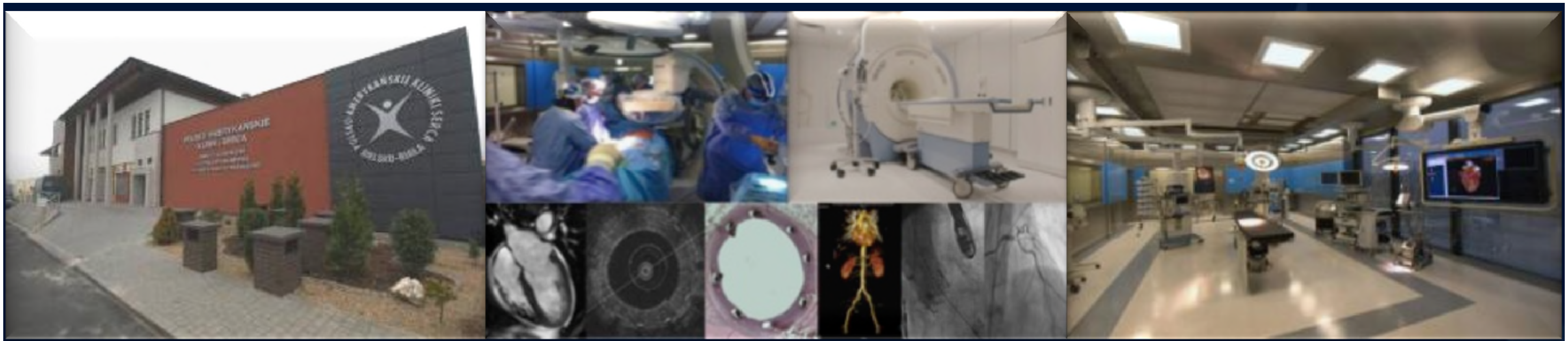

Design Constraints of Current Bioresorbable Scaffolds: Can We Improve Their Procedural Parameters? - Insights from Polish Apollo and BSM Projects

Associate Prof. Krzysztof Milewski, MD, PhD

Center for Cardiovascular Research and Development

American Heart of Poland SA; Katowice

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Summary of ABSORB II 3 year outcomes

- The trial did not meet its mechanistic co-primary endpoints of superior **vasomotor reactivity** because Xience showed unexpected vasomotion which had been hypothesised to be zero.
- The trial did not meet its co-primary endpoints of non-inferior **late luminal loss** with respect to Xience
- A higher rate of **device oriented composite endpoint** due to target vessel myocardial infarction largely driven by peri-procedural myocardial infarction was observed in the Absorb arm.
- The higher (although not statistically significant) incidence of **very late scaffold thrombosis** (>365 days)
- **The patient oriented composite endpoint**, exercise testing and anginal status (compliance: 93%) were not statistically different between both devices at 3 years

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We need second generation scaffolds!

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What parameters should be improved and how?

Parameter

- Strut thickness and geometry
- Tensile strength, stiffness and ductility
- Scaffold crossing profile, deliverability
- Storage conditions
- Inflation pattern, ability of scaffold to follow lesion and vessel geometry

Way of improvement

- Material / composition of polymers
- Processing of materials
- Different way of scaffold implantation (balloon vs self-expanding technology)

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“Playing” with materials and composition of different polymers

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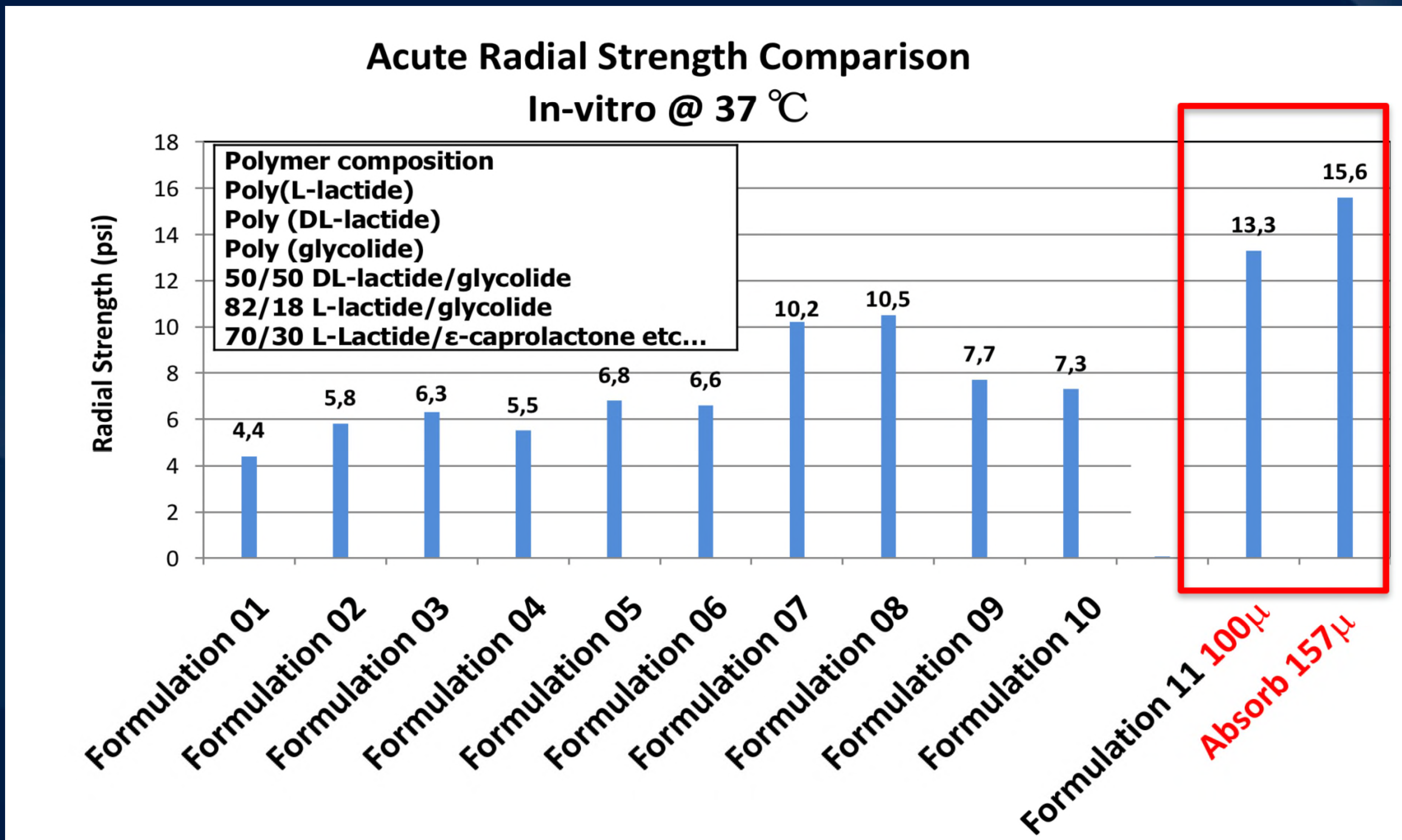

