Development of Textile Structures with Material-Intrinsic Shape Changing Capabilities for Regenerative Medicine (TexMedActor)

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Introduction and Objective

In Germany, both demographic changes in society and injuries resulting from trauma are leading to a high proportion of people with cardiovascular diseases or injuries to vessels and internal organs requiring treatment. Treatment of injuries to internal organs, vessels, or nerves usually requires complex procedures (anastomoses) that involve elaborate fixation and suturing. These complicated and elaborate procedures are often associated with long procedure times, which in turn directly correlate with increased complication rates [1-3]. Tubular plastic implants are increasingly being developed to bridge such defects. These single material structures do not allow tissue/ cell ingrowth. Therefore, they run counter to the concept of regenerative medicine, which aims to restore body tissues and cells. In addition, when the defects are filled, regeneration is often disturbed due to the structural-mechanical properties that are not adapted to biomechanics. Furthermore, the lack of interconnectivity of the pore spaces of the replacement structures prevents the cell ingrowth, cell growth, nutrient supply and the removal of metabolic products.

In the context of in vitro tissue engineering, in addition to static cell culture systems, dynamic systems are also being developed. These are based, for example, on continuous or pulsating fluid flows or on a cyclic stretching of a clamped cell support system or substrate [4]. However, a replication of natural mechanical growth stimuli is not possible with such bioreactor systems because, especially in larger structures, there is a locally increased flow velocity along the largest pores or only an overflow of the entire cell support system. Additionally, undesirable stress peaks and undefined distortions occur in the region of the clamps and supports in mechanically stimulated systems.

Since the native structure of the four most important tissue types (connective and supporting tissue, nervous, muscular and epithelial tissue) from which organs, such as bones, blood vessels, muscles, tendons and ligaments, are formed, consists of fiber-like constructs, these can be particularly well biomimicked with textile structures. With the help of pre-designed fiber arrangements, three-dimensional, complex geometries with interconnecting pore spaces can be built up. The cells can use these structures to orient themselves in their growth direction [5]. Therefore, fiber-based high-tech structures are particularly predestined to overcome the limitations of currently available implants.

Therefore, within the framework of the IGF research project TexMedActor (21022 BR/1) novel textile structures with material-intrinsic shape changing capabilities were developed for regenerative medicine with a variety of different application fields, especially anastomosis. The concept pursued envisages the textile-technological realization of structures with a shape memory effect. The textiles should be able to assume predetermined geometries in order to adapt interactively to defects and to simplify complex interventions to bridge or support defects in internal organs like vessel and nerves. Furthermore, these textiles are intended to enable electromechanical stimulation for the actively targeted stimulating of cell growth. In this way, regeneration is accelerated or even made possible in the first place, since the necessary stimuli for tissue- and cell-adapted growth stimulation are lacking, especially in the case of body tissues with weak or no blood supply, such as cartilage, tendons, ligaments, or in the case of wound healing disorders or chronic wounds. Furthermore, novel bioreactors based on the intrinsic properties of the textile structures will be developed, which use the mechanism of action for electromechanical stimulation to uniformly stimulate the cells at each site even in highly complex and large-scale cell carrier structures. Here, the mechanical stimuli originate from the material itself. This material-intrinsic stimulation represent a new method for optimal cell cultivation, by stimulating cell on the textile cell carrier structures without externally applied fluid flows or mechanical deformation. This is intended to overcome two recognized medical technology problems: 1) complicated, costly operations on internal organs, vessels or nerves that are difficult or impossible to perform with minimally invasive procedures, and 2) lack of tissue- and cell-adapted stimuli for promotion of growth in previously used replacement structures and materials as well as currently available dynamic cell culture systems.

Selected Results

Development of Thermoplastic Shape-Memory-Yarns and -Fabrics

First, it was necessary to develop yarns with a material-intrinsic shape-change capability whose activation temperature is in the range of the body core temperature (37 °C) or the body surface temperature (~20 – 25 °C). For this purpose, a thermoplastic urethane (TPU) was blended with polycaprolactone (PCL) of different molecular weights (1250 g/mol and 80000 g/mol). Differential scanning calorimetry (DSC) was used to determine phase transformation temperatures and the heat flow generated. Based on the amount of PCL added and its molecular weight, it was possible to adjust both the activation temperature of the shape memory effect and the amount of converted heat (Fig. 1). In particular, the use of low molecular weight PCL (1250 g/mol) led to application-specific activation temperatures.

