

Autogenous teeth used for bone grafting: a comparison with traditional grafting materials

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Objectives. This study evaluated the surface structures and physicochemical characteristics of a novel autogenous tooth bone graft material currently in clinical use.

Study Design. The material's surface structure was compared with a variety of other bone graft materials via scanning electron microscope (SEM). The crystalline structure of the autogenous tooth bone graft material from the crown (AutoBT crown) and root (AutoBT root), xenograft (BioOss), alloplastic material (MBCP), allograft (ICB), and autogenous mandibular cortical bone were compared using x-ray diffraction (XRD) analysis. The solubility of each material was measured with the Ca/P dissolution test.

Results. The results of the SEM analysis showed that the pattern associated with AutoBT was similar to that from autogenous cortical bones. In the XRD analysis, AutoBT root and allograft showed a low crystalline structure similar to that of autogenous cortical bones. In the CaP dissolution test, the amount of calcium and phosphorus dissolution in AutoBT was significant from the beginning, while displaying a pattern similar to that of autogenous cortical bones.

Conclusions. In conclusion, autogenous tooth bone graft materials can be considered to have physicochemical characteristics similar to those of autogenous bones. (Oral Surg Oral Med Oral Pathol Oral Radiol 2014;117:e39-e45)

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Bone graft materials that are presently used in dental clinics are autogenous bones, allogeneic bones, xenogeneic bones, and alloplastic materials. According to bone-healing mechanisms, they can be categorized into materials that induce osteogenesis, osteoinduction, and osteoconduction. Among the many different types of bone graft materials, autogenous bones are the most ideal. They are capable of osteogenesis, osteoinduction, and osteoconduction. Their advantage is rapid healing time without immune rejection.

Nonetheless, their biggest shortcomings are that the harvest amount is limited, bone resorption after graft is unavoidable, and the second defect is generated in the donor area. Therefore, to overcome such shortcomings, allogeneic bones and synthetic bones were developed and used in clinics, and efforts have been made to develop more ideal bone substitution materials.

Starting in 1993, we developed bone graft materials using human teeth with which we conducted experimental studies. In 2008, we developed an autogenous tooth bone graft material from extracted teeth prepared as a powder, which was grafted to the donor patient himself.¹⁻⁷ Mineral components of autogenous tooth bone graft materials consist of 4 stages (types) of calcium phosphate (hydroxyapatite [HA], tricalcium phosphate [TCP], octacalcium phosphate [OCP], and amorphous calcium phosphate [ACP]). Under scanning electron microscopic (SEM) examination, HA crystalline structures and collagen fibers around the dentinal

tubules were detected.⁸ Short-term clinical studies have reported that even when wounds became dehiscent, the bone graft materials were not infected and good second healing was achieved.⁹

In this study, bone graft materials that were prepared as powder by separating the crowns and roots of extracted teeth were compared with the structural and physicochemical characteristics of allogeneic bones, xenogeneic bones, and synthetic bones that are used commonly in clinics. This enabled the examination of whether their characteristics were similar to those of autogenous bones.

MATERIAL AND METHODS

After obtaining approval from the Institutional Review Board of Seoul National University Bundang Hospital (B-1105-049-003), our study involving the treatment and analysis of autogenous bones and autogenous teeth was performed.

Bone graft materials

Control: autogenous mandibular block bone. After obtaining consent from patients, orthognathic surgery was performed and resected buccal cortical block bone was selected as the control group. Because cortical bones are compact, their early mechanical strength is excellent. Nonetheless, after transplantation, the rate of revascularization is slow and healing via osteoconductive mechanisms is observed.¹⁰

Autogenous tooth bone graft material. The extracted teeth were immersed in 70% ethyl alcohol and delivered to a specialized treatment company (Korea Tooth Bank Co., Seoul, Korea), where any soft tissues, calculus, and foreign materials (e.g., prostheses and endodontic filling materials) attached to the teeth were removed, while the crown and the root portions of the teeth were divided and crushed. Particle sizes ranged from 0.5 to 1.0 mm. The crushed tooth particles were added to a solution of distilled water and hydrogen oxide, and were later washed by ultrasonography washer to remove residual foreign materials. The washed tooth particles were dehydrated with ethyl alcohol solution and defatted with ethyl ether solution. Subsequently, after the lyophilization procedure, the tooth particles were sterilized with ethylene oxide gas and packaged as 2 types of materials (AutoBT crown and AutoBT root).

