Preparation of a poly(L-lactic acid) braided stent with high radial force

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Abstract: In this paper, a poly(L-lactic acid) (PLLA) braided stent with high radial force is prepared by optimizing the processes of monofilament forming and stent annealing. Firstly, three kinds of PLLA monofilaments with different diameters are prepared by melt extrusion, then two kinds of thicker monofilaments are further solid-state drawn to have diameters similar to that of the third thinner monofilament. The monofilament that is solid-state drawn at the larger draw ratio shows sufficient tensile mechanical properties and can be used for braiding stents, which is owing to the promotion of oriented crystallization. Secondly, PLLA braided stents are annealed at different temperatures. Stent not annealed shows much lower chronic outward force (COF) and much higher radial shrinkage rate (RSR) than those of annealed stents. Moreover, the COF is increased by 115% and the RSR is decreased by 59% as the annealing temperature is gradually increased from 80°C to 160°C. Therefore, PLLA braided stents can be annealed at higher temperatures below their melting temperature to enhance the radial force. These results are due to the improved crystallinity induced by the thermal motion of molecular chains. This study may provide helpful suggestions for the preparation of biodegradable braided stents with high radial force.

1. Introduction

Biodegradable materials have been widely used in various biomedical fields by virtue of excellent biodegradability and biocompatibility [1]. Recently, biodegradable braided stents (BBS) as emerging medical devices have shown unique advantages over traditional metallic braided stents in treating peripheral vessel stenosis and digestive tract obstruction [2, 3]. BBS not only avoid the trouble of subsequent removal but also effectively reduce the incidence of adverse clinical events such as inflammation [4, 5]. Despite these encouraging results, BBS have poor mechanical properties especially low radial force, which may lead to the constrictive remodeling of lumen.

Over the past few decades, poly(L-lactic acid) (PLLA) has been extensively used for constructing biodegradable coronary stents, and many products have shown good clinical outcomes and been on the market [6, 7], which promotes its further applications in the field of BBS. Recently, some theoretical explorations on PLLA braided stents have shown good results [8]. However, preliminary animal experiments on PLLA braided stents show that the lesions need to be predilated before implantation, and reexpansion is also needed immediately after deployment to prevent the occurrence of nonadherence even migration [9]. Both inconveniences are ascribed to the low radial force of PLLA.
braided stents [9], which may further induce more severe clinical accidents like stent collapse even restenosis, restricting their broad applications. Therefore, it is necessary to prepare PLLA braided stents with high radial force.

Scholars have adopted many strategies to improve the radial force of BBS. Im et al. optimized the parameters of solid-state drawing (SSD) and prepared a PLLA monofilament with high stiffness and strength to braid springs, which are further annealed at the optimal temperature to have high compressive resistance and recovery rate [10]. Wang et al. enhanced the radial force of PLLA Z-structure stents by optimizing the parameters of strand like monofilament diameter [11]. Zhao et al. increased the local and whole compressive properties of poly(p-dioxanone) (PDO) braided stents by raising the annealing temperature and introducing the axial runners, respectively [5, 12]. Han et al. developed a PDO/PLLA sheath-core biphasic monofilament, which is braided into stents with radial force nearly twice that of PDO braided stents [13]. All these researches prove that optimizing manufacturing processes can effectively improve the radial force of BBS. However, how to prepare a PLLA braided stent with high radial force by optimizing its manufacturing processes has been rarely reported before.

The purpose of this paper is to prepare a PLLA braided stent with high radial force by optimizing the processes of monofilament forming and stent annealing. Firstly, some PLLA monofilaments with specific diameters are prepared by melt extrusion and SSD, then the tensile mechanical properties of these monofilaments are compared and the feasibility of using them to braid stents is discussed. Secondly, PLLA stents are braided by the selected monofilament, then they are annealed at different temperatures and their radial force is compared. In addition, the crystalline properties of monofilaments and stents prepared by different process parameters are compared to explain the differences in mechanical properties. This study can bring new ideas for manufacturing BBS with fine mechanical properties.

2. Materials and Methods

2.1. Material

PLLA powder with brand of RESOMER® L210 S and intrinsic viscosity of 3.3-4.3 dL g⁻¹ is purchased from Evonik (Germany).

2.2. Preparation of Monofilaments

Firstly, the PLLA powder is melted and extruded into three kinds of monofilaments with diameters of 0.60±0.02 mm, 0.40±0.02 mm and 0.20±0.02 mm, respectively, and they are designated as ME0.60, ME0.40 and ME0.20, respectively. Secondly, ME0.60 and ME0.40 are further solid-state drawn to have diameters of 0.23±0.02 mm and 0.21±0.02 mm, respectively, and these two kinds of monofilaments are designated as SSD0.23 and SSD0.21, respectively. The draw ratio (DR) is calculated according to the following formula:

\[ DR = \left( \frac{D_0}{D_1} \right)^2 \]  

where \( D_0 \) and \( D_1 \) are the monofilament diameter before and after SSD, respectively. Therefore, the DR of SSD0.23 and SSD0.21 is 6.8 and 3.6, respectively.

