Anisotropic Elastomers for Polymer Heart Valves

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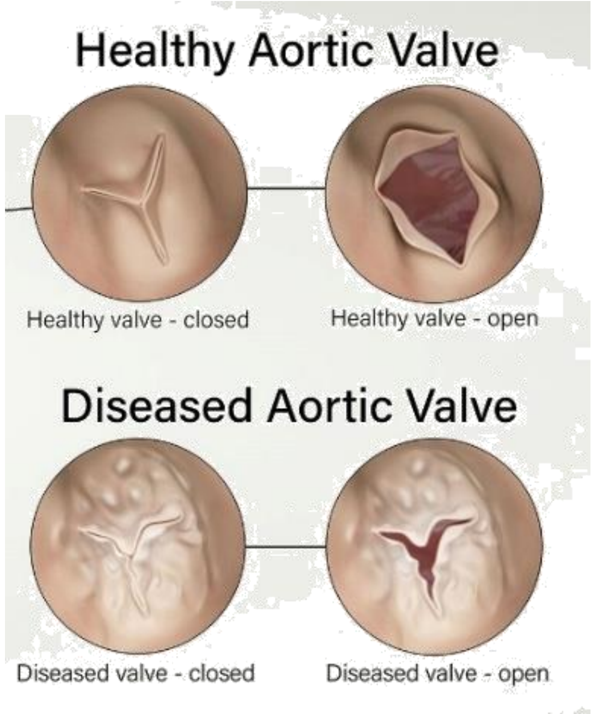
HEART VALVE DISEASE

- Valvular heart disease (VHD) affects over 100 million people globally
- Aortic valve disease is the most prevalent VHD
- Types: - Stenosis: heart valve does not open fully
  - Regurgitation: heart valve does not close fully
- Causes: - Congenital conditions
  - Degenerative conditions
  - Rheumatic fever related



Source: https://patientdecisionaid.org/aortic-stenosis/

Clinical treatment: Heart valve replacement surgery → 500,000 a year, a figure expected to double in the next 50 years

CURRENT HEART VALVE PROSTHESIS

Mechanical replacements

- Hard, man-made materials

✓ Long-term durability (~20 years)

× Requires patient to take life-long anticoagulants

Biological replacements

- Porcine or bovine tissue leaflets

✓ Biocompatibility

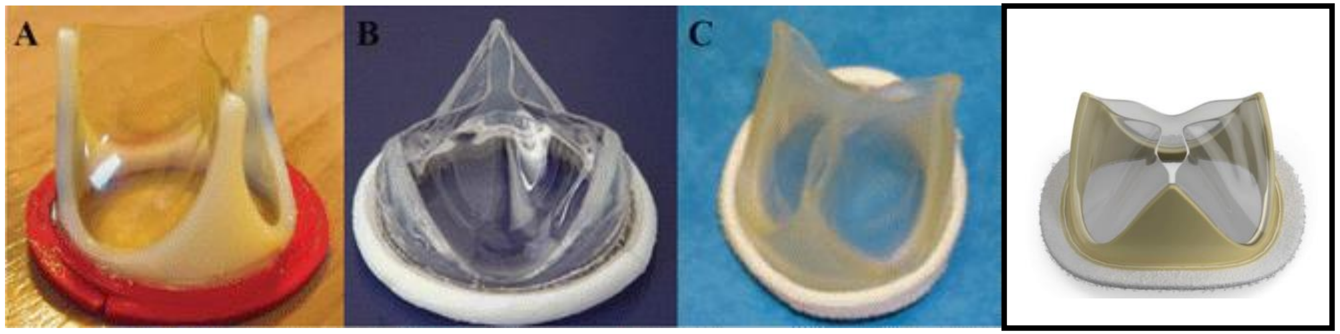
× Lower durability (10-15 years), leading to repeat operation

Research aim: To meet the need for a prosthesis that is suitable for all patients

POLYMER HEART VALVES

A potential solution: A flexible leaflet polymer heart valve (PHV) that mimics the hemodynamic performance of the native heart valve

Materials used in different attempts to design a PHV:



- *MM Rozeik et al. The aortic valve: structure, complications and implications for transcatheter aortic valve replacement*, 2014.

- *Foldax, Tria heart valve, Source: https://foldax.com*

Silicone

Polyurethanes

Polytetrafluoroethylene (PTFE)

Polyesters (e.g. PET)

Styrenic thermoplastic elastomers

POLYMER HEART VALVES

Opportunities:

- Cheaper and easier to manufacture
- Potential for no anticoagulation therapy

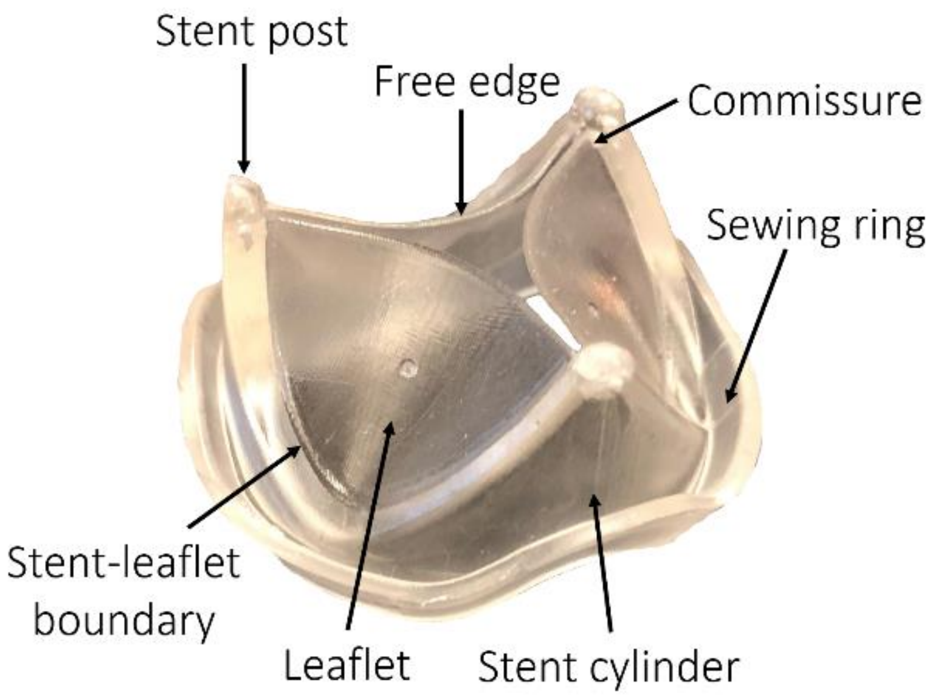
Limitations so far:

- Mechanical failure (tearing of leaflets)
- Calcification

How can durability be improved?

