Paclitaxel-Eluting Biodegradable Synthetic Vascular Prostheses
A Step Towards Reduction of Neointima Formation?

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Background—Clinical small-caliber vascular prostheses are unsatisfactory. Reasons for failure are early thrombosis and late intimal hyperplasia. We thus prepared biodegradable small-caliber vascular prostheses using electrospun polycaprolactone (PCL) with slow-releasing paclitaxel (PTX), an antiproliferative drug.

Methods and Results—PCL solutions containing PTX were used to prepare nonwoven nanofibre-based 2-mm ID prostheses. Mechanical morphological properties and drug loading, distribution, and release were studied in vitro. Infrarenal abdominal aortic replacement was carried out with nondrug-loaded and drug-loaded prostheses in 18 rats and followed for 6 months. Patency, stenosis, tissue reaction, and drug effect on endothelialization, vascular remodeling, and neointima formation were studied in vivo. In vitro prostheses showed controlled morphology mimicking extracellular matrix with mechanical properties similar to those of native vessels. PTX-loaded grafts with suitable mechanical properties and controlled drug-release were obtained by factorial design. In vivo, both groups showed 100% patency, no stenosis, and no aneurysmal dilatation. Endothelial coverage and cell ingrowth were significantly reduced at 3 weeks and delayed at 12 and 24 weeks in PTX grafts, but as envisioned, neointima formation was significantly reduced in these grafts at 12 weeks and delayed at 6 months.

Conclusions—Biodegradable, electrospun, nanofibre, polycaprolactone prostheses are promising because in vitro they maintain their mechanical properties (regardless of PTX loading), and in vivo show good patency, reendothelialize, and remodel with autologous cells. PTX loading delays endothelialization and cellular ingrowth. Conversely, it reduces neointima formation until the end point of our study and thus may be an interesting option for small caliber vascular grafts. (Circulation. 2009;120[suppl 1]:S37–S45.)

Key Words: coronary disease ■ endothelium ■ intimal hyperplasia ■ paclitaxel elution ■ vascular prostheses

Cardiovascular diseases are one of the major causes of death, and an increasing number of revascularization procedures are required, partly because of aging of the population.1 Up to now, blood vessels are replaced either by autologous veins or arteries or by biostable synthetic vascular grafts such as expanded polytetrafluoroethylene (e-PTFE) and polyethylene terephthalate (Dacron). These synthetic grafts show very good properties to replace large diameter vessels, but they lead to specific problems for small diameters (<6 mm) such as coronary artery bypass grafts.2 In particular, they are prone to acute thrombosis when associated with reduced flow, which can lead to graft occlusion with fatal clinical outcome. Furthermore, their inadequate mechanical properties (compliance mismatch) and lack of biocompatibility (no endothelium) are responsible for the appearance of intimal hyperplasia, leading to a thickening of the arterial wall, mainly at the anastomoses, and a narrowing of the lumen.3 It is therefore clear that novel small-diameter vascular grafts with an acceptable clinical outcome are needed.

We recently proposed an optimized small-diameter degradable vascular graft based on poly(e-caprolactone) (PCL) nano- and microfibres suitable for in vivo vascular regeneration.4,5 Using the advantages of the electrospinning technique, which allows the preparation of extracellular matrix-like scaffolds, the slow degradation rate of PCL, and its better mechanical properties compared to other described synthetic
or natural polymers, we showed that the PCL grafts were successful as abdominal aorta replacements in rats up to 6 months. They were fully patent at 24 weeks with no thrombosis, stenosis, or aneurysmal dilatation, and histological analyses revealed a homogeneous cellular infiltration associated with polymer degradation and extracellular matrix formation, as well as a rapid and complete endothelialization, though some neointima formation was observed. Nevertheless, this was significantly less pronounced than for ePTFE grafts. Yet it would be interesting to minimize neointima formation applying similar drug-eluting PCL grafts, which deliver an antiproliferative drug in situ.

Recently, stents coated with slow-releasing paclitaxel (PTX) have been used successfully in the experimental model and in patients to reduce in-stent restenosis by inhibiting the cellular proliferation attributable to high local drug concentration with minimal systemic side effects. Drug incorporation in fibers using standard or coaxial electrosprinning of drug-loaded solutions have been described for various compounds and is promising for controlled drug delivery applications related to tissue engineering. Some groups prepared PTX-eluting fibers for biomedical applications based on PLA or PLGA. However, recent reports have shown that these polymers do not possess the adequate mechanical properties to be used as vascular grafts in the systemic circulation. Hence, our aim was to prepare and assess in vitro and in vivo, a PTX-eluting biodegradable vascular graft, which would combine the positive findings of our previously described PCL grafts with the ability of the drug to prevent intimal hyperplasia formation.

