Ridge Preservation After Tooth Extraction With Buccal Bone Plate Deficiency Using Tunnel Structured β-Tricalcium Phosphate Blocks: A 2-Month Histologic Pilot Study in Beagle Dogs

Takahiro Ikawa,* Tatsuya Akizuki,*† Takanori Matsuura,* Shu Hoshi,* Shujaa Addin Ammar,* Atsuhiro Kinoshita,‡ Shigeru Oda,§ and Yuichi Izumi*

Background: Reduction in alveolar ridge volume is a direct consequence of tooth extraction. Tunnel β-tricalcium phosphate (β-TCP) blocks were manufactured from randomly organized tunnel-shaped β-TCP ceramic. Efficacy of these blocks compared to extraction alone for alveolar ridge preservation after tooth extraction with buccal bone deficiency was evaluated.

Methods: Maxillary first premolars of six beagle dogs were extracted after removing the buccal bone, and bone defects of 4 × 4 × 5 mm (mesio-distal width × bucco-palatal width × depth) were created. Fresh extraction sockets with buccal bone defects were filled with tunnel β-TCP blocks at test sites. Two months after the operation, histologic and histometric evaluations were performed.

Results: Regarding histologic sections, coronal and middle horizontal widths of the alveolar ridge were significantly greater at test sites (3.2 ± 0.5 and 3.6 ± 0.4 mm, respectively) than at control sites (1.2 ± 0.3 and 2.0 ± 0.6 mm, respectively). The amount of woven bone was significantly greater at test sites (62.4% ± 7.9%) than at control sites (26.8% ± 5.3%), although that of connective tissue and bone marrow was significantly greater at control sites (38.1% ± 6.2% and 16.0% ± 6.9%, respectively) than at test sites (10.7% ± 5.7% and 4.1% ± 2.2%, respectively). Regarding basic multicellular units, no statistically significant difference was found between the test and control sites (0.5% ± 0.1% and 0.6% ± 0.1%, respectively).

Conclusion: Tunnel β-TCP blocks represent an effective bone-graft material for alveolar ridge preservation in fresh extraction sockets with buccal bone defects. *J Periodontol 2016;87:175-183.*

KEY WORDS

Alveolar ridge augmentation; beta-tricalcium phosphate; biocompatible materials; dogs; osteogenesis; tooth extraction.

* Department of Periodontology, Graduate School of Medical and Dental Science, Tokyo Medical and Dental University, Tokyo, Japan.
† Division of Periodontology, Department of Oral Science, Graduate School of Dental Science, Kanagawa Dental University, Kanagawa, Japan.
‡ Department of Educational Media Development, Institute for Library and Media Information Technology, Tokyo Medical and Dental University.
§ Oral Diagnosis and General Dentistry, University Hospital of Dentistry, Tokyo Medical and Dental University.

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Optimal positioning of dental implants is crucial for achieving predictable functional and esthetic restorations and depends on the bone tissue available.[1] Unfortunately, tooth extraction triggers changes in the residual alveolar bone and results in an inadequate volume of the recipient site for crown-oriented implant placement.[2-6] These morphologic changes are caused by bone remodeling in the healed socket.[4,7] In curable sockets, the average width and height of reductions of the alveolar ridge are 3.87 and 1.67 mm, respectively.[6] Resorption of the alveolar ridge is more pronounced on the buccal than on the lingual aspect of extraction sockets because of the thin buccal plate.[3,5] It is known that alveolar ridge preservation depends on the type of bone defect accompanying tooth extraction, particularly when dealing with buccal bone loss.[8] Extraction sockets with buccal bone deficiency were shown to display greater bone remodeling without the use of graft materials in rats[9] and beagle dogs.[10] Thus, these changes represent a real challenge for clinicians in implant dentistry.