POLIVALVE

Surgical PoliValve – An entirely **injection moulded** polymer heart valve made from styrenic thermoplastic elastomers, designed and developed by the Structured Materials group

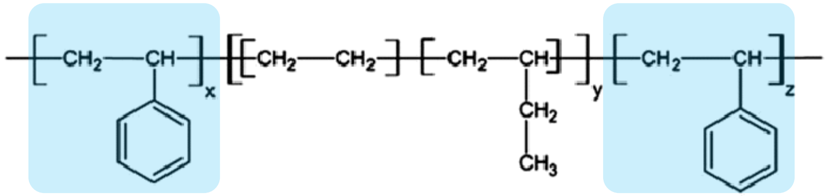


STYRENIC THERMOPLASTIC ELASTOMERS

- PoliValve is made of thermoplastic elastomers (SEBS grades)
- These are block copolymers which phase separate
- Styrene blocks forms hard, crystalline phases
- Central blocks form soft, rubbery phases

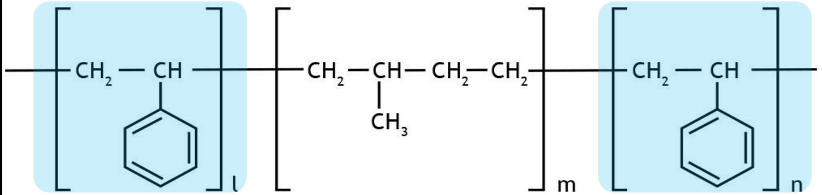
Varying functional group, styrene content and molecular weight strongly affects material performance

SEBS



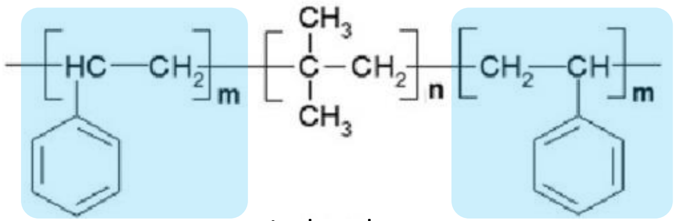
Ethylene-Butylene

SEPS



Ethylene-Propylene

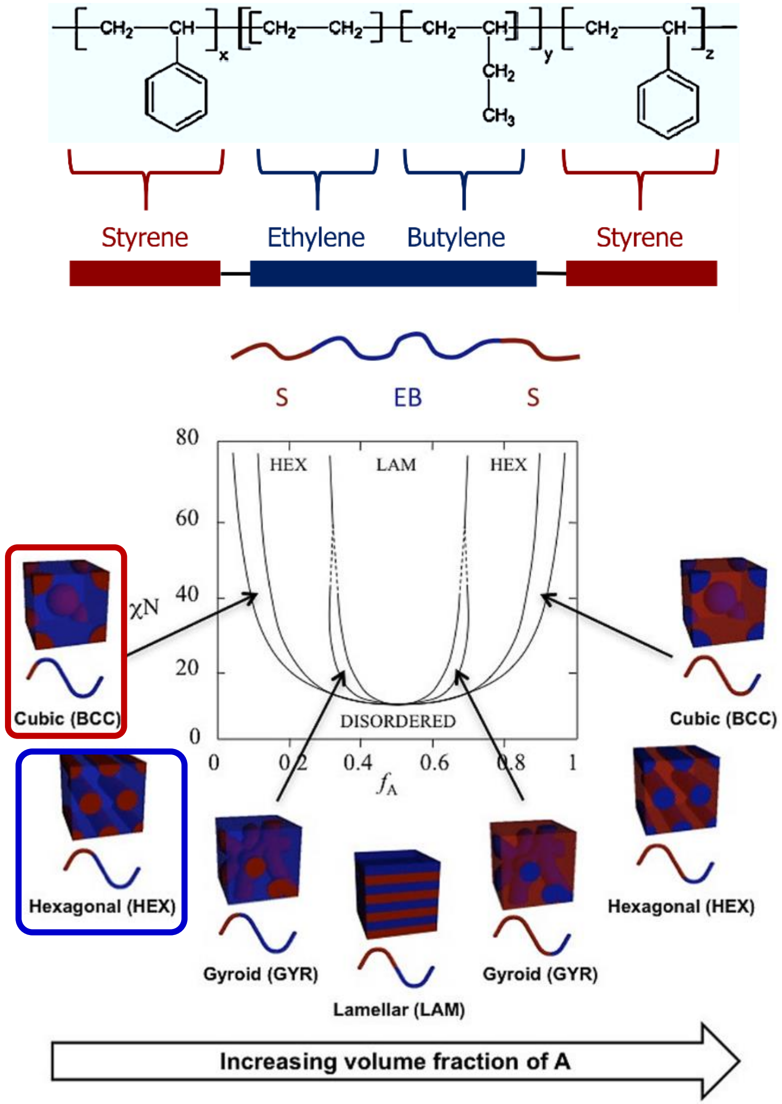
SIBS



Isobutylene

STYRENIC THERMOPLASTIC ELASTOMERS

Depending on styrene content and molecular weights, phase separation induces various morphologies:



