

Alveolar Ridge Preservation With the Socket-Plug Technique Utilizing an Alloplastic Putty Bone Substitute or a Particulate Xenograft: A Histological Pilot Study

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Following tooth extraction, ridge preservation procedures are employed to regenerate bone in the extraction socket, limit consequent ridge resorption, and provide a stable base for implant placement. The purpose of this study is to histologically evaluate and compare bone regeneration in extraction sockets grafted with either a putty alloplastic bone substitute or particulate anorganic bovine xenograft utilizing the socket-plug technique. Nineteen patients underwent 20 tooth extractions and ridge preservation following a standardized protocol. Ten sites were grafted with calcium phosphosilicate putty (CPS group) and the remaining 10 with anorganic bovine bone substitute (BO group). Patients were recalled after 4–6 months to evaluate the bone regeneration and to proceed with implant placement. A bone core was obtained during the implant procedure from each site and was used for histologic analysis. Histomorphometry revealed that residual graft values were significantly higher in the BO group ($25.60\% \pm 5.89\%$) compared to the CPS group ($17.40\% \pm 9.39\%$) ($P < .05$). The amount of new bone regenerated was also statistically significant higher in the alloplast group ($47.15\% \pm 8.5\%$) as compared to the xenograft group ($22.2\% \pm 3.5\%$) ($P < .05$). Results suggest that ridge preservation using a putty calcium phosphosilicate alloplastic bone substitute demonstrates more timely graft substitution and increased bone regeneration when compared to an anorganic bovine bone xenograft.

Key Words: ridge preservation, socket, collagen plug, putty, xenograft, bone regeneration

INTRODUCTION

The success of osseointegrated implants rests in the quality and quantity of residual bone at the recipient site at the time of implant placement.¹ Loss of bone occurs due to ridge resorption. Increased resorption may occur due to the presence of endodontic pathology, periodontitis, trauma, or aggressive maneuvers during extraction. The degree of ridge resorption greatly increases with the time elapsed since extraction, with the greatest amount occurring in the immediate postextraction period.^{2,3} Schropp et al⁴ in a 12-month prospective study showed that a 50% decrease in bone width occurred following extraction, with two-thirds of the estimated loss occurring in the first 3 months.

In an attempt to preserve the alveolar bone and to avoid ridge augmentation prior to implant placement, numerous

biocompatible regenerative materials have been used to fill the postextraction socket.^{5–8} The regeneration of bone in the postextraction socket has been documented with the use of a variety of grafts and/or guided bone regeneration membranes as opposed to healing of the extraction socket alone.^{9,10}

Autogenous bone grafts have always served as a gold standard for regeneration.¹¹ However, problems such as their procurement, quantity obtained, unpredictable resorption, and need for a second surgical site makes their use in ridge preservation procedures questionable.

Allografts have been frequently used for various regenerative treatment purposes including augmentation of extraction sockets. However, issues have been reported regarding their immunogenicity and immunologic reactivity.^{12,13} Allografts are generally considered to possess osteoconductive properties. Demineralized freeze-dried bone may exhibit osteoinductive properties, but this varies with each donor and each tissue bank, and it may even vary between batches within the same bank.^{14,15}

Xenografts have been used with good results in oral osseous surgeries. A bovine xenograft derived from hydroxylapatite that is deproteinated has enjoyed frequent use in ridge preservation. This bone substitute has been documented to retain its natural microporous structure following processing so

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DOI: 10.1563/AAID-JOI-D-13-00025

that it supports cell proliferation and migration and enhances blood vessel formation through the coarse meshed interconnecting pore system. It possesses a large internal surface, which enables an intensive contact with new bone tissue and a fine crystalline structure, which permits integration into the natural bone remodeling process. Several animal studies have shown this material to be promising in comparison with other bone substitutes.^{16,17} According to Klinge and colleagues,¹⁸ bovine xenografts provide an ideal scaffold for new bone formation and support osteoblastic cell attachment and proliferation when used in rabbits. However, histologic studies have revealed the presence of remnants of amorphous graft particles even several months following its implantation *in vivo*.^{19,20}