2.3. Characterizations of Monofilaments

2.3.1. Tensile Test The tensile mechanical properties of monofilaments are measured using a homemade tensile tester. The test is conducted under environmental conditions with room temperature of 20-30°C and relative humidity of 40-60%. The tensile speed is 10 mm min⁻¹. The stress-strain curve can be obtained, and then some indexes can be analyzed.

2.3.2. X-Ray Diffraction (XRD) The XRD test is carried out using a X-ray diffractometer (Rigaku Smartlab (3)). The Cu kne radiation is used. The scanning range is from 5° to 35°, the speed is 6° min⁻¹,
and the step is 0.02°. The monofilaments are positioned with their axes parallel to the radiation.

2.3.3. Differential Scanning Calorimetry (DSC) The DSC test is performed using a differential scanning calorimeter (Mettler-Toledo DSC3). The monofilaments are cut into pieces weighing 3-6 mg, which are then sealed into an aluminum crucible with volume of 40 μl. The heating range is from 25°C to 220°C, the rate is 10°C min⁻¹, and the nitrogen flow is 50 ml min⁻¹. The crystallinity (χc) is calculated according to the following formula:

\[ \chi_c = \frac{\Delta H_m - \Delta H_c}{\Delta H_0} \times 100\% \]  

(2)

where \( \Delta H_m \) and \( \Delta H_c \) are the enthalpy of fusion and cold crystallization, respectively, both of which are obtained from the DSC thermogram, and \( \Delta H_0 \) is the melting enthalpy of 100% crystalline PLLA (93.7 J g⁻¹) [14].

2.4. Preparation of Stents
Firstly, SSD0.23 and copper molds are used to braid stents with inner diameter of 8 mm, length of 20 mm, pin number of 6 and pitch of 7.74 mm. Secondly, these stents are annealed in a vacuum oven at different temperatures for 1 h. The chosen annealing temperatures include 80°C, 100°C, 120°C, 140°C and 160°C, and the corresponding stents are designated as SA80, SA100, SA120, SA140 and SA160, respectively. The stent not annealed is designated as SNA. Thirdly, all stents are removed from the molds.

2.5. Characterizations of Stents

2.5.1. Radial Force The radial force of stents is tested using a radial force tester (Blockwise TTR2) according to the standard ASTM F3067-14. The testing temperature is 37°C. The chamber firstly contracts to compress a stent to 4.5 mm in diameter, then keeps static for 600 s, and finally expands to drive the stent to expand by itself until they are no longer in full contact. Both loading rate and unloading rate are 0.02 mm s⁻¹. The radial force normalized by the stent length is adopted.

2.5.2. Differential Scanning Calorimetry (DSC) The DSC test of stents is the same as that of the monofilaments and performed as per Section 2.3.3.

3. Results & Discussion

3.1. Tensile Mechanical Properties of Monofilaments

![Stress-strain curves of PLLA monofilaments](image)

Figure 1. Stress-strain curves of PLLA monofilaments, the inserted figure is the enlarged view of the elastic and yield stages, the inserted table lists the indexes of tensile mechanical properties.
Monofilaments as the most basic skeletons must have fine tensile mechanical properties to make braided stents of sufficient radial force [15]. Under this premise, monofilaments preferably have a smaller diameter to reduce the overall dimension of braided stents for convenient delivery. To assess the feasibility of using PLLA to construct BBS, five kinds of PLLA monofilaments with specific diameters are prepared and their tensile mechanical properties are compared in Figure 1. The monofilament of ME0.20 is too fragile to be tested.

Three indexes can be obtained from the stress-strain curves. The elastic modulus (E) is the slope of the initial elastic stage which is linear, the elongation at break (ε) and tensile strength (σ) are the maximum strain and the maximum stress, respectively. As shown in the enlarged view, ME0.60 and ME0.40 have lower E of 2.2 GPa and 2.6 GPa, respectively. In contrast, SSD0.23 and SSD0.21 have much higher E of 6.9 GPa and 4.1 GPa, respectively, which are enhanced by 214% and 58%, respectively. The enlarged view also shows that ME0.60, ME0.40 and SSD0.21 have obvious yield stage. The σ of ME0.60 and ME0.40 is their yield strength of 62.9 MPa and 63.8 MPa, respectively, while the σ of SSD0.21 is its breaking strength of 78.0 MPa. In contrast, SSD0.23 has no obvious yield stage, and the σ is its breaking strength of 582.8 MPa, which is 7.5 to 9.3 times as high as that of the others. Furthermore, the ε of monofilaments is greatly increased from 9.0-10.8% to 34.8-36.5% by SSD. These results indicate that the melt-extruded PLLA monofilaments show inferior tensile mechanical properties, behaving much too softly, brittlely and weakly, while SSD not only reduces the diameter of PLLA monofilaments but effectively improves their tensile mechanical properties, making them stiffer, more ductile and stronger. Moreover, a larger DR can more significantly improve both E and σ of PLLA monofilaments when the final target diameter is close. Overall, the monofilament of SSD0.23 that is solid-state drawn at the larger DR of 6.8 has enough E, ε and σ, making it endurable to big deformation and high stress and suitable for braiding stents.

