Original

Physical Properties and Hydroxyapatite Formation of Fast Self-setting Biphase Calcium Phosphate Cement

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Abstract: Biphase calcium phosphate (BCP) cement, consisting of an α -tricalcium phosphate-tetracalcium phosphate as the only solid phase and a calcium phosphate solution (Ca-P soln) as the liquid phase, was formerly reported. The BCP cement was easy to prepare, and was expected to show desired handling properties and to form hydroxyapatite (HA) for clinical applications. The objective of the study was to evaluate physical properties and HA formation of the BCP cement. The solid phase of the cement was a BCP (Ca/P of 1.8) prepared in a furnace and ground to a median size of 9.96 μ m. The liquid phase of the BCP cement consisted of an acidic Ca-P soln, which was produced by mixing phosphoric acid with calcium carbonate (CaCO₃) and diluted 3.0-fold, 3.5-fold, 4.0-fold with H₂O. Additionally, trisodium citrate anhydrous and polyvinylpyrrolidone were included as a water reducing agent and washout resistance enhancer, respectively. Cement powder and liquid were mixed (P/L=3.0) to produce samples for setting time, diametral tensile strength (DTS) and compressive strength (CS) measurements. X-ray powder diffraction (XRD) analyses and microscopic observations by FE-SEM and atomic force microscope (AFM) were also performed to identify HA conversion in set samples with time chronologically. BCP cement showed good washout resistance when immersed in water. The setting times (n=5) were 3.0-fold: 5.24 $\pm$ 0.01min, 3.5-fold: 7.39 $\pm$ 0.01min and 4.0-fold: 9.06 $\pm$ 0.01min at 25 $\pm$ 1°C. Differences were apparently existed between each sample (p <0.05). One-day wet DTS (n=5) values were 3.0-fold: 7.07 $\pm$ 0.51MPa, 3.5-fold: 5.98 $\pm$ 0.91MPa and 4.0-fold: 5.07 $\pm$ 0.51MPa and CS (n=5) values were 3.0-fold: 46.58 $\pm$ 3.21MPa, 3.5-fold: 47.75 $\pm$ 2.55MPa and 4.0-fold: 45.53 $\pm$ 1.97MPa. No difference was exhibited between DTS results for each sample except between 3.0-fold and 4.0-fold samples (p <0.05), and CS results showed no apparent difference existed among all samples (p <0.05). XRD analyses showed that BCP cement mostly converted to HA and microscopic features exhibited that HA crystals were clearly observed on surfaces of the BCP-cement at 24hours after mixing. The newly developed BCP cement was found to have adequate physical properties and HA formation for clinical use.

Key words: BCP cement, Physical property, HA conversion

Introduction

A number of calcium phosphate cements (CPCs) have been used for clinical treatments for almost three decades with satisfactory results. In addition to high biocompatibility and osteoconductivity, many advantages of CPCs as a class of bone graft substitute material are derived from their self-hardening properties. The pasty consistency and washout resistance of CPCs allows close adaption or direct contact to the irregular contours of bone surfaces. However, there have been concerns of difficult handling properties and insufficient physical properties to allow perfect placement and shaping of the graft. Thus, CPCs may be made more clinically useful by improvements in their handling and physical properties.

Furthermore, commercially available CPCs consist of two or more calcium phosphates, calcium-containing or phosphate-containing compounds as the solid phase and a sodium phosphate solution or organic acid, such as citric, tartaric, malic, lactic acid, as the liquid phase¹⁻⁵⁾. These CPC's powder compounds, which need to be manufactured separately

and each ground to the required particle size distribution, are then thoroughly blended to produce a homogeneous mixture. The cement powders exhibited poly-modal size distributions. Therefore, the handling, hardening, mechanical, and most importantly *in vivo* properties of CPC products depend strongly on the composition and size distributions of the CPC powders. In addition, the CPC, the powder was consisted of an α -tricalcium phosphate (α -TCP)-tetracalcium phosphate (TTCP) at different molar ratio and the liquid consisted of a sodium dihydrogen phosphate, was previously reported⁵⁾. However, the cement took a few weeks to cure and showed insufficient physical strength for clinical use. Even after full cure, most of the hardened cement mass still did not convert to hydroxyapatite (HA)^{5,6)}.