Materials and Methods

In Vitro Studies
Preparation of Unloaded and PTX-Loaded Vascular Grafts by Electrospinning
Preparation of 2-mm inner diameter PCL grafts after an optimization process by a factorial design approach and the in vitro and in vivo assessments have been reported in detail elsewhere. In a similar factorial design approach, various optimized PTX-loaded vascular grafts (PCL-PTX) were prepared, and the effect of different PTX concentrations on fiber morphology, graft tensile stress, and strain behaviors were investigated. The PTX-loaded vascular grafts were prepared like the nonloaded controls by electrospinning of PCL solutions (7.5, 9 and 12% [wt/vol]) containing different amounts of PTX (0.25, 0.5, 0.75 and 1% [wt/wt]). The generated fibers were collected on a rotating (4500 rpm) and translating (200 rpm, 4-cm amplitude) mandrel to form a nonwoven tubular PCL graft. The grafts were dried at 37°C under vacuum overnight. Residual solvents were analyzed with a Headspace Sampler (HP7694, Hewlett-Packard) coupled to a gas-chromatography system (GC System, 6850 Series, Agilent Technologies) equipped with an HP-1 capillary column (Agilent Technologies). All vascular grafts were γ-sterilized at 25 kGy before characterization and in vivo use.

Assessment of PTX Loading and Distribution in the Vascular Graft
The extent of drug loading and the incorporation efficiency were assessed by high performance liquid chromatography (HPLC) analysis on 2.5-cm long PTX-loaded vascular grafts with theoretical loadings of 0.25%, 0.5%, 0.75%, and 1% (wt/wt). Additionally, the homogeneity of PTX distribution along the vascular grafts (n=3) was verified by cutting 4 1-cm-long pieces from a 4-cm PTX-loaded graft, theoretically loaded with 0.5% and 0.75% (wt/wt).

PTX Release Studies In Vitro
Vascular grafts theoretically loaded with 0.5%, 0.75%, and 1% of PTX (n=3 each for graft type) were placed in vials with a measured amount of release medium of phosphate buffered saline (pH=7.4) containing 0.05% (vol/vol) Tween 20. The vials were kept at 37°C with rotational mixing at 100 rpm for 1, 5, and 16 hours and 1, 6, 8, 12, 14, 16, 20, and 27 days. At each time point, 1-mL aliquots of the release medium were taken for PTX quantification. The remaining release medium was aspirated and fresh release medium was added between each time point to maintain sink conditions.

Mechanical and Morphological Properties Evaluations
Fiber diameter and morphology of the grafts were investigated using a scanning-electron microscope (SEM; JEOL JSM-6400, Jeol Ltd). Tensile stress and strain were measured on complete vascular grafts using a mechanical testing bench from Schenck AG (Nänikon, Switzerland) with a cross-head speed of 10 mm/min at room temperature.

In Vivo Studies
The PCL-PTX graft chosen for in vivo evaluation was made from a 12% w/v PCL solution with PTX drug-loading of 0.75% because it showed similar fiber morphology and mechanical properties to plain PCL grafts used previously.

Experimental Rat Model
Our experimental rat model, including anesthesia, surgery, and the follow-up protocols for digital subtraction angiography (DSA) imaging and sampling of the vascular graft, was described in details previously. Briefly, 18 male Sprague-Dawley rats (375 g) were anesthetized and operated according to this protocol (Janvier S.A.S., Le Genest-St-Isle, France). PCL (n=9) and PCL-PTX (n=9) grafts were implanted randomly into the abdominal aorta of the rats and follow-up times were 3, 12, and 24 weeks (n=3 for each time point in each group). No anticoagulation or antiplatelet drugs were given. At the conclusion of the study period, DSA images were obtained after blood sampling for PTX blood levels, and rats were euthanized after explantation of the vascular graft with the adjacent abdominal aorta segments. The experimental protocol has been approved by the Animal Experiments Ethical Committee of the University of Geneva (Protocol No. 06/52) and the Veterinary Office of State of Geneva, Switzerland (No. 1081/3232/11), and carried out in conformity with the Guide for Care and Use of the Laboratory Animals (National Research Council, Washington, DC: National Academy Press; 1996).

