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In vivo biocompatibility study of degradable homo- versus multiblock copolymers and their (micro)structure compared to an established biomaterial

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Abstract. Copolyetheresterurethane (PDC) is a biodegradable, shape-memory biomaterial, which has been shown to be of low toxicity and pro-angiogenic in vitro. In the present study we examined the in vivo compatibility of PDC as a compression molded film and as electrospun scaffolds and its well established constituent, the homopolymer poly(p-dioxanone) (PPDO), which were compared with the clinically used poly[(vinylidine fluoride)-co-hexafluoropropene] (PVDF) as reference material. The materials were implanted in the subcutaneous tissue of mice and the host responses were analyzed histologically 7 and 28 days after implantation.

All materials induced a foreign body response (FBR) including the induction of foreign body giant cells and a peripheral fibrous capsule. PDC, PPDO and PVDF films showed no signs of degradation after 28 days. PDC films showed a significantly reduced associated macrophage layer and fibrous capsule on their surface. Few fragments of PDC and PPDO scaffolds were present at the implantation site, while PVDF scaffolds were still present in large amounts at day 28. Especially aligned electrospun PDC scaffold induced a significantly thinner fibrous and a slightly reduced inflammatory response after 28 days of implantation. In addition, only PDC aligned fibrous scaffold structures induced a significant increase in angiogenesis.

In summary, PDC films outperformed PPDO and PVDF films in terms of compatibility, especially in capsule and macrophage layer thickness. Through microstructuring of PDC and PPDO into scaffolds an almost complete degradation was observed after 28 days, while their respective films remained almost unchanged. However, the capsule thickness of all scaffolds was comparable to the films after 28 days. Finally, the parallel arrangement of PDC fibers enabled a strong enhancement of angiogenesis within the scaffold. Hence, material chemistries influence overall compatibility in vivo, while angiogenesis could be influenced more strongly by microstructural parameters than chemical ones.

Keywords: Degradable polymer, electrospinning, scaffold, microstructure, in vivo compatibility, foreign body reaction, neovascularization, tissue integration, shape-memory polymer, homopolymer, copolymer

1. Introduction

A biomaterial-based device modulating tissue regeneration should temporarily, spatially and mechanically substitute damaged and lost tissue, fully degrade over time providing the in-growth of regenerating host tissue without a damaging foreign body reaction (FBR).

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The foreign body reaction is composed of five reaction phases, i.e. protein adsorption, acute inflammation, chronic inflammation, foreign body giant cell formation and fibrosis or fibrous capsule formation [1–3]. A challenge in the design of a biomaterial is keeping a balance between the foreign body reaction and inducing the growth of regenerating tissue to avoid pronounced scarring [4–6].

In recent years considerable efforts have been made to examine the influence of materials chemical structure and microstructure to promote tissue in-growth and reduce adverse implant encapsulation. Several studies showed promising effects of filamentous structures in tissue engineering and regenerative medicine applications [7–10]. Electrospun scaffolds, multifilaments [11, 12] or grafts [13] possess a high porosity and surface area to volume ratio favouring cell adhesion, infiltration [14–18] and angiogenesis [19]. In addition, fiber alignment was shown to affect cell morphology and differentiation [20–23]. One example was the regulation of the myogenic differentiation of myoblasts by the aligned orientation of PPDO fibers in electro spun scaffolds [24].

Copolyetheresterurethane (PDC) is a flexible biodegradable multiblock copolymer with shape-memory capability. The latter allows PDC to expand in a defined matter after being introduced into the body in a compressed form via minimal invasive surgery. PDC is composed of poly(ε-caprolactone) (PCL) and poly(p-dioxanone) (PPDO). It is supporting adhesion of endothelial cells and suppression of smooth muscle cell attachment in vitro; both as a flat film as well as electro spun scaffolds [25, 26]. In comparison, neither the degradable homopolymer PPDO, a constituent of PDC, nor poly[(vinylidene fluoride)-co-hexafluoropropene] (PVDF) intended for long-term implantation exhibited a comparable cell-selective adhesion. In addition, the tunable degradation rate, adjustable mechanical properties, shape-memory capability, low thrombogenicity [27] and pro-angiogenic properties [28] make PDC an interesting candidate as clinical option for blood-contacting applications such as e.g. synthetic vascular grafts or cell-selective stents.

