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INDIVIDUAL AND AGE PECULIARITIES OF THE CORTICAL BONE TISSUE ADAPTATION PROCESS IN HUMAN FEMUR

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Abstract: The mathematical model of the cortical bone tissue adaptive remodeling recently developed by the authors contains the parameters that allow to take into account the effects of the individual and age peculiarities on the rate and the character of the adaptation process. The technique and the results of numerical investigation of the character and the rate of the bone tissue properties adaptive change are presented in the given paper. The analysis of the dependence of this adaptive process on the bone cells activity, bone tissue calcification level, morphological architecture and strength under the steady load variations has been carried out.

Key words: adaptation, individual peculiarities, bone cells activity, calcification, mechanical characteristics

Introduction

It is well known from the literature that the bone tissue mechanical characteristics are influenced by the loading history [2, 3, 5, 8, 9, 14]. In response to altered physiological load, the bone begins to remodel adequately its internal structure. For example, the total hip joint replacement causes the altered load environments and decreased level of patient motional activity. Both these facts give rise to the adaptive remodeling of bone architecture and mechanical characteristics around the implant's stem. When the elastic modulus is decreased, the implant's loosening and reduction of its lifetime are possible. The biomechanical model of relationship between the magnitude of external bone loading and the bone tissue mechanical characteristics ought to take into account the patient's age and individual peculiarities. Such a model will allow minimize the unfavourable changes in the cortical bone and increase the implant's lifetime by its individual fitting. In the given paper we study the possibilities of our recent model of cortical bone adaptive remodeling to take into account the effects of individual and age peculiarities on the rate and the character of the adaptive process. The paper contains an analysis of the dependence of the bone tissue porosity and elastic modulus on the bone cells activity, the bone tissue calcification level, morphological structure and strength characteristics.

Materials and methods

The given study employs the model of the cortical bone adaptive remodeling presented in the recent authors' paper [23]. The cortical bone is considered as a linear elastic anisotropic binary composite material. It is assumed that the matrix (the interstitial lamellae) is reinforced by the hollow cylinder inclusions (the osteons with the central Haversian canals).

These central osteon's canals are considered as a cylinder cavities with a zero elastic modulus, $E_{hav} = 0$. The presence of lateral canals does not taken into account. The values of the elastic constants are taken from the experimental study [17].

Let us consider the dependence of the cortical bone mechanical characteristics on the bone tissue morphological structure. For example, the effective longitudinal elastic modulus is calculated with the assumption that the contribution of the each phase is proportional to its volumetric content:

$$E_{11} = (\lambda_{ost} - \lambda_{hav})E_{ost} + \lambda_{lam}E_{lam} + \lambda_{hav}E_{hav}, \tag{1}$$

where λ_{ost} and E_{ost}, λ_{lam} and E_{lam} are the relative contents and elastic moduli of the osteons and interstitial lamellae respectively; and λ_{hav} is the relative content of the Haversian canals.

The intermediate lamellae are the remains of osteons that have been destroyed during the uninterrupted process of bone tissue remodeling [12]. The mechanical characteristics of the intermediate lamellae differ from the osteon's characteristics by two main reasons. Firstly, they have different levels of accumulated fatigue damage, and secondly, the characteristics of existent osteons and the osteons' remains that form the intermediate lamellae, are adapted to different loads. Therefore we suppose:

$$E_{lam} = K_E E_{ost}. \tag{2}$$

We consider that the osteons' tissue is an isotropic medium with a small volume fraction (2%) of absolutely rigid spherical inclusions (lacunae with osteocytes) [7, 19], and the tissue of interstitial lamellae is a medium with cavities (hollow lacunae with the cellular fragments). Therefore, with the findings of study [6], we have $K_E = 0.92$ for any Poisson's ratio.

It is assumed in the present paper that the number of osteons as well as elastic characteristics of matrix and inclusions are the constant values, and the alteration of the cortical bone mechanical properties is completely dependent on the radius of the osteon's Haversian canal. For the cylindrical form of the Haversian canal we have:

$$\lambda_{hav} = \pi n r_{hav}^2, \tag{3}$$

where n is the osteons number in 1 mm^2, and r_{hav} is the radius of osteon's Haversian canal.