Spherical morphology
→ Isotropic properties

Cylindrical morphology
→ Anisotropic properties

STYRENIC THERMOPLASTIC ELASTOMERS

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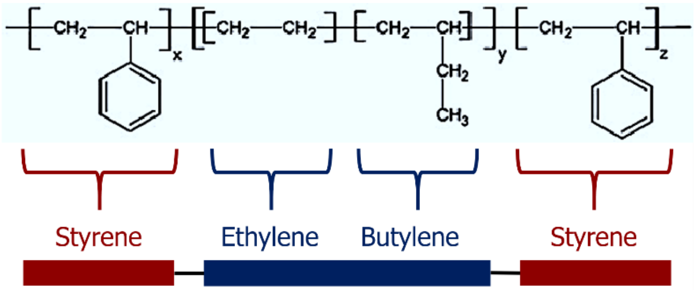
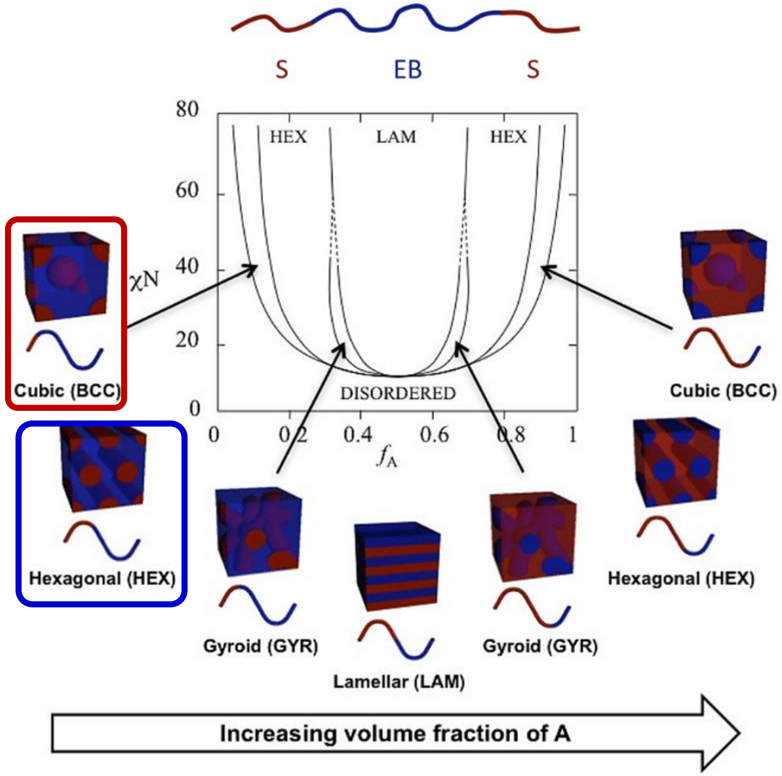


PoliValve: Stent – Hard SEBS, Leaflets – SEBS 20

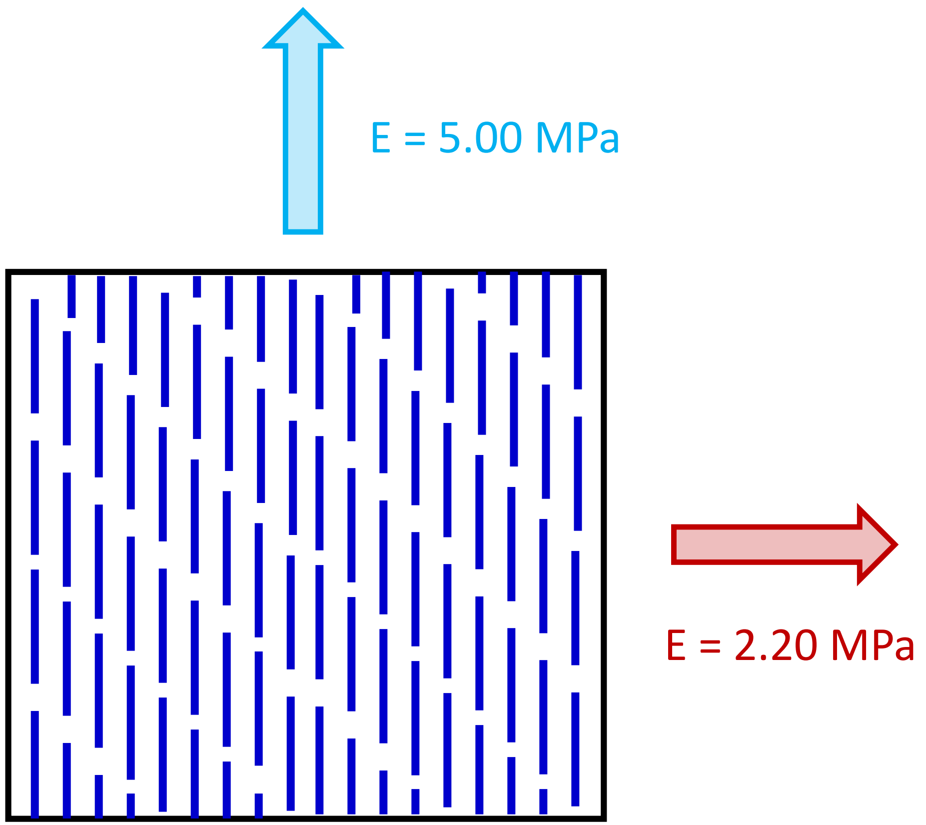
Material	Molecular weight (g/mol)	Morphology	Styrene fraction (% wt.)
Soft SEBS	High	Spherical	<20
Hard SEBS	High	Spherical	<20
SEPS-22	71, 697	Cylindrical	19.2
SEBS-29	74, 837	Cylindrical	28.4
SEBS-20	111, 327	Cylindrical	19.6
SIBS-19	High	Cylindrical	19.0

Table of styrenic block copolymers studied for PHV application.



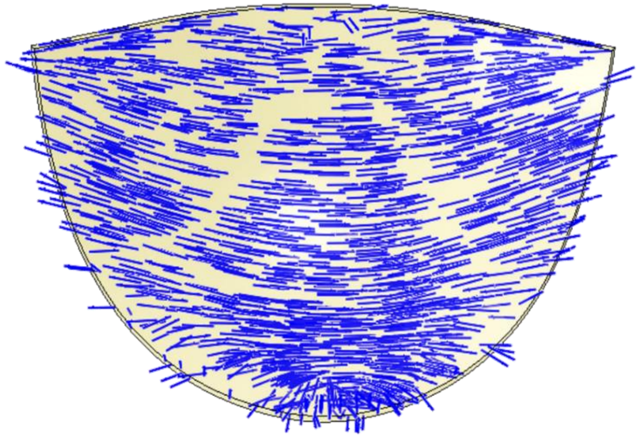
STYRENIC THERMOPLASTIC ELASTOMERS

- Mechanical properties measured in anisotropic styrenic thermoplastic elastomers vary based on cylinder orientation
- Anisotropy is flow induced during polymer processing
- For an oriented sheet of SEBS 20 (leaflets) the Young's modulus measured for parallel and perpendicular orientation follows a 2.3 : 1.0 ratio