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Patrick W. Serruys, TCT 2016

"Playing" with composition of polymers - mechanical properties and degradation time

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Polymer composition	Tensile modulus of elasticity (Gpa)	Tensile strength (Mpa)	Elongation at break (%)	Degradation time (months)
Poly(L-lactide)	3.1-3.7	60-70	2-6	>24
Poly (DL-lactide)	3.1-3.7	45-55	2-6	12-6
Poly (glycolide)	6.5-7.0	90-110	1-2	6-12
50/50 DL-lactide/glycolide	3.4-3.8	40-50	1-4	1-2
82/18 L-lactide/glycolide	3.3-3.5	60-70	2-6	12-18
70/30 L-Lactide/å-caprolactone	0.02-0.04	18-22	>100	12-24
Cobalt chromium	210-235	1449	～40	Biostable
Stainless steel 316L	193	668	40+	Biostable
Nitinol	45	700-1100	10-20	Biostable
Magnesium alloy	40-45	220-330	2-20	1-3

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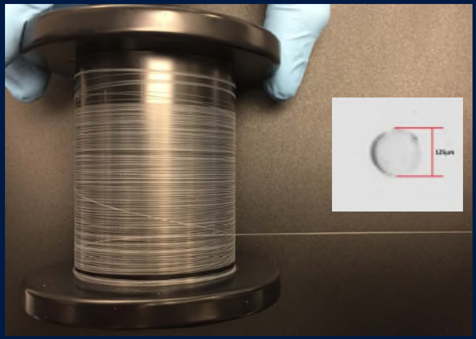
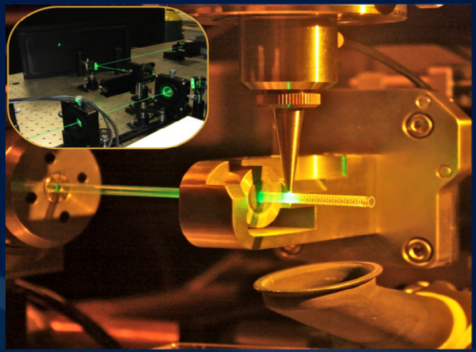
Processing methods

The current limitations of BRS including low tensile strength, stiffness (which require thick struts to prevent acute recoil) and insufficient ductility (which limits the range of scaffold expansion) could be addressed by different processing methods of materials

	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)
Amaranth Medical	Dip coating on mandrel to form a tube from PLLA solution	PLLA (in-house polymer synthesis and dissolved in an organic solvent)





Patrick W. Serruys, Yoshinobu Onuma, TCT 2015

Polish BRS projects

American Heart of Poland

Apollo:

- balloon-expandable
- use of alternative materials / composition of polymers
- optimize processing of materials

BSM Stent:

- self-expandable scaffolds
- use of alternative materials / composition of polymers
- optimize processing of materials (injection moulding)

- thinner struts and lower scaffold profile
- improved mechanical parameters (tensile strength, stiffness, ductility)
- optimized storage conditions
- increase range of scaffold sizes
- shorter bioresorbtion process with minimal inflammatory reaction
- minimized thrombogenicity of polymers and their degradation products

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APOLLO PROJECT

The First Polish Biodegradable Stent

Title: *Development and Comprehensive Evaluation of the First Polish, Next Generation, Thin Strut Biodegradable Polymer and Elastic, Sirolimus Eluting Vascular Scaffold*

The main goals of the project include:

1. Thin struts with optimized geometry to improve healing, reduce rate of restenosis and improve procedural parameters
2. Alternative polymers with optimal biocompatibility
3. Optimize and the speed of polymer biodegradation

- *The prototype will be evaluated in the in-vivo preclinical setting, aiming to prove feasibility and safety with comprehensive evaluation of vascular healing, biocompatibility and polymer degradation in a series of large animal experiments*
- *Clinical implementation and certification steps will be executed*