The values of λ_{ost} and λ_{lam} are subject to the relationship

$$\lambda_{ost} + \lambda_{lam} = 1, \tag{4}$$

therefore we obtain from Eqs. (1) and (3) the following equation:

$$\frac{dE_1}{dt} = -2n\pi \cdot r_{hav} \cdot E_{ost} \frac{dr_{hav}}{dt}. \tag{5}$$

According to data of study [16]: $\lambda_{hav} = 0.037$, $\lambda_{ost} = 0.460$, $\lambda_{lam} = 0.540$, $r_{hav} = 0.03$ mm, $n = 13.2$.

It is supposed that the deviation of longitudinal strain from some homeostatic value produces an effect on the volume fraction of active bone cells. Therefore the time derivative of internal radius of the osteon's Haversian canal has the equation:

$$\frac{dr_{hav}}{dt} = \begin{cases} 0 & r_{min} > r_{hav}, \\ \dfrac{(\lambda_b a_b + \lambda_c a_c)}{\varepsilon_{max} - \varepsilon_{min}}(\varepsilon_{11} - \varepsilon_{hom}) & r_{max} \ge r_{hav} \ge r_{min}, \\ 0 & r_{hav} > r_{max}, \end{cases} \tag{6}$$

where a_b and a_c are the rates of bone apposition / resorption by osteoblasts / osteoclasts; λ_b and λ_c are the parts of the bone endosteal surface occupied by osteoblasts / osteoclasts;

ε_{11} and ε_{hom} are the current and the homeostatic values of longitudinal strain; $\varepsilon_{\max}$ is the given value of the longitudinal strain under which all the osteoclasts are in active state, and all the osteoblasts are not active; $\varepsilon_{\min}$ is the given value of the longitudinal strain under which all the osteoclasts are not active, and all the osteoblasts are in active state; $r_{\max}$ and $r_{\min}$ are the maximum and minimum radii of osteon's central Haversian canal.

The parameters λ_b and λ_c obey the relationship

$$\lambda_b + \lambda_c \leq 1 , \tag{7}$$

and in accord with the data of papers [1, 12, 13] it may be assumed $\lambda_b = 0.94$ and $\lambda_c = 0.06$.

It is well known that bone resorption and apposition are the interdependent processes [2, 12, 21]; we suppose the relation between a_b and a_c to be linear:

$$a_c = K_{bc} a_b . \tag{8}$$

In paper [12] the quantitative methods of investigation of the bone tissue histological specimens are described, these methods allow to determine the individual parameters of the bone remodeling. It is stated that the rate of apposition has not any substantial relation to gender and age; according to morphometric studies $a_b = 0.6 \div 0.7$?m per day. Rozhinskaya [13] has been obtain the rate of osteoid sediment $a_b = 1.0 \div 2.0$?m per day. According to data by Starichenko et al. [14], the rate of the bone tissue apposition $a_b = 0.5 \div 2.8$?m per day, and it is nearly the same for cortical and trabecular bone tissue. In study by Dempster [21] the following data on the rate of apposition and resorption are presented: $a_b = 0.06 \div 0.49$?m per day, and $a_c = 0.89 \div 1.74$?m per day, i.e. the proportion between the mean rates of osteoblasts and osteoclasts activity is $K_{bc} = 3.5 \div 14.8$.

According to data by Knets [5], the longitudinal compressive stress in the cortical bone under the normal physiological load is $\sigma_{hom} = 2$ kg/mm^2 (20 MPa). Hence, with the experimentally measured longitudinal elastic modulus $E_{11}^{hom} = 1872$ kg/mm^2, the cortical bone strain is $\varepsilon_{hom} = -0.107\,\%$. As a maximum strain ε_{max} we assume the failure tensile longitudinal strain $\varepsilon_{max} = 1.54\%$ [5]. To determine minimum strain ε_{min} we apply the relationship that follows from the condition of remodeling absence under при $\varepsilon_{11} = \varepsilon_{hom}$:

$$\varepsilon_{min} = \frac{(\lambda_b + K_{bc}\,\lambda_c)\,\varepsilon_{hom} - \lambda_b\,\varepsilon_{max}}{K_{bc}\,\lambda_c}, \tag{9}$$

The kinetic equation of internal remodeling may be written in the form

$$\frac{dE_1}{dt} = -C(\varepsilon_{11} - \varepsilon_{hom}), \tag{10}$$

where C is the factor of the cortical bone adaptive response on the longitudinal strain variations; with Eqs. (3) and (5) we have:

$$C = \frac{2n\pi \cdot r_{hav} E_{ost} (\lambda_b + K_{bc}\lambda_c) a_b}{\varepsilon_{max} - \varepsilon_{min}}. \tag{11}$$

The described model correlates with the data by Doktorov et al. [3] concerning the influence of the load decrease / increase on the magnitude of the bone balance during the remodeling cycle. The equations employed in the model balance do not conflict with the principles of adaptive changes in the human organism [15].

