Mechanical Properties and *In Vitro* Degradation of Bioresorbable Fibers and Expandable Fiber-Based Stents

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Abstract: Bioresorbable polymeric support devices (stents) are being developed in order to improve the biocompatibility and drug reservoir capacity of metal stents, as well as to offer a temporary alternative to permanent metallic stents. These temporary devices may be utilized for coronary, urethral, tracheal, and other applications. The present study focuses on the mechanical properties of bioresorbable fibers as well as stents developed from these fibers. Fibers made of poly(L-lactide) (PLLA), polydioxanone (PDS), and poly(glycolide-co-ϵ-caprolactone) (PGACL) were studied *in vitro*. These fibers combine a relatively high initial strength and modulus together with sufficient ductility and flexibility, and were therefore chosen for use in stents. The effect of degradation on the tensile mechanical properties and morphology of these fibers was examined. The expandable stents developed from these fibers demonstrated excellent initial radial compression strength. The PLLA stents exhibited excellent *in vitro* degradation resistance and can therefore support body conduits such as blood vessels for prolonged periods of time. PDS and PGACL stents can afford good support for 5 and 2 weeks, respectively, and can therefore be utilized for short-term applications. The degradation resistance of the stents correlates with the profile of mechanical property deterioration of the corresponding bioresorbable fibers. © 2005 Wiley Periodicals, Inc. J Biomed Mater Res Part B: Appl Biomater 74B: 792–799, 2005

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INTRODUCTION

Stents are playing an increasingly important role in percutaneous coronary interventions. Various metal stents have been shown to reduce the restenosis rate compared with angioplasty alone. This success has prompted the expansion of stent usage to peripheral arteries, the urethra, trachea, esophagus, and gastrointestinal tract.[1] Reports of resorbable and nonresorbable polymeric stents have recently appeared. The rationale for nondegradable stents is improved biocompatibility over the metal stent and convenient drug loading. Nonresorbable polymers being investigated for stent use include polyethylene terephthalate, polyurethane, and polydimethyl siloxane. The rationale for bioresorbable stents is support of body conduits only during their healing, delivery of drug and/or gene therapy agents from an internal reservoir to the surrounding tissue, and no need for surgery to remove the device. The most frequently used polymers for bioresorbable stents are aliphatic polyesters, such as poly(L-lactic acid) (PLLA), poly(glycolic acid) (PGA), and poly(ϵ-caprolactone) (PCL).[2]

Bioresorbable stents have been reported for a variety of applications.[3–5] Ye et al.[3] developed a tubular PLLA/PCL microporous stent for delivering gene transfer vectors to the arterial wall. Kemppainen et al.[4] reported a spiral PLLA stent, and Brauers et al.[5] described tubular PDLLA and poly(DL-lactic-co-glycolic acid) stents, both for urethral applications. None of these stents are expandable. Several early designs of expandable bioresorbable stents have been developed as alternatives for metallic stents.[6–9] Agrawal and Clark[6] developed and investigated a PLLA stent, based on a slotted polymer fiber design, that can withstand compression pressures of up to 1000 mmHg. *In vivo* studies have demonstrated minimal thrombosis and inflammatory responses and moderate neointimal growth. Gao et al.[7] have reported a PDLLA/PCL stent with an inner heparin layer, deployed with a

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balloon catheter, employing heating and pressurization. This stent produced mild neointimal proliferation in swine carotid artery models after 2 months. Yamawaki et al.[8] reported a PGA coil stent that exhibited thrombus deposition in canine implant studies, but no subacute closure. Tamai et al.[9] described a bioresorbable PLLA zigzag coil stent used in a human coronary artery. This stent required a combination of heating and pressurization for expansion. A film-based expandable stent containing dexamethasone has been developed and studied.[10,11] This stent, designed as a tracheal stent for supporting the neonatal trachea, demonstrated very good mechanical properties. Preliminary *in vivo* studies demonstrated good proof of principle and tolerable biocompatibility.

