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Combining 3D Printing and Electrospinning for the Fabrication of a Bioabsorbable Poly-p-dioxanone Stent

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Abstract. For a good radial strength and small volume, the metal stent is widely applied in treating vascular disease. However, because metal stents can form a fixed stenosis in the treated area of vascular disease, it is not appropriate for treating children who are growing up. Bioabsorbable vascular stent (BVS) is the ideal choice for children. Aiming at overcoming the defects in mechanical properties of existing vascular stents, a sliding-lock bioabsorbable poly-p-dioxanone (PPDO) vascular stent, which is fabricated through combining 3D printing and electrospinning technology, is proposed herein. The results of experiments show that when the thickness of a stent is constant, the stent combined with electrospinning is obviously better than one fabricated through 3D printing. In addition, it is very favorable for the growth and proliferation of cells. This fabrication process lays the foundation for further applying the stent in treating vascular disease in children.

Keywords. 3D printing, Absorbable vascular stent, Electrospinning, Mechanical property, Composite forming.

Introduction

Cardiovascular disease is one of the leading causes of death worldwide [1]. Currently, due to it being minimally invasive and efficient, the intervention therapy has become a primary method for treating coronary heart disease [2]. Metal stents have better radial strength, and they have been widely used in clinics [3]. Although these materials have good mechanical properties and biocompatibility, the usually are not biodegradable. The implantation will form a fixed diameter of blood vessels, which is not suitable for children's vascular growth and may affect the further development of blood vessels [4,5]. This situation often requires reoperation, which limits its application in pediatric patients. In addition, stenosis rate and thrombosis rate using metal stents is also high, [6]. Due to degradation, BVS can disappear gradually, and therefore can avoid the occurrence of the abovementioned phenomenon [7]. Therefore, BVS is ideal for pediatric patients.

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At present, the preparation methods of bioabsorbable polymer vascular stent use 3D printing, weaving, laser engraving, coating method and so on. 3D printing is a process for producing 3D solid objects of virtually any shape from a digital model using a layer-by-layer (LBL) process [8]. 3D printing has received much attention in the biomedical field in recent years for its potential many useful applications [8]. 3D printing technology for BVS fabrication provides new theoretical and technical support.

The bioabsorbable polymeric material often cannot achieve the strengths of the metallic material such as toughness and elasticity. Currently BVS remains in the initial developing stage, mostly prepared using bioabsorbable polymeric materials. Using bioabsorbable polymers for preparing polymer stents results in the strength being far less than the metal stent. SUN Kun et al [9] designed a sliding-lock PPDO stent for children with congenital stenosis. This sliding-lock slide stent is produced through 3D printing (fused deposition modeling, FDM). B.Stepak et al [6] adopted laser engraving to prepare vascular stents. Ligang et al [10] reported a home-made PPDO monofilament line weft woven tubular scaffolds, next to treat intestinal stenosis lesions.

As mentioned above, the stents were prepared with bioabsorbable polymer. Because of relative poor strength compared with the metal stent, the application in clinics is limited. Were the intensity of the stent increased, the thickness of the stent could be increased, leading to its large initial diameter, poor expansibility, inability to reach a satisfactory balance between mechanical properties and delivery of the stent result in the stent being unable to meet the children's congenital vascular narrow clinical needs.

Electrospinning technique has important applications in biomedicine. Nanofibers have received considerable attention in the tissue engineering field because of their distinctive properties, including high surface-area-to-volume ratio, biomimicry of the structure and functions of extracellular matrix of human body tissues, etc[11].

In this study, in order to offset the defect of bioabsorbable polymer vascular stent prepared by 3D printing, nanofibers were added to its surface by electrospinning to increase the effect of toughness, which inhibits the proliferation of vascular endothelial abnormalities in the stents.

1. Test platform for combining 3D printing with electrospinning for the fabrication of BVS

In order to increase the effect of combining two processes: in 3D printing and electrospinning, the proposed complex foming system includes a motion platform subsystem, multi-temperature field controlling subsystem, high voltage electric field controlling subsystem, Taylor cone monitoring subsystem, 3D printing feeding subsystem and electrospinning feeding subsystem, shown in Figure 1.

Motion platform subsystem is mainly used for receiving nozzle forming material from the typical three-axis gantry mechanism with PMAC motion control according to a planned path route.