Irradiated cancellous bone. Irradiated mineralized allogeneic cancellous bone (ICB) (Rocky Mountain Tissue Bank, Aurora, CO, USA) and marrow is a graft material that shows healing by osteoinduction and osteoconduction, and was supplied in the wet state.

BioOss. Currently, BioOss (Geistlich Pharma AG, Wolhusen, Switzerland) is a representative xeno-

neic bone graft material that is most commonly used in dental clinics. It has been reported to show effective healing by osteoconduction. BioOss is made from the mineral part of the bones that originates from Australian cattle. During manufacturing, the organic constituents are removed via a special treatment process, so that the hard bone structure consisting of calcium compounds remains. Particle sizes range from 0.25 to 1.00 mm.

Micromacro biphasic calcium phosphate. Micro-macro biphasic calcium phosphate (MBCP) (Biomat-lante, Vigneux de Bretagne, France) is biphasic ceramic that is composed of HA and β -TCP. Two-thirds of the material consists of 300- to 600- μ m macropores, whereas the remaining third consists of micropores smaller than 10 μ m in diameter. MBCP is an osteoconductive alloplastic material that is absorbed slowly over time. Particle sizes range from 0.5 to 1.0 mm.

Scanning electron microscopy. A scanning electron microscope (S-4800, Hitachi, Tokyo, Japan) was used to examine the surface structure of a variety of bone graft materials. SEM revealed that the surface of all samples (AutoBT crown, AutoBT root, BioOss, MBCP, ICB, autogenous mandibular cortical bone) was covered with 7-nm-thick platinum (Pt) coating when the instrument was operated at 15 kV.

High-resolution x-ray diffraction analysis. The individual samples were inserted into an analytical glass holder, and the diffraction patterns were measured using an x-ray diffractometer (D8 Advance, Bruker AXS GmbH, Karlsruhe, Germany) with copper (Cu) radiation ($\lambda = 1.5218 \text{ \AA}$) over 10 to 60° at a rate of 1 second/step.

From the x-ray diffraction (XRD) graphs, the full width at half maximum (FWHM) values of the crystallite sizes of the bone graft materials were obtained by measuring the widths of the apexes of the measured peaks as well as the center areas of the base. The domain size of each graft material was calculated by applying the Scherrer equation (Fig. 1).¹¹

Ca/P ion dissolution test. A total of 0.5 g of each graft material was added to 10 mL of 1 \times phosphate-buffered saline (PBS) (WelGENE Inc., Daegu, Korea), and maintained in a drying oven (Hanbaek Scientific, Bucheon, Korea) at 37°C under the condition of blocking from the outside. They were stored for 3, 7, or 14 days, and were later centrifuged (Hanil Scientific, Gangneung, Korea) at 1000 rpm for 5 minutes. A total of 10 mL of supernatant was obtained, excluding the graft materials. The released amounts of calcium and phosphorus ions present in the supernatant were measured by inductively coupled plasma-mass spectrometry (ICP-MS) ELAN DRC-2 (PerkinElmer, Waltham, MA).

