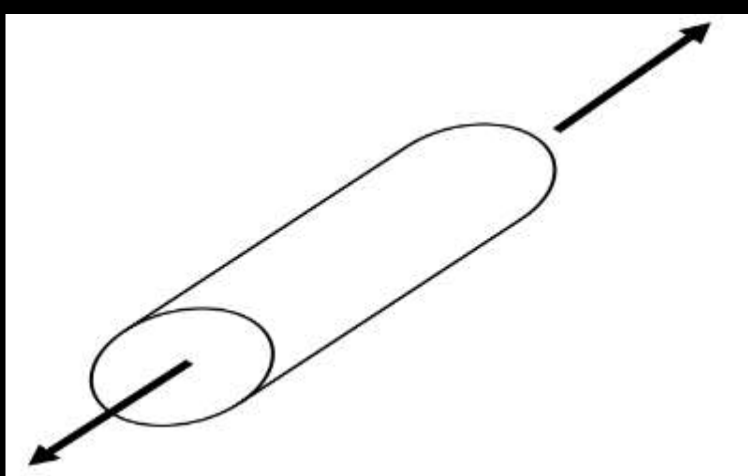


Melt spinning



Stretching/Spinning/MicroBraiding

- Stretching the fibers extends the molecular chains to increase the strength of the fibers from 70 to 620 Mpa (reference: strength of stainless steel 316L = 500MPa)
- A bioresorbable scaffold comprised of fibers is strengthened by stretching or drawing the fibers.



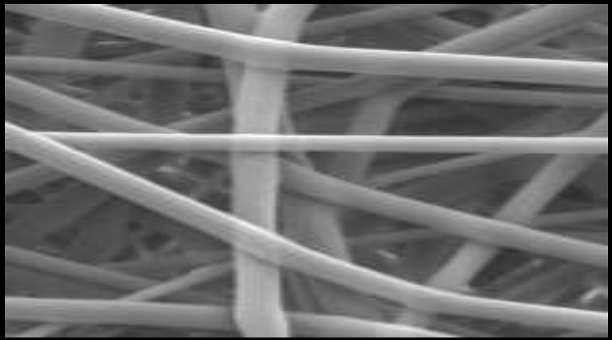
Example PLLA	As-polymerized Material [1]	Fiber
Tensile Strength*	60-70 MPa	<2.3 GPa[2]- Solution <0.6 GPa[2]- Melt
Elongation to break*	2-6%	<25%[3]
Modulus*	3.1-3.7 MPa	4-10 GPa[2]

Forming Interconnected fibrous network

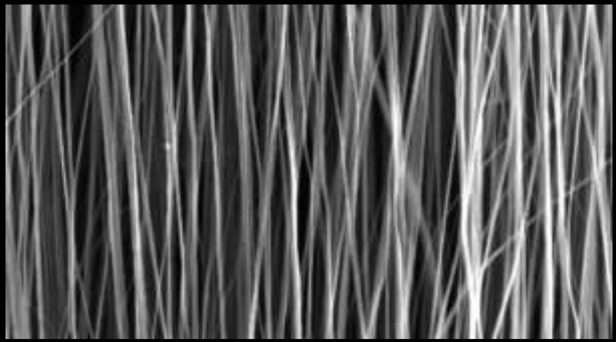
Fiber by itself is useless.