APOLLO PROJECT

The First Polish Biodegradable Stent

The **BIOSTENT** CONSORTIUM members:

- **Center for Cardiovascular Research and Development, American Heart of Poland SA – leader of the project**
- **BALTON Ltd. Warsaw**
- Centre of Polymer and Carbon Materials, Polish Academy of Sciences, Zabrze
- Silesian University of Technology, Faculty of Biomedical Engineering
- Silesian Center for Heart Diseases
- Military University of Technology, Faculty of Mechanical Engineering
- Innovations for Heart and Vessels Sp. z o. o. – I4HV

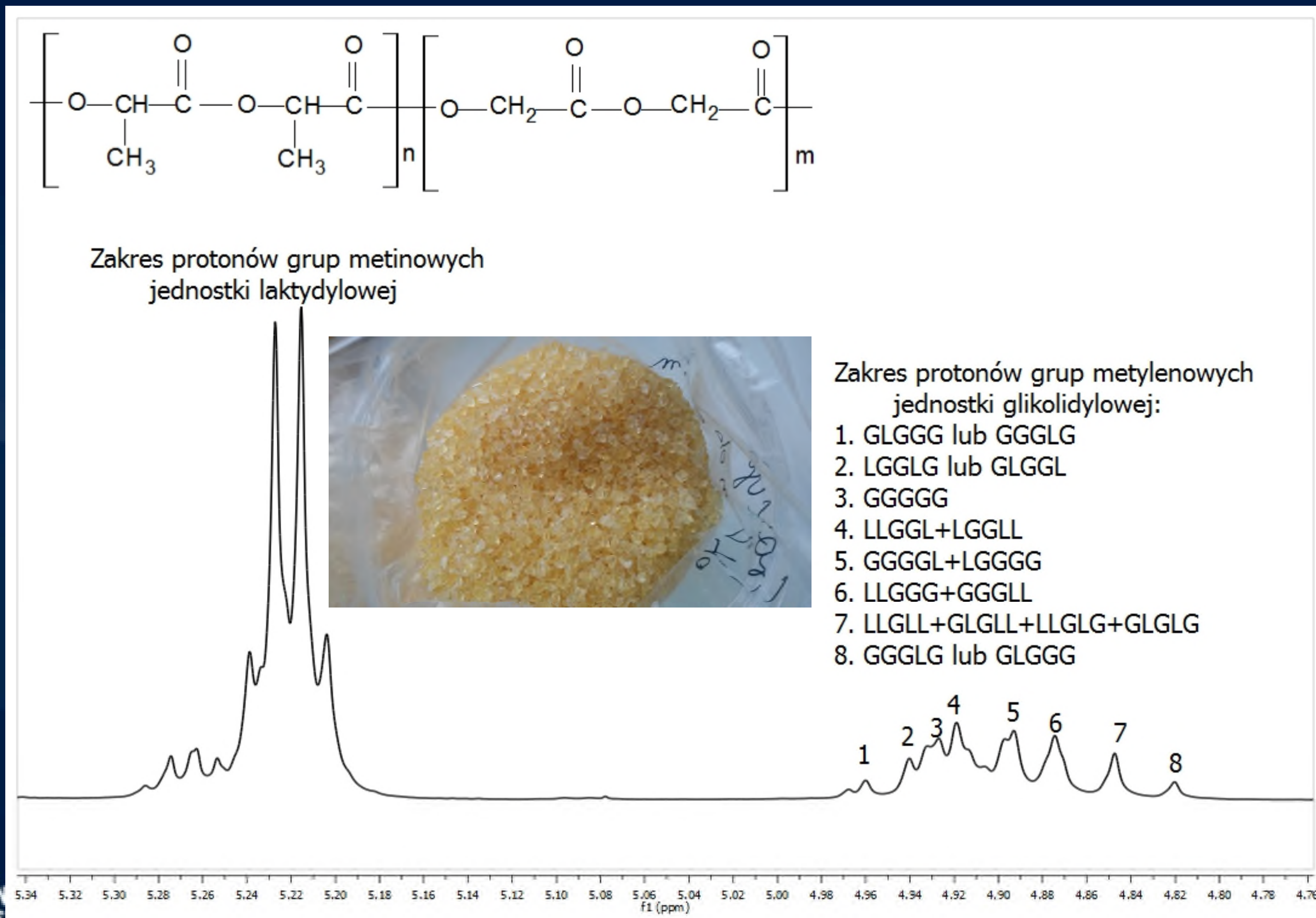
Budget: 14 312 450 pln (funding – 11 448 705 pln)

Duration of the project: 36 months

APOLLO PROJECT

PLGA_poly(lactic-co-glycolic acid)

- poly(glycolic acid) (PGA) – high strength, fast degradation profile (ca 6 months)
- poly-L-lactide (PLLA) - thermoplastic aliphatic polyester with long degradation time



APOLLO PROJECT

- project progress

Material / composition of polymers	PLGA 1 (PLA : PGA) formulation 1	PLGA 2 (PLA : PGA) formulation 2	PLGA 3 (PLA : PGA) formulation 3
Pipe ready for processing	1.8 x 1.6mm 3.0 x 8.0mm 3.5 x 15mm	failure	in progress
Stent	3.0 x 8.0mm 3.5 x 15mm - 150ųm (target = 100ųm)		
Implantation	Success		

