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Strut size and surface area effects on long-term *in vivo* degradation in computer designed poly(L-lactic acid) three-dimensional porous scaffolds

Eiji Saito [a], Yifei Liu [a], Francesco Migneco [a], Scott J. Hollister [a,b,c,*]

[a] Department of Biomedical Engineering, University of Michigan, Ann Arbor, MI 48109-2099, USA
[b] Department of Mechanical Engineering, University of Michigan, Ann Arbor, MI 48109-2125, USA
[c] Department of Surgery, University of Michigan, Ann Arbor, MI 48109-2110, USA

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ABSTRACT

Current developments in computer-aided design (CAD) and solid free-form fabrication (SFF) techniques enable fabrication of scaffolds with precisely designed architectures and mechanical properties. The present study demonstrates the effect of precisely designed three-dimensional scaffold architectures on *in vivo* degradation. Specifically, three types of porous poly(L-lactic acid) (PLLA) scaffolds with variable pore sizes, strut sizes, porosities, and surface areas fabricated by indirect SFF. In addition, one experimental group of PLLA solid cylinders was fabricated. The scaffolds and cylinders were subcutaneously implanted into mice for 6, 12 and 21 weeks. The solid cylinders exhibited a faster percentage mass loss than all porous scaffolds. Among the porous scaffolds the group with the largest strut size lost percentage mass faster than the other two groups. Strong correlations between surface area and percentage mass loss were found at 12 ($R^2 = 0.681$) and 21 ($R^2 = 0.671$) weeks. Scaffold porosity, however, was not significantly correlated with degradation rate. Changes in molecular weight and crystallinity also resulted in changes in the chemical structures due to degradation, and the solid cylinders had faster crystallization due to more advanced degradation than the porous scaffolds. Scaffold compressive moduli decreased with degradation, but the resulting modulus was still within the lower range of human trabecular bone even after 21 weeks. The loss in compressive moduli, however, was a complex function of both degradation and the initial scaffold architecture. This study suggests that CAD and fabrication, within a given material, can significantly influence scaffold degradation profiles.

1. Introduction

Bone graft substitutes, such as metal, have been historically used to repair bone defects. However, these implants are not ideal since they do not degrade in the body, which may lead to chronic problems such as implant loosening and infection. Furthermore, most metal implants are much stiffer than bone, often causing stress shielding and bone resorption. As an alternative approach, tissue engineered scaffolds have been developed using biodegradable materials. The role of tissue engineered scaffolds is to fill defects and support new tissue generation during the healing process. During the process scaffolds should degrade in concert with the formation of newly generating bone, providing a smooth transition in load bearing from scaffold to tissue [1].

The rate of scaffold degradation is affected by various factors, including molecular weight, ratio of co-polymers, crystallinity, morphology, stress, the *in vitro* or *in vivo* environment, and implantation sites [2–4]. An influence of polymer scaffold architecture on degradation has been widely postulated. For example, poly(lactic-co-glycolic acid) (PLGA) films or solid materials degrade faster than porous PLGA scaffolds, and more homogeneous degradation occurs in the scaffolds than films [5,6]. A lower porosity and permeability accelerate PLGA scaffold degradation *in vitro* [5,7]. Several studies have examined the degradation of porous poly(L-lactic acid) (PLLA) scaffolds *in vitro* [8–13] and showed that thicker walls degrade faster than thinner ones due to the autocatalysis of lactic acid, and a higher surface per volume ratio decreases the degradation rate [11,13].

Although previous studies examined the relationship between scaffold architecture and degradation behavior, most of the porous scaffolds were sponge-like or nanofibrous scaffolds whose internal architectures, such as pore interconnectivity, location, and strut size, could not be rigorously controlled and did not have adequate mechanical properties for bone tissue engineering applications [14–19]. Significant architectural variations often lead to conflicting and confusing conclusions. For example, porous scaffolds were found to degrade faster than solid block polymers [20,21], which contradicts the aforementioned results of faster degradation in

* Corresponding author at: Department of Surgery, University of Michigan, Ann Arbor, MI 48109-2110, USA. Tel.: +1 734 647 9962.
E-mail address: scottho@umich.edu (S.J. Hollister).

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