Forming an interconnected fibrous network is critical:

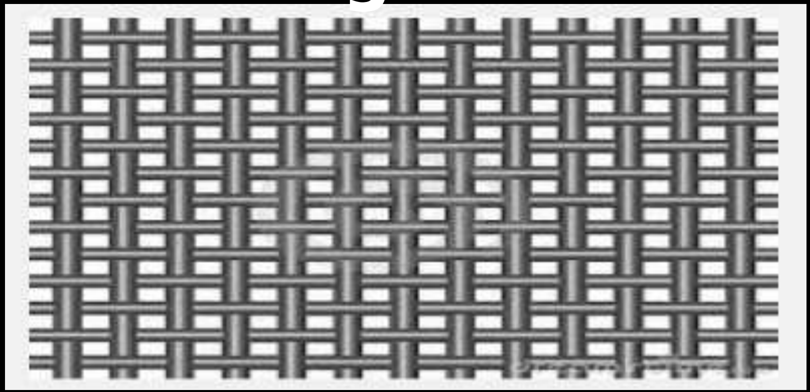
- **Fiber-to-fiber junctions**
- **Fiber alignment**
- **Consolidation vs. porosity**
- **Polymer morphology**



Random



Aligned



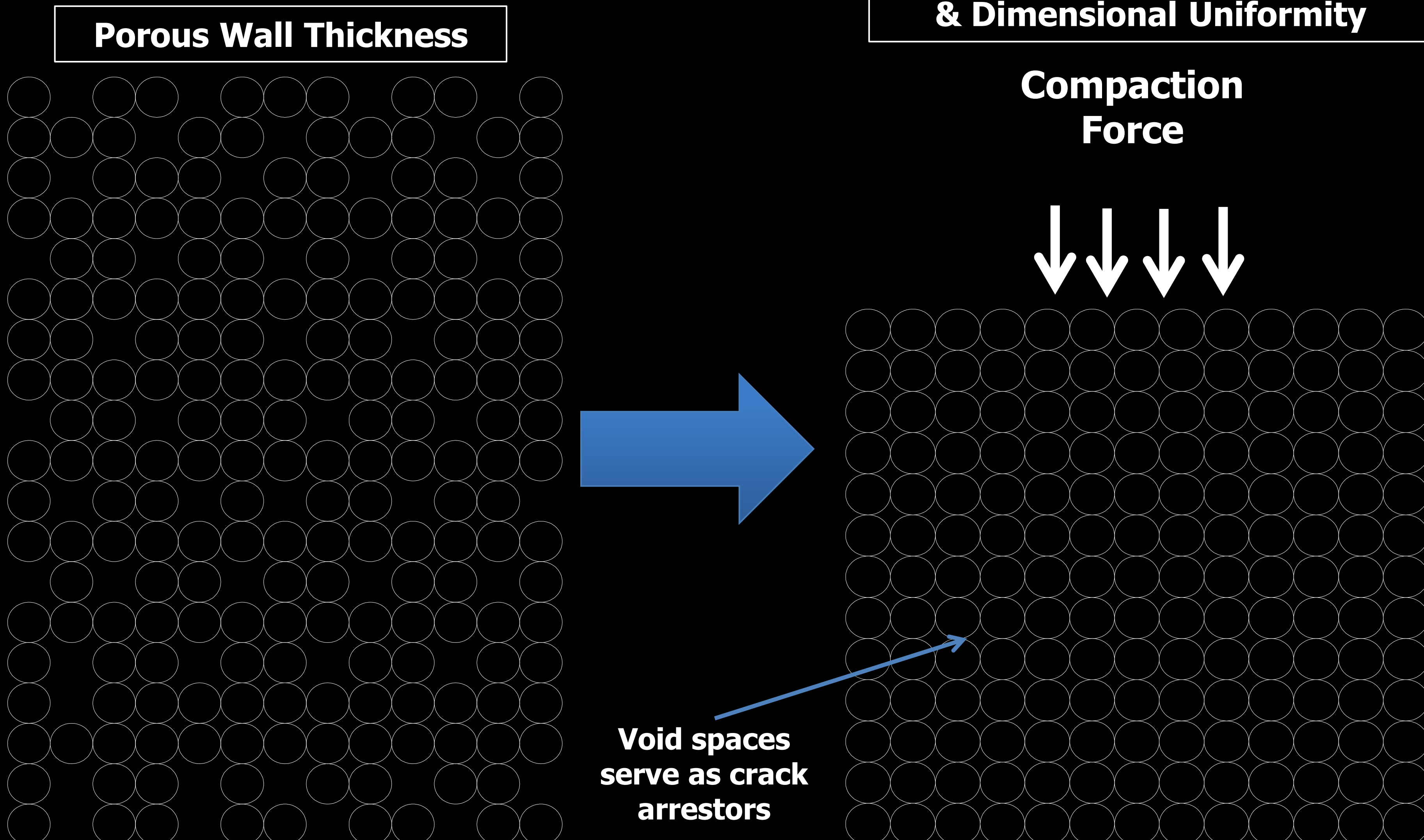
Woven

In collaboration with Jack Scanlon (Heartlon)

Forming Interconnected fibrous network

Consolidation

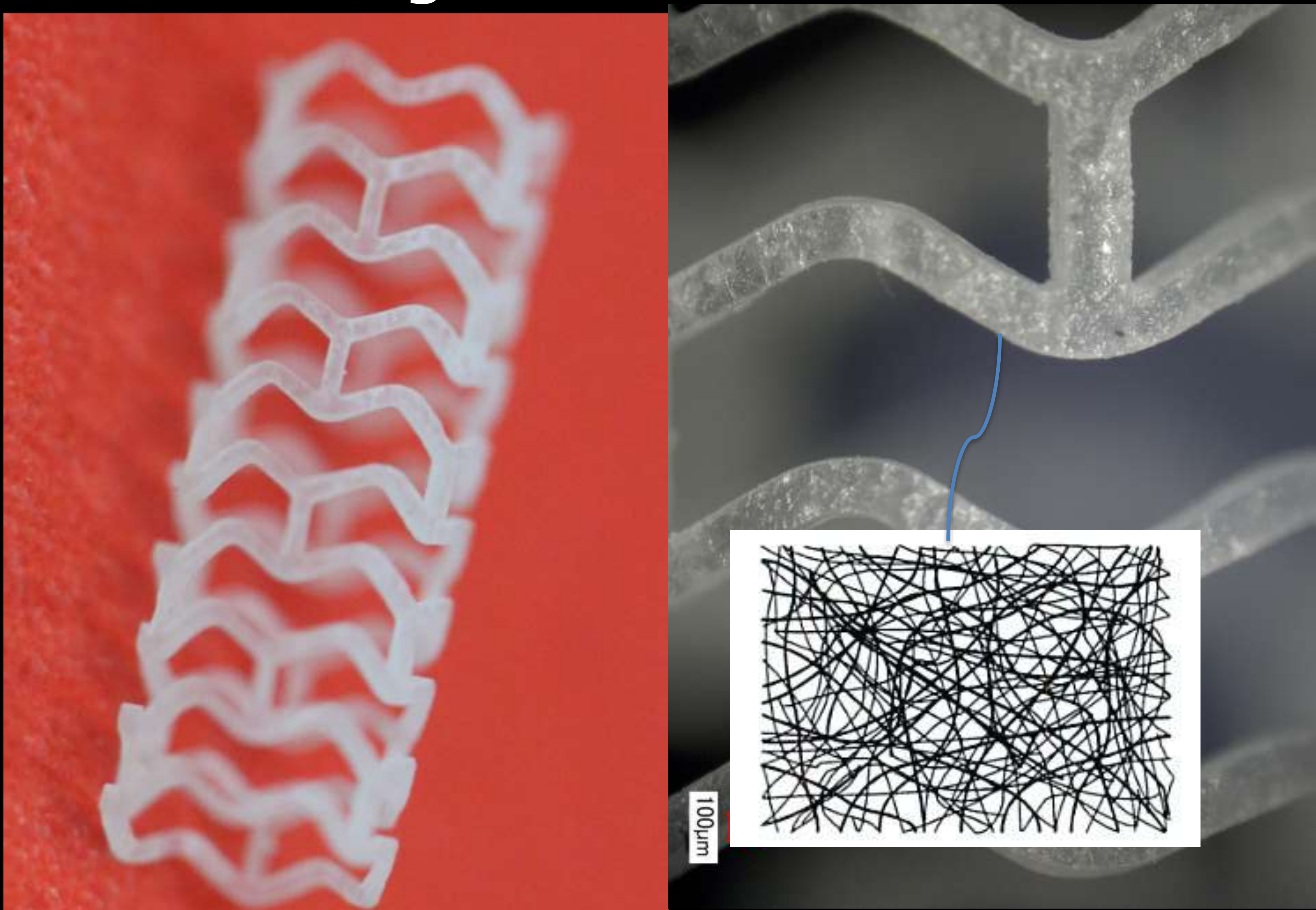
Consolidation Forms Network Imparting Stiffness & Dimensional Uniformity