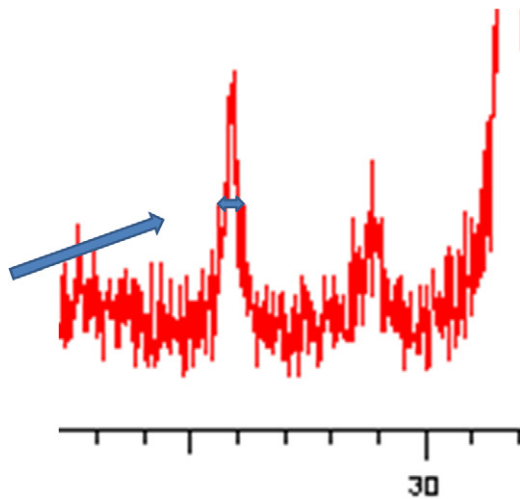


Fig. 1. Measurement of domain size using the Scherrer equation. D_p , crystallite size; λ , 1.54; θ , diffraction peak angle; $\beta_{1/2}$, FWHM.

RESULTS

SEM

AutoBT roots were cut in a parallel direction to dentinal tubules. The surfaces were generally homogeneous, and minute longitudinal sections of the dentinal tubules were observed. In high-magnification photographs, the surfaces between the dentinal tubules present at 5- to 10- μm intervals showed slightly rough patterns (Fig. 2, A and B). AutoBT crown surfaces of the sections were generally homogeneous, with small dentinal tubules of 1.0 to 1.5 micrometer in length. In comparison with AutoBT root sections, these showed a more compact pattern. Moreover, small particles that were speculated to be hydroxyapatite were observed between the dentinal tubules (Fig. 2, C and D). The autogenous block bone surfaces showed wave-shaped compact patterns. Under high magnification, irregular fiber patterns and a mixture of ribbon-shaped structures of varying sizes was shown (Fig. 2, E and F). The allogeneic bone surfaces were the smoothest among all samples. A homogeneous compact surface was displayed as well. High-magnification photographs revealed thin fibers that were arranged very tightly, as well as isolated openings that were 5 μm in width and 20 μm in length (Fig. 2, G and H). In comparison with ICB and autogenous block bones, the section surfaces of the xenogeneic bone graft material BioOss were less compact, whereas a regular arrangement of small tubules of 5 μm in width was observed (Fig. 2, I and J). On the surfaces of the alloplastic material MBCP, hulled millet-form fragments of 5 to 10 μm in diameter were observed (Fig. 2, K and L).

XRD

The crystalline structures of the AutoBT root and allogeneic bones showed patterns that were most similar to those of autogenous bones. The peak for AutoBT crown was narrower than that for the root, displaying a very sharp pattern. The peak for BioOss was similar to that of MBCP. Nevertheless, the peak for BioOss displayed a pattern that was more horizontally spread out. The peak for MBCP was sharper than those of other bone graft materials, showing narrow width patterns (Fig. 3). The results of the domain size measurements for each bone graft material are shown in Table I. AutoBT root and allogeneic bones (ICB) showed sizes that were relatively similar to those of autogenous bones.

Ca/P ion dissolution test

AutoBT and autogenous block bones showed similarly extensive calcium dissolution during the early phase, in comparison with MBCP, ICB, and BioOss. MBCP showed the highest dissolution of phosphorous, whereas BioOss showed the lowest dissolution. AutoBT, autogenous block bones, and ICB showed relatively similar degrees of dissolution (Tables II and III).

DISCUSSION

An autogenous tooth bone graft material was developed in 2008, which has been actively used in clinical settings. The organic and inorganic components of the crown and root portions of teeth are different, which results in different healing mechanisms after bone graft procedures.⁷⁻⁹ ICB consists of irradiated allogeneic cancellous bones, which is supplied in the wet state and displays both osteoinductive and osteoconductive healing. BioOss consists of anorganic bovine bones, which have a bimodal pore structure and display osteoconductive healing. MBCP consists of alloplastic synthetic materials with both micropores and macropores, and it shows osteoconductive healing.