The present in vivo study aimed at the exploration of the histocompatibility, degradability and tissue regeneration capability of PDC as a potential implant biomaterial. On this account, PDC, PPDO and PVDF scaffolds and films were implanted into murine subcutaneous tissue to analyze the progress of degradation, extent of foreign body reaction, tissue integration and regeneration.

2. Materials and methods

2.1. Polymers

A degradable shape-memory copolyetheresterurethane (PDC) was considered, which is composed of poly(ε-caprolactone)- (PCL) and poly(p-dioxanone)- (PPDO) segments that are connected via an aliphatic diurethane linker as junction unit [29]. Briefly described, for synthesis of PDC equal amounts of PCL-diol ($M_n = 2000$ g·mol$^{-1}$; Solvay Caprolactones, Warrington, U.K.) and PPDO-diol ($M_n = 5300$ g·mol$^{-1}$) as obtained by ring-opening polymerization [30] were dissolved in dimethylcarbonate (Acros Organics, Geel, Belgium) and reacted at 85°C with hexamethylene diisocyanate (>99%; Fluka, Buchs, Switzerland) for 48 hours. PDC with an average molecular weight $M_w$ of 75 kg·mol$^{-1}$ was obtained as determined by gel permeation chromatography (GPC). PPDO (Resomer X® with a $M_w$ of 100 kg·mol$^{-1}$ [31], Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany) and PVDF (Solef® 21216, with $M_w$ of 570–600 kg·mol$^{-1}$ [32], Solvay Solexis, Tavaux, France) were used as received. The chemical formula of the explored polymer materials is displayed in Scheme 1.

2.2. Production of polymeric films, random or aligned fibrous scaffolds

Films were produced from the melt by compression molding on a Collin P 200 E (Dr. Collin GmbH, Ebersberg, Germany) at 100 °C and 130 bar for PDC, 120°C and 50 bar for PPDO and 140 °C and
Scheme 1. Chemical structure of the polymers used for this study. (A) PDC, (B) PPDO, and (C) PVDF.

100 bar for PVDF. The obtained film thicknesses were 300 ± 50 μm (PDC), 100 ± 20 (PPDO) and 200 ± 30 for PVDF. Subsequently, disc-shaped films with a diameter of 13 mm were punched out.

Electrospinning of PDC and PPDO was conducted from a 1,1,1,3,3,3 hexafluoro-2-propanol (HFP) solution with a concentration of 11% (w/v) according to the method with the electrospinning setup described in [29]. PVDF was dissolved in a N,N-dimethylformamide/acetone mixture (3:1 v/v) with a concentration of 40% (w/v). The fibers were collected on a polypropylene foil fixed on a mandrel at different speeds. To collect random fibers a rotary mandrel velocity of 1 rpm (surface velocity: 0.005 m·sec⁻¹) was chosen, while aligned PDC fibers were collected at 2000 rpm (surface velocity: 10.5 m·sec⁻¹). The obtained electrospun scaffolds had thicknesses ranging from 250 μm to 300 μm.

