Clinical and Histological Evaluation of Ceramic Matrix in a Collagen Carrier for Socket Preservation in Humans

Edgard S. El-Chaar, DDS, MS

Introduction: *A case series was used to evaluate the efficacy and predictability of a ceramic matrix in a putty-like collagen carrier in immediate extraction sockets.*

Methods: *A single failing tooth was atraumatically extracted from each of 10 subjects. The sockets were debrided and grafted with ceramic matrix in a putty-like collagen carrier (15% hydroxyapatite, 85% β-tricalcium phosphate complex). A bovine pericardium membrane was draped over the graft site and a tension-free primary closure was obtained. After 6 months of healing, a trephine biopsy was taken from the center of each graft and a dental implant was placed. Two subjects were withdrawn from the study and were considered treatment failures. One of them moved to another state and the second exhibited delayed healing that required debridement of the grafting material from the socket.*

Results: *After 6 months follow–up, there was a mean reduction of ridge width of 1.667 mm and mean reduction of ridge height of 0.483 mm after graft healing and integration. Over a 24-month follow-up, mean new bone fill was 40.25% and implant osseointegration was 100%.*

Conclusion: *Ceramic matrix in a putty-like collagen carrier maintained ridge dimensions and, despite ongoing bone turnover, produced adequate mineralized tissue that enabled implant placement at 6 months. (Implant Dent 2016;25:149–154)*

Key Words: tricalcium phosphate, hydroxyapatite, putty graft material, human alveolar socket repair, socket grafting

A horizontal and vertical volume change of the alveolar ridge after tooth extraction and healing of the undisturbed socket is a normal phenomenon that has been extensively studied and reported. These dimensional changes become more extensive if the socket's residual alveolar walls are either damaged or missing. Considerable loss of ridge height and width after tooth extraction and healing can lead to less-than-ideal implant placement, especially in the anterior maxilla, where bone volume is both biologically and esthetically important.[1–4] To limit and combat these dimensional changes, surgical procedures such as guided bone regeneration and socket preservation are employed.[5,6] These surgical procedures have been successfully executed and documented using allografts, autografts, and xenografts.[7–9]

Many histologic and radiographic evaluations of osseous tissue formation with the use of synthetic graft materials have been reported using animal models and human studies. Two examples of synthetic graft materials that have been researched are bioceramics made of hydroxyapatite (HA) and β-tricalcium phosphate (β-TCP). Bioceramics made of hydroxyapatite (HA) have been widely used as bone substitutes in bone grafting and dental devices.[10–12] HA-based ceramics can induce mesenchymal cells to differentiate into osteoblasts and therefore HA can be used as scaffold material for bone tissue engineering. This has been shown in 2 experiments, one with rat marrow-derived cells placed onto an HA scaffold,[13] and another with an osteoblastic-like cell line seeded onto HA discs.[14] Bioceramic grafts with β-TCP were shown to induce osteogenesis in the calvaria of rats, by Kojima et al,[18] when using a bone regeneration induction method consisting of a combination of the bone-filling material atelocollagen, bovine granules, and thermoplastic bioabsorbable plates. In another study of synthetic grafting materials, Fujita et al[19] embedded a block of HA and β-TCP subperiosteally in the parietal region of rats, then histologically compared the β-TCP and HA. Both areas

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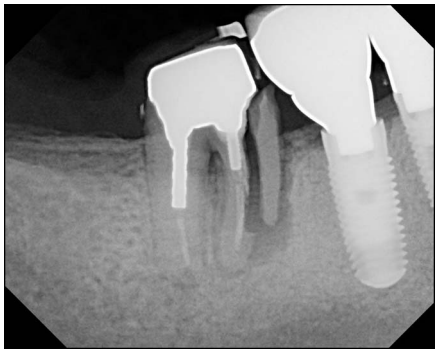

Fig. 1. Subject 1: Periapical radiograph of a failing mandibular right second molar treatment planned for extraction and restoration with a single implant fixture. Note the fracture of the mesial root.

