JOURNAL OF THE MECHANICAL BEHAVIOR OF BIOMEDICAL MATERIALS 34 (2014) 37–46

Available online at www.sciencedirect.com

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Research Paper

3D braid scaffolds for regeneration of articular cartilage

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ARTICLE INFO

Article history:
Received 18 October 2013
Received in revised form
7 January 2014
Accepted 8 January 2014
Available online 28 January 2014

Keywords:
3D braid scaffold
Axial yarn gradient
Unit cell
Finite element method
Articular cartilage

ABSTRACT

Regenerating articular cartilage in vivo from cultured chondrocytes requires that the cells be cultured and implanted within a biocompatible, biodegradable scaffold. Such scaffolds must be mechanically stable; otherwise chondrocytes would not be supported and patients would experience severe pain. Here we report a new 3D braid scaffold that matches the anisotropic (gradient) mechanical properties of natural articular cartilage and is permissive to cell cultivation. To design an optimal structure, the scaffold unit cell was mathematically modeled and imported into finite element analysis. Based on this analysis, a 3D braid structure with gradient axial yarn distribution was designed and manufactured using a custom-built braiding machine. The mechanical properties of the 3D braid scaffold were evaluated and compared with simulated results, demonstrating that a multi-scale approach consisting of unit cell modeling and continuum analysis facilitates design of scaffolds that meet the requirements for mechanical compatibility with tissues.

1. Introduction

Articular cartilage is a soft tissue sustaining the pressure at joints between the hard ends of bones, and is thereby frequently damaged by wear. Articular cartilage consists mainly of collagen fibers and proteoglycan matrix, which is a type of fiber-reinforced composite (Mow and Guo, 2003). Fig. 1 shows a schematic diagram illustrating typical articular cartilage. Within articular cartilage, chondrocytes maintain the tissue structure by synthesizing and modulating collagen fibers and proteoglycan. Chondrocytes may be cultivated outside the body and implanted within artificial articular cartilage (e.g., scaffolds) to regenerate the articular cartilage (Buschmann et al., 1992). To provide a supportive environment for chondrocytes to produce

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1751-6161/$ - see front matter © 2014 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.jmbbm.2014.01.004

articular cartilage and survive, the mechanical properties of scaffold must be as close as possible to those of natural articular cartilage (Cohen et al., 1999). The mechanical properties of articular cartilage are anisotropic and heterogeneous. Furthermore, due to its gradient structure (Fig. 1), the mechanical properties of articular cartilage also vary along a gradient (Akizuki et al., 1986; Buckwalter and Mankin, 1998; Cohen et al., 1998), making the development of scaffolds for regenerating articular cartilage challenging.

Woven composite scaffolds have been developed that can readily mimic the mechanical properties of natural articular cartilage. Woven composite scaffolds with uniform in-plane structure and isotropic mechanical properties have been proposed as a cartilage scaffold (Hutmacher, 2000; Temenoff and Mikos, 2000). Because their isotropic mechanical properties did not match those of anisotropic articular cartilage, the woven composite scaffolds could only be implanted into a limited, local region of the articular cartilage (Woodfield et al., 2004). Later, an anisotropic three-dimensional woven composite scaffold was developed that can mimic natural human cartilage; however, the structural variation of this scaffold did not match the layer-like structure of cartilage through thickness (Moutos et al., 2007). Recently, multi-layered composite scaffolds with aligned and randomly distributed fiber structures have been developed (McCullen et al., 2012). Even though their structure mimics native articular cartilage, creating scaffolds with gradient properties is only possible using quite complex manufacturing processes, necessitating the adoption of new technologies. To address the need for straightforward methods of manufacturing multi-layered scaffolds, this study introduces 3D braid composites as a feasible scaffold for articular cartilage due to the ability to control the mechanical properties by adjusting the processing parameters.

Braid composites, a type of 3D textile composite, are high-performance structural materials with high impact resistance, high failure strength, and long fatigue life, and have been used in the high-end automobile, aerospace, and sporting goods industries (Tate et al., 2006). Several studies have used unit cell modeling to numerically predict the elastic properties of 3D braid composites (Zuorong et al., 1999). Moreover, the mechanical analysis of braid composites using FE approach has been well developed (Miravete et al., 2006; Yu and Cui, 2007). In addition to braiding yarns, axial yarns have also been introduced into 3D braid composites. As the axial yarns are additional straight yarns introduced between the braiding yarns, they improve in-plane mechanical stiffness and enhance shape stability, damage tolerance, and fatigue resistance by increasing the fiber volume fractions (Karbhari and Wang, 2007; Potluri et al., 2003). In summary, braiding is a well-developed, established technology allowing the virtual design of anisotropic 3D braid scaffolds with gradient fiber volume fraction in a specific direction that may then be manufactured by varying processing parameters such as braiding angle, yarn density, and number of layers. The structure of braided scaffolds closely matches the fiber structure within human organs; they have thus been examined as potential ligament replacement materials (Freeman et al., 2007; Ide et al., 2001).

This study aimed to develop biocompatible 3D braid scaffolds that can degrade completely following the regeneration of articular cartilage (Athanasiou et al., 1991; Dai et al., 2010). For this purpose, a new unit cell model was developed to predict the mechanical performance of braid composites and optimize their internal structure in virtual space. Using the unit cell model and finite element analysis, an optimal structure that mimics the gradient mechanical properties of natural articular cartilage is proposed.

2. Methods: designing new 3D braid scaffolds and experimental

In addition to functioning physiologically, scaffolds intended to support regeneration of articular cartilage should be mechanically stable; otherwise, their malfunction causes unbearable pain. Producing mechanically stable scaffolds requires careful design, for which mechanical modeling of scaffolds is well suited. Here, a unit-cell approach; i.e., mathematical modeling of unit cell geometry and its finite element analysis using the actual material properties, was employed to predict the mechanical properties of 3D braid scaffolds.

2.1. *Mathematical modeling of unit cell geometry in 3D braid scaffold*

The unit-cell of 3D braid scaffolds can be modeled mathematically, provided that the running paths of individual yarns inside the braid are determined by the manufacturing process (in this case, circular braiding) (Fig. 2). The yarn carriers on concentric layers in the braiding bed move

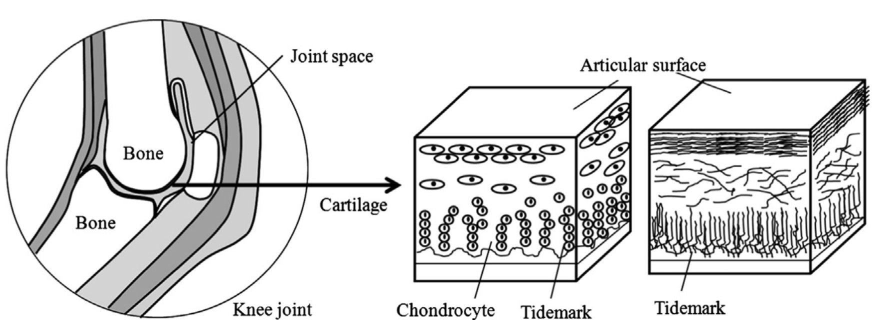

Fig. 1 – Schematic diagram of the knee joint and articular cartilage structure (Buckwalter and Mankin, 1998; Cohen et al., 1998). Left and right schemes of the articular cartilage represent variable distribution and density (from high at the surface area to low at the bottom) of chondrocytes and fibrous structure, i.e., its gradient structure.