Histological Assessment and Morphometric Analysis
For histological investigations, explanted grafts with both anastomoses were fixed in 4% formaldehyde for 24 hours, cut into 2 longitudinal halves, and then embedded into paraffin. Histological sections of 4 μm were stained with Hematoxylin-Eosin (H&E) for cellular ingrowth, neointima formation, and tissue reaction, Miller and Masson for elastin fibers and collagen deposition, and immunohistochemistry with an anti-CD31 antibody (Santa Cruz Biotechnology, Inc. PECAM-1 [M-20]) for endothelial cells and neangiogenesis. Histological slides were also analyzed quantitatively by computed histomorphometry using a Leitz Medilux (Leica) motorized microscope, a Sony 3CCD color-video camera, and the software Leica Q-win standard version Y2.3 for image analysis. “Endothelial coverage” was defined as the length of endothelial cell layer on the luminal surface and expressed as the percentage of total graft length. “Neointima formation” was defined as the area between the endothelial layer and luminal surface of the prosthesis and calculated per unit length of graft (mm/mm) and per unit length of neointima (mm/mm) reflecting the mean thickness of neointima. “Transmural cellular ingrowth” was defined as the percentage of graft area which was penetrated densely by host cells from the adventitial tissue toward luminal surface. Additionally, SEM pictures were taken at 5 different locations with 3 different magnifications to assess the luminal surface and endothelial coverage.
At the conclusion of the study, a blood sample was taken from each rat to assess the systemic PTX concentration. After sample treatment of the serum by an online column switching technique, PTX was quantified by HPLC with UV detection at 205 nm with a lowest detection limit of 500 ng/mL.

Statistical Analysis
Statistical tests were performed using SPSS (version 16.0). Results for continuous variables are expressed either as mean±SD for in vitro results (Table and Figures 1 and 2) or, as mean±SEM for in vivo results (all other figures). Mann–Whitney U test was used to compare nonparametric values at each time point, as well as comparison between time points in the same group. At each time point and in each group, the sample size is 3 for the in vivo part. The level of significance was set at \( P<0.05 \).

Statement of Responsibility
The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

Results

In Vitro Studies

Mechanical Properties and Fiber Morphology
A complete mechanical and morphological study of the PCL-PTX compared to the nonloaded grafts was carried out. These results will not be presented in detail because they are beyond the scope of this article. Briefly, for the same PCL concentration, PTX-loaded grafts have higher maximal stress and strain values than nonloaded grafts, and PTX-loading had the same effect as a PCL concentration increase. In terms of morphology, fewer beads and larger fibers were found at higher PCL concentrations. Fiber diameters were 500±210 nm, 640±540 nm, and 1640±1000 nm for nonloaded grafts obtained with PCL concentrations of 7.5, 9, and 12% (wt/vol), respectively. When PTX was added into the PCL...

![Figure 2. In vitro drug release profiles of PTX from PCL vascular grafts containing 0.5, 0.75, and 1% (wt/wt) PTX over 27 days in PBS pH 7.4-Tween 20 at 37°C. Data are expressed as an average of results obtained from 3 grafts at each time point (mean values±SD, n=3).](image)

![Figure 3. Histological analysis of PCL (A and B) and PCL-PTX (C and D) grafts at 3 weeks. A, Full thickness of PCL graft showing cellular infiltration of the external part (H&E, ×100 magnification). B, Endothelialization on the luminal side of a PCL graft (H&E, ×400 magnification). C, Full thickness of a PCL-PTX graft with no cellular ingrowth (H&E, ×100 magnification). D, No endothelial cell coverage on the luminal side of PCL-PTX graft (H&E, ×400 magnification).](images)
solutions, the beads disappeared and the fibers became 80% larger at PCL concentrations of 7.5 and 9%, whereas no significant differences in beads and/or fibers were observed at 12%.

Evaluation of PTX-Loading and Incorporation Efficiency
Studies have been carried out to analyze the extent of the PTX loading into the vascular grafts. PCL-PTX graft loading in the range from 0.2% to 1% (wt/wt) have been prepared successfully, with a high incorporation efficiency of 80% to 100% representing 50 to 200 μg PTX respectively for 2.5-cm long grafts (Figure 1). PTX distribution was homogeneous along the grafts, with no significant difference in the amount of drugs recovered from different parts of the grafts (Table). Therefore, the final product chosen for rat implantation had comparable PTX amount as reported for the Taxus and Express stents, which contain 151 μg of PTX per 2.4 cm stent length (http://www.fda.gov).

