Numerical simulation of tooth extraction socket: alveolar bone regeneration

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Abstract
Recently, regenerative medicine has received attention owing to the progress of an aging society. Regenerative dentistry, such as bone regenerative therapy and implant treatment to regain bone loss as a result of active periodontal disease, is actively performed. The alveolar bone is a functional bone that supports teeth and buffers occlusal pressure. In the implant treatment, the implant is inserted into the tooth after it has been extracted. After the implant is inserted, the alveolar bone will regenerate over about three months and the implant will be fixed in place. During this process of alveolar bone regeneration, there have been problems with the implant and alveolar bone not bonding. This work was contributed to dental regenerative medicine by building a simulation model of alveolar bone regeneration. After tooth extraction is performed, the alveolar bone regenerates by chemically converting calcium (Ca) secreted from the newly formed blood vessels into hydroxyapatite, which is the main component of bone. Thus, its internal structure and external shape are mechanically affected around the bone. The main purpose of this study is to establish a mathematical model, introduced as the Ca transport model that is secreted from the newly formed blood vessels, and mechanical factor model expressed as bone remodeling for analyzing and predicting the interaction of angiogenesis and bone regeneration. As a result, we were able to obtain a good agreement between the qualitative features of the experimental images and the simulation results.

Keywords: Alveolar bone, Angiogenesis,

1. Research background
In recent years, regenerative medicine has been attracting attention in Japan due to the aging population and the discovery of iPSC cells (Induced pluripotent stem cells). Regenerative medicine is the most advanced medical technology to regenerate tissues and organs that have been damaged by disease or injury using one's own cells. In this study, we focused on dental regenerative medicine, which is performed on periodontal tissues such as gums and bones that support teeth. A typical example of dental regenerative medicine is implant treatment. Implant therapy is a treatment in which an artificial tooth root made of titanium is implanted in the alveolar bone (Fig. 1) [1], which is the bone that supports the teeth, and is bonded to the alveolar bone, which is then covered with artificial bone. In the process of alveolar bone regeneration, the implant does not bond with the alveolar bone, leading to treatment errors.

Therefore, alveolar bone regeneration is important in dental regenerative medicine, and we aim to contribute to dental regenerative medicine by elucidating this phenomenon.
2. Object of analysis
After dentification, the holes (Figure 1) require 90 days to regenerate under the influence of gravity and other mechanical loads and calcium (Ca) secretion from blood vessels [2]. At intervals of 14, 30, and 90 days, the regenerated bones are referred to as new bone, juvenile bone, and osteoblastic structures, respectively (Figure 2(a), (b), (c)) [3].

3. Calculation model

3.1 Angiogenesis
Initially, vascular triggers (blood clots) are placed at random numbers. Next, a search is performed around the calculation point (particle) that represents the tip of the blood vessel, and a calculation point suitable for new blood vessel formation is determined based on the value of the inducing substance and other factors, and the blood vessel is renewed toward that calculation point. The bifurcation angle was set to 60-80° based on fractal nature [4].
3.2 Ca transportation
The main component of bone is hydroxyapatite, a hard crystalline form of basic phosphate $Ca^{2+}$, which is formed from $Ca^{2+}$ secreted from neovascular vessels, as shown in equation (1) [5].

$$10Ca(OH)_2 + 6H_3PO_4 \rightarrow Ca_{10}(PO_4)_6(OH)_2 + 18H_2O \quad (1)$$

Using Reynolds’ transport theorem, which considers $Ca^{2+}$ secreted from the neovascular system in migration phenomenology, equation (2) can be expressed as

$$D\nabla^2 A = \frac{1}{\beta} \Delta \rho. \quad (2)$$

However, the convection term was neglected under the assumption that the effect of convection by the secretion of $Ca^{2+}$ from neovascular tissue is small. Moreover, the nonstationary term was ignored under the assumption of steady-state secretion and diffusion of $Ca^{2+}$. Because the local bone formation and $Ca^{2+}$ consumptions are conservative, the generation term is defined as the local bone formation rate $\Delta \rho$.

3.3 Bone remodeling
The phenomenon of bone remodeling refers to a change in the bone structure due to the surrounding mechanical load. For example, the bones of a sick, bedridden person or an astronaut become brittle because of a lack of mechanical load.