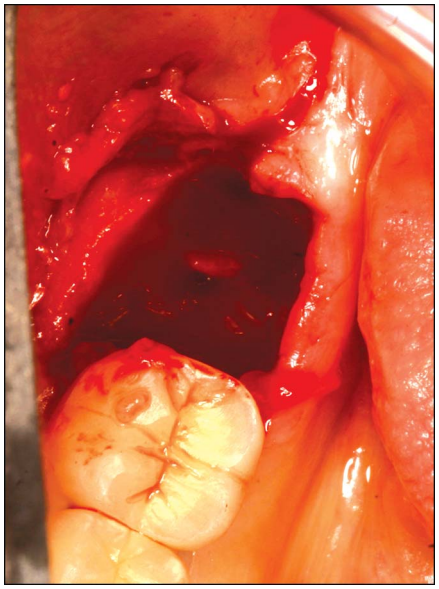

Fig. 2. Subject 1: Extraction socket of the right mandibular second molar after full thickness flap elevation, tooth sectioning, and sequential root removal. The extraction sockets are thoroughly debrided to remove any granulation tissue and rinsed with a saline solution before placement of the bone graft.

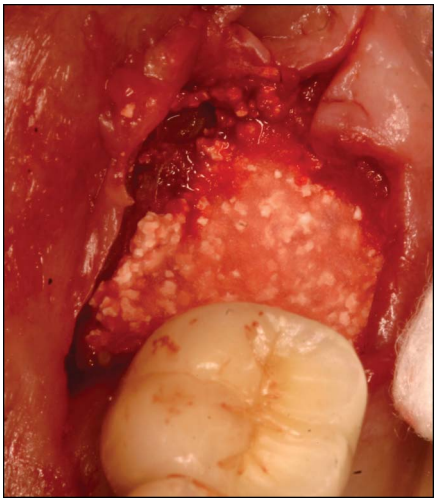

Fig. 3. Subject 1: The MASTERGRAFT putty graft material (Medtronic, a composite consisting of 15% HA and 85% β-TCP placed in a carrier made from a combination of insoluble/soluble collagen strands) was placed to fill the extraction socket and was contoured to recreate the dimension of the alveolus before tooth extraction.

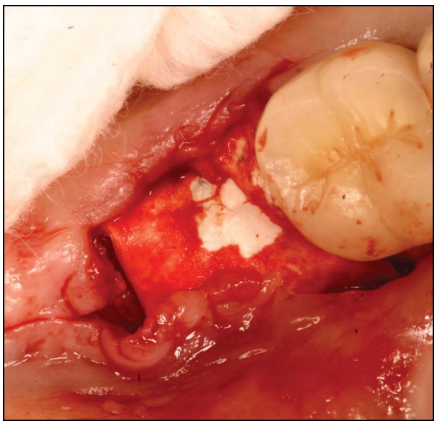

Fig. 4. Subject 1: A bovine pericardium (Copios; Zimmer Dental, Inc.) was trimmed and draped over the graft site, containing the graft material and allowing for epithelial cell exclusion during initial healing. Tension-free primary closure was achieved over this membrane with 5 to 0 polyglactin 910 (Vicryl; Ethicon, Johnson and Johnson Company) sutures.

were found to have formed membranous bone but it was reported that the HA site showed higher osteogenesis capability than β-TCP.

All of the included studies reported good bone repair, with the use of synthetic graft materials but very few studies to date include a histological examination of the course of bone repair following implantation of synthetic graft materials in the human jaw. Because of this lack of histologic evidence, the detailed course of bone repair in human jaws surrounding synthetic grafts remains unclear.

