Demineralized Bone Matrix in Extraction Sockets: A Clinical and Histologic Case Series

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Purpose: *To evaluate its efficacy and predictability in immediate extraction sockets, this case series used demineralized bone matrix in a puttylike carrier (DBM putty) with and without mineralized bone chips. Each preparation was made from the long bones of the same tissue donor; the only excipient material was water.*

Material and Methods: *A single failing tooth was atraumatically extracted from each study subject, and the socket was debrided. Intact sockets were grafted with DBM putty (n = 6), and sockets with buccal defects were grafted with DBM putty with bone chips (n = 6). A bovine pericardium membrane was draped over the graft site, and tension-free primary closure was obtained. After 6 months of healing, a trephine biopsy was taken from the center of each graft, and then, a dental implant was placed. Two subjects were withdrawn, and histologic data could not be obtained from 2 other patients.*

Results: *Mean new bone fill was 40.28% for DBM putty (n = 5) and 44.60% for DBM putty with bone chips (n = 4).*

Conclusions: *Both preparations maintained ridge dimensions and, despite ongoing bone turnover, produced adequate mineralized tissue that enabled implant placement at 6 months. This finding warrants further research. (Implant Dent 2013;0:1–7)*

Key Words: DBM, demineralized bone matrix, extraction socket, ridge preservation technique, dental implant placement

Numerous investigators[1–6] have reported the osteoinductive capacity of demineralized bone matrix (DBM). The process of removing calcium from allogenic bone tissue (demineralization) results in exposure of the inner bone matrix that contains growth factors and bone morphogenetic proteins. Demineralized freeze-dried bone allograft, the earliest commercially available form of DBM, has been clinically used in blocks, particulates, and powders for more than 40 years and offers a suitable matrix for osteoconduction. To improve handling and delivery, more recently DBM powders have been suspended in various types of synthetic or biologic carriers and used extensively as graft extenders or bone graft substitutes in orthopedic[7–11] and dental[12–18] applications. Several factors have been reported[19–21] to be capable of diminishing the osteoinductive capacity of DBM, however, and some clinicians have advocated testing of DBM to verify its osteoinductivity before use[22] or only using DBM to augment composite grafts.[23] Nonetheless, continuing DBM research has resulted in a proliferation of new products in recent years.

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One area of contemporary research has been the influence of the carrier itself on the osteoinductive capacity of DBM putties and gels. Water is known to facilitate protein breakdown by keeping proteases in a hydrated state. One concern has been that DBM preparations that are reconstituted in water may experience a progressive loss of osteoinductive potential. Han et al[24] used *in vitro* culture assays and *in vivo* intramuscular implantations in nude rats to evaluate the effects of moisture and storage temperature on DBM osteoinductivity. In a dry state, DBM preserved its osteoinductive capacity when temperatures reached 65°C (149°F) but lost nearly 90% of its activity when suspended in a moist carrier up to 5 weeks at the same temperature.[24] The researchers[24] also reported that the collagen network of DBM controlled the release rate of osteoinductive growth factors and served as a scaffold for proliferation and differentiation of osteogenitor cells. Materials made from 100% DBM evaluated in the rat model have been reported to resorb at the same rate in which new bone is formed,[25] but further research is needed to confirm this finding in humans.

Peterson et al[9] evaluated 3 commercial DBM preparations for spinal fusions

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in the rat model and reported that DBM suspended in a glycerol carrier was more effective in developing early fusion than DBM preparations suspended in either 4% sodium hyaluronate or a combination calcium sulfate hemihydrate and carboxymethylcellulose carrier custom-mixed with a proprietary aqueous solution. It is unknown, however, whether the disparate outcomes[9] were attributable to differences in DBM carriers, residual calcium content (range = <0.5% to <8%) in the processed tissues, or other unidentified variables that affected the osteoinductivity of the DBM materials. Other toxicology testing of a commercial DBM preparation in the rat model reported a 90% death rate caused by hemorrhagic necrosis of the kidneys, which the researchers believed to be caused by toxic effects of the glycerol carrier.[26] However, the researchers[26] noted that the amount of DBM preparation used in the rats was 8 times the maximum volume used in humans and that the human-derived DBM was a xenograft in the rat model. DBM in a xenogenic (porcine) carrier has reportedly achieved highly variable results in humans.[27,28]

This article reports on the short-term clinical and histologic outcomes of fresh tooth extraction sockets immediately augmented with DBM in 12 consecutive patients.

