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Controllable aligned nanofiber hybrid yarns with enhanced bioproperties for tissue engineering

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6 **Keywords:** electrospinning, aligned nanofibers, microfibers, core-shell yarn, tissue
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8 engineering
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10 11 Abstract

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14 Electrospun nanofibers have large surface area, high porosity and controllable orientation
15 while conventional microfibers have appropriate mechanical properties such as stiffness,
16 strength, and elasticity. Therefore, the combination of nanofibers and microfibers can provide
17 building elements to engineer biomimetic scaffolds for tissue engineering. In this study, a
18 core-shell structured fibrous structure with controllable surface topography was created by
19 electrospinning polycaprolactone (PCL) nanofibers onto polyglycolic acid (PGA) microfibers.
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21 The surface morphology, surface wettability and mechanical properties of resultant core-shell
22
23 structure were characterized. FE-SEM images reveal that the orientation of PCL nanofibers
24 on the yarn surface can be tuned by the fiber collector and rotating disks. Benefiting from the
25 introduction of the shell of aligned PCL nanofibers on the core of PGA yarn, the uniaxially
26 aligned PCL nanofiber covered yarns (A-PCLs) exhibited higher hydrophilicity, porosity, and
27 mechanical properties than the core PGA yarns. Moreover, A-PCLs promoted the adhesion
28 and proliferation of BALB/3T3 (mouse embryonic fibroblast cell line), and guided cell
29 growth along the biotopographic cues of the PCL nanofibers with controllable alignment. The
30 developed core-shell yarn that can have both the desired surface topography of PCL
31 nanofibers and mechanical properties of PGA microfibers has demonstrated great potential in
32 constructing various tissue scaffolds.
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1. Introduction

Tissue engineering, also known as regenerative medicine, is based on biological and engineering disciplines, and it mainly refers to the preparation of human tissue substitutes to promote the repair of human injury tissue or organ.^[1] Extracellular matrix (ECM) primarily containing some polysaccharides and proteins is a micro-nanoscale network of macromolecules distributed on the cell surface or among cells.^[2] ECM can provide a suitable microenvironment for cell behavior, and affect the cell shape, metabolism, function, migration, proliferation and differentiation through the biophysical and biochemical signal.^[3,4] One of the main research contents of tissue engineering is to generate the biocompatible scaffold that will imitate ECM and three-dimensional (3D) structure of diverse tissues. Recently, some properties of the 3D bioengineered scaffold including strength, porosity and configuration have been examined to improve diverse ECM platforms.^[5,6] In particular, there have been numerous reports on cell growth and related behavior of 3D scaffolds which possessed aligned biotopographical cues due to the regular organization of most of the structures of native tissues.^[7-9] For example, skeletal muscle tissue is composed of aligned myofibers, and blood vessel is made up of aligned vascular endothelial cells along the axial direction. Various methods such as freeze-drying,^[10] molecular self-assembly,^[11] photo-lithography,^[12] micro-grooving,^[13] 3D printing^[14] have been employed for the preparation of 3D well-organized tissue scaffolds. However, in clinical and commercial considerations, these methods involve complex process, expensive cost, or low resolution, and are difficult to adapt to the complexity of the size, configuration, and strength of the target tissue/organ.

The application of textile materials in tissue repair can be traced back to 5000 BC when the ancients used cotton or flax to suture the wound.^[15] At present, different textile structures including woven, knitted and nonwoven fabrics have been used as supports for tissue/organ repairing/regeneration, such as 3D woven cartilage scaffold, nonwoven scaffolene® and 3D knitted cardiac scaffold.^[16,17] They have 3D structures and can be served as guiding and ECM mimicking structures for soft tissue, ligament or cartilage. However, cells cultured on conventional scaffolds made of macroscale fiber or yarn materials lack sufficient contact guidance so that cells cannot effectively deposit ECM mimics to generate a micro-nanoscale environment that can promote growth, differentiation, and migration.^[18] Electrospinning is a well-established technology for the production of nanofibers, which was first reported by Formhals.^[19] Besides low cost and simple operation, some of the known features of electrospun fibers include a large specific surface area, nano-sized diameter, and high porosity.^[20,21] Aligned electrospun fibers or yarn prepared by the modified electrospinning process can provide improved mechanical properties and effective biotopographic cues highly desired by anisotropic tissue scaffolds such as tendon, ligament and cardiac tissues.^[22,23] It was also found that aligned electrospun nanofibers could promote adhesion and growth of some cells (nerve, smooth muscle cells, and myofiber, etc.).^[24-27] Electrospun aligned nanofibers with sufficient mechanical strength can be used as scaffolds alone or combined with textile technologies such as weaving, knitting or braiding to engineer 3D nanofiber scaffolds. The resultant scaffolds can effectively simulate the microstructure of ECM to a great extent, including simulation of the 3D structure of heart,^[28,29] muscle,^[30-32] vascularization,^[33] nerves,^[34,35] and cartilage.^[36-37] However, pure electrospun fibers remain