When using a composite of 2 different bioceramics, an important element to look for is close matching of the resorption to the bone deposition rate. This is an important concern when selecting biomaterial grafts because a rapidly resorbing scaffold might induce bone volume reduction, whereas one that resorbs too slowly, or not at all, would slow down bone deposition limiting tissue remodeling and maturation for implant placement.[15–17] Identifying the most appropriate bioceramic or bioceramic composite bone substitute for ridge preservation before implant placement is a controversial point, because, to date, there have been few reports that would give insight on whether such grafts can support functioning dental implants.

In this study, a bioceramic combination of HA- β-TCP in a putty-like collagen carrier was used in socket preservation after tooth extraction before dental implant placement. The dimensional changes of the ridge were noted to help determine the graft material's efficiency in preserving ridge dimension after tooth extraction and 10 cores were harvested from the grafted sites to evaluate the bone generated. The implants placed in these sites were followed for a period of 24 months as a means of assessing implant survival in areas grafted with the employed synthetic graft material. The purpose of this study was to determine the capability of a bioceramic combination of HA-β-TCP in a putty-like collagen carrier to preserve alveolar ridge dimension after tooth extraction, generate osseous tissue in a grafted site, and support implants for a period of approximately 24 months.

MATERIALS AND METHODS

This nonrandomized case series considered systemically healthy patients who presented to the author's private practice for implant restoration of a single unsalvageable tooth (Fig. 1) and who lacked adequate bone volume for immediate implant placement. Each patient's medical and dental history was reviewed to identify any contraindications to tooth extraction and augmentation surgery. A thorough clinical examination was also performed to determine oral health status and to identify any existing pathologies that needed to be corrected before surgery. A cone-beam computed tomography (CBCT) scan was taken to further evaluate general dental health and to assess

Table 1. Histologic Analysis Data

Specimen Identification	Total Area	Vital Bone Area	NonVital Bone Area	NonBone Area	Percent Spec = Bone	Percent Total Bone = VITAL	Percent ALLOGRAFT = NONVITAL	Percent Marrow or Fibrous Tissue	Percent Spec = NonBone
Specimen-1	651,114	163,459	0	135,593	25	100	0	54	21
Specimen-2	632,123	374,484	0	21,772	59	100	0	37	3
Specimen-3	854,029	408,574	0	0	48	100	0	52	0
Specimen-4	570,564	169,611	0	90,548	30	100	0	54	16
Specimen-5	227,252	61,485	0	40,895	27	100	0	55	18
Specimen-6	730,047	300,382	0	0	41	100	0	59	0
Specimen-7	553,809	217,845	0	80,494	39	100	0	46	15
Specimen-8	467,855	248,202	0	48,383	53	100	0	37	10

The cases were distributed as follows: 4 maxillary posterior, 6 mandibular posterior. The new and existing bone and residual graft material are distinguished by (1) density of the osteocytes in the matrix, (2) alignment of the cement lines, (3) erosion by osteoclasts, and (4) staining intensity. The histologic analysis resulted in 40.25% (25%–59% range) vital bone, 10.38 (3%–21% range) residual graft material, and 49.25% (37%–59% range) marrow.
Spec indicates specimen.

the volume of bone and the status of the buccal plate of the tooth scheduled for extraction. A total of 10 patients (7 women, 3 men), ranging in age from 38 to 83 years (mean of 59.25), were consecutively treated (Table 1) after signing an informed consent form.

Medications

Antibiotic prophylaxis with amoxicillin (500 mg) or clindamycin (150 mg) (Cleocin; Pantheon YM, Inc., Toronto, ON, Canada), for patients with hypersensitivity to penicillin-based medications, was administered 1 hour before surgery and prescribed for 7 postoperative days (amoxicillin 500 mg 1 tablet 3 times a day or Clindamycin 150 mg 4 times a day). Chlorhexidine gluconate (0.12%; Peridex; Zila Pharmaceuticals, Inc., Fort Collins, CO) mouth rinse was also prescribed 2 minutes before surgery and twice daily for 1 week afterward. For the first 24 hours after surgery, patients were prescribed acetaminophen and hydrocodone (500 mg; 1 tablet 2–3 daily; Vicodin; Abbott Laboratories, Abbott Park, IL) as an analgesic and, to help control swelling, diflunisal (500 mg; 1 tablet 2–3 daily; Dolobid; Merck & Co., Whitehouse Station, NJ), a nonsteroidal anti-inflammatory medication.

