Textile-reinforced Hydralese™ Leaflets with High Toughness and Low Flexural Stiffness

Mohamed A. Elkhodiry, Ph.D., Amanda Weber, Andrew Metzger, Stephanie Reed, Ph.D.

secant group
PARTNERS FROM INSPIRATION TO REALIZATION

Bioprosthetic Heart Valves

- Most utilized form of replacement heart valves in North America
- Matches native valve hemodynamics
- No need for prolonged anti-coagulation


(© Cleveland clinic)
Fig.1. Representative design of current bioprosthetic heart valves

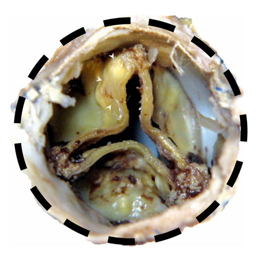


Fig.2. Valve leaflet calcification (Saleeb *et al.*, **Circulation**, 2014)

- Persistent leaflet calcification and degeneration problems
- Often requires re-intervention with a new prosthetic
- Difficult to scale for a global market

Polymeric Heart Valves

- Synthetic polymers offer a fully optimizable platform for superior long-term performance
- Extremely scalable and cost-effective
- Can be shaped into more effective 3D geometries

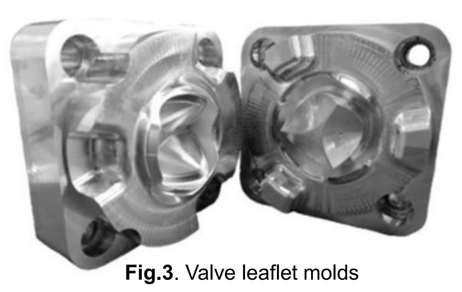


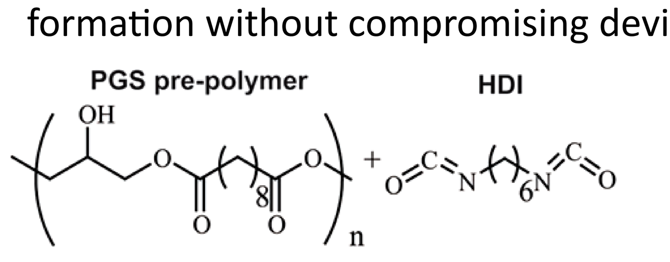
Fig.3. Valve leaflet molds (Stasiak*et al.*, **Biomaterials Science**, 2020)


Fig.4. Molded polymeric heart valve (Stasiak*et al.*, **Biomaterials Science**, 2020)

- Leaflets made from elastic thin polymer films often lack strength and durability
- Bio-stable synthetic polymers have unknown long-term biocompatibility and limited bio-integration

Hydralese™: Poly(glycerol sebacate) Urethane

- PGSU is a biodegradable elastomer with excellent in vivo biocompatibility (as per full ISO 10993 testing)
- It offers a more compliant polymer system than can better match native tissue compared to other bioresorbable polymers (Table 1).
- PGSU's slow surface-based degradation allows for gradual neo-valvular tissue formation without compromising device functions



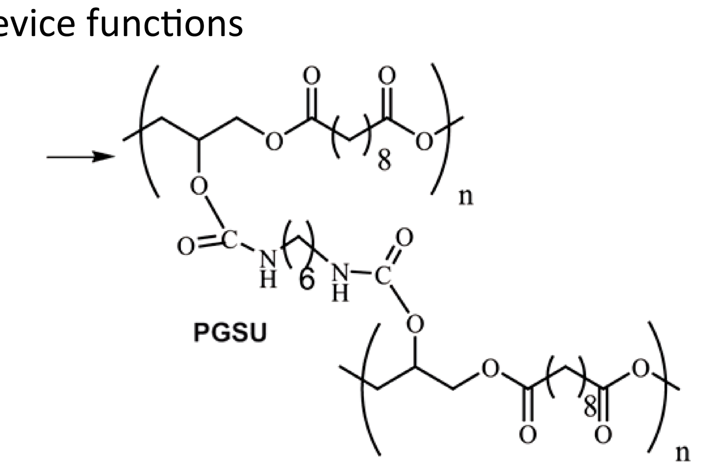



Fig.5. ASTM dog-bone die cut from thin PGSU film

- Thin PGSU films can offer a fully synthetic bioresorbable alternative to xeno-derived tissue
- Yet, they lack sufficient tear strength, suture retention for standard assembly and durability testing of replacement heart valves.