challenging to process into 3D structures due to low mechanical properties, and therefore limit their practical uses. For example, the tensile strength of nanofiber yarn scaffolds for skeletal muscle tissues reported by Wang et al.^[30] was less than ~ 5 cN (1 MPa), which failed to meet the requirement in the repair of tendons and ligaments that usually have tensile strength from 15 to 100 MPa.^[38] To overcome this limitation, the concept of core-shell yarns has been conceived and tested on a specially designed electrospinning setup.^[39] This method combines conventional bio-braided fibers acting as the core materials to provide the required strength for post processing, with aligned electrospun nanofibers serving as the shell to provide biotopographic cues.

In this study, core-shell yarns with tunable nanofiber orientations on the surface were developed and their effects on hydrophilicities, mechanical properties, and in vitro biological performance as tissue scaffolds were assessed. Aligned polycaprolactone (PCL) nanofibers beneficial to the promotion of cell adhesion and growth were electrospun onto polyglycolic acid (PGA) yarns, which were biocompatible and could provide an excellent mechanical strength and a stable size. The morphological structure of the scaffolds composed of aligned PCL nanofiber covered yarns (A-PCLs) was analyzed by SEM, and the BALB/3T3 (mouse embryonic fibroblast cell line) cells were cultured on these scaffolds. The effect of nanofiber arrangement on performance of the scaffolds in terms of cell morphology, adhesion, and growth was also evaluated. Results showed that the scaffolds with controllable aligned nanofibers possessed controllable guidance for cell growth, and the mechanical properties of the scaffolds reached practical level (372 MPa) for weaving or other post-treatments. Aligned PCL nanofibers on the surface could also improve the hydrophilicity (surface contact angle

reduced from 134° to 94°) and porosity (increased from 19% to 90%) of the scaffolds. This type of nanofiber covered yarn can potentially be used in the biomedical textiles such as 3D scaffolds for diverse tissue engineering applications.

2. Experimental Section

Materials: The PGA yarn sized 2 (~0.5 mm diameter) was purchased from Shandong WeiGao Group Medical Polymer Co., Ltd., China. PCL (Mn=80000) (Sigma-Aldrich, MO, USA) solution with the concentration of 10 wt% was prepared by dissolving it in 60/40 (v/v) mixture of dichloromethane (DCM) and *N,N*-dimethylformamide (DMF) (Tianjin Kermel Chemical Reagents Co., Ltd., China). PGA yarn and PCL were chosen as raw materials, because PGA yarn exhibits good biocompatibility and is often used as the suture, and PCL shows good biocompatibility and biodegradability. DCM and DMF were used without further purification. BALB/3T3 cells were obtained from the Cell Bank of the Chinese Academy of Sciences (Shanghai, China). Medium and other reagents for cell culture were purchased from Hyclone (USA).

Fabrication of nanofiber covered yarn scaffolds: The electrospinning setup comprises of a syringe pump (Zhejiang Smith Medical Instrument Co., Ltd., China), a high voltage power supply (Dalian ZhiDian Electronic Technology Co., Ltd., China), a grounded collector (consisted of two parallel aluminum flakes), and two rotating disks with two rotating rollers. In the electrospinning process, PCL solution in a 20 mL syringe was pushed by a syringe pump at an infusion rate of 0.8 mL h⁻¹ to a spinneret with the inner diameter of 1.65 mm. Two parallel aluminum flakes (length of 20 cm, span distance of 3 cm) were used as the grounded collectors below the spinneret. A voltage of 15 kV was applied between the spinneret and the

grounded collector. The distance between the spinneret tip and the upper edges of collector was 15 cm. When aligned PCL nanofibers were suspended over the edges of the two parallel aluminum flakes, PGA yarn was conveyed at a controlled speed into the spinning zone by an unwinding roller. Meanwhile, two disks were rotated at the same speed and direction to allow the aligned PCL nanofibers to uniformly cover the PGA yarn and form a core-shell structure. This electrospinning process was carried out at 20±2 °C and 65±5 RH%. All prepared scaffolds were kept in a ventilated environment for 24 h to allow any residual organic solvent to evaporate completely.

