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Material Properties

Experimental mechanical testing of Poly (L-Lactide) (PLLA) to facilitate pre-degradation characteristics for application in cardiovascular stenting

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ABSTRACT

Next-generation stents made from Biodegradable Polymers (BPs) aim to address the long-term risks (i.e. late restenosis and in-stent thrombosis) associated with both Bare Metal Stents and Drug Eluting Stents, whilst aiming to reduce the healthcare costs associated with secondary care. However, the true potential of BPs for cardiovascular load bearing applications does not appear to be fully realised. While the literature provides data on stiffness and strength of BPs, it is lacking pre-degradation experimental data on the recovery behaviour and temperature and strain rate dependency. In this paper, an experimental study is undertaken to address this knowledge gap using Poly (L-Lactide) (PLLA) samples, subjected to tensile testing. Stress-strain characteristics, recovery, relaxation and creep data at body temperature are reported and considered in the context of real-life stent deployment. The experimental data herein reveal a strong temperature and strain rate dependency, whilst demonstrating associated plasticity within the material. The work provides a physical evaluation of PLLA's pre-degradation behaviour, establishing key data points to allow the assessment of PLLA as a viable material in the wider context of stent deployment and load carrying capacity.

1. Introduction

Biodegradable Polymers (BPs), in particular Poly (L-Lactide) (PLLA), have emerged as a favourable choice for use in orthopaedics and interventional cardiology medical devices [1,2]. On a small clinical scale, PLLA's reliability as a viable stent material, chosen to overcome complications experienced with conventional metal stents (e.g. restenosis and thrombosis), has been demonstrated [3]. More specifically, the potential attractiveness of PLLA is confirmed by the commercialisation of the first fully biodegradable polymer stent "Absorb" (Abbott Vascular, USA), whilst there are a number of other competitive products in the pipeline [4–6]. To date, the benefits of non-permanent stents are increasingly recognised and widely reported in numerous publications [7–9]. The main advantages include (i) reduced in-stent restenosis, (ii) minimisation of late thrombosis risk, and (iii) reduction in restriction that the flexibility of a polymer affords for artery expansion and contraction, minimising physical changes in everyday function [10].

Given these recent advancements coupled with the capabilities of simulation software, it could be assumed that the mechanical performance of PLLA in the context of the stent application is understood and widely reported. However, this is far from being the case due to the confidential nature of the medical device industry, further complicated by the small volume and short-term existence of these products on the market. As a consequence, there is still a substantial lack of knowledge regarding the loading capacity, plastic deformation, recovery and general behaviour of PLLA, as reported by Bobel et al. [11]. Such mechanical uncertainty poses unpredictable risks as the loading characteristics are vital for safe and effective clinical performance of cardiovascular stents. A lack of confidence in reliable performance has had a negative impact on BPs becoming a disruptive technology as an alternative to BMS and DES [7]. The capability of computational modelling is also compromised; without this accurate experimental data, simulative design optimisation studies cannot reach their full potential (i.e. reduce costs, predict long-term performance, inform decisions based on reliability, etc.).

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A number of clinical trials that may help our understanding and generate further confidence in bioabsorable stents are either underway or in the planning phase. Abbott Vascular recently announced a clinical trial involving 3000 patients for their next generation stent, the Absorb IV [12]. The Amaranth FORTITUDE stent successfully completed clinical trials and further studies for the second-generation FORTITUDE stent are planned [13]. Elixir DESolve and REVA Fantom completed first-in-man trials and additional clinical trials involving >100 patients [14,15]. In contrast, there are no clinical performance progress reports published recently on the Arterial Remodelling Technologies (ART) stent or the first fully bioabsorable stent, the Igaki-Tamai stent. Interestingly, a recent study by Varcoe et al. [16] indicates a high Target Lesion Revascularisation (TLR) rate in the long term study of the Igaki-Tamai stent, strongly suggesting that this particular stent system is not suitable for clinical consideration.

The existence and increasing availability of degradation performance data for PLLA is apparent [17], unfortunately, this is not the case for pre-degradation mechanical performance data. For example, PLLA is known to degrade slowly (>24 months), meaning it can provide mechanical stability for >6 months [18,19]. The limited amount of pre-degradation data is surprising when considering the importance of loading capacity, plastic deformation and recoil at stent deployment. More specifically, the mechanical properties of PLLA, such as elastic modulus, mechanical strength and ductility, are of major interest and importance when the material is subjected to high loads during stent deployment [20]. The mechanical properties are strongly related to the physical properties of the material, e.g. molecular weight, inherent viscosity and crystallinity, as well as melting and glass transition temperatures [21]. The molecular weight of a polymer strongly affects the mechanical behaviour and degradation rate [20]. The inherent viscosity is linked to the molecular weight defined by the Mark–Houwink equation [22], and an increasing molecular weight leads to a rise in inherent viscosity. The deployment instructions for Abbott's Absorb stent suggest a slow and gradual expansion with a balloon pressure increase of 2 atm every 5 s to a maximum pressure of 16 atm. This indicates a dependency of the material behaviour on the deployment rate.