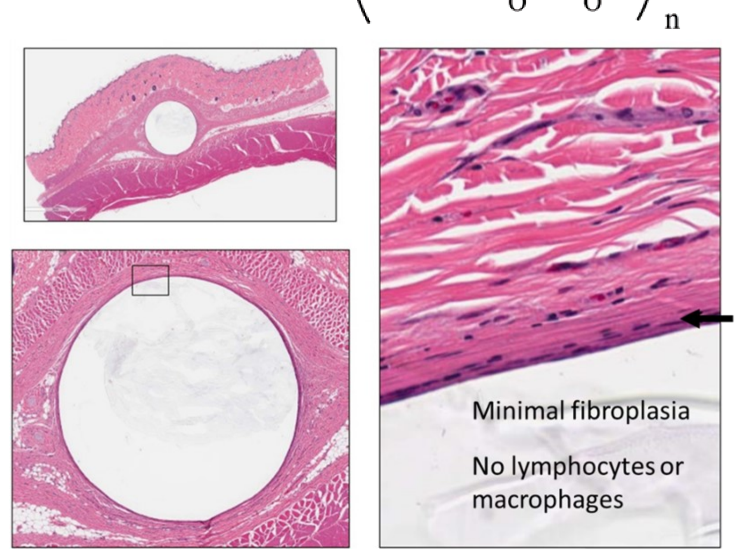


Fig.6. *In vivo* histological images of PGSU constructs implanted subcutaneously

Table. 1. Properties of PGSU compared to other common biodegradable and biostable polymers

	PGSU	PGA	PLGA 50:50/75:25	PLGA 80:20/85:15	PDLLA	PLLA	PCL	TPU	PU	PDMS
Polymer Type	Thermoset	Thermoplastic	Thermoplastic	Thermoplastic	Thermoplastic	Thermoplastic	Thermoplastic	Thermoplastic	Thermoset	Thermoset
Tg, Tm	-80C, none	40C, 220C	45C, amorphous	55C, 140C	50C, amorphous	60C, 185C	-60C, 60C	-40C, 180C	-50C, none	-125C, none
Flexibility	++	--	-	-	--	--	-	++	++	++
Flexural Modulus	3-20 MPa	9-10 GPa	2-3 GPa	1.5-2.5 GPa	3-6 GPa	3-6 GPa	200-600 MPa	15-900 MPa	20-900 MPa	1-900 MPa
Tensile Elastic Modulus	4-12 MPa	6.5-7.0 GPa	3.4-3.8 GPa	3.3-3.8 GPa	3.1-3.7 GPa	3.1-3.7 GPa	200-300 MPa	10-900 MPa	4-250 MPa	1-900 MPa
Strain at Break	20-100%	1-2%	1-4%	2-6%	2-6%	2-6%	300%	200-700%	15-800%	10-800%
Degradation Mechanism	Hydrolysis, enzymatic, pH	Hydrolysis, enzymatic, pH	Hydrolysis, enzymatic, pH	Hydrolysis, enzymatic, pH	Hydrolysis, enzymatic, pH	Hydrolysis, enzymatic, pH	Hydrolysis, enzymatic, pH	None	None	None
Degradation timeframe	3-24 months, tunable	1-6 months	1-4 months	12-18 months	12-16 months	>24 months	>24 months	Permanent	Permanent	Permanent
Inflammatory Response	-	++	++	+	+	+	+	-	-	+

Textile-reinforced PGSU Leaflets

PGSU was combined with PET textiles of different densities to create a range of tough-soft composites with superior tear strength and tunable tensile and flexural properties.

fracture energy

$$\Gamma = W \cdot l_T$$

energy dissipation density of the dissipation zone

energy dissipation zone size

(Cui *et al.*, **Advanced Materials**, 2020)

- The resulting PGSU-textile composite were tensile tested uniaxially.
- All composites showed higher toughness and resilience compared to either the uncoated textile or the neat PGSU films.
- Increasing the PGSU : textile ratio resulted in significant reduction in the elastic modulus of the composite compared to the uncoated textile.
- Th flexural moduli of all tested composites were below 10 MPa with no significant differences between the composites and controls.