Different ridge preservation therapies have been developed.[11,12] Some studies have recommended the immediate placement of dental implants[13,14] and grafting in extraction sockets.[15,16] However, controversial results were evidenced by a few studies that showed buccal bone loss in animal and human experiments with these procedures.[17-19]

Various bone-graft materials, such as autografts,[20,21] allografts,[20,22,23] xenografts,[24-26] and alloplastic materials,[27-30] have been used for alveolar ridge preservation. Autogenous bone, which has osteoconductive, osteoinductive, and osteogenic properties, is considered the gold standard bone-graft material.[31] However, second surgery is required with subsequent increased morbidity.[32] As an option, β-tricalcium phosphate (β-TCP) is a biocompatible alloplastic material that is replaced with newly formed bone.[33,34]

The geometric structure of graft materials influences bone formation.[35,36] In a rabbit model, significantly higher vascularization was observed in graft materials with a pore size of 300 μm than those with smaller pore diameters.[37] Based on this concept, tunnel-shaped β-TCP, with an inner diameter of 300 μm, an outer diameter of 500 μm, and a length of 1 mm, was fabricated.[38,39] A block-type graft material was manufactured by randomly aggregating these particles.[38,39] These particles proved effective for periodontal regeneration in one-wall intrabony defects[39] and Class III furcation defects,[38] particularly in terms of new bone formation. In this pilot study, the effect of tunnel β-TCP blocks on alveolar ridge preservation is evaluated in extraction sockets with deficient buccal bone plates at 2 months in beagle dogs.

MATERIALS AND METHODS

Preparation of Tunnel β-TCP Blocks

The preparation of tunnel β-TCP blocks was performed as described previously.[38,39] In brief, β-TCP slurry was prepared by mixing a paste of TCP, polyvinyl alcohol, and distilled water at a molar ratio of 8:2:10. Extrusion molding was used to prepare a distinctive luminal structure, with an inner diameter of 300 μm, an outer diameter of 500 μm, and a length of 1 mm. Tunnel β-TCP blocks were manufactured by gathering and fixing randomly organized tunnel β-TCP particles. The blocks were sintered at a maximum temperature of 1,100°C. The porosity of the tunnel β-TCP blocks was ≈70%. The material was shaped into blocks measuring 5 × 5 × 5 mm.

Surgical Procedure

The ethics committee of the Animal Research Center at the Tokyo Medical and Dental University, Tokyo, Japan, approved this research protocol (0140321A). Six male beagle dogs, aged ≈1 year and weighing ≈10 kg, are used in this study. Premedication with 0.5 mg/kg medetomidine hydrochloride‖ was injected intramuscularly. Thiopental¶ (0.005 mL/kg) was administered intravenously during surgical procedures as a general anesthetic. Local anesthesia, 2% lidocaine hydrochloride with epinephrine (1:80,000), was induced.# Crestal incisions were performed from the maxillary canine to the second premolar in each dog, and a full-thickness mucoperiosteal flap was elevated. The buccal bone plate covering the root surface of the first premolar (P1) was removed using steel burs. The size of the defect created was 4 × 5 mm (length × height; Fig. 1A). Furthermore, P1 was removed carefully using forceps, and soft tissue in the extraction socket was completely curetted. The bone defect was trimmed to 4 mm in the mesio-distal direction, 4 mm in the bucco-palatal direction, and 5 mm in the apical direction (Fig. 1B). Bilateral defects were designated randomly as test or control by tossing a coin. The fresh extraction sockets with buccal bone defects were filled with tunnel β-TCP blocks at the level of the adjacent bone in the test group (Fig. 1C). In contrast, no graft materials were placed in the control group. A release incision was performed on the periosteum of the flap to cover the defect, which was then sutured.** After the operation, an antibiotic†† and an analgesic agent‡‡ were administered for 3 days, and chemical plaque control using a 2% solution of chlorhexidine gluconate§§ was performed

‖ Dormitor, Orion, Espoo, Finland.
¶ Ravonal, Tanabe Pharmaceutical, Osaka, Japan.
# Xylocaine, Fujisawa Pharmaceutical, Osaka, Japan.
** GORE-TEX CV-5 Suture, W. L. Gore & Associates, Newark, DE.
†† Penicillin G, Meiji Seika Pharma, Tokyo, Japan.
‡‡ Vetorphale, Meiji Seika Pharma.
§§ Hibitane Concentrate, Sumitomo, Osaka, Japan.