Characterization of scaffolds: The morphology of scaffolds was characterized by a field emission scanning electron microscope (FE-SEM) (Quanta-450-FEG, FEI, England). FE-SEM images were analyzed using Smileview (JEOL) software to determine fiber diameter and pore diameter through the selection of five random fields of each image. Optical images of the prepared yarns were recorded by a digital camera (HDR-SR11E, SONY, Japan). Modified Fast Fourier Transform (MFFT) technique was employed to characterize the alignment of nanofibers from the FE-SEM images.^[40,41] The porosity of scaffolds was measured according to the liquid displacement method.^[42] Before test, scaffolds were placed in a desiccator (Shanghai SuoPu Instrument Co., Ltd., China) for drying 2 h and were then put into measuring cylinders that were filled with a certain volume of ethanol. The porosity (P) of scaffolds was calculated as follows:

$$P(\%) = \frac{V_1 - V_3}{V_2 - V_3} \times 100\% \quad (1)$$

Where V_1 is the volume of ethanol in a measuring cylinder, V_2 refers to the volume of ethanol and scaffold; V_3 is the volume of remaining ethanol after the scaffold was taken out.

Mechanical properties of scaffolds were evaluated by an electronic strength tester (5565, Instron, USA). All scaffolds for testing were cut into 15 cm and pulled at a speed of 10 mm min^{-1} . To study the hydrophilicity of scaffolds, water contact angle was measured with 2 μL water using a contact angle analyzer (OCA15EC, Dataphysics, Germany) at ambient temperature. The morphology of water drops at randomly distributed positions of the scaffolds was recorded and then analyzed. Wicking height (W) was utilized to evaluate water absorption capacity of scaffolds by a wicking property tester (YG(B)871, China). The average value of W was calculated as follows:

$$W = \frac{\sum_{i=1}^n w_i}{n} \quad (2)$$

Where w is the height of the water along the fiber.

Biological assessment in vitro: BALB/3T3 cells were cultured in DMEM culture medium with 10% FBS and 1% antibiotics. All prepared scaffolds were placed in the bottom of 24-well tissue culture plate (TCP), washed 3 times with PBS, sterilized for 12 h under UV radiation, and subsequently incubated with DMEM for 24 h before cell seeding. Cells were detached by trypsin/EDTA when cells were grown to 90% confluency. A hemocytometer was used to count the viable cells and then cells were seeded onto scaffolds at a density of 1×10^4 cells/well. Afterwards, cells were cultured in the standard culture condition (37 $^{\circ}\text{C}$, 5% CO_2 , and 95% humidity). The medium was refreshed every 48 h. To study the cell proliferation on different scaffolds, viable cells were determined by using methylthiazol tetrazolium (MTT)

1 assay. After 1, 3, and 5 days of cell seeding in a 24-well plate, cells were washed with PBS
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3 and incubated in 400 μ L MTT solution. After incubation at the standard culture condition for
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6 3 h, the MTT solution was removed from each well and 400 μ L DMSO was appended. The
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9 plate was gently shaken for 20 min in order to dissolve the formazan precipitate. A
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12 spectrophotometric plate reader was used to measure the absorbance of the content of each
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15 well at 492 nm. Cells grown on the 24-well TCP was used as the control. The morphology of
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18 cells on scaffolds was examined by FE-SEM. After 3 days culture, cell-scaffolds were
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21 washed with PBS and fixed with 3% glutaraldehyde for 2 h, followed by dehydrating through
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24 gradient ethanol solution (30, 50, 70, 90, 100% v/v) and drying 12 h at room temperature.
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26 Completely dried cell-scaffolds were coated with gold for the analysis of cell morphology.
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29 The elongation of BALB/3T3 cells on prepared scaffolds was measured by aspect ratio,
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32 which was evaluated by the longest and shortest length of cell on FE-SEM images. Confocal
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35 laser scanning microscope (CLSM) (FV1200, Olympus, Japan) was used to visualize cell
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38 cytoskeletal structure and distribution on the scaffolds. The process can be briefly described
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41 as follows: cell-scaffolds were washed three times with PBS, fixed with 4%
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44 paraformaldehyde for 60 min, permeabilized with 1mL 0.1% Triton X-100 (AMRESCO USA)
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47 for 10 min after culture of 3 days. The cells on scaffolds were stained for 30 min with
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50 FITC-Phalloidin and then stained by DAPI for 5 min after being washed another three times
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53 with PBS. The nuclei and cytoskeletons of cells were finally visualized by CLSM. The
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56 alignment of cells was determined from CLSM images by MFFT technique.
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Statistical analysis: Results were presented as mean value and standard deviation (SD). Statistical analysis was performed by one-way analysis of variance (ANOVA). $P < 0.05$ were considered statistically significant.

