A Mechanobiological Modeling of the Endochondral Ossification Process: An Experimental and Computational Analysis

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ABSTRACT

Long bone formation starts early during embryonic development through a process known as endochondral ossification. This is a highly regulated mechanism that involves several mechanical and biochemical factors. Due to the fact that long bone development is an extremely complex process, it remains unclear how biochemical regulation is affected when static and dynamic loads are applied, and also how biochemical and mechanical factors affect the shape acquired by the bone during early development. Therefore, in this study a mechanobiological model was implemented which is based on reaction-diffusion and poroelastic equations to simulate the endochondral ossification process and the change of long bone shapes during embryonic stages. Moreover, a morphological characterization of femur development in embryonic mice was carried out to validate the model. The computational model was performed in an incremental-iterative scheme which allows to compute the evolution of the negative-feedback loop between Ihh/PTHrP and the diffusion of VEGF molecule. Additionally, static and dynamic loading by an applied load in the distal and proximal rudiment were represented. The results evidenced the molecular variation of Ihh/PTHrP and VEGF allowing the formation of the main structures within long bones such as the primary ossification center, the bone collar, the growth plates and the cartilaginous epiphysis. Additionally, it is evidenced that static and dynamic hydrostatic compressions have an influence bone shape, and also that the poroelastic formulation affects in a small proportion the molecular concentration which leads the ossification process. The implication of this research is that it provides a novel and relevant understanding into normal long bone development, and it helps the understanding of how mechanical and biomechanical factors depend on each other to form long bones during embryonic development.