Evaluation of Bone Quality near Metallic Implants with and without Lotus-Type Pores for Optimal Biomaterial Design

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The stress shielding effect often degrades the quality and quantity of bone near implants. Thus, the shape and structure of metallic biomaterials should be optimally designed. A dominant inorganic substance in bone is a biological apatite (BAp) nanocrystal, which basically crystallizes in an anisotropic hexagonal lattice. The BAp c-axis is parallel to elongated collagen fibers. Because the BAp orientation of bones is a possible parameter of bone quality near implants, we used a microbeam X-ray diffractometer system with a beam spot, which had a diameter of 50 or 100 μm, to evaluate the BAp orientation of bones.

Two animal models were prepared: (1) a nail model (Ø 3.0 mm, SUS316L), which was used to understand the stress shielding effect in a rabbit tibial marrow cavity, and (2) a model of a lotus-type porous implant (Ø: 3.4 mm, mean pore diameter: 170 μm, SUS304L), which was used to understand the effect of the unidirectional-elongated pore direction in an anisotropic bone tissue of a beagle mandible. The porous implants were implanted so that the pore direction was parallel or perpendicular to the mesiodistal axis of mandible.

For the porous implant model, new bone formation strongly depended on the elongated pore direction and the time after implantation. For example, four weeks after implantation, new bone formed in pores of the implants, but the BAp orientation degree in the new bone was more similar to that in the original bone in the elongated pores parallel to the mesiodistal direction than that in the perpendicular pores. These differences in bone formation inside the parallel and perpendicular pores may be closely related to the anisotropy of original bone tissues such as the orientations of collagen fiber, BAp, and blood vessels. The orientation degree of BAp also changed in the nail model. The stress shielding effect decreased the orientation degree of the BAp c-axis in the tibia along the longitudinal axis.

Thus, optimal design of metallic biomaterials such as implant shape, pore size, elongated pore direction, etc., should be based on the anisotropy of the bone microstructure. [doi:10.2320/matertrans.47.2233]

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1. Introduction

Bone has a well organized microstructure and is composed of inorganic biological apatite (BAp) and organic collagen fiber, which provide reinforcement and pliability, respectively.¹ The microstructure under various scale levels shows anisotropy, which depends on the type of bone and the related stress distribution in vivo.²,³ Therefore, variations in the stress distribution on bones after implantation of biomaterials should change the bone microstructure on the nanoscale level. In fact, the stress shielding effect is a dominant factor for loosening orthopedic and dental implants in bones due to the quantitative changes in the total bone mass and bone mineral density (BMD).⁴,⁵ These changes are due to the bone functional adaptation for constructing a load bearing structure.⁶

To prevent the stress shielding effect and to maintain normal functional adaptation in bone tissue near implants, the material properties and design of shape for implants should be optimized. One possible optimization method is to bring the stiffness of the implants closer to that of bones, i.e., 10–30 GPa in the cortical bone.⁷ Because metallic and ceramic materials show higher Young’s modulus values than cortical and trabecular bones, new materials, which have decreased modulus values, have been developed for bone replacements.⁸ β-Titanium alloys, which have a bcc lattice and a low concentration of toxic elements, are promising as a bone implant material. In addition, porous materials have received attention as coating materials on the bone implant and as an implant, itself. Fixation of porous coated implants relies on the adaptive potential of the bone to provide a long lasting, biologically integrated interface.⁹ Moreover, the apparent stiffness in porous implants decreases compared to dense bulk materials. Thus, the implantation of porous materials may suppress the stress shielding effect on bones.

Recently, a new type of porous materials, which has long cylindrical pores that are aligned in one direction, has been fabricated by a unidirectional solidification process in a high pressure gaseous atmosphere.¹⁰,¹¹ The porous material, called the lotus-type porous material, may have potential as a bio-implant material because of the low apparent Young’s modulus and anchor effects by the in-growth new bones, which allows strong bonding at the bone-implant interface. Moreover, the anisotropy of the lotus-type porous implants may match the anisotropic microstructure found in bones.

In this article, changes in bone quantity and quality are examined after implantation of nails and lotus-type porous materials in a rabbit tibia and beagle mandible, respectively. Our studies focus on the stress shielding effect and anisotropy of bone microstructure. Bone quality is evaluated by the orientation of the BAp c-axis and the related collagen fiber direction because the BAp orientation is a very sensitive parameter, which is closely related to both the in vivo stress distribution and the bone mechanical function in normal, regenerate, and pathological hard tissues.²,³,¹²-¹⁴
2. Experimental Procedure