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STRATEGMED

APOLLO PROJECT

Attempts to cut scaffolds

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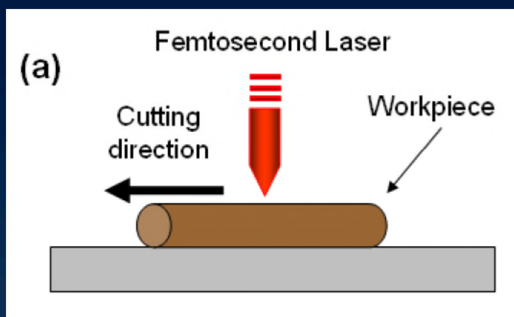
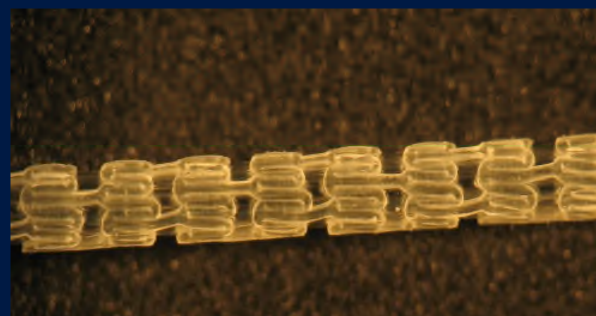
PLGA1 Ø 3,0 mm

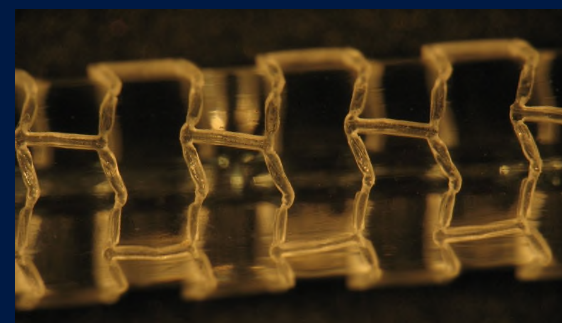
- Stent cutting using femtosecond laser (in assistance of argon and cold)
- Crimping T = 53,1±0,5 ºC
- Balloon expansion: T=37,0 ºC



Laser cutting



Stent crimped on the balloon (3,0 x 18 mm)



Fully expanded stent

	APOLLO
Material	**PLGA**
Polymer	**Biodegradable**
Size (diameter)	**3.00– 3.50 mm**
Strut thickness	**150ɥm**
Profile of stent crimped on the balloon	**.043" (1,0 mm)**

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Courtesy Balton Company

STRATEGMED

First preclinical application

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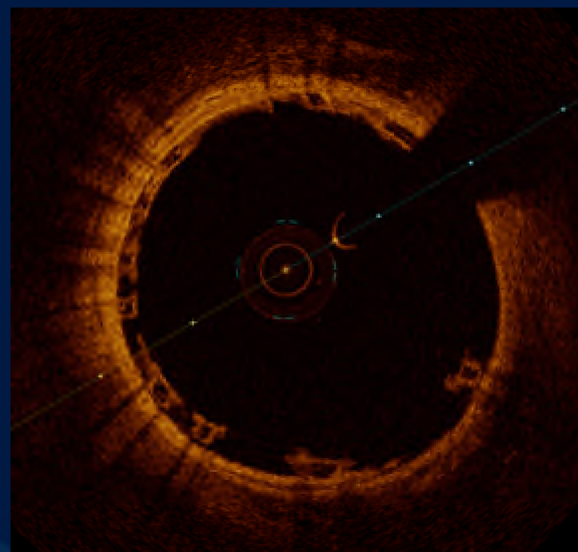

