Available online at www.sciencedirect.com
SCIENCE DIRECT®
Biomaterials 26 (2005) 6323–6334
Biomaterials
www.elsevier.com/locate/biomaterials

Compositional effects on the formation of a calcium phosphate layer and the response of osteoblast-like cells on polymer-bioactive glass composites

Helen H. Lu*, Amy Tang, Seong Cheol Oh, Jeffrey P. Spalazzi, Kathie Dionisio

Biomaterials and Interface Tissue Engineering Laboratory, Department of Biomedical Engineering, Columbia University, 351 Engineering Terrace Building, MC 8904, 1210 Amsterdam Avenue, New York, NY 10027, USA

Received 20 October 2004; accepted 12 April 2005
Available online 24 May 2005

Abstract

Biodegradable polymer-ceramic composites are attractive systems for bone tissue engineering applications. These composites have the combined advantages of the component phases, as well as the inherent ease in optimization where desired material properties can be tailored in a well-controlled manner. This study focuses on the optimization of a polylactide-*co*-glycolide (PLAGA) and 45S5 bioactive glass (BG) composite for bone tissue engineering. The first objective is to examine the effects of composition or overall BG content on the formation of a Ca–P layer on the PLAGA–BG composite. It is expected that with increasing BG content (0%, 10%, 25%, 50% by weight), the required incubation time in a simulated body fluid (SBF) for the composite to form a detectable surface Ca–P layer will decrease. Both the kinetics and the chemistry will be determined using SEM + EDAX, FTIR, and μ-CT methods. Solution phosphorous and calcium concentrations will also be measured. The second objective of the study is to determine the effects of BG content on the maturation of osteoblast-like cells on the PLAGA–BG composite. It is hypothesized that mineralization will increase with increasing BG content, and the composite will support the proliferation and differentiation of osteoblasts. Specifically, cell proliferation, alkaline phosphatase activity and mineralization will be monitored as a function of BG content (0%, 10%, 50% by weight) and culturing time. It was found that the kinetics of Ca–P layer formation and the resulting Ca–P chemistry were dependent on BG content. The response of human osteoblast-like cells to the PLAGA–BG composite was also a function of BG content. The 10% and 25% BG composite supported greater osteoblast growth and differentiation compared to the 50% BG group. The results of this study suggest that there is a threshold BG content which is optimal for osteoblast growth, and the interactions between PLAGA and BG may modulate the kinetics of Ca–P formation and the overall cellular response.

Keywords: Polymer-ceramic composite; Bioactivity; Degradable polymers; Bioactive glass; Osteoblasts; Mineralization

1. Introduction

Orthopedic implants constitute over 50% of all implantation procedures performed in the United States, and bone is the most often replaced organ of the body, with over 500,000 bone repair procedures surgeries performed annually [1]. Clinically, both biological and synthetic grafts have been utilized for bone repair. The preferred grafts of choice are autografts harvested from the iliac crest which have a success rate of 80–90% with minimal risk of immune rejection, infection, or disease transfer [2]. However, autografts are limited in supply, restricted by anatomical incompatibilities, and are associated with donor site morbidity. These limitations have prompted significant interest in alternatives such as tissue-engineered grafts. Tissue-engineered bone grafts are attractive because they can be designed to exhibit many advantages of autografts,

*Corresponding author. Tel.: +1 212 854 4071; fax: +1 212 854 8725.
E-mail address: hl2052@columbia.edu (H.H. Lu).

0142-9612/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.biomaterials.2005.04.005

without the aforementioned limitations. First, since these grafts are populated with autogenous cells, the issue of graft rejection is obviated. Second, with the addition of appropriate growth factors, the grafts can be engineered to be osteoinductive. Lastly, by utilizing a biomaterial substrate whose physical and structural properties mimic those of biological bone, an osteoconductive and osteointegrative construct can be engineered.