Biphase calcium phosphate cement (BCP-cement), consisting of an α -TCP- TTCP as the only solid phase and a calcium phosphate solution (Ca-P soln) as the liquid phase, was previously reported⁶⁻¹⁶⁾. The powder phase of BCP consists of a single solid-solution compound with a mono-modal size distribution. The compound is synthesized in a single manufacturing process, and ground to a single size distribution. When the hardening reaction of the BCP cement proceeded, the BCP cement mostly converted to HA, which is the main inorganic component of

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Table 1. Materials used in this study

Materials	Manufactures
Powder phase :	
Tetracalcium Phosphate (TTCP): $\text{Ca}_4(\text{PO}_4)_2\text{O}$	Taihei Chemical Industrial Co. Ltd., Osaka, Japan
α -Tricalcium Phosphate (α -TCP): $\text{Ca}_3(\text{PO}_4)_2$	Taihei Chemical Industrial Co. Ltd., Osaka, Japan
Dicalcium Phosphate Anhydrous (DCPA): CaHPO_4	Taihei Chemical Industrial Co. Ltd., Osaka, Japan
Trisodium Citrate Anhydrous (Na_3Cit): $\text{Na}_3(\text{C}_3\text{H}_5\text{O}(\text{COO})_3)$	Wako Pure Chemical Industries, Ltd., Osaka, Japan
Calcium Carbonate: CaCO_3	Wako Pure Chemical Industries, Ltd., Osaka, Japan
Liquid phase :	
Polyvinylpyrrolidone-k25 (PVP-k25): $(\text{C}_6\text{H}_9\text{NO})_n$	BASF Japan Ltd., Tokyo, Japan
Phosphoric Acid: H_3PO_4	Wako Pure Chemical Industries, Ltd., Osaka, Japan
Calcium Carbonate: CaCO_3	Wako Pure Chemical Industries, Ltd., Osaka, Japan
Sterile purified water: H_2O	Nichi-Iko Pharmaceutical Co., Ltd.

Figure 1. Schematic drawing and particle size distribution of BCP powder particles. The powder phase of BCP cement was a solid solution of TTCP and α -TCP. BCP powder showed mono-modal particle distribution, and the median particle size of the powder was 9.96 μm .

bone, as the final product within 24 hours after mixing^{6-10,16}. Our former study reported that the BCP cement had excellent biocompatibility and osteoconductivity compared to the control cement. Micro-CT results showed the cement maintained its original graft shape and adaptability through the entire experimental period, and also exhibited excellent washout resistance to bodily fluid when applied to bone defects. These results indicated that the BCP cement was successfully retained and had adequate physical properties after the filling.

Physical properties were essentially related to clinical application, and HA conversion was directly related to biocompatibility and bone formation. The purpose of this study was to examine washout resistance, physical properties, HA conversion and microscopic observations of the BCP cement.

Materials and Methods

The materials used in this study are shown in Table 1.

The powder phase of BCP cement was a solid-solution of α -TCP-TTCP. It was prepared by heating a mixture of dicalcium phosphate anhydrous (DCPA) and calcium carbonate (CaCO_3) in a furnace, and ground to a mono-modal size distribution with median size of 9.96 μm . Solid-solutions with compositions ranging from 95% α -TCP/5% TTCP to 5% α -TCP/95% TTCP are contemplated. In general, the corresponding molar Ca/P ratios of the powder range from 1.52 to 1.97, and a Ca/P ratio of 1.8 was used in this study. The scheme and the distribution of BCP powder particle are shown in Fig. 1. The liquid phase of BCP cement consisted of an acidic Ca-P soln (pH 2.1), which was produced by mixing phosphoric acid with CaCO_3 and diluted 3.0-fold, 3.5-fold and

4.0-fold with H_2O , and then used as the cement liquid.

Additionally, tri-sodium citrate anhydrous (Na_3Cit) in the powder phase and polyvinylpyrrolidone-k25 (PVP-k25) in the liquid phase were included as a water reducing agent and a washout resistance enhancer, respectively⁶⁻¹⁶. The samples were prepared by mixing BCP powder with the cement liquid at a P/L ratio of 3.0. The components and the setting reaction of the BCP cement are shown in Fig. 2. The total amount of Na_3Cit in the sample was adjusted to 1.5 mol/l. Na_3Cit achieved high zeta-potentials of CPCs caused by adsorption of multiple charged citrate ions at the solid-liquid interface, enabling the effective dispersion of cement particles⁶⁻¹⁶. Using the Na_3Cit solution decreased the viscosity, achieved injectability, and improved the strength of the cement paste when used as a bone graft material^{6, 11-18}. In this study, the powder contained Na_3Cit and each liquid contained 0.75wt% of PVP-k25. Ca-P solns of the 3.0-fold, 3.5-fold and 4.0-fold dilution with H_2O were used for physical property and XRD analyses of the BCP cement, and microscopic observations were performed for the BCP cement using Ca-P soln of 3.5-fold dilution with H_2O .

