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Calcium-Phosphate Formation on Titanium Modified with Newly Developed Calcium-Hydroxide-Slurry Treatment

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Authors developed a new surface-modification method with calcium-hydroxide slurry, which make it possible to treat a titanium surface by contacting with an alkaline agent containing high concentration of calcium. The objective of the new surface modification method was to improve a bone conductivity of titanium with simple and low-cost processes. The calcium-hydroxide slurry was prepared by mixture of calcium-hydroxide reagent and deionized water. A titanium plate was completely buried in the calcium-hydroxide slurry, and the slurry including the titanium was heated in air at 873 K for 7.2 ks, followed by washing in deionized water, and drying in air. Characterization with X-ray photoelectron spectroscopy revealed that chemical state of the surface-modified-titanium surface was the same as that of calcium titanate. X-ray diffraction pattern showed that the perovskite-type calcium titanate was formed in the surface-modified layer, and depth profile by Auger electron spectroscopy titanium indicated that dioxide layer was formed under the calcium-titanate layer. When the surface-modified titanium was immersed in a Hanks' balanced saline solution for 9 d, hydroxyapatite was formed on the surface-modified-titanium surface, while was not formed on the unmodified-titanium surface without surface modification. However, after 18-d immersion, hydroxyapatite was also formed on unmodified-titanium surface. X-ray diffraction pattern showed that thickness of the hydroxyapatite layer formed on the surface-modified-titanium surface was thicker than that on the unmodified-titanium surface. These results indicated that the calcium-hydroxide-slurry treatment improves the performance of calcium-phosphate formation of titanium. Therefore, the new treatment technique is one of the promising methods for improvement of bone conductivity of titanium. [doi:10.2320/matertrans.48.105]

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Keywords: surface modification of titanium, calcium-hydroxide slurry, calcium titanate, calcium-phosphate formation, bone conductivity

1. Introduction

Titanium has been used as biomaterials, such as stem of artificial joints and dental implant, because of its excellent biocompatibility¹⁻⁴⁾ and mechanical strength,⁵⁻⁷⁾ whereas, it takes several months to obtain good fixation between the titanium and bone. Although bulk properties dictate the mechanical properties of biomaterials, tissue-biomaterial processes are surface phenomena and they are governed by surface properties. In order to activate bone conduction, therefore, various surface modification techniques have been attempted. Hydroxyapatite (HAP) coating is the most popular method, and plasma-splaying process is employed for the coating.⁸⁻¹²⁾ With coating of HAP, good biomaterial-bone fixation is obtained.^{10,11)} However, a fracture at the HAP-titanium interface or in the HAP itself is often observed after a long-term use.¹³⁾ Therefore, it can be said that long-term stability of the plasma-sprayed HAP coating is insufficient.

Surface modifications improved the defects of the HAP coating are also studied by some researches. The most important requirement for the improvement is to obtain an unclear interface between the surface-modified layer and titanium substrate, yielding non-destructive interface. Hanawa *et al.* reported that implantation of calcium-ions with an energy of 18 keV modifies titanium surface to be bioactive.^{14,15)} The surface-modified layer of calcium-ion-implanted titanium consists of calcium oxide/hydroxide, titanium oxide, and calcium titanate,^{16,17)} and they concluded that calcium titanate causes of the bioactive surface.¹⁸⁾ Kokubo *et al.* showed that titanium bond to living bone directly if the titanium is treated by soaking in sodium-hydroxide solution

and the subsequent heating.¹⁹⁻²¹⁾ A surface of the treated titanium has sodium-titanate layer with gel-like structure.^{22,23)} After immersed in a simulated body fluid (SBF), sodium in the layer rapidly dissolved in the fluid, calcium in the SBF is taken in the layer instead of sodium, and then, calcium titanate is formed in the treated-titanium surface.^{24,25)} In the above two surface modification methods, calcium titanate is key material for the improvement of bone conductivity.