A novel multiple-lobe, expandable, bioresorbable stent made of PLLA fibers, for coronary application, has been reported.[1,12–14] The stent fabrication method, its mechanical properties, *in vitro* degradation, and approaches to improve its biocompatibility were described. This fiber-based stent demonstrated excellent initial radial compression strength and good *in vitro* degradation resistance, which makes it applicable for supporting blood vessels for at least 20 weeks. Furthermore, a method was developed to incorporate drugs and protein into the stent without affecting its mechanical properties.[14] The present research explores the expansion of this stent design to other possible applications by using additional bioresorbable polymers. It focuses on the mechanical properties of polydioxanone (PDS) and poly(glycolide-co-ε-caprolactone) (PGACL) fibers and stents prepared from these fibers. The effect of *in vitro* degradation on the mechanical properties of the fibers and stents was also studied. The chosen polymers, PDS and PGACL, exhibit moderate and fast degradation rates, respectively. The results are compared with those of the PLLA fibers and stents, which degrade relatively slowly.

EXPERIMENTAL

Bioresorbable Fibers

Bioresorbable poly(L-lactide) (PLLA) fibers were prepared from a relatively high molecular weight polymer, RESOMER L210 (inherent viscosity = 3.6 dL/g in $CHCl_3$ at 30°C), Boehringer Ingelheim, Germany. The PLLA fibers were melt-spun at 190°C in a batch mode (Alex James, Greer, SC) and then drawn at 80°C to a draw ratio of 8:1. PDS II™ monofilament sutures (Ethicon, Inc.) were used as polydioxanone (PDS) fibers. MONOCRYL™ monofilament sutures, copolymer of glycolide and ε-caprolactone (Ethicon, Inc.), were used as poly(glycolide-co-ε-caprolactone (PGACL) fibers. Initial diameters were 0.15 mm for the PLLA and PDS fibers and 0.20 mm for the PGACL fiber.

Expandable Stent Preparation

A four-lobe fiber-based stent was designed with the use of a linear, continuous coil array principle, by which four furled lobes convert to a single large lobe upon balloon expansion.

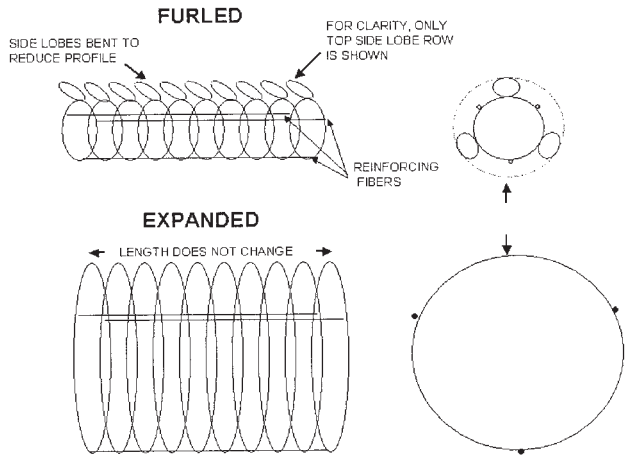

Figure 1. A schematic diagram showing the stent design and manufacturing. The coil fiber is wound continuously over four mandrels to obtain the four-lobe structure (one central, three peripheral). The side lobes are flattened passively or by using a sheath during delivery. These lobes can also be wound inside the basic coil to reduce the profile during delivery. Both designs open readily upon balloon expansion.

Fibers were woven continuously around a four-mandrel array (one central, three peripheral) into a four-lobe configuration. Three longitudinal fibers were interwoven and glued to the coil for mechanical support. The glue used here was a relatively viscous solution of PLLA in chloroform. It was applied at the binding sites, that is, at the interfaces between the coil fiber and the longitudinal support fibers. After fabrication, a conventional angioplasty balloon catheter was inserted in the central lobe and the stent was deployed. A pressure of 3 atm was used to fully expand the furled stent to its final dimensions. The structure of the fully expanded stent is that of a helical coil with three longitudinal reinforcing fibers. A schematic diagram showing the basic elements of this stent design and manufacturing is presented in Figure 1. The initial and final diameters of the stents are adjustable by various combinations of the sizes of the central and peripheral rod mandrels. Stents of 15-mm length, 3.0-mm final (dilated) diameter, and 1.8-mm predilated diameter were used in this study. Both single- and double-fiber designs were investigated for PLLA stents, whereas only a single-fiber design was investigated for PDS and PGACL stents.