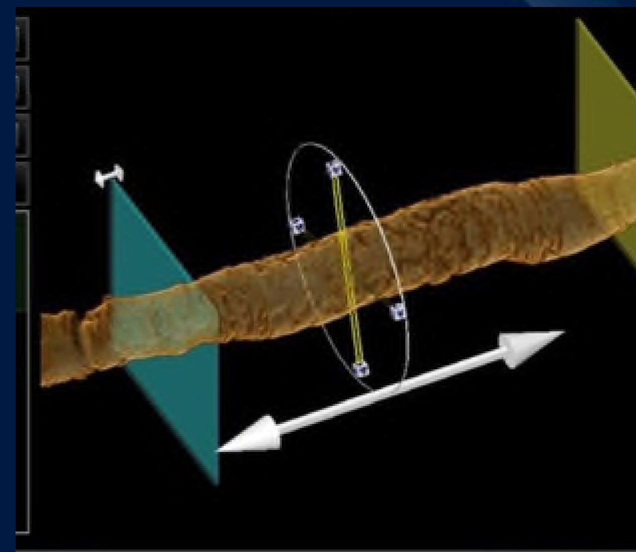

	n=6
Deliverability	6/6
Expansion	6/6
Postdilatation	6/6
Procedural efficacy	6/6

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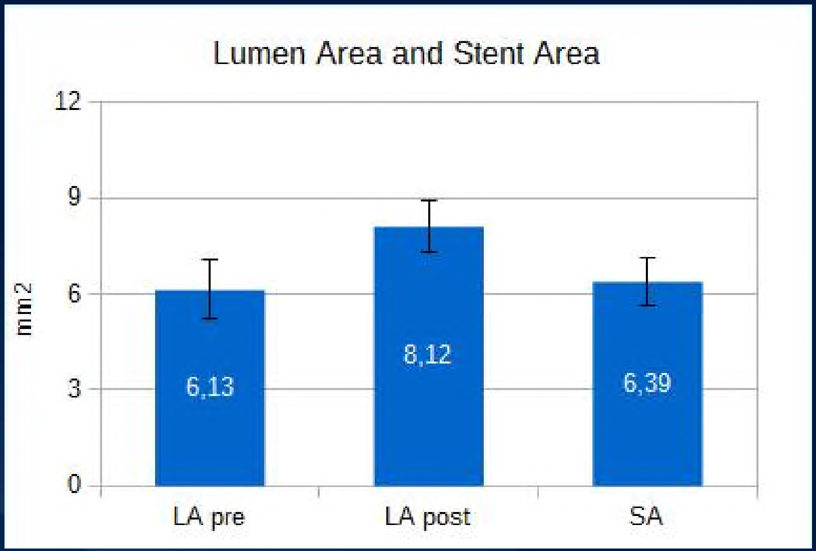
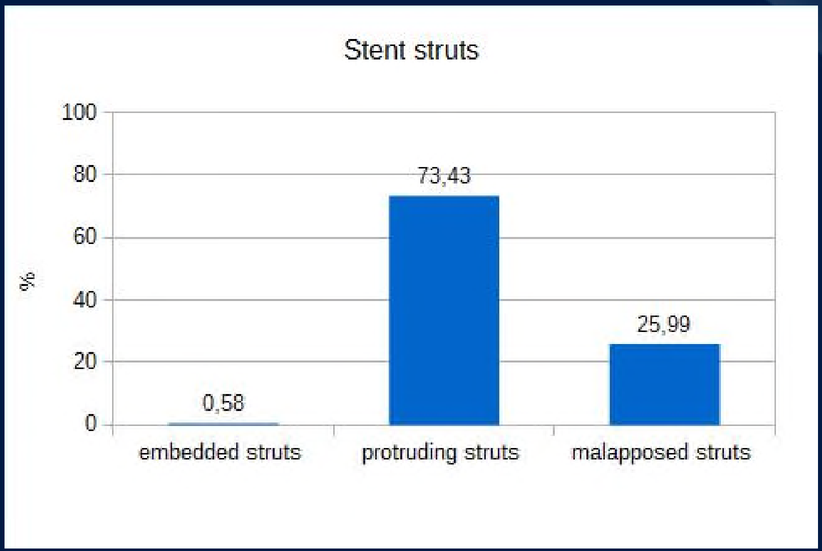
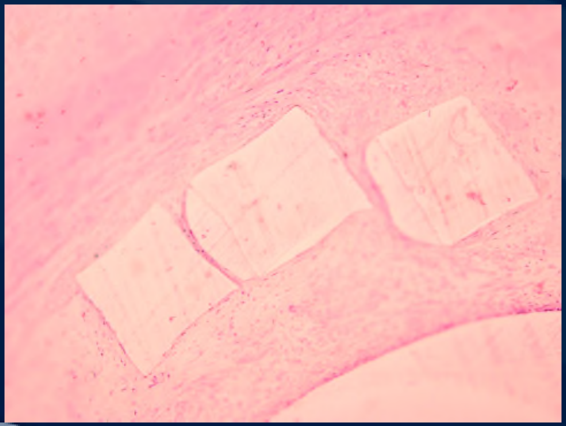
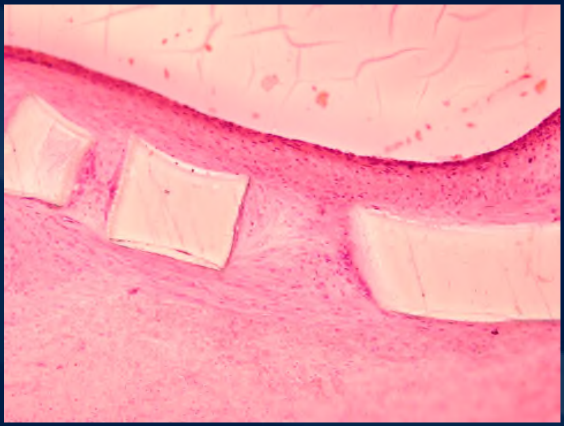
APOLLO PROJECT

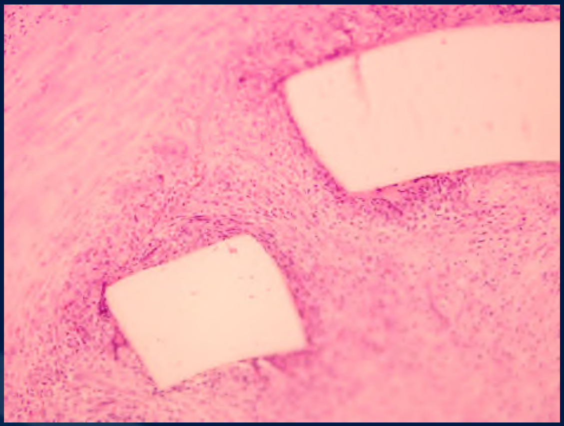
1 months results











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Narodowe Centrum Badań i Rozwoju