In SEM analysis, AutoBT dentin surfaces were generally homogeneous, and minute longitudinal sections of the dentinal tubules were observed. And also, AutoBT crown surfaces were generally homogeneous, with small dentinal tubules. However, these showed a more compact pattern. Most AutoBT crowns consist of dentin, and only a portion of the upper area is covered with enamel. Therefore, the result that was cut rectangular to the dentinal tubule direction was obtained. The autogenous mandibular block bones primarily consisted of cortical bones. The allogeneic bone graft material ICB was composed of cancellous bones. So the autogenous block bone surfaces showed wave-shaped compact patterns and the allogeneic bone surfaces were the smoothest among all samples.

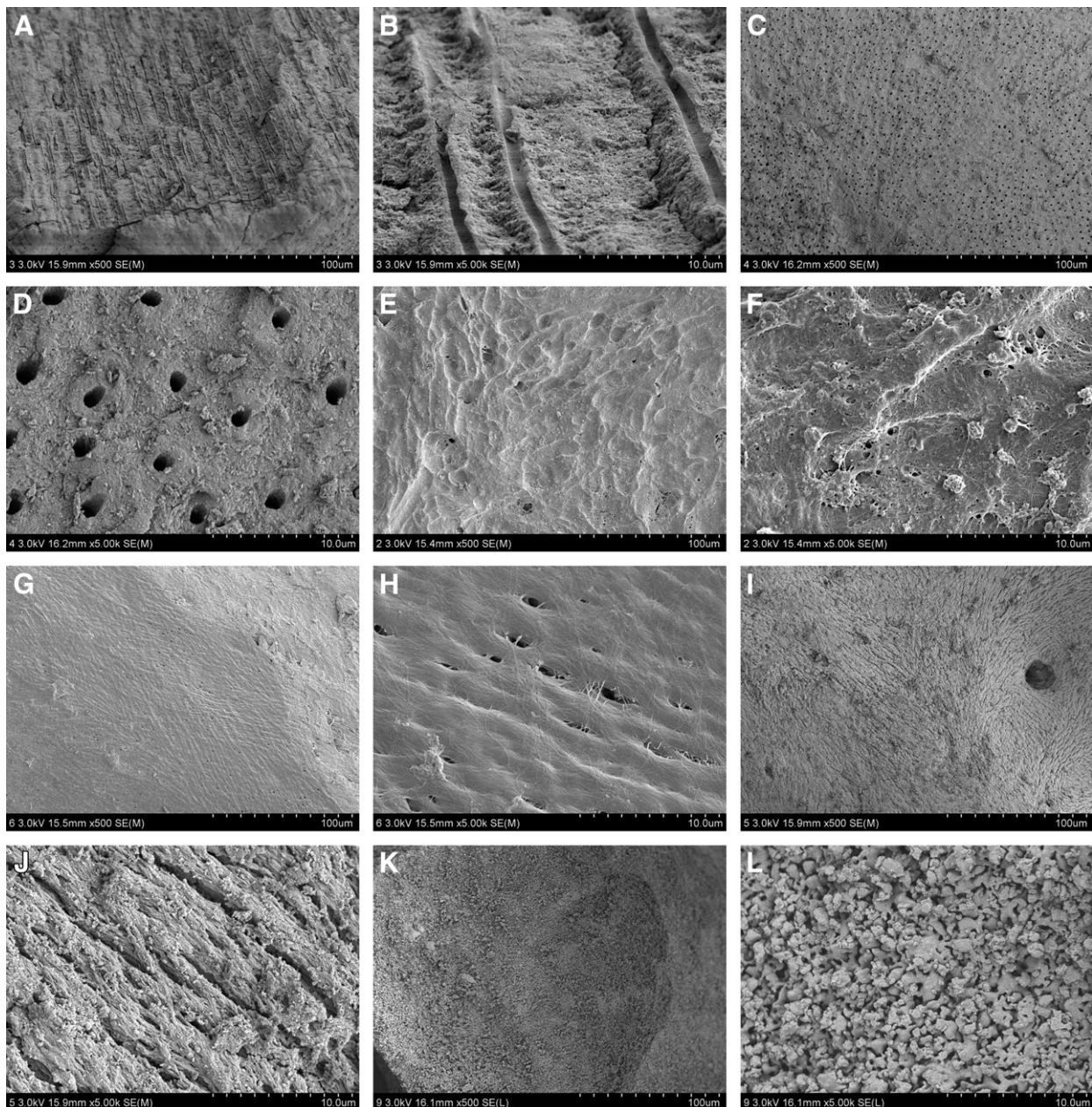


Fig. 2. SEM views of the different types of bone graft materials. **A**, AutoBT crown ($\times 500$); **B**, AutoBT crown ($\times 5000$); **C**, AutoBT root ($\times 500$); **D**, AutoBT root ($\times 5000$); **E**, autogenous cortical bone ($\times 500$); **F**, autogenous cortical bone ($\times 5000$); **G**, ICB ($\times 500$); **H**, ICB ($\times 5000$); **I**, BioOss ($\times 500$); **J**, BioOss ($\times 5000$); **K**, MBCP ($\times 500$); **L**, MBCP ($\times 5000$).