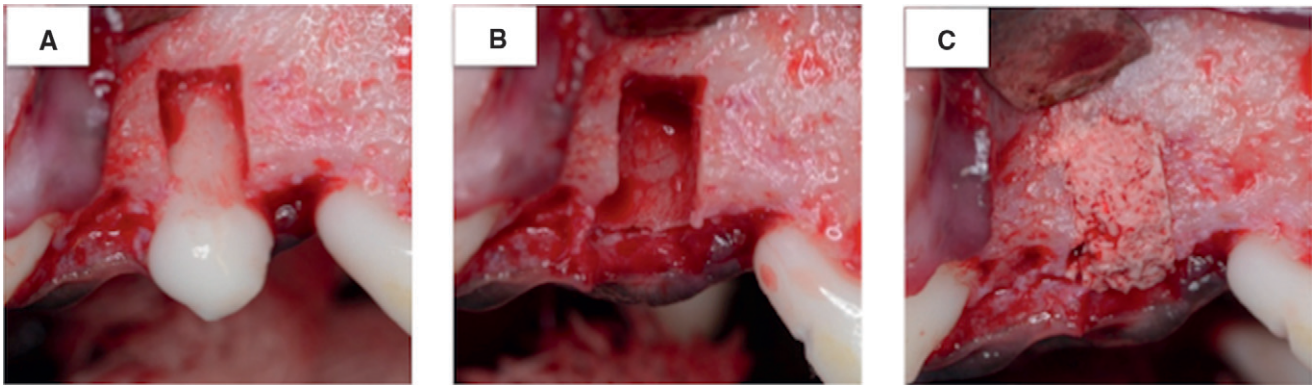

Figure 1.
A) *Buccal bone defects on the first premolar of the maxilla were made using steel burs.* ***B)*** *Tooth extraction was performed carefully, and the bone defects were trimmed to 4 × 5 × 4 mm (length × height × depth).* ***C)*** *Tunnel β-TCP blocks were grafted at the experimental sites, whereas the control sites received no graft.*

three times a week without general anesthesia. At 14 days after surgery, the sutures were removed. During the experiment, the animals were fed a soft-pellet diet.

After a healing period of 2 months, the dogs were euthanized using an overdose of sodium thiopental and perfused with a fixing solution of 4% formaldehyde through the carotid arteries. The maxillae were removed and soaked immediately in 10% neutral-buffered formaldehyde.‖‖

Histologic Analyses

The specimens were decalcified in hydrochloric acid,¶¶ embedded in paraffin,## and cut into 5-μm-thick sections*** in the bucco-palatal plane. The histologic section of the most central portion of the defect was selected using the electric counter of the microtome, confirmed by the picture obtained by computed tomography, and stained with hematoxylin and eosin. The width of new bone formation was measured histologically in the coronal (1 mm), middle (3 mm), and apical (5 mm) positions from the top of the palatal plate under a light microscope††††‡‡‡ (Fig. 2A). The region of interest (ROI) corresponded to the size of the bone defect (5 × 4 mm; Fig. 2B). The measurement of these parameters was performed according to a previous study.[40] New bone formation in the ROI, including bone marrow, basic multicellular units (BMUs), woven bone formation, and residual TCP, were measured using image processing software.§§§

Statistical Analyses

Differences between the test and control groups were calculated, and the data were expressed as means and standard deviations. Sample distribution was investigated using the Shapiro-Wilk test for each parameter, and statistical analysis was performed using the Student *t* test ($P < 0.05$)‖‖‖‖ for normally distributed samples or Wilcoxon rank-sum tests ($P<0.05$) for the rest of them.¶¶¶

Sample size was decided using previous studies[4,17,18,21] as reference, and the power calculation was based on the horizontal widths according to a previous study,[40] differences of 1 mm between groups equated to an SD of 0.6 mm, significance level of 5%, and a power of 80%.

RESULTS

Clinical Observations

No dogs exhibited inflammation or wound dehiscence at either test or control sites throughout the study.

Histologic Observations

New bone formation was evident inside the tunnel β-TCP blocks in the test group (Fig. 3A). At control sites, a limited amount of new bone and a larger amount of connective tissue (CT) were evident on buccal bone (Fig. 3B).