### 2.3. Morphological and mechanical analysis of scaffolds

Fibrous PDC scaffolds were investigated by scanning electron microscopy (SEM). Prior to examination with the SEM (Gemini Supra 40 VP, Zeiss, Jena, Germany) the samples were sputtered with a thin conductive layer to improve the contrast. Fiber diameter and alignment were determined by the image processing software ImageJ (1.44; National Institutes of Health) [33] with an average of 10 measurements. Pore dimensions were determined by measuring the area in between embracing fibers of the in-focus plane from the top-view SEM images. By anticipating a spherical pore void model the apparent pore diameter was calculated. The air/water contact angle was assessed for PDC film as well as random and aligned scaffolds in a captive bubble experiment (DSA 100, Krüss GmbH, Hamburg, Germany). Before testing the samples were immersed in deionized water for 24 h. The mechanical properties of electrospun scaffolds and PDC film were examined by unidirectional tensile tests at ambient temperature utilizing a standard tensile tester (Zwick, Ulm, Germany). Scaffold test specimens were cut into rectangular stripes with the dimensions 40 × 10 × 0.1 mm³, while for PDC film standard test specimens of type DIN EN ISO 527 1BB (L₀ = 20 mm; b₁ = 2 mm) were applied.

### 2.4. Subcutaneous implantation of polymers

Animals used in this study were handled in accordance with institutional and federal animal care guidelines. The protocol was approved by the local Ethical Committee for Animal Experiments (reference number G0175/10). Eight to ten weeks old male C57Bl/6 mice (Charles River, Sulzfeld, Germany) were anaesthetized with isoflurane and surgical anesthesia was maintained by delivery of 1.5 vol% isoflurane through a vaporizer with 100% oxygen. Surgical procedures were performed under a Leica dissecting microscope (Leica Microsystems, Wetzlar, Germany) on a heated surgical pad. Seven mice were included per material and time point. An incision of 1.5 cm was made about 2 cm below the neck and a subcutaneous pocket of approximately 1 cm above the incision was prepared by blunt dissection to minimize the effect of wound healing on the FBR. PVDF, PPDO and PDC films (approx. 0.8 × 0.8 cm²) as well as PVDF, PPDO and PDC electrospun scaffolds with a random (ran) fiber orientation and
PDC scaffold with aligned (ali) fiber orientation were inserted into the subcutaneous pocket and the incision was closed with 6.0 Prolene sutures.

2.5. Histology, immunohistochemistry and image analysis

Seven or 28 days after implantation mice were anesthetized; implants with surrounding tissue were removed and fixed overnight with 4 vol% formalin/PBS-buffered. After embedding in paraffin, 3 μm-thick tissue sections were stained with Hematoxylin and Eosin (HE) or Masson’s trichrome (MT) according to standard procedures. Vascularization was evaluated by immunostaining with a rabbit polyclonal anti-CD31/PECAM-1 serum (Santa Cruz) followed by incubation with AlexaFluor488-labeled goat anti-rabbit secondary antibodies (Invitrogen, Darmstadt, Germany). Images of 200x fields acquired with a Zeiss Axioskop (Carl Zeiss Microscopy, Germany) microscope were analyzed by a blinded person using ImageJ (1.44; National Institutes of Health) software.

Capsule thickness was determined on both sides of the capsule (proximal and distal) at six different locations of the MT- and HE-stained tissue sections. Inflammatory cell numbers/FBGC and capillary density (CD31 positive structures) were analyzed in six to eight high-power fields (HPF) (40x) and were expressed as cell numbers per mm². All measurements were performed in six to eight sections (n = 4–7 for each material and time point).

2.6. Statistical analysis

Data were reported as arithmetic mean ± standard deviation, and were analyzed by two-tailed unpaired Student’s t-test. A p value of less than 0.05 was considered significant (*p < 0.05; **p < 0.01).

3. Results and discussion

3.1. Morphological and surface properties

PDC, PPDO and PVDF films with a smooth surface exhibiting low roughness profiles with a root-mean-squared roughness $R_q$ of 0.23 ± 0.02 μm were obtained by compression molding method as previously reported [26]. Porous (80 ± 10% porosity) scaffolds were produced with random and aligned fiber arrangement (PDCali) by electrospinning [25]. Representative SEM images obtained for the fibrous scaffolds are shown in Fig. 1.