In Vitro PTX Release Profile
The results of PTX release from the electrospun vascular grafts in vitro are summarized in Figure 2. All PCL-PTX vascular grafts with 3 different PTX concentrations demonstrated triphasic release profiles which is typical for a degradable polymer. The 3 phases correspond to (1) an “initial slight burst release” of around 20% of the incorporated PTX within hours, (2) followed by a “slower, sustained release” by a drug diffusion controlled process over the following 22 days, and which led to the cumulative release of around 20% to 30% after 6 days, and between 45% to 60% after 22 days, and (3) a “final plateau phase” with a much slower release, which may be governed by the release of the remaining PTX from slow degrading of PCL fibers or by a high interaction between drug and polymer.

In Vivo Studies
Experimental Rat Model
PCL and PCL-PTX grafts were easily implanted into the rats using standard microsurgical techniques. No significant bleeding was observed in either group. All animals survived until the end of follow-up, and all grafts were patent in both groups. DSA revealed no significant stenosis, nor aneurysm formation in either group.

Histological Evaluation of PCL and PCL-PTX Grafts
PCL and PCL-PTX grafts were analyzed at all time points. Major differences were found between these 2 groups at 3 weeks. Firstly, PCL grafts were infiltrated from the adventitial side by fibroblasts, macrophages, and giant cells (Figure 3A) and showed an endothelialization with CD31-positive endothelial cells (data not shown) starting from both anastomoses (Figure 3B). On the contrary, PCL-PTX grafts had no cellular infiltration (Figure 3C) and no endothelial coverage on the luminal side (Figure 3D). At 12 weeks, PCL-PTX grafts showed cellular infiltration and CD31-positive endothelial coverage (Figure 4D and 4E; see inset) similar to PCL grafts (Figure 4A and 4B). Neointima formation was minimal including 2 or 3 spindle-shaped cell layers in the PCL-PTX grafts without any elastin fibers (Figure 4F). Neointima was composed of 6 to 10 spindle-shaped cell layers with homogenous elastin fiber deposition (Figure 4C) in the PCL group.

At 24 weeks, confluent endothelial coverage was found in both groups (by morphometry and SEM). No differences in cellular infiltration were observed in either group (Figure 5A and 5B). Neangiogenesis was present in both groups (Figure 5C and 5F). Neointima formation was different, with more cell layers and some elastin fibers in the PCL group compared to the PCL-PTX group. We observed comparable amount of
collagen deposition within the graft in both groups, as demonstrated by Miller and Masson staining (Figure 5B and 5E). As previously reported for PCL vascular grafts, we observed chondroid metaplasia in both groups at 12 weeks within the neointima, but this was less important in the PCL-PTX group than the PCL group. In both groups, this disappeared almost completely at 24 weeks, leaving some neointima calcification (data not shown).

**Morphometric Analysis**

Quantitative morphometric comparison between the PCL and the PCL-PTX groups over time (3, 12, and 24 weeks) demonstrated a significantly delayed endothelialization in PCL-PTX grafts compared to the PCL grafts. However, at 24 weeks, 99% of the PCL-PTX grafts were covered by the endothelium (Figure 6A). Cellular infiltration was also reduced significantly at 3 weeks in the PCL-PTX grafts; additionally 37% and 35% of these grafts were infiltrated at 12 and 24 weeks, respectively. Despite the lack of statistical significance, the cellular infiltration of PCL-PTX grafts was less than that of PCL grafts at all time points (Figure 6B). Neointima formation was negligible in both groups at 3 weeks and showed a significant increase at 12 and 24 weeks in the PCL group, but remaining stable and significantly lower in the PCL-PTX group. Additionally, the area and mean thickness of neointima formation was reduced by more than half in the PCL-PTX grafts at 12 and 24 weeks when compared to PCL group (Figure 7A and 7B).

**Paclitaxel Blood Levels**

None of the samples collected at the conclusion of the study showed a detectable PTX concentration, indicating a subclinical level of PTX in the systemic circulation (<500 ng/mL).

