

## Original

# Chemical Analysis of a Novel Coating Material, CaTiO<sub>3</sub>-aC

Mika Okauchi-Yabuuchi<sup>1)</sup>, Ryo Tamamura<sup>1)</sup>, Noriyuki Nagaoka<sup>1)</sup>, Shin Takagi<sup>2)</sup>, Etsuo Kishimoto<sup>3)</sup>, Tohru Takagi<sup>1,4)</sup>, Andrea Rodriguez<sup>1)</sup>, Miho Inoue<sup>1)</sup>, Hitoshi Nagatsuka<sup>1)</sup>, Masaru Akao<sup>4)</sup> and Noriyuki Nagai<sup>1,4)</sup>

<sup>1)</sup> Department of Oral Pathology and Medicine, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences

<sup>2)</sup> Department of Oral and Maxillofacial Reconstructive Surgery, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences

<sup>3)</sup> Department of Oral Health, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences

<sup>4)</sup> Center of Oral Health Science, International Dental Hygienist College in Okayama, Motoyama Gakuen

(Accepted for publication, October 25, 2008)

**Abstract:** In the current study, we compared the recently developed CaTiO<sub>3</sub>-amorphous carbon (CaTiO<sub>3</sub>-aC) as a bone inducing coating material with HA from aspects of surface electric charge and solubility. CaTiO<sub>3</sub>-aC had negative surface electric charge similar to HA. Thus similar tissue reaction and bone inducing ability were considered to obtain.

On the other hand solubility of CaTiO<sub>3</sub>-aC coating was lower than HA. Moreover though CaTiO<sub>3</sub>-aC itself showed low solubility, CaCO<sub>3</sub> was found to be included in it, and long-term slow Ca<sup>2+</sup> release occurred. Thus the sample was suggested to be used as an ion exchange material.

When the implant using Ti/CaTiO<sub>3</sub>-aC/HA double layer coating was developed, first bioactive state of the implant will continue due to HA character. Then even early resorption of HA occurs, bioactive state will continue due to CaTiO<sub>3</sub>-aC layer. Therefore Ti base will not expose. This result is supposed to contribute long term success of the implant.

**Key Words:** CaTiO<sub>3</sub>-aC, Hydroxyapatite, Implant, Coating material, Titanium

## Introduction

It has been reported that CaTiO<sub>3</sub> like substrates generally form during coating of hydroxyapatite (HA) over the titanium surface under high temperature conditions (1200 °C) by thermal decomposition method<sup>1)</sup>. Nagai et al. has recently reported that the coating material formed over the titanium surface by a newly developed modified thermal decomposition method (sintering at 650 °C using an organic solvent) was a film-like CaTiO<sub>3</sub>-amorphous Carbon compound (CaTiO<sub>3</sub>-aC)<sup>2)</sup>. This compound includes amorphous carbon and is different than the previous materials prepared by the dry method. In the dry method, perovskite (CaTiO<sub>3</sub>) compound is formed as a main component after heating of CaCO<sub>3</sub>-TiO<sub>2</sub> mixture at 1200 °C, while formation of CaTiO<sub>3</sub>-aC material was shown by Nagai et al<sup>2)</sup>.

Since the compound is a novel bioactive material, its basic character is needed to be identified. For a good implant coating material, strong bonding as well as long period of bone inducing ability is required. Regarding with the bonding ability, it has

recently been demonstrated in the article by Nagai et al<sup>2)</sup>. On the other hand, for character of the coating material with bone inductivity as in the representative material of HA, electric charge of the material surface has been known to be negative<sup>3-6)</sup>. As mentioned above, low solubility for a long period, a different point from HA or TCP, is an important factor<sup>2, 3)</sup>.

Thus we examined the differences of bone inducing ability between the novel material of CaTiO<sub>3</sub>-aC and HA by focusing the surface electric charge and solubility.