Fiber diameters of the prepared scaffolds ranged from 4.0 ± 0.3 μm for PPDO scaffolds, 3.0 ± 1.0 μm (PVDF scaffolds) to 2.0 ± 0.04 μm for PDCran scaffolds, while PDCali scaffolds exhibited the smallest fiber diameter with 1.6 ± 0.5 μm. The apparent pore diameter, calculated by assuming a spherical pore geometry based on the determined areas between the fibers in the top view SEM images, was found to be around 10 ± 1 μm for all random scaffolds, whereas the parallel arranged fibers in PDCali scaffolds exhibited a lower apparent pore diameter of 7 ± 1 μm. The determined apparent pore diameters suggest that all scaffolds enable cell infiltration. The alignment of the fibers in the PDCali of the scaffolds showed was almost parallel with an alignment angle of 12 ± 10°. In contrast to the rigid films the fibrous constructs behave like a textile and can adapt to the tissue curvature of the implantation site. Tensile tests of films revealed a low Young’s modulus (E) in combination with a high deformability (elongation at break: $\varepsilon_b$) for PDC with $E = 20 ± 1$ MPa and $\varepsilon_b = 420 ± 30\%$, while $E = 170 ± 20$ MPa and $\varepsilon_b = 370 ± 90\%$ were found for PVDF and PPDO exhibited a Young’s modulus of $E = 230 ± 10$ MPa and $\varepsilon_b = 150 ± 30\%$ [26]. All prepared electrospun scaffolds showed increased E values (PDCran: 50 ± 10 MPa; PVDFran: 180 ± 30 MPa; PPDOran: 350 ± 30 MPa) and reduced
Fig. 1. Representative SEM images of electrospun scaffolds. PDC scaffolds with randomly (A) and parallel arranged fibers (B). PVDF scaffolds with random fibers prepared from PVDF (C) and PPDO (D), all scale bars = 10 μm.

deformability (PDCran: 210 ± 30%; PVDFran: 230 ± 30%; PPDOran: 130 ± 10%) when compared to their film counterparts [25]. These changes in the mechanical properties can be attributed to an increased degree in molecular orientation of the macromolecules in the electrospun microfibers. For PDC scaffolds with parallel arranged fibers a further increase in Young’s modulus to 190 ± 30 MPa and a decrease in εb to 150 ± 30% was observed, which can be related to a smaller fiber diameter and an additional straining of the fibers during the collection on the fast rotating mandrel. Figure 2 illustrates the difference in the stress-strain behavior obtained for PDC film and scaffolds.

PDC films showed an advancing contact angle of 63 ± 4°, which can be classified as hydrophilic as determined by contact angle measurements at the air/water interface utilizing the captive bubble method. While for PPDO and PVDF films more hydrophobic advancing contact angles of 74 ± 6° and 100 ± 3° were found [26]. Both PDC scaffolds exhibited lower apparent advancing contact angles of 56 ± 5° (PDCran) and 42 ± 5° (PDCali), whereby only a slight hysteresis <5° was observed between advancing and receding contact angle. Here, the mm-sized air bubble is probing both the scaffold fibers and water situated in between the fibers of the fully soaked scaffold and thus resulting in lower apparent contact angles.

3.2. Macroscopic evaluation of implantation sites and retrieved implants

3.2.1. Films

After 7 and 28 days, subcutaneously implanted polymeric films together with peri-implant tissue were removed. These time points were chosen because they most likely reflect the transition from the acute inflammatory response to the end stage foreign body reaction. Implantation sites of films did not show any macroscopic signs of inflammation, i.e. swelling, redness or heat, during the entire observation period in the live animals. After explantation, all films were only loosely attached to the
surrounding subcutaneous tissue without macroscopic signs of degradation, fragmentation or altered physical appearance after seven or 28 days.