Recently, alloplastic bone substitutes that include synthetically derived biomaterials have been used extensively for regeneration in extraction socket. A third-generation bioactive glass alloplastic putty has been included in this study. This bone substitute is a premixed composite of bioactive calcium phosphosilicate particulate and a synthetic absorbable binder in a putty form. The bioactive particulate is composed solely of elements that exist naturally in bone such as Ca, P, Na, Si, and O, with the binder being a combination of polyethylene glycol and glycerin.²¹ The surface reactions lead to the formation of a calcium phosphate layer which serves as a scaffold for new bone growth. This graft material has the ability to adhere to normal bone, aid its remodeling, and enable hemostasis.²² It has been successfully used in various osseous defects with no reported adverse event and good patient acceptability.

The aim of the present pilot study is to evaluate the quality of bone formation in extraction sockets following implantation with either a particulate bovine xenograft (Bio-Oss, Osteohealth, Shirley, NY) (BO) or a calcium phosphosilicate putty alloplastic bone substitute (NovaBone Dental Putty, NovaBone Products, Alachua, Fla) (CPS putty).

MATERIALS AND METHODS

The present study included 19 patients presenting with 20 single-rooted teeth that were scheduled for extraction. Ten of these cases were treated in a private practice in Greece and the remaining ten in a private practice in India. Each of these patients had no systemic health issues with any underlying medical conditions that could affect the surgical or regenerative procedure. The exclusion criteria for this study were:

- medical history that contraindicates oral surgical treatment;
- chronic therapy with nonsteroid anti-inflammatory drugs and/or corticosteroids;
- pregnancy;
- severe periodontal disease;
- prior mucogingival or periodontal surgery at the experimental site;
- loss of more than 50% of the buccal plate at the time of extraction; and
- heavy smoking (>10 cigarettes per day).

Subjects smoking less than 10 cigarettes per day were included in the study, and they were encouraged to abstain

from smoking 1 week before as well as 4 weeks after the surgery.

Following a thorough oral evaluation, patients were informed about the diagnosis and treatment alternatives. Willing participants signed the consent form and were enrolled in the study. The study was conducted in accordance with the Helsinki Declaration of 1975, as revised in 2000.

The patients were then stratified into 2 test groups following a simple random allocation approach at the site-level according to a computer-generated randomization list: group BO and group CPS. In each of the groups, the tooth scheduled for extraction was removed using a flapless technique under local anesthesia (2% lidocaine with 1:100 000 epinephrine). Ridge preservation was performed according to the socket-plug technique as previously described by Kotsakis et al.²³

Briefly, the extraction sockets of group BO were immediately grafted with particles of bovine xenograft and those of group CPS were filled with calcium phosphosilicate putty. Following grafting, a collagen plug (CollaPlug, Zimmer Dental, Carlsbad, Calif) was placed over the graft to occlude the socket, and it was secured using a horizontal mattress technique with 4-0 Vicryl suture material. Placement of removable interim prosthesis over the healing socket was avoided, and the edentulous sites were provisionally restored with either a resin-fiber retained partial denture fixed on the neighboring teeth or left as it was according to the patients' esthetic demands.

Antibiotics (amoxicillin 500 mg 3 times a day for 7 days) and nonsteroid anti-inflammatory analgesics (ibuprofen 400 mg 4 times a day for 3 days) were prescribed postsurgically. The patients were advised to follow a cold/soft diet for 24 hours and use a chlorhexidine 0.2% oral gel for topical application 2 times daily for 2 weeks. Postoperative evaluation was done at 1, 3, and 6 weeks to check for complications including infection, wound dehiscence, and resorption.

Periapical radiographs were taken at 5 to 6 months after grafting to confirm radiographic bone healing of the extraction defects. At this stage, implant placement was planned and samples for histologic analysis were to be obtained simultaneously with the surgical procedure. Mucoperiosteal flaps were raised to gain access to the underlying alveolar bone. Bone cores were obtained using a 2.7-mm inner diameter trephine bur. The cores obtained were stored in 10% buffered formalin and sent for histopathologic examination.

