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MODELING OF BONE FRACTURE HEALING

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Fracture healing is a complex process controlled by the number of biological and mechanical factors. The successful healing is determined by the way of treatment, i.e. the stabilization method and the rehabilitation applied. The paper deals with modeling of the fracture healing process. The mechanobiological model of evolution of tissues in the fracture callus is elaborated, focusing on the influence of mechanical environment. The model will be implemented to Finite Element Method code and simulations will be performed in order to propose the effective way of dynamization of the fracture.

Keywords: *fracture healing, mechanobiological modeling, numerical simulations, FEM*

1. INTRODUCTION

Fractures of long bones occur quite often, creating patients disability due to long term healing causing the limitation of normal activities, and significant social cost and charge of health care system.

It is well recognized that the healing process is strongly affected by the mechanical environment at the fracture site determined by the way of treatment, i.e. the stabilization method, applied dynamization with the range and duration of allowed movements and loads, and also the decision of removing the stabilization.

Usually the way of treatment (stabilization and rehabilitation) depends first of all on experience of the orthopedic surgeon, supported by the radiological images of the affected bone. In clinical practice any diagnostic method allowing for quantitative evaluation of the progress of healing is not standard procedure.
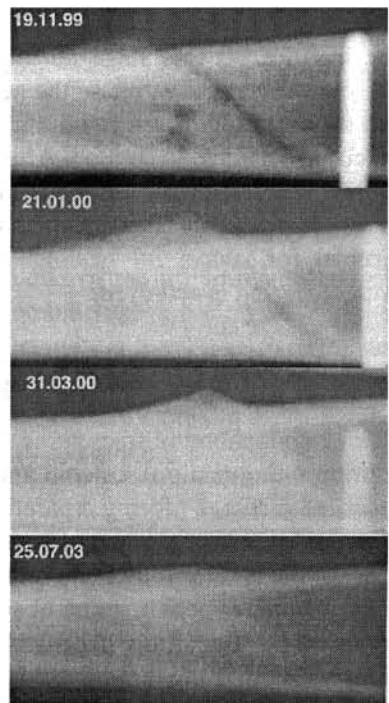

Fig. 1. Radiogram of fracture of tibia at different stages of healing.

Several theories trying to cope with the process of fracture healing have been elaborated, starting from the qualitative Pauwels theory [5], through the simple interfragmentary strain theory of Perren [6] and the deformation/pressure theory of Blenman and Carter [2], until the mechanobiological models of Lacroix and Prendergast [4] and Bialón-Plaza and van der Meulen [1], taking into account the activity of osteogenic cells and influence of growth factors.

In this paper we focus on modeling of the mineralization process of callus. The mineral fraction assures the strength necessary for the weight-bearing and correct junction of the broken bone, therefore this process seems crucial for the successful treatment.

2. BIOLOGICAL ASPECTS OF FRACTURE HEALING

The bone fracture is healed in two ways, primary or intramembranous ossification and secondary, or endochondral ossification, usually occurring simultaneously, but with different intensity.

The intramembranous ossification can be observed in the distal parts of the callus adjacent to the periosteum, and may also occur on the surfaces of fracture if contact of bone fragments is accurate and intrafragmentary movements are strongly restricted. The mechanisms of this type of healing is similar to that of remodeling - the bone is formed by osteoblasts activity.

During the endochondral ossification three phases are distintinguished: (i) inflammatory, (ii) reparative and (iii) remodeling. During the inflammation the hematoma surrounding the fracture is formed, and next granulation tissue is created, providing initial stability for the fracture. At this stage no influence of mechanical environment has been observed. During the reparative phase the activity of osteogenic and chondrogenic cells takes place. Firstly the osteoid is formed and next by means of mineralization the woven bone and calcified cartilage is created. After the reparative phase no more stabilization is required. During the last phase - remodeling, the bone regains the physiological stage, periosteal and endosteal callus are resorbed, and haversian structure is reconstructed.

Crucial for successful healing is the second stage, when the strength sufficient for weightbearing is achieved.