In test sites, the newly formed bone was observed both close to and far from the original bone. The dome-shaped contour of the buccal bone, like pristine bone, was found to include minimal new bone formation, CT, and residual issue particles (Figs. 4A, 4D, and 4G). New bone formation and angiogenesis were mostly visible inside the luminal structure of the tunnel β-TCP block (Fig. 4B), and the tunnel β-TCP interface was filled with new bone containing BMUs

‖‖ Mildform 10 N, Wako Pure Chemical Industries, Osaka, Japan.
¶¶ K-CX, Falma, Tokyo, Japan.
Tissue-TEKVIP5Jr, Sakura Finetek Japan, Tokyo, Japan.
*** AP 300-3, Microm International, Walldorf, Germany.
††† ECLIPSE Ni-U, Nikon, Tokyo, Japan.
‡‡‡ DP70, Olympus, Tokyo, Japan.
§§§ ImageJ v.1.43u, National Institutes of Health, Bethesda, MD.
‖‖‖‖ Microsoft Excel v.2011, Microsoft, Redmond, WA.
¶¶¶ Microsoft Excel v.2011, Microsoft.

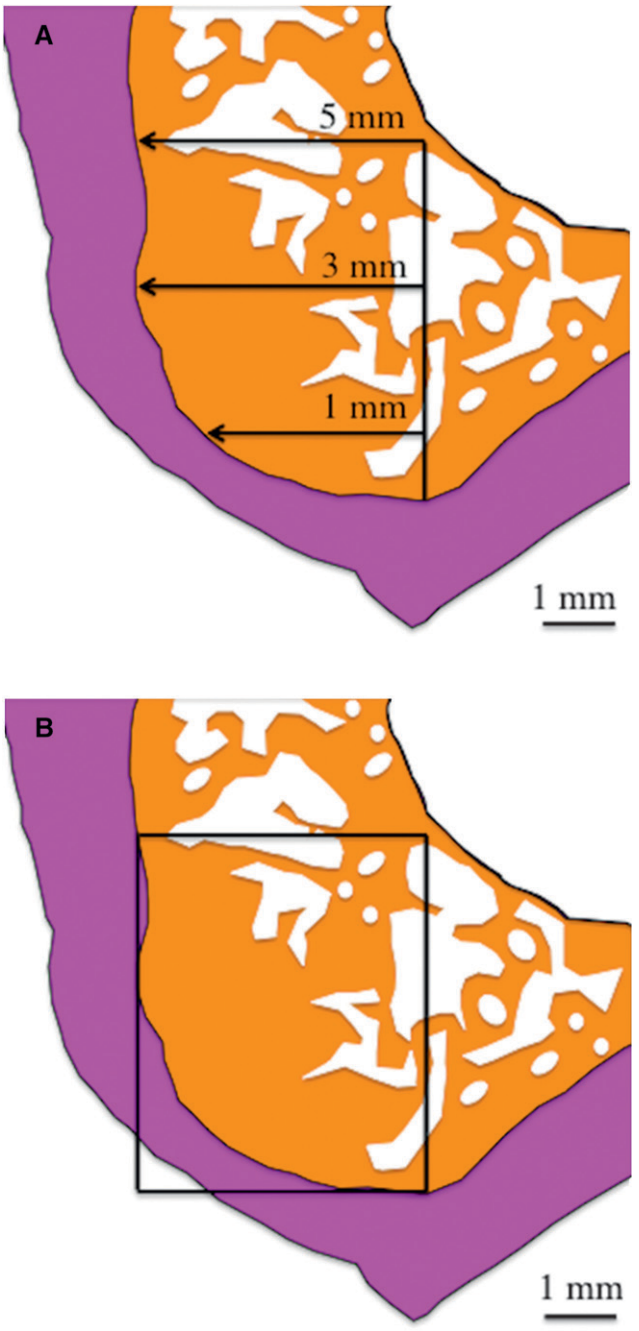

Figure 2.
A) *Liner measurements were made to evaluate the horizontal widths of the alveolar ridge bone 1, 3, and 5 mm from the top of the palatal plate on photomicrographs.* ***B)*** *The ROI was the same size as the bone defect (5 × 4 mm). Scale bars = 1 mm.*

