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Influence of mechanical impact on bone tissue regeneration in porous scaffold

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Abstract. The three-dimensional finite element model of biomechanical system was built. The model includes the fixer, tibia bone's simulator, callus and porous scaffold. By using author's program code the bone tissue regeneration was calculated in the volume of porous scaffold with increasing external loading. The obtained results allow us to estimate the influence of mechanical loading on the process of regeneration. The presented data can be used in a clinical condition for treatment of the injured bone.

1. Introduction

Bone fractures and fracture healing are so common in our lives that it is easy to lose sight awesomeness of this biomechanical phenomenon. Unlike other adult biological tissues that regenerates with the formation of scar tissue, the bones regenerates with the formation of bone. A new bone is formed and continuously remodeled until its properties are restored and the initial part of the fracture is not distinguishable from the healthy part of the bone. It is known that bone substance is a highly structured biological composite material formed by a matrix of collagen and hydroxyapatite crystals and a complex hierarchical system of pores filled with vascular and interstitial fluid. Since the bulk of peculiar bone cells are located on the walls of the tubules and the surfaces of the lagoons forming the micropore system, it is assumed that perturbations introduced by an external mechanical load into the steady fluid motion in the bone transport system can ensure the transfer of control signals between the bone cells during its structural adjustment.

Structural adjustment of undeveloped soft substance into dense bone tissue occurs as a result of differentiation of bone cells, for example, during restoration of bone integrity after fracture and implantation of skeletal implants into bone substance, which leads to the start of reparative bone regeneration in the area of contact with the surface of a foreign object or between bone fragments.

There is a hypothesis that has clinical evidence that, after the initial differentiation of the soft matter of bone callus to successfully complete the process of osteosynthesis of fractures of long tubular bones, dosed loading on the limb is necessary [1]. The lack of mechanical stress leads to inhibition of the process of ossification of jelly-like callus and the formation of predominantly fibrous or cartilage tissue from it. It was experimentally shown that decisive for the initiation of growth processes is not the peak value of tissue deformation, but a certain value of the lower limit of deformation, above which the tissue neoplasm processes prevail over resorption [2]. It has also been established that other characteristics of mechanical stress, such as the distribution of stresses and fluxes of interstitial fluid in the pores of the bone substance, the duration and frequency of force are of

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certain importance [3, 4]. It has been suggested that dynamic, in particular periodic, loads are more effective for stimulating reparative bone regeneration than static [5, 6].

Mechanical action may cause destruction of fracture, or change its biological path. However, the mechanisms that are caused by mechanical excitation, passing into a biological respond, remain partially unknown. A deeper understanding of these processes will enable the development of more accurate and rational fracture treatment strategies and will open up an unlimited area of research in other disciplines of regenerative medicine.

2. Materials and methods

The article describes the three-dimensional model of the tibia, the formulation of the problem of tissue regeneration and the tests conditions. The results of the study of bone tissue regeneration processes in the volume of scaffold with different porosity under the dynamic influence of increasing frequency are also presented.

The model includes a tibial bone, a fixation frame, a porous scaffold and a callus (Figure 1). For construction, a spatial finite element with parabolic interpolation of geometry and functions was used [5]. By studying the convergence of the test numerical solution, an adequate grid was selected, consisting of 3,600 finite elements and 16,276 nodes.

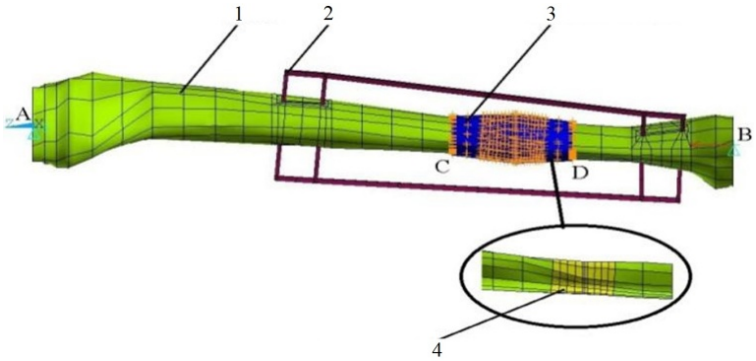


Figure 1. Model: 1) a tibial bone; 2) a fixation frame; 3) a callus; 4) a porous scaffold