## Materials and Methods

### *Experiment 1. Comparison of Zeta potentials of CaTiO<sub>3</sub>-aC, CaTiO<sub>3</sub> and HA (Sintering at 650 °C as well as 1200°C)*

Powders of each of CaTiO<sub>3</sub>-aC, CaTiO<sub>3</sub> and HA (sintering at 650 °C as well as at 1200 °C) were used. For CaTiO<sub>3</sub>-aC, commercial material was used (Aldrich®, Sigma). Powders of CaTiO<sub>3</sub>-aC and HA (sintering at 650 °C) were synthesized by thermal decomposition method as shown in the below. Each coating material prepared according to the method of Nagai et al<sup>2)</sup> was put in a crucible, followed by wind drying in the draft for a week, and then overnight drying at 110 °C. Then each material was rapidly heated at 650 °C for 2 hours. HA (sintering at 1200

Corresponding to: Hitoshi Nagatsuka DDS.PhD. Department of Oral Pathology and Medicine, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Shikatacho, 2-5-1, Okayama City, 700-8525, Japan. Tel: 086-235-6652. Fax: 086-235-6654. E-mail: jin@md.okayama-u.ac.jp

°C) was prepared as in the following way. 0.5 M phosphoric acid was gradually dropped into 0.5 mol Ca (OH)<sub>2</sub> suspension and white gel like precipitation was prepared. The material was filtrated, dried at 60 °C, and then heated at 1200 °C for one hour under the conditions of a temperature increase of 100 °C /h. 0.1 g of each of the prepared powders was crushed to pieces with a mortar, and then mixed with 100 ml of distilled water. Then each solution was homogenized with an ultrasonic homogenizer (vibra cell, SONIC) for 5 hours. Zeta potential of each material was then measured with a zeta seizer (Nano-ZS, Malvern Instruments) at room temperature.

Particle diameters of each particle calculated with Nano-ZS zeta sizer were 396 ± 46 nm for CaTiO<sub>3</sub>-aC, 1170 ± 219 nm for CaTiO<sub>3</sub>, 351 ± 42 nm for HA (sintering at 650 °C), and 463 ± 56 nm for HA(sintering at 1200 °C).

**Experiment 2. Comparison of solubility of CaTiO<sub>3</sub>-aC, CaTiO<sub>3</sub>, and HA**

**A. Comparative experiment of CaTiO<sub>3</sub>-aC, CaTiO<sub>3</sub>, and HA (sintering at 650 °C as well as 1200 °C) particles**

The samples were powders of each of CaTiO<sub>3</sub>-aC, CaTiO<sub>3</sub> and HA (sintering at 650 °C as well as 1200 °C) as used in experiment 1. 0.1 g of each sample was added into 100 ml of 10 mM Tris buffer solutions with various pH (PH 4.8/ 7.0/ 7.8), and mixed with a continuous stirrer at room temperature. Then 10 ml solution was collected at various time periods (1<sup>st</sup> day, 3<sup>rd</sup> day, 7<sup>th</sup> day and 4 weeks later) and centrifugally separated. Ca and Ti concentrations in each collected solution were measured with ICP-AES (Inductively Coupled Plasma) (SPS-7700, Seiko Instruments).

**B. Comparative experiment of solubility of CaTiO<sub>3</sub>-aC as well as HA coating film prepared by modified thermal decomposition method using Ti plate**

Coating of Ti plate was performed as previously reported by the method of Nagai et al<sup>2)</sup>. Solubility of Ca and Ti from Ti plate into neutral buffer was measured by ICP as in experiment A. Ti plates coated with each of CaTiO<sub>3</sub>-aC and HA were soaked in 100 ml of each of Tris buffer (pH 7.4) and physiologic salt solution (pH 7.4) at room temperature. Two Ti plate with size of 3.5 cm x 3.5 cm were used. Each was coated 3 times with CaTiO<sub>3</sub>-aC as well as HA. Ca and Ti concentration in each solution was calculated at 1<sup>st</sup> day, 3<sup>rd</sup> day, 7<sup>th</sup> day, 14<sup>th</sup> day and 28<sup>th</sup> day. The experiment was repeated 3 times.

**Results**

**Experiment 1. Comparison of Zeta potentials of each of CaTiO<sub>3</sub>-aC, CaTiO<sub>3</sub>, and HA (sintering at 650 °C as well as 1200 °C)**

As shown in table 1, Zeta potential of CaTiO<sub>3</sub>-aC particle was -22.2 mV similar to negative charge of HA particle (-9.13 mV, sintering at 650 °C, modified thermal decomposition method).