Mechanical Property Measurements of Bioresorbable Fibers and Stents

The mechanical properties of the fibers were measured at room temperature in unidirectional tension at a rate of 50 mm/min (ASTM D 638-98), with the use of a Universal Testing System machine, MTS Systems Corporation, Eden Prairie, MN. The tensile strength was defined as the maximum strength in the stress–strain curve, the maximal strain as the breaking strain, and Young's modulus as the slope of the stress–strain curve in the elastic (linear) region. Five samples were tested for each point. The mean values and standard

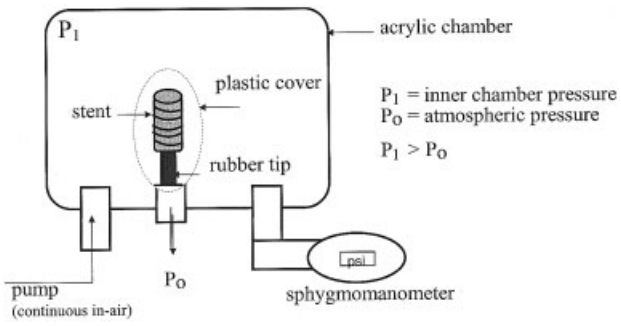

Figure 2. A schematic representation of the radial compression test chamber (see text for a description).

deviations are presented in the graphs. Fiber samples were immersed in phosphate-buffered saline (PBS) (pH 7.4) at 37°C. Samples were removed every week, dried in a vacuum oven, and tested for deterioration of their tensile mechanical properties.

The radial compression strength of stents formed from fibers was measured with the use of a special chamber constructed in the laboratory. This chamber, described in Figure 2, permits the application of hydrostatic pressure to the external surface of the stent. A dilated stent is located on a rubber tip and a small plastic bag, placed over it, is closed airtight with wire. The chamber is ported to a manual air pump for pressurization, and a sphygmomanometer is used to measure the pressure in the chamber. The external surface of the stent was exposed to the pressure in the chamber while the internal surface of the stent was exposed to atmospheric pressure. The pressure difference across the stent wall was increased gradually, and the resulting changes in the stent shape and diameter were observed. Stents were immersed in PBS (pH 7.4) at 37°C. Samples were removed every week, dried in a vacuum oven, and tested for deterioration in their radial compression strength.

Morphological Characterization

The fibers were observed using a Jeol JSM 840A scanning electron microscope (SEM) at an accelerating voltage of 5 kV. The SEM samples were Au/Pd sputtered prior to observation.

In Vitro Retention of Weight

The polymer fibers were weighed and then immersed in PBS (pH 7.4) at 37°C in order to determine retention of their weight profile. Samples were removed every week, dried in a vacuum oven, and weighed. The weight retention was calculated as

$$\text{Weight retention } (\%) = 100 \times \left(1 - \frac{w_0 - w_f}{w_0}\right), \qquad (1)$$

where w_0 and w_f are the weights of the dried fibers before and after exposure to water, respectively. Five samples were tested for each point. The mean values and standard deviations are presented in the graphs.

RESULTS AND DISCUSSION

Bioresorbable Fibers

The bioresorbable polymers chosen for this study enable a variety of degradation times. Poly(L-lactic acid) (PLLA) is one of the most important biodegradable polymers, and is used in a wide range of clinical applications, such as devices for orthopedic[15–17] and cardiovascular surgery,[18] sutures,[19] and as drug-delivering implants.[20,21]

PLLA is a very good choice for the first three mentioned applications, where high mechanical strength and toughness are required. This polymer can be formed into films, fibers, tubes, and matrices using standard processing techniques such as molding, extrusion, spinning, and solvent casting.[19] Its total degradation time is approximately 24 months.

Polydioxanone (PDS) has gained increasing interest in the medical and pharmaceutical fields due to its excellent biocompatibility.[19] It has been introduced into the market as a suture and as a bone pin (ORTHOSRB[22,23]). Its total degradation time is 6 months. Poly(glycolic-co-ε-caprolactone) (PGACL, trade name: Monocryl) is a block copolymer of glycolide and ε-caprolactone. This unique bioresorbable polymer degrades completely within 3-4 months. It offers reduced stiffness compared with pure poly(glycolic acid) and has been introduced into the market by Ethicon as a monofilament suture (Monocryl).