Histologic technique

Hard Tissue Research Laboratory, University of Minnesota, Minneapolis, Minnesota performed nondecalfied histology and provided histomorphometric data on the specimens from the cases that were treated in Greece. Upon receipt, specimens were dehydrated with a graded series of alcohols for 9 days. Following dehydration, the specimens were infiltrated with a light-curing embedding resin (Technovit 7200 VLC, Heraeus Kulzer, Wehrheim, Germany). This was followed by 20 days of infiltration with constant shaking at normal atmospheric pressure; the specimens were then embedded and polymerized by 450-nm light. Care was taken during specimen preparation that the temperature of the specimens never exceeded 40°C; the specimens were then cut and ground. Specimens were



FIGURES 1 AND 2. **FIGURE 1.** Representative radiograph of a socket regenerated with calcium phosphosilicate putty at 5 months. Note that the radiodensity in the socket area is very similar to the adjacent ungrafted area. **FIGURE 2.** Representative radiograph of a socket regenerated with bovine bone substitute at 6 months. Note that the socket area exhibits higher radiodensity indicative of residual graft particles.

prepared in an apicocoronal direction, parallel to the long axis and were cut to a thickness of 150 μm on a cutting/grinding system (EXAKT Technologies, Oklahoma City, Okla). The cores were polished to a thickness of 45–65 μm with a series of polishing sandpaper disks from 800 to 2400 grit, using a microgrinding system, which was then followed by a final polish with 0.3- μm alumina polishing paste. The slides were stained with Stevenel blue and Van Gieson picrofuchsin and a cover slip was placed for histologic analysis using bright field and polarized microscopy. Histomorphometric measurements were completed using a combination of spot insight program and Adobe PhotoShop (Adobe Systems, San Jose, Calif). At least two slides of each specimen were evaluated.

The Department of Oral Pathology, Oxford Dental College in India processed the cores that were obtained in India. All CPS putty samples were subjected to microwave decalcification with 5% nitric acid solution (95 mL deionized water with 5 mL nitric acid). The tissue specimen was immersed in the above solution and placed in a microwave and heated up to 800 W for 20 seconds; this cycle was repeated 3 times with a 1-hour interval between each cycle. This was followed by routine automatic tissue processing, embedding, sectioning, and finally staining of the sections with hematoxylin and eosin (H & E). The above-mentioned modified technique was utilized for the CPS cores because, based on the authors' experience, hard tissue microtomy of CPS cores can cause artifactual voids due to the residual graft particles being separated particularly from the marrow portion of the cores. To prevent inconsistencies in the histomorphometric analysis, the protocol of the Department of Oral Pathology includes this modified technique for handling bioglass cores. Microwave demineralization

is a rapid method of partial demineralization to the point that the tissue is soft enough to cut with a routine soft tissue microtome. CPS cores being a bioactive glass do not undergo demineralization with nitric acid to the same extent as hydroxyapatite in bovine xenograft. As a result, there was no volumetric loss of CPS putty at the end of processing and no consequent effect on the histomorphometric analysis. All BO specimens were routinely processed in an automatic tissue processor, embedded in self-cure acrylic resin, mounted on a hard tissue microtome (Leica SP 1600 saw microtome, Leica Biosystems, Buffalo Grove, Ill) and 50- μm sections were obtained, which were further ground by hand on an Arkansas stone, and stained routinely with H & E.