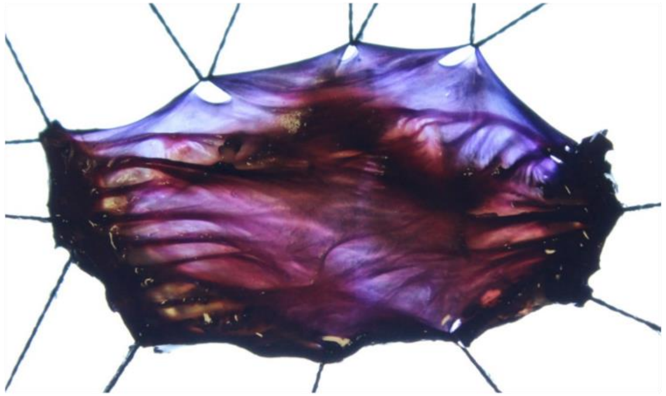


MODELLING ANISOTROPY IN STYRENIC ELASTOMERS

- Computational modelling used to **tailor anisotropy** in the leaflet
- Optimisation shows **circumferential alignment** of cylinders along the maximum stress direction
- Orientation achieved by having **injection point** at **centre** of leaflet
- Fatigue lifetime model **under predicts** durability in the PHV → needs further development



Optimised cylinder orientation

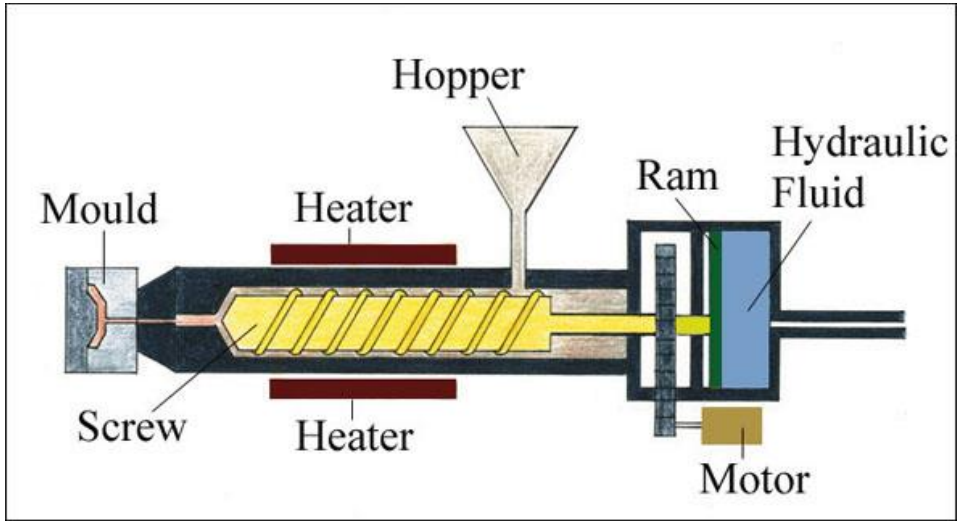


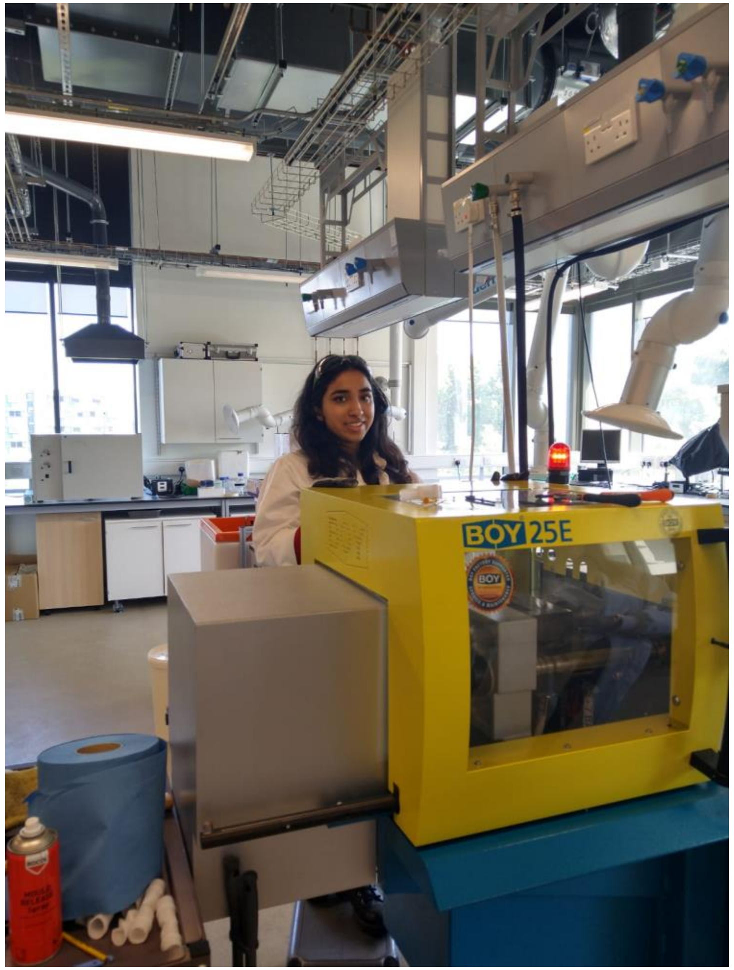
Natural tissue leaflet

- *M. Serrani et al., "A Computational Tool for the Microstructure Optimization of a Polymeric Heart Valve Prosthesis," J. Biomech. Eng., vol. 138, no. 6, pp. 16–20, 2016.*
- *J. Brubert, "A novel polymeric prosthetic heart valve: design, manufacture, and testing,", p. 296, 2015.*

Injection moulding

- Fit moulds into machine and load polymer
- Establish screw and mould temperatures
- Optimise holding pressure and cooling procedure
- Inject polymer into mould, cool and remove part