We previously analyzed the surface structures of autogenous tooth bone graft materials via SEM. We found that the surface pattern was very compact in the enamel portion in comparison with other parts. This is because enamel is composed of 97% HA with high crystallinity. Dentin was abundant on the breaking surfaces, presenting as long dentinal tubules of approximately 1 to approximately 2 μm in length. They showed a regular arrangement at intervals of approximately 10 μm . HA was the primary mineral found

between the tubules, giving this material low crystallinity. A mixture of calcium phosphate and organic substances, such as collagen, was also present. The cementum part was also composed of an organic-inorganic complex of minerals with low crystallinity and organic collagen substances.¹²

In our study, the density, roughness, and homogeneity of AutoBT were shown to be relatively similar to those of autogenous cortical bones. The irregular surface between AutoBT and the dentinal tubules, as well

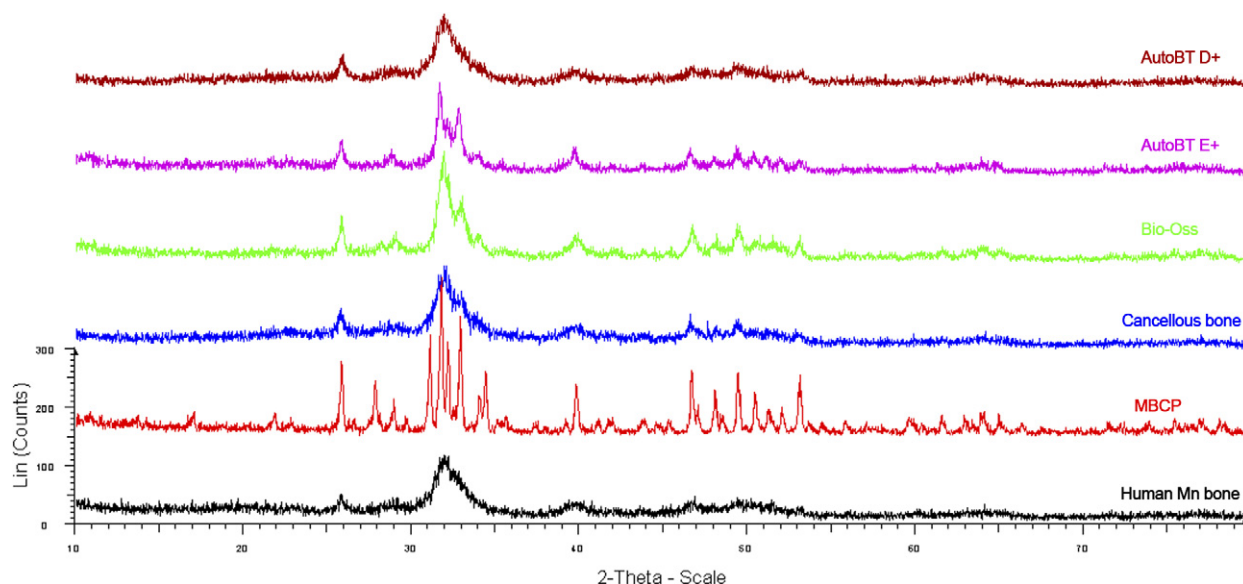


Fig. 3. The results of the XRD analysis. AutoBT D+: AutoBT root, AutoBT E+: AutoBT crown, cancellous bone: ICB.