The initial stress–strain curves of the three polymers are presented in Figure 3 and their exact tensile mechanical properties are presented in Table I. PLLA exhibits a yield point (Figure 3), whereas the other two polymers, PDS and PGACL, do not demonstrate a clear yield point and may therefore do not undergo any plastic deformations. PLLA

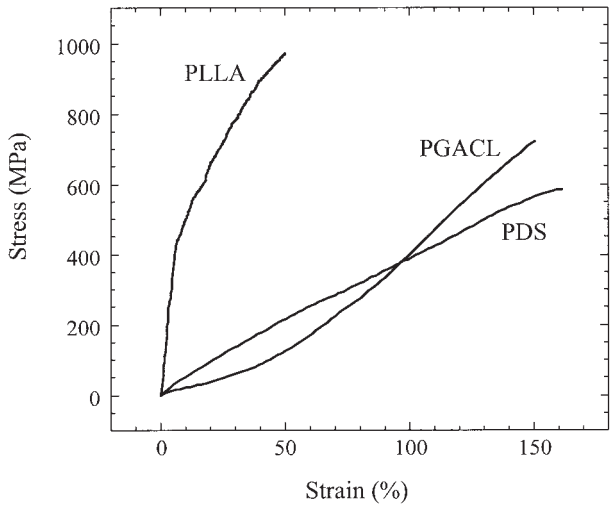

Figure 3. Stress–strain curves of bioresorbable fibers. The materials are indicated.

TABLE I. Tensile Mechanical Properties of Bioresorbable Fibers

Fiber	Tensile Strength (MPa)	Modulus (MPa)	Strain (%)
PLLA	967	5,000	50
PDS	583	367	161
PGACL	721	477	151

demonstrated a very high tensile strength and modulus and a moderate ultimate strain (ductility), PDS showed moderate tensile strength and modulus and a relatively high ductility, and PGACL exhibited high tensile strength and ductility and moderate modulus. The tensile strengths and modulus values of PDS and PGACL are similar to those that appear in literature.[24] These three polymers are thus totally different from each other and exhibit a relatively large variety of initial mechanical properties. It should be emphasized that in order to be able to produce stents from these fibers they should combine relatively high strength with sufficient ductility and flexibility. All three fiber types exhibited these required properties.

The fibers were immersed in PBS at 37°C, and samples were removed every week in order to investigate the effect of their *in vitro* degradation on their mechanical properties. The tensile strengths, moduli, and strains of the three polymers as a function of degradation time are presented in Figure 4(a–c), respectively. As expected, PLLA, which has the lowest degradation rate, exhibited almost no change in mechanical properties during the 6 studied weeks; that is, its good mechanical properties are preserved for at least 6 weeks. A previous study [14] showed that PLLA fibers still retain good mechanical properties even after 24 weeks of degradation in aqueous medium. Their tensile strength decreased from 967 to 676 MPa, Young's modulus from 4500 to 4100 MPa, and ultimate tensile strength: from 50 to 32%. Thus, they preserved good strength and flexibility. Although PDS has moderate initial tensile strength and modulus, it lost only approximately 30% of its initial strength in 3 weeks and 60% of its initial strength in 6 weeks of degradation (Figure 4). The 3-week result is in agreement with the manufacturer's (Ethicon) results and other studies,[24] but the 6-week result is different. The literature shows a strength loss of 75%. This difference probably results from different test conditions. The fibers in this study were tested *in vitro*, whereas the manufacturer tested them *in vivo.* Under *in vivo* conditions degradation of PDS by microorganisms may occur in addition to the chemical degradation by water. That is, the sutures were in contact with the typical inflammatory/immunological response of the organism and to other agents (such as enzymes) that speed up the degradation process of PDS. In contradistinction, PGACL, which demonstrated a relatively high initial tensile strength and ductility, totally lost its strength and modulus after 3 weeks of degradation [Figure 4(b)]. The results are in agreement with those obtained by the manufacturer (Ethicon) and other researchers,[24] who suggest that this polymer has 50–60% strength retention after 1 week of degradation and 20–30% after 2 weeks of degradation.