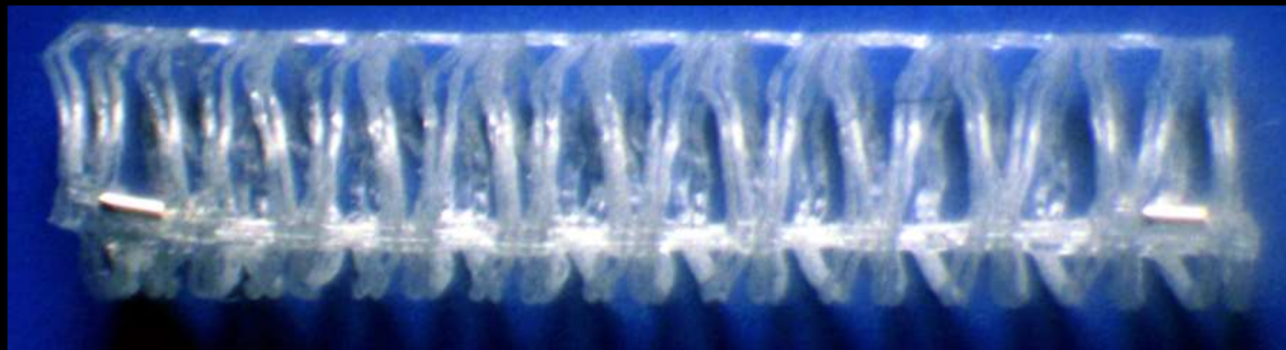
In collaboration with Jack Scanlon (Heartlon)

Microbraiding

In collaboration with Jack Scanlon (Hartlon)