Multi-temperature field control subsystem is mainly used for stabilizing the material temperature at the nozzle. And the appropriate temperature can ensure the material at the nozzle has a good liquidity, which is favorable for adopting 3D printing technology to prepare the stent.

High-voltage electric field controlling subsystem can supply a high voltage power for composite forming electrospinning to meet the requirements of electrospinning

forming processes. The voltage in this subsystem can be rapidly regulated over the range of 0 ~ 50 KV.

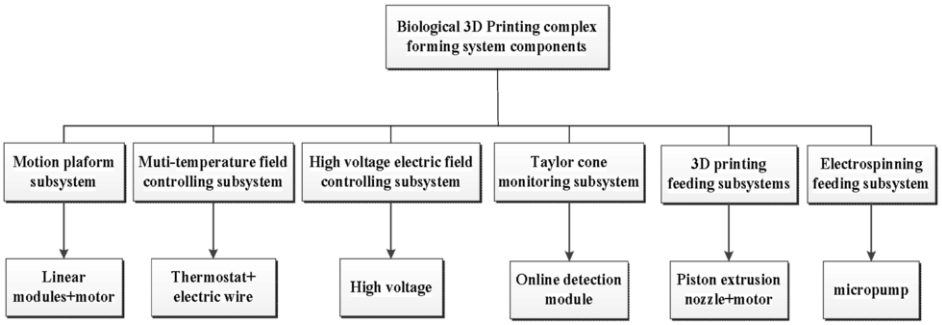

Figure 1. Components of 3D printing biological complex forming system.

The main function of the Taylor cone monitoring subsystem is for achieving real-time monitoring of the Taylor cone form, realizing the monitoring of the spinning process. This subsystem is equipped with high-speed CCD camera, and the processed information is sent to the control system for adjusting the process parameters.

3D printing feeding subsystem is mainly used for preparing the macro-part of stent.

Electrospinning feeding subsystem is primarily used for preparing the micro-part of stent.

2. Test for combining 3D printing with electrospinning for the fabrication of BVS

2.1. Experimental methods

The test platform, as shown in figure 2, was built by our team is based on the combination of 3D printing and electrospinning technology to prepare the BVS.

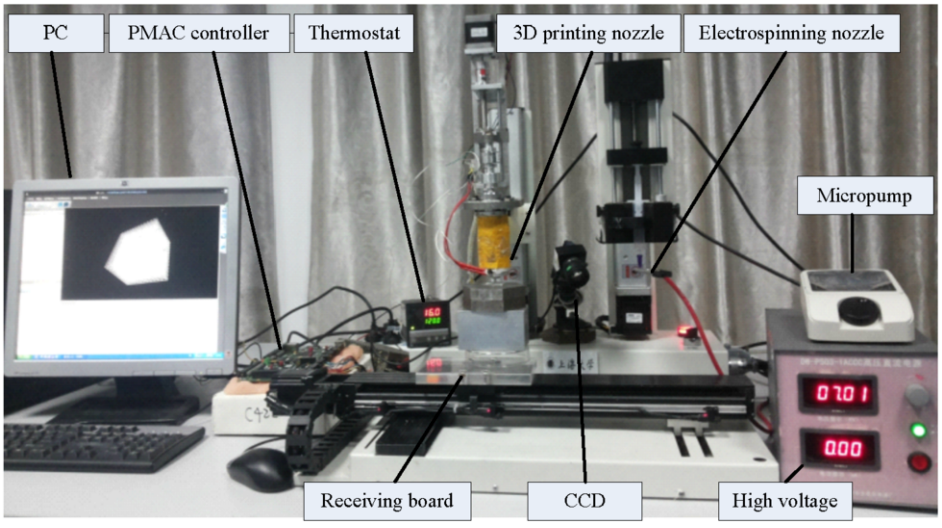

Figure 2. Test platform of biological 3D printing complex forming vascular stents.

Experiment materials and process parameters are shown as follows:

Material used for preparation of the stent is granular Poly-p-dioxanone (Germany Evonik Röhm AG); molecular formula: -(C4H6O3)n-. Poly-p-dioxanone(PPDO) is a kind of aliphatic polyester-polyether with excellent biodegradability, biocompatibility and bioabsorbability. Its application has already been approved by the FDA as the base body material of medical absorbable suture (trade name PDS), and it also has utilization potential in the fields of orthopedic fixation materials, drug carriers, etc[12].