Two animal models were prepared: (1) a nail model, which was used to analyze the stress shielding effect, and (2) a model, which used a lotus-type porous implant, to understand the effect of elongated pore direction in an anisotropic bone tissue. A nail (ø: 3.0 mm, SUS316L) was inserted in the marrow cavity of a rabbit left tibia (a 5-month-old female) from a hole drilled in the distal cartilage. The rabbit was sacrificed one year after the operation. Cylindrical lotus-type porous implants (ø: 3.4 mm, height: 4.0 mm, SUS304L) (See Fig. 1(a)) were inserted in a cortical portion of beagle mandible. The porous implants contained unidirectional-elongated pores with a mean diameter of 170 μm and a total porosity of 60 vol.%. They were fabricated by the continuous zone melting technique under hydrogen at a growth rate of 330 μm/s. Complete details are described in previous papers.10,11) The lotus-type porous implant was implanted so that the elongated pore direction was parallel or perpendicular to the mesiodistal axis as schematically shown in Fig. 1(b). It should be noted that the c-axis of BAp, collagen fibers, and blood vessels preferentially align parallel to the mesiodistal axis in the mandibles.2,15) The beagles were sacrificed at four and thirteen weeks after implantation. The bone specimens were removed and then immersed into 10 vol% formalin neutral buffer solution to prevent denaturation of the organic matrix.

The preferred orientation of the BAp crystallites in the bone specimens was analyzed by a microbeam X-ray diffractometer (Mac Science, M18XHF22-SR, Japan) using Cu-Kα radiation operated at 90 kV and 40 mA. Because the incident beam collimated into a circular spot of 100 and 50 μm in diameter by metal collimators, X-ray diffraction peaks were obtained from a surface radiation area, which had a diameter of approximately 500 and 250 μm in the nail model and porous implant model, respectively. The preferred orientation of the BAp c-axis was evaluated as the relative intensity ratio of the (002) diffraction peak to the (310) peak from the X-ray profile measured along the longitudinal axis of the long bone. Complete details of the microbeam X-ray diffraction analysis are described in our previous paper.2)

The bone mineral density (BMD) and morphology of the bone specimens were measured in dry conditions by peripheral quantitative computed tomography (pQCT) (XCT Research SA+; Stratec Medizintechnik, GmbH, Germany) with a voxel size of 80 μm × 80 μm × 460 μm. The cortical bone was detected as the CT values of more than 690 kg/m³. The data is presented as a mean value ± standard deviation (SD). The Student’s t-test was used for statistical analysis.

3. Results and Discussion

3.1 Stress shielding effect in the nail model

Figure 2 shows the X-ray radiographic images one year after implantation of the nail in the left tibia of a rabbit. The entire length of left tibia was slightly shorter than that of right tibia, which did not have a nail. No significant inflammation

Fig. 1  Schematic illustrations, which show a lotus-type porous implant (a), conditions of the elongated pore direction for implantation in a mandible (b), and a method for estimating the distance, d, from the surface of the implant with elongated pores parallel to a mesiodistal direction (c). The BAp c-axes are preferentially oriented to the mesiodistal axis in the mandibles. d is estimated by eq. (2), where r is the diameter of cylindrical porous implant (= 3.4 mm), q is half the width of the cross-section of the implant, and p is the distance from the center line.
was observed around the nail. Even if Ni is dissolved from the nail, it does not cause an apparent toxic reaction. Four positions, a, b, c, and d, which were used to analyze the BMD and the BAp orientation in each tibia, are also described. Figure 3 shows the positions, A, B, C, D, E, F, and G, which were used to analyze the BMD and the BAp orientation in each tibia, are also described.
orientation in each cross-section of the four slices as described in Fig. 2. Positions A–F are in the original bone, but position G is in the new formed bone due to the in vivo change in the stress distribution after implantation of the nail in the left tibia.

The nail induces a stress shielding effect on the cortical bone of the left tibia mainly due to bending stress in addition to the axial stress because Young’s modulus of SUS316L (~161 GPa) for the nail is much higher than that of cortical bone (~20 GPa). Consequently, numerous pores appear in the cortical portion of the left tibia. The volume fraction of pores can be quantitatively evaluated from the pQCT images taken in the cross-section perpendicular to the bone longitudinal axis using eq. (1).

Porous volume (%) 
\[
= 100 \times \frac{\text{number of voxels satisfying } BMD < 690 \text{ [kg/m}^3\text{]}}{\text{number of voxels in the original cortical portion}}
\]  

The volume in the voxel is 80 μm × 80 μm × 460 μm. The 460 μm side is parallel to the longitudinal direction. A value of 690 kg/m³ corresponds to the threshold value of the minimum density of the cortical bone. The new bone (named G) is formed on the posterior side of the left bone as shown in Fig. 3, but the area of new bone was not used to calculate the porous volume. Finally, the porous volume is 1.3 ± 0.9% for the right tibia, which is used as a control, but the porous volume for the left tibia is 6.2 ± 3.0%. Since the porous volume of the left tibia, which contains the nail, is statistically higher than that in the right tibia, which lacks a nail (P < 0.05), it is concluded that stress shielding by the nail clearly promotes the introduction of pores in the cortical portion.