Table 1. Zeta potentials of CaTiO<sub>3</sub>-aC, CaTiO<sub>3</sub> and HA (sintering at 650 °C as well as 1200 °C)

Sample	Zeta potential (mV)
CaTiO <sub>3</sub> -aC (650°C)	-20.6
CaTiO <sub>3</sub> (1200°C)	-31.2
HA(650°C)	-9.13
HA(1200°C)	-8.93

**Experiment 2. Comparison of solubility of CaTiO<sub>3</sub>-aC, CaTiO<sub>3</sub>, and HA**

**A. Comparative experiment of CaTiO<sub>3</sub>-aC, CaTiO<sub>3</sub>, and HA (sintering at 650 °C as well as 1200 °C) particles**

As shown in figure 1, solubility of Ca was highest in CaTiO<sub>3</sub>-aC sample, followed by HA sample (sintering at 1200 °C) in all buffer solutions and time periods. Though HA (sintering at 650 °C) and CaTiO<sub>3</sub> showed similar Ca solubility, both levels were low. Liquefaction volume of Ti was in undetectable level in all materials except the CaTiO<sub>3</sub> sample.

**B. Comparative experiment of solubility of CaTiO<sub>3</sub>-aC as well as HA coated Ti plate prepared by modified thermal decomposition method**

As shown in figure 2, Ti plate coated with CaTiO<sub>3</sub>-aC by modified thermal decomposition method showed lower level of Ca solubility than Ti plate coated with HA (sintering at 650 °C) by the same method in all experiment periods. Liquefaction volume of Ti was in undetectable level in both samples.

**Discussion**

We recently developed an ultra thin coating material of CaTiO<sub>3</sub>-aC/HA by a novel modified thermal decomposition method<sup>2)</sup>. In this method, bonding ability with Ti was 2.5 times stronger as compared to HA only coating. Moreover proliferation, differentiation and calcification ability of the osteoblastic cells were shown in investigations of Rodriguez as well as Inoue (article in preparation). Herein, we evaluated the physical properties of CaTiO<sub>3</sub>-aC and HA by the new method.

Correlation of bone induction ability and character of implant surface

Efficacy of bone induction ability by bioactive material has been known to be affected by property of the material. As conditions of surface which promote differentiation of osteoblast<sup>7-9)</sup>:

1. Minus electric charge of the surface<sup>3-6)</sup>
2. Continuous liquefaction of Ca<sup>2+</sup><sup>10)</sup>

For example, HA has been known to be associated with minus surface electric charge<sup>3-6)</sup> and liquefaction of Ca<sup>2+</sup> in normal body<sup>11)</sup>. Mechanism of early bone induction is as follows:

1. Though macrophage with positive surface electric charge recognizes the negatively charged HA material as a foreign

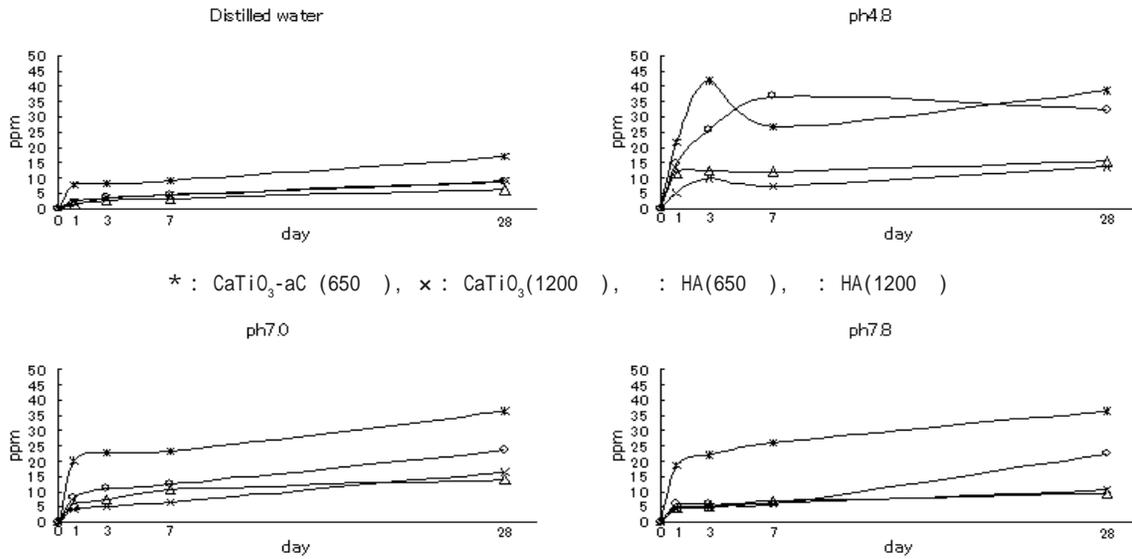


Figure 1. Solubility of CaTiO<sub>3</sub>-aC, CaTiO<sub>3</sub>, HA (sintering at 650 °C), and HA (sintering at 1200 °C). y axis shows Ca concentration. Ti elution was undetectable level in all samples except CaTiO<sub>3</sub>.