3. PHYSICAL AND MECHANICAL PROPERTIES OF TISSUES DURING FRACTURE HEALING

During endochondral fracture healing the following tissues are formed: granulation tissue (during inflammation), osteoid and cartilage, gradually transformed into woven bone and calcified cartilage (during reparative phase) and lamellar bone as the result of remodeling. These tissue are composed of liquid phase (mainly water), organic part (collagens of type I, II, or X, and various non-collagenous proteins, including growth factors). All tissues except lamellar bone may be treated as isotropic, and their mechanical properties are determined by the volume fractions of organic and mineral parts. Experimental investigations show that the Young modulus varies from *3 MPa* for the connective tissue until about *20 000 MPa* for the cortical bone. Values of mechanical properties used for nu-

merical simulations can be found, for instance in Claes and Heigele [3], or in Blenman et al. [2].

4. EXISTING MODELS OF SIMULATION OF HEALING PROCESS

Several models dealing with evolution of tissues during healing process are known. Historically the first is the approach of Blenman and Carter [2], in which authors hypothesized that the vascularity level as well as magnitude and type of mechanical stress (octahedral and dilatational) determine the tissue differentiation.

Lacroix and Prendergast [4] modeled the callus area as the biphasic (fluid-solid) medium and proposed the fluid flow and tissue shear strains to be the mechanical factor affecting the fracture healing process.

Bailón-Plaza and van der Meulen [1] took into account the time-dependent growth factor and cellular event to control the production of tissues.

5. NEW APPROACH

In this contribution we focus on the reparative phase of fracture healing. First of all, this phase is crucial for successful treatment. Moreover, during this phase the evolution of tissue is strongly affected by the mechanical factors.

During the reparative phase the activity of osteogenic and chondrogenic cells take place, leading to the formation of collagenous matrix followed by the mineralization of bone.

Our goal is the elaboration of new mathematical model of the fracture healing process and its numerical implementation. We treat the tissue formed during the process as the isotropic viscoelastic material. Its mechanical properties, more precisely the Young modulus E and viscosity η are determined by volume fractions of organic ingredient φ_c and mineral ingredient φ_m ; it means that

$$E=E(\varphi_c, \varphi_m), \ \eta=\eta(\varphi_c, \varphi_m) \tag{1}$$

vary from point to point, so the resulting material is inhomogeneous.

As the initial stage of our considerations we assume the end of the inflammatory stage, when callus is composed of the connective tissue. The connective tissue contains some amount of organic matter denoted as φ_{cg}, but no mineral ingredient is present, therefore at this stage $\varphi_c=\varphi_{cg}$, $\varphi_m=0$.

Following [4] we assume that progenitor cells invade the fracture callus and proliferate and differentiate. Their spreading is described by the diffusion equation

$$\frac{dn}{dt} = D\nabla^2 n \tag{2}$$

The collagen is synthesized by cells, and the rate of synthesis is moderated by the mechanical factor. Therefore that the rate of the volume fraction of organic ingredient φ_c is assumed to be the function of cell concentration n, the mechanical stimulus S, and the value of φ_c itself, namely

$$\frac{d\varphi_c}{dt} = F_c(n, S, \varphi_c) \tag{3}$$

The mineralization follows the creation of collagenous matrix. This process covers nucleation, crystal growth and proliferation. Most of nucleation sites are associated with collagen fibrils, therefore it is justified to correlate the rate of volume fraction with φ_c. The growth of mineral phase takes place on surfaces of crystals, and is strongly affected by the presence of inhibitors synthesized by cells. In order to incorporate these dependencies in the mathematical model, we propose the equation of evolution of the mineral content in the form

$$\frac{d\varphi_m}{dt} = F_m(n, S, \varphi_c, \varphi_m) \tag{4}$$

The sequence of events during the bone fracture healing is well recognized, nevertheless the way how the physical environment affects the process is under discussion. Therefore alternate propositions for incorporation the influence of mechanical factor [1,2] will be studied.

Particular case of relations (1)-(4) will be implemented to Finite Element Code, and parametric study of the solution will be done in order to investigate the influence of biological and mechanical factors on the modeled process. It is believed that after validation and verification the model will be useful for planing the stabilization method, as well as the rehabilitation process.

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