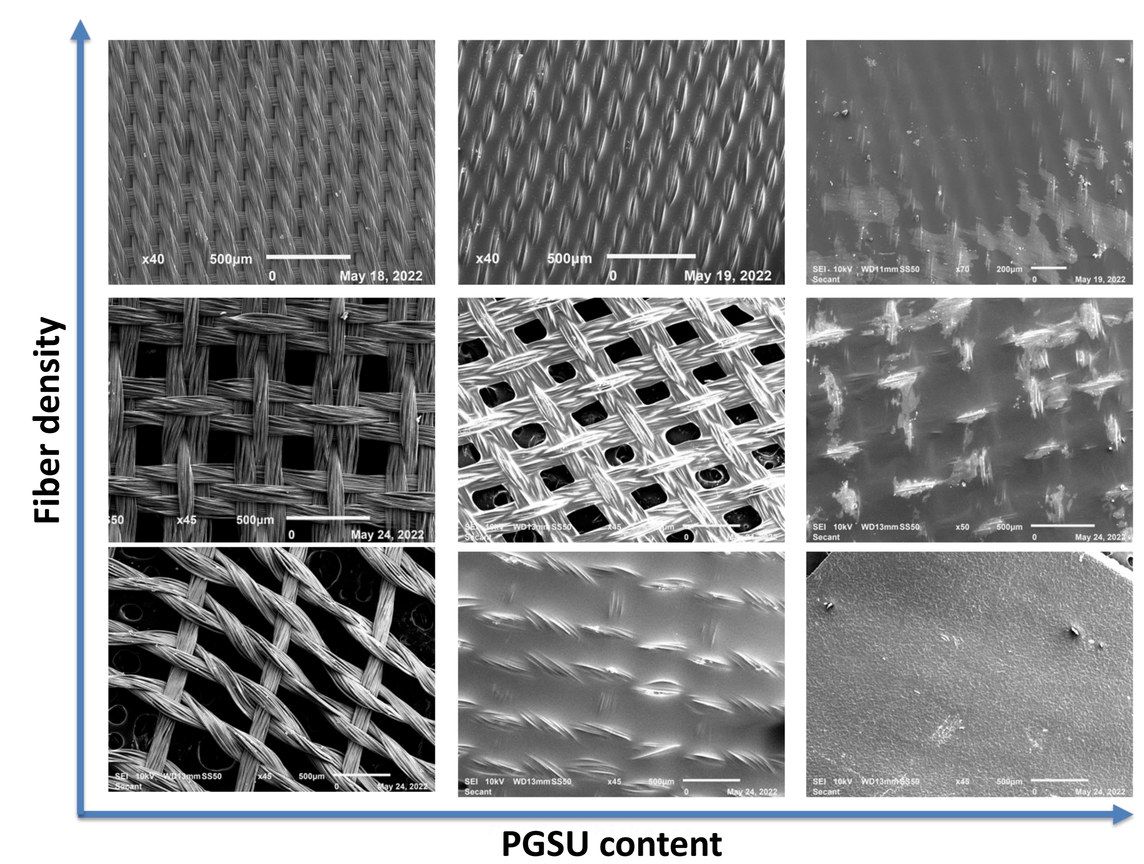


Fig.7. SEM images of textiles and their corresponding PGSU composites

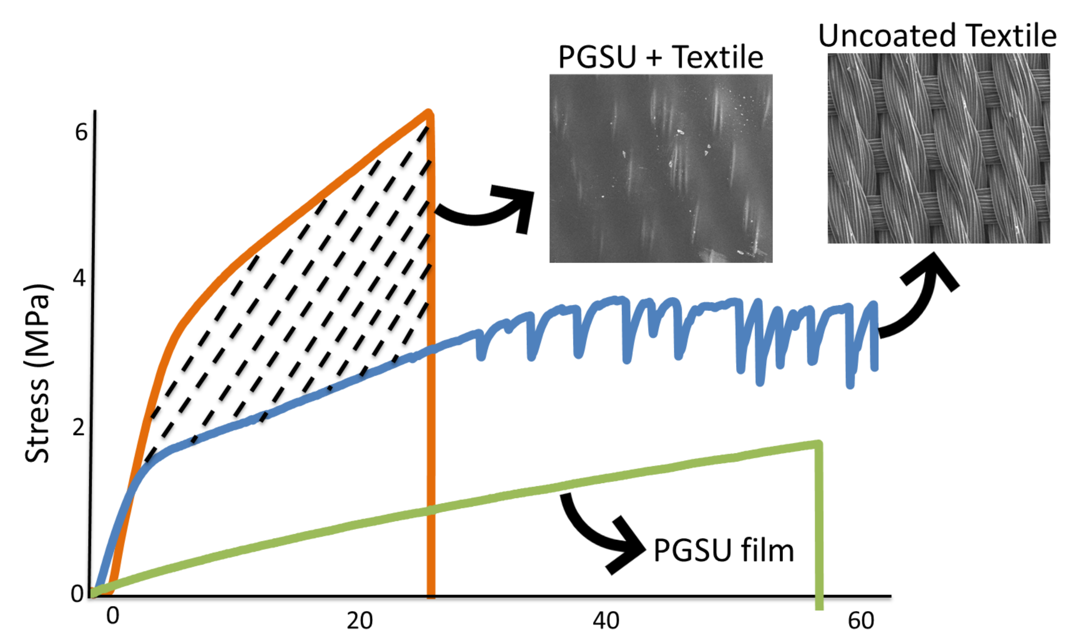


Fig.8. Tensile of high density textile composite vs. controls

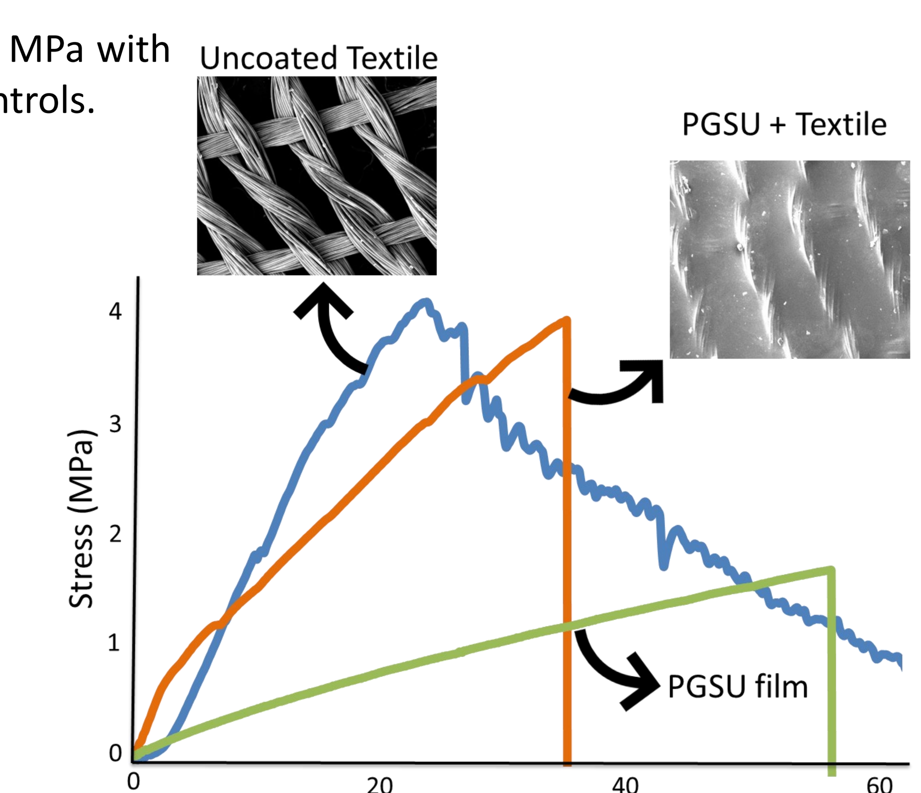


Fig.9. Tensile testing of low density textile composite vs. controls

Fatigue resistance

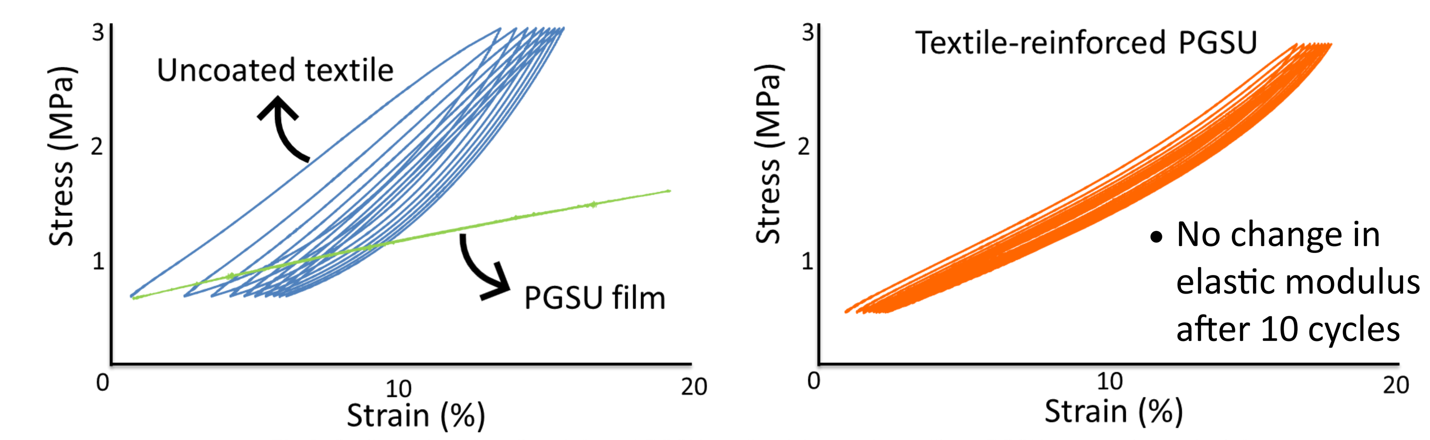