**Discussion**

Although intensive research has been initiated in recent years toward the preparation of small-diameter vascular grafts suitable for clinical use, none of this has led to a functional candidate yet. Among the various causes responsible for failure, thrombosis, aneurysms, and intimal hyperplasia are leading. As a consequence, it would be of great interest to dispose of novel vascular grafts having both very good mechanical properties and a nonproliferative therapeutic effect. Our approach aimed at preparing biodegradable PTX-eluting small-diameter vascular grafts made of PCL for clinical applications. In fact, PTX is a well-known mitotic inhibitor used in cancer chemotherapy, but it is also used in some cardiovascular applications, like coronary stents, to prevent restenosis by limiting the growth of neointima. Its mechanism of action is related to the hyper-stabilization of microtubules through its binding with the β-subunit of tubulin, which results in a blocked mitotic cycle at the G2/M stage. Beside this antiproliferative effect, the stability of PTX during the electrospinning process, its solubility in the solvents used with PCL and its resistance to γ-sterilization render it a valuable candidate for the formulation of novel vascular grafts.

However, one has to keep in mind that inclusion of drugs into nano- or microfibre polymers does influence their basic properties, both mechanically and morphologically. In addition, it has been demonstrated that the drug release from such fibers is strongly dependent on the nature of the incorporated drug. Because intimal hyperplasia tends to appear within the first months after implantation, it is of importance to have a slow and controlled release of PTX over this period of time, to ensure an adequate antiproliferative effect and to avoid a burst release of massive doses of PTX, which could result in an acute cytotoxicity for the surrounding tissues. Therefore, the influence of various PTX loadings into PCL vascular grafts was investigated in the present study, first in vitro for fiber morphology, mechanical properties, drug distribution, and drug release profiles; second, for in vivo effects of
time-released PTX from the grafts implanted in the rat abdominal aorta.

The results obtained from PCL-PTX grafts are consistent with our previous study on nonloaded PCL grafts. Tensile stress values of PCL grafts were increasing with PCL concentration up to 12% (wt/vol), which corresponded to a maximum of 5 MPa, and decreased with further PCL concentration increase. In this study, drug loading might have the same effect as an increase of the PCL concentration leading to better mechanical properties observed for electrospun grafts from low PCL concentrations. The factorial design process led to the preparation of an optimized vascular graft spun from a 9% PCL solution containing 0.5% of PTX. It should be noted that the tensile stress values of the drug-loaded grafts after γ-sterilization were always above 2 MPa, which is the maximum stress value for the natural vessels of rats and pigs and is considered as a lower limit value for implanted synthetic grafts into the systemic circulation.

Along with the incorporation of PTX, an increase of the fiber diameters of 80% was observed, which led to higher tensile stress values of drug-loaded vascular grafts in comparison to the nonloaded ones.

PTX incorporation efficiency into the nanofibres was high (80% to 100%) and homogeneous along the graft. This is very important for a controlled drug release. As outlined above, optimized grafts with a PTX concentration as described for Taxus and Express stents were prepared and could be implanted successfully. PTX in vitro release was controlled over a time period of 30 days with only a little burst at the initial phase, and 60% of PTX was released over 22 days. It is assumed that the remaining PTX would be released in small concentrations along with time-dependent degradation of the PCL fibers. Previous human studies involving Taxus and Express stents demonstrated that low-dose PTX release over several days was efficacious, and completion of release was expected at 6 months. The results from our PTX-eluting PCL vascular grafts are promising, and may provide a step toward reduction of intimal hyperplasia in small-diameter grafts.

We preferred to use PTX as a suitable drug, for its known potent antiproliferative effect on the neointima formation, and its continuous local release from the graft. The analysis of blood samples confirmed that concentration of the antimitotic drug was below the detection limit in the systemic circulation, which may not be sufficient to create toxic side effects.