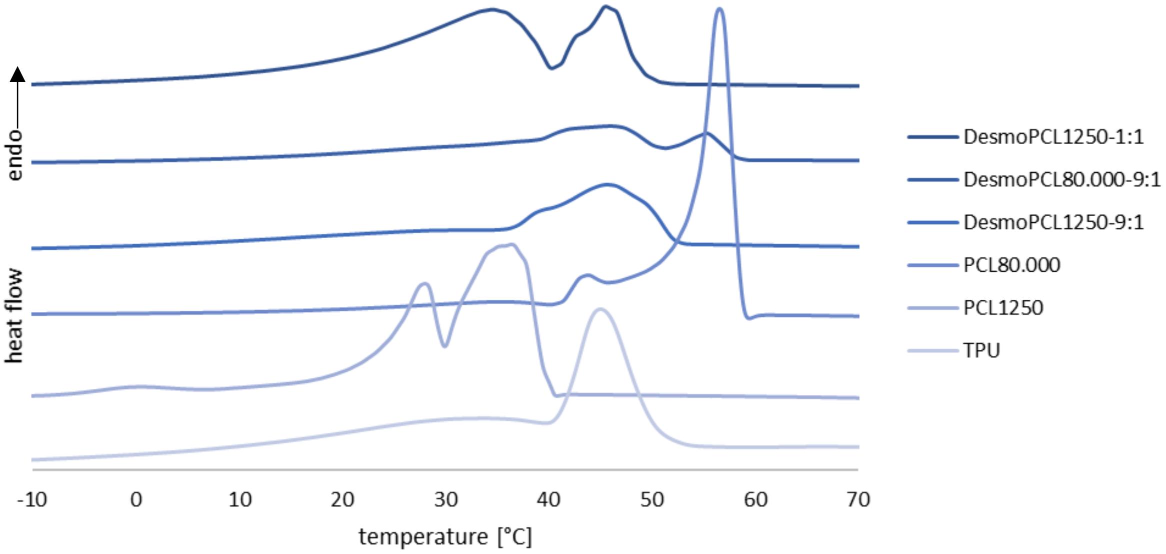


Figure 1: DSC curves of the investigated TPU-PCL blends and the individual components

The yarn production was first tested by means of melt spinning. It was shown that TPU can be successfully spun in reproducible quality with a fineness of 42 tex. However, the blend materials could only be processed to a limited extent. Due to the low molar mass of PCL, incipient decomposition of the polymer already occurred at temperatures of approx. 200 °C, which are absolutely necessary for melting the TPU. Therefore, a solvent wet spinning process was established, with which PCL contents of up to 33 % in the yarn can be realized without decomposition. In this process, the polymer blends were dissolved in DMF at room temperature and coagulated in water.

The generated melt-spun as well as wet-spun yarns exhibited pronounced shape memory properties with activation temperatures at the level of the body core or body surface temperature (depending on the PCL content) and were thus able to achieve high contraction rates after prior programming. However, for anastomosis therapy, 3D rolling rather than simple contraction of the yarns is required.

Therefore, a graded weave structure from a plain weave to a twill weave to a five-bind atlas weave was chosen when processing as a fabric (Fig. 2A). As a result, the weft yarns in the different fabric layers are bound to different extents, which leads to friction differences and thus to a different degree of contraction of the shape memory yarns after activation. Thus, a rolling of the fabrics at body temperature could be realized (Fig. 2B+C).