Recently, some of the authors (N. Ohtsu and T. Hanawa) attempted to improve surface of titanium by calcium-titanate coating with radiofrequency magnetron sputtering.²⁶⁻³⁰⁾ The deposited calcium-titanate layer without some post-treatment has an amorphous structure,^{28,29)} is dissolved in a physiological solution rapidly,²⁷⁾ and is not effective for the improvement.²⁹⁾ Whereas, if successive heating is carried out after the deposition, the calcium-titanate coating is crystallized to be a perovskite structure,^{28,29)} not dissolved easily, and facilitates new bone formation on titanium in hard rat tissue.³⁰⁾ These results indicate that the calcium-titanate coating with perovskite structure modifies titanium surface to be bioactive. However, sputtering technique requires a complex instrument equipped with an ultra-high vacuum system and further is inapplicable to complex-shaped biomaterials. Therefore, the sputtering technique is sometimes not suitable for commercialization, and development of new calcium-titanate coating technique with simple and low-cost is required.

Hanawa *et al.* attempted to form a calcium-titanate on titanium by soaking in a calcium-oxide solution.¹⁸⁾ After soaking in the solution, calcium is taken in the surface, however, the atomic ratio of calcium to titanium (Ca/Ti) is

about 0.1 in the surface,¹⁸⁾ and this ratio much smaller than that of stoichiometric calcium titanate. Hamada *et al.* attempted by hydrothermal modification in calcium-oxide solution.³¹⁾ Although the hydrothermal modification enhances the synthesis of calcium titanate, the atomic ratio of calcium to titanium is still lower than that of stoichiometric calcium titanate, and the calcium-titanate layer is not crystallized to be a perovskite structure. One simple method to increase the concentration of calcium in the modified surface is to treat titanium with an alkaline solution containing high concentration of calcium. However, since the water solubility of calcium oxide and hydroxide is extremely low, it is impossible to prepare the alkaline solution with high calcium concentration.

Authors developed a new surface modification method using calcium-hydroxide slurry. The new method makes it possible to modify titanium surface by contacting with alkaline agent containing high concentration of calcium. The objectives of this study were to characterize a surface of titanium modified with the newly developed calcium-hydroxide-slurry treatment and to estimate performance of calcium-phosphate formation in a SBF. The surface of surface-modified titanium was characterized with grazing incident angle X-ray diffractometry (GI-XRD), X-ray photoelectron spectroscopy (XPS), and depth analysis by Auger electron spectrometry (AES). The surface-modified titanium was immersed in Hanks' balanced saline solution (HBSS), and thereafter, the calcium phosphate formed in the solution were observed with scanning electron microscopy (SEM), and phase of the calcium phosphates were identified with GI-XRD.

2. Experimental Procedures

2.1 Surface modification with calcium-hydroxide-slurry treatment

Commercially available grade 1 pure Ti (cpTi; Furuuchi Chemical Co, Japan) with a disk shape (8 mm in diameter \times 1 mm in thickness), was mechanically polished with SiC paper (#1500) to obtain a rough surface. The titanium plate was soaked in 6 mol L⁻¹ HCl solution at 353 K for 60 s to etch the surface oxide, followed by gently rinsed in deionized water, and dried at 333 K in air. Calcium-hydroxide slurry for the treatment was prepared by a mixture of 1 g of reagent-grade calcium-hydroxide reagent (Nacalai Tesque, Inc) with 1 mL of deionized water (Millipore). Immediately after the mixture, the etched titanium plate was completely buried in the slurry. Then, the slurry containing the titanium plate was heated at 873 K for 7.2 ks in air with an electric furnace. After the heating, the slurry changes to a dry solid with many cracks due to vaporization of water. The titanium plate was retrieved from the slurry, washed ultrasonically in distilled water, and dried at 333 K in air.

2.2 Characterization of surface for the modified-titanium surface.

Chemical state and its composition in the surface were characterized with XPS. The photoelectrons were excited by Al K α radiation ($h\nu = 1486.6$ eV) from a monochromatized X-ray source (SSX-100, Surface Science Inc, U.S.A.). The

Table 1 Ion concentrations of Hanks' balanced saline solution (HBSS).

	Concentration (mol L ⁻¹)
Na ⁺	1.42×10^{-1}
K ⁺	5.81×10^{-3}
Mg ⁺	8.11×10^{-4}
Ca ²⁺	1.26×10^{-3}
Cl ⁻	1.45×10^{-1}
HPO ₄ ²⁻	7.78×10^{-4}
SO ₄ ²⁻	8.11×10^{-4}
CO ₃ ²⁻	4.17×10^{-3}

spot size of the X-ray was about 300 \times 500 μ m. The binding energy of Au 4f_{7/2}, Ag 3d_{5/2} and Cu 2p_{3/2} were 84.0, 368.3 and 932.6 eV, respectively and the FWHM of the Au 4f_{7/2} peak was 1.1 eV. Atomic ratio of calcium to titanium (Ca/Ti) was evaluated from the integrated intensities of Ca 2p_{3/2} and Ti 2p_{3/2}, where the sensitive factors installed in the standard SSI software were used for the calculation.