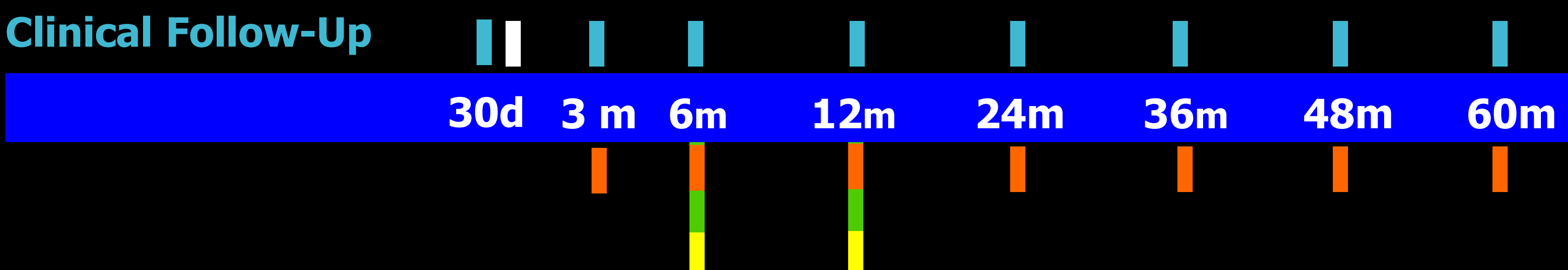


MIRAGE Microfiber Sirolimus-Eluting Coronary Scaffold Study Design



PI: T. Santoso and P.W. Serruys

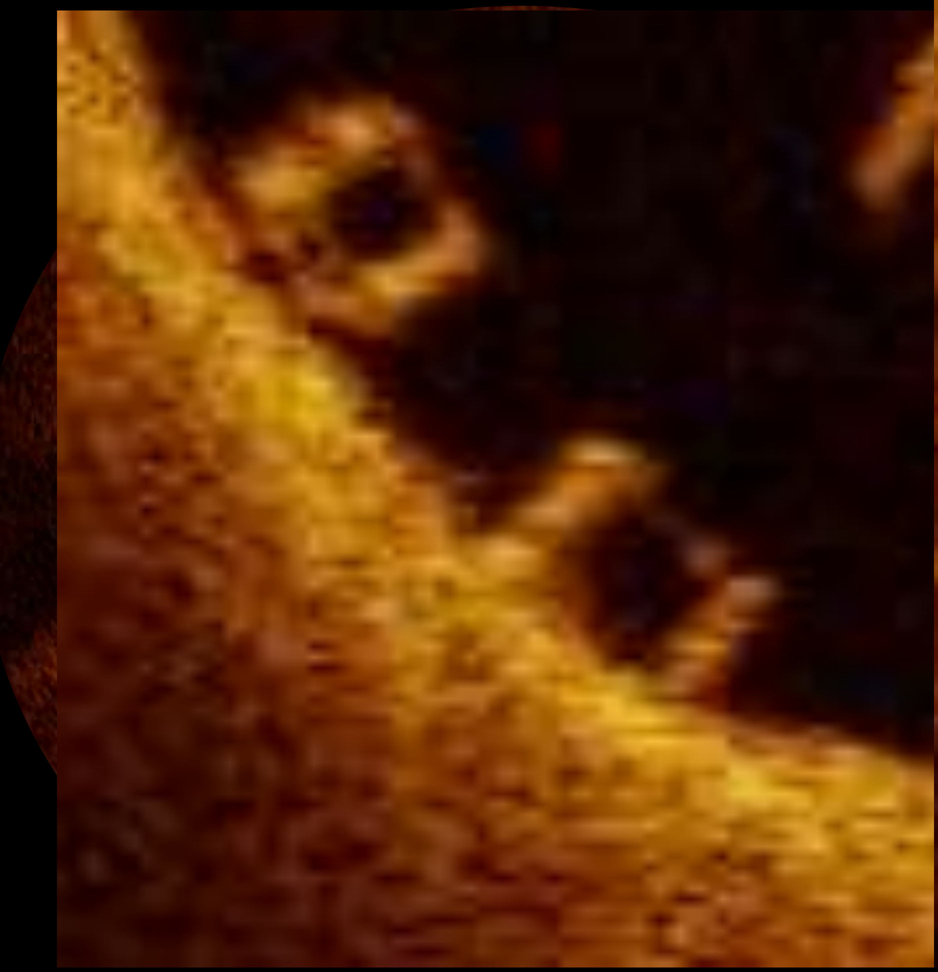
65 subjects (including 5 pilot)
Randomized 1:1 MMSES:Absorb BVS / 2 sites (Indonesia and Malaysia)