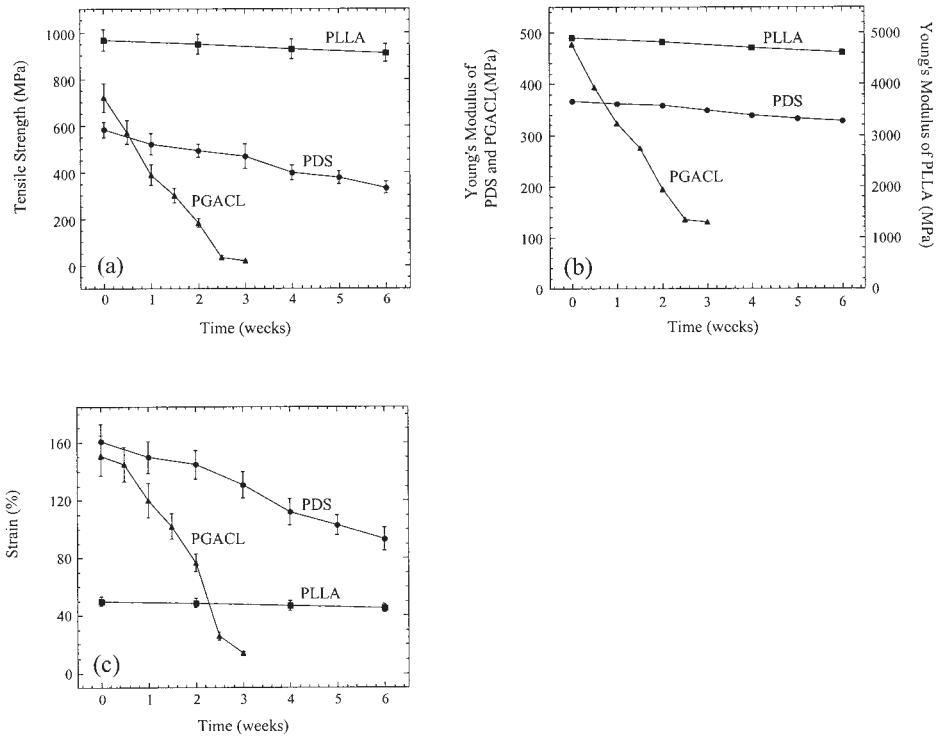

Figure 4. Tensile mechanical properties of: PDS (circles), PLLA (squares), and PGACL (triangles), as a function of degradation time in PBS at 37°C: (a) strength, (b) Young's modulus, (c) strain.

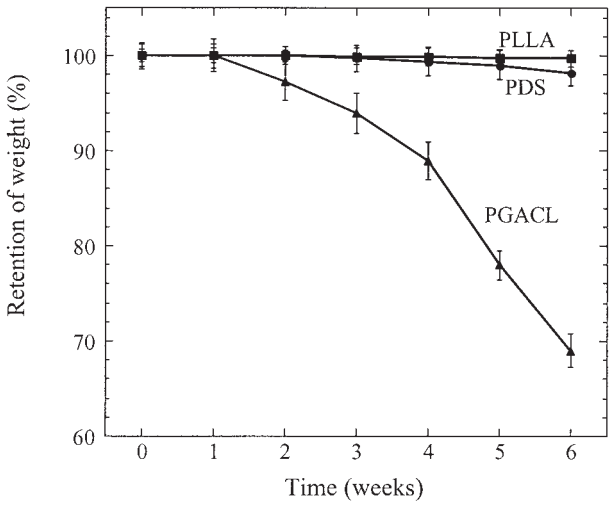

Figure 5. Retention of weight as a function of degradation time in PBS at 37°C: PDS (circles), PLLA (squares), and PGACL (triangles).

The weight-retention profiles of the three fibers are presented in Figure 5. PLLA did not exhibit any weight loss due to exposure to the aqueous medium during the 6 weeks of study, PDS lost approximately 2% of its initial weight, and PGACL gradually lost 30% of its initial weight within 6 weeks of immersion in aqueous medium. SEM micrographs showing the structure of the fibers after 6 weeks of degradation are presented in Figure 6. The PLLA fiber exhibited a smooth surface [Figure 6(a)], whereas the characteristic features of the PDS fiber showed small particles on its surface [Figure 6(b)]. These fragments probably resulted from surface delamination after a certain degree of degradation. After 6 weeks of degradation the PGACL fiber was torn into small pieces and therefore could not bear any load [Figure 6(c)]. When the internal parts of the fiber were exposed, it was found to be composed of many thin microfibrils in which the polymer chains are probably aligned in the direction of the fiber's axis.