Depth profiles of the elements were determined with AES (JAMP-7100E, JEOL, Japan) with Argon-ion sputtering. The acceleration voltage of electron probe was fixed to 10 kV and that of Ar ions for ion etching was fixed to 3.0 kV. The etching rate estimated with SiO₂ layer was 0.3 nm s⁻¹. The profiles were determined by monitoring of differential spectra for Ti L₃M₂₃M₂₃, Ca L₃M₂M₃, and O KVV transition lines.

Crystallinity of the surface was identified by GI-XRD with a step-scanning mode at 0.8 deg min⁻¹ and the X-ray incident angle $\alpha = 1.0$ degree against the specimen surface (Rotaflex RU-200B, Rigaku, Japan).

2.3 Evaluation of performance for calcium-phosphate formation in HBSS

HBSS was employed as a SBF to evaluate the performance of calcium phosphate formation, whose inorganic contents was similar to that of human blood plasma. The ion concentrations of the HBSS are listed in Table 1. The HBSS was prepared by dissolving prescribed amount of reagent-grade NaCl, KCl, MgSO₄·7H₂O, Na₂HPO₄, KH₂PO₄, and NaHCO₃ (Nacalai Tesque, Inc) in deionized water (Millipore). The pH value of the HBSS immediately after preparation was about 7.4. Four plates of the surface-modified titanium were immersed in 12.6 mL of the HBSS at 310 K. Also, four unmodified-titanium plates, which mechanically polished with SiC paper (#1500), was immersed in HBSS as a control material. Avoiding Si contamination eluted from the vessels,³²⁾ specimens were immersed in the vessels made of perfluoroalkoxy fluoroplastic (Teflon[®] PFA) and the vessel was completely sealed. In order to avoid the increase of the pH, HBSS were changed once every three days. Two specimens were retrieved from the HBSS after immersion for 9 d; the other two specimens were retrieved after immersion for 18 d. After retrieval, the specimens were gently rinsed with distilled water, and dried at 313 K in air.

Performance for calcium-phosphate formation of the each specimen was estimated by observations of surface using scanning electron microscopy (SEM), where the acceleration voltage of SEM was 10 kV. Phase of the calcium phosphates