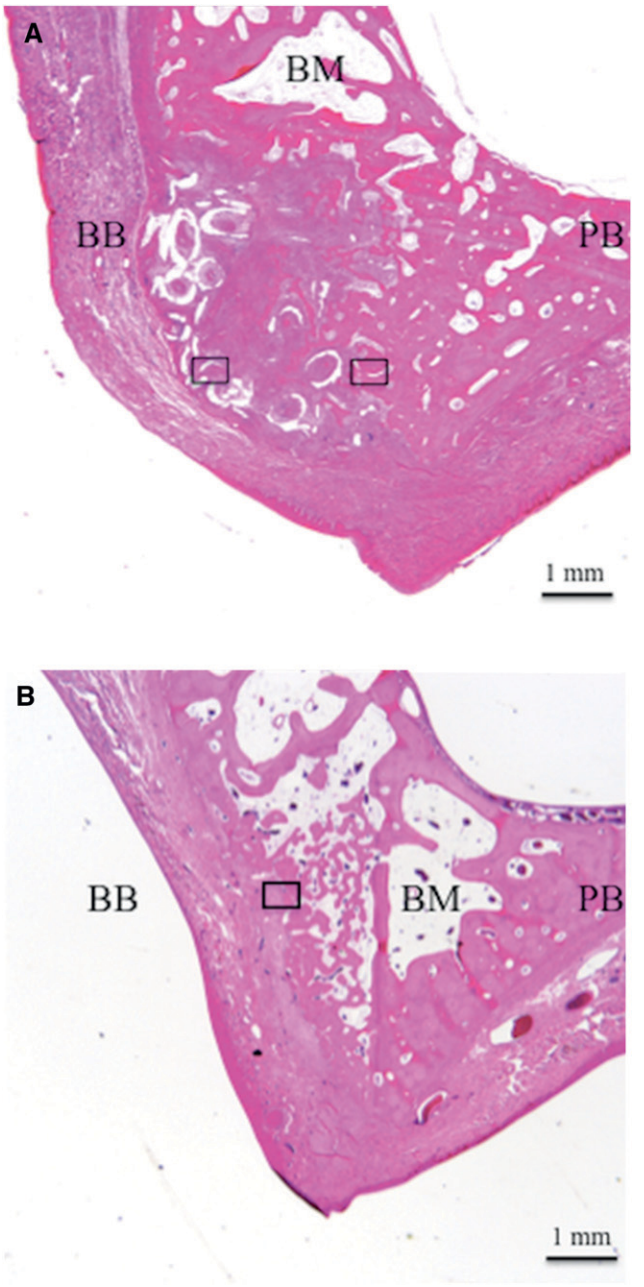

Figure 3.
Photomicrograph of a bucco-palatal section. ***A)*** *The widths of new bone formation and residual β-TCP were observed histologically at the test sites.* ***B)*** *Although mature bone formation from the original bone was observed at the control sites, a limited amount of new bone and a larger amount of connective tissue (CT) were evident on the buccal bone. BB = buccal bone wall; BM = bone marrow; PB = palatal bone wall. Scale bars = 1 mm (original magnification).*

(Figs. 4E and 4H). Furthermore, the absorption of β-TCP was evident.

In control sites, the surface of the original bone was occupied by mature bone formation, composed of bone marrow and woven bone, and containing a large number of primary osteons (Figs. 4C, 4F, and 4I).

Regarding buccal bone, the width of new bone at test sites was 3.2 ± 0.5, 3.6 ± 0.4, and 3.4 ± 0.2 mm in the coronal, middle, and apical positions, respectively. In contrast, the width of new bone was 1.2 ± 0.3, 2 ± 0.6, and 3 ± 0.6 mm at control sites. The width of newly formed bone was significantly greater in the