Table I. Estimation of domain sizes from diffraction peak broadening

Diffraction line index	(002)	(210)	(211)	(310)	(222)	(231)	(004)
2θ at Cu Kα λ = 1.54 Å = 0.154 nm	25.9	28.95	31.8	39.83	46.73	49.5	53.1
AutoBT root	16	11	8	7	11	10	11
AutoBT crown	27	19	19	33	28	40	25
BioOss	21	19	9	11	17	17	20
ICB	17	18	11	11	16	20	21
MBCP	42	42	35	30	43	40	36
Autogenous cortical bone	16	13	8	8	13	20	21

ICB, irradiated cancellous bone; MBCP, micromacro biphasic calcium phosphate.

Table II. Ca (m/z; 42.959) ion dissolution

Day	MBCP	ICB	BioOss	AutoBT crown	AutoBT root	Auto bone
3 d	54.2	97.7	35.5	230.7	280.0	246.8
7 d	48.6	71.7	33.6	162.7	255.2	189.2
14 d	62.7	97.6	35.1	144.5	180.6	180.6

ICB, irradiated cancellous bone; MBCP, micromacro biphasic calcium phosphate; m/z, mass-to-charge ratio.

as the circular- or ribbon-shaped structures of autogenous cortical bones, suggest the presence of both mineralized materials and organic materials.

XRD is a method used to examine the crystalline structure of solid materials by analyzing the x-ray diffraction patterns of powder samples. Even if the chemical compositions of different materials are identical, their crystalline structures may be different. As such, diffraction analysis enables the estimation of the sizes of different crystalline

Table III. P (m/z; 30.994) ion dissolution

Day	MBCP	ICB	BioOss	AutoBT crown	AutoBT root	Auto bone
3 d	301.7	217.8	174.0	269.8	269.4	260.5
7 d	311.4	191.2	151.7	282.8	230.2	282.8
14 d	302.5	165.4	148.7	253.8	229.0	245.3

ICB, irradiated cancellous bone; MBCP, micromacro biphasic calcium phosphate; m/z, mass-to-charge ratio.

structures. To assess crystalline size, the Scherrer equation is applied.¹¹ The 2 θ (theta) value, which indicates the peaks for HA, beta-TCP, and other patterns, was constant. JCPDS is a database showing the locations of the peaks as well as the relative peak sizes of each mineral. Therefore, after measuring the XRD of the different bone graft materials and referring to the database, the crystalline structure of different materials can be analyzed. Wide XRD peaks are associated with low crystallinity, whereas narrow peaks are associated with high crystallinity.^{11,13-15}

In our study, the diffraction peaks for the control group (autogenous cortical bones) were broad, whereas the peaks for AutoBT root and allogeneic bones (ICB) showed similar patterns. The crystalline structure of the mineral components of human alveolar bones displayed low crystallinity. The peak for AutoBT crown was narrower than that for the root, displaying a very sharp pattern. This indicates that the tooth crown only partially contains enamel; in comparison with the root portion, both the mineral content and crystallinity are higher in the crown. The peak for BioOss was similar to that of MBCP. Nevertheless, the peak for BioOss displayed a pattern that was more horizontally spread out. In other words, this was associated with low crystallin-

ity and crystalline size (domain).¹⁶ The peak for MBCP was sharper than those of other bone graft materials, showing narrow width patterns. Thus, we determined that these bone graft materials had high crystallinity.