CASE SERIES

Patients who presented at the author's private practice for implant restoration of a single unsalvageable tooth (Fig. 1) but who lacked adequate bone volume for immediate implant placement were considered for this nonrandomized case series if they were systemically healthy. Each patient's medical and dental histories were reviewed to identify any contraindications to tooth extraction and augmentation surgery, and a thorough clinical examination was performed to determine oral health status and 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 assess the volume of bone and status of the facial plate of the tooth scheduled for extraction. A total of 12 patients (6 women and 6 men), ranging in age from 38 to 83 (mean = 59.25) years, were consecutively treated after providing signed informed consent (Table 1).

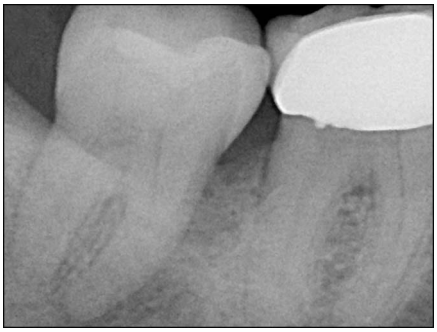

Fig. 1. Subject 1: failing mandibular right second molar.

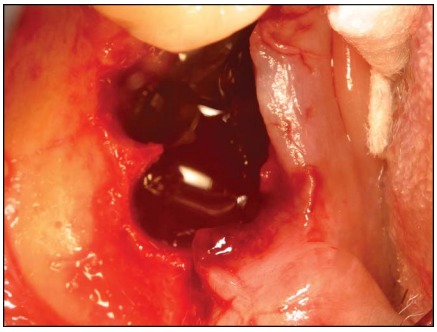

Fig. 2. Subject 1: double-rooted extraction socket after tooth sectioning and sequential root removal.

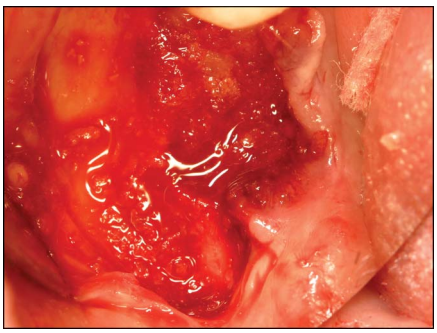

Fig. 3. Subject 1: DBM putty injected into the socket.

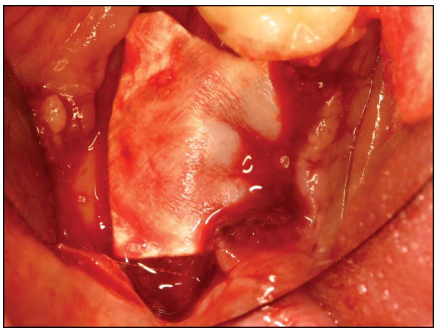

Fig. 4. Subject 1: bovine pericardium membrane draped over the graft site.

Medications

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

Atraumatic Tooth Extraction and Socket Augmentation

On the day of surgery, anesthesia was administered via 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).

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Table 1. Patient Demographics, Treatment Data, and Histology Findings