3.2.2. Scaffolds

The implanted PDC scaffolds degraded over time (in 3 cases the scaffolds degraded completely after 28 days). After explantation, all scaffolds were only loosely attached to the surrounding subcutaneous tissue. No signs of inflammation around the scaffolds were visible. A more or less pronounced vascularization in and around the scaffolds had developed.

Within the study no adverse events that could point to implant rejection, infection or toxicity of the implanted material occurred. All retrieved implants showed no signs of necrosis, bleeding or chronic inflammation.

3.3. Histological signs of polymer degradation

Biodegradability of biomaterials has a high impact on foreign body reaction and tissue regeneration. Preferentially the degradation rate should match the rate of tissue regeneration and degradation products should be non-toxic and completely metabolizable [34]. In contrast to films, fibrous scaffolds are described with a differential degradation behavior depending on surface-volume ratio, crystallinity, porosity, fiber diameter and orientation [34].

3.3.1. Films

While PVDF is intended for long term implantation, PPDO and PDC are degradable materials. However, macroscopic and light microscopic examination revealed no obvious signs of degradation of the polymeric films after 28 days (Fig. 3).

3.3.2. Scaffolds

On the other hand, PPDO and PDC scaffolds showed considerable fragmentation after 7 days and were barely detectable after 28 days at the implantation site (in three cases no material at all could be found after 28 days) (Fig. 4A-C). The PVDFran scaffold fragments were still present in large amounts in the histological sections (black arrows) infiltrated by fewer macrophages and foreign body giant
Fig. 3. Histological appearance of polymer films at day 28 after implantation. A) PDC film. The not visible PDC film is surrounded by thin layer of macrophages (grey arrow) and a thin fibrous capsule (*). B) PPDO film. Remnants of the PPDO film are still present in the histological sections (black arrows). The implant is surrounded by a thin macrophage layer (grey arrow) and a thin fibrous capsule. C) PVDF film. The PVDF film is still present in the histological sections (black arrows). It is surrounded by a thin layer of macrophages (grey arrows) and a thin fibrous capsule (*). All section stained with H/E, all bars = 50 μm.

Fiber breaking has also previously been shown to occur for degradable polymers such as PGA, PLLA and PCL (for review see [34]).

A combination of two effects is responsible for degradation of Poly(α-hydroxy acids), hydrolytic degradation under aqueous conditions and enzymatic degradation in *in vivo* conditions. For scaffolds especially, the enzymatic degradation effect is strongly enhanced due to the much larger surface compared to the respective films, which might explain the strongly altered scaffold structure after 28 days [29].

### 3.4. Foreign body reaction against film and scaffold polymers

In order to analyze the inflammatory response, inflammatory cells, namely fibrocytes and general leukocytic infiltration around the implants were quantified.

#### 3.4.1. Films

Capsule infiltration with inflammatory cells was similar for all tested polymer films at both investigated time points and showed no significant changes during the time of observation (Fig. 5A).
Fig. 4. Histological appearance of polymer scaffolds at day 28 after implantation. A) PDC aligned fiber scaffold (PDCali). Remnants of the PDCali are visible as grayish material or empty intra-lesion spaces (black arrows). The site of implantation is infiltrated by numerous leukocytes and foreign body giant cell (grey arrows). There is a thin fibrous capsule (*) around the infiltrated implantation site. B) PDC random fiber scaffold (PDCran). Areas with homogeneous light eosinophilic material are suspicious for remnants of the PDCran (black arrows). The site of implantation is infiltrated by numerous leukocytes and foreign body giant cells (grey arrows). There is a thin fibrous capsule (*) around the infiltrated implantation site. C) PPDO random fiber scaffold (PPDOran). Remnants of the PPDOran are still present as grayish material or empty spaces in the histological sections (black arrows). The site of implantation is infiltrated by numerous leukocytes and foreign body giant cells (grey arrows). There is a thin fibrous capsule (*) around the infiltrated implantation site. D) PVDF random fiber scaffold (PVDFran). PVDFran scaffold fragments are still present in large amounts in the histological sections (black arrows). They are infiltrated by fewer macrophages and foreign body giant cells (grey arrows) and a thin outer fibrous capsule (*). All section stained with H/E, all bars = 50 μm.

