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Electrospinning and characterisation of biomimetic scaffolds for cardiac implants

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Introduction

Due to the rising numbers of people diagnosed with heart insufficiency, the clinical relevance of the development of new long-lasting and reliable biomimetic materials for functional heart implants is higher than ever. Native porcine pericardium currently acts as the gold standard despite the drawbacks of the intensive decellularisation processes involved therein. To provide an alternative that mimics the non-linear mechanical properties of porcine pericardium, we aim at developing a novel biomimetic electrospun hybrid consisting of polyurethane and collagen as part of a cardiac support system for patients with left ventricular heart failure.

Material Development

NIPU synthesis

- High valuability of non-isocyanate polyurethane (NIPU) production
- High-molecular weight NIPUs were synthesized through a transurethanization reaction of
  - dimethylhexane-1,6-diyldicarbamate (1,6-HDC)
  - polycarbonate diols with different M_w
- The chemical structure of the NIPUs were characterized by NMR- and FTIR spectroscopy.

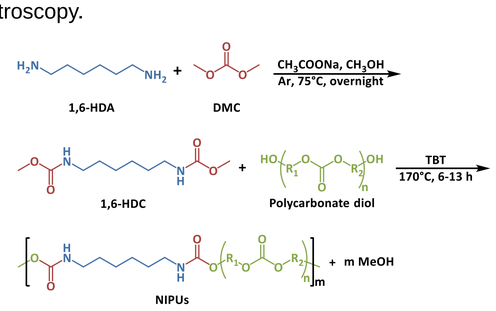

Figure 1: *Synthesis of high-molecular weight NIPUs.*

Table 1: *GPC and DSC characterisation of the synthesized NIPUs.*

NIPU	M_n of polycarbonate diol (g/mol)	M_w of NIPU (g/mol)	PDI	T_g (°C)	T_m of NIPU (°C)	ΔH_m (J/g)
NIPU16	500	26 200	1.85	-29	108	23.5
NIPU24	500	58 600	2.41	-26	107	37.5
NIPU15	1000	14 500	1.64	-38	64	19.1
NIPU17	2000	18 700	1.80	-42	44	27.8

Electrospun Scaffolds

- Versatile method to create porous structures that closely resemble the natural extracellular matrix, with fibre diameters ranging from a few nanometers to over one micrometer.
- Mechanical stability, fibre morphology, and fibre sizes can be influenced, by varying the system and process parameters.
- Various electrospun scaffolds were created by electrospinning NIPU and rat tail collagen

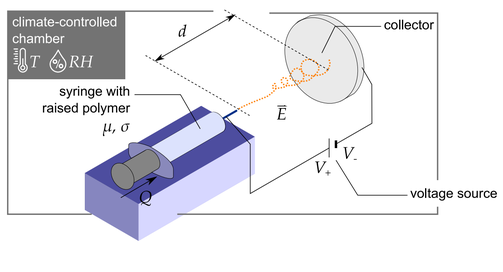

Figure 2: *The electrospinning process. Dissolved or molten polymer is pumped through the capillary and gets collected in a small conic-shaped droplet (Taylor cone) on the tip of the capillary, when a high voltage is applied. If the electrical field is appropriately increased, a fibre will eject from the Taylor cone and travel in spinning motion towards the collector, while the solvent evaporates.*

Outlook

- Mechanical characterization of electrospun scaffolds.
- Minimisation of solvent impact on collagen.
- Simulated biostability tests for long-term stability assessment.

References

[1] Zeugolis, D. I. et al. (2008) Biomaterials, 29(15), 2293-2305.

Electrospinning

- Various electrospun scaffolds were created by electrospinning NIPU and rat tail collagen

Collagen

- could be spun from non-fluorinated, acidic solutions
- well-defined fibrous morphology
- fibre morphology improved with faster solvent evaporation

NIPU

- well spinable out HFP with tuneable fibres dependent on Mw
- cytotoxicity tests showed good biocompatibility

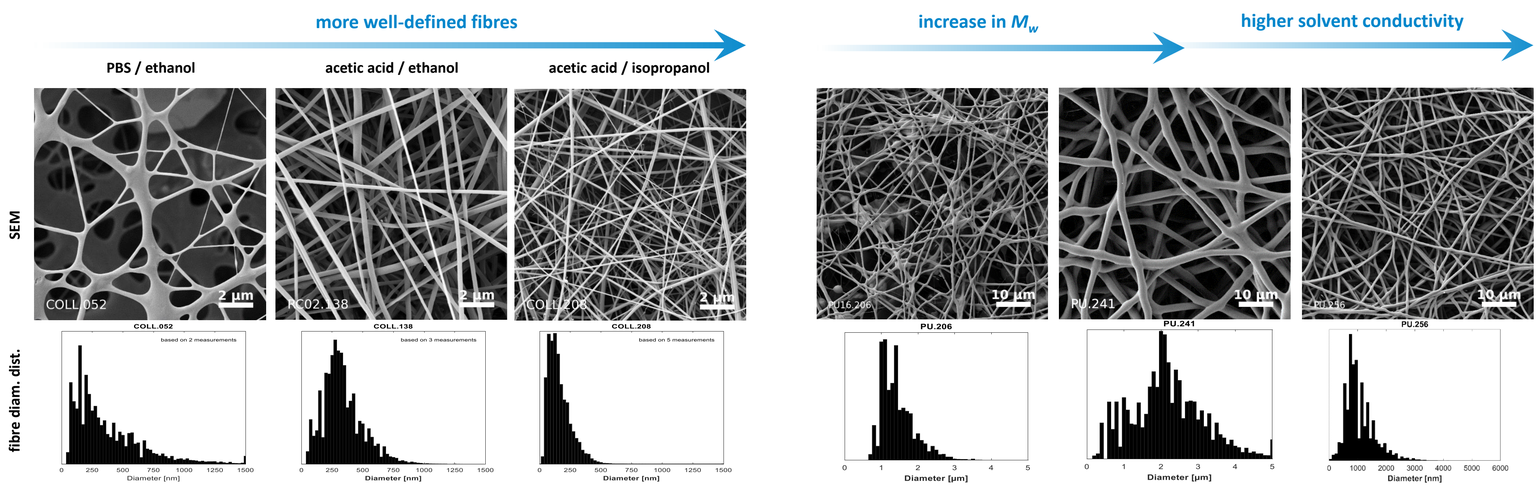

Figure 3: *The top row shows SEM images of electrospun rat tail collagen (left) and NIPU (right). The bottom row shows the distribution of fibre diameters.*