Fig.9. Cyclic testing of textile-reinforced PGSU (on the right) vs. the textile or PGSU separately (on the left)

The composites were also studied beyond the ultimate tensile strength to test the limits of PGSU-PET bonding.

Stretching the composite structures to failure led to:

- A single break
- No cracks
- No delamination

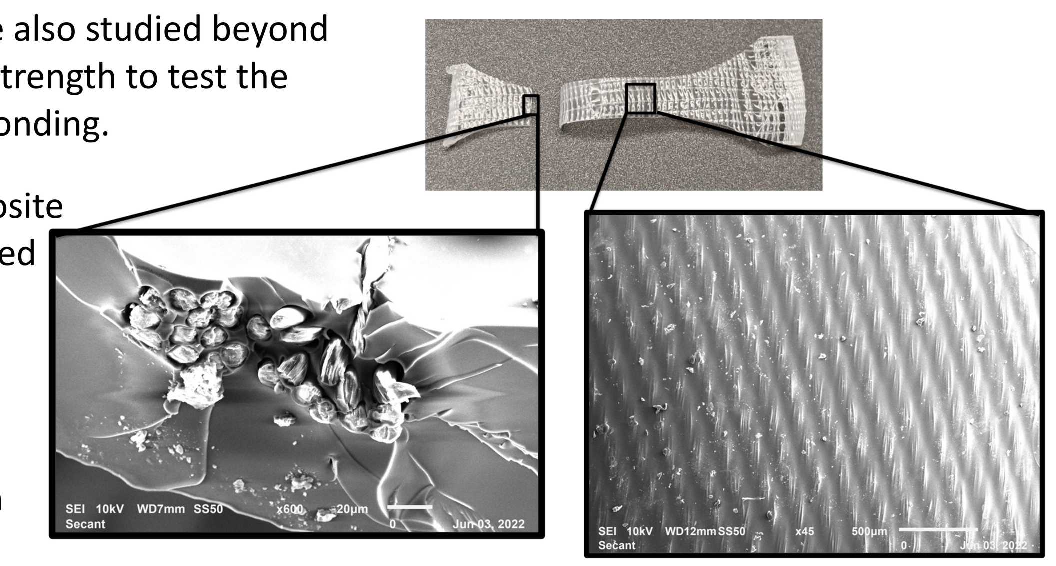


Fig.10. SEM images of textile-reinforced PGSU after tension until failure

Textile-induced anisotropy

- Using combination textiles with two fibers with different mechanical properties results in an anisotropic textile that mimics native valve tissue anisotropy.
- Incorporating PGSU within the textile did not jeopardize the anisotropy and increased overall toughness