3. Results and discussion

3.1 Morphology and characterization of the prepared scaffolds

Figure 1. Schematic of the device used to prepare A-PCLs.

First, A-PCLs were prepared by homemade electrospun apparatus (**Figure 1**), which have been reported in our previous work.^[39, 43] In brief, the morphology of the A-PCLs was affected by the speed of the unwinding rollers and rotating disks. The rotation of the disks controls the covering cycle of PCL nanofibers onto the PGA yarn. **Figure 2a, b, and c** show the prepared A-PCLs at 300, 500, and 700 rpm disk speeds. The speed of the winding and unwinding rollers was fixed at 30 rpm. The resultant A-PCLs named as 300-PCLs, 500-PCLs, and 700-PCLs have different nanofiber alignment angles (the angle between direction of nanofibers and axial direction of the core yarn). It is found that the angle of the PCL nanofibers along the axial direction increases from 3° through 35°, to 85° with the increase of the rotation speed, indicating that the nanofibers are close to the axial direction at a lower rotation speed and close to vertical direction at a higher rotation speed. It is for this reason

that this method allows us to design different scaffold materials which have different topographic cues as needed. We can also change the raw polymer materials or add drugs into the nanofibers according to requirements through this process. Random PCL nanofiber membranes (R-PCLs) were manually wrapped on the core yarn at the same electrospinning time and used as the control scaffold (**Figure S1a**). The surface morphology of R-PCLs is shown in **Figure S1b**.

Figure 2 Schematic illustration of the A-PCLs fabrication procedure: (a)-(c) Fabrication process and surface morphology for the 300-PCLs, 500-PCLs, 700-PCLs.

FE-SEM images in **Figure 2a-c** show that the surface of 300-PCLs, 500-PCLs, and 700-PCLs was smooth and nanofibers were aligned at an increasing angle from 3°, 35°, to 85° with reference to the axial direction. Surface morphology images (**Figure 3a-c**) and corresponding fiber alignment curves (**Figure 3a'-c'**) show that nanofibers on the scaffolds were neatly aligned with peaks of 3°, 35°, and 85°, respectively. This further proves the

change in the fiber alignment angle on the surface of A-PCLs prepared at different disk rotating speeds. As shown in **Figure 3d**, nanofibers on R-PCLs are randomly arranged, and the fiber arrangement curve (**Figure 3d'**) exhibits a profile different from those in **Figure S1** where peaks are present. The fiber diameter, pore size and porosity of these scaffolds have also been characterized and regarded as important parameters for regulating cell proliferation and differentiation.^[44] As shown in **Table 1**, the mean fiber diameter of R-PCLs (444 ± 59 nm) is slightly larger than that of 300-PCLs (388 ± 33 nm), 500-PCLs (415 ± 31 nm), and 700-PCLs (349 ± 43 nm). The reason might be the stretching of the aligned nanofibers during the covering process at a high rotation speed. However, the difference of average fiber diameter among these scaffolds was not obvious, which might be due to the similarity of polymer jet instability under the same electrospinning condition. The pore size of 300-PCLs (2281 ± 836 nm), 500-PCLs (1914 ± 773 nm), and 700-PCLs (2194 ± 640 nm) has been greatly improved compared with that of R-PCLs (1482 ± 334 nm). This may be attributed to the aligned state of nanofibers deposited on the core yarn. The porosity of these scaffolds shows basically consistent. Moreover, the porosity of A-PCLs is significantly increased compared with that of the core yarn. This is because the small size of nanofibers has improved the porosity of scaffolds significantly. In comparison to the previous study,^[45] the A-PCLs not only have a higher porosity but also controllable-alignment topographic cues.

Figure 3 FE-SEM images of different scaffolds at a high magnification (a)-(d) and corresponding curves of fiber arrangement on the surface of different scaffolds (a')-(d').

Table 1 Fiber diameter, pore diameter and porosity of different scaffolds. *, $p < 0.05$.