Clinical Data					Histologic Data				
Case No.	Age (Years)	Sex	DBM Type	Tooth Location	New Bone (%)	Residual Graft (%)	Fibrous Tissue (%)	Marrow (%)	Total (%)
1	60	F	Putty	Mandibular right second molar	52.08	2.11	6.46	39.35	100
2	67	M	Putty	Maxillary left second premolar	42.16	8.88	5.55	43.41	100
3	68	F	Putty with chips	Mandibular right central incisor	—*	—*	—*	—*	—*
4	38	F	Putty	Mandibular left second molar	—†	—†	—†	—†	—†
5	57	M	Putty with chips	Mandibular right second molar	44.44‡ 50.95§	13.25‡ 3.99§	6.42‡ 15.60§	35.89‡ 29.47§	100‡ 100§
6	50	M	Putty with chips	Maxillary right first molar	47.03	3.17	1.74	48.06	100
7	46	M	Putty with chips	Mandibular left first molar	—‖	—‖	—‖	—‖	—‖
8	70	F	Putty	Mandibular right second molar	19.49	12.54	6.03	61.94	100
9	83	M	Putty	Mandibular right first molar	26.07	14.41	4.53	54.99	100
10	40	F	Putty with chips	Maxillary left second premolar	—¶	—¶	—¶	—¶	—¶
11	61	F	Putty	Mandibular right first molar	61.62	1.66	2.38	34.34	100
12	71	M	Putty with chips	Mandibular right second molar	36.00	11.75	8.15	44.09	100
All subjects (mean)					42.20	7.97	6.32	43.50	100

*Narrow ridge; no biopsy taken but implant was successfully placed.
†Subject moved and was lost to follow-up.
‡Mesial root biopsy was taken in a molar site with 2 augmented root areas.
§Distal root biopsy was taken in a molar site with 2 augmented root areas.
‖Subject had a preexisting infection, and primary closure could not be achieved after grafting; no biopsy taken but implant was successfully placed.
¶Poor histology sample could not be accurately analyzed.

Augmentation Materials and Procedures

DBM with and without mineralized corticocancellous bone chips (Puros DBM Putty; Zimmer Dental, Inc., Carlsbad, CA) was used to augment the sockets in an attempt to minimize postextraction atrophy and help preserve the dimensions of the alveolar ridge. The 100% biologic carrier had a puttylike consistency (putty) and was manufactured from the long bones of the same tissue donor that provided the DBM and bone chips in every lot; the only excipient material was sterile water. The tissue demineralization process was similar to that used by Urist and Dowell,[29] with several additional washing procedures designed to remove residual chemicals from the demineralized tissues.[30] Final DBM particles ranged from 125 to 850 mm in size, which was obtained by sieving the bone before and after demineralization.[30] After packaging, the DBM preparations were subjected to low-dose (17.8–20.1 kGy) gamma irradiation, which has been reported to be capable of killing or inactivating bacteria, viruses, fungi, and spores while preserving the osteoinductivity of the bone morphogenetic proteins.[30,31] Packaged materials were stored at a controlled room temperature of 15°C to 25°C (59°F–77°F) in accordance with the manufacturer's (RTI Biologics, Alachua, FL) instructions. Each lot was tested for osteoinductive potential using an athymic rat model. The definitive material had a puttylike consistency that could be adapted to various defect shapes and sizes, and rat ectopic assays have shown the material to be capable of maintaining its osteoinductive potential over the period of its shelf life if stored as indicated.

The type of DBM selected for the patient was determined by the status of the extraction socket. Subjects with relatively intact, 4-walled sockets were treated with DBM putty, and patients with buccal wall defects were treated with DBM putty with chips (Table 1). The augmentation material was injected directly into the extraction socket with its applicator (Fig. 3) and a bovine pericardium membrane (Copios; Zimmer Dental, Inc.) 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[32] and 5-0 polyglactin 910 (Vicryl; Ethicon, a Johnson and Johnson Company, Somerville, NJ) sutures.

Postoperative Monitoring

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. A standardized (XCP-DS; Rinn Dentsply, York, PA) fitted for a digital sensor

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(Dexis, LLC, Hatfield, PA) was used to take a periapical radiograph after graft placement and again at 1 and 6 months postoperative to monitor healing. At the 6-month monitoring appointment, another CBCT scan was taken using the same radiographic template. The patient was anesthetized via 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 2.1 × 10 mm from the center of the graft site (Fig. 5). Additional drills were used to further prepare the biopsy site for placement of a dental implant (Tapered Screw-Vent; Zimmer Dental, Inc.) according to the product's instructions for use. The soft tissue flap was mobilized for tension-free closure and sutured (5-0 Vicryl; Ethicon a Johnson and Johnson Company). Sutures were removed 7 to 14 days later, and the implant was first provisionally and then definitively restored with a single-tooth restoration (Fig. 6).