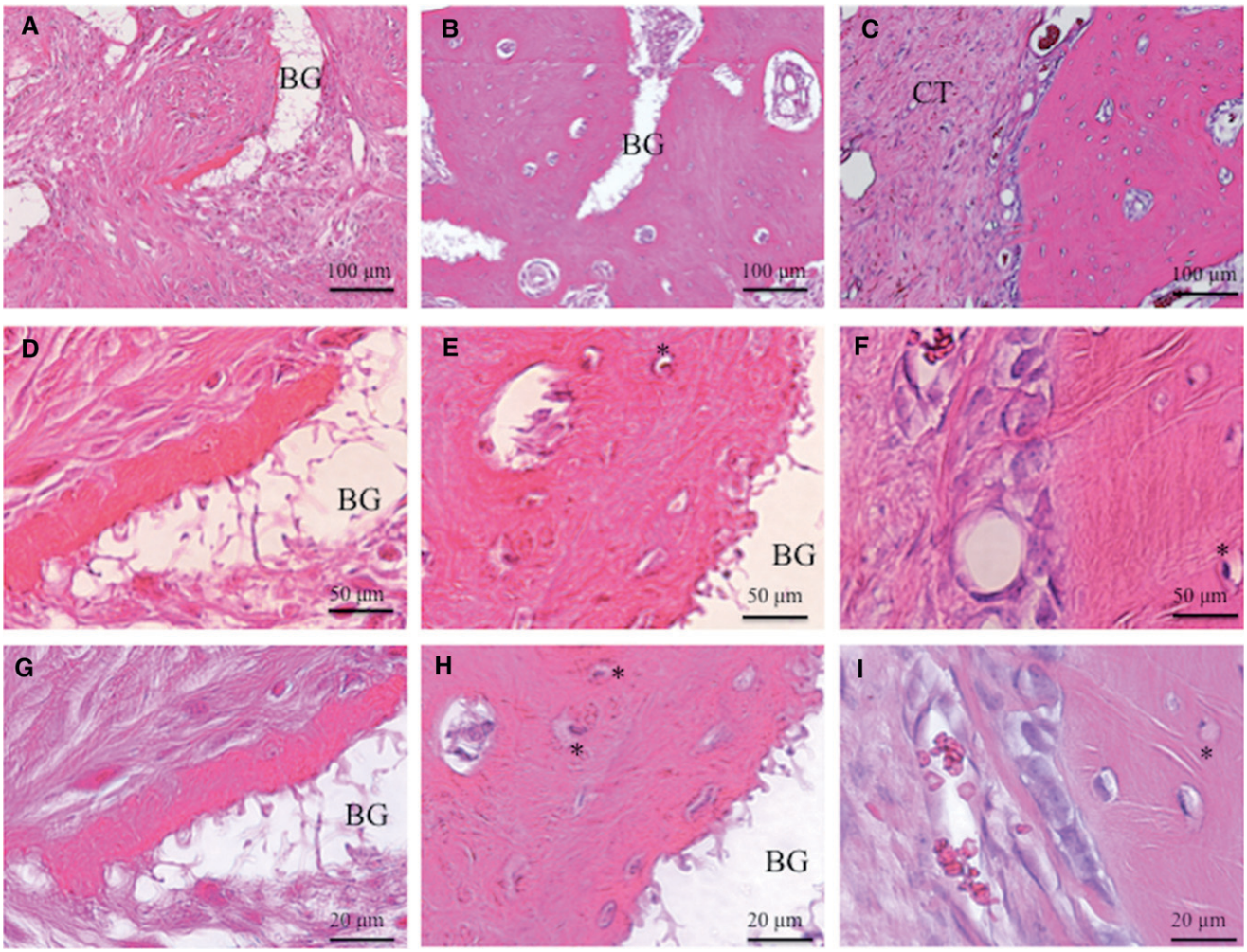

Figure 4.
Higher magnification of the boxed area of the buccal bone ***(A, C, D, F, G*** *and* ***I)*** *and boxed area adjacent to the original bone* ***(B, E,*** *and* ***H)*** *in Fig. 3. A, B, D, E, G, and H) The presence of residual* ***β****-TCP (BG) surrounded by newly formed bone and BMUs (asterisks) were observed at the test sites. C, F, and I) In the control sites, mostly CT was found, but the large area was occupied by mature newly formed bone and BMUs. A through C) original magnification ×20, scale bars = 100 μm; D through F) original magnification ×40, scale bars = 50 μm; G through I) original magnification ×100, scale bars = 20 μm.*

test group than in the control group at the coronal and middle positions ($P = 0.000003$ and 0.0006, respectively; Table 1). The composition of the ROI is shown in Table 2. The amount of woven bone at test sites (62.4% ± 7.9%) was significantly greater than that at control sites (26.8% ± 5.3%). The percentage of BMUs did not significantly differ between the test and control sites (0.5% ± 0.1% and 0.6% ± 0.1%, respectively). However, the amount of bone marrow was 4.1% ± 2.2% at test sites and 16.0% ± 6.9% at control sites, and the amount of CT was 10.7% ± 5.7% at test sites and 38.1% ± 6.2% at control sites; both outcome measures were significantly greater at control sites than at test sites ($P = 0.0005$ and 0.0006, respectively).