It may be stated in addition that the presented model allows simulate the changes in the external femur geometry too. The periosteum and endosteum surfaces are also the bone parts that respond to the external load alteration. The relationships similar to Eq. (6) are valid for the surface remodeling. By considering the femoral diaphysis as a hollow cylinder with external radius R_{ext} and internal radius R_{int}, we can write the equations of the bone dimensions variations:

$$\frac{dR_{int}}{dt} = \frac{(\lambda_b + K_{bc}\lambda_c)a_b}{\varepsilon_{max} - \varepsilon_{min}}(\varepsilon_{11} - \varepsilon_{hom}), \tag{12}$$

$$\frac{dR_{ext}}{dt} = -\frac{(\lambda_b + K_{bc}\lambda_c)a_b}{\varepsilon_{max} - \varepsilon_{min}}(\varepsilon_{11} - \varepsilon_{hom}). \tag{13}$$

The total area of the osteon's central Haversian canals in the cortical bone tissue of the human femoral diaphysis is an order of magnitude greater than the external surface area (periosteum and endosteum). Consequently, the main mechanism of bone adaptation to the varying load is the change of the cortical bone internal structure. The adaptive change of the femur external geometry has been observed in the cases when the external load considerably differs from the physiological norm for a long time, and the internal adaptive mechanisms become insufficient to compensate the load change [10].

To study the dynamics of the mechanical characteristics variations in the femoral cortex, let us consider the bone tissue specimen oriented along the osteon's axis with the cross section of 1 mm^2. Under the normal physiological activity, the dominant load on the human femoral cortex is the longitudinal compressive load. Therefore we load the model bone tissue specimen by the longitudinal force that maintains the specimen's strain between the limits ε_{min} and ε_{max}. The longitudinal strain is determined by Hooke's law

$$\varepsilon_{11} = \frac{\sigma_{11}}{E_{11}}, \tag{14}$$

where σ_{11} is the longitudinal stress (the longitudinal force per unit of the specimen cross section).

It is indicated in the histological studies that the remodeling cycle runs in the volume of 0.05 mm^3 [3] (or $0.05 \div 0.1$ mm^3 [13]). The average osteon's radius is 0.11 mm [1, 17], hence the length of the remodeling region has to be more than 1.32 mm. According to data by Dempster [21], the length of the remodeling cone in the cortical bone is 2.5 mm. In the considered specimen the number of potential regions of remodeling is small (the number of osteon's central Haversian canals n is 13.2 per mm^2), and the volume of the remodeled bone substance is comparable with the representative volume. Hence some incorrectness arises in application of the continuous media model to the remodeled bone. Despite of this fact, the presented approach allows to consider the femoral cortex as the inhomogeneous continuous media, and reflects experimentally observed differences of bone tissue porosity and mechanical characteristics in different parts of the cortical layer.

The set of equations (6), (10), (11) and (14) allows to calculate the variations of the Haversian canal radius and the effective longitudinal elastic modulus under the longitudinal strain alteration in the cortical bone. When the load corresponds to with the physiological norm, the strain ε_{11} is equal to ε_{hom}, and the bone structure remains unchanged. The external load increase or decrease causes the deviation of longitudinal strain from its homeostatic value, and the adaptive mechanisms became activated. The numerical solution of set of equation (6), (9), (10) was performed by the Euler method with the time increment of 12 days. It is much higher than described by Starichenko et al. [14] 24-hour, 48-hour and week rhythms of bone apposition, but this time increment ensures good convergence of the numerical method.