3.2. Crystalline Properties of Monofilaments

![Figure 2. Crystalline properties of PLLA monofilaments: (a) XRD curves; (b) crystallinity.](image)

The crystalline properties of these PLLA monofilaments are further compared to explore the effect mechanism of forming processes on the tensile mechanical properties. As shown in Figure 2 (a), the peak of (110)/(200) reflection at 2θ of ~16.4° which corresponds to the α-crystal [16] is almost undetectable in ME0.60, ME0.40 and ME0.20 while clear and obvious in SSD0.23 and SSD0.21. In addition, this peak of SSD0.23 is much intenser and sharper than that of SSD0.21. These results indicate that the melt-extruded PLLA monofilaments are poorly oriented and crystallized while SSD promotes the α-crystal orientation and growth via stress, and this promotion is positively correlated with the DR [16]. As confirmed in Figure 2 (b), ME0.60, ME0.40 and ME0.20 have the lowest crystallinity of 12.6-16.8%, SSD0.21 has a higher crystallinity of 39.9%, and SSD0.23 has the highest crystallinity of 65.2%. The differences in the orientation and crystallinity of various PLLA monofilaments can well explain the differences in their tensile mechanical properties.
3.3. Radial Force of Stents

Figure 3. Radial force of PLLA braided stents: (a) a diagram of radial force-diameter curve, the inset shows the shapes of stents before and after testing; (b) indexes at different annealing temperatures.

Annealing is an essential process when preparing BBS, and the annealing temperature is a crucial parameter affecting their mechanical properties. To explore the optimal annealing temperature for improving the radial force of PLLA braided stents, a kind of stent with specific geometric structure is braided by SSD0.23 and then annealed at a series of temperatures between its glass transition temperature and melting temperature [17]. The radial force of PLLA braided stents annealed at different temperatures is compared in Figure 3.

As shown in Figure 3 (a), the radial force-diameter curve of PLLA braided stents consist of three stages: compression, static and expansion. Since the most important performance of braided stents is the self-expanding ability, the chronic outward force (COF) which is the expansion force between the indicated use diameters (IUD) is mainly analyzed [18]. Furthermore, an index of radial shrinkage rate \( RSR \) is introduced and calculated according to the following formula:

\[
RSR = \frac{(OD_0 - OD_1)}{OD_0} \times 100\%
\]  

where \( OD_0 \) and \( OD_1 \) are the stent outer diameter before and after radial force testing, respectively, as shown in the inset.

As shown in Figure 3 (b), SNA has the lowest COF at IUD of 6.5 mm of 0.003 N mm\(^{-1}\) and the highest RSR of 21.5%. Moreover, the COF at IUD of 6.5 mm is gradually increased from 0.041 N mm\(^{-1}\) to 0.088 N mm\(^{-1}\) and the RSR is gradually decreased from 11.0% to 4.5% as the annealing temperature gradually rises from 80°C to 160°C. These results indicate that raising the annealing temperature improves the ability of PLLA braided stents to expand by themselves and recover to the original state before compression. Therefore, PLLA braided stents can be annealed at higher temperatures below their melting temperature to improve the radial force.

3.4. Crystallinity of Stents

Figure 4. Crystallinity of PLLA braided stents annealed at different temperatures.
The crystallinity of these PLLA braided stents are further compared to explore the effect mechanism of annealing temperature on the radial force. As shown in Figure 4, the crystallinity of SNA is the same as that of SSD0.23 of 65.2% and the lowest among all stents. In addition, the crystallinity is gradually increased from 66.1% to 70.6% as the annealing temperature gradually rises from 80°C to 160°C [19]. These results indicate that annealing promotes the recrystallization of PLLA braided stents by inducing the thermal motion of molecular chain [12], and this promotion becomes stronger at a higher temperature owing to a better chain movement ability. Therefore, PLLA braided stents annealed at a higher temperature are stiffer and stronger and have higher radial force.

4. Conclusions
In this paper, both processes of monofilament forming and stent annealing are optimized to prepare a PLLA braided stent with high radial force. It is found that the melt-extruded PLLA monofilaments showing poor tensile mechanical properties need to be solid-state drawn at a larger DR, by which they can have sufficient stiffness, toughness and strength to be suitable for braiding stents. Furthermore, annealing can improve the radial force of PLLA braided stents, and a higher annealing temperature increases the COF and decreases the RSR. The enhancements in the mechanical properties of both monofilaments and stents are attributed to the improved crystalline properties. In conclusion, PLLA braided stents can be made of solid-state drawn monofilaments with larger DR and then annealed at higher temperatures below their melting temperature to improve the radial force.

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