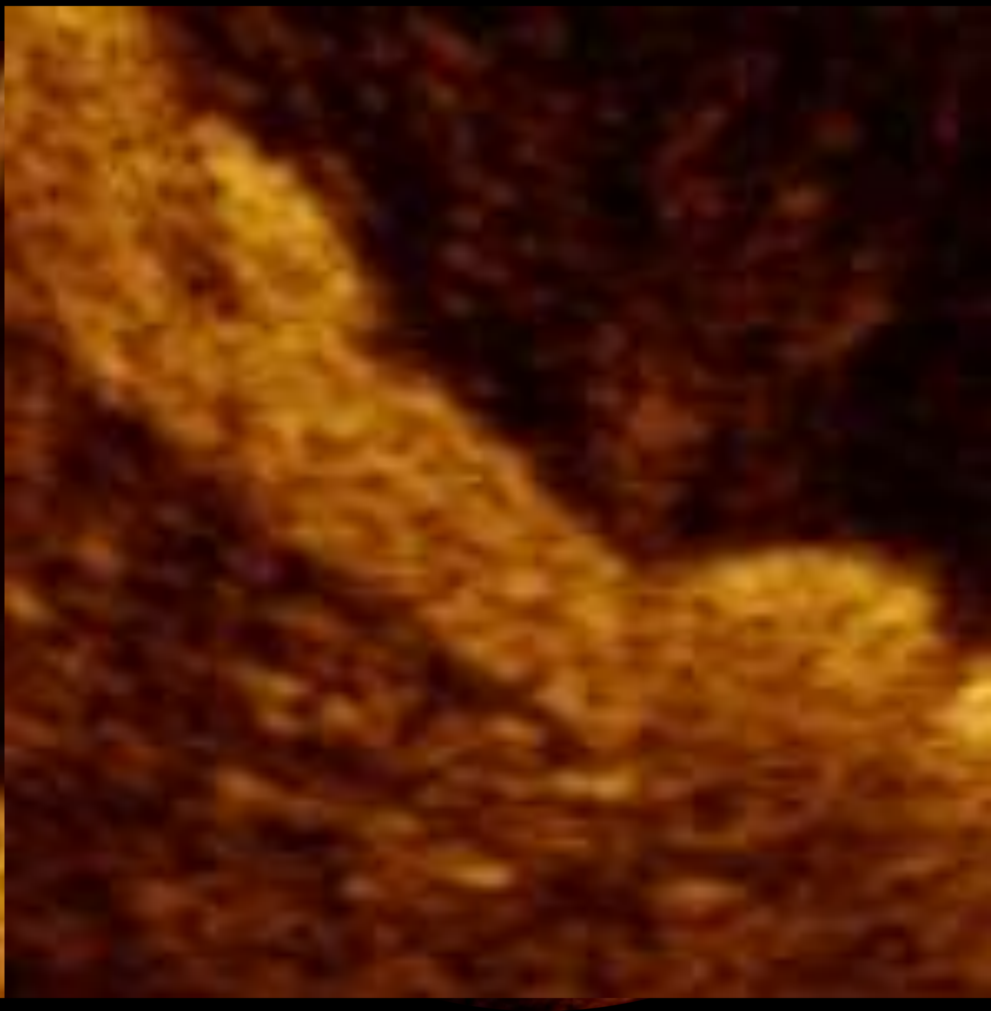
MACE & its individual end points at follow-up
Angio (all), IVUS (30 cases), OCT (all) follow-up