To examine the adequacy of the used model, we performed a numerical simulation of the experiment described in study [12]. According to data of this study, the bone loss was

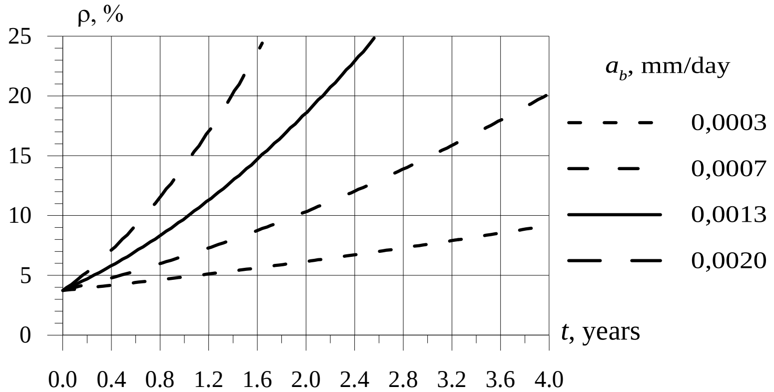

Fig. 1. The porosity variations under total patient immobilization, with different rate of osteoid forming.

4.2% after 8 months of patient total immobilization. The Fig. 1 shows that such a bone loss may be described by our model with $a_b = 1.3$?m per day.

It is known from the literature [3, 18] that normally about 5% of the cortical bone has been replaced in a year, with nearly zero balance between bone resorption and apposition. In this case the volume fraction of the active bone cell has to be 2÷4% under the physiological values of a_b and λ_b. However in our model the volume fraction of the active bone cell is about 50% under the zero bone balance. This difference may be explained by the following way. Our model describes the cells' activity within the regions of adaptive remodeling (even with zero bone balance). Meanwhile, the integral factor (5% of replaced bone) was calculated for the whole skeletal cortex, including the unchanged region of bone tissue too. The experimental verification of the used parameters validity is the volume fraction of active cells in a child organism (when the active remodeling runs in the all the skeletal bones) is up to 60%.

The model parameters characterize the patient's individual and age peculiarities and may be varied within some physiological range. It is necessary to access the effect of each parameter on the adaptive changes in the bone calculated by the presented model. We has been investigate the numerical solution dependence on the following parameters:

- the rate of osteoid forming a_b,
- the osteon's elastic modulus E_{ost},
- the number of osteons *n*,
- the osteons-interstitial lamellae elastic moduli ratio K_E,
- the resorption-reposition rates ratio K_{bc},
- the longitudinal strain ε_{max}.

The cortical bone effective elastic modulus and porosity were calculated. In Table 1 the normal values and variation ranges of the investigated model parameters are presented.

The choice of varied parameters is justified by the experimentally observed individual and age changes in the cortical bone structure and mechanical characteristics. The limitations on the radius of osteon's central Haversian canal are the minimal value observed in histological studies, and the maximal value equal to the osteon's radius. The choice of minimal value is caused by the requirements on the transport of nutritives and the removal of the bone cells metabolism products. The choice of the central Haversian canal maximal value is caused by the selected structural model of the cortical bone.

Table 1. The normal values and the ranges of the model parameters.

Parameter	Normal value	Range of variations
a_b , ?m per day	1.3	0.3÷2.0
K_{bc}	10	5÷15
E_{ost} , kg/mm^2	1776	1558÷2670
K_E	1.0	0.6÷1.4
n, the canals number per 1 mm^2	13.2	5.2÷17.2
ε_{max} , %	1.54	1.24÷1.84
ε_{hom} , %	-0.107	const
ε_{min} , %	-2.68	calculate by Eq. (9)
r_{max} , mm	0.11	const
r_{min} , mm	0.01	const
λ_b , %	94	const
λ_c , %	6	const

The main age group of patients who are in need of the total hip joint replacement consists of people older than 50 years. The aim of the surgical intervention is to recover the supportive function of the extremity, and as far as possible ensure the reliable implant's operation up to the end of patient's life without relapses. The mean length of human life in the developed countries exceeds 70 years, therefore in the calculations we consider the adaptive changes in the bone during the time interval more than 20 years. The main complication that decreases the endoprostesis lifetime is the implant's aseptic unstableness, and the cause of the implant's loosening is decreasing of the bone bearing capacity due to the changes in structure and mechanical properties of femoral cortex. It is known from experimental studies [20, 22], that after installation of the hip joint endoprostesis the decrease of longitudinal strains in the cortical layer of femur along the implant's stem was observed. Hence all calculation were performed with 30% bone underloading.

