

RESUMO N° 223

THE EFFECT OF BMP-2 ON LARGE BONE DEFECTS: AN IN SILICO STUDY

Frederico Ribeiro, fredericoribeiro@ist.utl.pt

LAETA, IDMEC, Instituto Superior Técnico, Universidade de Lisboa, Portugal

Maria-José Gómez-Benito, gomezmj@unizar.es

Multiscale in Mechanical and Biological Engineering (M2BE), Aragón Institute of Engineering Research (I3A), University of Zaragoza, Spain

João Folgado, jfolgado@dem.ist.utl.pt

LAETA, IDMEC, Instituto Superior Técnico, Universidade de Lisboa, Portugal

Paulo Fernandes, prfernand@dem.ist.utl.pt

LAETA, IDMEC, Instituto Superior Técnico, Universidade de Lisboa, Portugal

José-Manuel García-Aznar, jmgaraz@unizar.es

Multiscale in Mechanical and Biological Engineering (M2BE), Aragón Institute of Engineering Research (I3A), University of Zaragoza, Spain

Keywords: Fracture Healing, Large Bone Defect, Critical Size Fracture, Bone Morphogenetic Protein-2, Hydrogel, Computational Mechanobiology

During the last decade, healing of large bone defects revealed itself a challenge for both bone tissue engineering and modern orthopaedics. To our knowledge, this problem was mainly addressed from a mechanical perspective, either focusing on mechanoregulatory models or on the stability provided by rigid scaffolds. Thus, the influence of chemical factors and its delivery devices has been somehow disregarded. From the myriad of chemical factors that affect and influence bone healing, bone morphogenetic protein-2 (BMP-2) has shown to be a very powerful osteoinductive factor. Therefore, the aim of this work is to develop in silico a mechano-chemical model that combines both the mechanical stimulus with the chemical stimulus provided by BMP-2. The proposed model is then used to study how exogenous BMP-2 delivered in a large bone defect affects its healing.

First, we collected quantitative experimental data concerning the effect of BMP-2 on cell behavior, i.e, cell proliferation, migration, differentiation, maturation and extracellular matrix production. The data gathered were used to define the mechano-chemical model with which we investigated large bone defect healing under different conditions: normal healing without any scaffold, healing with only hydrogel, and healing with a hydrogel soaked with different BMP-2 doses. To validate the model, the in silico predictions were compared qualitatively and quantitatively with the results from a previous in vivo study. Qualitatively, the predictions presented similar bone tissue formation and bone tissue distribution across the defect during healing. Quantitatively, the amount of bone formed in the defect was assessed: the in silico predictions diverged from the in vivo measurement by no more than 10%.

The model was validated and has shown to provide accurate predictions of BMP-2 effect on bone defect healing. This new in silico model can be a helpful tool to develop future bone tissue regeneration strategies.