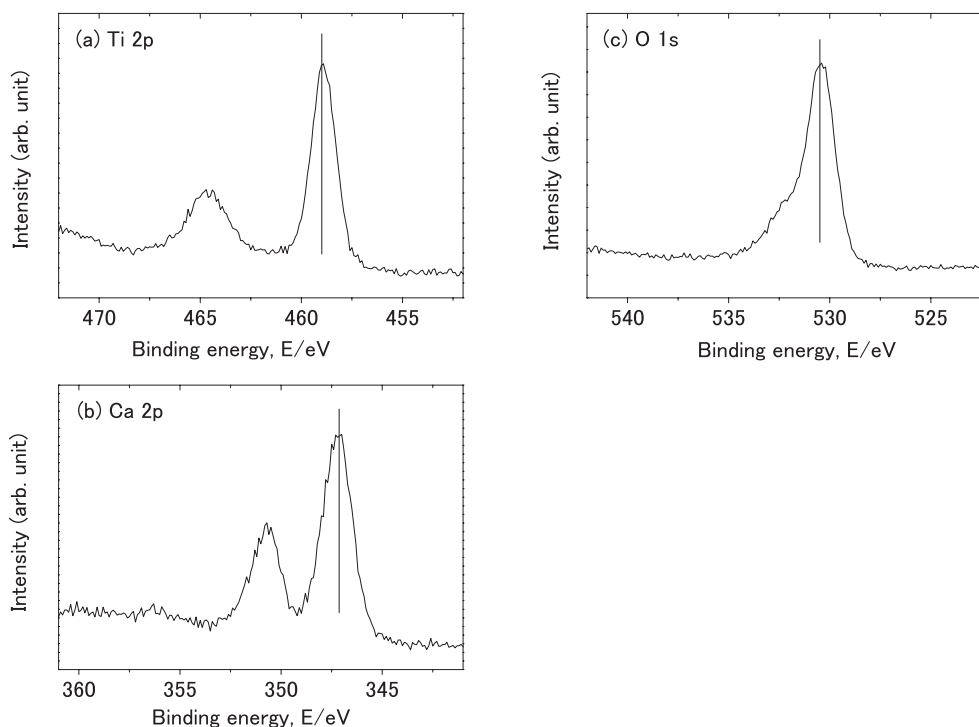


Fig. 1 XPS spectra for the surface-modified-titanium surface: (a) Ti 2p, (b) Ca 2p, and (c) O 1s regions.

were identified with GI-XRD. The measurement conditions of the GI-XRD measurement were the same as the conditions mentioned in the above.

3. Results and Discussions

3.1 Characteristics of the surface-modified-titanium surface

In the XPS survey spectrum for the surface-modified-titanium surface, peaks originated from calcium, titanium, oxygen, and carbon were observed. The binding energy of C 1s peak was 284.8 eV, and origin of carbon was surface contamination adsorbed by exposure to atmosphere. Figures 1(a) and 1(b) show the XPS spectra for Ti 2p and Ca 2p regions, respectively. FWHM of Ti 2p and Ca 2p peaks are 1.4 and 1.8 eV, respectively, and shapes of the peaks are almost symmetry. The results indicate that the chemical states of Ti and Ca consist of one state. Figures 1(c) shows the XPS spectrum for O 1s region. The O 1s peak has small tail in high energy side due to water adsorbed in atmosphere and/or hydroxyl group existing at the outermost surface. It is impossible to estimate which states are dominant in the tail. Binding energies for the modified surface and a calcium titanate of single-crystal are shown in Table 2. The binding energies for the modified surface almost agree with those of the calcium titanate of single-crystal.³³⁾ Furthermore, results of quantitative calculation showed that the atomic ratio of calcium to titanium (Ca/Ti) was 1.0. According to these results, it is concluded that chemical state of the modified surface within the XPS effective depth is calcium titanate.

Depth profile of elements for the modified surface is shown in Fig. 2. The profile of calcium shows that calcium is taken into the surface oxide layer up to ca. 10 nm from the

Table 2 Binding energies of Ti 2p_{3/2}, Ca 2p_{3/2}, and O 1s peaks for the surface-modified-titanium surface and single-crystal calcium titanate.

Electron orbital	Binding energy (eV)	
	Modified surface	Calcium titanate ³²⁾
Ti 2p _{3/2}	459.1	459.1
Ca 2p _{3/2}	347.2	347.3
O 1s	530.5	530.5

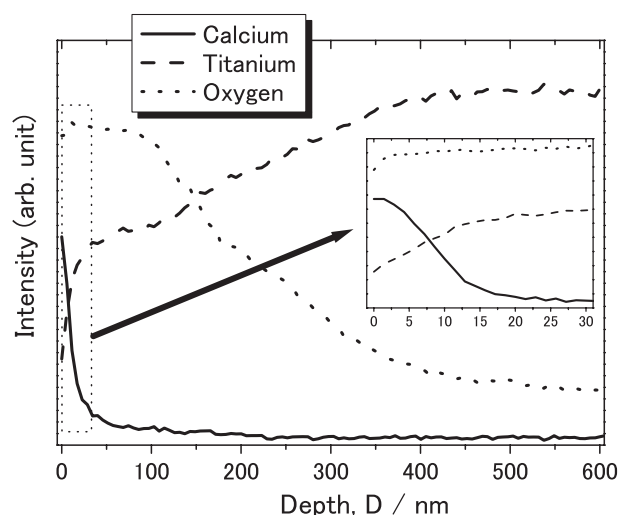


Fig. 2 Depth profile of calcium, titanium, and oxygen for the surface-modified-titanium surface. Inserted figure is enlargement of outermost surface region, which is enclosed by dash line.

outermost surface by the calcium-hydroxide-slurry treatment and the concentration of calcium gradually decreases towards to interior. The profile of oxygen shows that concentration of