Results and discussion

The results of the calculations are presented in Figs. 1–7. These graphs shows that under the cortical bone underloading the compensatory increase of porosity is developed, and as a result the bone mechanical properties became weakened. The investigated model parameters have different effects on the rate of this process.

The factors a_b and K_{bc} have similar effects on the dynamics and non-linearity of adaptive processes in the cortical bone (Figs. 2, 3). The variations of $\varepsilon_{\max}$ in the given range of magnitudes have not substantial influence on the rate of the porosity increase in the bone tissue (Fig. 4). The change of the number of osteons per 1 mm^2 n exerts an exert on the total increase of bone porosity (Fig. 5), and under $n = 5.2$ osteons per 1 mm^2 the radius of osteon's central Haversian canal runs into its maximum in 18 years. The elastic modulus of osteon's material has a significant effect on the rise of the bone tissue porosity (Fig. 6). The increase of this parameter results in rapid (in 10 years) growth of osteoporosis in the cortical bone. Assuming that the rise of elastic modulus is concerned with the level of bone tissue calcification, the given changes may be a cause of brittle failure of the femoral side adjoined to the prosthesis. In turn, it will cause the loss of implant's stable fixation that may significantly complicate the subsequent treatment of the given joint. The effect of the factor K_E is inconsiderable, especially within the first 6-12 years (Fig. 7). Under small values of the parameter K_E the osteons carry the main load. Therefore the change of radius of the central Haversian canal effects stronger on the magnitude of strain, and as a result of it the porosity increases slower. Under large values of the parameter K_E the part of the load carried by osteons is insignificant, and the normalization of strains requires the more substantial porosity increase.

Conclusions

In the given paper the recently presented by the authors biomechanical model of cortical bone tissue adaptive remodeling has been employed. The effects of internal parameters of the model on the dynamics of changes of the porosity and elastic modulus of cortical bone tissue in the human femur have been studied. It has been received the qualitative correspondence between the obtained results and the present knowledge on the influence of age changes on the bone structure and mechanical characteristics. The present study contains the estimation of the degree of different parameters' influence on the rate of adaptive processes. It has been revealed that the parameters ε_{max}, n and K_E does not exert a substantial effect on the numerical solution, therefore the calculations may be performed with the average statistical values of these parameters. We suppose that the given assumption will allow to carry out the individual calculations of the predicted time intervals of the implant's stable fixation using the standard techniques of determination *in vivo* the other parameters without any considerable loss of the solution accuracy.

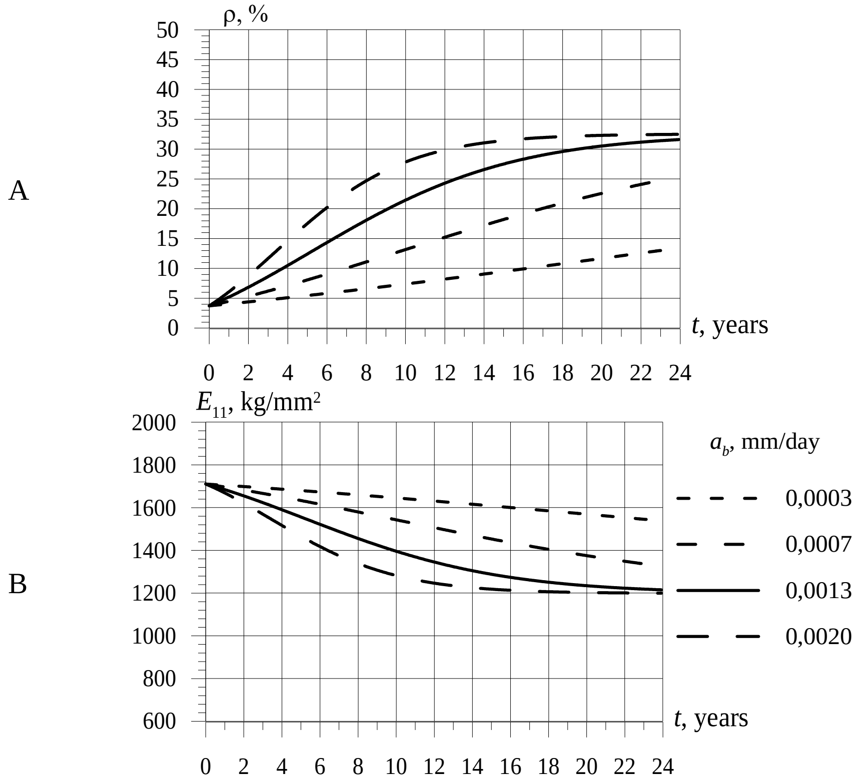

Fig. 2. The time variations of the porosity (A) and elastic modulus (B) under different rates of osteoid forming a_b.