There are a limited number of experimental studies evaluating the mechanical performance of pure PLLA. Among the few reports that are available, Grabow et al. focused on the stent application and examined various different mechanical characteristics of fully polymeric PLLA stent deployment (stent recoil and shortening, pressure vs. diameter change and creep at constant pressure) [23]. An earlier study by Grabow et al. investigated mechanical properties of rod and dumbbell samples of pure PLLA and PLLA/TEC [24]. A retardation curve (creep and relaxation behaviour), as well as modulus and tensile strength, with modulus variation as a function of temperature, were presented. A study by Eswaran et al. [25] presented cyclic data of a PLLA single stent ring element. Wong et al. [26] reported strain rate dependency of PLLA at body temperature and stress-strain behaviour at body temperature and glass transition temperature (50 °C). In contrast, the change in properties during degradation for PLLA has been more extensively studied, for example [17,27]; consideration was also given to a variety of material compositions of PLLA, and how these combinations could enhance performance in comparison to pure PLLA.

Given the lack of full mechanical characterisation data for pure PLLA material pre-degradation, there is an absence of a comprehensive reported evaluation of PLLA in relation to the loading histories that are experienced during real-life stent deployment, and this has hindered the progression of the use of this material. Specific characterisation data such as that related to unloading behaviour, including recoverable elastic strain, viscoelastic strain and permanent plastic deformation, are largely absent in the reported literature. The authors strongly believe that the presentation of such data can facilitate the development of enhanced BP stents by addressing the gap in reported knowledge and the related uncertainty of performance prediction.

In view of the limitations summarised above, this paper presents an experimental characterisation of PLLA material relevant to the stent application in the pre-degradation state. The study focuses on mechanical performance, i.e. stress-strain behaviour, addressing strain rate dependence, relaxation, recovery, temperature dependence and plastic deformation. It is acknowledged that temperature dependent data is vital for accurate stent deployment assessment. Such data can vary between room temperature (pre-implantation) and values exceeding normal body temperature up to 42 °C (possible reaction/inflammation to the implant). To this end, the significant role of temperature variation and strain rate dependency is reported.

2. Materials and methods

2.1. Material

The PLLA polymer used in this study, Purasorb® PL 65, was supplied by Corbian-Purac Biomaterials (Gorinchem, Netherlands) in granular form. This high molecular weight PLLA has an inherent viscosity of 6.5 dL/g and a molecular weight of 481,500 g/mol. The solvent dichloromethane (DCM) was purchased from Sigma-Aldrich (County Wicklow, Ireland).

2.2. Sample preparation

Test specimens were prepared by solvent casting. PLLA was dissolved in DCM with a concentration of 0.03 g/ml (see Fig. 1) at room temperature under constant stirring over a period of 72 h or until fully dissolved. The solution was then poured into a glass petri dish with a diameter of 10 cm to generate a thin film sheet with a thickness of 200 μm (±30). The dish was covered with a lid until the DCM was fully evaporated, which was subsequently confirmed by a constant weight of the PLLA sheet.

The authors are cognisant of the potential impact that the manufacturing technique can have on the mechanical performance of the material. The solvent casting method was selected as a proven thin film production technique for tensile sample preparation, ensuring the preparation of uniform specimens of a stent application size-scale. The ease of use of this method allows faithful control of thickness throughout the sample. However, it is acknowledged that there is a range of component/device manufacturing processes that could be used in practical application and that these would have an impact on mechanical properties.

Dumbbell shaped specimens were cut from the thin sheet with a gauge length of 10 mm (±0.3) and a width of 4 mm (±0.5) (according to ISO 527-3 and ISO 527-1) for mechanical testing. A stiff rubber pad was glued on each end of the specimen to help avoid slip during testing. A number of grips were examined prior to the experiments described below. A glued rubber strip was found to prevent slippage with reasonable reliability.

2.3. Testing

2.3.1. Equipment

A Zwick bi-axial tensile testing machine (Zwick, Ulm, Germany) with a 100N load cell, TestXpert software, and a connected video extensometer with VideoXtense software was used, in uni-axial mode, to determine the mechanical performance of the material. Specimens tested at temperatures higher than room temperature