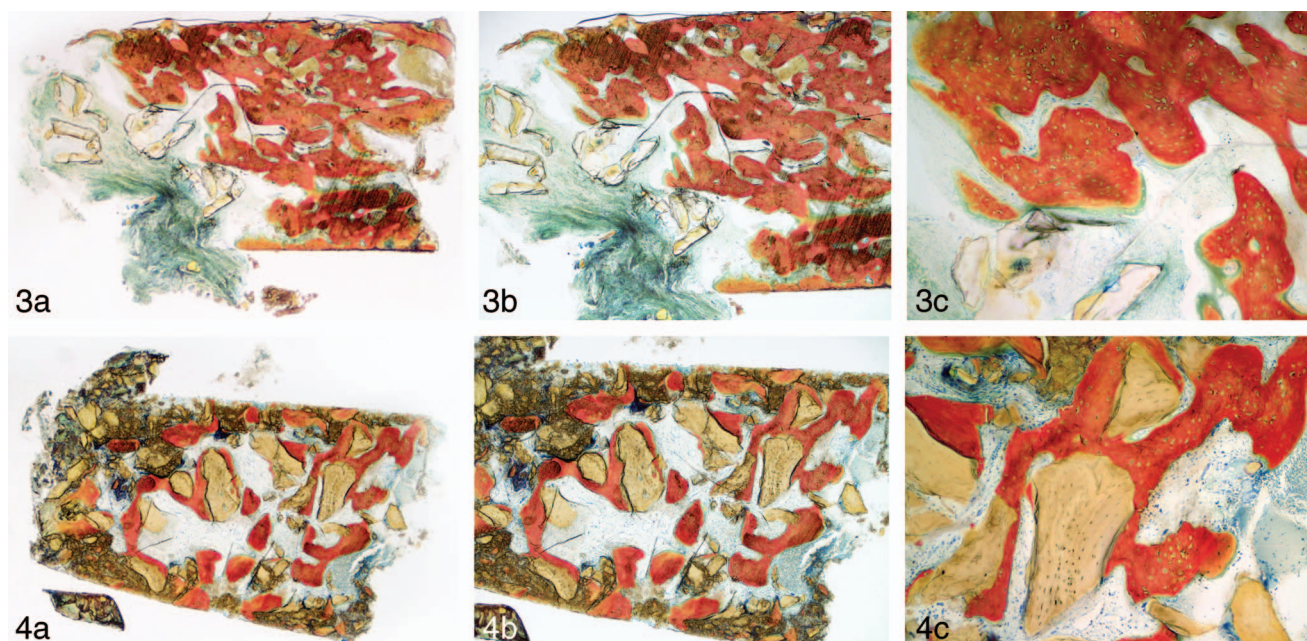
Statistical analysis

A 2-tailed, independent *t* test was performed to compare histomorphometric results regarding new bone formation and residual bone graft between the 2 groups. The level of statistical significance was set at $P < .05$. Results from the histologic analysis of the samples were presented descriptively.

RESULTS

Clinically and radiographically, all sites healed without any complications or adverse reactions. No signs of infection or inflammatory response were observed during the healing period.

Periapical radiographs taken at 5 to 6 months post grafting (5.25 ± 0.2) showed radiodensity similar to the adjacent bony structures in the CPS group (Figure 1), while cases in the BO



FIGURES 3 AND 4. FIGURE 3. Representative images of calcium phosphosilicate putty core at 6 months: (a) medium ($\times 20$), (b) high ($\times 40$), and (c) very high ($\times 100$) magnifications. The red-stained tissue is mineralized, newly regenerated bone with visible cell nuclei. Some residual graft particles can be seen in all of the microphotographs. **FIGURE 4.** Representative images of bovine bone substitute core at 6 months: (a) medium ($\times 20$), (b) high ($\times 40$), and (c) very high ($\times 100$) magnifications. Large remnants of residual graft particles can be noted. Red area denotes newly formed bone with visible cell nuclei.

group showed a greater level of radio-opacity (Figure 2). During surgical reentry of the surgical sites, visual inspection revealed bone regeneration in the healed ridges with both test materials. The sockets that had been grafted with the xenograft presented visible residual particles on the area of the regenerated bone. This newly formed structure was regarded as bone, and histologic analysis was done to confirm clinical findings. All sockets received implants; results regarding primary implant stability and implant survival will be presented in a separate publication.