In order to ensure that vascular stents have an uniform pore structure, forming process parameters are set via a pre-processing module of biological 3D printing complex forming system: h- layer height, and λ- scanning line pitch bewteen formed fibers. Pre-processing module generates a machine-made path that follows particular parameters set by the generation document holder.

Based on the path documents obtained, in order to ensure the that the system can prepare satisfactory VBS, the system's feeding speed is set to 2.5 mm/min, the velocity of the platform is 40 mm/min, and the nozzles diameter of 3D printing feeding subsystem is 0.51mm, through post-processing module of biological 3D printing complex forming system on the basis of previous experience.

Experiment material of the composite electrospinning is a mixed solution of PVA-chitosan. In this study, chitosan and PVA were blended. Meanwhile, acetic acid and water were used as solvents. Firstly, PVA (grades JP233, degree of polymerization 3500, alcoholysis degree of 88%, Kuraray Company of Japan, Ltd.) was dissolved in hot water with 8wt%. This solution was heated until boiling on a magnetic stirrer and stirred until it was completely dissolved. Secondly, chitosan (viscosity-average molecular weight Mη=112×105, degree of deacetylation 82.5%, Zhejiang Golden-Shell Biochemical Co., Ltd.) was dissolved in the solvent of 10% acetic acid solution. Finally, the PVA solution and chitosan solution were mixed with a volume ratio of 2:1 and stirred well.

In order to obtain a high quality of electrospinning, distance from the nozzle to the receiving plate was set to 150 mm through the PC, the high-voltage DC power supply voltage was set to 15 KV through the micropump, and the solution was fed through a 26G needle with a feed rate of 20ul/min.

2.2. Fabrication of vascular stents

Test platform of biological 3D printing complex forming vascular stents as shown in Figure 2 was used to fabricate the vascular stents. Briefly, PPDO was inserted into a stainless steel syringe and heated using an electric wire. When the polymer reached the molten phase, PPDO was extruded through a nozzle and deposited on a continuously moving platform controlled by a computer. The vascular stent was fabricated by depositing PPDO fibers along the predefined path (Figure 3). Finally, Type I stents were fabricated by only using the 3D printing technology. On this basis, the system automatically turns on the micropump and high voltage when the motion platform subsystem control on the receiving board moves below the electrospinning nozzle. Nanofibers were added onto the Type I stents' surface by electrospinning technology. Type II stents were fabricated by this complex forming technology.

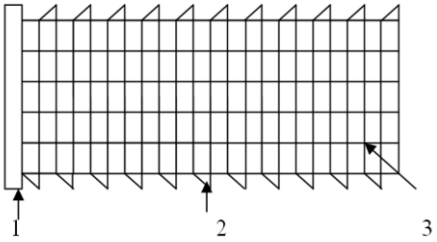

Figure 3. Test Schematic illustration of a PPDO BVS with the sliding-lock structure (1.framework, 2.barbs, 3.lamellar mesh structure).

2.3. Experimental results

In order to compare the differences in the mechanical properties of bioabsorbable PPDO stents prepared through only 3D printing technology and complex forming]technology, two kinds of stents were prepared. These two kinds of stents have two macro layers. Figure 4(a) is a Type I stents that was made using only 3D printing technology. The length of the stent is 40mm and the width of the stent is 20mm. The width of the strent and the pores between the stent is approximately 0.8 mm. Figure 4(b) is a local-enlarged view of Type I stents. We can get a local-enlarged view of the stents through the image measuring instrument (Suzhou Yixin Photoelectric Technology Co. Ltd). Figure 5(a) depicts prepared Type II stents through complex forming technology. Figure 5(b) is a local-enlarged view of Type II stents. When comparing Type II stents with Type I stents, many nanofibers adhere to Type II stents.

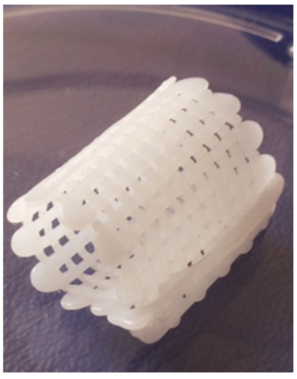

Figure 4(a). Type I stents.

