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The effects of tensile stress on degradation of biodegradable PLGA membranes: A quantitative study

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ABSTRACT

The inhomogeneous stress distribution of biodegradable stents after implantation affects the local degradation rate of the stents, leading to stress concentration and hence stent fracture. The quantitative relationship between the tensile stress and degradation rate of stent polymer is first investigated in this work. To implement the study, an in vitro degradation of poly(L-lactide-co-glycolide) (PLGA) membranes was incubated in deionized water under different applied tensile stress levels from 0.1 MPa to 0.5 MPa. By a special designed device, the tensile stress level can be maintained constant during degradation. The mass loss and mechanical properties of the membranes during the degradation were sampled each week until the membranes broke. The experimental results showed that over a range of tensile stress, higher tensile stress might lead to quicker loss of mechanical properties. Specifically, remarkable decreases of elastic modulus and tensile strength in 0.5 MPa group were observed. As the magnitude of tensile stress increased, more mass loss was observed in the loaded groups. In conclusion, the mass loss rate and mechanical properties of PLGA was sensitive to the tensile stress level during the in vitro degradation. The load dependency of our data demonstrates the importance of quantifying the effects of tensile stress on the degradation of biodegradable polymers. Moreover, this quantification model could be used as a prediction tool for the optimization of biodegradable polymer stents.

1. Introduction

The biodegradable polymers have been widely used in biodegradable stent (BDS). The BDS could release the sustained drug with degrading into nontoxic compounds [1,2]. It offers the potential to improve long-term patency rates by providing support just long enough for the artery to heal [3]. However, the stress distribution of BDS after implantation has shown to be quite non-uniform, which may cause the undesirable degradation and compromise the long-term function of the stent.

As demonstrated previously, the external environment where the degradation occurs influence degradation process greatly [4,5]. One of the most important factors is mechanical load [6–8]. In vitro experiments have reported that loading could accelerate the degradation of poly (glycolide-co-L-lactide) (PDLLA) [9], and the dynamic loading exhibited a significantly faster rate than that under static loading [10]. Moreover, the mechanical environment of the implanted stent was quite complicated, which make it difficult to control the degradation rate and predict the mechanical behavior of the stent. Thus, it is necessary to quantify the effects of mechanical load on the polymer degradation.

In order to clarify the impacts of load on polymer degradation, strain controlled [11]and stress controlled experiments [12]were carried out separately. As acknowledged by Deng et al. [13], strain controlled experiments resulted in stress relaxation of the polymer and a limit on its deformation, while stress controlled experiments may result in polymer creep and significant dimensional changes. Moreover, the creep loading during degradation attenuates mechanical property loss in PLGA [14]. Due to these outcomes, the

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effects of mechanical loads on the degradation rates have not been quantified. Once the BDS was implanted, the complex in vivo mechanical environment could cause non-uniform degradation and may lead to undesirable clinical function in long-term.

Therefore, the aim of this research is to develop a model to describe the relationship between the tensile stress and degradation rate of stent, by which we can also predict the mechanical behavior of stent during the polymer degradation. Different levels of tensile stress were applied on an exemplary biodegradable polymer, PLGA, during its vitro degradation. The relationships between tensile stress and mass loss, tensile strength, elastic modulus and the surface morphology of the membranes were investigated.

2. Materials and methods

2.1. Fabrication of the PLGA membranes

PLGA (with a copolymerization ratio of LA/GA = 50/50) with molecular weight of 9×10^4 was supplied by Jinan Daigang Biomaterial Co., Ltd. PLGA membranes were prepared by a solvent-casting method. Every 1500 mg of PLGA powders were put into 25 ml chloroform to produce a polymer weight to solvent volume ratio of 6% (w/v). After the dissolution, the solution was poured into a customized glass mould (60 mm length × 5 mm width) which was fixed on a horizontal table. The membranes with thickness of 0.2 mm were cut into strips of 60 mm in length and 5 mm in width.