Substrate	Fiber diameter (nm)	Pore diameter (nm)	Porosity (%)
Core	—	—	19.01±3.89*
R-PCLs	443.5±59	1482±334	76.38±5.73
300-PCLs	387.7±33	2281±836	89.97±6.74
500-PCLs	414.8±31	1914±773	85.66±7.07
700-PCLs	348.6±43	2194±640	84.28±7.16

3.2 Effect of nanofiber arrangement on hydrophilicity of different scaffolds

Hydrophilicity of the scaffold is the key issue for cell adhesion and proliferation, because hydrophilicity can affect the adhesion of serum proteins.^[46] **Figure 4** presents the

hydrophilicity of different scaffolds including surface contact angle analysis and wicking effect measurement. The water contact angle of 300-PCLs, 500-PCLs, and 700-PCLs is $94\pm5^\circ$, $97\pm7^\circ$, and $109\pm6^\circ$, respectively, which are significantly lower than that of R-PCLs ($134\pm8^\circ$; $P<0.05$) shown in **Figure 4a**. Wicking effect is usually used in the textile field to characterize the hydrophilicity of fibers or yarns. **Figure 4b** gives the wicking height of different scaffolds. It is evident that the wicking property of the core yarn improved significantly when the yarn surface were covered with aligned nanofibers. Wicking height of 300-PCLs (10.4 ± 0.7 cm), 500-PCLs (9.3 ± 0.8 cm), and 700-PCLs (9.0 ± 0.8 cm) exhibit a slight decrease but they are all higher than that of R-PCLs (8.3 ± 0.6 cm). The reason behind this result can be explained as wicking effect according to our previous study.^[39] More capillaries formed between aligned nanofibers are beneficial to water diffusion. The increase of alignment angle results in a more inclined route and greater resistance to water diffusion. However, R-PCLs have more inefficient capillaries because of random fiber arrangement.

Figure 4 Effect of arrangement of surface PCL nanofibers on water contact angle (a) and wicking height (b) for the different scaffolds.

3.3 Effect of nanofiber arrangement on mechanical properties of different scaffolds

Figure 5a shows the stress-strain curve and Young's modulus of different scaffolds. It is illustrated that the Young's modulus of different scaffolds remains unchanged at the initial elastic region. However, tensile strength and break strain of 300-PCLs (372 MPa; 28%),

500-PCLs (345 MPa; 26%), and 700-PCLs (335 MPa; 25%) increase compared to the core yarn (290 MPa; 19%) because of the inclusion of electrospun PCL nanofibers. The PCL nanofibers broke after the failure of the core yarn so a smaller alignment angle of the nanofibers on the surface of the scaffolds could lead to a higher tensile strength and break strain of A-PCLs (Figure 5b, c).

Figure 5 Stress-strain curve, Young's modulus (a), tensile strength (b), and break strain (c) of different scaffolds. *, $p < 0.05$.

3.4 Cellular morphology on different scaffolds

In vitro biological assessments were carried out by using BALB/3T3 cells. The morphology of cells on different scaffolds was visualized by FE-SEM and CLSM after 3 days of cell seeding. Figure 6 shows the FE-SEM images of cells on the surface of 300-PCLs, 500-PCLs, 700-PCLs, and R-PCLs scaffolds. Clearly BALB/3T3 cells prefer to attach to and grow on the biotopographic cues provided by A-PCLs scaffolds and tend to proliferate along the aligned PCL nanofibers (Figure 6a-c), while the morphology of cells on the R-PCLs scaffolds show an irregular oval form (Figure 6d). The growth patterns of BALB/3T3 cells on different biotopographic cues of scaffolds were characterized by measuring the aspect

ratio of the cell lines in the FE-SEM images (**Figure 6e**). Cellular aspect ratio on 300-PCLs (8.20 ± 1.5), 500-PCLs (7.31 ± 0.33), and 700-PCLs (6.91 ± 0.89) is significantly higher than that on R-PCLs (1.75 ± 0.29) shown in **Figure 6f**.

Figure 6 FE-SEM image of morphology of BALB/3T3 cells on different scaffolds (300-PCLs (a), 500-PCLs (b), 700-PCLs (c), R-PCLs (d)) after 3 days of cell culture, and statistical analysis of aspect ratio of cell lines on A-PCLs and R-PCLs. *, $p < 0.05$ (e, f).

