Acta Biomaterialia 8 (2012) 3997–4006

Contents lists available at SciVerse ScienceDirect

Acta Biomaterialia

journal homepage: www.elsevier.com/locate/actabiomat

# Biomimetic poly(lactide) based fibrous scaffolds for ligament tissue engineering

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ARTICLE INFO

*Article history:*
Received 13 February 2012
Received in revised form 9 July 2012
Accepted 12 July 2012
Available online 22 July 2012

*Keywords:*
Poly(lactide)
Electrospinning
Crimp-like
Collagen
Fascicles

ABSTRACT

The aim of this study was to fabricate a fibrous scaffold that closely resembled the micro-structural architecture and mechanical properties of collagen fibres found in the anterior cruciate ligament (ACL). To achieve this aim, fibrous scaffolds were made by electrospinning L-lactide based polymers. L-Lactide was chosen primarily due to its demonstrated biocompatibility, biodegradability and high modulus. The electrospun fibres were collected in tension on a rotating wire mandrel. Upon treating these fibres in a heated aqueous environment, they possessed a crimp-like pattern having a wavelength and amplitude similar to that of native ACL collagen. Of the polymer fibre scaffolds studied, those made from poly(L-lactide-*co*-D,L-lactide) PLDLA exhibited the highest modulus and were also the most resilient to in vitro hydrolytic degradation, undergoing a slight decrease in modulus compared to the other polymeric fibres over a 6 month period. Bovine fibroblasts seeded on the wavy, crimp-like PLDLA fibres attached, proliferated and deposited extracellular matrix (ECM) molecules on the surface of the fibrous scaffold. In addition, the deposited ECM exhibited bundle formation that resembled the fascicles found in native ACL. These findings demonstrate the importance of replicating the geometric microenvironment in developing effective tissue engineering scaffolds.



## 1. Introduction

Ligaments are load-bearing, soft fibrous connective tissues that connect bones within joints [1–3]. The ligament that is ruptured the most and that is predominantly studied is the anterior cruciate ligament (ACL) [1–5]. The ACL has a low self-healing propensity as it is surrounded by synovial fluid, which prevents clot formation, thereby impeding the wound-healing cascade [6,7]. Additionally, the high extracellular matrix (ECM) density and organization along with the presence of few or no blood vessels further hinder self-healing [5,6]. The inability of the ACL to self-repair has led to the study and design of functional synthetic constructs to replace damaged ACL using tissue-engineering principles [5–8]. Even though tissue engineering holds promise, the constructs developed to date do not completely restore normal tissue function, ultimately leading to construct failure [9–12]. This failure can be attributed to the lack of similarity of the scaffolds that have been investigated to the microstructural architecture (crimp pattern) and mechanical properties of the native ACL [10–12].

We have previously shown that electrospun polymer fibres can be fabricated with a crimp-like pattern with amplitude and wavelength similar to that observed in the collagen fibres of the ACL [10,12]. From a mechanical standpoint, the presence of crimp is advantageous as it provides scaffolds prepared with the fibres with a non-linear stress–strain behaviour, similar to that exhibited by the ACL under physiologic loading [13]. In addition, a scaffold designed for tissue engineering should support cell attachment and proliferation, and be biodegradable [6]. Poly(L-lactide) has been extensively studied as a scaffold material to replace damaged connective tissue, primarily because of its good in vivo track record as a biomaterial [14–17]. However, poly(L-lactide) is hydrophobic [18] and semi-crystalline, with a typical crystallinity ($X_c$) of ~37% [19–21]. Poly(L-lactide) is brittle because of its semi-crystalline nature [19–21], making the produced microfibres difficult to handle. The lack of poly(L-lactide) compliance makes it unsuitable as a fibrous scaffold in applications that undergo dynamic loading. By copolymerizing L-lactide with other known biodegradable monomers, the biodegradability and handling of the resultant copolymer fibres can be improved [18], while still benefiting from the good mechanical properties poly(L-lactide) has to offer.

Thus, the polymers examined in this study to fabricate a biomimetic fibrous ligament scaffold included: poly(L-lactide-*co*-glycolide), poly(L-lactide-*co*-D,L-lactide), poly(D,L-lactide) and poly (L-lactide). These polymers were chosen as they are biocompatible and biodegradable, possess glass transition temperatures ($T_g$) above 37 °C and hence have a high modulus at physiologic temperature,

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http://dx.doi.org/10.1016/j.actbio.2012.07.012