

Mechanobiology of Soft Skeletal Tissue Regeneration

The material properties of multipotent mesenchymal tissue change dramatically during the differentiation process associated with skeletal regeneration. Using a mechanobiological tissue differentiation concept and a fiber-reinforced poroelastic model of soft skeletal tissues, we have developed a mathematical approach for describing time-dependent material property changes during the formation of cartilage, fibrocartilage, and fibrous tissue under various loading histories. In this approach, intermittently imposed fluid pressure and tensile strain regulate proteoglycan synthesis and collagen fibrillogenesis, assembly, cross-linking, and alignment to cause changes in tissue permeability (k), compressive aggregate modulus (H_A), and tensile elastic modulus (E). Cyclic fluid pressure causes an increase in proteoglycan 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 stiffness added by newly synthesized type II collagen. Tensile strain increases the density, size, alignment, and cross-linking of collagen fibers thereby increasing E while also decreasing transverse k as a result of an increased flow path length. The Poisson's ratio of the solid matrix, ν_s , is assumed to remain constant (near zero) for all soft tissues. Implementing a computer algorithm based on these concepts, we simulate progressive changes in material properties for differentiating tissues. Beginning with initial values of $E = 0.05$ MPa, $H_A = 0$ MPa, and $k = 1 \times 10^{-13}$ m⁴/Ns for multipotent mesenchymal tissue, we predict final values of $E = 11$ MPa, $H_A = 1$ MPa, and $k = 4.8 \times 10^{-15}$ m⁴/Ns for articular cartilage, $E = 339$ MPa, $H_A = 1$ MPa, and $k = 9.5 \times 10^{-16}$ m⁴/Ns for fibrocartilage, and $E = 1000$ MPa, $H_A = 0$ MPa, and $k = 7.5 \times 10^{-16}$ m⁴/Ns for fibrous tissue. These final values are consistent with the values of E , H_A , and k reported by other investigators and the time-dependent acquisition of these values is consistent with current knowledge of the differentiation process.