The thickness of the macrophage layer on the polymeric films was measured 7 and 28 days after implantation. After 7 days huge variations of the size of the cellular layer within groups became evident. Although not statistically significant, PDC showed the smallest macrophage layer after 7 days (Fig. 5B). Layer thickness decreased for PDC and PPDO films between days 7 and 28 with a significantly lower layer thickness for PDC compared to PVDF and PPDO films (Fig. 5B).
Fig. 5. Inflammatory response to different polymeric films 7 or 28 days after subcutaneous implantation. (A) Polymer films. General leukocyte/fibrocyte density in the peri-implant fibrous tissue at days 7 and 28. (B) Polymer films. Leukocyte layer on film surface at days 7 and 28. (C) Polymer scaffolds. General leukocyte/fibrocyte density in the peri-implant fibrous tissue at days 7 and 28. (D) Polymer scaffolds. Density of infiltrated leukocytes in the scaffold material. Data represent means ± SEM (n = 3–7 per group are shown). ¶p < 0.1; ∗∗p < 0.05; **p < 0.01.

3.4.2. Scaffolds

Similar to films, scaffolds with random fiber orientation showed no significant differences in the number of inflammatory cells in the capsule surrounding after 7 days (Fig. 5C). Notably, inflammatory cell density of the capsule after 7 days tended to be higher in PDCali scaffolds compared to PVDFran, PPDOran and PDCran (Fig. 5C). However, PDCali displayed a drastic decline in inflammatory cell density leading to the lowest leukocyte/fibrocyte density in the capsule of all tested materials after 28 days. In contrast to polymer films, all polymer scaffolds showed a leukocyte infiltration into the implanted material. The density of leukocytes/fibrocytes in the implants showed considerable differences between tested materials after 7 days, with PPDOran showing the lowest inflammatory cell density. PDCali was the only material that showed a significant decline of inflammatory cell density within the observation period of 28 days (Fig. 5D).
Foreign body giant cells (FBGC) were not a feature of the immune reaction against any of the polymer films. Only around one PVDF film very few FBGC were observed. In contrast, all scaffolds elicited a foreign body reaction response that was characterized by moderate to severe formation of FBGC without any clear differences between the different scaffolds.

3.5. Peri-implant fibrous capsule formation

The capsule thickness was measured 7 and 28 days after implantation for all materials (Fig. 6A-C).

3.5.1. Films

At day 7, the fibrous capsule around polymer films, if present, were in general thin and mostly infiltrated by varying amounts of diverse inflammatory cells without significant differences in capsule thickness among PVDF, PPDO and PDC films (Fig. 6A). This is most likely due to the mechanical
pressure applied subcutaneously that squeezes the scaffold. Between days 7 and 28 capsule thicknesses significantly increased for PVDF films, while capsules around PPDO and PDC films did not significantly change in their thickness over time (Fig. 6A). The expansion of the fibrous capsules might presumably be a consequence of the infiltration and proliferation of invading cells as well as a production of ECM. However, at day 28, the capsule around PDC films was significantly thinner than around PVDF and PPDO films (Fig. 6A).

3.5.2. Scaffolds

Capsules around PVDF and PPDO scaffolds were stable between days 7 and 28. In contrast, capsules around PDCran and PDCali scaffolds were significantly decreasing in thickness between days 7 and 28 (Fig. 6B). After 28 days, both PDC scaffolds exhibited a significantly thinner capsule than PVDFran and PPDOran scaffolds. Of note, PDCali, with aligned fiber orientation, displayed a lower capsule thickness than the PDCran, with random fiber alignment (Fig. 6B). Interestingly, capsule thickness after 28 days showed no significant differences between identical materials in form of films and scaffolds (Fig. 6C).

