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Homeostasis-based aging model for trabecular changes and its correlation with age-matched bone mineral densities and radiographs

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ABSTRACT

Purpose: This paper aims (1) to propose a novel bone adaptation model for age-related trabecular changes by adopting two implicit parameters in optimization, (2) to compare the simulated bone volume fraction (BV/TV) with the reported bone mineral density (BMD), and (3) to review the simulated trabecular architectures with the age-matched radiographs.
Materials and methods: The proposed model simulated the trabecular changes for an age span of 32–80 years. Quantitative comparison was conducted in terms of BMD and other morphometric indices. Then, two radiologists scored the simulated trabecular architectures using the age-matched radiographs. This protocol was approved by the hospital institutional review board.
Results: The simulated BV/TV was well correlated with BMD reported in the literature ($R^2 = 0.855$; $p < 0.05$). In comparison with age-matched radiographs, the consensus scores of agreement of the trabeculae were higher in age groups over the 50s, and the means of the Ward's triangle areas were strongly correlated with those in the age-matched radiographs ($R^2 = 0.982$; $p < 0.05$).
Conclusion: The proposed model could reflect the targeted trabecular changes in proximal femur with age. With further follow-up measurements, this research would contribute to the development of patient-specific models that assist radiologists in predicting skeletal integrity with aging.

1. Introduction

Bone is an organ that undergoes consistent metabolic processes in order to adapt to the surrounding mechanical demands, which is well known as Wolff's law [1]. This homeostatic bone regulatory mechanism is executed through the dynamic coupling of bone forming and bone resorbing cells that function on the trabecular surface. However, the modulation is often disturbed through reduced physical activity, endocrinologic conditions, and other factors. In particular, osteoporosis is the common metabolic bone disorder that leads to a deterioration of bone strength [2]. These phenomena generally occur in the elderly and lead to increased bone fracture risk. The traditional evaluation of fracture risk has been based on the average bone mineral density (BMD) value of a specific site (e.g., femoral neck and lumbar spine) using a dual energy X-ray absorptiometry (DXA) or quantitative computed tomography (QCT) [3]. However, considering that bone strength depends on both bone quantity (e.g., BMD) and bone quality (e.g. bone macro- and micro-structures), finite element analysis (FEA) has been adopted to quantify "current" bone strength [4]. In particular, high resolution peripheral quantitative computed tomography (HR-pQCT) and micro-magnetic resonance imaging (μMRI) have been recently introduced to construct patient-specific μFE models at the trabecular level [5,6]. However, due to dynamic features of bone, there are unmet demands for quantitatively predicting "future" bone strength.

In order to reflect the dynamic features of bone, many researchers have focused on the development of numerical models for bone remodeling. The early models had a phenomenological nature that only captured the net metabolic expressions [7,8]. Since the mid-1990s, *in silico* models have evolved to include more physiological mechanisms in which the osteocytes are distributed in the FE models with experimentally observed densities [9,10]. The current *in silico* models can consider the trabecular changes through the relationship between the osteoclast resorption and osteoblast formation using μFE models [11].

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As an alternative approach, optimization-based bone remodeling models have been proposed on the basis of the mathematical understanding of Wolff's law. Hollister et al. used the homogenization method to obtain the microarchitecture of the trabecular bone [12]. Jang and Kim examined the effects of the loading alteration due to disc degeneration on the trabecular architecture in young and old lumbar vertebrae using topology optimization [13]. Optimization can also be used to determine (or, at a minimum, estimate) the optimized bone structure under the given loading conditions through representing osteoblastic bone formation and osteoclastic resorption [14,15]. Thus, the optimization-based models have the potential to be utilized for predicting age-related changes in bone structures.

However, little literature to date has reported the clinical feasibility of age-related (or aging) bone remodeling models. Therefore, this paper aims (1) to propose a homeostasis-based aging model through introducing and adjusting two implicit parameters in optimization, (2) to evaluate the chronological morphometric changes of the simulated trabecular bone in comparison with reference data, and (3) to compare the simulated trabecular architectures with age-matched radiographs in terms of characteristic trabecular patterns in proximal femur.

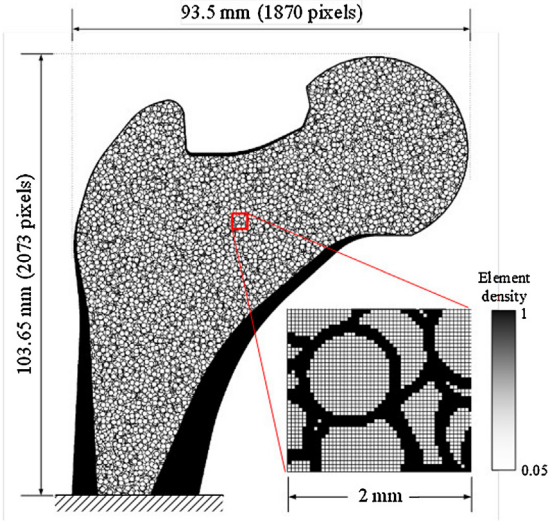

Fig. 1. FE model for initial bone architecture of human proximal femur.

