Dual-layer scaffolds for small-caliber blood vessel tissue engineering

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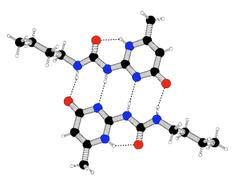

Dual-layer Scaffolds for Small-caliber Blood Vessel Tissue Engineering

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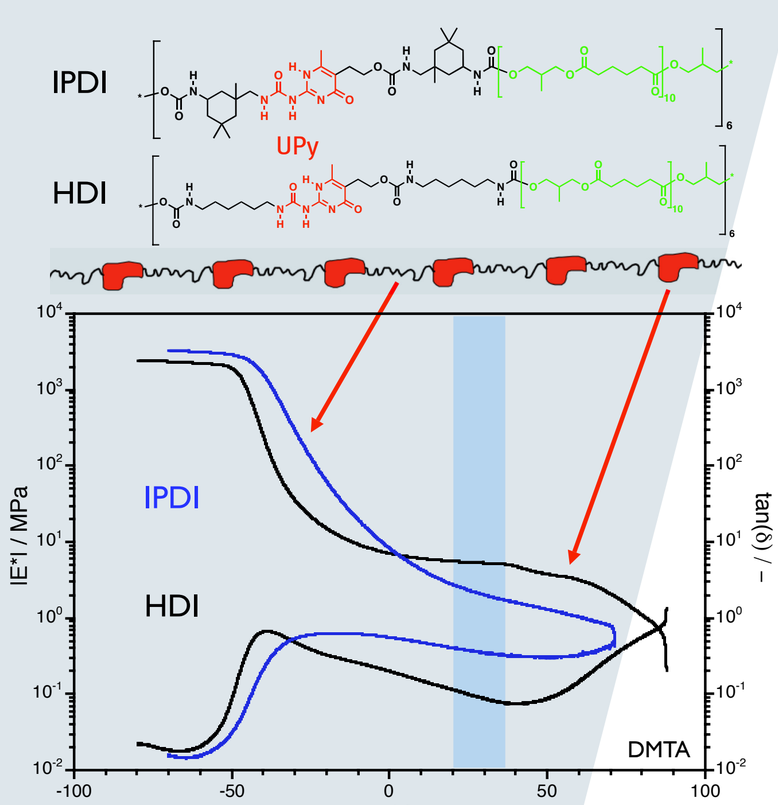
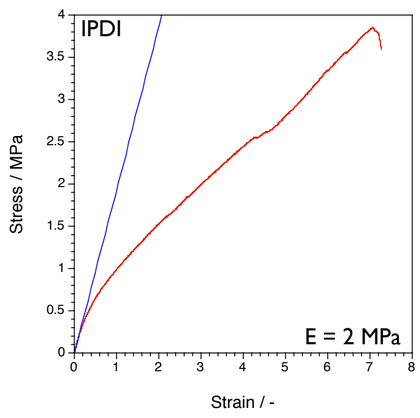
Introduction

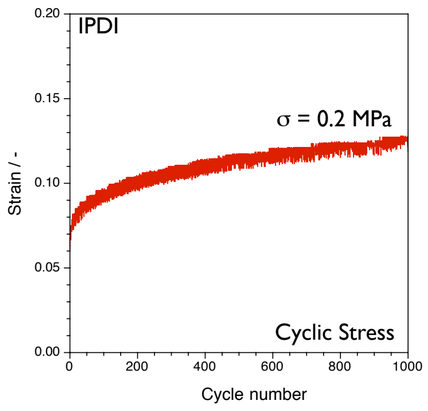
Currently, there are no successful artificial small blood vessels for medical use. Methods and materials that have been useful in the surgical repair of large vessels (e.g. synthetic grafts) are non-effective in small vessels, because blood coagulation leads to rapid occlusion of these vessels. This project aims to use a tissue engineering approach to construct a more advanced artificial vessel, that is mechanically similar to a natural blood vessel, and that supports both smooth muscle cells within their natural extracellular matrix and an intact lining of endothelial cells. To this end a novel elastic material will be synthesized and evaluated for the controlled culture of smooth muscle cells and endothelial cells on a porous tubular scaffold in a pulsed bioreactor.