DISCUSSION

In this study, the use of tunnel β-TCP blocks for alveolar ridge preservation in extraction sockets with buccal bone defects is compared to no grafts. To the best of the authors' knowledge, this is the first study to evaluate the efficacy of this novel material on alveolar ridge preservation after tooth extraction. Clinically, the healing was uneventful, and the use of this material in extraction sockets appeared to be safe. The histologic evaluations showed statistically significant differences between the two groups. At test sites, the percentage of new mineralized tissue and the horizontal width of new bone were greater than at control sites. However, the percentage of bone marrow was significantly larger at control sites than at test sites. This suggests that tunnel β-TCP block is effective for ridge preservation after tooth extraction with deficient buccal bone but requires more time to be replaced by new bone.

Many histologic studies on animals have demonstrated that grafting with biomaterials reduces buccal

bone resorption after tooth extraction,[41-43] but these alveolar ridge-preservation experiments were performed using flapless tooth extraction with an intact buccal bone plate. In the present study, buccal bone deficiency was created at the maxillary first premolar. Few studies have examined this type of defect.[9,10] One of them examined extraction sockets with buccal bone loss in the distal root of the second and third maxillary premolars in beagle dogs.[10] In this study, the bone-regenerative potential for alveolar ridge preservation of a composite of β-TCP and a collagen sponge is evaluated. At 2 months, the areas of new bone in the β-TCP granules,### collagen, β-TCP granules plus collagen, and no-graft groups were 6.35 ± 2.07, 4.87 ± 1.88, 7.09 ± 1.81, and 4.80 ± 1.39 mm^2, respectively, and the percentages of new bone in these groups were 33.76% ± 9.86%, 30.24% ± 8.95%, 23.19% ± 8.62%, and 22.86% ± 6.62%, respectively. Furthermore, the areas of residual β-TCP granules in the β-TCP granules and β-TCP granules plus collagen groups were 0.77 ± 0.52 mm^2 (3.67% ± 2.48%) and 0.87 ± 1.09 mm^2 (4.14% ± 5.19%), respectively. Compared to these results, the present study evidenced larger percentages of new bone and residual graft material after the use of tunnel β-TCP blocks (68.9% ± 7.6% and 14% ± 7%, respectively). Another study on rats also examined the healing of extraction sockets with buccal bone defects using different time points (1, 3, 6, 9, 15, and 21 postoperative days).[9] It showed that more alveolar resorption occurred in extractions sockets with deficient buccal bone than in extraction sockets with intact buccal bone. Two studies in humans[24,44] confirm the findings of these animal experiments. It has been suggested that alveolar ridge resorption after tooth extraction is more pronounced when buccal bone is compromised. In these experiments, tooth extraction with buccal bone loss results in atrophy of the alveolar ridge at the control site. Therefore, this finding is consistent with the clinical situation. It is known that V-shaped defects are most commonly encountered after tooth extraction in clinical settings. However, in this study, rectangular rather than V-shaped defects are used for comparing the results with previous study.[10] Additional studies are necessary to test the utility of tunnel β-TCP blocks for ridge augmentation in defects of various shapes after tooth extraction.

Table 1.

Mean ± SD (mm) of Linear Measurements Made to Evaluate Horizontal Widths of Alveolar Ridge Bone

Position	Test Sites (mm)	Control Sites (mm)
Coronal (1 mm)	3.2 ± 0.5*	1.2 ± 0.3
Middle (3 mm)	3.6 ± 0.4*	2.0 ± 0.6
Apical (5 mm)	3.4 ± 0.2	3.0 ± 0.6

* P <0.05, statistically significant difference by Student t test; n = 6.

Table 2.