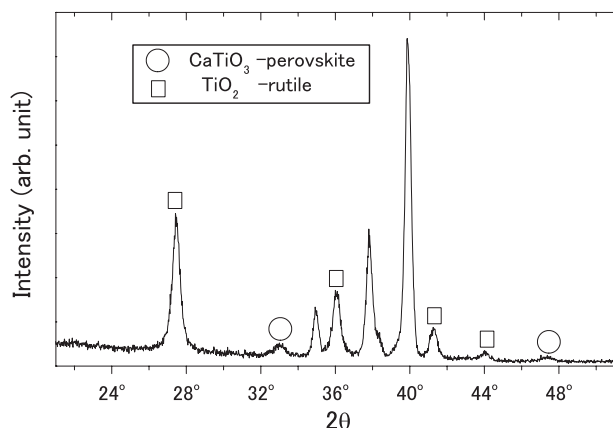


Fig. 3 GI-XRD pattern for the surface-modified-titanium surface.

oxygen diffused into the surface-modified titanium is almost constant up to 120 nm from the outermost surface. Eventually, the surface oxide layer was thickened. The depth range is much larger than that of calcium. These results indicate that surface of the modified titanium has double-layered structure; the outer layer consists of calcium, oxygen, and titanium, and the inner layer consists of oxygen and titanium. Furthermore, in the interface region between the inner layer and titanium substrate, oxygen gradually decreases towards to the substrate. The results indicate that the interface of the modified surface is unclear, that is expected to give non-destructive interface.

Figure 3 shows GI-XRD patterns of the modified surface. Detected peaks except peaks originated from titanium-substrate are identified as those of calcium titanate with perovskite structure and titanium dioxide with rutile structure. It is clear that calcium titanate and titanium dioxide existed at the outer layer and the inner layer, respectively, in the double-layered modified surface.

Some of authors discussed in the previous reports on the characteristics of calcium-titanate film prepared with radio-frequency magnetron sputtering.²⁸⁻³⁰ In the reports, it is concluded that calcium-titanate film which can activate the bone formation should have following two properties: chemical state of calcium is calcium titanate and the film crystallized to be a perovskite-type calcium titanate.^{29,30} Results of the characterization in this study indicated that the calcium-hydroxide-slurry treatment changed titanium surface to the calcium-titanate layer whose characteristics satisfied the requirement for the activation.

3.2 Performance of calcium-phosphate formation in HBSS

SEM images for surfaces of the unmodified and surface-modified titanium after immersion in HBSS for 9 d are shown in Figs. 4(a) and 4(b), respectively. On the surface-modified-titanium surface, many sphere-like precipitates with about 1- μ m diameter are observed. The precipitates are piled up and completely covered the modified surface. On the other hand, no precipitates are observed on the unmodified-titanium surface.

Figure 5 shows the SEM images of the surfaces of the unmodified and surface-modified titanium after immersion in HBSS for 18 d. Also, reduced images are inserted in the upper quarter part of the figures. Both the unmodified and modified surfaces were covered with the precipitate layer. Cracks observed in the layer are due to the evacuation of the water in an ultra-high vacuum. It is clear that the layer formed on the modified surface was thicker than that on the unmodified surface. A part of the layer formed on the modified surface is peeled off. The phenomenon is explained by the effect of stress concentration due to the thick precipitate layer. Peeling off is not observed on the unmodified surface because the layer is not so thick.