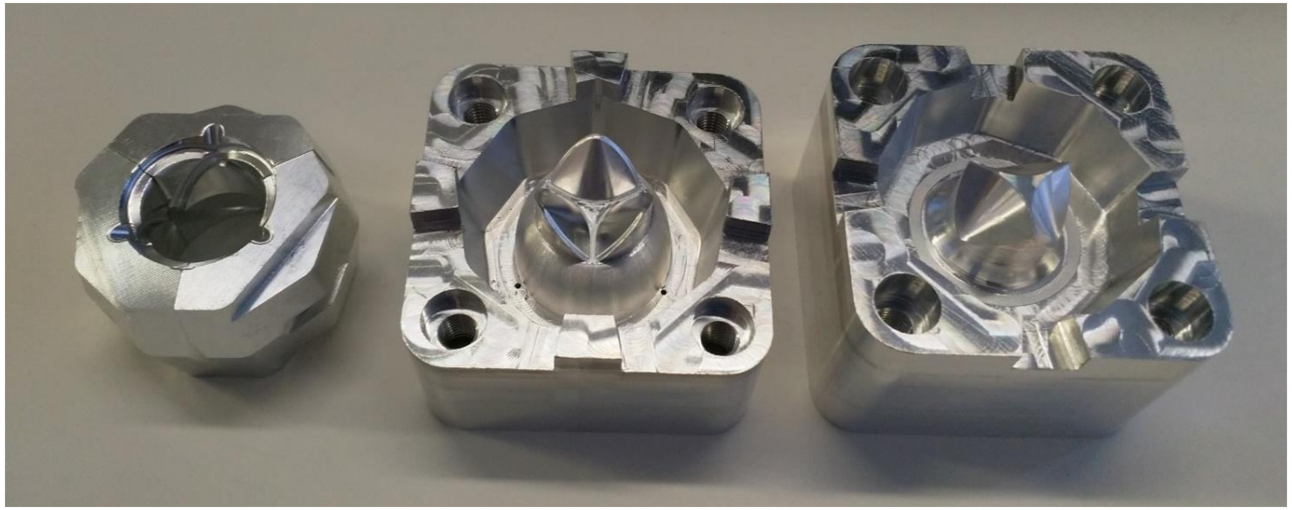
MANUFACTURING PROTOTYPES

CNC Machining

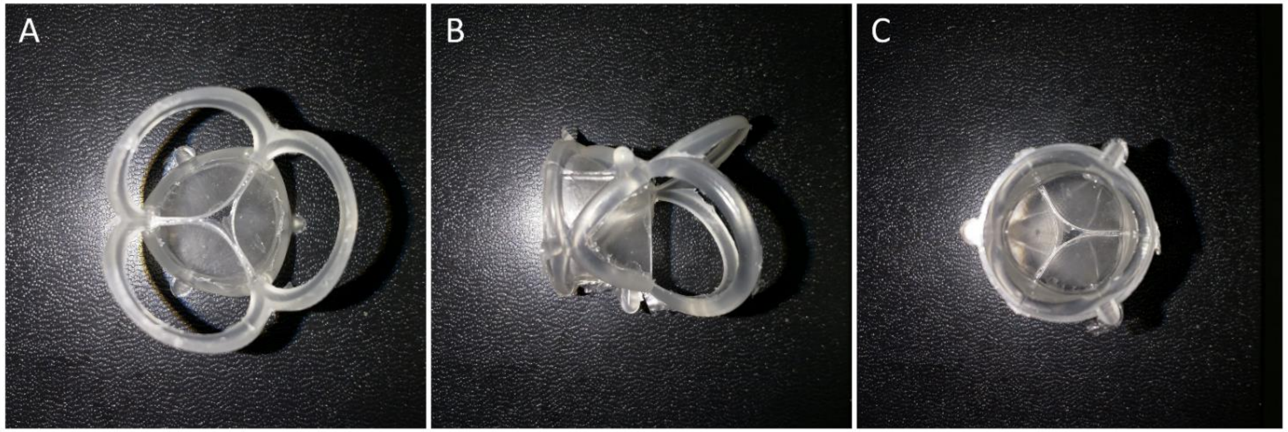
- Program tool paths
- Set up tools and stock block
- Perform machining steps

