INTRODUCTION: Mesenchymal tissue is capable of differentiating into a variety of soft skeletal tissues including cartilage, fibrocartilage, and fibrous tissue. Although it is widely accepted that mechanical stresses play a role in the process, the mechanobiological mechanisms affecting material property adaptations during differentiation are not completely understood. Previous research has proposed a qualitative tissue differentiation concept relating hydrostatic stress and tensile strain to the formation of bone, cartilage, fibrous tissue, and fibrocartilage. By expanding these concepts, we implement a fiber-network reinforced, poroelastic model of mesenchymal tissue to introduce an analytical model describing the differentiation of mesenchymal tissue in response to simulated applications of tensile stress and fluid pressure.

METHODS: Using a time-dependent algorithm (Fig. 1), we simulate changes in three material properties of differentiating mesenchymal tissue: tensile elastic modulus (E), compressive aggregate modulus (H_A), and permeability (k). In this approach, fluid pressure and tensile strain regulate changes in k, H_A, and E in differentiating tissue through their effects on proteoglycan synthesis and collagen fibrillogenesis. Fluid pressure causes an increase in both proteoglycan and type II collagen synthesis, resulting in a decrease in k and increase in H_A due to the hydrophilic nature and large size of the aggregating proteoglycans. It further causes a slight increase in E due to the formation of type II collagen and increased aggregate modulus. Tensile strain causes a much greater increase in collagen formation, resulting in an increase in E due to the elevated number, size, and cross-linking of collagen fibers and a decrease in k due to the increased flow path length. The input tensile and fluid stresses, initial and final constitutive values of the regenerating tissue, and the rate parameters describing the time-dependent nature of differentiation were determined from various experimental data obtained from the literature.

RESULTS: The simulations predict the largest increases in tensile elastic modulus during differentiation of mesenchymal tissue into fibrous tissue (E = 1000 MPa) and the smallest with differentiation into articular cartilage (E = 1 MPa). Fibrocartilage experiences much greater levels of tensile strain than articular cartilage but less than fibrous tissue. Accordingly, its final E (333 MPa) is much higher than that of articular cartilage, but still less than pure fibrous tissue (1000 MPa). Development of fibrocartilage also includes exposure to fluid pressure, resulting in an E(p) equal to 6 MPa as was seen with articular cartilage development but not with fibrous tissue development. Final permeabilities exhibited a reverse trend from tensile elastic moduli results. Articular cartilage had the highest permeability (k = 4.8 x 10^{-15} m^4/Ns) and fibrous tissue the lowest (k = 7.5 x 10^{-16} m^4/Ns) (Table I). A function of fluid pressure alone, k(p) is of equal magnitude for both articular cartilage and fibrocartilage (5 x 10^{-15} m^4/Ns) and is two orders of magnitude lower than k(p) of fibrous tissue (1 x 10^{-13} m^4/Ns). Fibrous tissue, having no exposure to fluid pressure, has a k(p) equal to k_m, the initial mesenchymal tissue permeability (Table I). However, fibrous tissue permeability experiences a large decrease due to the extended flow path length associated with greatly increased collagen fibrillogenesis and fiber density (Fig. 1). These final calculated values of k(p,E) are consistent with permeabilities determined experimentally by other investigators for articular cartilage, fibrocartilage, and fibrous tissues.

The aggregate modulus, a function of proteoglycan content generated by fluid pressure (Fig. 1), exhibits no change during differentiation into fibrous tissue (H_A = 0 MPa). Mesenchymal tissue differentiation into articular and fibrocartilage, however, include high levels of fluid pressure so they attain the maximum aggregate modulus (H_A = 1 MPa) within 90 days (Table I).


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