Figure 6 shows the GI-XRD patterns for the unmodified-

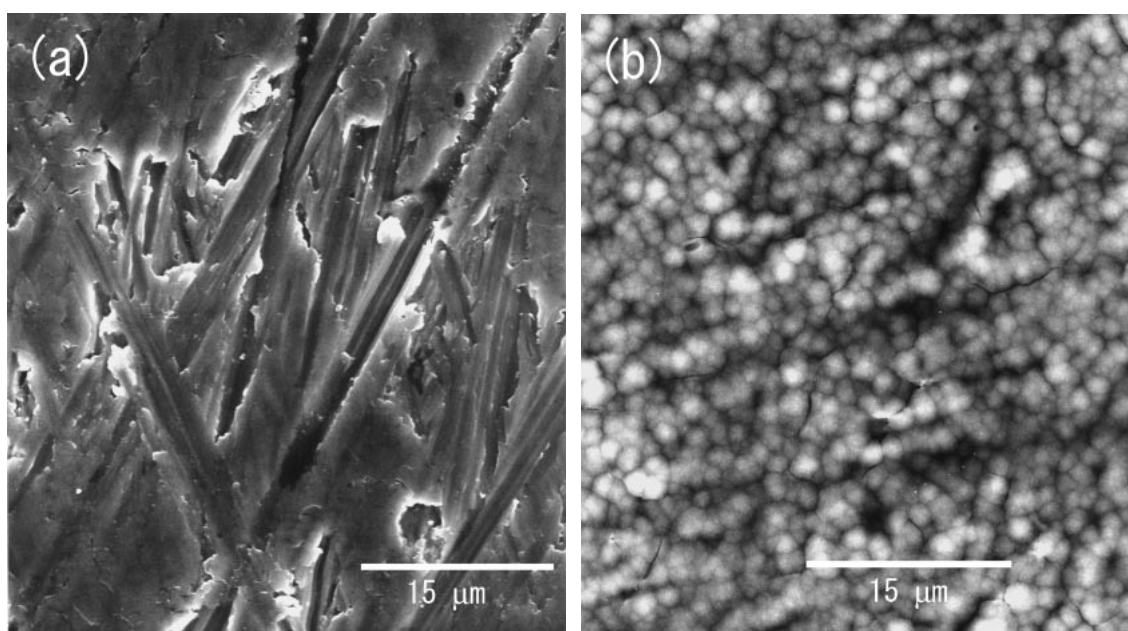


Fig. 4 SEM images for the surface after immersion in HBSS for 9 d: (a) unmodified-titanium surface, and (b) surface-modified-titanium surface.

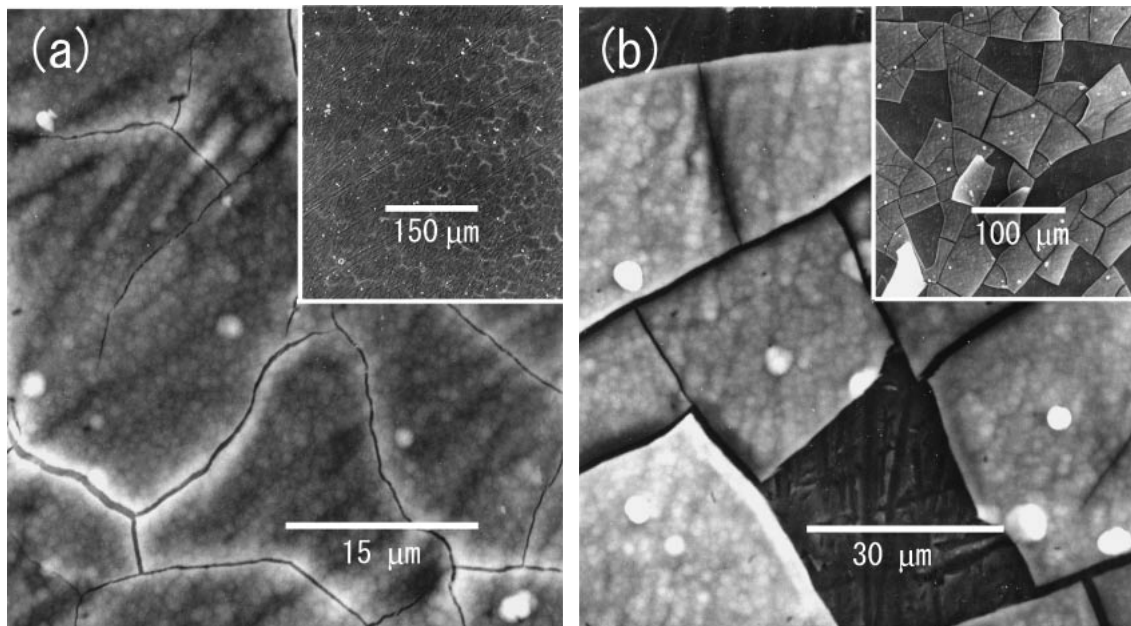


Fig. 5 SEM images for the surface after immersion in HBSS for 18 d: (a) unmodified-titanium surface, and (b) surface-modified-titanium surface. Inserted figures in upper quarter part are reduced SEM images.