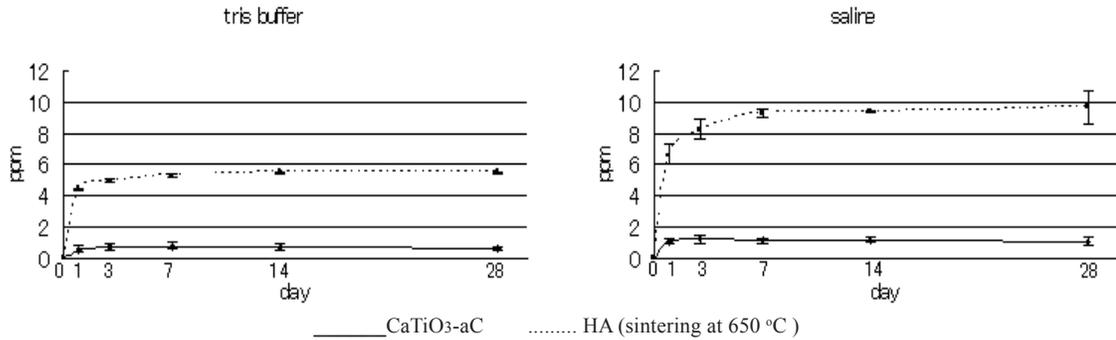
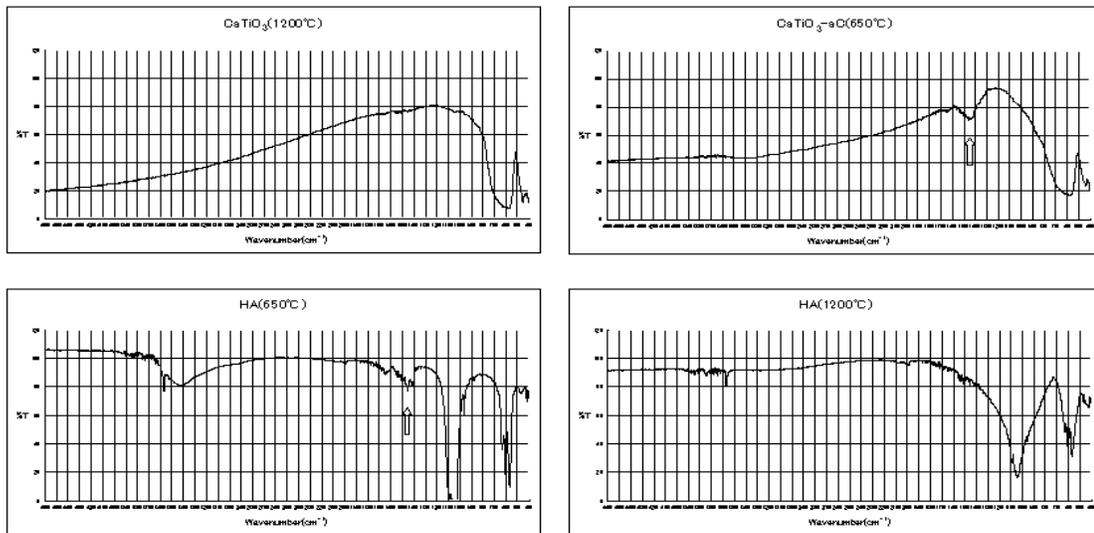


Figure 2. Solubility of CaTiO<sub>3</sub>-aC as well as HA (sintering at 650 °C) coating film prepared by modified thermal decomposition method on Ti plate. y axis shows Ca concentration. Ti elution was undetectable level.



↑  
CO<sub>3</sub><sup>2-</sup>

Figure 3. FT-IR spectrum of powder sample. CO<sub>3</sub><sup>2-</sup> group was identified in CaTiO<sub>3</sub>-aC as well as HA sample (sintering at 650 °C). Presence of CO<sub>3</sub><sup>2-</sup> group suggests that CaCO<sub>3</sub> exists in CaTiO<sub>3</sub>-aC and carbonate apatite forms in HA sample (sintering at 650 °C).