Atraumatic Tooth Extraction and Socket Augmentation

On the day of surgery, anesthesia was administered through local infiltration with 2% lidocaine and 1:100,000 epinephrine. An intrasulcular incision and circular fibrotomy were performed around the tooth to be extracted, and the incision was extended crestally to at least 1 adjacent tooth bilaterally. Buccal and lingual full-thickness flaps were elevated to expose the underlying alveolar process. In the case of single-rooted teeth, an ultrasonic surgical device (Piezosurgery; Mectron Medical Technology, Carasco, Italy) was used to section the periodontal ligament and mobilize the teeth. Once mobility was achieved, the teeth were gently extracted with forceps. Teeth with multiple roots, such as molars, were first sectioned before using the ultrasonic surgical device to remove each root segment in the same manner as single-rooted teeth. The alveolar socket was thoroughly debrided, irrigated with sterile saline solution, and carefully inspected to assess facial plate status (Fig. 2).

Augmentation Materials and Procedures

Grafts were performed using ceramic matrix in a putty-like collagen

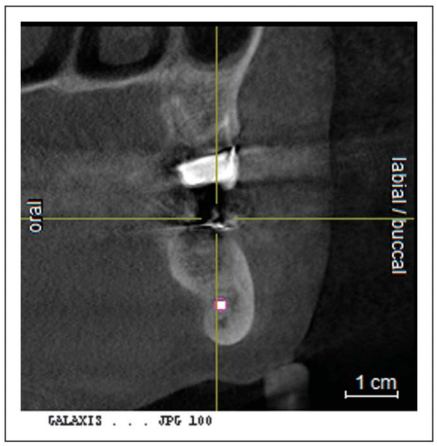

Fig. 5. Subject 1: CBCT sagittal cross section in the area of the mandibular second molar 6 months post grafting. Note the buccal lingual ridge thickness.

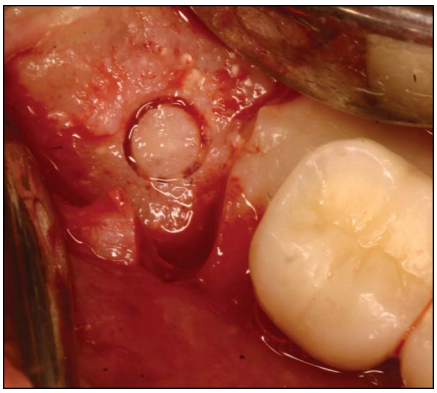

Fig. 6. Subject 1: 6 months after augmentation, the site was re-entered to allow for implant placement. The area was grossly evaluated at this time and a 3.0 mm diameter trephine core biopsy was taken before completion of the osteotomy for histologic analysis.

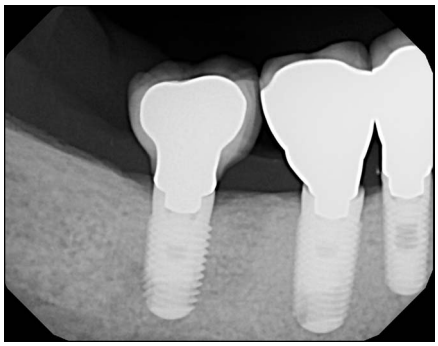

Fig. 7. Subject 1: A periapical radiograph of the implant in the area of mandibular right second premolar with the final restoration in place.