Material Characterisation

- Need for characterization of collagen due to collagen's susceptibility to electrospinning solvents [1].
- **HAc/EtOH** reduced intact triple-helix content
- **HCl/EtOH** more preserved intact triple-helix content

Raman Spectroscopy

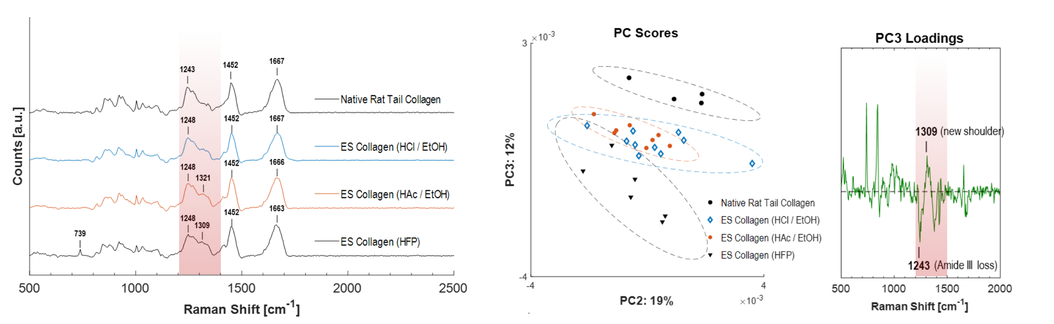

Figure 4: *Raman spectroscopical analysis of native, denatured and electrospun rat tail collagen. Raman spectroscopy enables the non-destructive differentiation between native and denaturised collagen. Amide III (~1248 cm^{-1}) proves to be an important marker.*

Enzymatic Digestion

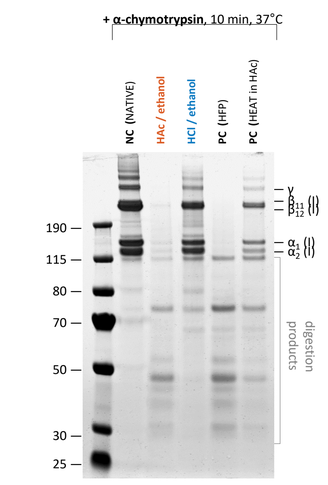

Figure 5: *SDS-PAGE analysis show the better preservation of the α_1 and α_2 chains in collagen spun out of HCl/ethanol after enzymatic digestion with α-chymotrypsin.*

Cell Adhesion, Viability, and Morphology

- Cell adhesion an viability showed by means of Live/Dead Staining
- Morphology visualised by means of an F-Actin staining.
- hFFs and hMCs show good adhesion and viability on electrospun NIPU, as well as on electrospun collagen.

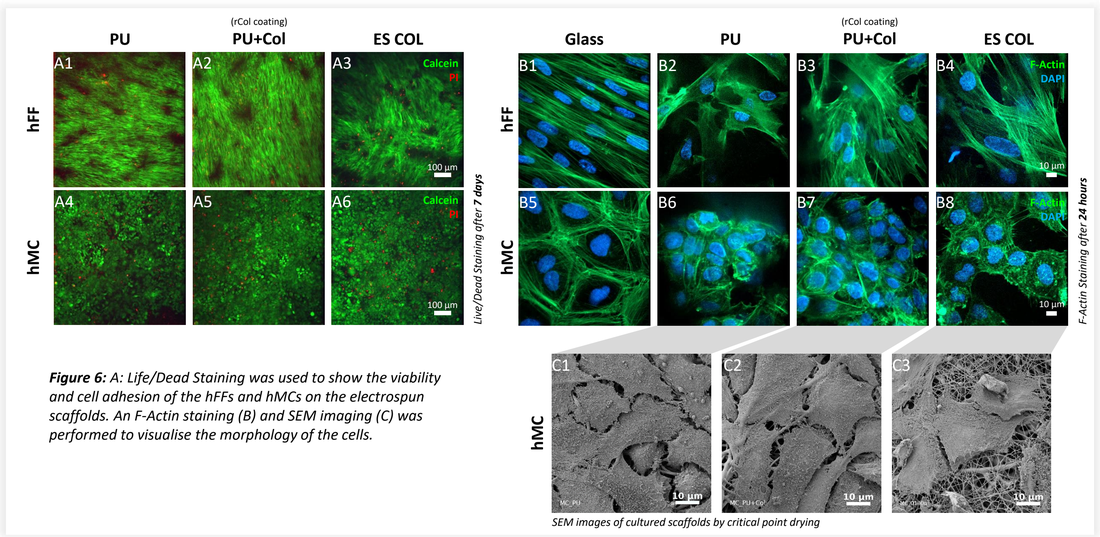

Figure 6: *A: Life/Dead Staining was used to show the viability and cell adhesion of the hFFs and hMCs on the electrospun scaffolds. An F-Actin staining (B) and SEM imaging (C) was performed to visualise the morphology of the cells.*

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