Histology and histomorphometric analysis

Histologic analysis of all samples consistently showed the presence of vital, healthy trabecular and woven bone and bone marrow with evidence of remodeling, indicated by resting and reversal lines with variable quantities of residual bone graft material. These sections were then analyzed at $\times 20$, $\times 40$, and $\times 100$ magnifications to ascertain the area occupied by bone tissue and residual bone graft. Figure 3a, b, and c shows histology sections of a representative CPS putty case at 6 months. At all magnifications, the sections show vital lamellar bone, highly vascular bone marrow, and some residual graft particles. Figure 4a, b, and c shows histology sections of a representative BO case at 6 months. At all magnifications, the sections show viable bone with marrow tissue and residual graft substitute. A higher number of residual graft particles can be clearly observed in the sections with BO as compared to CPS putty.

Table 1a displays vital bone in defects filled with CPS putty that ranges from 36%–57% (average $47.15\% \pm 8.5\%$). Residual bone graft (RBG) was found to range from 30% at 4 months to a

TABLE 1a			
Vital bone and residual graft values for the calcium phosphosilicate putty group*			
Tooth No.	Time, mo	Vital Bone, %	RBG, %
11	4	55	18
11	4	36	30
14	6	55	3
21	4	40	28
21	5	41	26
24	6	41	13
24	6	57	8
25	5	55	8
35	4	38	24
44	5	54	16

TABLE 1b			
Vital bone and residual graft values for the bovine bone substitute group*			
Tooth No.	Time, mo	Vital Bone, %	RBG, %
11	6	24	20
13	6	19	24
15	6	21	28
23	6	22	26
24	6	27	18
25	6	22	23
33	6	26	22
35	5	26	26
44	4	18	32
45	4	17	38

*RBG indicates residual bone graft.

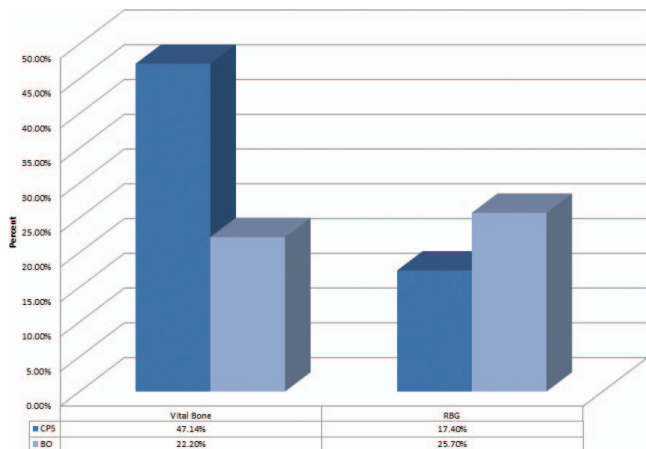


FIGURE 5. Graphical representation of the percentage of vital bone and residual bone graft in both groups.

minimum of 3% at 6 months and an average of 17.4% ± 9.4%. The vital bone values in the BO group (Table 1b) ranged between 17% and 27% (average 22.2% ± 3.5%). The difference in vital bone volume between the 2 groups was found to be statistically significant in favor of the CPS putty group (*P* < .05). Specimens in the BO group showed a range of RBG of a maximum of 38% at 4 months to a minimum of 18% at 6 months with an average of 25.7% ± 5.9% (Figure 5).

The amount of RBG was found to be significantly higher in the BO group (*P* < .05). Table 2 presents a comparison of RBG between the study groups at 2 different observation intervals, at 4 and at 6 months. At 6 months, there was a highly statistically significant reduction in residual graft volume in the CPS putty group when compared to that in the BO group (*P* < .001).

DISCUSSION

Extraction site reconstruction is employed frequently for alveolar ridge preservation when future placement of implants is the treatment of choice. Immediately following extraction of a tooth, a cascade of inflammatory events are initiated, and a blood clot is formed which further directs the migration and proliferation of cells and the release of growth factors. By 4–6 weeks, most of the alveolus is filled with woven bone (osteoid tissue), while the soft tissue becomes keratinized. After a 4- to 6-month period, the mineralized tissue within the socket reorganizes into layers of lamellar bone.²⁴ Many biomaterials have been used in an attempt to enhance bone regeneration in the postextraction socket. A clinical study by Becker et al²⁵ showed that when bovine bone is used in ridge preservation it does not promote extraction socket healing. Bovine xenografts also do not contribute significantly to bone-to-implant interface. The same study also indicated that these grafts appeared inferior to the normal extraction socket healing, though they maintained ridge width, possibly due to extended resorption time.