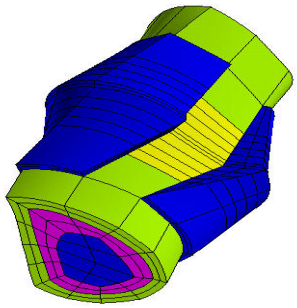


Figure 2. The area is considered: "scaffold - callus"

The loading conditions of the model can also be seen in Figure 1. In section A the bone is rigidly fixed, at the location CD the pore fluid pressure of the poroelastic medium acts on the callus. Static and harmonic loads act perpendicular to section B. The developed mathematical model and program allow us to investigate the influence of the type and parameters of the mechanical factor on the structural adjustment of bone tissue in the volume of a scaffold filled with biological tissue (Figure 2) [7, 8]. As the load applied in section B of the bone, consider the sum of a slowly varying compressive force, constant at each time step, and a fast component varying harmonically with a relatively high frequency:

$$\mathrm{F}(\mathrm{t},\tau,\omega) = \mathrm{F}_{sta}(\mathrm{t}) + \mathrm{F}_{dyn}(\mathrm{t})\mathrm{e}^{i\omega\tau} \ , \ \ \mathrm{F}_{dyn} = k\mathrm{F}_{sta} \qquad (1)$$

F – the total force depending on the slow t and fast τ times and frequency ω; F_{sta} – a static force that depends only on the slow time t (a graph of the static force versus time is shown in Figure 3); F_{dyn} – the amplitude of the harmonic force, also dependent on the slow time t.

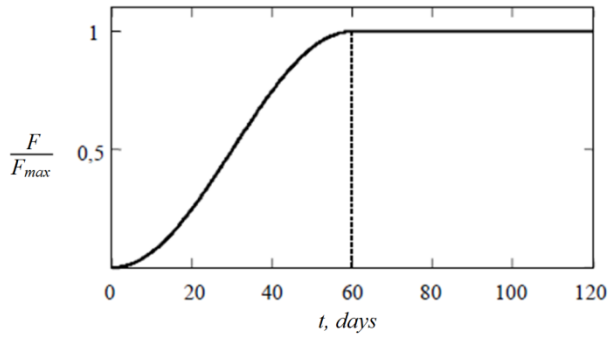


Figure 3. Graph of the normalized harmonic force change. T_1 = 60 days - time for which the force F_{sta} reaches a maximum

The task of penetration of mesenchymal stem cells in the zone of a scaffold with a porosity of 50 or 90% was solved for the period of 120 days. The diffusion coefficient is J = 0.65 mm^2/day. The initial conditions are the concentration of active cells in the volume of callus C_{vc} = 80% and in the volume of scaffold C_{vs} = 30%. The boundary condition is the concentration of cells at the border of the callus C_b = 100%. To study the effect of the harmonic load a solution is given for values of the frequency *f* equal to 10, 100, 200 Hz and the harmonic load factor *k* = 0.01.

The results of the tissue structural adjustment calculation with a time step equal to one day are displayed in the form of graphs that show the dependence of the physical-mechanical properties of the bone on time at specified points in the area under study (Figure 4) with variation of key parameters.

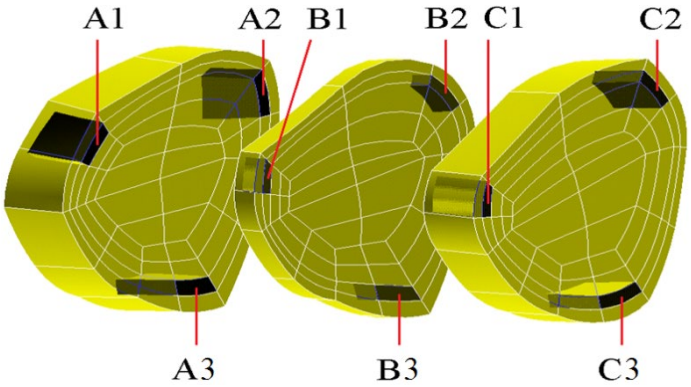


Figure 4. Points in the scaffold volume to output the results

The density of the tissue is considered as the main variable characterizing the process of regeneration. Successful is the process of regeneration with the yield of density curves at values close to the maximum - 1416 kg·m^{-3} [6].

3. Results and discussion

Graphs of changes in tissue density (for scaffold with a porosity of 50% - figure 5-7, with a porosity of 90% - Figure 8-10) show that the frequency of the applied harmonic load influences the convergence of the results and, consequently, the formation of mature bone tissue.

