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Nonlinear Mathematical Modelling of Bone Damage and Remodelling Behaviour in Human Femur

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Abstract

The simulation of bone remodelling is highly complex due to the high nonlinear coupled relations between the damage and repair behaviours. In this paper, a new bone remodelling model based on the fatigue damage mechanism is proposed. Then the repair process of the human femur is simulated based on the finite element method. The results show that the new damage model can well simulate the bone damage evolution caused by overloadings. This indicates that the new mathematical model suggested in this paper can simulate the effect of external load on the cortical bone density and the related mechanical properties of the cortical bone.

Keywords: bone remodelling, bone damage, human femur, finite element method**AMS 2010 codes:** ???

1 Introduction

Bone is a hierarchically structured biomaterial consisting of collagen and hydroxyapatite. These two constituents are coupled to form mineralized collagen fibres at nanoscale. The lamellar structure is made up of fibres. The thick and thin lamellar structures are organized circularly into osteons, which are the main structural unit of the cortical bone. Compared with single collagen or hydroxyapatite, the mechanical properties of bones are significantly superior. Bone has a high level of damage tolerance because of the toughening effect related to its complex structures. But bone can also be weakened by fatigue and finally lead to fracture resulting from daily loading activities. Fortunately, bone has an ability to find such damages and heal them by a metabolic process called remodelling [1–3]. The most important feature of bone damage resistance is the self-healing mechanism of bone and its adaption to environmental conditions. This adaption is the process by which bone

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can adjust its structure and other mechanical properties to adjust with the outer loadings. However, if extremely high cycle-loadings are applied, the damage growth may be beyond the bone's repair capacity and may result in bone fractures. Taylor et al. [4] evaluated the fatigue of bones using an experimental method. The results showed that the fatigue life of bones subjected to repeated loadings without repairing is within only 3 years.

Since the damage repair is performed by remodelling, it is reasonable that micro-damage in bone can stimulate the bone remodelling [5–10]. Evidence shows that if the remodelling process of bones was suppressed by drugs or genetic manipulation [11], the damages would not be repaired although bones formed and grew. The accumulations of the damage made bone tissues more vulnerable to fatigue. Besides repairing the fatigue damage, bone remodelling also adapted its structures and mechanical properties to the changing mechanical loadings. Thus, fatigue damage has both mechanical and biological consequences. It not only plays a negative role for bone materials as for the artificial ones, but it also has a positive aspect of strengthening and renewing the bone. Then the bone damage repair process can be seen as in Figure 1.

Fig. 1 Bone damage repair process.

The damage resistance mechanism of bones has aroused the interest of scientists and engineers for many years. It is difficult to predict the process of bone remodelling and damage healing in a single mathematical framework. Researchers have proposed a number of models to simulate the external factors (electromechanical environment [12–14], the electromagnetic field [15, 16], etc.) and internal factors (micro-damage [17–21]) that may play a potential role in the remodelling process. Many researchers believe that damage caused by fatigue is the trigger for bone repairing. Taylor et al. [4] suggested that bone is a mechanical system including micro-crack growth and repair. The relationship between damage evolution and osteocyte behaviour has attracted extensive attention. Results [22] show that micro-damage can sense many unknown physiological signals to initiate the repairing process. This point has received great attention from researchers, and it is believed that the micro-fluid potential and damage of osteocytes are related to micro-crack. McNamara et al. [23] proposed a mechanical regulation system combining strain and micro-damage stimulation to model the formation and repair of trabecular bones. In this model, the propagation/healing process of trabecular bone micro-damage subjected to mechanical loadings was well studied. The stimulation factors to activate bone healing are stress, strain and the damage evolution rule, which is defined by the Miner's rule [24]. Wang et al. [25] proposed a remodelling model for dental implant models. In this theory, strain is assumed to be the dominant factor in remodelling when the damage is below the critical value. However, if it exceeds the critical threshold, the damage model should be used to simulate the damage evolution.

To better understand this process, it is necessary to use the damage theory under the condition of small strain in elasticity to study its mechanical response. From a biomechanics point of view, it is of great importance to put the theoretical framework in which a hypothetical statement can be made, considering the damage in the process of remodelling of bone. Mathematical modelling proved to be a helpful and useful way in the biomedical area for simulation of the complex and nonlinear biomedical process [26–28]. The purpose of this paper is to develop a complete remodelling-damaging model to simulate bone adaption to mechanical loadings. The relationship between the apparent density of bone and its effective anisotropy was established using the experimental data of other researchers. Then the new model coupling the remodelling is used to simulate a two-dimensional human femur remodelling and predict the density and damage change in this adaptive process.