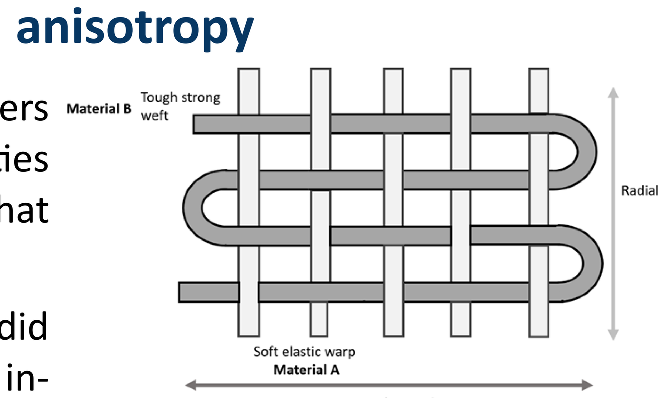


Fig.11. Design of woven anisotropic textile

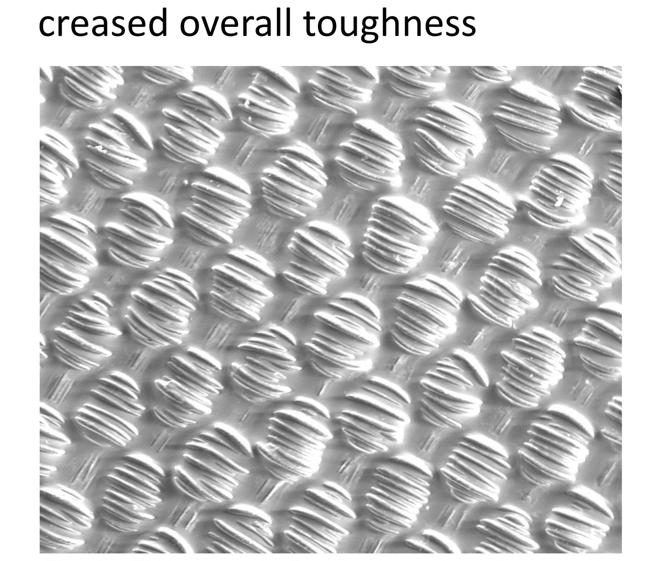


Fig.12. SEM image of the PGSU-anisotropic textile composite

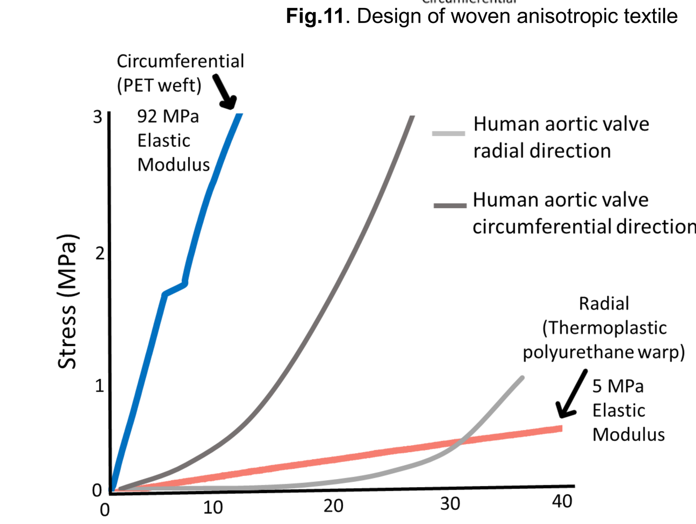


Fig.13. Tensile testing of the anisotropic textile along the two fiber directions

Conclusion

- PGSU provides a compliant slow degrading material ideal for heart valve leaflet substitutes
- Textile-reinforced PGSU creates a hybrid thin structure with superior toughness, tunable stiffness, and excellent flexural properties
- The PGSU-textile composite structure creates superior fatigue profile to either materials independently which is ideal for valve durability

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