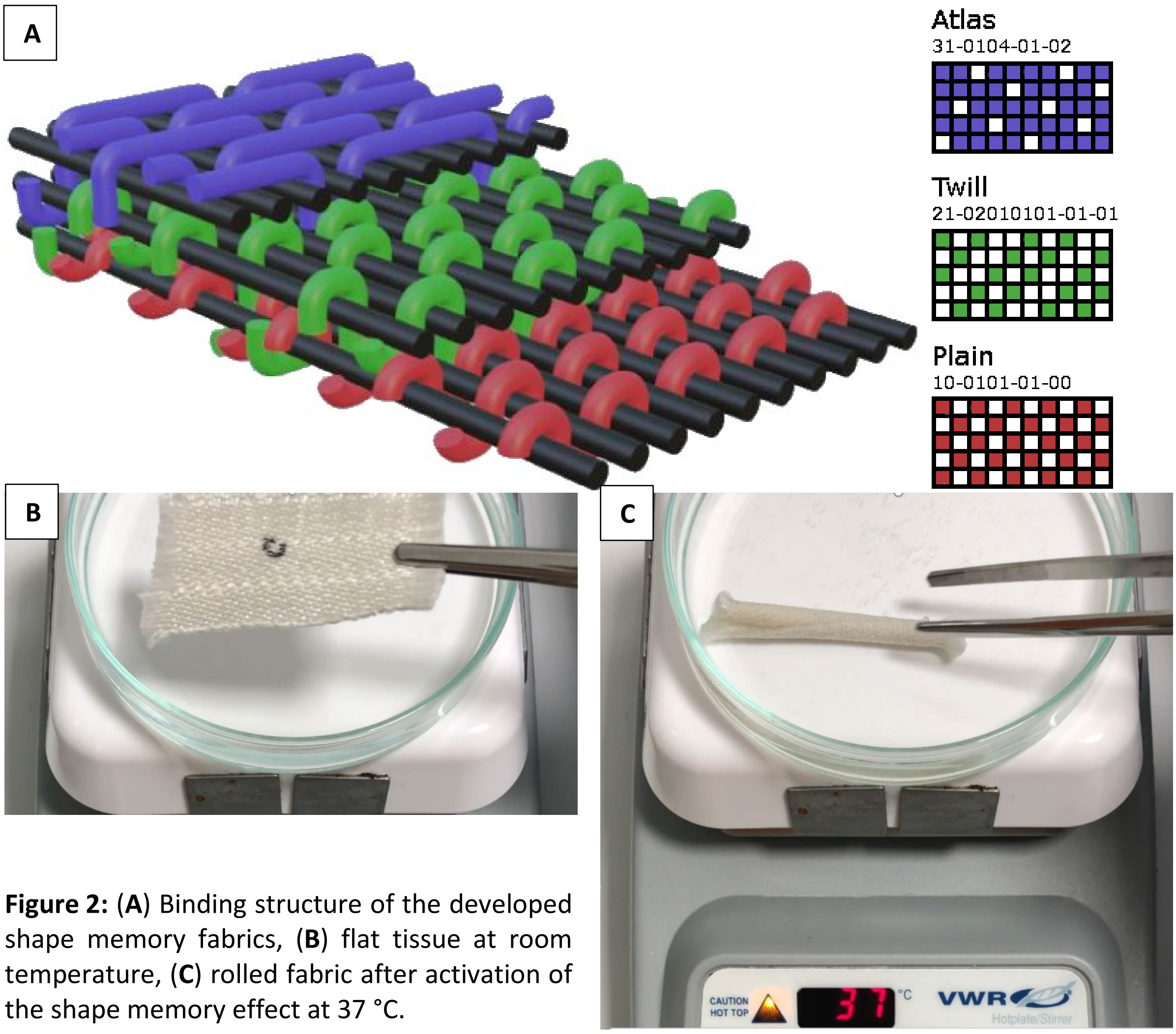


Figure 2: (**A**) Binding structure of the developed shape memory fabrics, (**B**) flat tissue at room temperature, (**C**) rolled fabric after activation of the shape memory effect at 37 °C.

Development of Piezoelectric Yarns

Electroactive yarns were developed on a PVDF basis by means of a melt spinning process. The polymer exhibits pronounced piezoelectric properties in its polar crystal phases (namely β and γ). For use as textile bioreactor systems, however, an increase in the piezoelectric properties is necessary in order to realize the greatest possible mechanical stimulation at very low current strengths in the µA range, which are harmless to cells. Therefore, by specific adjustments of the spinning parameters, the melt draw ratio (MDR), as well as the post-draw, methods were developed to increase the polar phase fraction of the PVDF yarns. The phase fractions were determined via quantitative analysis of Fourier-transformed infrared spectra. An increase in the polar β- and γ-phases from about 45 % to over 60 % was found.

