



Through-thickness control of polymer bioresorption via electron beam irradiation

Marie-Louise Cairns^{a,*}, Alice Sykes^a, Glenn R. Dickson^b, John F. Orr^a, David Farrar^c, Arthur Dumba^d, Fraser J. Buchanan^{a,*}

^aSchool of Mechanical and Aerospace Engineering, Queen's University Belfast, Belfast BT9 5AH, UK

^bSchool of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast, Belfast BT9 7BL, UK

^cSmith & Nephew Group Research Centre, York Science Park, Heslington, York YO1 5DF, UK

^dIsotron Ltd., Thornhill Road, South Marston, Swindon SN3 4TA, UK

ARTICLE INFO

Article history:

Received 7 June 2010

Received in revised form 4 August 2010

Accepted 8 September 2010

Available online 16 September 2010

Keywords:

Bioresorption

Electron beam

Degradation

Poly(lactic acid)

Surface modification

ABSTRACT

Predicable and controlled degradation is not only central to the accurate delivery of bioactive agents and drugs, it also plays a vital role in key aspects of bone tissue engineering. The work addressed in this paper investigates the utilisation of e-beam irradiation in order to achieve a controlled (surface) degradation profile. This study focuses on the modification of commercially and clinically relevant materials, namely poly(L-lactic acid) (PLLA), poly(L-lactide–hydroxyapatite) (PLLA–HA), poly(L-lactide–glycolide) co-polymer (PLG) and poly(L-lactide–DL-lactide) co-polymer (PLDL). Samples were subjected to irradiation treatments using a 0.5 MeV electron beam with delivered surface doses of 150 and 500 kGy. In addition, an acrylic attenuation shield was used for selected samples to control the penetration of the e-beam. E-beam irradiation induced chain scission in all polymers, as characterized by reduced molecular weights and glass transition temperatures (T_g). Irradiation not only produced changes in the physical properties of the polymers but also had associated effects on surface erosion of the materials during hydrolytic degradation. Moreover, the extent to which both mechanical and hydrolytic degradation was observed is synonymous with the estimated penetration of the beam (as controlled by the employment of an attenuation shield).

© 2010 Acta Materialia Inc. Published by Elsevier Ltd. All rights reserved.

1. Introduction

The current philosophy behind the development of biomaterials is that a material should no longer perform merely as a functional, but benign, replacement of tissue but rather as an interactive system capable of responding to the biological environment [1–4]. In this regard, bioresorbable polymers have shown significant potential due to their abilities to have their material properties manipulated. However, the real impact of their potential has only been realised in recent years and it is envisaged that they will have a significant impact in several fields, including drug delivery, tissue engineering and regenerative medicine.

Bioresorbable materials are defined as those that degrade via a process of removal by cellular activity and/or dissolution of a material into a biological environment [5]. To date, one of the most successful commercial applications of bioresorbable polymers is the use of poly(hydroxyacids) in orthopaedic applications [6,7]. More specifically, polylactic acid (PLA), poly(L-lactic acid) (PLLA), poly(L-lactide–DL-lactide) co-polymer (PLDL), poly(glycolic

acid) (PGA) and poly(lactide–co-glycolide) (PLG) have been used as tissue fixation devices (pins, rods, screws or plates) and as replacement tendons and ligaments. Although these bioresorbable polymers have shown a degree of bioactivity in vivo, i.e. allowing tissue in-growth, there remain a number of issues to be addressed in order to accomplish full exploitation of their potential. Such issues include matching the polymer degradation to the rate of new bone formation, assurance of mechanical integrity and the negation of premature mass loss. Furthermore, there is a need for new bioresorbable polymers to exhibit early resorption within months rather than years [8]. A key factor addressing these issues is the prediction and control of their degradation profiles.

In vivo degradation of bioresorbable polymers occurs due to hydrolysis of the polymer chains. Random hydrolytic chain scission of backbone ester bonds occurs and carboxylic acid end groups are produced. The eventual monomer components that remain, namely lactic and glycolic acids, are metabolised through the tricarboxylic acid cycle and then safely eliminated by the body as carbon dioxide and water. This hydrolytic degradation causes an initial drop in molecular weight, a loss of strength and, ultimately, a loss of mass [9–11]. The rate at which degradation proceeds, and the time to complete resorption, depends on a range of factors, including the

* Corresponding authors. Tel.: +44 (0) 2890 974509; fax: +44 (0) 2890 661729.
E-mail addresses: m.cairns@qub.ac.uk (M.-L. Cairns), f.buchanan@qub.ac.uk (F.J. Buchanan).

chemical structure, crystallinity, molecular weight, glass transition temperature, processing conditions, shape and size [9,12–14].

The mechanism of degradation of bioresorbable polymers can be classified as either surface erosion or bulk erosion [15]. Surface erosion would be the more desirable mode of degradation whereby the rate of degradation of polymer bonds is faster than the rate at which water can diffuse into the matrix. Thus the device will degrade from surface to core. However, in many cases “bulk erosion” is seen, whereby water diffuses into the material at a faster rate than the bonds degrade, causing hydrolysis of polymer bonds throughout the entire matrix. The inner core may even degrade at a faster rate than the surface, which not only leads to an early loss of mechanical integrity before any significant mass loss but also the build up of acidic degradation products within the core. The subsequent sudden release of these acidic degradation products is referred to as the “acid burst” phenomenon and is known to cause inflammation [11]. Control of the degradation rate is not only central to the development of bioresorbable polymers from a bone tissue engineering perspective but is also critical to the avoidance of an early loss of mechanical strength and the “acid burst” effect. Manipulation of polymer degradation rates and enhancement of material bioactivities have been investigated using a number of methods, including co-polymerisation, addition of lauric acid and ceramic/polymer blends [12,16]. These techniques have proved successful in modifying the polymer degradation rate. However, the materials are treated in their entirety, which leads to a uniform reduction in bulk mechanical properties during degradation. In order to achieve a more subtle control of degradation an alternative approach would be to induce the preferential modification of the surface in the first instance, i.e. to initiate pseudo-surface erosion.