The average initial elastic modules of samples were measured as 441.5 ± 39.9 MPa, and the average tensile strengths were 4.57 ± 0.15 MPa. The smooth and transparent PLGA test-piece was stored at −20 °C.

2.2. Experimental device

The loading device was showed as Fig. 1. The device consists of one organic glass pedestal and two stainless steel grips to fix the specimens and hang the weights. The grip on the downside is fixed on the organic glass pedestal directly; the other side is connected with the weights. The values of applied stress can be regulated by changing the weight.

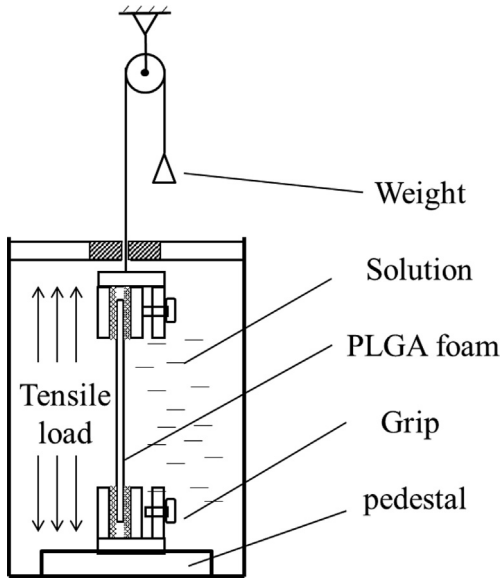

Fig. 1. Self-made load-providing device.

2.3. In-vitro degradation experiments

To investigate the influence of tensile stress on degradation, five constant loadings (0.1, 0.2, 0.3, 0.4, 0.5 MPa) were applied to the specimens by hanging a dead weight during the in vitro experiments. Due to the creep of the polymer, the weights were changed with the cross-sectional area to ensure the constant tensile stress. Another group without loading was taken as the control group. Each group has five samples. All PLGA specimens were immersed in deionized water (pH, 7.4). The degradation of PLGA was carried out in a super-clean lab at room temperature of 25 °C. The pH values of the deionized water were closely monitored during the experiments. Although no measurable changes in pH were observed, the solution was changed at least once a week. At each degradation time point, specimens were removed from solution and evaluated for mass loss and strength retention.

2.4. Morphologies

Environmental Scanning Electron Microscopy (ESEM) (Quanta FEG 250, FEI) was employed to observe the surface morphology of PLGA specimens at 1200× magnification as they degraded over time. ESEM observation was carried out at 30 kV. Before that, all the samples were washed with deionized water three times and then dried under vacuum at room temperature over 72 h.

2.5. Mechanical properties

Each specimen was cut into 50 mm long, 10 mm wide strips for mechanical test. The tensile elastic modulus E and tensile strengths σ of the specimens before and after in vitro degradation were measured using a materials testing machine (ElectroPuls™ E10000, INSTRON, USA). A 250N tension sensor was chosen, and measurements of the specimens were run at 1 mm/min. All tests were conducted at room temperature E and σ of PLGA were calculated according to the following expressions:

$$\mathrm{E} = \frac{Fl_0}{A\Delta l} \tag{1}$$

$$\sigma = \frac{F}{A} \tag{2}$$

Where

F is the tension load the specimen subjected (N),
l_0 is the original length of the tested specimens (mm),
A is the area of cross-section (mm^2) (measured at each sample interval before mechanical testing),
Δl is the elongation of the specimens (mm),

2.6. Mass loss

The solid specimen in deionized water solution was collected and dried until the masses were unchangeable. Then the masses were measured by a microbalance (Shanghai Balance Instrument Factory, JA1003). The mass loss was defined as

$$\text{Mass loss}(\%) = \frac{m_0 - m}{m_0} \times 100\% \tag{3}$$

Where m_0 is the weight of initial specimen and m is the weight of the degraded specimen after drying at room temperature.