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Mini Review

Strategies for the Tendon Ligament-To-Bone Insertion in Tissue Engineering

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Abstract

Reattachment of a mineralized connective tissue to the bone is frequently required following these injuries. The fibro cartilaginous transition region in the uninjured tendon/ligament-to-bone insertion is a functionally graded material that shows a gradual transition from soft tissue to hard tissue. By lowering interfacial stress concentrations that could be harmful, this transition is thought to make force transmission between the two different tissues easier. The tissue is at risk of re-injury because the transition region is impaired or lost when a tendon or ligament is injured and does not regenerate after surgical repair or natural healing. A number of tissue engineering repair methods have been inspired by the requirement to regenerate a strong tendon-to-bone insertion. The present and future approaches to engineering the tendon/ligament-to-bone insertion are discussed in the context of this review, which views the tendon-to-bone insertion site as a mechanical tissue structure.

Keywords: Engineering of graded tissues, Tendon-To-bone insertion site, Fibrocartilage, Mineralized fibrocartilage, Enthuses, Mechanical conditioning of engineered tissues

INTRODUCTION

Typically, a tendon must be surgically attached to its bony insertion in order to repair tears in the cruciate ligaments of the knee and the rotator cuff tendons of the shoulder, for example (Thomopoulos S, 2006). There is a transitional region in uninjured insertions between soft tissue and bone with gradations in cell phenotype, organization, composition, and mechanical properties. By reducing the potential for damaging stress concentrations to form at the interface, the gradations make it easier for the effective transfer of load between two materials that have very different mechanical properties (Genin GM, 2009). This transitional area does not regenerate after surgical or natural repair procedures. Instead, mechanically inferior fibro vascular tissue forms at the repair site during tendon-to-bone healing (Newsham-West R, 2007). The insertion is subjected to high stresses as a result, increasing the likelihood of failure. Consequently, current surgical repair methods have a high rate of re-injury; Up to 94% of massive rotator cuff tears that are repaired fail, and 56% of ACL reconstruction patients suffer from knee pain one year after their procedure. Soft tissue healing is influenced by a number of biological and mechanical factors, but many patients have subpar outcomes (Galatz LM, 2005). For tendon/ligament-to-bone repair, researchers have begun to focus on tissue engineered structures. In order to create constructs with the biological and mechanical properties necessary for insertion site repair, various current and emerging methods will be discussed in this review (Silva MJ, 2006). Healing of the bone to tendon insertion site the tendon ligament to bone insertion site presents a functionally graded material system that gradually transitions from mineralized tissue to mineralized fibrocartilage to mineralized tissue, with no distinct boundaries between tissue regions. This presents challenges for surgical procedures. Collagen type I and tendon/ligament cells are arranged in highly ordered arrays in the direction of tensile force in tendon and ligament. There is a lot of collagen type II in fibrocartilage, as well as a lot of per cellular collagen type III and little decor in and aggrecan, collagen types I and X. The majority of the mineralized fibrocartilage is composed of collagen type II,

with significant amounts of collagen type and aggrecan. Mineralized fibrocartilage has significantly less organized fibrol alignment than fibrocartilage and the tendon itself (Rodeo SA, 1993). Finally, a relatively stiff carbonated hydroxyl apatite mineral within a type I collagen scaffold makes up about half of bone's volume. As a result, the insertion site has a gradational increase in mineral content and a gradational decrease in the organization of the tissue as it moves from the tendon/ligament to the bone. A region of tissue between tendon and bone that is more flexible than either tendon or bone is the result of these competing gradations.

Strategies for repairing damaged tissue

Three primary obstacles emerge when looking at the tendon-to-bone insertion site from the mechanical perspective. During healing, the tendon-to-bone insertion site must first be mechanically stabilized. Second, reconstruction of a natural, graded tissue must be guided by the structure that is present during healing (Corry IS, 1999). Thirdly, it must end in a tissue system that maintains a graded mechanical structure and a spatially varying population of cells while recursively maintaining a graded mechanical structure. The second challenge is the focus of this review, which is presented from the viewpoint of cell populations, mechanical functions, and stimuli. In the design of a tendon/ligament-to-bone construct, two fundamental paradigms have been established (Yang PJ, 2009). The first method makes use of stratified constructs in which each biomaterial stratum is held together in series and seeded with a distinct type of cell that is relevant to a specific area of the insertion. In this model, it is hypothesized that cell-mediated metaplasia will start when multiple cell phenotypes are close to one another, creating an insertion site similar to graded tissue (Spalazzi JP, 2006). The second strategy makes use of a single type of pluripotent cell that is stimulated by varying degrees of local stimuli. Biochemical and mechanical stimuli are hypothesized to promote local cell differentiation, resulting in graded changes in cell and tissue type in this paradigm. Because they can be isolated from a variety of tissues and then differentiate into insertion-relevant cell types, adult mesenchyme stem cells are typically used (Benjamin M, 2002).

Constructed by stratified insertion

At the interface of the two types of cells, they hypothesized that fibrocartilage cell Tran's differentiation would occur as a result of fibroblast-osteoblast interaction. Fibroblasts and osteoblasts were plated opposite one another in a tissue culture dish with a gate separating the two cell populations for a two-dimensional co-culture study. The increased expression of cartilage-specific type collagen and COMP genes by migrating cells at the co-culture interface suggests that fibroblast-osteoblast interactions may promote insertion-related Trans differentiation. Spalazzi, others then looked into how cell-cell interactions worked in a three-dimensional, three-phase co-culture model. The region where tendon formation took place was Phase A, which was a porous poly matrix that was seeded with fibroblasts. To represent the bone phase, the sintered PLGA and 45S5 glass microspheres that made up Phase C were seeded with osteoblasts. PLGA made up the unneeded fibrocartilage phase. Phase B saw migration of osteoblasts and fibroblasts, significant deposition of collagen type I in phases A and B, and high mineralization in faze C. A fibro cartilaginous region in phase B was not realized, despite the formation of tendon-like and bone-like structures in the extremities of the stratified scaffold. Chondrocytes were included in Phase B and examined in a subcutaneous co-culture system to create a fibrocartilage region. Tissue continuity across the three phases, mineralization in phase C, and fibrocartilage between phases A and B were all achieved by utilizing three distinct cell populations, indicating that a representative ligament-to-bone construct could be produced by employing a stratified strategy with the appropriate cell types and extracellular matrix components.

CONCLUSIONS

The grade tissue interface does not regenerate in the current treatment methods for injured insertions. Bioactive tissue engineering solutions are required due to poor clinical outcomes and inadequate tissue sources for grafts. The continuous, graded nature of the native insertion should be taken into account when designing the scaffold. Because these cells can be stimulated by local factors to regulate cell differentiation and form functionally graded tissues, strategies involving multipotent mesenchyme stem cells are appealing. Although MSCs have been used in the majority of orthopaedic tissue engineering studies, ASCs may eventually be a more appealing source of cells for clinical use. A functionally graded construct design, a thoughtful recapitulation of the natural insertion's temporally and spatially resolved cues, and the careful selection of a clinically attractive and abundant source of pluripotent cells are all necessary for the successful development of a tissue engineered tendon/ligament-to-bone insertion. Before these objectives can be realized, there are numerous scientific obstacles. The fundamental mechanics behind a strong tendon-to-bone attachment remain a topic of on-going research. The minimum design requirements for an efficient tissue replacement at the tendon-to-bone insertion site are not clear.

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