Mold making considerations

- High quality finish
- Tolerances and undercuts
- Injection point position

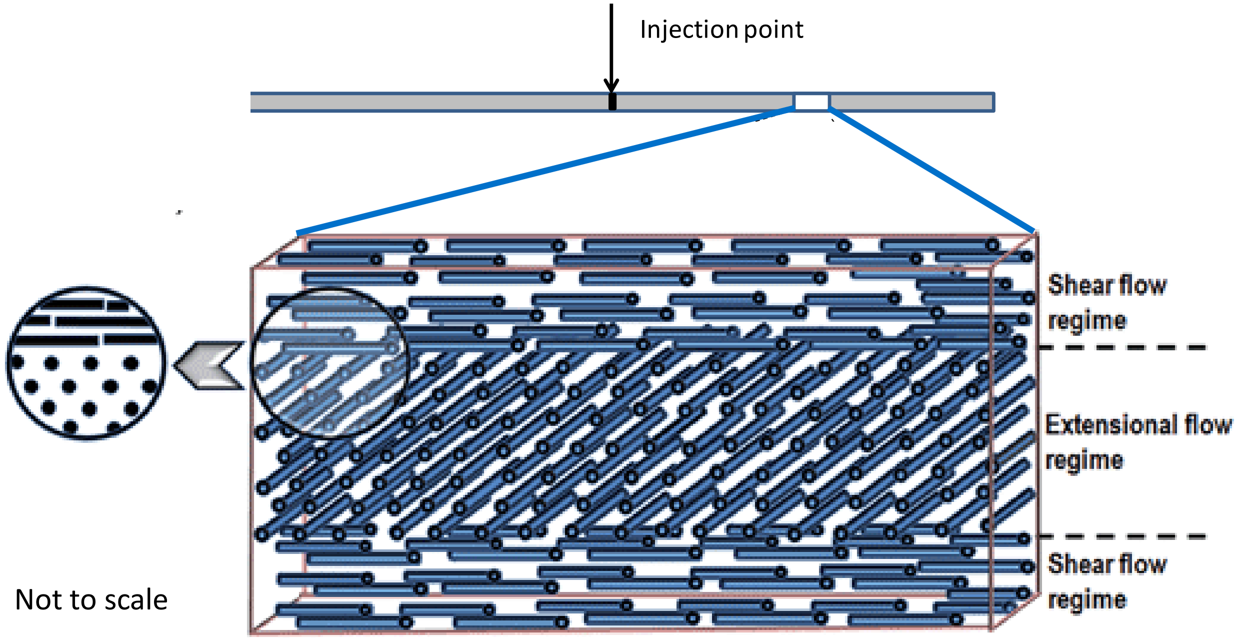


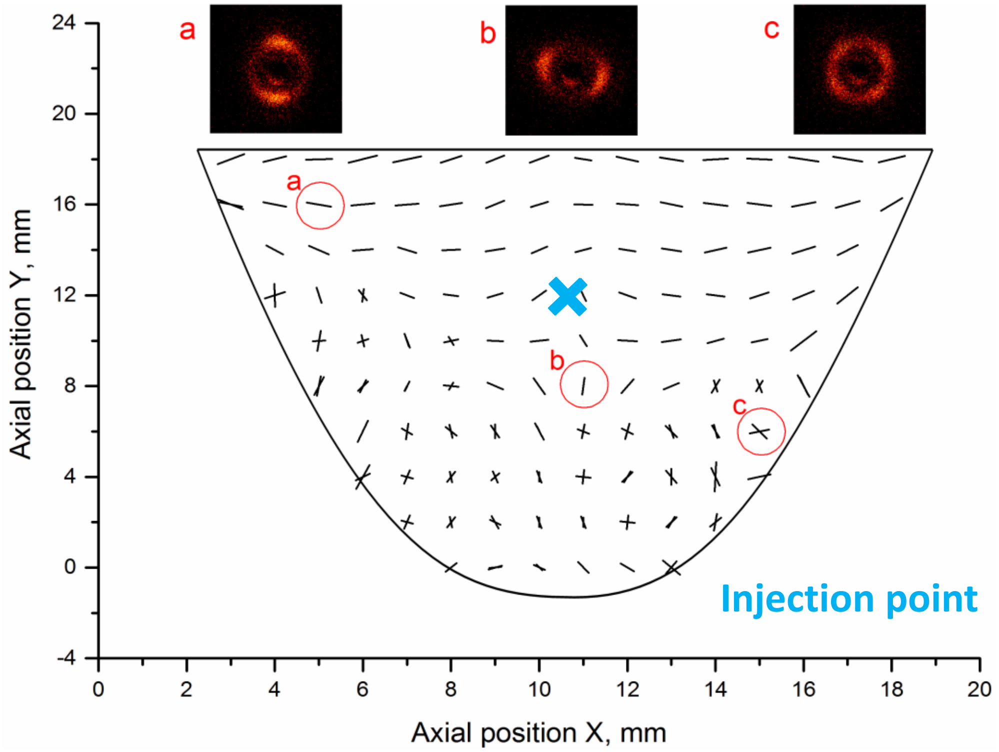
CNC machined inserts (left), female mould (centre), male mould (right).



Top view (A), side view (B) and bottom view (C) of injection moulded transcatheter PHV

ANISOTROPY IN PHV LEAFLET





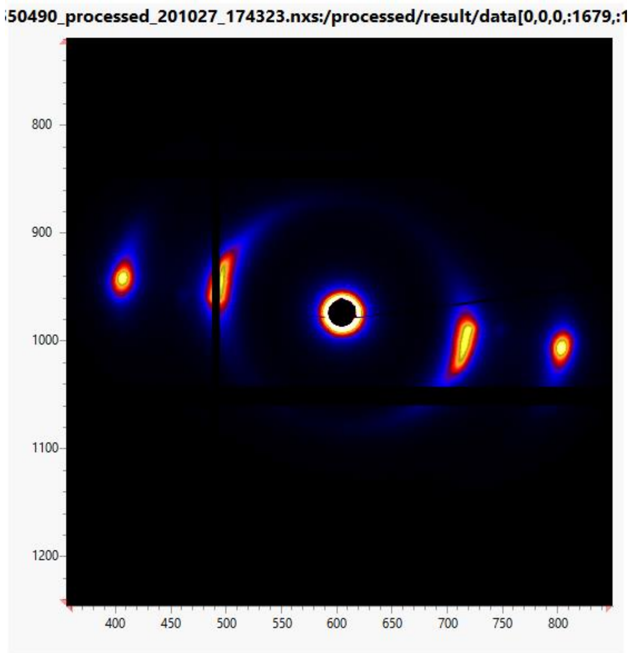
Alignment of cylinders in an injection moulded sample

Small angle X-ray scattering images

- J. Stasiak et al, A bio-inspired microstructure induced by slow injection moulding of cylindrical block copolymers, 2014.

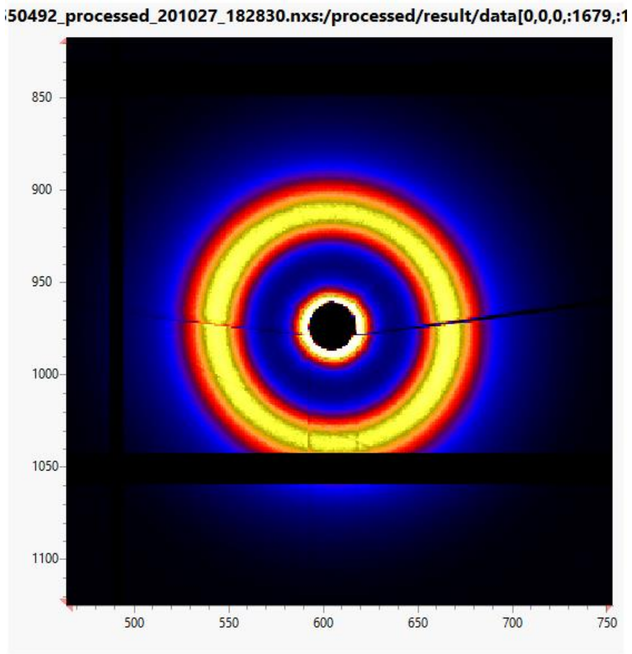
- J. Stasiak et al, Design, Development, Testing at ISO standards and in-vivo feasibility study of a novel Polymeric Heart Valve Prosthesis," 2020.