Analyzing the results, it can be seen that the recovery process of tissue properties depends on scaffold porosity: for a more rigid scaffold (with less porosity), a successful recovery requires a higher frequency load than for a less hard scaffold. It is not shown on the graphs, but it follows from the calculation, that a purely static load, which is not capable of generating forced flows of interstitial fluid in the system of pore channels, does not lead to the formation of bone tissue.

Analyzing the results for a scaffold with a 90% porosity it can be seen that at low frequencies the recovery process is unstable and leads to the formation of tissues of the fibro-cartilage type with low mechanical characteristics. An increase in the harmonic load plays a positive role in the formation of bone tissue in the scaffold volume.

After all experiments we can conclude that the task of regenerating active stem cells brings the model of the "bone – scaffold" system considered in computational experiments to the actual processes of bone restoration during structural adjustment by porous scaffolds.

According to the obtained graphs, it is clear that the density of the formed bone tissue in the scaffold increases throughout the entire volume of the area under consideration, which confirms the beneficial effect of the harmonic load on the tissue regeneration processes in the volume of the porous scaffold.

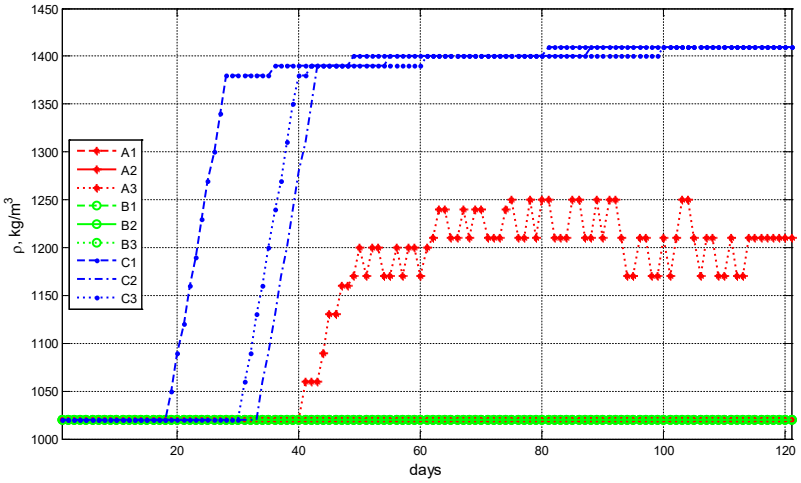


Figure 5. Bone density at selected points of a scaffold with a 50% porosity at a loading frequency 10 Hz

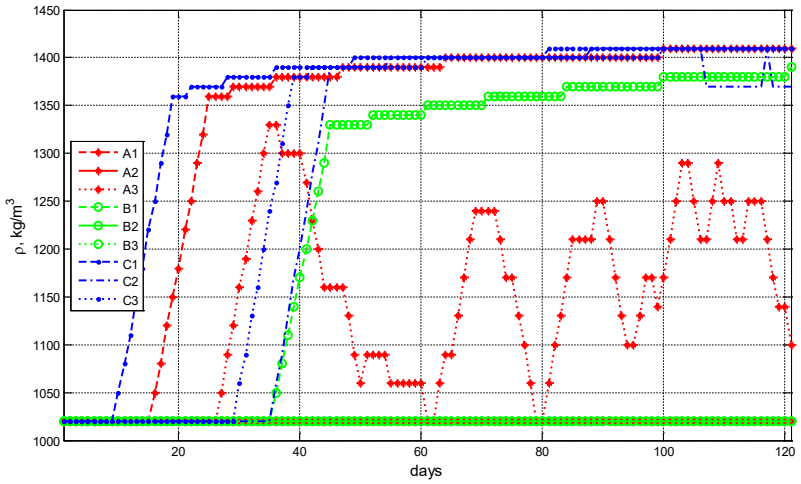


Figure 6. Bone density at selected points of a scaffold with a 50% porosity at a loading frequency 100 Hz