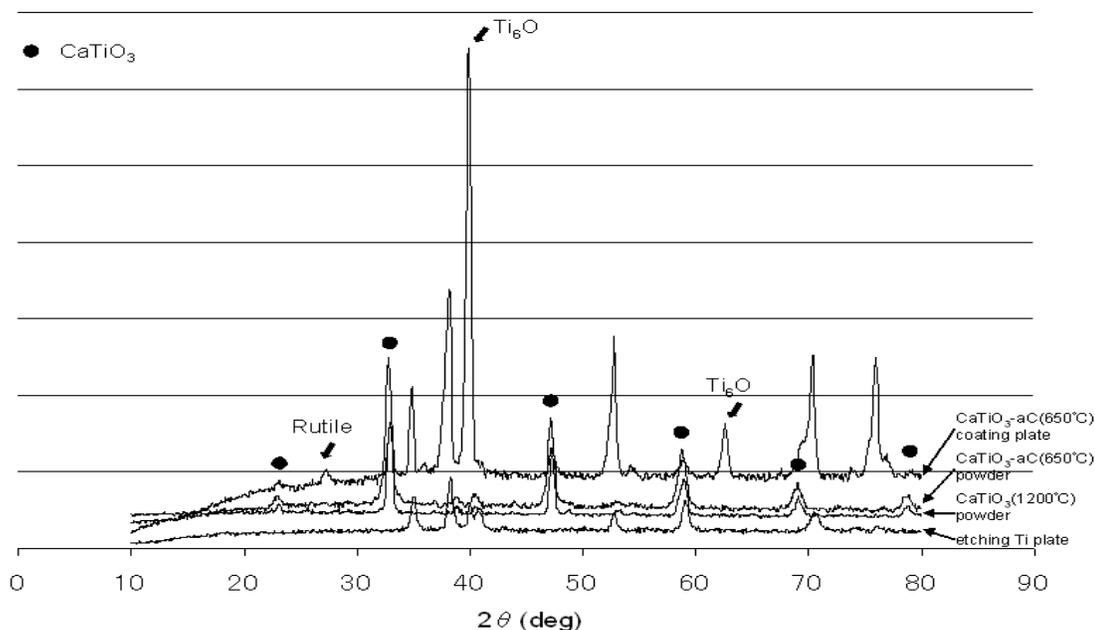


Figure 4. XRD diffraction pattern of CaTiO<sub>3</sub>-aC and CaTiO<sub>3</sub> powders as well as CaTiO<sub>3</sub>-aC coating plate. As a reference substrate, diffraction pattern of Ti base plate with etching is shown.

- body, phagocytosis cannot be done<sup>12</sup>).
2. Ca<sup>2+</sup> released from HA material re-deposits on HA surface and makes it with positive electric charge. Thus interstitial proteins with minus electric charge such as fibronectin and vitronectin precipitate<sup>13</sup>). On the other hand, host bone-marrow derived mesenchymal stem cells with minus charge avoids from the surface<sup>14</sup>).
  3. Mesenchymal stem cells differentiate into osteoblasts and attach to HA surface through interstitial proteins and Ca<sup>2+</sup>. These cells then secrete non-collagenous as well as collagenous matrixes<sup>9</sup>).

Since experiment 1 showed that CaTiO<sub>3</sub>-aC had negative surface electric charge similar to HA, the tissue reaction and bone bonding ability are supposed to be same with HA material. In fact, proliferation, differentiation and calcification ability of the osteoblastic cells were shown for CaTiO<sub>3</sub>-aC material in *in vitro* investigations of Rodriguez as well as Inoue (article in preparation).

#### Solubility and continuity of bioactive condition

From the results of comparative experiment 2 of CaTiO<sub>3</sub>-aC, CaTiO<sub>3</sub> and HA solubility, the following 2 questions arise:

1. Although Ca released from CaTiO<sub>3</sub>-aC sample (powder as well as coating plate), Ti liquation was undetectable level.
2. Regarding with Ca liquation level, it was higher in CaTiO<sub>3</sub> aC than HA in powder material and lower in CaTiO<sub>3</sub>-aC than HA in plate.