SMALL ANGLE X-RAY SCATTERING



Cylindrical morphology

- SEBS 20 (leaflet)

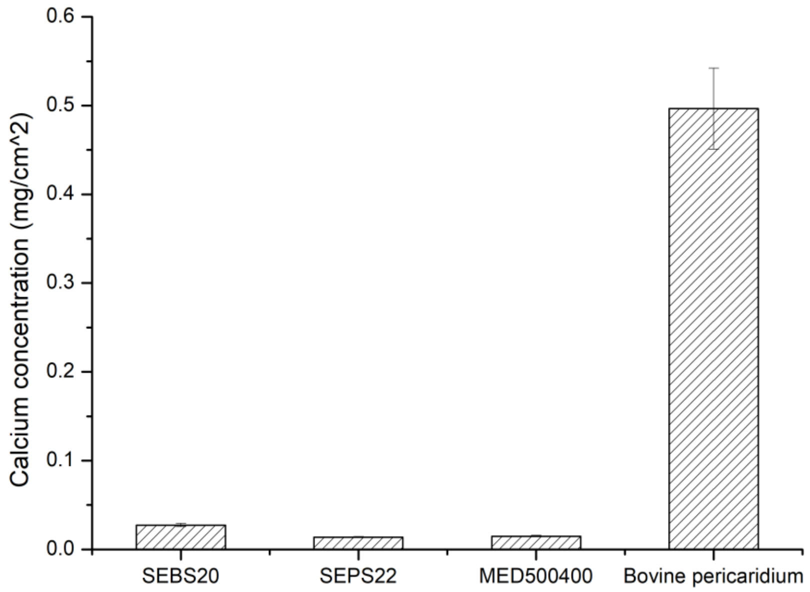


Spherical morphology

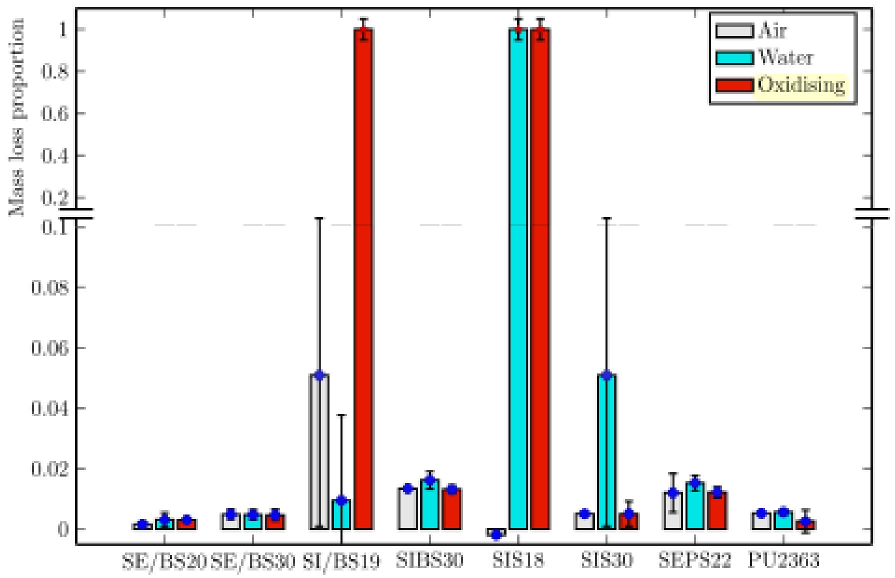
- Hard SEBS (stent)

Source: Synchrotron SAXS on beamline I22 at Diamond Light Source, Harwell, UK.

CALCIFICATION AND OXIDATION



Significantly lower susceptibility to calcification than bovine pericardium



- Very low mass loss seen for SE/BS20 and SEPS22

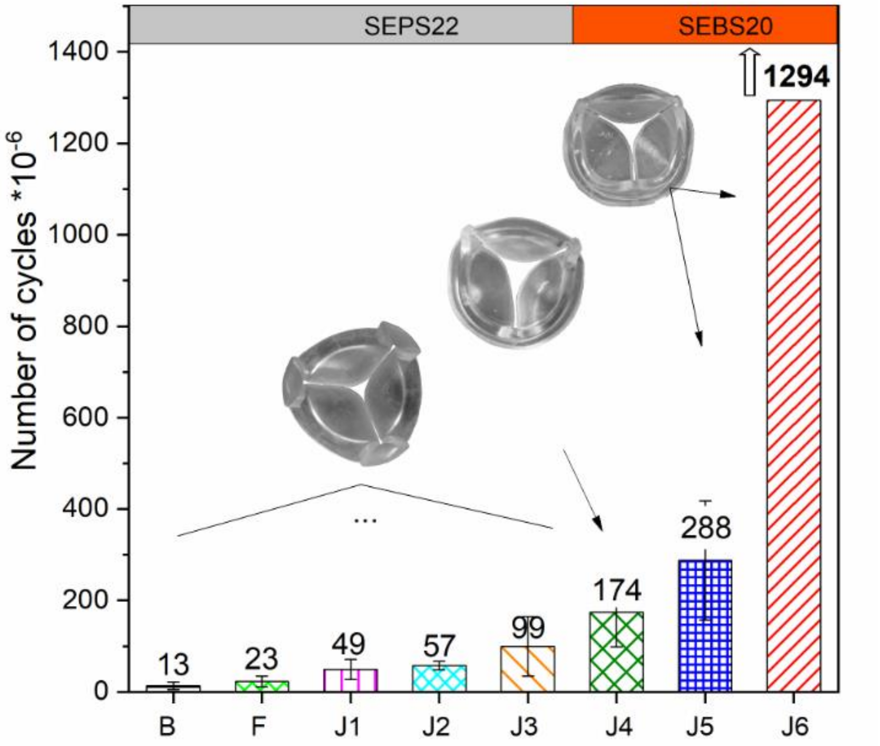
- More detailed studies on calcification and oxidation are in progress

Source: - Experiment and data collected by E. Okafor and J. Allford

- J. Brubert, "A novel polymeric prosthetic heart valve: design, manufacture, and testing.", 2015.