BSM STENT

American Heart of Poland

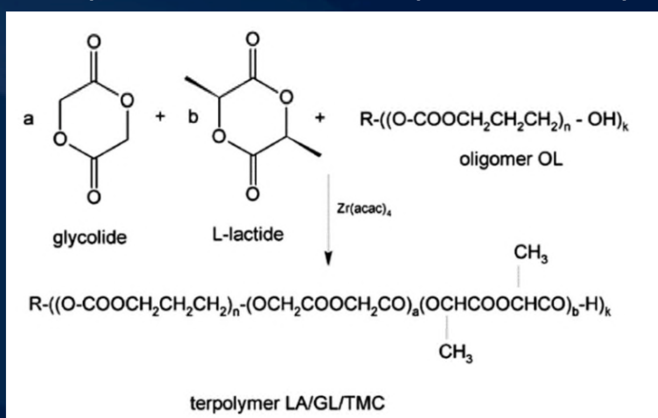
”Development of self-expandable bioresorbable scaffolds”

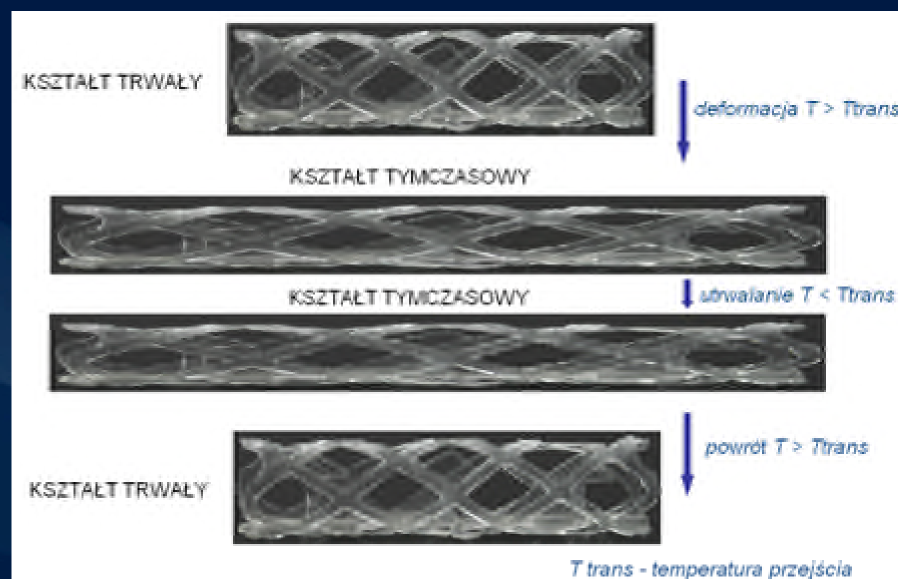
The target: coronary and peripheral aplications

CMPW PAN Centrum Materiałów Polimerowych i Węglowych Polskiej Akademii Nauk

American Heart of Poland

Terpolimer with shape memory





Courtesy prof. J. Kasperczyk

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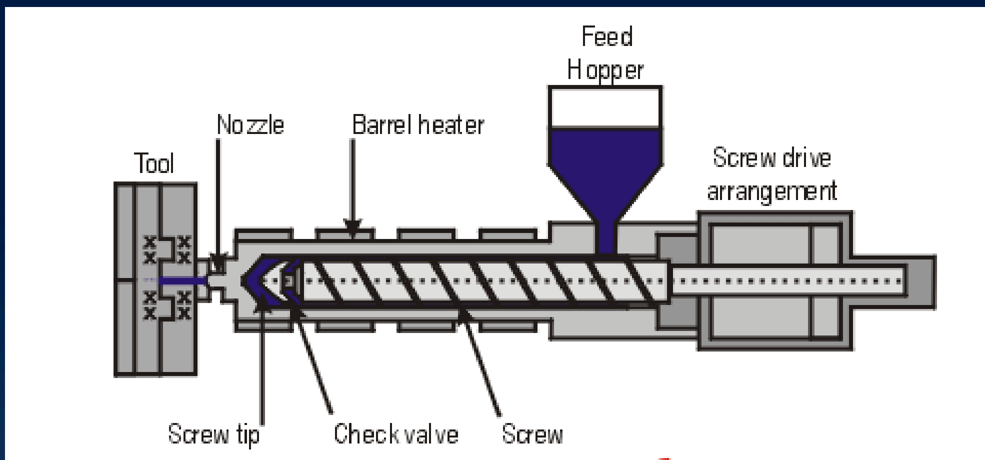
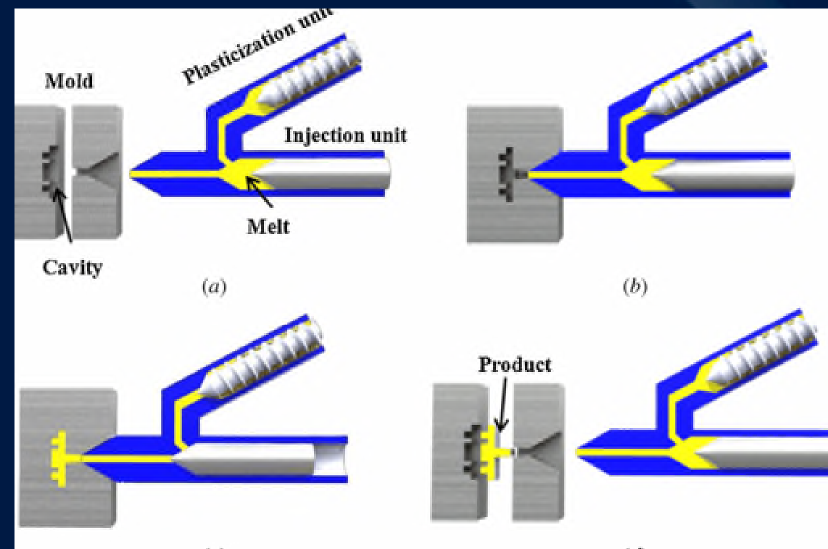
Production of scaffold prototypes