The experiments conducted by Goodship et al. showed a correlation between local strain and remodeling, and this correlation is based on the mechanical stimulus [6]. When the mechanical stimulus is locally strong, a microscopic level of remodeling formation occurs. Conversely, when the mechanical stimulus is locally weak, remodeling absorption occurs.

The mathematical model proposed by Huiskes et al. uses strain energy density $U$ to represent mechanical stimuli and expresses bone growth in terms of Young’s modulus $E$ [7]. It is modeled as in equation (3), assuming that there is a threshold of strain energy density toward bone growth and absorption.

$$\frac{dE}{dt} = C(U - U_h), \quad (3)$$

where $C_U$ denotes the rate constant and $U_h$ represents the reference strain energy density.

The relationship of equation (4) is also experimentally demonstrated in the report by Carter et al. [8]

$$E = 3790 \cdot \dot{\epsilon}^{0.06} \cdot \rho^3, \quad (4)$$

where $\dot{\epsilon}$ is the strain rate.

From equations (3) and (4), equation (5) is realized.

$$\frac{d\rho}{dt} = \frac{C_U}{3\rho^2} (U - U_h) \quad (5)$$

3.4 Bone Formation Equation
From terms 2-1 and 2-2, the bone structure formation equation is modeled using Equation (6) [9]

$$\frac{d\rho}{dt} = C_A(A - A_h) + \frac{C_U}{3\rho^2}(U - U_h) + dp \nabla^2 \rho \quad (6)$$

where $A$ represents the concentration of $Ca^{2+}$ secreted by neovascularization and $A_h$ denotes the concentration of a reference $Ca^{2+}$ in the blood.

We introduced $\nabla^2 \rho$, which is responsible for locally flattening the formation and absorption effects of modeling. $dp$ is the diffusion constant.

The various parameters are set as shown in $C_A=20$, $Cu=3.0\times10^{-3}$, $dp=8.64\times10^{-3}$.

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4. Analysis conditions

4.1 Initial conditions
The extraction socket was modeled using particles (Fig. 3). Each particle was considered as a cell, and an analytical model close to the real phenomenon was constructed.

For simplicity, a three-dimensional cubic region of 12 mm per side was used as the analysis area, and a total of 729,000 computational nodes (particles), 90 of which were placed in each direction, were placed. The extraction sockets (Figure 2) were 8 mm in diameter and 12 mm in height. The time tick width was set to 0.1 day/step. The initial bone density $\rho$ immediately after tooth extraction was randomly assigned in the range of $10^{-6} \leq \rho \leq 10^{-3}$. The initial Ca concentration was set at 4.95 [mg/dl].

4.2 Boundary conditions
The upper surface of the extraction socket region was set as a free particle as a boundary condition, and the forced displacement as shown in Figure 3 (b) was applied as a mechanical stimulus for analysis. The sides were set as particles with a calcium concentration and bone density of 0.

5. Analysis result

5.1 Angiogenesis and vascular regression
In the analysis, the vessels in the region of tooth extraction fossa actively regenerated up to the 15th day after tooth extraction, buried in the bone by the 30th day, and retracted by the 90th day. Thus, the results of the analysis are shown in Figure 3, which represents the above characteristics.
5.2 $Ca^{2+}$ transport analysis
The results of the $Ca^{2+}$ transport analysis (Figure 5) shows that $Ca^{2+}$ was secreted from the vessels and evenly diffused throughout the extraction fossa as time progressed from day 30 (Figure 4 (a)) to day 90 (Figure 4 (b)).

5.3 Bone formation analysis
The results of the bone formation analysis (Figure 6) showed bone formation overtime at 14, 30, and 90 days. These results (Figure 6) corresponded to the experimental results of (Figure 2) and showed agreement in qualitative features.

6. Conclusions
1) Alveolar bone regeneration after tooth extraction was reproduced by simulation using particles.
2) In order to simulate the real world, we have formulated a bone formation equation that takes into account calcium transport from blood vessels and mechanical stimulation, which are major factors in bone regeneration. agreement with the realized life.
3) The analysis results of bone formation analysis (Figure 6) were compared with those of the experimental data (Figure 2) and were found to be qualitatively consistent.
4) In the future, we would like to conduct a quantitative evaluation of the simulation results and change the conditions by gender and age.
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