Actin behavior was regarded to play a great role on the adhesion, migration and proliferation of cells.^[47,48] **Figure 7a** simulations that the biotopographic cues of scaffolds can induce the contact direction of actin, and determine the direction of cell secretion of ECM. At a relatively high magnification as shown in **Figure 7b-d**, BALB/3T3 cells grow

within the structure of A-PCLs scaffolds and elongate in the direction of the aligned fibers leading to a larger aspect ratio because cell bodies bridge up among aligned nanofibers. In order to further determine whether the A-PCLs scaffolds have a controllable alignment to guide the cells to grow in diverse directions, the cell distribution and morphology on scaffolds were measured by CLSM (**Figure 8**). The 3D views and top views of fluorescent staining images show that aligned BALB/3T3 cells distribute regularly and fully fill on the peripheral surface of 300-PCLs (**Figure 8a**), 500-PCLs (**Figure 8b**), and 700-PCLs (**Figure 8c**) scaffolds. The angular arrangements of the cells are approximately 3° , 35° , and 85° relative to the axial direction of the scaffolds, which match the trend of fiber alignment curves mentioned in **Figure 3a'-c'**. These data further confirm that A-PCLs having a controllable alignment can provide effective biotopographic cues for the cells.

Figure 7 Simulations of the cell elongation and actin organization (a), and FE-SEM images of BALB/3T3 cells on 300-PCLs (b), 500-PCLs (c) and 700-PCLs (d) after 3 days of cell seeding.

Figure 8 CLSM images of 3D view and top view for the F-actin and DAPI staining morphology of BALB/3T3 cells after 3 days of culture, and relative cell alignment curves of 300-PCLs (a), 500-PCLs (b), 700-PCLs (c).

3.5 Cell proliferation on different scaffolds

MTT assay was carried out to evaluate the cell proliferation of BALB/3T3 cells on 300-PCLs, 500-PCLs, and 700-PCLs. **Figure 9a** shows that BALB/3T3 cells proliferate slowly at 1 day of culture, and then the proliferation rate increases during the period from 3 to 5 days. The proliferation of cells on these scaffolds does not show any significant difference at the same culture time, suggesting that A-PCLs have the same trend for proliferation of BALB/3T3 cells. In comparison to R-PCLs and Core (TCP as control), A-PCLs have a significant proliferation difference as shown in **Figure 9b**, in which MTT result of BALB/3T3 on A-PCLs refers to the mean value on 300-PCLs, 500-PCLs, and 700-PCLs. It is observed that proliferation of control group is higher than that of the other three scaffolds at the beginning of culture for BALB/3T3, because the cells need to adapt to new environment. But there is a significant difference between nanofiber covered yarns

(R-PCLs and A-PCLs) and core yarn within 1 day culture because cells can easily attach to and proliferate on PCL nanofibers. However, after 3 and 5 days of cell culture, proliferation of BALB/3T3 on the A-PCLs is enhanced significantly compared to that on the R-PCLs and TCP. This can be explained by the following aspects: firstly, PCL nanofibers have high porosity and large specific surface area which provide more space for cell attachment and proliferation and thus improve the biocompatibility of the core after covering nanofibers; secondly, A-PCLs have a higher hydrophilicity than R-PCLs, and are more beneficial to cell growth; thirdly, controllable biotopographic cues can guide cells grow into aligned state.

Figure 9 MTT results of BALB/3T3 on A-PCLs (a), and various substrates (b) after 1, 3, and 5 days of cell culture. *, $p < 0.05$.

4. Conclusions

In this work, A-PCLs were developed for tissue engineering scaffolds by a novel electrospinning process which could be adjusted to control the alignment direction of nanofibers on the outer periphery of the core material. The core and covered material can be selected according to different tissue engineering requirements. The prepared scaffolds possessed well aligned nanofibers with a large porosity and hydrophilicity which were found to be advantageous to cell growth. In vitro biological performance showed that cell adhesion and proliferation were evidently promoted on the A-PCLs scaffolds, and cells were able to

1 identify the biotopographic cues provided by the surface aligned nanofibers. Furthermore, the
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3 A-PCLs had sufficient mechanical properties for weaving or other post-treatments. Therefore,
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6 these core-shell structure of A-PCLs scaffolds have significant potential for constructing
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9 different 3D tissue bioengineered structures.
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11 **Supporting Information**

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13 Supporting Information is available from the Wiley Online Library or from the author.
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40 **Conflict of Interest**

41
42 The authors declare no conflict of interest
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