

A MECHANO-REGULATION ALGORITHM OF STEM CELL DIFFERENTIATION AND COMPARABLE HISTOLOGY DURING BENDING STIMULATION

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Introduction: Tissue differentiation during healing of a bone fracture is heavily influenced by mechanical stimuli.^{1,2,3} Accurate characterization of this mechano-regulatory effect has great therapeutic potential. Several mechano-regulation algorithms have been developed that predict the course of fracture healing under a variety of mechanical conditions.^{4,5,6} One of the most thoroughly tested algorithms was developed by Prendergast *et al.*^{7,8} However, the ability of this algorithm to describe non-union has yet to be explored. The goal of this study was to test this algorithm in a non-union scenario in which a cyclic bending motion applied to an osteotomy gap results in the formation of cartilage, rather than bone.^{9,10}

Methods: A 3-D finite element model of a rat femur with transverse osteotomy was created using μ CT images of a physical sample (**Figure 1**). Poroelastic material properties were assigned according to values in the literature.⁸ The callus tissue was assumed to be granulation tissue at the start of the stimulation regimen. Boundary conditions were chosen to correspond to previous studies that applied a cyclic bending motion of $\pm 6^\circ$ about the center of the osteotomy gap.^{9,10} This motion was achieved in the model by applying displacements to the cortical bone at the right end and fixing the cortical bone at the left end. The mechano-regulation algorithm⁸ was then implemented in each element of the fracture callus. Briefly, the stimulus factor was calculated from the maximum octahedral shear strain and fluid velocity found in each element throughout the stimulation. Material properties were updated accordingly assuming that one iteration represented one day of stimulation. Twenty iterations were applied in order to simulate four weeks of stimulation applied for five days per week.

Results: Intramembranous ossification was predicted along the surface of the cortical bone outside the osteotomy gap. Clusters of cartilage were predicted within the gap (**Figure 2**), while small clusters of fibrous tissue were predicted to form between the regions of cartilage and bone.

Discussion: Consistent with published histology results (**Figure 3**)^{9,10} the algorithm predicted the formation of large masses of cartilage in the osteotomy gap. However, the predicted presence of fibrous tissue within the gap did not match the experimental observations. Thus, while the mechano-regulation algorithm correctly predicted non-union as a result of the bending stimulation, some features of

the patterns of tissue formation were not successfully replicated.

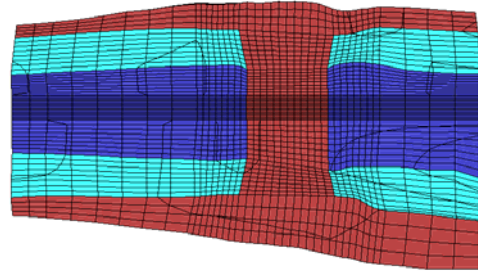


Figure 1: Cross section of the finite element model of the fracture callus: cortical bone is light blue, bone marrow is dark blue, and callus tissue is red.

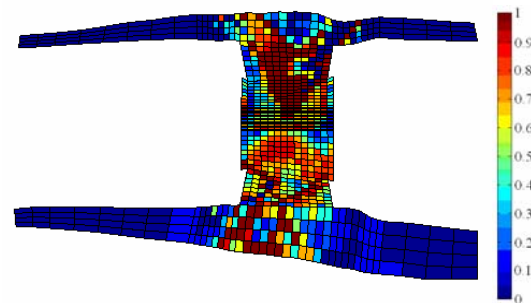


Figure 2: Ratio of cartilage tissue to total tissue in each element predicted after four weeks of bending stimulation.

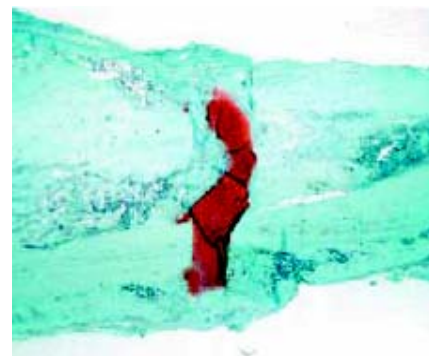


Figure 3: Histology slide of a mid-sagittal section of an osteotomized rat femur after four weeks of bending stimulation.¹⁰ The tissue has been stained with Safranin-O (coloring cartilage red) and Fast Green (coloring bone green).

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