It is proposed that this can be achieved with electron beam (e-beam) radiation. Earlier reports have shown that controlled dosage e-beam irradiation is able to modify polymer degradation predictably by altering the physical properties of polymers. Specifically, e-beam irradiation can cause a decrease in average molecular weight (through chain scission), advancing the process of hydrolytic degradation [17–19]. Moreover, previous work by the authors has illustrated the potential to influence molecular weight, strength and corresponding degradation in a depth-dependent manner [19]. E-beam irradiation has the potential to be a major underpinning technology in achieving predictable and controlled degradation of bioresorbable polymers. Furthermore, this can then allow degradation to proceed in a manner occurring from the outside of the device towards the centre, engendering early stage mass loss, maintenance of internal mechanical strength and, ultimately, the provision of optimum conditions for tissue healing.

The work addressed here investigates the utilisation of e-beam irradiation in order to achieve a predictable surface engineered degradation profile. Moreover, particular focus is given to refinement of the technology so that it may be applied on a scale relevant to currently used medical devices, i.e. ACL interference screws (of approximately 8×20 mm). This study focuses on the e-beam modification of commercially and clinically relevant materials, namely PLLA, PLG, PLDL and PLLA-HA.

2. Materials and methods

2.1. Materials

PLLA (PURASORB PLLA PL38), PLG (85:15) (PURASORB PLG 8531) and PLDL (70:30) (PURASORB PLDL 7038) were supplied by Purac Biomaterials (The Netherlands). A commercial polymer/ceramic blend containing PLLA-HA was supplied by Smith & Nephew (York, UK).

2.2. Sample preparation

A Collin P200 P computer controlled platen press was used to manufacture polymer sheets. A mould with a thickness of 1.0 mm was used to shape the samples. In practice this was found to produce sheets with a thickness of 1.1 ± 0.04 mm. For all materials a moulding temperature of 200 °C at a pressure of 10 MPa was used. ISO6602 flexural bar samples (80×10 mm) were then cut from the resultant compression moulded sheets. To equilibrate crystallinity and reduce any stressing in the material all samples were then annealed in a pre-heated air circulating oven at 120 and 100 °C for PLLA/PLLA-HA and PLG/PLDL, respectively.

Acrylic frames, as illustrated in Fig. 1, were manufactured to support the samples during e-beam irradiation. For selected samples acrylic lids with a thickness of 0.5 mm were used to provide a shielding layer as a technique to further control the penetration depth of the e-beam. The thickness of shielding required was determined from previous work [20].

2.3. E-beam irradiation

A 1.5 MeV Dynamatron Continuous DC e-beam unit (Isotron, UK), with the beam energy reduced to 0.5 MeV, was used for irradiation of the PLLA, PLLA-HA, PLG and PLDL samples. Irradiation was performed in the presence of air and samples were treated with delivered surface doses of 150 and 500 kGy (with (S) and without (NS) a 0.5 mm acrylic attenuation shield). To avoid excessive rises in sample temperature during e-beam irradiation the delivery of 500 kGy was staggered in a series of individual treatments of 150, 150, 100 and 100 kGy, with a 2 min cool down period between each dose. To verify the accuracy of the delivered irradiation dose, dosimetry was carried out in accordance with Isotron protocols and in-house standards. Briefly, thin film dosimeters (Far West Technology) were used for calculations of dose rates. The discolouration of the dosimeters by the radiation was then quantified using a Thermo Unicam UV2 Spectrophotometer.

2.4. Gel permeation chromatography (GPC)

The treated surface region of the irradiated samples was manually excised from the bulk sample prior to determination of molecular weight and polydispersity of irradiated samples by GPC. The excised region was of approximately 1 mm depth, as indicated by scanning electron microscopy (SEM) and predicted by CASINO modeling (not shown here). The software program CASINO (version 2.42), developed and tested by Drouin et al., utilises Monte Carlo simulation to predict electron distributions in materials [21–23].

Triplicate samples were prepared in chloroform (Sigma lot 7353 M) at concentrations of approximately 1 mg ml^{-1} and the resultant solutions were filtered through $0.45 \mu\text{m}$ polytetrafluoroethylene (PTFE) syringe filters before analysis. GPC was performed

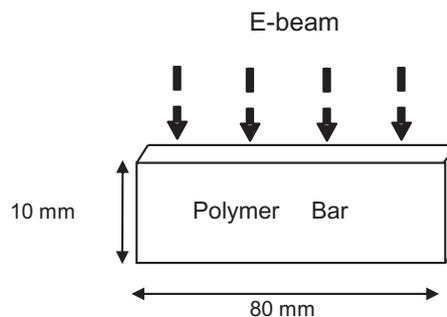


Fig. 1. Schematic representation illustrating the sample arrangement during irradiation.

ID	Title	Pages
962	Through-thickness control of polymer bioresorption via electron beam irradiation	10

Download Full-Text Now



<http://fulltext.study/article/962>



-  **Categorized Journals**
Thousands of scientific journals broken down into different categories to simplify your search
-  **Full-Text Access**
The full-text version of all the articles are available for you to purchase at the lowest price
-  **Free Downloadable Articles**
In each journal some of the articles are available to download for free
-  **Free PDF Preview**
A preview of the first 2 pages of each article is available for you to download for free

<http://FullText.Study>