The harvested bone core was fixed in 10% buffered formalin for 10 to 12 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-μm-thick sections with a high-precision diamond disc and then ground down to about 30 μm in thickness with a specially designed grinding machine. The resulting slides were stained with hematoxylin and eosin and sent to an independent laboratory (PharmaLegacy Laboratories, Inc., Pudong, Shanghai, China) for histologic analysis. Quantitative histomorphometry was conducted using software (OsteoMeasure; OsteoMetrics, Inc., Atlanta, GA), which interfaced with a light fluorescence microscope (eg, Olympus TIRFM; Olympus Corporation, Tokyo, Japan) and digital camera (eg, Olympus Microfire; Olympus Corporation). Quantitative histology of hematoxylin and eosin-stained slide sections was assessed according to the methods of Parfitt et al[33] for various histology features and scored using a stratified 5-point scale and a simplified 2-point scale that collapsed findings into 2 broad categories for clinical relevance.

Clinical and histologic results are summarized in Table 1. The new and existing bone and residual graft material are distinguished by (1) the density of the osteocytes in the matrix, (2) the alignment of the cement lines, (3) the erosion by osteoclasts, and (4) staining intensity (Figs. 7–10). New bone matrix tends to have high osteocyte number, little or no cement lines, rarely with osteoclastic erosion surfaces, and stained

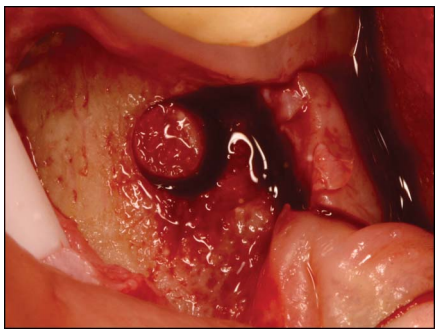

Fig. 5. Subject 1: biopsy at 6 months.

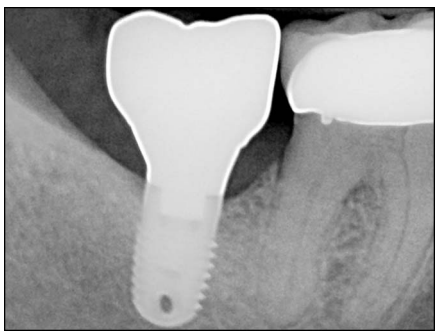

Fig. 6. Subject 1: final restoration, radiographic view.

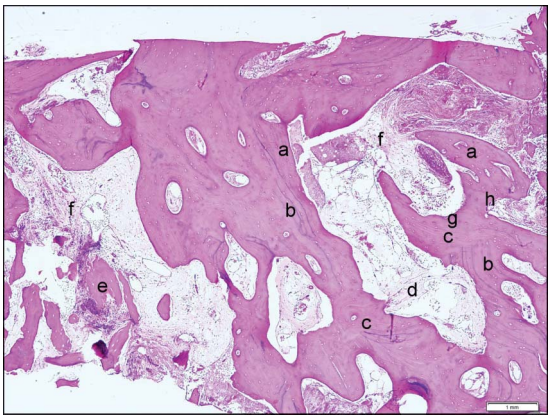

Fig. 7. Subject 1, DBM putty: (**a**) new bone, (**b**) residual graft material, (**c**) existing bone matrix, (**d**) mild marrow fibrosis, (**e**) biopsy debris, (**f**) moderate marrow fibrosis, (**g**) osteoblasts, and (**h**) osteoclasts (×4).

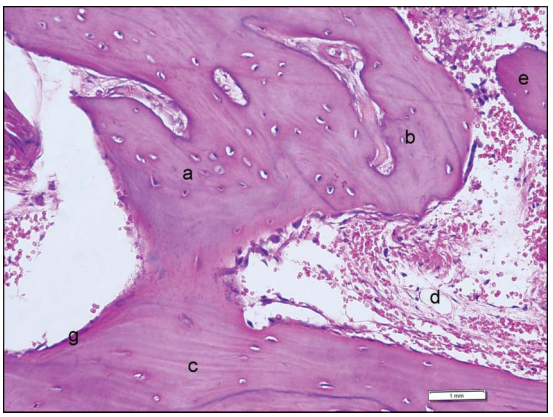

Fig. 8. Subject 1, DBM putty: (**a**) new bone, (**b**) residual graft material, (**c**) existing bone matrix, (**d**) mild marrow fibrosis, (**e**) biopsy debris, and (**g**) osteoblasts (×20).