The present study was conducted to comparatively assess the relative efficacy of BO to a newly developed putty alloplastic bone substitute using a flapless ridge preservation

TABLE 2
Comparative evaluation of the residual bone graft (RBG) percentages between the 2 study groups at 2 time interval†

RBG	CPS Putty (%)	BO (%)
4 Months	23.67 ± 5.57*	35.00 ± 4.24
6 Months	8.00 ± 4.08**	23.14 ± 3.44
All samples	17.40 ± 9.39*	25.60 ± 5.89

†CPS indicates calcium phosphosilicate; BO, bovine bone substitute.
*Indicates a statistically significant (*P* < .05) reduction in RBG values in favor of the CPS putty group.
**Indicates a highly statistically significant (*P* < .001) reduction in RBG values in favor of the CPS putty group.

approach. CPS putty is a third generation bioactive glass. Bioglass has been successfully implanted for over a decade in craniofacial surgeries, in dental bone grafting, and in orthopedic and spine indications.²⁶ Though an excellent bone filler, BO resorbs very slowly and has been shown to exhibit a high percentage of residual graft particles for extended periods of time following its implantation. CPS putty not only provides an osteoconductive scaffold but also functions by a process of osteostimulation.²⁷ It stimulates osteoblast recruitment, proliferation, and differentiation at the defect site and increases the rate of bone formation not just at the edges but throughout the defect. It has been engineered to exhibit faster rate of particle resorption and bone regeneration. In a recent study, Gonshor et al²⁸ concluded that a high percentage of vital bone (48.2%) was noted in a series of 22 sockets that were restored with CPS putty. In comparison, results of a clinical study where BO was left to heal in extraction sockets for 9 months showed that the amount of osseous tissue in the superficial area of the healed socket was 17.1%. The average bone tissue fraction increased to 48.3% in the midsection area, but it displayed 4 times more woven bone than lamellar. Bone tissue reached 63.9% only in the most apical site of the healed socket after 9 months of healing.²⁹

In our study, a collagen wound dressing material that was used instead of a membrane helped in achieving excellent hemostasis and induced blood clot formation along with stabilization of the blood coagulum.^{30,31} This collagen barrier is an integral biomaterial when utilizing the socket-plug technique and has been found to stimulate platelet aggregation and enhance fibrin linkage. It has also been demonstrated to be chemotactic for fibroblasts in vitro which might promote cell migration and primary wound coverage.³² Histologic results of this study point out that the collagen plug is an adequate barrier for ridge preservation when most of the buccal plate is maintained following extraction since no epithelial infiltrate was noted in the regenerated sockets.

CONCLUSION

Both BO and CPS putty showed regeneration of bone within the socket; thus, both can be considered clinically viable alternatives for alveolar ridge preservation. While at 4 months the RBG between the 2 study groups was comparable, CPS putty showed a significantly less percentage of RBG and a

greater amount of bone regeneration at the 6-month interval than BO.

Consequently, CPS putty may present a clinical advantage in terms of the quality of the regenerated bone over BO when reduced treatment time between ridge preservation and implant placement is required. Large-scale randomized clinical studies are required to evaluate the clinical efficacy of CPS putty bone substitute and reaffirm our findings.

ABBREVIATIONS

BO: bovine bone substitute
 CPS: calcium phosphosilicate
 H & E: hematoxylin and eosin
 RBG: residual bone graft

ACKNOWLEDGMENTS

The authors wish to thank Mr Srinvas Katta, Director of Dental Products, Novavone LLC, Alachua, Florida, for providing partial material support for this study. The authors are also grateful to Panagiotis Stanitsas, MSc, Transportation Engineering, University of Minnesota, Minnesota, for his help with the statistical analysis presented in the manuscript.

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