Table 2. Quantitative Measurements (in millimeters)

Subject	1	2	3	4	5	6	7	8	9	10
At graft horizontal	9.61	12.80	13.56	Unav	9.92	8.88	9.15	9.14	10	11.50
At graft vertical	8.79	6.73	7.85	Unav	9.52	6.50	10.29	13.37	8.36	9.46
Post-graft horizontal	6.64	13.24	11.19	16.91	7.91	8.47	Unav	8.83	8.06	7.73
Post-graft vertical	6.81	4.79	7.36	11.13	11.03	3.89	Unav	11.61	7.86	9.48
Results										
Horizontal	−2.97	+0.44	−2.37	Exe	−2.01	−0.41	Exe	−0.31	−1.94	−3.77
Vertical	−1.98	+1.94	−0.49	Exe	+1.51	−2.61	Exe	−1.76	−0.5	+0.02

Above is the pre and 6 months post operative measurements of the grafted sites in both vertical and horizontal dimensions for each subject. The resulting change in each dimension for each subject is also recorded in the Table Above. A negative indicates net loss, while positives are recorded net gain in dimension.
Overall Horizontal changes: −1.667.
Overall Vertical changes: −0.483.
Unav indicates unavailable; Exe, excluded.

carrier (MASTERGRAFT putty; Medtronic, Minneapolis, MN), a composite consisting of 15% HA and 85% β-TCP placed in a carrier made from a combination of insoluble/soluble collagen strands laced throughout the product to help maintain graft integrity. During manufacturing, the ceramic particles are evenly mixed throughout the putty in a ratio of 80% ceramic and 20% collagen, resulting in a porosity of 80%, a mean pore size of 500 μm, and an interconnected diameter of 125 μm. After tooth extraction and debridement, the synthetic graft material was hydrated with sterile saline and molded into the extraction socket (Fig. 3). A bovine pericardium membrane (Copios; Zimmer Dental, Inc., Carlsbad, CA) was draped over the entire graft site (Fig. 4). Tension-free soft tissue closure was achieved with soft tissue grafts or rotated pedicle palatal connective tissue flaps[20] and sutured with 5 to 0 polyglactin 910 (Vicryl; Ethicon, Johnson and Johnson Company, Somerville, NJ) sutures. To monitor healing, a standardized XCP-DS (Rinn Dentsply, York, PA) fitted for a digital sensor (Dexis, LLC, Hatfield, PA) was used to take a periapical radiograph after graft placement and again at 1 and 6 months postoperatively. The sutures were removed 7 to 14 days after surgery, and oral hygiene instructions were reviewed with the patient. Immediately after surgery, a radiographic template was placed in the patient's mouth and a CBCT scan was taken. Six months post operatively, the same radiographic template was put in place and new CBCT scan was taken (Fig. 5). The radiographic template was to standardize the site for measurement of ridge width and height initially and 6 months after graft healing and integration (Table 2).

Core Harvesting

The patient was anesthetized through local infiltration and the graft site was surgically exposed using crestal and buccal releasing incisions followed by elevation of a full-thickness mucoperiosteal flap. A trephine drill, 3.0 mm in outside diameter, was used to retrieve a bone core measuring approximately 2.13 × 10 mm from the center of the graft site (Fig. 6). Additional drills were used to further prepare the biopsy site for placement of a dental implant according to the product's usage instructions. The soft tissue flap was mobilized for tension-free closure and sutured (5–0 Vicryl; Ethicon, Johnson and Johnson Company). The sutures were removed 7 to 14 days later and the implant was finally restored 4 months post placement (Fig. 7).