First regarding for the question one, crystal structure of CaTiO<sub>3</sub>-aC did not dissolve, but it is suggested that another compound within CaTiO<sub>3</sub>-aC crystal which consists of calcium could release

Ca. Since CaO forms as a starting substance from preparation of CaTiO<sub>3</sub>-aC<sup>2</sup>), the possible compound which generates from this step could be CaCO<sub>3</sub> or Ca(OH)<sub>2</sub>. Thus to confirm existence of carboxyl (CO<sub>3</sub><sup>2-</sup>) and hydroxyl (OH<sup>-</sup>) group, FT-IR spectrophotometric analysis was performed. A FT/IR-350 type Fourier Transform Infrared Spectrometer (JASCO Corporation) was used, and measurement was done with KBr method with a spectrum of 400-4600 cm<sup>-1</sup> of frequency range. The result of IR spectrum demonstrated presence of CO<sub>3</sub><sup>2-</sup> group within powder sample of CaTiO<sub>3</sub>-aC as well as HA (sintering at 650 °C) (Figure 3). Though the presence of CO<sub>3</sub><sup>2-</sup> within CaTiO<sub>3</sub>-aC sample was detected as CaCO<sub>3</sub>, carbonate apatite<sup>15, 16</sup>) was formed within HA powder sample. Both compounds show similar composition to HA of the living body. On the other hand, CO<sub>3</sub><sup>2-</sup> group was not detected within CaTiO<sub>3</sub> sample and little amount was found within HA (sintering at 1200 °C).

Next, to evaluate crystal structure of CaCO<sub>3</sub> XRD analysis was performed. For the measurement of XRD pattern, the instrument RINT2500 (Rigaku) was used under the conditions of 50mA, 200kV with Cu-Kα ray irradiation. The analysis did not show presence of CaCO<sub>3</sub> crystal within CaTiO<sub>3</sub>-aC sample (powder as well as coating) (Figure 4). And since background of XRD pattern of CaTiO<sub>3</sub>-aC coating was high, presence of amorphous compound within the coating material was suggested. Thus it has been considered that CaCO<sub>3</sub> crystal amount within CaTiO<sub>3</sub>-aC sample was either very low or was in amorphous state. In case of amorphous state, liquation of Ca has been considered to be easy. Though a strong peak different than the base material Ti peak was detected from analysis of diffraction pattern of CaTiO<sub>3</sub>-aC

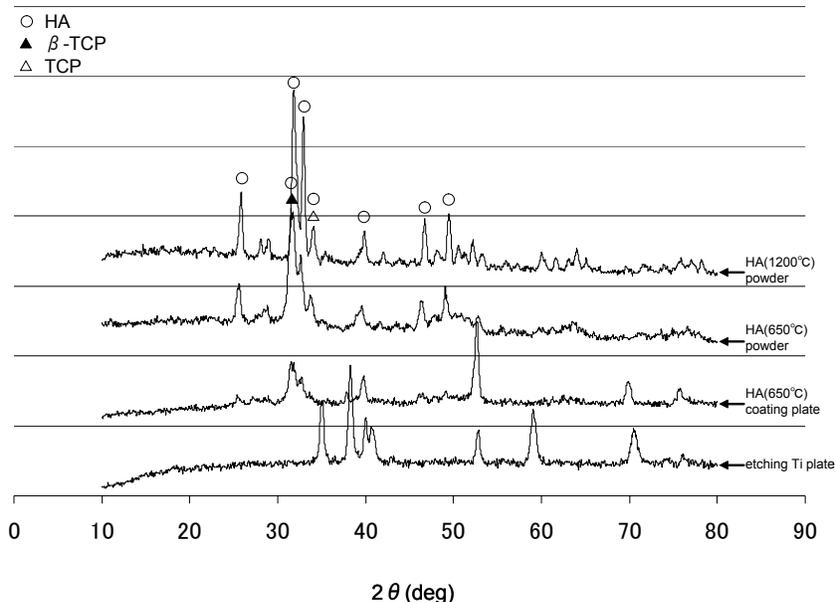


Figure 5. XRD diffraction pattern of HA (sintering at 650 °C as well as sintering at 1200 °C), and HA coating plate. As a reference substrate, diffraction pattern of Ti base plate with etching is shown.

coating, this was most likely compatible with Ti<sub>6</sub>O (hexagonal, space group: P31c, a=5.14, b=5.14, c=9.48) diffraction pattern. This group was considered to be formed from oxidization of Ti base in low oxygen environment between Ti base and CaTiO<sub>3</sub>-aC coating during sintering. And though TiO<sub>2</sub> (Rutile) peak formed from oxidization of Ti base was also seen, Rutile amount was very low and only strongest peak was detected.