Previously, Kim et al.¹ reported that HA and β -TCP were the major components of tooth ash that was treated with high temperatures. On the other hand, autogenous tooth bone graft materials were observed to contain 4 types of calcium phosphate, whereas the XRD patterns of the crown and root portions were different. In other words, this indicates that the root area consists of dentin and cementum and therefore has low crystallinity, whereas the crown area contains abundant levels of enamel components and therefore has high crystallinity.^{7,8}

In an in vitro dissolution test, AutoBT showed excellent biodegradability, whereas apatite reprecipitation was actively visible immediately after transplantation. We conjecture that this material plays an effective role in the induction of bone regrowth. Priya et al.¹⁷ reported that the extensive dissolution of calcium phosphate composites, which releases calcium and phosphorous ions, induces the reprecipitation of the apatite onto the surfaces. They suggested that the combination of dissolution and reprecipitation were the mechanisms behind apatite formation. Apatite layer formation was expected to encourage the osseointegration of bioceramic composites. They also observed that the calcium phosphate composite revealed the formation of macroporous regions, given the considerable dissolution resulting from the α -TCP and CaO phases. The formation of macroporous regions and rough surfaces created during dissolution allowed the proliferation of both biological cells and bone growth.¹⁷ It is desirable for biocompatible materials to be completely absorbed in vivo via biodegradation. Poor biodegradation prevented natural bone growth for extended periods.¹⁶

Numerous authors have reported that highly crystalline apatites are insoluble, whereas low crystalline apatites have higher relative solubilities. In studies assessing the solubility and dissolution rates of different types of HAs, elevated levels of calcium measured in poorly crystalline HA products were associated with higher relative solubility values when compared with more crystalline materials.^{18,19}

Nelson²⁰ and LeGeros²¹ suggested that the solubility of apatites increases with increasing ionic substitutions into the apatite lattice and with decreasing crystallinity. Synthetic calcium phosphate ceramic surfaces can be transformed to biological apatite through a sequence of reactions that includes dissolution, precipitation, and ion exchange.²²

Both the organic and inorganic compositions differ between crown and root of autogenous tooth bone graft

materials. Thus, when the material is grafted, crown and root show different healing mechanisms. Apatites present in bone tissues form a ceramic/high molecular weight nanocomplex pattern.²³ Apatites present in human bone tissues have low crystallinity, with crystal sizes that are several tens of nanometers. On the other hand, HAs that are prepared via the sintering process at high temperatures have high crystallinity. Grain growth occurs during the sintering process, resulting in sizes that are at least 10 times larger than those apatites present in bone tissues.²⁴ The biodegradation of large particles with high crystallinity is almost impossible. Their osteoconduction capacity is very low and osteoclasts cannot degrade them. Low-crystalline carbonic apatites show the best osteoconduction effects. Some authors have suggested that small crystallite sizes of HAs can enhance biodegradation as a result of higher solubility.^{18,25}

CONCLUSIONS

Our results showed that autogenous tooth bone graft materials have structures and physicochemical characteristics that are most similar to those of autogenous cortical bones. Autogenous tooth bone graft materials are biodegradable biomaterials with compact microporous and low crystalline structures.