2 Method and Model

2.1 Method

In this paper, the remodelling model [29, 30] was used to simulate the bone remodelling and damage growth/repair. In this model, the apparent density was used to evaluate the mechanical properties of bone tissues and was considered as a single scalar. The changing rate of bone density is

$$\dot{\rho} = k\dot{r}S_v\hat{\rho} \quad (1)$$

where ρ is the apparent density, which represents the internal structural characteristics of bones. The change in bone density $\dot{\rho}$ is assumed to be related to the maximum density $\hat{\rho}$ and S_v denotes the internal surface per unit volume. It can be expressed as

$$S_v = 0.02876P^5 - 0.10104P^4 + 0.13396P^3 - 0.09304P^2 + 0.03226P \quad (2)$$

where P is the porosity of the bone. The relation between the apparent density and porosity is (3)

$$\rho = (1 - P) \times \rho_0$$

where ρ_0 is the tissue density, which is a constant; k is the ratio of the available remodelling surface and the total bone internal surface; and $\dot{r}$ is the change rate of bone remodelling after considering the dead zone.

Then the damage can be included in the model. First, we define ω as a damage value to evaluate the damage of bones. The damage rate is $\dot{\omega} (\dot{\omega} = \frac{1}{N_f})$ [24] according to Miner's rule, where N_f is the number of cycles to reach failure for the bones at a given stress level. Then it can be calculated using $\log N_f = H \log \sigma^i + JT + K\rho^i + M$, where σ is the stress (Mpa), T is the temperature ($^{\circ}\text{C}$) and ρ^i is the density of bones (gcm^{-3}), respectively [31]. Here $K = 2.364$, $H = -7.789$, $M = 15.47$ and $J = -0.0206$ are all constants. Then, the damage can be calculated as

$$\omega = \int_0^t \dot{\omega} dt, \omega \leq 0.98 \quad (3)$$

where ω is the local bone to be repaired and t is the remodelling duration.

The damage threshold $\omega_{crit} = 2.6 \times 10^{10}$ is obtained when the damage reaches $3,500\mu\epsilon$ during one cycle.

If damage ω is less than ω_{crit} , adaptive remodelling is activated. Strain energy density at location i can be calculated as $U^i = \frac{\epsilon^i E^i \epsilon^i}{2\rho^i}$, where E^i is the elastic modulus (MPa) at location i (assumed isotropic), ϵ^i is the strain and the unit of U^i is $\text{MPa}(\text{gcm}^{-3})^{-1}$. At a given location i , the stimulus for the element is S^i , defined as $S^i = U^i - U_{ref}$.

The changing rate of density is

$$\frac{d\rho(x^j, t)}{dt} = C_1 S_{strain}^j \quad (4)$$

where ϵ^{ref} is dependent on the strain of the element j and ϵ^j is determined based on the following criteria: If the strain of the element $\epsilon \leq 1,000\mu\epsilon$, $\epsilon^{ref} = 1,000\mu\epsilon$ and $C_1 = 3.87$; if the strain $1,000\mu\epsilon < \epsilon \leq 2,000\mu\epsilon$, $\epsilon^{ref} = 1,000\mu\epsilon$ and $C_1 = 0$; If the strain $2,000\mu\epsilon < \epsilon \leq 3,500\mu\epsilon$, $\epsilon^{ref} = 1,000\mu\epsilon$ and $C_1 = 198$.

If damage accumulation ω exceeds the critical value ω_{crit} , the damage process happens.

Thus

$$\frac{d\rho_a(x_j, t)}{dt} = B \sum_{j=1}^N f^j(a, x^j) S^j(x) \quad (5)$$

where ρ_a is the bone density of bone remodelling, parameter B and ρ_{max} are the proportion coefficients and the maximal bone density. $B = 0.05(\text{gcm}^{-3})^2 \text{MPa}^{-1} \text{day}^{-1}$ and $\rho_{max} = 1.80 \text{gcm}^{-3}$. $f^i(x, x^i)$ is spatial influence

function, denoting the decay in signal intensity relative to distance $d(x, x^i)$ and decay parameter D . Then E and ν can be expressed as

$$E = \begin{cases} 1,007 \times \rho^2, & \text{if } 0.01\text{g/cm}^{-3} \leq \rho < 0.25\text{g/cm}^{-3} \\ 255 \times \rho, & \text{if } 0.25\text{g/cm}^{-3} \leq \rho < 0.40\text{g/cm}^{-3} \\ 2,972 \times \rho^2 - 933 \times \rho, & \text{if } 0.40\text{g/cm}^{-3} \leq \rho < 1.20\text{g/cm}^{-3} \\ 1,763 \times \rho^{3.25}, & \text{if } 1.20\text{g/cm}^{-3} \leq \rho \leq 1.80\text{g/cm}^{-3} \end{cases} \quad (6)$$

$$\nu = \begin{cases} 0.2, & \text{if } 0.01\text{g/cm}^{-3} \leq \rho < 1.20\text{g/cm}^{-3} \\ 0.32, & \text{if } 1.20\text{g/cm}^{-3} \leq \rho < 1.80\text{g/cm}^{-3} \end{cases} \quad (7)$$

2.2 Numerical finite element model of human bones

A human femur bone model was used to predict the change in bone density and damage under different loadings by finite element method (FEM) (Figure 2) to show how the micro-damage-based mechanism works in the clinical practice.