From the rectangular shape of the struts into the ovoid shape

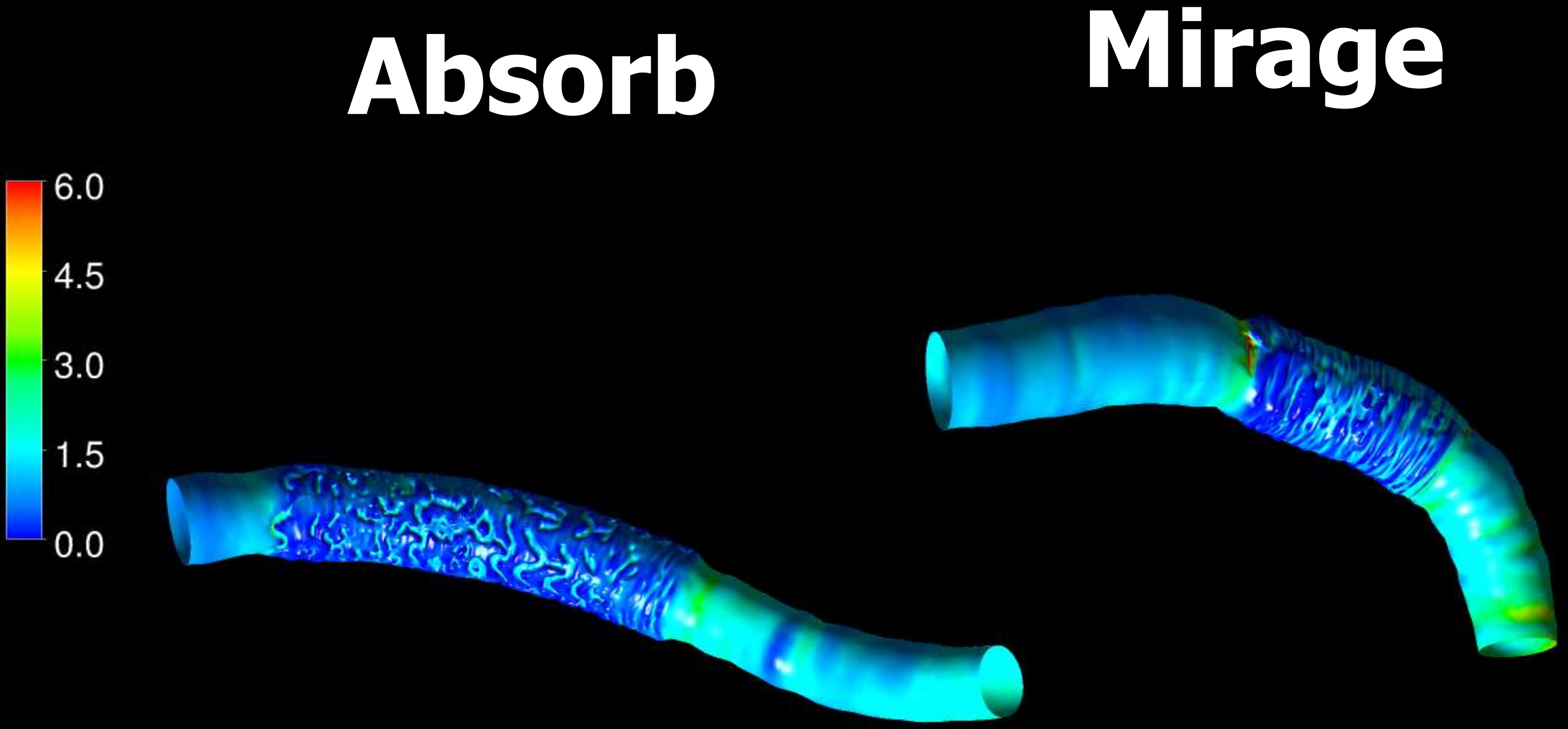
Absorb



Mirage



Currently the impact of strut shape on EES/flow is investigated in a preclinical model