Expandable Stents Prepared from Bioresorbable Fibers

As previously shown, all fibers exhibited high tensile strength and modulus combined with good ductility and flexibility. Stents were therefore prepared from these fibers. The design consisted of a linear, continuous coil array principle, by which four lobes convert to a single large lobe upon balloon expansion, as presented in Figure 7. Three longitudinal fibers were interwoven and glued to the coil for mechanical support. As a result, the structure of the fully expanded stent was that of a helical coil with three longitudinal reinforcing fibers, as shown in Figure 7(b,d).

The initial and final diameters of stents are adjustable by various combinations of the sizes of the central and peripheral rod mandrels. Stents with 15-mm length, 3.0-mm final (dilated) diameter, and 1.8-mm predilated diameter were used in this study. Most of the study focused on single-fiber stents, but PLLA double-fiber stents were also investigated. Each dilated coil stent contained 12 loops, each bonded to three longitudinal support fibers, that is, 36 binding points per single-fiber stent and 72 binding points per double-fiber stent. The initial radial compression strength of the dilated form of

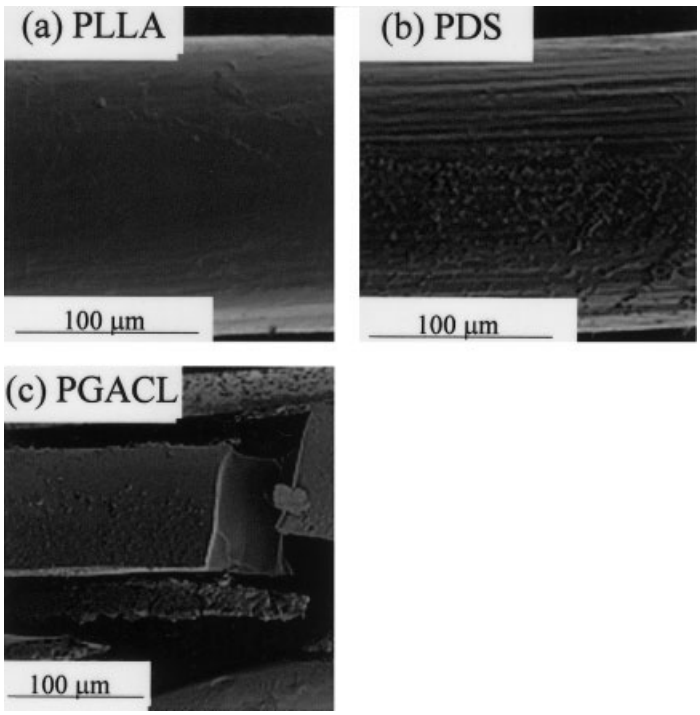

Figure 6. SEM micrographs of: (a) PLLA, (b) PDS, and (c) PGACL fibers, after 6 weeks of degradation in PBS at 37°C.