The samples were prepared by mixing BCP (Ca/P ratio=1.8) powder with the cement liquid for 30sec at P/L ratio of 3.0⁶⁻¹⁰, and then used for washout resistance, setting time (Gilmore needle), diametral tensile strength (DTS) / compressive strength (CS) measurements, XRD analyses and microscopic observations. Experimental procedures are described as bellow.

Washout resistance and setting time

For the measurement of washout resistance, 3.0-fold/3.5-fold/4.0-

• Components

Powder Ca/P=1.8 Median size: 9.96 μ m containing 1.5mol/L Na ₃ Cit	+	Liquid pH 2.1 calcium phosphate solution (Ca-P soln), with 3.0-fold,3.5-fold,4.0-fold dilution with H ₂ O, containing 0.75wt%PVP
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• Setting reactions

Figure 2. Components and setting reaction of the BCP cement. Three kinds of Ca-P soln., diluted with 3.0-fold, 3.5-fold and 4.0-fold H₂O, were used as the cement liquid. Na₃Cit in the powder phase and PVP-k25 in the liquid phase were included as a water reducing agent and a washout resistance enhancer, respectively. During the setting reaction proceeded, the BCP cement mostly converted to HA as a final product.

fold cement pastes were manually shaped into a ball and immersed in water at 3 min after mixing. The samples were visibly checked for shape at 10min after mixing. The samples were also taken out from water by tweezers and their shape-integrities were observed at 15 min after mixing. The cement was considered to pass the washout resistance test if the paste sample kept original shape and did not visibly disintegrate in water.

The setting time of 3.0-fold/3.5-fold/4.0-fold cement paste was estimated by the results of a Gilmore needle method test. The Gilmore needle method test was performed using a needle with a tip diameter of 2.12 mm loaded with 453.5 g. The hand-mixed pastes were filled into the mold (2.0 cm in diameter, 3 mm in thickness) on a glass plate, and were stored in 50% relative humidity at 23 $\pm$ 1 $^{\circ}$ C. In this method, the cement was considered to set when the needle with the load failed to make a perceptible indentation on the surface. The data of each sample was used to calculate the group mean ($\pm$ SD). A Tukey-Kramer test was used to establish statistical significance ($p < 0.05$).

Mechanical strengths

The 3.0-fold/3.5-fold/4.0-fold cement pastes were filled into a glass mold (6.0 mm in diameter, 12.0 mm in thickness) and kept in 100% humidity at 37 $^{\circ}$ C for 2 h. After removal from the mold, each sample was stored in 30 ml of H₂O for 22 h and used for CS and DTS measurements immediately. The mechanical strength of the sample was measured using a Universal Testing Machine (TG-5KN, Instron Japan Co. LTD, Kanagawa, Japan) at cross head speed of 1 mm/min. DTS values were calculated using the equation; DTS (MPa)=2P/ π DH, and CS values were calculated using the equation CS (MPa)=2P/DH. The data of each sample were used to calculate the group mean ($\pm$ SD) and underwent a Tukey-Kramer test for individual comparison with a 0.05 level of significance. (P: load, D: diameter, H: height)

X-ray diffraction (XRD) analysis

HA formation of the BCP cement was examined by powder X-ray diffraction (XRD) analysis^{9,10}. The 3.0-/3.5-fold/4.0-fold cement pastes were filled into a glass mold (ϕ 6.0 mm $\times$ H 12.0 mm) and kept in 100% humidity at 37 $^{\circ}$ C for 2 h, and then removed from the mold and stored in 30 ml of H₂O for 22 h. After storage, the samples were dehydrated in acetone for 1 h and dried in the desiccator for 23 h, and then ground to fine powder by mortar and pestle for XRD. XRD analyses of the 3.5-fold samples at 6, 12, 24 and 48 h were also performed to examine chronological HA conversion.