The stress shielding effect also appears in the distribution of the BMD in the cortical portion as shown in Fig. 4. The peak in the BMD distribution shifts to lower side in the left tibia, which contains the nail, compared to the right tibia, which does not have a nail. The mean BMD values (see arrows) are quite different from the peak values, but have similar tendencies. The mean BMDs in the left tibia, which has the nail, and the right tibia, which is the control, are 1336 ± 40 kg/m³ and 1444 ± 48 kg/m³, respectively (P < 0.05).

Figure 5 shows the effect of the nail implant on the intensity ratio of (002)/(310), which corresponds to the orientation degree of the BAp c-axis along the longitudinal bone axis. The randomly oriented apatite has a ratio of two. There is not a statistical difference in the BAp orientation, which depends on the analyzed portion within the same slice of the right tibia (control: A–F) and the original left tibia (nail: A–F). Thus, Fig. 5 adopts the mean values within the same slice. In the original cortical bone (A–F), the degree of the preferred orientation of the BAp c-axis along the longitudinal bone axis tends to decrease due to implantation and related stress shielding. In a previous study using a rabbit ulna model with a defect, it was reported that the degree of the BAp orientation decreases during an unloading condition. Moreover, the new bone portion (G) has a much lower degree of BAp orientation than the original cortical bone.

Figure 6 shows the correlation between the BMD and the orientation degree of the BAp c-axis in each analyzed portion. The stress shield promotes a decrease in both the BMD and the BAp orientation. The BMDs in the original cortical portion and new bone in the left tibia, which contains the nail, do not differ, but the BAp orientation in the new bone is statistically lower than that in the original one. In general, bone can adapt its mechanical function as a load bearing structure, which is called functional adaptation. Therefore, the changes in the BMD and also the BAp orientation depend on the applied stress field, which is based on the functional adaptation of the bone.

3.2 Optimal design of elongated pore direction in the lotus-type porous implant model

New bone, which contains calcified or fibrous tissue, forms
in the cylindrical pores. This formation of new bone depends on the elongated pore direction and the time after implantation in the lotus-type porous implants. Figure 7 shows example cross-sections of the lotus-type porous implant with parallel pores (Fig. 7(a)) and perpendicular pores (Fig. 7(b)) in a mandible along the mesiodistal axis. The porous implants are fixed in the cortical portion of mandible and new bone tissue macroscopically invades the elongated pores in the implants.

Figure 8 shows the existence ratio of bone tissue as a function of distance, d, from the porous implant surface. The distance from the implant surface, d, can easily be estimated by eq. (2) in a cross-section of the porous implant with the elongated pores parallel to the mesiodistal axis.
lattice with a \( P6_3 \) space group. The degree of calcification and the subsequent orientation of BAp are larger in the elongated pores parallel to the mesiodistal axis. Detailed studies on the effects of Ni dissolution, stress shielding, and pore size in new bone formation inside pores are currently under way and will be reported elsewhere.

The optimal design of metallic biomaterials such as the shape of the implant and pores, pore size, elongated pore direction, etc., should be considered on the basis of the anisotropy of the bone microstructure. Until now, biomechanical modeling in biomechanics has been used in the design and preclinical analysis of orthopedic devices. The biomechanical models show a very important aspect for design of these devices on the basis of the shape and BMD of the bone near the devices. In the future, however, the BAp orientation degree must be an additional parameter for understanding the detailed bone microstructure in relation to the stress distribution in vivo and bone mechanical function for the optimal biomaterial design. Moreover, metallic implants are recognized to be the only replacement, which supports body weight. In this study, the optimal design of metallic implants may induce and control new bone tissue, which improves bone functions. “Material Biology” is the term we coined to describe this novel relationship between biological tissue and materials, which improve the “Quality of Life”.

4. Conclusion

Variations in the bone microstructure after implanting metallic implants with and without lotus-type elongated pores were examined and the BAp orientation and the BMD of bones were analyzed. The following conclusions were reached by focusing on the anisotropy of the bone microstructure and stress conditions in bones near the implant.

1. The stress shielding effect by the metallic nail diminishes both the BMD and the orientation degree of the BAp c-axis along the longitudinal bone axis in the cortical portion of a tibia. After stress shielding occurs in the tibia, numerous pores appear, which result in a peak shift to lower side of the BMD distribution.

2. The formation of new bone tissues in the pores of lotus-type implants strongly depends on the elongated pore direction and the time after implantation. A lotus-type porous implant with the elongated pores parallel to the longitudinal axis can induce the new bone formation more effectively than that with perpendicular pores.
owing to the anisotropy of the original bone tissues such as the orientation of collagen fiber, BAp c-axis, and blood vessels.

(3) The BAp orientation of new bone even in the pores of the lotus-type porous implants can be analyzed by using a microbeam X-ray diffractometer system. The preferred orientation of the BAp crystallite/collagen fiber is an important parameter for the evaluation of the bone quality as well as BMD in bones near metallic implants.

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