- The injection moulding technique is a highly accurate and largely automated process
- This is relatively cheap technology allowing for fast stents production (stents can be made each 10-30 seconds on a single machine)

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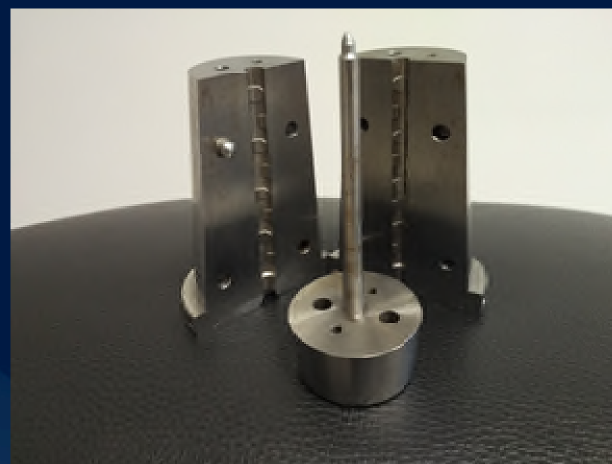
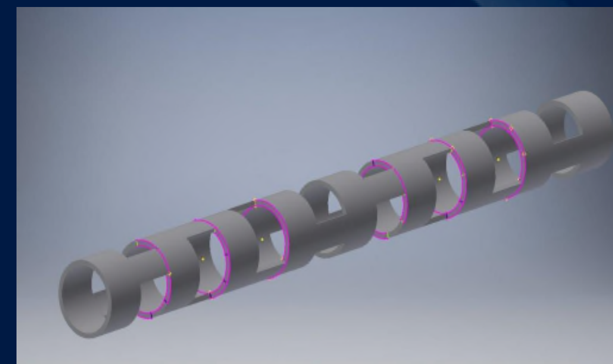
The laboratory injection molding machine

Laboratory extruder - injection moulding machine Haake



Injection mould



Project of the stent

First self-expandable stent prototype: 6 x 60mm with wall thickness of 400 µm

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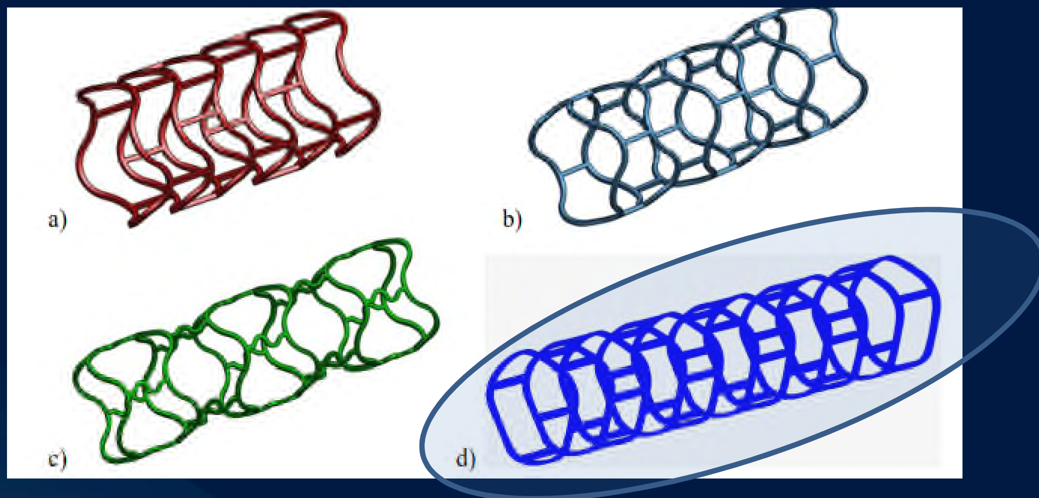
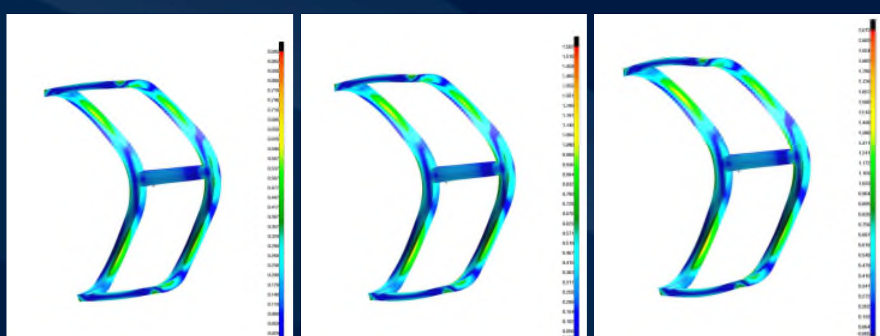
Production of scaffold prototypes



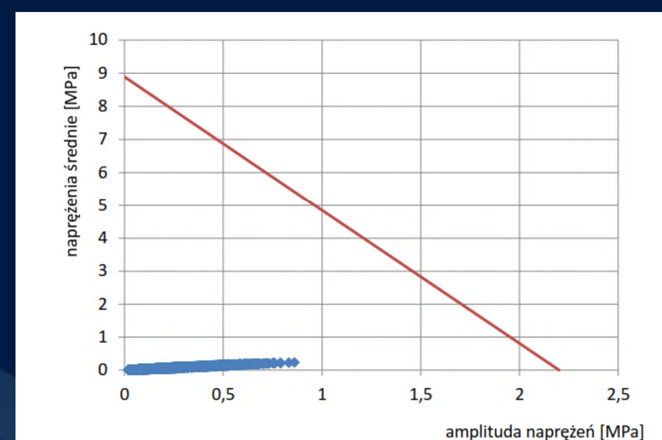
Selected shape:

Stent dimensions 30mm x 6 mm, wall thickness 200 µm at present with 100 µm as a target

fatigue resistance



a pressure of 50 100 150 mmHg



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Should present sufficient mechanical properties, easy to crimping, obtainable in the way of injection moulding (the possibility of filling of all caves in injection mould)

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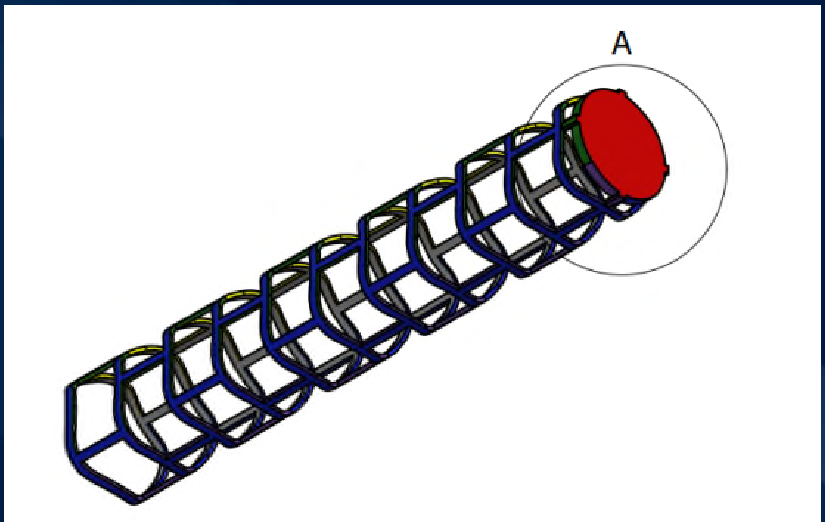
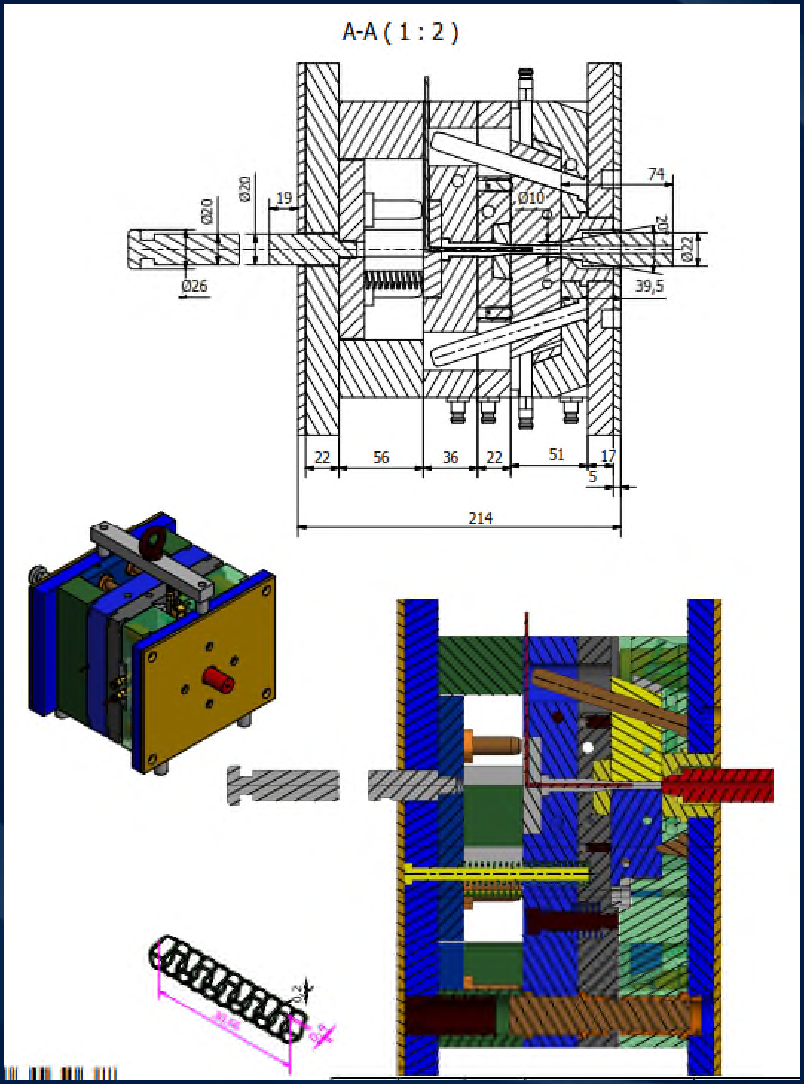
The project of injection mold

precise form, with four sliders,core, heating and cooling channels, vacuum channels special ejectors





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CONSLUSIONS

- Second generation BRSs should remove most limitations of 1st generation devices thus theoretically producing better clinical outcomes and more user-friendly technologies
- In our Polish projects we expect:
  - easier implantation techniques (lower profile, better deliverability)
  - increased overexpansion capabilities
  - broader range of scaffold sizes
  - shorter (but still well balanced) degradation time
  - better biocompatibility and lower thrombogenicity of polymers and their degradation products

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