Powder XRD patterns, obtained with a powder x-ray diffractometer (Multi Flex, Rigaku Corporation, Tokyo, Japan), were used to determine phase compositions of the hardened samples. The XRD patterns were recorded with use of a vertical-mounted diffractometer system with graphite-monochromatized CuK α radiation (λ =0.154nm) generated at 40 kV and 20 mA, and scanning speed 2 $^{\circ}$ /min. The sample was scanned from 10 to 60 degrees 2 θ in a continuous mode, and peak intensities were recorded on a computer. Analysis of the detected diffraction pattern was performed in comparison with standard powder X-ray diffraction data (Powder Diffraction File: PDF) for each substance, and the chronological formation of HA from α -TCP/TTCP as the original substance was confirmed.

Microscopic observations

The 3.5-fold samples were prepared by same procedures as for the XRD samples until drying in the desiccator, and then were broken for fractures. Observations of the fracture surface of the samples were conducted by field emission-scanning electron microscope (FE-SEM) and atomic force microscope (AFM).

FE-SEM observations for 24 h and 48 h samples were performed us-

ing SEM (SU8020, Hitachi high technologies, Tokyo, Japan) at an accelerating voltage of 07V. Prior to the observation, samples were fixed on stubs without sputtered coating. Observations were carried out up to where the crystalline form of HA could be distinguished. AFM observations for 24 h and 48 h samples were carried out in a completely non-contact state using AFM (NX-20 type, Park Systems Japan, Tokyo, Japan) and cantilever (OMCL-AC160TS, Park Systems Co. Japan, Tokyo, Japan), under conditions of 256×256 and 512×512 pixels and a scan rate of 0.2 - 1Hz. Firstly, observations of the surface of each sample were carried out in the range of 20×10 μ m, then observations were performed while sequentially increasing the magnification ratio for parts where it was considered to be necessary. Observations were carried out up to the range of magnification whereby objects of about 100 nm could be identified and where the crystalline form of HA could be distinguished. Also, differential image Enhanced Color (EC) displays were made for the purpose of confirming the parts that were difficult to distinguish due to large surface forms and the presence of unevenness etc., and for clarifying three-dimensional discrimination in the AFM image. Furthermore, the surface roughness corresponding to each AFM image was given by line profile.

Results

Washout resistance and setting time

Three kinds of Ca-P soln diluted with 3.0-fold, 3.5-fold and 4.0-fold H_2O , were used as cement liquid. After the mixing, all BCP cement pastes were an injectable phase through a cannula (2 mm in diameter), then became a moldable phase with shape integrity, and hardened stiffly. Fig. 3 shows the washout resistance results for the cement pastes. All samples showed that no noticeable disintegration and negligible debris were observed at 10 min after the mixing (A). All samples set into solid masses, so the samples were taken out from water by tweezers without any collapse. The samples were observed in dry condition at 15 min after mixing (B). Observations for the samples, which were continuously preserved in water, made at 24 h later were also the same as (A), with

Figure 3. Washout resistance and handling properties of the BCP cement. All samples showed that no noticeable disintegration and negligible debris were observed at 10 min after the mixing (A). All samples set into solid masses, so the samples were taken out from water by tweezers without any collapse. The samples were observed in dry condition at 15 min after mixing (B). The cement was considered to pass the washout resistance test if the paste sample kept original shape and did not visibly disintegrate in water.

no further disintegration from the 10min-samples.

Following previously studies¹⁸⁻²⁰, the sample was considered to pass the washout resistance test if the paste did not visibly disintegrate. Therefore, all BCP cements were considered to have excellent washout resistance when preserved in water.

The setting time of each cement paste is shown in Fig. 4. The cement showed injectable phase initially and exhibited moldable phase, and then hardened stiffly. The setting time of each sample (n=5) to harden was 3.0-fold: 5.24±0.006 min, 3.5-fold: 7.39±0.006 min, and 4.0-fold: 9.06±0.006 min at 25±1°C. The 3.0-fold sample showed the shortest setting time until hardening among all samples, and there were apparent differences between each sample in hardening ($p<0.05$).

Figure 4. Setting time of the BCP-cement. The cement showed injectable phase initially and exhibited moldable phase, and then hardened stiffly. The 3.0-fold sample showed the shortest setting time until the hardening among all samples, and there were apparent differences between each sample in hardening ($p<0.05$).

Mechanical strengths

Mechanical strengths of the samples are shown in Figs. 5 and 6. Mean one-day wet DTS (n=4) values were 3.0-fold: 7.07±0.51MPa, 3.5-fold: 5.98±0.91MPa and 4.0-fold: 5.07±0.51MPa, and CS values were 3.0-fold: 46.58±3.21MPa, 3.5-fold: 47.75±2.55MPa and 4.0-fold: 45.53±1.97MPa.