Characterization of Textile Structures with Material-intrinsic Shape Changing Capabilities

The shape memory properties of the melt-spun or wet-spun yarns were investigated using the Zmart.Pro Z100 tensile testing machine (ZwickRoell GmbH & Co. KG, Germany) in combination with a heat chamber. The strain fixation and strain recovery behavior was determined cyclically at 300 %

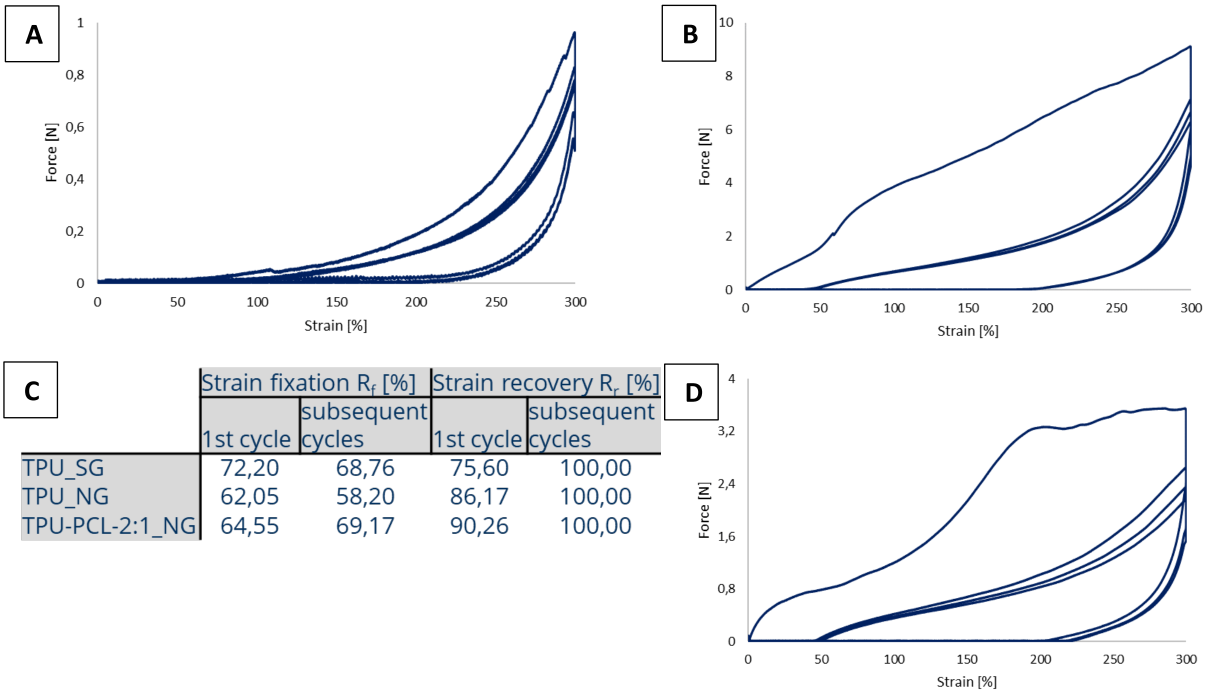
maximum elongation and thermal activation. The characteristic values were calculated using the following equations:

$$R_f(n) = (\varepsilon_f(n) - \varepsilon_p(n-1)) / (\varepsilon_m - \varepsilon_p(n-1)) \quad (1)$$

$$R_r(n) = (\varepsilon_m - \varepsilon_p(n)) / (\varepsilon_m - \varepsilon_p(n-1)) \quad (2)$$

R_f … strain fixation
R_r … strain recovery
ε_f … fixed strain
ε_p … initial strain
ε_m … maximum strain