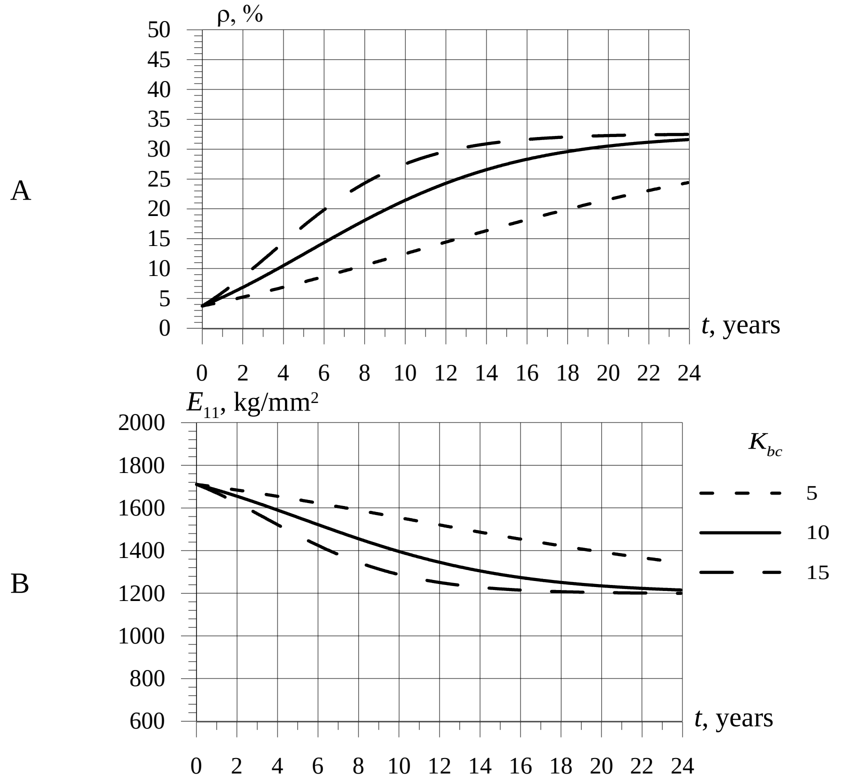

Fig. 3. The time variations of the porosity (A) and elastic modulus (B) under different resorption-reposition rates ratios K_{bc}.