DTS results showed that 3.0-fold sample exhibited the largest DTS value in all samples and a clear difference existed between it and 4.0-fold sample ($p<0.05$). No clear difference existed between 3.0-fold and 3.5-fold cement samples and also 3.5-fold to 4.0-fold samples. CS results showed no apparent difference existed among all samples ($p<0.05$).

XRD analysis

Powder XRD patterns of 3.0-fold/3.5-fold/4.0-fold samples at 24 h are shown in Fig. 7. The diffraction patterns of all the 24 h samples exhibited that the detection intensities and peaks of HA were quite similar to those of standard powder X-ray diffraction data (Powder Diffraction File: PDF). No apparent difference was found among the samples.

Figure 5. Diametral tensile strength (DTS) of the BCP cement. DTS results showed that 3.0-fold sample exhibited the largest DTS value in all samples and a clear difference existed between it and 4.0-fold sample ($p < 0.05$). No clear difference existed between 3.0-fold and 3.5-fold cement samples and also 3.5-fold to 4.0-fold samples.

Figure 6. Compressive strength (CS) of the BCP-cement. CS results showed no apparent difference existed among all samples ($p < 0.05$).

The α -TCP and TTCP diffraction patterns of 3.5-fold samples at 6, 12, 24 and 48 h were reduced and that of HA was clearly detected in 6 h samples. The diffraction pattern of 12 h sample showed that HA was the main phase (Fig. 8). The diffraction pattern of 48 h sample exhibited

Figure 7. XRD patterns of 3.0-/3.5-fold/4.0-fold samples at 24 h. The diffraction patterns of all the 24 h samples exhibited that the detection intensities and peaks of HA were quite similar to those of standard powder X-ray diffraction data (Powder Diffraction File: PDF). No apparent difference was found among the samples.

Figure 8. XRD patterns of the 3.5-fold samples at 6, 12, 24 and 48 h. The BCP cement formed HA chronologically and was mostly converted to HA after 24h from mixing.

Figure 9. FE-SEM micrographs of fracture surfaces of 24 h and 48 h samples. HA crystals were already found on the fracture surface of the 24 h sample, and apparent needle and rod shape crystals were clearly formed on the surface of the 48 h sample.

Figure 10. AFM images of 24 h sample. In the 3×3 µm image, fine HA crystals were formed on the entire surface and did not show constant regular arrangement or orientation. As was clear from the 1×1 µm enlarged image, HA crystals were clearly observed with fine crystallinity and the crystal size of the HA was approximately 20-50 nm in diameter and 200-400 nm in length.

that the intensities and peaks of HA were clearly observed compared with those of 24 h sample. Very small amounts of unreacted α -TCP and TTCP were still found in 24 h and 48h samples. XRD results indicated that the BCP cement formed HA within 6 h and changed into HA chronologically. It was nearly completely converted to HA after 24 h from mixing.

Microscopic observations

FE-SEM micrographs of fracture surfaces of the sample at 24 h and 48 h are shown Fig. 9. Small HA crystals were already found on the fracture surface of the 24 h sample, and apparent needle and rod shape crystals were clearly formed on the surface of the 48 h sample. FE-SEM images not only revealed the presence of HA crystals in the formed samples, but also showed clearly that the density of HA crystals increased with the increase of HA content.

Figs. 10 and 11 show the observed AFM images of 24 h and 48 h samples. In the $3 \times 3 \mu\text{m}$ image of Fig. 10, it was confirmed that fine needle

shape HA crystals were formed on the entire surface of the 24 h sample. It was clearly confirmed by EC that there were some crystals in the region where observation was difficult by AFM. As was clear from the $1 \times 1 \mu\text{m}$ enlarged image, HA crystals were clearly observed with fine crystallinity. The crystal size of HA observed in the 24 h sample was approximately 20-50 nm in diameter and 200-400 nm in length. In addition, it was confirmed that the HA crystals did not show constant regular arrangement or orientation. In the $3 \times 3 \mu\text{m}$ image of Fig. 11, the 48 h sample showed that larger density and more matured HA crystals formed on whole surface in comparison to the 24 h sample. The $1 \times 1 \mu\text{m}$ image exhibited that excellent cylindrical crystalline structures were formed on whole surface.