Fig. 2 2-D finite element model of the femur.

As is shown in Figure 2, a four-node quadrilateral plane strain element is used to generate mesh. It is assumed that bones are compressible isotropic materials. Therefore, Young's modulus, permeability and Poisson's ratio are preliminarily defined, all by mineral density. These parameters are all changing with time.

Bone tissue is affected by repeated loads during daily activities, and the peak value of cyclic loads is dominant in the remodelling process [32]. Therefore, the static force and fixed constraint are set as the boundary conditions of the model.

Based on the mechanical law, a remodelling and damage model of human proximal femur is established, which takes into account the strain energy and stress of each element under usual stimulation. In the initial model, bone remodelling was considered and the density distribution was uniform. The biomechanical stimulation of each unit was calculated and the bone mineral density (BMD) of each unit was updated. After 1,000 iterative steps, we can clearly see that two high-density cortical layers appear around the model and a low-density area corresponds to the medullary cavity. The density distribution of the femoral head is very complicated. Two high-density areas and two low-density ones can be seen in and around the femoral head. Then the damage

mechanism is introduced into the simulation model. The damage region is taken as the initial, and continuous simulation is carried out using the controlled boundary conditions. The initial damage is a constant higher than the damage threshold to activate the damage repair mechanism.

In addition, we divided the bone remodelling process into three stages: absorption period (20 days), recovery (10 days) and formation (90 days) [33]. During each cycle, the FEM was used to calculate and obtain the stresses and strains in the femoral model.

The model of bone remodelling is implemented using the finite element software ANSYS, and each element is regarded as a separate model. Bone remodelling algorithms can be summarized as follows. First, assume the initial properties of the material and apply the boundary condition. The stresses and strains can be obtained according to the formula. Then the mechanical signal of each sensor can be calculated in bones. It will be detected by the tissues and these signals are sent to initiate the bone remodeling. According to the magnitude of these signals, the change in cell density is simulated and the new density can then be calculated. For the element whose density has changed, a new elastic modulus is determined in the next step.

3 Results

To demonstrate how the above models work in simulating the damage and remodelling process of bone, several representative examples are presented under different loadings in what follows. First, we consider a normal bone remodelling subject to normal loadings. Then a pin is inserted into a broken bone to simulate the clinical case when the bone suffers from “stress shielding.”

3.1 Bone remodelling process considering bone damage and healing

In this case, all the material parameters comply with the above model and the loading condition is as shown in Figure 3 and Table 1.

Fig. 3 Bone loadings without a pin.

Table 1 Loading applied on the bone

	Joint (right)	Muscle (left)
Loadings	Value (N)	Value (N)
1	4	1
2	1	0.5
3	3	1

Figure 4 gives the change in mechanical property of the human femur during the remodelling and healing process. This phenomenon can be explained as follows. When the resorption is in progress for the first 20 days, the sensor cells can detect the damage and send out corresponding stimulation signals. Beyond the critical value, the damage remodelling will be dominant. In addition, after the absorption activity occurs, it often diffuses in the nearby area. The bone density in the model can be reduced to the minimum. Then a reversal period follows from day 20 to 50. It is assumed that the absorption and formation rates are the same. Finally, the formation stage starts from the 50th to the 100th day. With the deposition of new bone, the mechanical properties and microstructure of bone gradually returned to the original state. As is shown in Figure 3, our simulation result is very close to the real bone. The distribution of bone mass in the bone is similar to that of real ones.

Fig. 4 Bone density change in the remodelling.

In order to describe the damage rate represented by elastic modulus, damage D_j is introduced into the model, which is expressed as follows:

$$D_j = 1 - E_j/E_0 \quad (8)$$

Table 2 Loading condition for the first case.

Loadings	Implant (right)		Muscle (left)	
	Value (N)	Direction	Value (N)	Direction
1	2,317	145°	703	45°
2	1,158	105°	351	75°
3	1,548	165°	468	15°

where E_j is the elastic modulus of an element in step j and is the modulus of the element in the undamaged model. The bone damage evolution can be seen in Figure 5. It is shown that when remodelling reduces the elastic modulus of bones, the damage signal gradually diffuses to other areas near this position. We can draw the conclusion that a series of bone remodelling and repair behaviours are carried out not only in the damaged area but also in the whole femoral model. This influence relationship is mainly determined by the spatial influence function, so that when the signal is strong enough, the signal of damage element can be transmitted to the whole model.