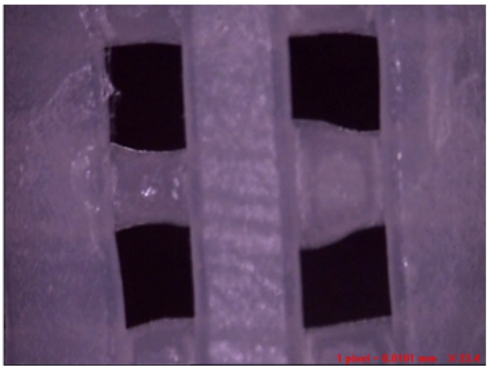

Figure 4(b). Type I stents.

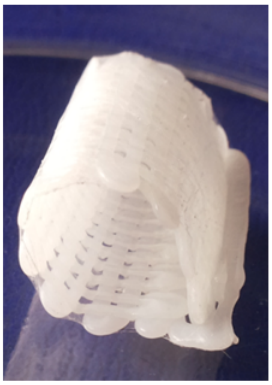

Figure 5(a). Type II stents.

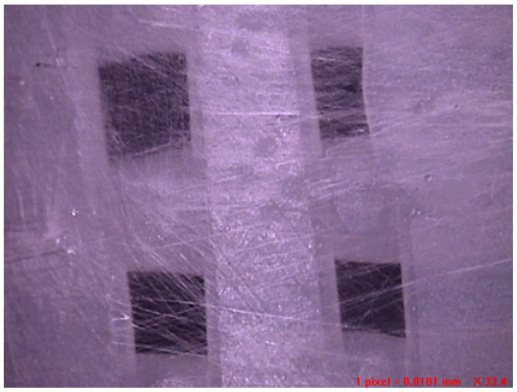

Figure 5(b). Type II stents.

2.3.1. Tensile strength test

Based on data from 10 samples of each group, tensile strength was measured for each group, and the average value was taken. Tensile strength of Type I stents is 16.5±1.3 MPa, Tensile strength of Type II stents is 17.8±1.6MPa. By contrast, we can clearly find that the tensile strength of Type II stents is a little bit greater than Type I stents. The tensile strength was defined as the maximum stress during the tensile test until fracture [13].

2.3.2. Radial strength test

Radial strength of the stent is the resistance of the stent towards radial outer pressure and it is one of the most important technical indicators of a stent. The experiment of the stents is conducted on a radial strength tester, RX550 (INSTRON company). The test chamber temperature is 37℃, the compression ratio is 50%, and the compression speed is 0.1mm/s. According to ISO13485 standard, when a stent is compressed to 88% of the diameter, the radial strength is the maximum value of the support stent. Based on data from the same 10 samples, the radial strength of Type I stents is 121±14.5 KPa and the radial strength of Type II stents is 124±13.6 KPa. Similarily to the tensile strength, the radical strength of Type II stents is a little bit greater than Type I stents; however, the thickness of the two kinds of stents have no significant differences.Test results on mechanical propensities of two groups of stents are shown in Table 1.

Table 1. Test results on mechanical propensities of two groups of stents

Stents type	Tensile strength MPa	Radial strength KPa
Type I stents	16.5±1.3	121±14.5
Type II stents	17.8±1.6	124±13.6

2.4. Experiment discussions

The reasons why Type II stents have good mechanical strength is because of its application of 3D printing technology, attachment of nanofibers on the stent increase

the overall effect of toughness. The literature [14] confirmed the orientation of nanofibers as a guiding role to cell growth. Electrospinning nanofibers can simulate the extracellular matrix environment [15]. According to studies, the best aperture of vascular endothelial cell growth is between 20-60μm. Advantages of the composite stents (Type II stents) are its conduciveness for cell growth, proliferation, and ability to speed up the repairing of vascular stenosis disease.

3. Conclusions

BVS can overcome the shortcomings of metal stents including impossible degradation and poor biocompatibility, but the bioabsorbable polymeric material often encounters difficultly in achieving the strength, toughness, and elasticity of the metal material. In this paper, we found that the radial strength and tensile strength prepared by combining 3D printing and electrospinning technology improve much more than the Type I stents prepared only by 3D printing technology. In addition, the adhesion nanofiber Type II stents are conducive to cell growth and proliferation and the acceleration of repairing stenosis. Our next task is to repair blood vessels in animals.

Acknowledgements

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