3.6. Angiogenesis

A prerequisite for material-tissue integration and tissue regeneration is the vascularization of implants that allows for deep cell in-growth.

3.6.1. Films

No vascularization was detectable within the solid polymeric films at the 7th and 28th days post implantation. However, vessel formation was detectable in the peri-implantary tissue of all films. The vascularization of tissue surrounding PPDO and PDC films was slightly higher than around PVDF films after 7 days without reaching statistical significance. After 28 days post implantation vessel density was similar between all films.

These results are in agreement with earlier studies, in which an angiogenic potential of PDC films (having a PPDO content of 33 wt% and linked with a mixture of 2,2,4- and 2,4,4-isomers of Trimethyl-1,6-diisocyanatohexane) was shown in vivo. Here, a PDC induced formation of blood microvessels in the peri-implantary tissue and newly grown vessels in a hen’s egg chorioallantoic membrane test were reported [28, 35].

3.6.2. Scaffolds

After seven days PVDFran and PDCran scaffolds showed moderate vessel formation, while there were no vessels visible in PPDOran and PDCali scaffolds (Fig. 7C). After 28 days vascularization was clearly visible even under low magnification conditions in PDCali scaffolds with an aligned fiber orientation (Fig. 7A right panel) but not in PDCran scaffolds with random fiber orientation (Fig. 7A left panel). All other tested scaffolds did not show newly formed vessels reaching into the implant. Quantification of newly formed vessels using immunofluorescence staining showed significantly elevated CD31 positive cells density in PDCali implants (Fig. 7C right panel) compared to PDCran implants (Fig. 7C left panel). In summary, all tested fibrous scaffolds showed considerable cell in-growth however, only aligned PDC fibers elicited vascularization providing an appropriate microenvironment for complete tissue regeneration. These results are in line with a study showing that aligned electrospun fibers may serve as a promising structural cue to guide the in-growth and direction of newly formed blood vessels to minimize host response, enhance tissue-scaffold integration, and elicit a thinner fibrous capsule [7].
Especially PDC scaffolds tended to an attenuated inflammatory response in the period of observation in terms of a decreased capsule thickness and decline of inflammatory cells infiltration in the scaffold. Interestingly we observed rather subtle differences concerning the foreign body reaction among different nanofibrous materials but significant differences due to fiber orientation.
4. Conclusion

A degradable multiblock copolymer termed PDC, a homopolymer and constituent of PDC termed PPDO and an established biomaterial termed PVDF were evaluated as flat films as well as fibrous scaffolds subcutaneously in mice with respect to their histocompatibility in vivo. PDC films outperformed PPDO and PVDF films in terms of histocompatibility, especially in capsule thickness and number of infiltrated macrophages. Hence, a copolymer can be tuned not only in its rate of degradation, but also in its compatibility towards the host. In addition, comparing films with a more natural fibrous scaffold microstructure, a significant morphological change was observed as PDC and PPDO scaffolds were almost fully degraded as opposed to the PDC and PPDO films, which remained mainly intact. On a macroscopic view, however, almost no change between films and scaffolds could be determined according to the capsule thickness after 28 days. Interestingly, a strong reduction in capsule thickness was found in PDC scaffolds from day 7 to day 28, which was not the case for PDC films in the same time period. Finally, the comparison of randomly oriented and aligned fibrous PDC scaffolds revealed a strong angiogenesis within the aligned PDC fiber scaffold, while almost no new vessels formed within the randomly oriented PDC fiber scaffold. In conclusion, the material chemistry has a strong influence on the overall histocompatibility under in vivo conditions, while microstructural parameters seem to have a more prominent influence on the vessel in-growth. The results obtained in this study suggest PDC scaffolds with parallel-arranged fibers as promising multifunctional biomaterial candidate for regenerative medicine applications.

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In vitro


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