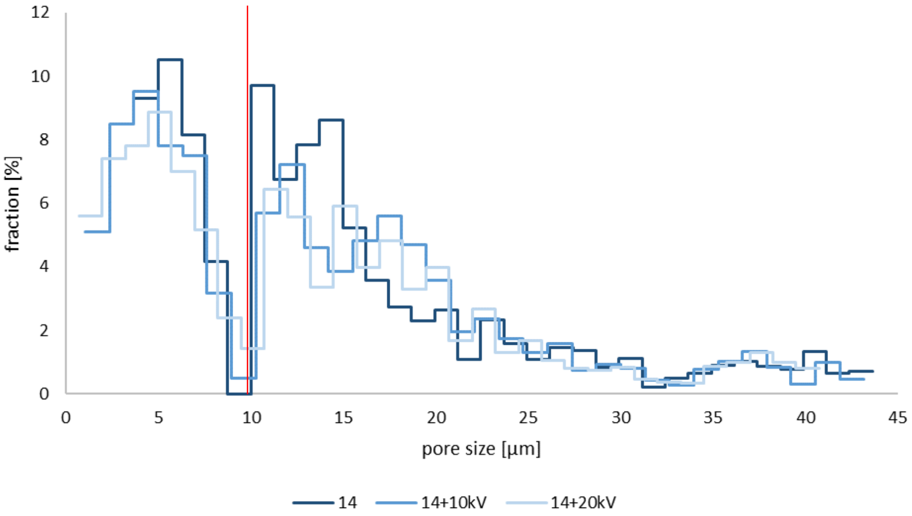
The generated force-elongation curves and the calculated characteristic values show, that both the spinning process and the PCL content have a considerable influence on the shape memory effect, in particular the force absorbed and the strain fixation (Fig. 3). Melt-spun yarns can achieve better strain fixation, but can absorb significantly reduced forces than wet-spun yarns. The addition of PCL can also improve the strain fixation behavior while reducing the force absorbed. Four elongation and contraction cycles were tested in which, with the exception of the first conditioning cycle, a perfect strain recovery of 100 % was achieved. No hysteresis of the shape memory behavior was observed over the testing period.



	Strain fixation R_f [%]		Strain recovery R_r [%]	
	1st cycle	subsequent cycles	1st cycle	subsequent cycles
TPU_SG	72,20	68,76	75,60	100,00
TPU_NG	62,05	58,20	86,17	100,00
TPU-PCL-2:1_NG	64,55	69,17	90,26	100,00

Figure 3: Force-elongation curves of the melt-spun (**A**) and wet-spun (**B**) TPU yarns and wet-spun TPU-PCL blends (**D**) and associated characteristic values (**C**)

For the development of textile cell support structures with integrated mechanical cell stimulation, plain weave fabrics with varying pore size were first generated by adjusting the warp and weft thread density. The developed piezoelectric PVDF yarns were used as weft yarns. For successful cell stimulation, micro-movements of the fabric fibers in frequencies of 1 – 3 Hz are necessary. This could be realized by integrating the woven fabrics into an alternating electric field. When applying voltages in the kilovolt range, currents of single-digit µA were measured. The in situ characterization of the pore sizes as a function of the applied electrical field was carried out with the aid of the capillary liquid porosimeter PSM165 (Topas GmbH, Germany) and a developed adapter for the integration of the measuring device into an electrical field. The obtained data (Fig. 4, here exemplary for a warp density of 14 yarns/cm) shows, that the pore size distribution changes in the electrical field. A pore size of 10 µm was defined as the threshold value for the visible effects, since this value forms the limit between the porosity of the multifilament yarn and the fabric itself. This is illustrated by the fact that no pores between ~8 µm and 10 µm were detected in the sample outside the electrical field. With increasing field strength, the percentage of pores < 10 µm increased significantly. This can only be attributed to the activated piezoelectric effect and the associated deformation of the PVDF yarn.



Pore fraction	14	14 + 10kV	14 + 20kV
below 10µm	32,13%	42,09%	45,66%
above 10µm	67,87%	57,91%	54,34%

Figure 4: Pore size distribution of the electroactive fabrics, here exemplary for a fabric with warp density 14 yarns/cm. The red line marks the self-defined threshold of 10 µm. The table shows pore fractions below and above this threshold as a function of the applied electrical field

Conclusion

In the IGF project 21022 BR/1 "TexMedActor", fabrics based on shape memory or electroactive yarns were developed which are capable of enclosing defects in hollow organs on the one hand and stimulating cells by micro-movements on the other. For this purpose, influences of spinning process and material composition on the shape memory behavior of TPU-based yarns were characterized and, in particular, the activation temperature was adjusted to values of the body core and body surface temperature. Furthermore, piezoelectric PVDF yarns were developed whose proportion of polar crystal phases was significantly increased by the spinning parameters and post-treatment, which also increased the piezoelectric behavior of the material. This allowed dynamic changes in pore size to be demonstrated in situ, which can have a stimulating effect on cells. With a new process and a new product group (textiles with intrinsic, active shape-changing capability), the results offer high innovation potential not only for medical devices, but also for a wide range of lucrative applications in a variety of niches, such as sports textiles and filter textiles. Furthermore, these can be used as a basis for the development of extracorporeal medical products such as compression textiles, bandages and orthoses.

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