NOVEL CARBON FOAM/POLYCAPROLACTONE SCAFFOLDS FOR TISSUE ENGINEERING APPLICATIONS

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Introduction

Scaffolds and implants play an integral part in tissue regeneration or reconstruction in the human body however success has been limited because of the complexity of tissues i.e. bone. The importance of the scaffold is that it provides a framework and initial support system for the cells to attach, proliferate and differentiate, and form a cellular matrix [1,2,3]. Several factors need to be considered in order for a tissue scaffold to be successful; the scaffold needs to be (1) biocompatible (2) be able to sustain applied loads and pressures (3) must be able to sustain cell attachment and growth and differentiation and (4) be able to be shaped or molded into a desired form. Recent development in design and fabrication technologies has made it possible to create scaffolds with a controlled architecture [4,5]. Polymer development has grown exponentially with the synthesis of numerous biocompatible and biodegradable polymers however many of these polymers lack the biological reactivity and mechanical strength needed to function as bone scaffolds. Degradation testing of polymeric scaffolds has been accomplished by subjecting the samples to simulated body fluid (SBF), a solution with ion concentrations and pH similar to that of human blood plasma [6]. Carbon foam research in biomedical applications has been limited. One group experimented with coating carbon foam with titanium to study the mechanical properties and found that it substantially increased the modulus and yield strength of the material and cell growth was satisfactory [7]. A recent study looked at pore control in carbon scaffold design [8] with hopes to determine ideal pore size for cellular applications. Our group has previously shown that osteoblast growth is dependent on orientation and crystallinity of carbon materials [9]. There have been no studies reported on the use of carbon foam combined with biodegradable polymers. This study investigates the novel application of porous carbon foam and polycaprolactone (PCL) as a scaffold or implant for bone replacement and is compared to trabecular bone.

Experimental

The open-cell carbon foam (CF) material was prepared by pressure foaming a pitch-based precursor using nitrogen gas (800-1000psi) and a temperature of 500-600°C [10]. The pressure and temperature were varied to change the structure of the foam. The study varies the pore size while keeping bulk porosity constant. The pore size of two different foams evaluated in this study, which was determined using optical microscopy and microCT X-ray analysis (MicroCT35, Scanco Medical, Zurich Switzerland), was 10 pores per inch and 100 pores per inch (ppi). The biodegradable polymer, PCL, was purchased from Sigma Aldrich (St. Louis, MO). This polymer has a molecular weight of 14,000M_w and a melting point of 60°C. Hybrid composites were formed by melt fabrication. Carbon foam and PCL was placed in a Teflon mold and the PCL was melted at 65°C (in a vacuum) until complete infiltration was accomplished. The composites were cooled at a constant rate. Composite samples were analyzed by microCT X-ray analysis to determine infiltration and defects within the material. Samples having less than five percent porosity were chosen as test samples. The composite samples were subjected to time-dependent degradation in a simulated biological environment (SBF at 37°C). Percent mass loss measurements are represented in Table 1. and Fig. 1. Mechanical compression testing was carried out using a MTS Mechanical Tester (MTS, Eden Prairie MN) with a 2200N load cell, in order to determine the maximum compressive load, compressive modulus (E_c) and compressive strength (σ_y). Results from the degradation study and mechanical tests were expressed as means ± SD of 10 samples per time point for each experimental group. Results are depicted in Table 1 and illustrated in Fig. 1 and 2. Statistical analysis was accomplished by carrying out multiple comparison procedures by one-way analysis of variance (ANOVA). The p-values equal to or less than 0.05 were considered significant.

Results and Discussion

The development of novel bone scaffolds in the past several decades has been limited. While bone-grafting materials are available they are often either not biologically reactive enough or limited in strength [11,12]. Recently, polymer materials such as PMMA and UHMWPE have found their way into implant design because of the durability and wear properties. Currently, natural and synthetic materials such as collagen, chitosan and biodegradable polymers are being processed and studied for their use as scaffold materials [13,14,15]. These materials offer advantages such as biological compatibility, controlled degradation, and ease of processing however they also often do not possess enough mechanical strength to function in load bearing applications.

Bone, is a porous composite material that is made of collagen and hydroxyapatite with infiltrated nerves, blood vessels and bone marrow. Several groups have attempted to create bone scaffolds from natural and synthetic materials [11,12,13]. It is often difficult to reach equilibrium to maximize both strength and biological reactivity. The porosity of a material will provide a framework for cellular integration, mineralization and vascularization by increasing surface area but has the drawback of decreasing the strength of the material. Open-cell carbon foam, for example, can be processed with varying porosity and pore size. The ability to vary the structure and geometry will in turn have an effect on the mechanical properties of the materials as well as provide

routes for vascularization. Table 1. illustrates that by increasing the pore size of the carbon foam the compressive properties decrease.