2. Materials and methods

2.1. Theory of the homeostasis-based aging model for trabecular changes with implicit parameters

In this paper, design space optimization (DSO) was adopted for the age-related bone remodeling simulation. DSO is a recently proposed optimization technique that consists of double loops: the inner loop is the same as the conventional topology optimization and the outer loop controls the design domain change [16,17]. When an optimization process in the inner loop converges with the current design domain, the outer loop seeks a better design domain through expanding and shrinking the design space.

Considering the relationship between the phenomenological bone remodeling algorithm and topology optimization [18,19], the proposed model is formulated to achieve the altered homeostasis of a target bone due to aging as follows:

$$\begin{aligned} &\text{Minimize } f(\boldsymbol{\rho}) = \sum_{j=1}^{m} c_j \left(\frac{1}{2}\mathbf{u}_j{}^T \boldsymbol{K}\boldsymbol{u}_j\right) + \alpha \sum_{i=1}^{N} \rho_i v_i \\ &\text{Subject to } \; g(\boldsymbol{\rho}) = \sum_{j=0}^{n_2}\sum_{i=1}^{n_1} h_2 |\rho_{(i,j)} - \rho_{(i-1,j)}| \\ &\quad + \sum_{j=1}^{n_2}\sum_{i=0}^{n_1} h_1 |\rho_{(i,j)} - \rho_{(i,j-1)}| \le P_0 \;, \\ &0.05 \le \rho_i \le 1.0 \end{aligned} \tag{1}$$

where $\boldsymbol{\rho} = \left\{\rho_1, \rho_2, \cdots, \rho_i, \cdots, \rho_N\right\}^T$ as a design variable vector; ρ_i and v_i are the relative density and volume of the ith finite element (up to N), respectively; c_j and $\mathbf{u}_j$ are the weighting factor and displacement vector for the jth load case (up to m), respectively; $\mathbf{K}$ is the stiffness matrix; h_1 and h_2 are the lengths of an element; and $\rho_{(i,j)}$ is the density of an element located in the coordinate of (i, j) in the background mesh. The detailed mathematical derivation is explained in the Appendix.

From the perspective of the multiobjective optimization, α can be regarded as the balance factor between the two competing measures in Eq. (1): the total strain energy $\left(\sum_{j=1}^{3} c_j \left(\frac{1}{2}\boldsymbol{u}_j{}^T \boldsymbol{K}\boldsymbol{u}_j\right)\right)$ and the total bone mass $\left(\sum_{i=1}^{N} p_i v_i\right)$. For example, if α increases, more emphasis is placed on minimizing the total bone mass rather than the total strain energy. Hence, Eq. (1) with increased α determines a set of the altered relative densities which represent the trabecular architecture with a lower bone mass and larger strain energy (i.e., lower bone stiffness). As for a constraint, P_0 in Eq. (1) has direct controllability over the trabecular number (Tb.N) because the degree of bone porosity corresponds to the perimeter of the bone architecture.

Considering that bone loss is the most prominent effect of aging and bone porosity changes correspondingly, the proposed aging model is based on the hypothesis that appropriately assigning α and P_0 in Eq. (1) can reproduce the targeted trabecular changes. Thus, in this paper, α and P_0 are modulated at every outer iteration in the DSO in order to represent the different equilibrium states (i.e., altered homeostasis) with aging.

2.2. Application of the homeostasis-based aging model to human proximal femur

As depicted in Fig. 1, the entire domain of the human proximal femur was discretized into 2.07 million bilinear quadrilateral elements (i.e., N = 2.07 million in Eq. (1)) with a size of 50 μm × 50 μm. For the initial trabecular architecture, hollow circular patterns were randomly generated in order to construct thin and near-isotropic patterns. In Fig. 1, a black pixel represents the maximum relative density (ρ_i = 1) for bone, whereas a white pixel denotes the minimum relative density (ρ_i = 0.05) for marrow. Three loading cases were considered to represent one- legged stance (6000 cycles per day), abduction (2000 cycles per day), and adduction (2000 cycles per day). Regarding this, the normalized weighting factors (c_j in Eq. (1)) for the one-legged stance, abduction, and adduction were set at 0.6, 0.2, and 0.2, respectively. The validity of the above finite element (FE) modeling can be found in the reference [14]. In this paper, it was assumed that only trabecular bone is adapted during the optimization with the cortex unchanged.

For the synthetic proximal femur, α and P_0 at each outer iteration were set as represented in Fig. 2. Note that α and P_0 were constant during the inner loop at the given outer iteration of DSO. Through Eq. (1) , the optimal values for ρ_i were obtained at each outer iteration to represent the chronological changes of trabecular architecture due to aging.