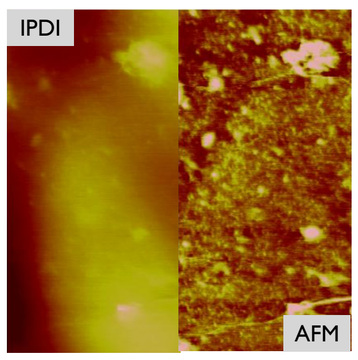
Mechanical Properties

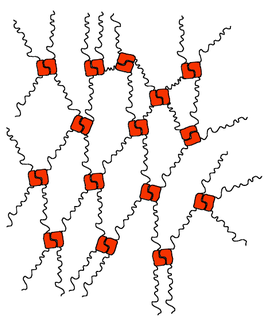
Two thermoplastic elastomers (TPEs) based on the strongly dimerizing UPy[1] moiety were evaluated, consisting of an amorphous polyester chain extended with an UPy bisisocyanate containing a bulky IPDI or a linear HDI spacer. The HDI material shows superior mechanical properties, presumably due to lateral stacking of dimerized UPy moieties, leading to higher stiffness and less plastic deformation on cyclic loading. The AFM data, showing hard blocks in a soft matrix, supports the assumption of lateral stacking (edge is 1 µm).

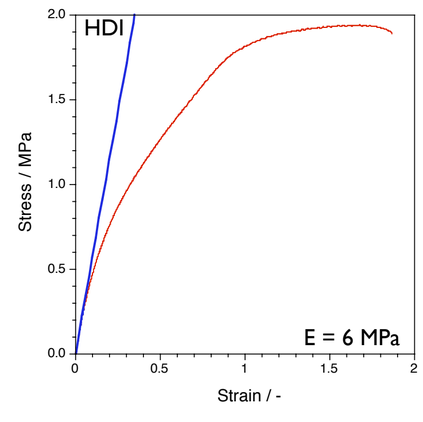


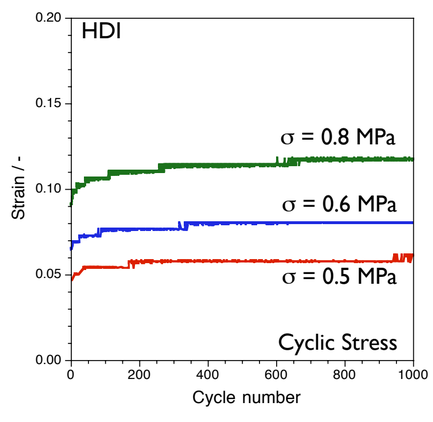


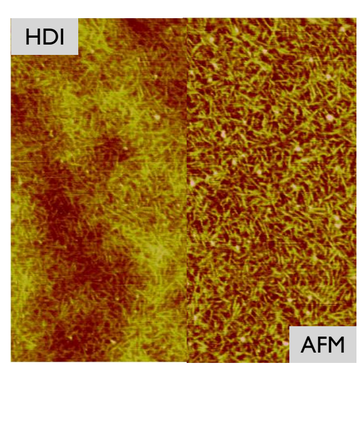


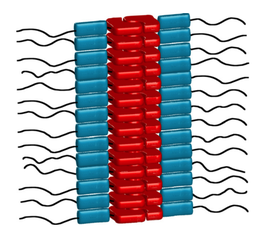






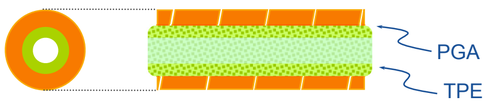


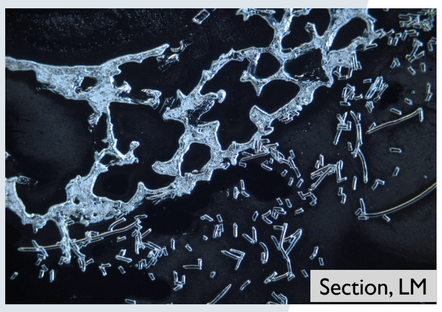


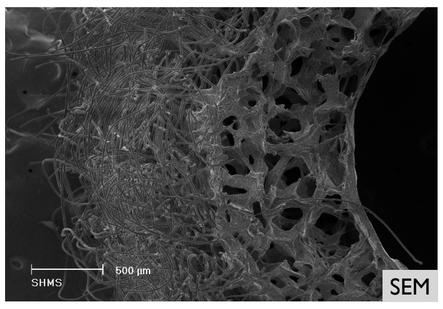


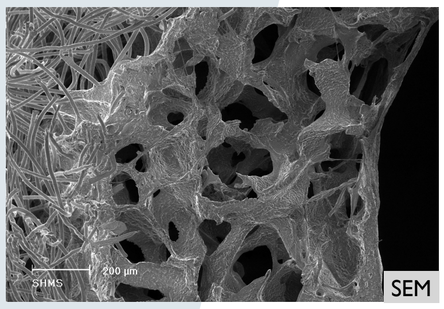
Scaffold

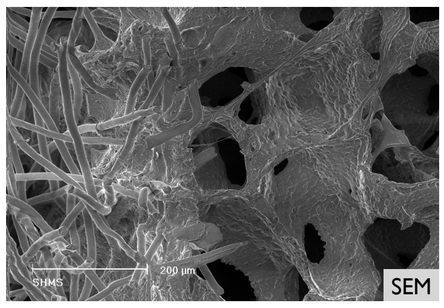
A dual-layer scaffold was constructed from the HDI based TPE and commercially available PGA felt. Light microscopy (LM) shows high porosity in both phases. Scanning Electron Microscopy (SEM) shows good integration between the two layers.





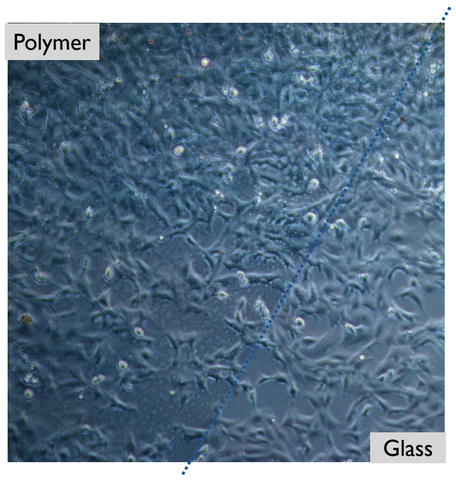






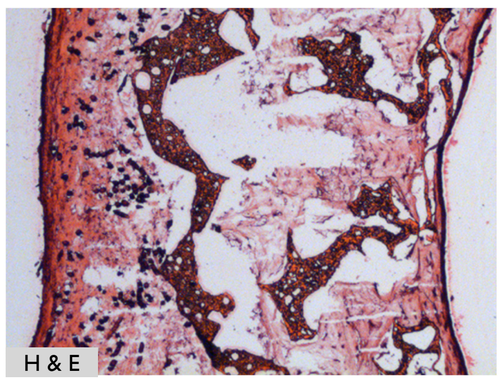
Cell Compatibility

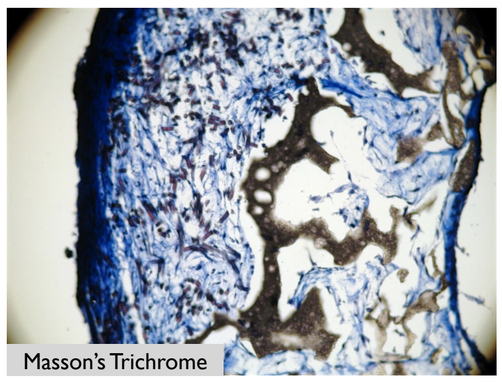
3T3 mouse fibrobasts were seeded on a cast of the HDI derivative on a glass cover slip. No discernable difference was observed in cell proliferation and adhesion between the polymer film and the glass surface.



Sheep myofibroblasts were subsequently seeded, in a fibrin gel supporting matrix, on the cylindrical dual-layer scaffolds displayed on the left. The resulting constructs were cultured statically for 18 days, and were subsequently harvested for analysis.

Histology below shows efficient seeding, with cells throughout the scaffold. The strongest proliferation and ECM deposition was, however, observed at the edges of the scaffold. Additionally, compaction of the construct is mostly observed in the PGA layer, and the adhesion of the EMC to the TPE material appears relatively poor.





Conclusions

These data show that UPy-based thermoplastic elastomers are cell-compatible, can be tailored to a specific (tissue engineering) application, and that it is possible to process them into a porous material. This material can then be employed to construct a functioning dual-layer vascular tissue engineering scaffold. The use of this advanced scaffold, in combination with mechanical and biochemical stimuli, may eventually lead to a significant improvement in the surgical applicability and specifically the in vivo patency of artificial small blood vessels.

References

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Acknowledgement

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