Material selection is a critical parameter in bone tissue engineering. A supporting scaffold is essential for maintaining mechanical strength, structural support, and for providing the optimal growth environment for bone formation during the early stages of the repair process [3–6]. Since no single existing material possesses all the necessary properties required for an ideal bone graft, there is a growing interest in the development of composite materials. The promise of combined advantages of the composite phases, as well as the inherent ease in optimization where desired material properties can be accentuated in a well-controlled manner, have made composites attractive for biomedical applications. From a biomimetic standpoint, various types of biological tissue such as bone are composite tissues with organic and inorganic phases, various cell types, extracellular matrix and bone mineral.

Several groups have begun to explore the potential of combining bioactive glass (BG) and polymers to form composite materials for bone tissue engineering [7–13]. The type of polymer–BG composite under research for bone repair has been predominantly particle-reinforced, with the exception of Marcolongo et al. [11] who implanted composite rods of polysulfone and BG fibers in rabbit femora. We recently combined polylactide-*co*-glycolide (PLAGA) 50:50 and 45S5 BG to engineer a degradable, three-dimensional composite (PLAGA–BG) scaffold [8]. The advantages of PLAGA are its documented biocompatibility, degradability, and relative ease of fabrication. However, PLAGA alone often does not have the necessary mechanical strength required for loading, lacks the ability to integrate with bone, and releases acidic degradation products which can have adverse effects on tissue response. BG was developed by Hench et al. [14,15] in the early 1970s, and it remains the most bone-bioactive material known to date [16–18]. Its bioactivity or osteointegration potential is directly related to the formation of a surface calcium phosphate (Ca–P) layer [19,20]. The biocompatibility, osteoconductivity, and osteoinductivity of BG have been well documented [19,21–26]. As such, the direct application of BG in load-bearing applications has been limited because BG is brittle and exhibits poor tensile and torsional properties [21,27,28].

The PLAGA–BG composite [8] was designed to integrate the advantages of the parent phases, while minimizing known limitations associated with each component. A significant advantage of PLAGA–BG over PLAGA is its osteointegration potential or the ability to form a surface Ca–P layer in vitro. Osteointegration is a critical factor in facilitating the chemical fixation of a biomaterial to bone tissue. The second advantage of the composite is that the addition of BG to the PLAGA matrix results in a structure with a higher compressive modulus than PLAGA alone. A successful tissue-engineered scaffold must exhibit mechanical properties similar to those of the tissue to be replaced, and the compressive strength and modulus of the composite do approach those of trabecular bone. Therefore, the PLAGA–BG composite would render greater functionality in vivo compared to the PLAGA alone. Moreover, the combination of the two phases serves to neutralize both the acidic byproducts produced during polymer degradation and the alkalinity due to the formation of the calcium phosphate layer [8]. Through hydrolysis reactions, PLAGA degrades into glycolic and lactic acids, the release of which can induce a biologically significant decrease in local pH. For BG to bond to bone, a surface Ca–P layer is formed through a series of dissolution, precipitation and ion exchange reactions which result in an elevated local pH due to the release of alkaline ions such as Si, Na, Ca and P. By combining PLAGA and BG, the acidic and basic degradation products are neutralized, a physiological pH is maintained and the composite supports the growth and differentiation of human osteoblast-like cells in vitro [8].

While significant progress has been made in the formation of PLAGA–BG composites, there is still a limited understanding of the interactions between the component phases of the composite, and a lack of insight into the design rules, which govern the extended functionality of this type of scaffold. It is critical that the kinetics of osteointegration, degradation, and new bone formation are precisely engineered such that the system is functional clinically. In order to optimize the PLAGA–BG composite for bone tissue engineering, the objectives of this study are two-fold. The first aim is to examine the effects of BG content on the formation of a Ca–P layer on the PLAGA–BG composite. It is expected that with increasing BG content, the required incubation time in a simulated body fluid (SBF) for the formation of a detectable Ca–P layer will decrease. Both the kinetics and the chemistry of the Ca–P layer will be examined. The second study aim is to determine the effects of BG content on the maturation of osteoblast-like cells on the PLAGA–BG composite. It is hypothesized that mineralization will increase with increasing BG content, and the composite will support the proliferation and differentiation of osteoblasts. Specifically, cell proliferation, alkaline phosphatase (ALP) activity and mineralization will be monitored as a function of BG content and culturing time.