XRD analysis with same conditions was also done for HA sample. The results showed that although β-TCP was detected in HA powder (sintering at 650 °C), it was not found in HA powder (sintering at 1200 °C) (Figure 5). However in HA powder (sintering at 1200 °C), TCP peak (rhombohedral, space group: R-3m, a=5.248, b=5.248, c=18.691) was detected. And α-TCP was not found in both HA sample. Regarding with HA powder (sintering at 650 °C), Ca liquation was considered from β-TCP (as well as carbonate apatite).

Regarding with question 2, two reasons were thought. First, surface volume of powder and coating plate of CaTiO<sub>3</sub>-aC is different. CaTiO<sub>3</sub>-aC coating is a structure of multicrystal composed of solidified microcrystals with a diameter of 10-20 nm (Figure 6). Thus though the surface volume dissolving due to solvent touch is small, long term slow Ca releasing character is likely to be. For the second reason, since Ca shows chemical binding with TiO<sub>2</sub> base (thus adhesive strength with Ti also improves) in CaTiO<sub>3</sub>-aC coating plate (different than powder), liquation of Ca is considered to be difficult.

In conclusion, although CaTiO<sub>3</sub>-aC itself did not dissolve, it becomes a Ca<sup>2+</sup> source through long term Ca<sup>2+</sup> release from CaCO<sub>3</sub>. Thus our results showed that the sample can be used as an ion

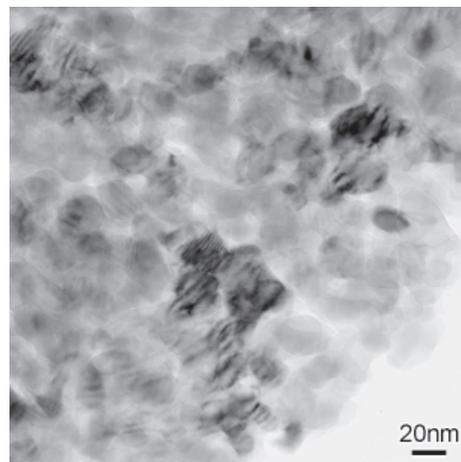


Figure 6. High power TEM image of CaTiO<sub>3</sub>-aC coating.

exchange material (coexistence of covalent and ion bonding). Presence of Ca<sup>2+</sup> has been reported to be effective for proliferation of osteogenic cells<sup>7,8,10,17,18</sup>.

In the current study, comparative experiment of solubility between HA (sintering at 650 °C) and HA (sintering at 1200 °C) showed that HA (sintering at 650 °C) clearly had lower solubility. Another point is that though HA (sintering at 650 °C) consisted of β-TCP, HA sample (sintering at 1200 °C) did not include β-TCP. Regarding with β-TCP, many researches have been recently conducted. Though bone affinity is low until 4 weeks as compared to HA, it is almost same after this time<sup>19</sup>. Moreover it shows similar mechanical character with HA<sup>20</sup>. Its solubility is also 20% of α-TCP<sup>20</sup>. Thus presence of β-TCP but absence of α-TCP in HA

material (sintering at 650 °C) is also a preferable result considering from good affinity and safety of  $\beta$ -TCP in the living organism.

On the other hand, as mentioned above, surface electric charge of  $\text{CaTiO}_3$ -aC is minus and its solubility is only 1/10<sup>th</sup> of HA (sintering at 650 °C). This result suggests that  $\text{CaTiO}_3$ -aC/HA double layer structure provides long term bioactive state than the previous plasma HA coating method. Zhou and Akao implanted  $\text{CaTiO}_3$ -aC/Ti to dogs, and showed long term successful results in terms of bone induction and bonding ability<sup>20</sup>. These results demonstrate persistent effect of  $\text{CaTiO}_3$ -aC.

When the implant using Ti/  $\text{CaTiO}_3$ -aC/HA (sintering at 650 °C) double layer coating was developed, first bioactive state of the implant will continue due to HA character. Then even early resorption of HA occurs, bioactive state will continue due to  $\text{CaTiO}_3$ -aC layer. Thus Ti base exposure will not occur. This result will be linked to long term success of the implant. Therefore current study introduces novel biomaterial of  $\text{CaTiO}_3$ -aC as a good implant coating material.

#### Acknowledgements

Our heartfelt appreciations go to Professor Miyake Michihiro, Department of Material and Energy Science, Okayama University Graduate School of Environmental Science and Associate Professor Sakae Toshiro, Nihon University Matsudo Faculty of Dentistry whose comments and suggestions were innumerable valuable throughout the course of our study.

