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Research Paper

Characterization of load dependent creep behavior in medically relevant absorbable polymers

Maureen L. Dreher[a,*], *Srinidhi Nagaraja*[a], *Hieu Bui*[b,1], *Danny Hong*[b,2]

[a]US Food and Drug Administration, Center for Devices and Radiological Health, Office of Science and Engineering Laboratories, Division of Solid and Fluid Mechanics, 10903 New Hampshire Avenue, Silver Spring, MD 20993, USA
[b]CDRH Medical Device Fellowship Program, Center for Devices and Radiological Health, Office of Science and Engineering Laboratories, Division of Solid and Fluid Mechanics, 10903 New Hampshire Avenue, Silver Spring, MD 20993, USA

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ABSTRACT

While synthetic absorbable polymers have a substantial history of use in medical devices, their use is expanding and becoming more prevalent for devices where long term loading and structural support is required. In addition, there is evidence that current absorbable medical devices may experience permanent deformations, warping (out of plane twisting), and geometric changes *in vivo*. For clinical indications with long term loading or structural support requirements, understanding the material's viscoelastic properties becomes increasingly important whereas these properties have not been used historically as preclinical indications of performance or design considerations. In this study we measured the static creep, creep recovery and cyclic creep responses of common medically relevant absorbable materials (i.e., poly(L-lactide, PLLA) and poly(L-*co*-glycolide, PLGA) over a range of physiologically relevant loading magnitudes. The results indicate that both PLLA and PLGA exhibit creep behavior and failure at loads significantly less than the yield or ultimate properties of the material and that significant material specific responses to loading exist. In addition, we identified a strong correlation between the extent of creep in the material and its crystallinity. Results of the study provide new information on the creep behavior of PLLA and PLGA and support the use of viscoelastic properties of absorbable polymers as part of the material selection process.

1. Introduction

Aliphatic polyesters are the most commonly used raw materials for commercial absorbable medical devices in the United States as well as Europe and have been processed into sutures, suture anchors, interference screws, plates, fracture fixation systems (Middleton and Tipton, 2000), sinus stents, annuloplasty rings, and adhesion barriers. Specifically, poly (lactide) and poly(glycolide), as well as their copolymers, are used most extensively. Medical devices manufactured from aliphatic polyesters degrade through hydrolysis of the polymer backbone primarily through a bulk degradation process

*Corresponding author. Tel.: +1 301 796 2505; fax: +1 301 796 9932.
E-mail address: Maureen.dreher@fda.hhs.gov (M.L. Dreher).
[1]Currently with: Georgia Institute of Technology, Institute of Electronics and Nanotechnology, 971 Atlantic Dr NW, Atlanta, GA 30332.
[2]Currently with US Patent and Trademark Office, 401 Dulany St, Randolph Building, 4B65, Alexandria, VA 22314.

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that includes decline of molecular weight, reduction in mechanical properties, and loss of mass (Lyu and Untereker, 2009; Middleton and Tipton, 2000). The ability to tailor the absorption rate of a medical device through control of the polymer's molecular weight, residual monomer content, and crystallinity makes this an attractive system for medical device development (Middleton and Tipton, 2000).

Specific polymers or copolymers are chosen for an intended device function and investigated pre-clinically for degradation kinetics, biocompatibility, and strength retention based on considerations of loading and biology at the implantation site (Mukherjee and Pietrzak, 2011). Traditionally, consideration of a device's strength performance over time is a primary consideration in the material selection process and is based on the kinetics of ultimate strength and/or stiffness loss according to standardized *in vitro* methods (e.g., ASTM F1635 (ASTM, 2009; International, 2009) that simulate hydrolysis in balanced salt solutions for an unloaded configuration. In contrast, detailed characterization of the mechanical behavior under long-term loading is not commonly completed for absorbable medical devices, even though they may be exposed to long term loading *in vivo* and failure driven by these loads is possible prior to degradation.