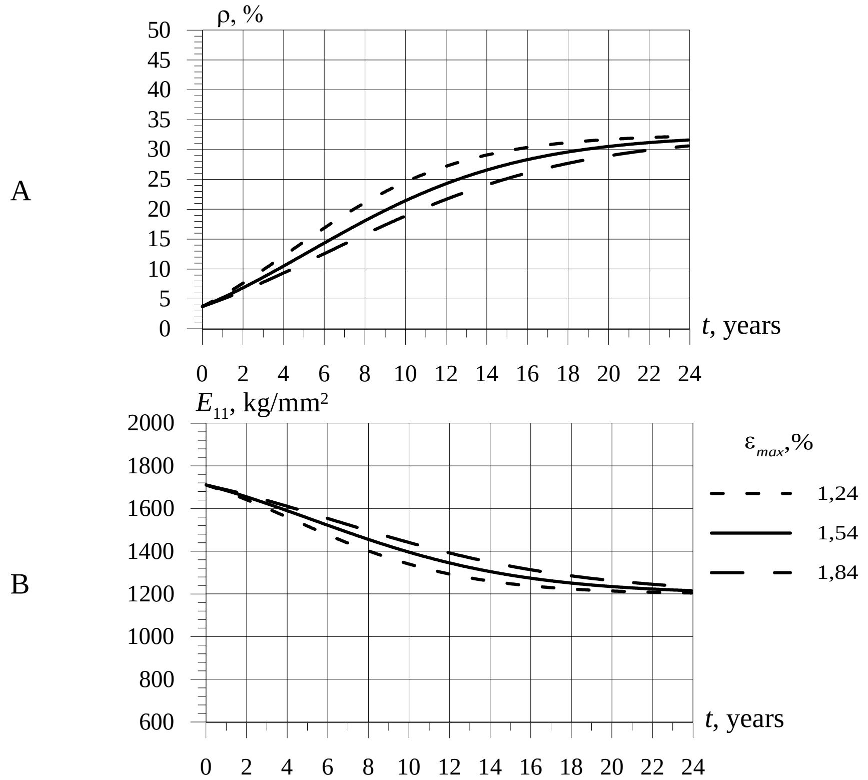

Fig. 4. The time variations of the porosity (A) and elastic modulus (B) under different values of maximum longitudinal strain ε_{max}.

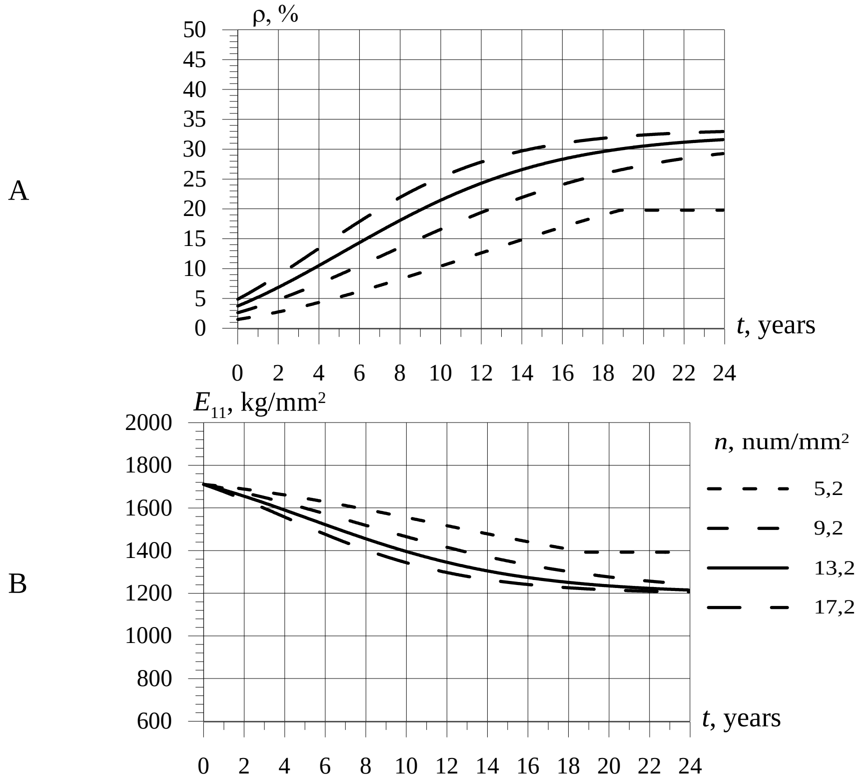

Fig. 5. The time variations of the porosity (A) and elastic modulus (B) under different osteons number per 1 mm^2 of the cortical bone cross-section area n.