Figure 6. Morphometric cellular repopulation of PCL and PCL-PTX grafts. A, Percentage of endothelial coverage at 3, 12, and 24 weeks. Note the absence of endothelial cells in PCL-PTX grafts at 3 weeks, and note the significant increase in endothelialization for both the PCL and PCL-PTX grafts between 3, 12, and 24 weeks, respectively. B, Percentage of transmural cellular ingrowth at 3, 12, and 24 weeks. Note that the ingrowth is delayed in the PCL-PTX grafts.
Nevertheless, the biological effect of PTX is well demonstrated histologically and leads to significant alterations mainly at the 3- and 12-week follow-up. The delayed endothelial coverage may represent a problem for early thrombogenicity. Virmani’s group has shown similar results in drug-eluting stents implanted in a rabbit model. Additionally, several well-documented clinical reports attribute the occurrence of coronary thrombosis after drug-eluting stent placement to the lack or incomplete endothelial coverage. Finally, using a similar model in the rat, we have previously observed enhanced thrombus formation in synthetic vascular grafts treated by systemic or local administration of rapamycin. However, in the present study, no occlusions were found, probably because of the high flow in the rat abdominal aorta. At 24 weeks, the endothelialization was nearly complete, indicative of a delay only in the PCL-PTX grafts. Simultaneously, the cellular ingrowth of the biodegradable prosthesis was also delayed, which may eventually delay the regeneration of an autologous arterial wall. This delay should not create any problems for the biomechanical properties of the graft during the vascular remodeling because PCL has a relatively slow degradation rate. Up to 6 months after implantation, no aneurysm formation was observed in our series. However, this hypothesis should be confirmed by other in vivo studies with longer follow-up.

Neointima formation, which normally progresses to intimal hyperplasia, and eventually stenosis and occlusion, is a major problem in small-diameter vascular grafts. Many attempts by several authors have been made to reduce intimal hyperplasia, such as the topical use of drug-releasing gel, including antimitotic drugs around the anastomosis, showing a reduction of intimal hyperplasia at the anastomosis with this method; however the method was relatively cumbersome, and drug release was not well controlled. In our PCL-PTX
grafts, a linear PTX release in vitro was observed over the first month. This in vitro drug release matches well the histological and morphological findings of neointima formation in vivo, which was significantly reduced after 12 weeks, compared to the control PCL grafts. This trend in histology and morphology extends to 24 weeks. Comparing the results of the present study with our previously published study in Circulation, which assessed PCL versus the classical ePTFE grafts, PCL-PTX grafts showed a delayed endothelialization similar to ePTFE grafts, but a significantly reduced neointima formation within the first 24 weeks when compared to ePTFE grafts.5

For the above described positive effect of the PTX-loaded grafts, further studies with longer assessment periods are needed because we have to follow the biological effect of the drug release and its consequences up to 1 or more years to exclude a “late catch-up phenomenon” as described for drug-eluting stents.23,24 Furthermore, the delayed endothelialization of the small-diameter drug-eluting PCL grafts may cause thrombosis and occlusions in low-flow conditions.

Currently, a direct application of these results is not yet possible for coronary bypass grafting in humans. First, longer follow-up studies have to evaluate complete degradation of the polymer scaffold, and second, a more relevant small caliber graft model has to be assessed in a larger animal.

Conclusions

Excessive growth of neointima in vascular grafts leads to graft failure in the long-term. This is even more pronounced in small-diameter grafts, such as coronary bypass grafts. Local delivery of PTX in the coronary arteries by drug-eluting stents has been shown to limit the growth of neointima, providing improved patency rates in the short-term. However, a “late catch-up phenomenon” has been described for such stents. PTX-loaded biodegradable vascular grafts may delay the excessive neointima formation in the grafts, whereas the scaffold degradation and an arterial regeneration process take place. Although topical application of antiproliferative drugs around vascular anastomoses have been reported with promising in vivo results, the use of a drug-eluting vascular graft has not yet been reported.

After our first report on biodegradable vascular prostheses in the arterial circulation, our present study is another step forward in this field. We first produced a PTX-loaded PCL vascular graft after a factorial design optimization process and performed in vitro tests to assess the mechanical and morphological properties of the graft after drug loading, the drug distribution in the graft body, and the early release from the graft. Our in vitro studies revealed that PTX loading influenced the mechanical and morphological properties of the PCL grafts, however this did not jeopardize their suitability for implantation. Then, the PCL-PTX grafts which showed the most relevant characteristics for in vivo application were chosen for implantation in the rat aorta. After 6 months follow-up, we observed the biological effects of local PTX release such as delayed endothelialization, limited neointima growth, and limited cellular infiltration. Despite these findings, the healing process of these biodegradable grafts was substantial, and the limitation of neointima formation was prominent. Based on our initial findings, we speculate that PTX-eluting PCL vascular grafts may potentially lead to better clinically applicable grafts in the future.

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Disclosures

None.

References


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