POLIVALVE PERFORMANCE SUMMARY

- PHV **injection moulded** from two styrenic block copolymers
- Leaflets have **tailored anisotropic properties** that mimic the native heart valve
- **Durability** improved by adjusting injection point position, leaflet shape and adding filets around leaflets
- Latest prototype lasts > **1 billion cycles** (~25 years) under accelerated fatigue testing
- Tested **in vitro** according to ISO 5840 standards and short term **in vivo** early feasibility study



J. Stasiak et al, Design, Development, Testing at ISO standards and in-vivo feasibility study of a novel Polymeric Heart Valve Prosthesis," 2020.

Conclusions & future work

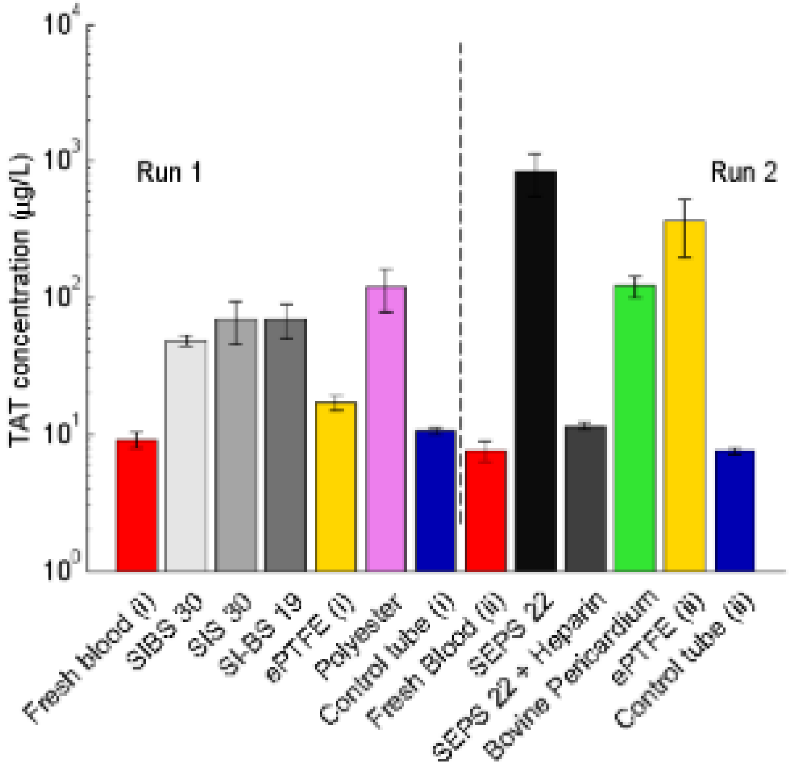
- Styrenic thermoplastic elastomers are effective materials for flexible leaflet PHV's that are **durable** and potentially **biocompatible**
- **Flow induced anisotropy** proves to be a useful tool to enhance durability in PHV leaflets
- Styrenic thermoplastic elastomers used in the Polivalve have demonstrated **good mechanical performance** and **resistance to calcification**

Future work:

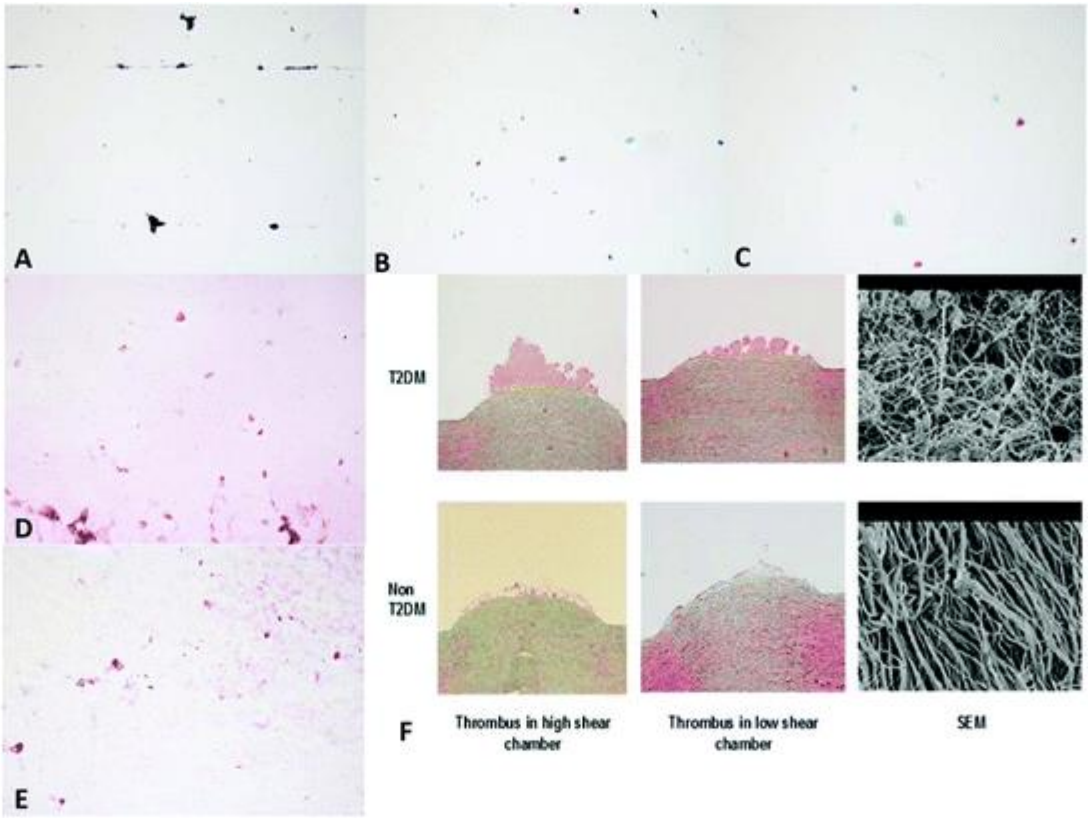
Continue to improve durability by studying anisotropy in styrenic block copolymers

Run tests to further study material biocompatibility (e.g. oxidation, calcification, biostability).

HEAMOCOMPATIBILITY



Thrombin is generated in the common pathway of the coagulation cascade as measured by the concentration of thrombin-antithrombin complex



- *J. Brubert, "A novel polymeric prosthetic heart valve: design, manufacture, and testing.", 2015.*