This work was supported by grant Grants-in Aid for Scientific Research(C)(20592200,20592454) and (19 · 07217, 19 · 45179) from the Japan Society for the Promotion of Science.

#### References

1. Ukegawa Y. Pull-out strength and bone tissue reaction of plasma-sprayed hydroxyapatite coatings with different thickness or substrates. *J Jpn Orthop Assoc* 66:688-702, 1992
2. Nagai N, Okauchi M, Rodriguez A, Mehmet G, Hu H, Nagaoka N, Nagatsuka H, Takagi T, Akao M. Development of New Titanium Coating Material ( $\text{CaTiO}_3$ -aC) with Modified Thermal Decomposition Method. *J Hard Tissue Biology* 17(2):47-54, 2008
3. Nakamura S, Kobayashi T, Yamashita K. Extended bioactivity in the proximity of hydroxyapatite ceramic surfaces induced by polarization charges. *J Biomed Mater Res* 61:593-599,2002
4. Nakamura S, Kobayashi T, Yamashita K. Enhanced osteobonding by negative surface charges of electrically polarized hydroxyapatite. *J Biomed Mater Res* 57:477-484, 2001
5. Itoh S, Nakamura S, Kobayashi T, Shinomiya K, Yamashita K, Itoh S. Effect of Electrical Polarization of Hydroxyapatite. *Ceramics on New Bone Formation. Calcif Tissue Int* 78:133-142, 2006
6. Kato R, Nakamura S, Katayama K, Yamashita K. Electrical polarization of plasma-spray-hydroxyapatite coatings for improvement of osteoconduction of implants. *J Biomed Mater Res* 74A:652-658, 2005
7. Park JW, Suh JY, Chung HJ. Effects of calcium ion incorporation on osteoblast gene expression in MC3T3-E1 cells cultured on microstructured titanium surfaces. *J Biomed Mater Res A* 86(1):117-126, 2008
8. Nayab SN, Jones FH, Olsen I. Effects of calcium ion implantation on human bone cell interaction with titanium. *Biomaterials* 26(23):4717-2477, 2005
9. Anselme K. Osteoblast adhesion on biomaterials. *Biomaterials* 21(7):667-681, 2000
10. Ma S, Yang Y, Carnes DL, Kim K, Park S, Oh SH, Ong JL. Effects of dissolved calcium and phosphorous on osteoblast responses. *J Oral Implantol* 31(2):61-67, 2005
11. Overgaard S, Lind M, Josephsen K, Maunsbach AB, Büniger C, Søballe K. Resorption of hydroxyapatite and fluorapatite ceramic coatings on weight-bearing implants: a quantitative and morphological study in dogs. *J Biomed Mater Res* 39(1):141-152, 1998
12. Ratner S, Schroit AJ, Vinson SB, Fidler IJ. Analogous recognition of phospholipids by insect phagocytes and mammalian macrophages. *Proc Soc Exp Biol Med* 182(2):272-6, 1986
13. Yoshinari M, Matsuzaka K, Inoue T, Oda Y, and Shimono M. *Materials Transactions* 43:2494, 2002
14. Eriksson C. Bone morphogenesis and surface charge. *Clin Orthop Relat Res* 121:295-302,1976
15. G.Montel. Sur l'étude physico-chimique des solides a structure d'apatite. *Ann,Chim* 4:255-266, 1969
16. Maitz MF, Pham MT, Matz W, Reuther H, Steiner G, Richter E. Ion beam treatment of titanium surfaces for enhancing deposition of hydroxyapatite from solution. *Biomol Eng* 19(2-6):269-272, 2002
17. Hanawa T, Kamiura Y, Yamamoto S, Kohgo T, Amemiya A, Ukai H, Murakami K, Asaoka K. Early bone formation around calcium-ion-implanted titanium inserted into rat tibia. *J Biomed Mater Res* 36:131-136,1997
18. Park JW, Park KB, Suh JY. Effects of calcium ion incorporation on bone healing of Ti6Al4V alloy implants in rabbit tibiae. *Biomaterials* 28(22):3306-3313, 2007
19. Aoki H, Innami Y, Ito A. TCP in Bioceramics-Development and Clinical Applications. Aoki H, Niwa S, eds. Quintessence, Tokyo:86-90, 1987
20. Zhou P, Akao M. Preparation and characterization of double layered coating composed of hydroxyapatite and perovskite by thermal decomposition. *Biomed Mater Eng* 7(1):67-81, 1997