Fig. 5 Change of bone damage in the model.

3.2 Bone remodelling process when an implant is applied in the bone

In this case, we will change the loadings to investigate the influence of those loadings on the bone remodelling process as shown in Tables 2 and 3 and Figure 6.

The results are shown in Figure 7. As is shown, the implant was tightly in contact with the bone when it was inserted into the tissue. But due to the stress shield effect, the loadings on the inner surface of the bone are not enough to support the normal condition of the bone. Then the inner bone began to absorb and led to a risk of loosening and failure of the structure. This is because the elastic modulus of the pin is much bigger than that of the bone. Most loadings are carried by the implant. The bone will fall into a condition called disuse. This is the main reason which causes the failure of a bone implant.

Fig. 6 Bone loadings with a pin. (a)First case; (b) Second case.

Table 3 Loading condition for the second case.

Loadings	Implant		Muscle (left)		Muscle (right)	
	Value (N)	Direction	Value (N)	Direction	Value (N)	Direction
1	1,700	145°	703	45°	613	145°
2	800	105°	351	75°	358	105°
3	1,100	165°	468	15°	448	165°

However, this condition can be improved by changing its loading condition. We can see in Figure 7(a) that the absorption mainly occurred on the left side. Then we adjust the forces on the right side. The results show that the absorption resulting from the disuse is less than that in the first case.

Fig. 7 Bone density change with a pin. (a) The first loading case; (b) The second loading case.

Under the condition of ensuring the support strength of a prosthesis, choosing a material with a smaller elastic modulus can also reduce the bone stress shielding effect. Scanell et al. [63] considered that the higher the elastic modulus, the greater the stress shielding and the more the bone absorption. Sumner et al. [64] found that the material stiffness has great influence on stress shielding. In order to study the influence of stiffness on the service life of a prosthesis, three kinds of prostheses with different elastic modulus are selected in this paper. The specific parameters are $E = 200, 100$ and 20 GPa. In order to study the stress shielding, the load

Fig. 8

Fig. 9

is still set according to the load distribution before adjustment. After 500 steps of simulation, the results are as shown in Figures 4–20. When the stiffness of the femoral prosthesis is in the range of 20a–200a, we can see that the stiffness of the femoral prosthesis increases slowly when the stiffness of the prosthesis is less than 20A. With a small axial load, the rate of bone formation in the femur is greater than that of bone resorption, and the combination of femur and prosthesis is better. When the prosthesis was 100 GPa, the number of bone units was very close to that of 20 GPa. This indicates that the 100 and 20 GPa prosthesis have almost the same effect in reducing stress shielding. This is consistent with the results of the influence of prosthesis stiffness on bone reconstruction analysed by Qu Chuanyong [10]. In order to ensure that the prosthesis has enough stiffness to provide support for patients, we will use a more moderate 100-GPa prosthesis for analysis of the disuse load of different ages.

4 Conclusions

In this paper, a remodelling model of human femur is established, and the damage-induced remodelling is simulated to illustrate the whole process of bone repair. In the bone remodelling model, both the mechanical stimulation and the damage sensors are considered to simulate the remodelling and damage repair process of the human femur. The numerical results obtained by simulation are very similar to the actual situation. Therefore, finite element simulation enables us to make a helpful and effective investigation on the bone damage and remodelling, which has become a very valuable reference for the clinical treatment [34]. The overall healing behaviour of the human proximal femur can be well simulated with the help of this model.

The main purpose of this paper is to study and simulate the remodelling of bone tissue with damage. In order to simplify the calculation, the isotropic elastic model was used to simplify the calculation. However, in reality, bone is a kind of living tissue with complex physiological functions and structures. It is of great importance to consider the anisotropic and heterogeneous nature of bone materials. This should be an important goal of biomechanics. On the other hand, finite element simulation needs a large number of biological experimental data as verification to support the model. However, due to the complexity of these experiments in vivo, more relevant biological or medical experiments are obviously needed to be carried out in the future. From the mechanical setting of daily load to the periodic tracking of damage repair model, targeted experiments are needed to be supplemented. Other drawbacks can be seen in our paper. For example, before triggering the repair process, the degree of damage must exceed a critical value. In the repair process, we did not consider the biological and metabolic effects, and the change in interface conditions. In the future, these models need to be further improved obviously, including some of their effects. Despite these limitations, as we have shown, this model can be used in the clinical setting, such as looking for suitable osteogenic physical activity, monitoring the long-term risk of stress fractures, prediction of bone tissue distribution after orthopaedic surgery and in some other diseases related to bone remodelling.

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