Mean ± SD (%) of Histometric Results

Region of Composition	Test Sites	Control Sites
Residual β-TCP	12.7 ± 6.3	
Woven bone	62.4 ± 7.9*	26.8 ± 5.3
Bone Marrow	4.1 ± 2.2	16.0 ± 6.9*
BMUs	0.5 ± 0.1	0.6 ± 0.1
CT	10.7 ± 5.7	38.1 ± 6.2†

* P <0.05, statistically significant difference by Student t test; n = 6.
† P <0.05, statistically significant difference by Wilcoxon rank-sum tests; n = 6.

Most previous studies on alveolar ridge preservation have used granular graft materials[41-43] because block-type graft materials are difficult to adjust to completely fill bone defects. Furthermore, an increased incidence of dehiscence was evident with the use of porous hydroxyapatite (HA) blocks compared to the use of granules for alveolar ridge augmentation in humans.[45] However, in the present study, alveolar ridge preservation was accomplished using β-TCP blocks, and immature new bone was observed in the buccal bone area, despite the fact that no membrane was used. This material was easy to trim and fit to bone defects of any size because of the weak connectivity between the tunnel β-TCP particles. In addition, the tubular structure of this material may promote angiogenesis and early stability through capillarity.[39,46] Commonly, alveolar ridge-preservation techniques use bone grafts with membranes to maintain the space and allow osteogenic cells to exclusively populate the defect.[47] However, previous studies have shown that resorbable and unresorbable membrane exposure has a poor effect on guided bone regeneration around dental implants.[48,49] Hence this material avoids the risk of a serious inflammatory reaction and the associated clinical healing problems that can be caused by membrane exposure.

In a previous study,[43] β-TCP, HA, biphasic calcium phosphate (BCP), or no graft were observed in extraction sockets in a canine model, and different healing patterns were found. At 2 months, the percentages of new bone formation in the β-TCP, HA, BCP, and no-graft groups were 48.6% ± 5.9%,

Osferion, Olympus Terumo Biomaterials, Tokyo, Japan.

32.3% ± 8.8%, 31.8%, and 62.0% ± 17.1%, respectively, and the percentages of residual biomaterial were 10.3% ± 4.1%, 48.1% ± 7.4%, and 32.4% ± 4.2%, respectively. In another study,[34] the bone formation and graft resorption properties of bovine bone substitute and β-TCP grafts were compared to those of autografts in minipigs; β-TCP was almost completely absorbed and replaced by newly formed bone (57.4% ± 5.3%), similar to autografts (54.5% ± 3.9%) at 2 months. In this study, the percentages of newly formed bone and residual β-TCP particles are 68.9% ± 7.6% and 14.0% ± 7.0%. When compared to previous studies, new bone formation was greater with tunnel β-TCP blocks than with other materials, whereas residual β-TCP was similar. In other words, this material has a potential similar to that of conventional β-TCP and was replaced equally by newly formed bone. β-TCP and bovine bone materials were also compared after 3-, 6-, 12-, and 24-month healing periods in dogs; β-TCP particles were absorbed completely only at 24 months.[50] In contrast, alveolar ridge preservation using β-TCP plus Type I collagen resulted in 62.6% mineralized bone and 16.3% residual β-TCP after 9 months in humans.[28] The 2-month healing period was chosen because most previous studies using similar models investigated the healing potential of biomaterials at 2 months, and this allowed the direct comparison of results.[7,10,40-43] Histologic studies suggest that a longer healing period is necessary to regenerate mature bone, thus suggesting that longer-term studies are required to understand the maturation time of new bone and graft material absorption. Moreover, although tunnel β-TCP blocks yielded significant histologic results in terms of the quality and quantity of newly formed bone, these results should be interpreted with caution because of the lack of clinical measurements at baseline and after treatment. Additional studies are needed to determine the clinical significance of these findings.

CONCLUSIONS

Tunnel β-TCP blocks significantly limited the absorption of the alveolar ridge after tooth extraction with deficient buccal bone compared to no-graft procedures. Furthermore, histologic analysis revealed significantly higher percentages of new bone formation and total mineralized tissue at augmented sites compared to control sites 2 months after tooth extraction and buccal bone defect creation.

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Correspondence: Dr. Tatsuya Akizuki, Division of Periodontology, Department of Oral Science, Graduate School of Dental Science, Kanagawa Dental University, 238-8580 Kanagawa, Japan. Fax: 81-46-822-8855; e-mail: akizuki.peri@tmd.ac.jp.

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