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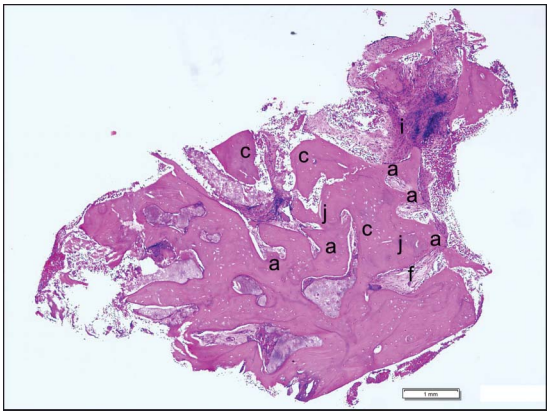

Fig. 9. Subject 5, DBM putty with bone chips: (**a**) new bone, (**c**) existing bone matrix, (**f**) moderate marrow fibrosis, (**i**) compressed bone fragments, blood clots (fibrin) and blood, and (**j**) residual bone chip (×4).

pinker in color (Figs. 7–10). Existing bone matrix tends to have low osteocyte number, a few cement lines, modest osteoclastic erosion surfaces, and stained lighter in pink color (Figs. 7–10). Graft material bone matrix tends to have low osteocyte number or empty lacunae, many cement lines, high osteoclastic erosion surfaces, and stained dark pink in color (Figs. 7–10). The majority of subjects (1, 2, 5, 6, 8, 9, 10, 11, and 12) were successfully treated, and biopsy samples were obtained (Table 1). One of these patients (patient 10) was a 40-year-old woman who exhibited a 4-mm-wide residual ridge with a vertical defect on the buccal wall after removal of a maxillary left second premolar (Table 1). Grafting and socket healing were uneventful. Secondary surgical exposure revealed that augmentation restored the vertical defect and preserved the 4-mm ridge width. Biopsy of the site and secondary dental implant placement were successfully achieved. Processing problems, however, resulted in a degraded biopsy sample that could not be accurately analyzed at the histomorphometric level. A second 57-year-old male subject (patient 5) had a residual ridge that measured 3 mm in width and 4.5 mm in height after extraction of a mandibular right second molar and a buccal plate dehiscence that extended to the root area of the extraction socket. After graft healing, the ridge lost 1.5 mm in vertical height, but its 3-mm-wide dimension was preserved. Two biopsies were taken (1 per tooth root area) of the site (Figs. 9 and 10), and dental implant placement was successfully

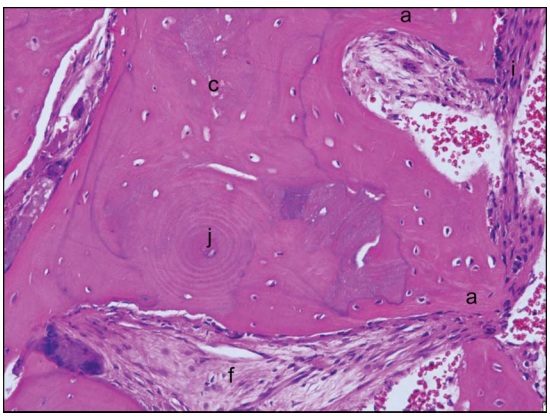

Fig. 10. Subject 5, DBM putty with bone chips: (**a**) new bone, (**c**) existing bone matrix, (**f**) moderate marrow fibrosis, and (**j**) residual bone chip (×20).

achieved. Despite the vertical bone loss, there was adequate bone volume to place a dental implant.