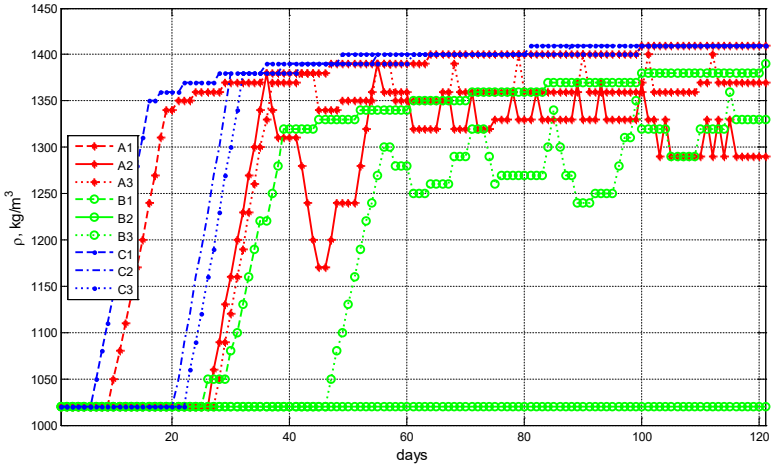


Figure 7. Bone density at selected points of a scaffold with a 50% porosity at a loading frequency 200 Hz

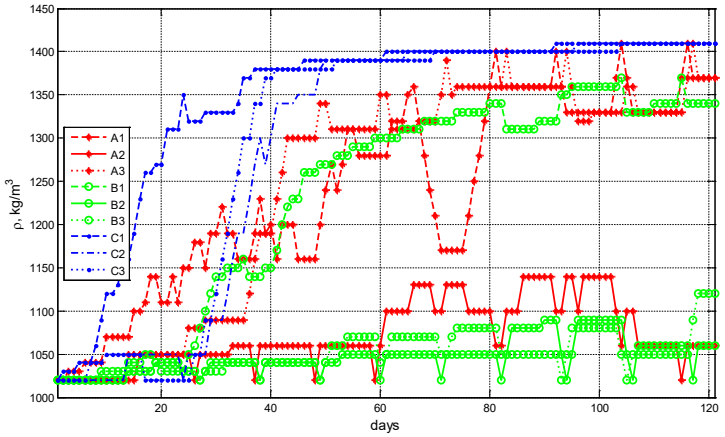


Figure 8. Bone density at selected points of a scaffold with a 90% porosity at a loading frequency 10 Hz

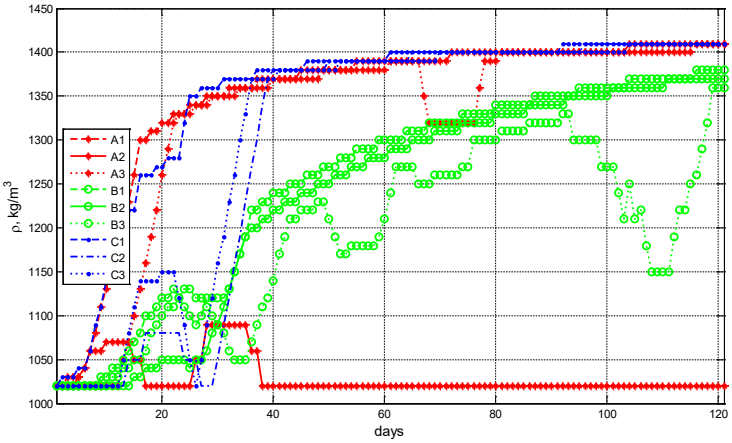


Figure 9. Bone density at selected points of a scaffold with a 90% porosity at a loading frequency 100 Hz

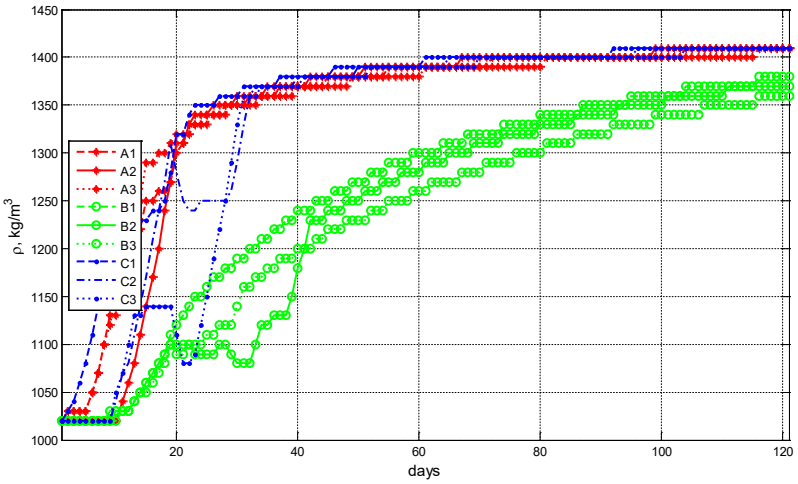


Figure 10. Bone density at selected points of a scaffold with a 90% porosity at a loading frequency 200 Hz

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