



Evaluation of residual stresses due to bone callus growth: A computational study

L.A. González-Torres, M.J. Gómez-Benito*, J.M. García-Aznar

Aragón Institute of Engineering Research (I3A), Universidad de Zaragoza, María de Luna 3, 50018 Zaragoza, Spain

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ABSTRACT

Mechanical environment in callus is determinant for the evolution of bone healing. However, recent mechanobiological computational works have underestimated the effect that growth exerts on the mechanical environment of callus. In the present work, we computationally evaluate the significance of growth-induced stresses, commonly called residual stresses, in callus. We construct a mechanobiological model of a callus in the metatarsus of a sheep in two different stages: one week and four weeks after fracture. The magnitude of stresses generated during callus growth is compared with the magnitude of stresses when only external loads are applied to the callus. We predict that residual stresses are relevant in some areas, mainly located at the periosteal side far from the fracture gap. Therefore, the inclusion of these residual stresses could represent a significant impact on the callus growth and predict a different evolution of biological processes occurring during bone healing.

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1. Introduction

Bone healing is a highly complex process that involves several coupled and simultaneous events. After a fracture different cells, extracellular matrix (ECM) and chemical substances (growth factors, cytokines, angiogenic factors) appear, and some physical phenomena (electrical, mechanical) and biological processes (inflammation, angiogenesis, ossification, chondrogenesis, remodeling of ECM, cell migration, proliferation and differentiation) are initiated. All these elements evolve in an orchestrated fashion aimed at the restoration of the shape and functionality of healthy bone, during the weeks following a fracture (Schindeler et al., 2008; Giannoudis et al., 2007).

From a mechanobiological point of view, biological processes are studied considering how they are affected by mechanical factors (Wang and Thampatty, 2006). Using this approach, bone healing has been experimentally (Augat et al., 1998; Wolf et al., 1998; Epari et al., 2006; Goodship et al., 2009) and computationally (Lacroix and Prendergast, 2002; Bailón-Plaza and van Der Meulen, 2003; García-Aznar et al., 2007; Geris et al., 2008; Isaksson et al., 2006, 2008; Boccaccio et al., 2008; González-Torres et al., 2010) studied, highlighting the relevance of the mechanical environment in the regulation of this process.

Different mechanobiological models have been proposed to study the evolution of bone healing (Lacroix and Prendergast, 2002; Bailón-Plaza and van Der Meulen, 2003; Geris et al., 2008; Isaksson et al., 2008; Gómez-Benito et al., 2005). In most of these studies different cell and tissue processes are included: cell

proliferation, differentiation, migration, apoptosis (programmed death), and also the synthesis and degradation of the ECM. Even though several aspects of the healing process are currently unknown and therefore not considered in models, they have been able to represent different features: the distribution of tissues inside the fracture zone (García-Aznar et al., 2007; Isaksson et al., 2008), the occurrence of some non-unions (Gómez-Benito et al., 2005; Chen et al., 2009), the callus growth (Gómez-Benito et al., 2005), the callus removal (Lacroix and Prendergast, 2002), and the fibrosis under excessive mechanical stimulation of the fracture zone (Lacroix and Prendergast, 2002; García-Aznar et al., 2007).

Nevertheless, despite computational models are able to simulate callus growth in function of the mechanical environment, as far as we know, no model has evaluated the value of residual stresses due to the non-uniform callus growth which actually occurs.

However, residual stresses generated during tissue growth and development may affect many biological processes (Taber, 1995; Lanir, 2009). In fact, a widely studied and proven issue is the existence and influence of residual stresses in the vascular system (Rachev, 2003; Cardamone et al., 2009). Currently, it is generally accepted that mechanical behavior of vessels is conditioned by residual stresses generated during their growth and remodeling. Similarly, in the digestive system, residual stresses have been found in the pig duodenum (Lu et al., 2005) and esophagus (Zhao et al., 2007), affecting the transport of bolus during digestion. Additionally, there are evidences suggesting that residual stresses are related to the growth of tumors. *In vitro* (Helmlinger et al., 1997) and theoretical studies (Jiang et al., 2005), have concluded that residual stresses are related to the size of a tumor.

Regarding bone, non-negligible residual stresses have been detected through X-rays (Almer and Stock, 2005). The presence of

* Corresponding author. Tel.: +34 976761000x5237.

E-mail address: gomezmj@unizar.es (M.J. Gómez-Benito).