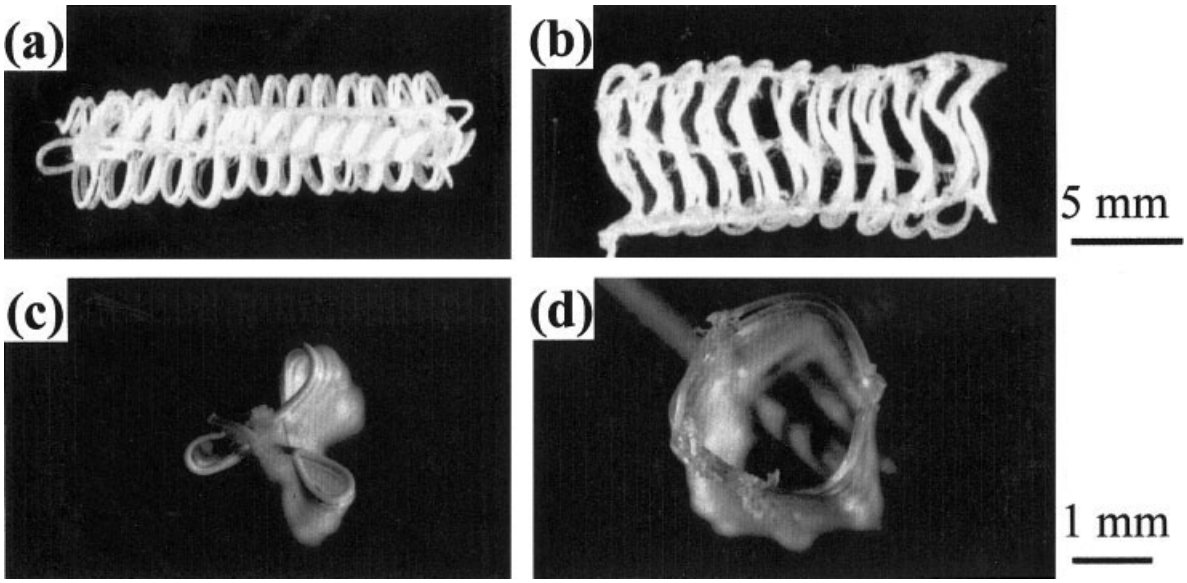

Figure 7. The expandable stent: (a) predilated; (b) dilated; (c) predilated, side view; (d) dilated, side view.

both types of stents was greater than 200 kPa. It should be mentioned that the maximal pressure that can be applied with the radial compression chamber used is 200 kPa. Higher pressures could therefore not be measured.

The stents were immersed in PBS at 37°C, and samples were removed periodically in order to investigate the effect of their *in vitro* degradation on their mechanical properties. The mode of failure observed was rupture of binding points, where the longitudinal support fibers were glued to the coil. The radial compression pressure needed in order to create a rupture of at least one binding point, in all types of stents, as a function of degradation time is presented in Figures 8 and 9. The number of ruptures (binding points that failed) for each degradation time is indicated in parentheses. The stents were observed under low magnifications after the pressure was released, and it appeared that they did not exhibit any distortion, even after rupture of several binding points.

The PLLA stents were studied for 20 weeks. Both single- and double-fiber types of stents did not undergo any failure throughout the first 8 weeks of exposure to aqueous medium. Afterwards, the radial compression pressure required to create a rupture at binding points exhibited a linear decrease with time, and the number of ruptures increased with time (Figure 8). Because the double-fiber design has more binding points than the single-fiber design, each binding point of the former is exposed to a smaller pressure. Thus, a higher total pressure is required to fail the double-fiber stent. In general, these stents exhibited good radial compression endurance. They resisted at least 150 kPa (approximately 75% of the initial strength), and exhibited only a few rupture points, while most of the binding points remained intact. The combination of the suggested design and the relatively high molecular weight PLLA may thus be applicable for supporting blood vessels for at least 20 weeks, and was chosen for further studies.

There is no ready answer for the question of how much compression resistance is sufficient. Lieu et al.[25] tested the mechanical performance of 17 intracoronary stent designs *in vitro*. None of these expanded stents deformed noticeably at radial compression pressures up to 30 kPa (0.3 atm). Beyond that pressure, stent compression performance differed. Because all 17 metal stents were already clinically proven to be capable of maintaining coronary artery patency, 30 kPa may be considered to be minimum required compression resistance for coronary applications. The current polymeric expandable stent design passes this minimum requirement, and its initial radial compression strength is higher than 200 kPa. Moreover, the radial compression strength of the PLLA stents is higher than 150 kPa after 20 weeks of degradation. Thus, this stent fulfilled the minimum requirement.

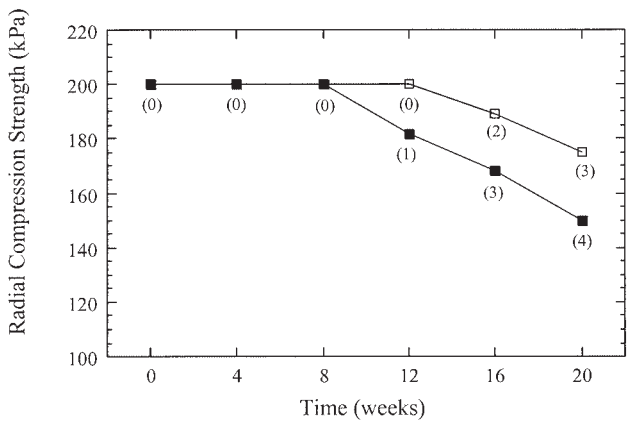

Figure 8. The radial compression strength of PLLA stents as a function of degradation time in PBS at 37°C: single-fiber design (solid squares), and double-fiber design (open squares). The number of ruptured points is indicated.