One subject (patient 4), a 38-year-old woman, presented with a residual ridge that measured 10 mm in width and 5 mm in height after extraction of a hopeless mandibular left second molar. After grafting with DBM putty, the patient moved and was lost to biopsy and follow-up. A second 58-year-old female patient (patient 3) treated for a mandibular right central incisor with a large buccal plate defect presented with a narrow ridge at secondary exposure. A clinical decision was made not to use a trephine to take a biopsy because it could jeopardize the stability of a 3.0-mm-diameter implant, which was successfully placed and restored (Table 1). A third subject (patient 7) was a 46-year-old man who presented for surgery with an active abscess on the mesiolingual tooth root and a lingual dehiscence that extended to the midroot of a failing mandibular left first molar. After tooth extraction and grafting, primary closure was not achieved and, because of secondary intention healing, resulted in vertical loss of graft volume. The site was regrafted with solvent-dehydrated mineralized cancellous bone allograft (Puros Cancellous Bone Allograft; Zimmer Dental, Inc.) after soft tissue maturation. This subject was withdrawn from the data analysis because of the preexisting infection and inability to achieve primary closure (Table 1).

Combined mean histologic outcomes for these 8 subjects with 9 successfully processed biopsies were 42.20% (range = 19.49%–61.62%) new bone formation, 7.97% (range = 2.11%–14.41%) residual graft material, 6.32% (range = 1.74%–15.60%) fibrous tissue, and 43.50% (range = 29.47%–54.99%) marrow (Table 1). All biopsied sites had adequate mineralized bone fill for implant placement. A small amount of residual graft material was present in all biopsy samples but widely varied among subjects (Table 1). DBM putty with bone chips also achieved 4.33% greater mean bone fill than DBM putty without bone chips, but sample sizes were inadequate to determine if this difference was statistically significant.

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DISCUSSION

Ridge resorption following tooth extraction has been traditionally considered inevitable.[34–38] 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 resorption over the next 2 years.[39,40] Ridge preservation techniques involve augmenting fresh extraction sockets with various bone graft materials to preserve or restore the natural ridge contours. For this reason, such ridge preservation techniques and are often used for development of future implant sites. Although there is currently insufficient clinical evidence to identify which socket graft materials may be optimal for ridge preservation, the dental literature does show that socket grafting may help to reduce both vertical and horizontal ridge resorption after tooth extraction.[41–43]

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. Because 80% (n = 8/10) of the augmented sockets in the present case series were large molars (Table 1), the finding that bone remodeling was still ongoing after 6 months of healing was not unexpected. 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 defect healing. Concerns that DBM efficacy may be affected by recipient age seemed to be supported by the present outcomes. The greatest percentage of bone fill was achieved by subjects (1, 2, 5, 6, and 11) who ranged in age from 50 to 68 years. In contrast, the majority of subjects (8, 9, and 12) with the slowest bone turnover rate (residual graft = 12.54%, 14.41%, and 11.75%, respectively) and the most modest percentage of regenerated bone (new bone = 19.49%, 26.07%, and 36%, respectively) were 70 years or older. However, it should be noted that, in subjects 70 years or older in this case series, DBM putty and DBM putty with chips were both effective for preserving or restoring adequate ridge dimensions for implant placement. More extensive research is needed to determine the actual effects of recipient age and other variables on DBM efficacy. Both preparations helped maintain ridge dimensions and enabled implant placement in mineralized tissue at 6 months despite signs of ongoing bone turnover.

As a clinical case series, the present study lacks the random allocation of patients into treatment and control groups and thereby represents a low-level of clinical evidence; however, studies such as this often represent the first line of clinical evidence, which underscores its clinical value. Based on the limited amount of comparable research literature,[12–14,17] it is reasonable to consider the present technique of immediately grafting extraction sockets with DBM putty as relatively new. Prospective, randomized, and controlled clinical studies are needed to fully elucidate the clinical behavior of DBM putty in tooth extraction sockets and to provide more scientific data on its efficacy as a ridge preservation technique.

CONCLUSIONS

DBM putty regenerated mineralized bone fill in extraction sockets and adequately preserved ridge dimensions for implant placement. More research is needed to adequately document this material and to determine the overall dimensions of ridge preservation that grafting of extraction sockets may provide.

DISCLOSURE

The author claims to have no financial interest in any of the companies or products used in this case series.

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