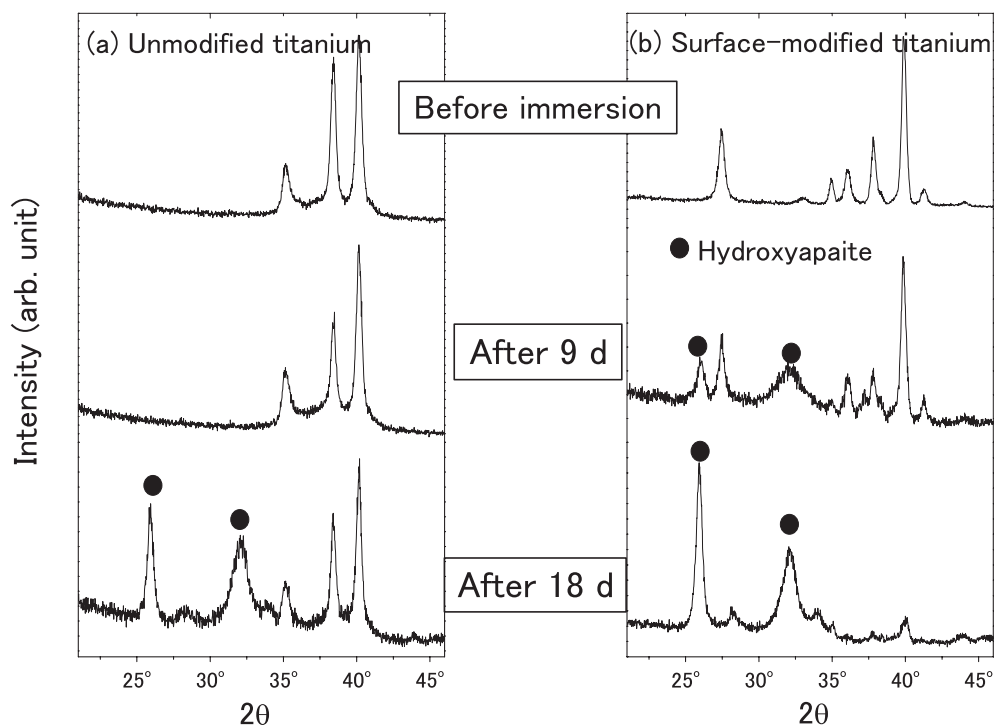


Fig. 6 GI-XRD patterns for (a) unmodified- and (b) surface-modified-titanium surfaces before and after immersion in HBSS for 9 and 18 d.

and surface-modified-titanium surface before and after immersion in HBSS for 9 and 18 d, respectively. New peaks appearing after the immersion are assigned to those of HAP. This result shows that the precipitates formed on the surfaces after the immersion are HAP. At 9 d, the peaks of HAP are observed only in the XRD patterns of the modified surface. This result corresponds to that of the SEM observation. At 18 d, the peaks of HAP are observed in the both modified and unmodified surface. On the other hand, the peaks of titanium

are disappeared in the modified-surface XRD pattern because the thickness of the precipitate layer formed on the modified surface exceeds the effective depth of the GI-XRD. The result indicates that the thickness of the HAP layer formed on the modified surface is thicker than that on the unmodified surface and corresponds to the result of the SEM observation.

The results of the SEM and GI-XRD show that the formation speed of HAP layer on the surface-modified-titanium surface is much faster than that on the unmodified-

titanium surface. Thus, it is concluded that the performance of the calcium-phosphate formation in HBSS is improved by the calcium-hydroxide-slurry treatment. In general, surface which can form calcium phosphates rapidly is bioactive. Therefore, the calcium-hydrate-slurry treatment is one of the promising treatments for improvement of bone conductivity.

4. Conclusion

By treating with newly developed calcium-hydroxide-slurry treatment, the surface of titanium changes to calcium-titanate layer with perovskite structure. Also, titanium-dioxide layer is formed under the calcium-titanate layer. The characteristics of the surface-modified titanium surface correspond to those of the calcium-titanate film prepared with radiofrequency magnetron sputtering and post-heating which can facilitate the bone formation. On the other hand, the interface between the modified layer and substrate is unclear, expected to give non-destructive interface. Speed of the hydroxyapatite formation on titanium in Hanks' balanced saline solution becomes faster by modifying with the calcium-hydroxide-slurry treatment, and thus, it is concluded that the treatment improve the performance of calcium-phosphate formation on titanium. The results show that the calcium-hydroxide-slurry treatment can modify titanium surface to a bioactive calcium-titanate layer with simple and low-cost, and it is indicated that the new technique is one of the promising treatments for improvement of bone conductivity.

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