FE-SEM and AFM images of the 3.0- and 4.0-fold cement samples taken in additional FE-SEM and AFM experiments at 24 h and 48 h exhibited quite similar to those of the 3.5-fold sample at 24 h and 48 h.

Figure 11. AFM images of 48 h sample. In the $3 \times 3 \mu\text{m}$ image, the sample showed that larger density and more matured HA crystals formed on whole surface in comparison to the 24 h sample. The $1 \times 1 \mu\text{m}$ image exhibited that excellent cylindrical crystalline structures were formed on whole surface.

Discussion

Previous studies¹⁹⁻³³⁾ have reported that the conventional CPCs were excellent materials for reconstructive surgery for alveolar bone deficiencies, orthopedic, and maxillofacial surgical applications, because most of CPCs formed low crystalline HA which was main inorganic component of bone. CPCs undergo the process of biodegradable and bioresorbable nature *in vivo*, so they work effectively for bone substitute materials³¹⁾. On the other hand, CPCs still had some difficulties for maintaining the original grafted shape and volume at defect site, because they did not have enough washout resistance and viscosity in body fluid^{6, 31, 32)}. These properties were caused by physical flow and chemical dissolution of the material components in the body fluid. Some CPCs took a long time to harden and showed inadequate physical properties and HA conversion for clinical uses even at 24 h after mixing. They also lack adequate controlled degradability for bone formation when implanted in the bone defect.

Therefore, a new bone substitute material was required to have sufficient physical strength and appropriate cellular affinity along with biodegradable and bioresorbable potential to facilitate the bone remodeling process³¹⁾. Above those reasons, we developed the BCP cement with improved washout resistance in body fluid, handling properties, mechanical strengths and rapid HA conversion compared to the conventional cements⁶⁻¹⁶⁾. In this experiment, physical properties of BCP cements when used the Ca-P soln diluted with 3.0, 3.5 or 4.0-fold of H₂O and mixed at P/L ratio of 3.0, such as DTS, CS, setting time and washout resistance, were examined. All BCP cements showed excellent washout resistance when immersed in water and set stiffly within 10 minutes. All BCP cements also showed almost same mechanical strengths, diffraction patterns of XRD and microscopic features. Even until the hardening, the cement paste kept original shape and did not visibly disintegrate in water. After the hardening, the BCP cement had sufficient mechanical strength for various clinical applications.

Based on the mode of bone reaction against HA in the *in vivo* environment, high temperature HA (HT-HA) with high crystallinity is reported to be suitable for HA coating for implant surfaces due to exhibiting osteoconductivity as a result of its bioactive/non-bioresorbable nature³³⁾. Low temperature HA (LT-HA) with low crystallinity produced at room temperature is reported to be suitable as a bone graft material due to bone substitution properties given by its bioactive/bioresorbable nature^{6, 31-33)}. When the hardening reaction of the BCP cement proceeded, the BCP cement gradually formed HA and was mostly converted to LT-HA, which is the main inorganic component of bone, as the final product within 24 h after the mixing⁷⁻¹⁰⁾. Therefore, the cement may show superior biocompatibility and osteoconductivity^{6, 8, 11-13, 15)}. HA crystals formed from the BCP cement were low-crystallinity and nano-meter size, which are the magnitude of those contained in bone, so it might be assumed that the HA crystals could be easily resorbed by osteoclasts and converted to natural bone, as which spontaneously occurred in bone remodeling³¹⁻³⁴⁾.

Our former study reported that the BCP cement, which was used for artificially created critical bone defects in rat calvaria, combined to residual bone firmly and converted to natural bone chronologically⁶⁾. This binding between the BCP cement and the residual bone increased the mechanical strength of the filling material and reduced its susceptibility to infections^{6-8, 11, 12)}. A recent study also reported that the BCP cement formed approximately 5wt% B-type carbonate apatite (CO₃-AP), essentially existing at 5-8wt% in natural bone, when implanted in subcutaneous tissues of rat for 8 weeks¹⁵⁾. These reports also explained that the BCP cement should convert to low crystalline HA like natural bone.

The BCP cement had superior handling properties and hardened stiffly and rapidly. It also showed excellent washout resistance and shape integrity in aqueous solution. Therefore, the BCP cement successfully retained the original graft shape⁶⁻⁸⁾. The BCP cement also had adequate physical properties and mostly converted to HA within 24h. These results strongly indicate that BCP cement could be an effective and suitable material for clinical uses.

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Conflict of Interest

The author has declared that no COI exists.

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