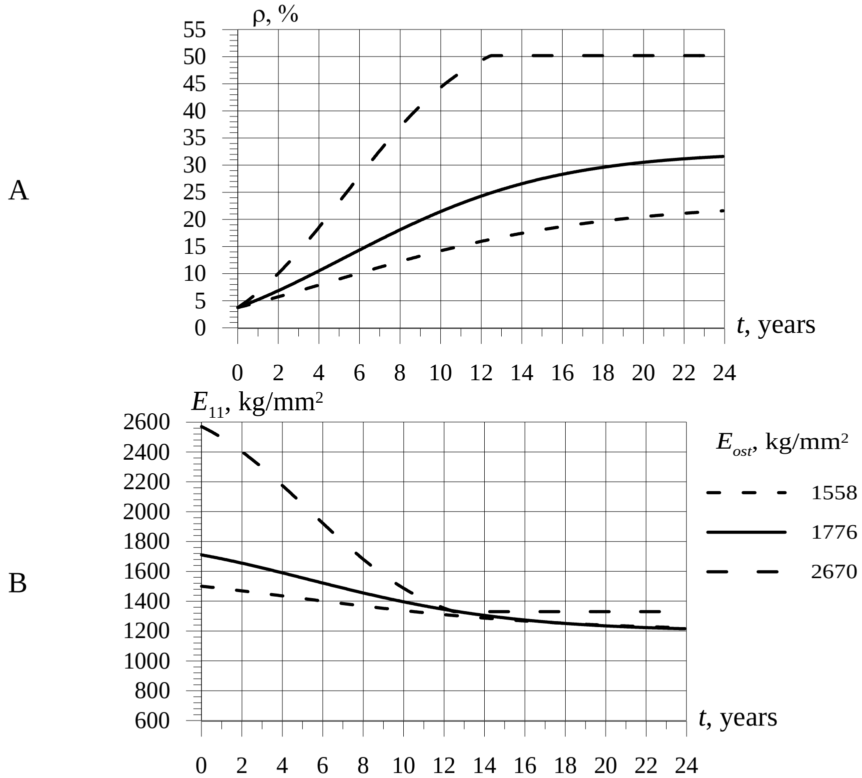

Fig. 6. The time variations of the porosity (A) and elastic modulus (B) under different values of osteon's material elastic modulus E_{ost}.

A

B

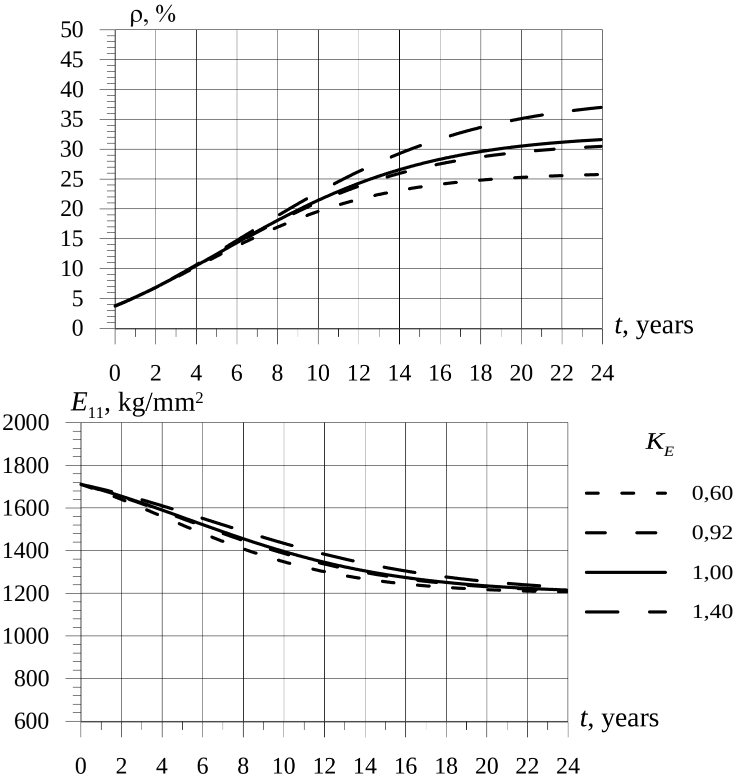

Fig. 7. The time variations of the porosity (A) and elastic modulus (B) under different osteons-interstitial lamellae elastic moduli ratios K_E.

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ИНДИВИДУАЛЬНЫЕ И ВОЗРАСТНЫЕ ОСОБЕННОСТИ АДАПТАЦИИ КОРТИКАЛЬНОЙ КОСТНОЙ ТКАНИ БЕДРА

А.В. Сотин, Ю.В. Акулич, Р.М. Подгаец (Пермь, Россия)

Разработанная авторами математическая модель адаптационной перестройки кортикальной костной ткани [23] содержит параметры, позволяющие учитывать влияние индивидуальных и возрастных особенностей на скорость и характер адаптационного процесса. В работе представлены методика и результаты численного исследования влияния активности костных клеток, уровня минерализации, морфологической структуры и прочностных свойств костной ткани на характер и длительность адаптационного изменения механических свойств ткани при установившемся изменении нагрузки. Библ. 23.

Ключевые слова: адаптация, индивидуальные особенности, активность костных клеток, минерализация, механические свойства

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