Characterization of the long term loading behavior in absorbable materials is critical for enhancing design and predicting failure not only for existing devices but also for emerging devices, such as tissue engineering scaffolds (Gloria et al., 2010; Gunatillake et al., 2006), spinal cages (Wuisman and Smit, 2006), and cardiovascular stents (Doyle and Holmes, 2009; Gonzalo and Macaya, 2012). While the overall failure rate for absorbable devices due to mechanical complications is generally considered to be low, there is evidence that absorbable implants have warped (exhibited out of plane twisting), bent (Brkaric et al., 2007; Nieminen et al., 2008) or developed significant unintended permanent deformations *in vivo* (Krijnen et al., 2006, 2004). These *in vivo* observations suggest that investigation of the long term loading performance for absorbable polymers is relevant to understanding the possible failure modes prior to degradation and adequately guiding material selection. In addition, recent evidence also suggests that the long term loading behavior of a polymeric device may influence the local biological response (Cameron et al., 2011), further supporting the need for long term characterization.

Distinct from metal medical devices, devices fabricated from absorbable and non-degradable polymers exhibit viscoelastic behavior and may be sensitive to time dependent failure through the accumulation of plastic deformation and creep rupture (Klompen et al., 2005; Schnabel, 1992). This study focuses on creep in absorbable polymers due to possible interactions between loading and degradation as well as the extensive use of absorbable polymers in existing and emerging devices with structural roles. In addition, exposure to mechanical loading can alter the molecular structure and/or degradation rate of absorbable polymers (Klouda et al., 2008; Li et al., 2010; Miller and Williams, 1984; Schnabel, 1992; Smutz et al., 1991; Zhong et al., 1993), which can in turn affect performance. Creep processes may not only induce macroscopic failure but can also limit structural performance prior to fracture through geometric changes. Therefore, investigation of creep accumulation and failure in absorbable materials and devices is an important component of design and pre-clinical evaluation, especially with the growing use of absorbable medical devices in loaded environments.

In general, data on the creep behavior of absorbable medical devices or their raw materials is limited. Early creep investigations into scaffolds manufactured through solvent-casting and particulate leaching from PLLA and P(D,L)GA suggested that the behavior may be material specific, at least at very low loads (Mikos et al., 1993). More recently, studies of absorbable craniofacial plates and spinal cages suggest that the creep rates are load dependent and that rupture can proceed well before the estimated degradation time (Engels et al., 2010; Pietrzak, 2012; Smit et al., 2010, 2008). While these studies provide useful creep information, the results are most applicable for the specific form of medical device studied and do not characterize creep from a material perspective or investigate its ability to recover from creep accumulation. The objective of the current study was to characterize the static and cyclic creep and recovery behavior for common medically relevant absorbable polymers over a range of load levels. A second objective of this study was to identify possible load and material dependencies of the creep response.

2. Materials and methods

2.1. Materials

Poly(L-lactide), i.e., PLLA (Resomer L210S) and poly(L-lactide-*co*-glycolide), i.e., PLGA (Resomer LG855S, 85:15) were acquired from Boehringer Ingelheim (currently, Evonik, Steinau, Germany) and injection molded into ASTM Type *V* tensile bars (Vaupell Inc., Constantine, MI) with a square cross section (3.25 mm per side) and an original gauge length of 9.53 mm. PLLA and PLGA were chosen based on their prevalence of use in medical devices and as being representative of polymers with moderate or nearly absent crystallinity, respectively. The 85:15 PLGA was chosen over other PLGA compositions because its initial inherent viscosity range was similar to that of the PLLA. Tensile bars from a single lot of each material were used for all creep evaluations. The inherent viscosity post molding was confirmed by the manufacturer to be ~2.5 dL/g and measured by gel permeation chromatography to have a poly(styrene) equivalent weight average molecular weight of ~250–300 kDa (PDI=1.4–1.7) for both materials.

2.2. Fluid equilibration

Prior to all mechanical testing, PLGA and PLLA tensile bars were allowed to uptake water while fully immersed in an environmental chamber at 37°C and 70% relative humidity over a 3 day period until a near constant mass was obtained (less than 0.25% change from prior day). Due to the relatively high initial molecular weight of the specimens, significant degradation did not occur during this time frame.

2.3. Monotonic characterization

In order to determine the relevant range of forces to apply during creep experiments, a subset of specimens ($n=4$ per