REFERENCES

1. Kim YK, Yeo HH, Ryu CH, Lee HB, UR B, Cho JE. An experimental study on the tissue reaction of toothash implanted in mandible body of the mature dog. *J Korean Assoc Maxillofac Plast Reconstr Surg* 1993;15:129-36.
2. Kim YK, Yeo HH, Yang IS, Seo JH, Cho JO. Implantation of toothash combined with plaster of paris: experimental study. *J Korean Assoc Maxillofac Plast Reconstr Surg* 1994;16:122-9.
3. Kim YK. The experimental study of the implantation of toothash and plaster of paris and guided tissue regeneration using lyodura. *J Korean Assoc Oral Maxillofac Surg* 1996;22:297-306.
4. Kim YK, Yeo HH. Transmitted electronic microscopic study about the tissue reaction after the implantation of toothash. *J Korean Assoc Oral Maxillofac Surg* 1997;23:283-9.
5. Kim YK, Kim SG, Lee JH. Cytotoxicity and hypersensitivity test of toothash. *J Korean Maxillofac Plast Reconstr Surg* 2001;23:391-5.
6. Kim YK, Kim SG, Lee JG, Lee MH, Cho JO. An experimental study on the healing process after the implantation of various bone substitutes in the rats. *J Korean Assoc Oral Maxillofac Surg* 2001;27:15-24.
7. Kim YK, Kim SG, Byeon JH, Lee HJ, Um IU, Lim SC, Kim SY. Development of a novel bone grafting material using autogenous teeth. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2010;109:496-503.
8. Kim YK, Lee HJ, Kim SG, Um IW, Im SC, Kim SG. Analysis of inorganic component and SEM analysis of autogenous teeth bone graft material and histomorphometric analysis after graft. *J Korean Acad Implant Dent* 2009;28:1-9.
9. Kim YK, Lee JY. The evaluation of postoperative safety of autogenous teeth bone graft. *J Korean Acad Implant Dent* 2009;28:29-35.

10. Garg AK. Bone. Biology, harvesting, grafting for dental implants. Rationale and clinical applications. Chicago: Quintessence Publishing; 2004. p. 3-20.
11. Holzwarth U, Gibson N. The Scherrer equation versus the 'Debye-Scherrer equation.' *Nat Nanotechnol* 2011;28:534.
12. Kim YK, Kim SG, Oh JS, Jin SC, Son JS, Kim SY, Lim SY. Analysis of the inorganic component of autogenous tooth bone graft material. *J Nanosci Nanotechnol* 2011;11:7442-5.
13. Tadic D, Epple M. A thorough physicochemical characterisation of 14 calcium phosphate-based bone substitution materials in comparison to natural bone. *Biomaterials* 2004;25:987-94.
14. Kirik SD, Solovyov LA, Blokhin AI, Yakimov IS. Structures of. *Acta Crystallogr B* 2000;56:419-25.
15. Balasundaram G, Sato M, Webster TJ. Using hydroxyapatite nanoparticles and decreased crystallinity to promote osteoblast adhesion similar to functionalizing with RGD. *Biomaterials* 2006;27:2798-805.
16. Adolfson E, Pter AH, Hermannson L. Phase analysis and thermal stability of hot isostatically pressed zirconia-hydroxyapatite composites. *J Am Ceram Soc* 2000;83:2798-802.
17. Priya A, Nath S, Biswas K, Basu B. In vitro dissolution of calcium phosphate-mullite composite in simulated body fluid. *J Mater Sci Mater Med* 2010;21:1817-28.
18. Fulmer MT, Ison IC, Hankermayer CR, Constantz BR, Ross J. Measurements of the solubilities and dissolution rates of several hydroxyapatites. *Biomaterials* 2002;23:751-5.
19. Lee DD, Rey C, Aioloiva M, inventors. Synthesis of reactive amorphous calcium phosphates. US patent 5,676,976; November 4, 1997.
20. Nelson DG. The influence of carbonate on the atomic structure and reactivity of hydroxyapatite. *J Dent Res* 1981;60:1621-30.
21. LeGeros RZ. Calcium phosphates in oral biology and medicine. *Monogr Oral Sci* 1991;15:1-201.
22. Ducheyne P, Radin S, King L. The effect of calcium phosphate ceramic composition and structure on in vitro behavior. I. Dissolution. *J Biomed Mater Res* 1993;27:25-34.
23. Glimcher MJ. Molecular biology of mineralized tissues with particular reference to bone. *Rev Mod Phys* 1959;31:359-93.
24. Lee SH. Low crystalline hydroxyl carbonate apatite. *J Korean Dent Assoc* 2006;44:524-33.
25. Lu J, Descamps M, Dejou J, Koubi G, Hardouin P, Lemaitre J, Proust JP. The biodegradation mechanism of calcium phosphate biomaterials in bone. *J Biomed Mat Res Appl Biomater* 2002;63: 408-12.

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