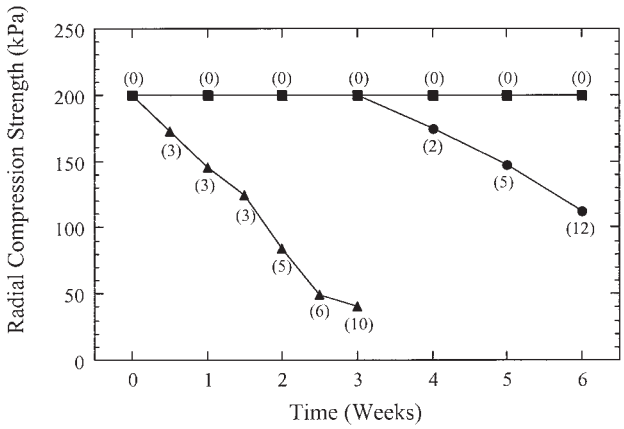

Figure 9. The radial compression strength of single-fiber bioresorbable stents as a function of degradation time in PBS at 37°C: PLLA (squares), PDS (circles), and PGACL (triangles). The number of ruptured points is indicated.

The radial compression strength as a function of degradation time for PDS and PGACL single-fiber stents compared to that of PLLA stents is presented in Figure 9. The PDS stents began losing mechanical strength after 3 weeks of degradation, but preserved good strength for 6 weeks. In contradistinction, PGACL demonstrated a faster decrease in radial compression strength (the slope of the curve) that began immediately after exposure to the aqueous medium. This study thus indicates that PLLA stents can support body conduits for relatively long periods of time (20 weeks) and can therefore be used as endovascular stents. PDS stents can afford good support for 5–6 weeks, and PGACL stents can be applied for only 2 weeks. PDS and PGACL stents are therefore utilizable for short-term applications, such as local support of the urinary track after surgery, as well as after other interventions.

PDS fibers lost 50% of their tensile strength after 6 weeks of degradation [Figure 4(a)] and PDS stents lost 44% of their radial compression strength (Figure 9). PGACL fibers lost 74% of their tensile strength after 2 weeks of degradation, and PGACL stents lost 60% of their radial compression strength; PGACL fibers and stents lost their strength completely after 3 weeks of degradation. The decrease in the radial compression strength of the stents corresponds to the decrease in the fiber's tensile strength. It should be noted that the weak points of this stent design are the binding points between circumferential and longitudinal fibers. These points tend to fail when the stent is exposed to external loading, and their rupture occurs even before the fiber undergoes any significant degradation. A more effective binding process that will be less sensitive to degradation should be developed in order to improve the stent strength. If such a binding process succeeds, the deterioration in the stent's radial compression strength will be slower than the deterioration in the fiber strength, as demonstrated with the film-based stent design.[10]

CONCLUSIONS

The present study focuses on the mechanical properties of bioresorbable fibers as well as medical support devices (stents) developed from these fibers. Fibers made of poly(L-lactide) (PLLA), polydioxanone (PDS), and glycolide-co-ε-caprolactone (PGACL) were studied *in vitro*. Examination focused on the effect of degradation on the tensile mechanical properties and morphology. The effect of the polymer's degradation on the radial compression strength of the stents was also studied.

The three studied fibers combine a relatively high initial strength and modulus together with sufficient ductility and flexibility. These fiber properties enable stent preparation and are also required for high-strength stents. Degradation studies of these fibers indicate that PLLA undergoes slow degradation and can therefore preserve good mechanical properties for 24 weeks. Despite losing 2 wt %, PDS partially preserves its mechanical properties for 6 weeks, whereas the PGACL fiber totally loses its strength after 3 weeks, because of a high degradation rate.

The expandable stents developed from these fibers demonstrated excellent initial radial compression strength. The PLLA stents exhibited very good *in vitro* degradation resistance and can therefore support body conduits such as blood vessels for prolonged periods of time. PDS and PGACL stents can afford good support for 5 and 2 weeks, respectively, and are therefore utilizable for short-term applications. The degradation resistance of the latter stents can be improved by using a double-fiber design and also by applying an effective binding process between the longitudinal fibers and the coils.

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