The use of a polymer melt fabrication method in scaffold design has been well documented [16,17]. PCL is a biodegradable polymer that is non-toxic and is approved for use in biomedical applications. Carbon foam has also been shown to be biocompatible and therefore a promising bone replacement [7,8]. Previously, our group demonstrated that osteoblast cell growth on carbon materials is dependent on crystallinity and orientation. Higher orientation and higher crystallinity increases attachment and cell growth [9].

The hybrid composite is formed from carbon foam, a porous, oriented material and PCL, a biodegradable material. While the degradation of PCL has been studied both in vitro and in vivo, it has not been reported in combination with carbon foam. It is important to understand how this material will behave in a simulated body environment and how the mechanics will change as a function of time. The novelty of this study is that by combining the oriented carbon foam with the biodegradable polymer an environment with controllable mechanical properties, degradability and tissue permeability is created. This study demonstrates that after infiltration the mechanical properties exceed that of trabecular bone (Table 1.). In bone regeneration the initial strength of the material as well as the strength after degradation is critical. The ability to tailor the mechanical properties also creates avenues for use in multiple applications. Our group has demonstrated that after 52 weeks of degradation both hybrid scaffolds exhibited a 5-6 percent loss in mass which was accompanied with a 20-30 percent loss in mechanical strength (Table 1., Fig 1., Fig 2.). While the loss in mass was minimal there was a greater loss in mechanical strength. The interaction of two materials is of key importance and there is a possibility that the SBF could permeate through the surface defects and degrade the polymer material that is bound to the carbon ligaments thus having a greater impact on mechanical stability. The ability to tailor this interaction and vary how the scaffold behaves would be advantageous in tissue integration and repair.

Table 1. Properties of Carbon and Hybrid Composites: Post 52-Week Degradation

Material	Percent Weight Loss (%)	Compressive Modulus (MPa)	Compressive Strength (MPa)
10 ppi Carbon Foam	0.5 ± 0.01	34 ± 1.5	0.31 ± 0.03
100 ppi Carbon Foam	0.5 ± 0.03	62 ± 2.8	0.48 ± 0.06
10 ppi Hybrid Composite	5.0 ± 0.3	150 ± 13	10 ± 1.1
100 ppi Hybrid Composite	6.0 ± 0.35	275 ± 17	13 ± 0.9
Trabecular Bone	NA	110	5

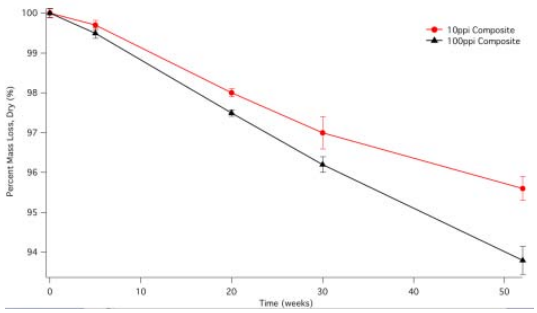

Fig. 1 Percent Weight Loss of Hybrid Composites

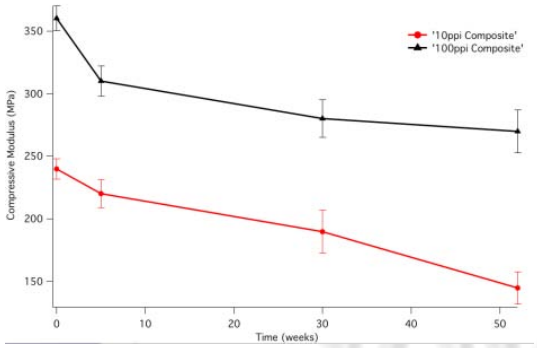

Fig. 2 Time Dependent Change of Compressive Modulus in Hybrid Composites

Conclusions

The balance between strength, biological integration and vascularization has made it a challenge to regenerate bone. Novel hybrid composites made from carbon foam and PCL were successfully processed using melt fabrication and are mechanically compared to trabecular bone. Processing of hybrid composites offers controllable and predictable architecture, geometry, and degradation. Degradation tests revealed that up to 6 percent of mass was lost after 52 weeks and compressive properties decreased 20 to 30 percent. However, the compressive properties of hybrid composites before and after degradation exceeded those of trabecular bone. This study demonstrates that combining carbon foam with biodegradable polymer shows promise in the area of scaffolding for bone. By varying the pore size and adding a biodegradable material can one can control the mechanical properties, degradation and the permeability of host tissue.

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