Histologic Analysis

The harvested bone core was fixed in 10% buffered formalin for 10 to 12

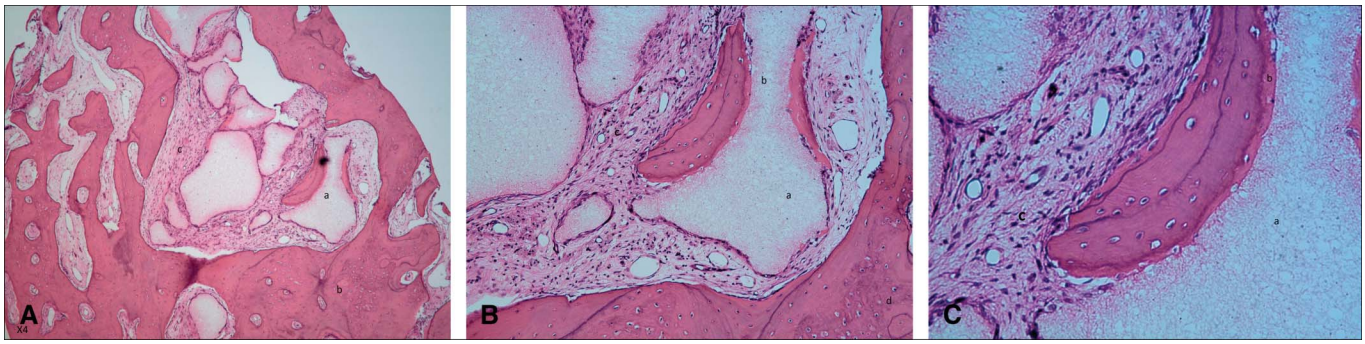

Fig. 8. **A**, Histologic view (×4) with hematoxylin and eosin: (**A**) Residual MASTERGRAFT particle with newly deposed bone, (**B**) existing bone matrix highly active with primary osteons and secondary osteons, and (**C**) moderate marrow fibrosis. **B**, Histologic view (×10) with hematoxylin and eosin: (**A**) Residual MASTERGRAFT particle showing line of deposition inside graft, (**B**) osteoblast lining on the demarcation line between new bone deposition and residual graft particle, and (**C**) moderate marrow fibrosis. **C**, Histologic view (×20) with hematoxylin and eosin: (**A**) MASTERGRAFT particle showing line of deposition inside of the residual graft, (**B**) newly deposited bone with lacunae filled with osteon, and (**C**) moderate marrow fibrosis.

hours and cut into thinly ground longitudinal sections using a precision cutting instrument (Microtome; Nanjing Everich Medicare Import & Export Co., Ltd., Nanjing, China). The specimen was dehydrated in an ascending series of alcohol rinses and embedded in a glycolmethacrylate resin (Techonovit 7200 VLC; Kulzer, Wehrheim, Germany).

After polymerization, the specimen was longitudinally cut into 150-mm thick sections with a high-precision diamond disc and then ground down to about 30 mm in thickness with a specially designed grinding machine. The resulting slides were stained with hematoxylin and eosin and sent to an independent laboratory (Hard Tissue Research Laboratory, University of Minnesota) for histomorphometric analysis. All the specimens were digitized at the same magnification using a NIKON ECLIPSE 50i microscope (Nikon Corporation, Tokyo, Japan) and a SPOT INSIGHT 2 mega sample digital camera (Diagnostic Instruments Inc., Sterling Heights, MI). Histomorphometric measurements were completed using a combination of spot insight program and Adobe Photoshop (Adobe Systems Inc., San Jose, CA) At least 2 slides of each specimen were evaluated.

Histomorphometric analysis will include the following parameters: percentage of the total core area, total bone area, vital bone formation, new bone formation, residual graft material, and marrow space.

Clinical and histologic results are summarized in Table 1. The new and existing bone and residual graft material are distinguished by (1) density of the osteocytes in the matrix, (2) alignment of the cement lines, (3) erosion by osteoclasts, and (4) staining intensity (Fig. 8, A–C). A new bone matrix tends to have a high osteocyte number, little or no cement lines, rarely any osteoclastic erosion surface, and a deep pink stain (Fig. 8, A–C). In contrast, existing bone matrix tends to have a low osteocyte number, few cement lines, modest osteoclastic erosion surfaces, and a light pink stain (Fig. 8, A–C).