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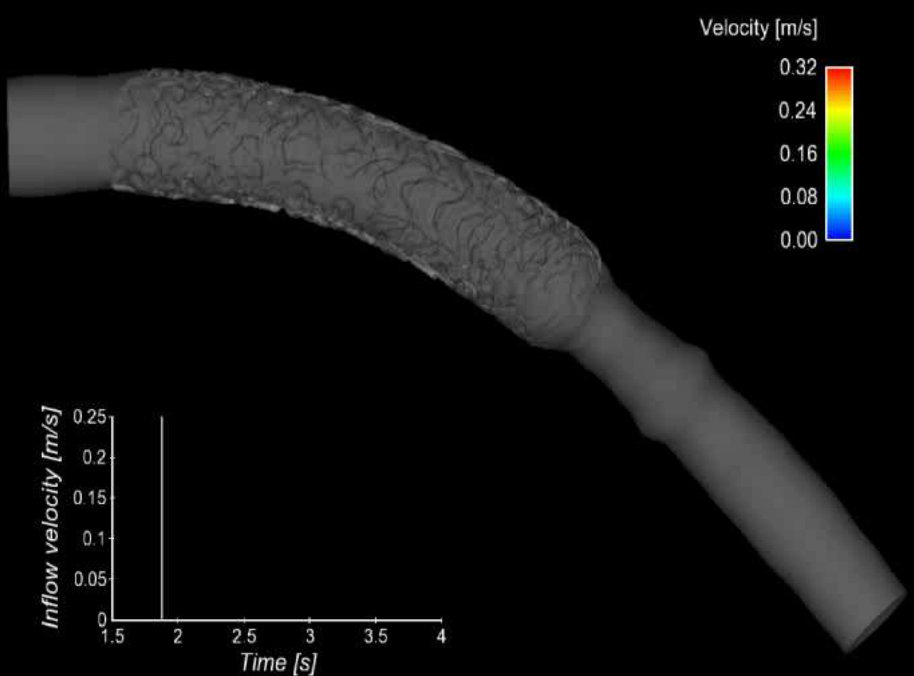
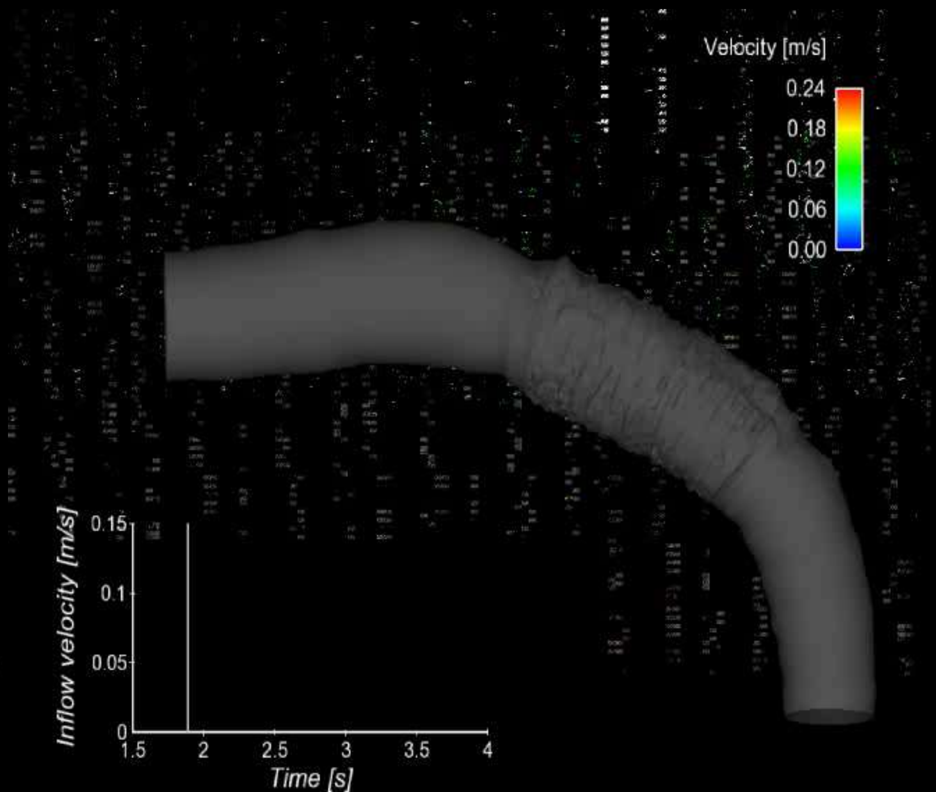
Absorb



Mirage



Conclusions

Future struts of BRS are to be:

- **Stronger and ductile**
- **Thinner**
- **More quickly bioresorbable**

… Yes, we can!