RESULTS

Of the 10 subjects treated 2 patients were removed from the analysis of ridge width. One was removed because the patient refused an immediately postoperative CBCT and ridge width and height measurements before graft healing, and integration could not be collected. Another was removed because of delayed healing that presented as a dry socket. For the patient with delayed healing, the graft was removed from the site and the socket ended up healing uneventfully. Those 2 subjects were eliminated from the quantitative results.

Biopsy samples were obtained from all patients except the patient that formed a dry socket and another patient that relocated. The cores were submitted for histologic analysis (Table 1). All of the 8 placed dental implants successfully osseointegrated, restored, and followed for an average of 24 months after restoration.

The histologic analysis resulted in 40.25% (25%–59% range) vital bone, 10.38 (3%–21% range) residual graft material, and 49.25% (37%–59% range) marrow (Table 1). All biopsied sites had adequate mineralized bone fill for implant placement and resulted in 100% implant osseointegration (Table 2). The quantitative results show mean reduction of ridge width of 1.667 mm and mean reduction of ridge height of 0.483 mm after graft healing and integration. The change in ridge dimension for each patient is reported in Table 2.

DISCUSSION

Ridge resorption after tooth extraction has traditionally been considered inevitable.[1,21–24] After tooth loss, alveolar sockets tend to rapidly resorb, with approximately 23% of the residual ridge mass lost within the first 6 months, followed by another 11% of bone mass over the next 2 years.[25,26] Ridge preservation techniques involving socket grafting with various bone graft materials aim to preserve or restore the natural ridge contours. For this reason, such ridge preservation techniques are often used to develop future implant sites. Although there is currently not enough clinical evidence to identify which socket graft materials are optimal for ridge preservation, the dental literature does show that socket grafting may help reduce both vertical and horizontal ridge resorption after tooth extraction.[27,28]

The dimensional changes noted with site preservation through the use of ceramic matrix in a putty-like collagen carrier is consistent with the changes noted in other studies and various graft materials.[1,29,30] Based on clinical observations in this case series, healing of all grafts appeared to begin along the border of the socket and advance inward at the rate of approximately 1 mm per month. Of the augmented sockets in this case series, 62.5% (n = 5/8) were molar sites and the remaining 37.5% (n = 3/8) were premolar sites. These 2 locations are considered large sites, supported by the finding that bone remodeling was still going on after 6 months of healing. Biopsy cores were taken from the center of each graft where bone turnover was still in process. After removing the centers of the bone grafts, implants were placed in fully mineralized bone tissue. Thus, the residual graft material present in the histologic data represented a state of defective healing.

In all subjects, ceramic matrix in a putty-like collagen carrier was effective in preserving or restoring adequate ridge dimensions for implant placement. It also allowed for successful implant placement in mineralized tissue at 6 months despite signs of ongoing bone turnover.

As a clinical case series, this study lacks the random allocation of patients into treatment and control groups, and thereby represents a low level of clinical evidence. However, studies like this are valuable as they often are the first line of clinical evidence. Based on the limited amount of comparable research literature using a composite of HA–β-TCP,[19,20] it is reasonable to consider that the present technique of immediately grafting extraction sockets with ceramic matrix in a putty-like collagen carrier is relatively new. And given the success rate of the placed dental implants, a ceramic matrix in a putty-like collagen carrier can be a good option if an artificial graft material is the clinician's modality of choice.

Prospective, randomized, and controlled clinical studies are needed to fully elucidate the clinical behavior of ceramic matrix in a putty-like collagen carrier in tooth extraction sockets and to provide more scientific data on its efficacy as a ridge preservation technique.

CONCLUSION

Ceramic matrix in a putty-like collagen carrier has regenerated mineralized bone fill in extraction sockets and has adequately preserved ridge dimensions for implant placement. The placed dental implants have had a 100% survival rate over a 24 month follow-up period. More research is needed to adequately document this material and to determine the overall dimensions of ridge preservation that grafting of extraction sockets with this material may provide.

DISCLOSURE

The author claims to have no financial interest, either directly or indirectly, in the products or information listed in the article.

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