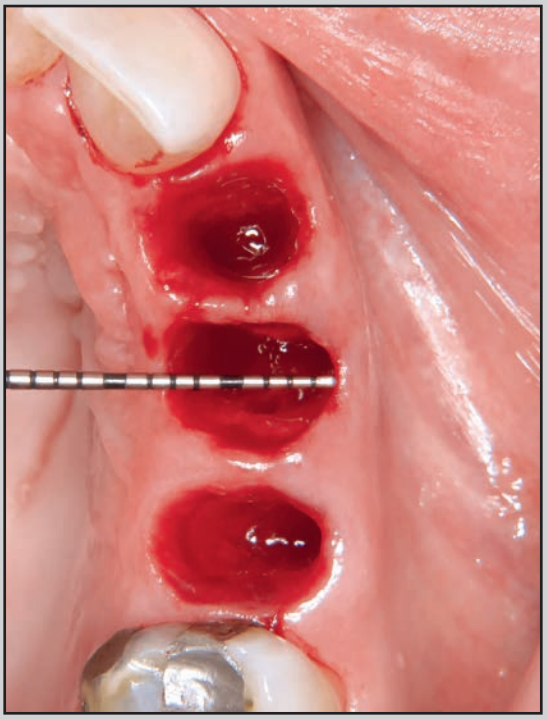
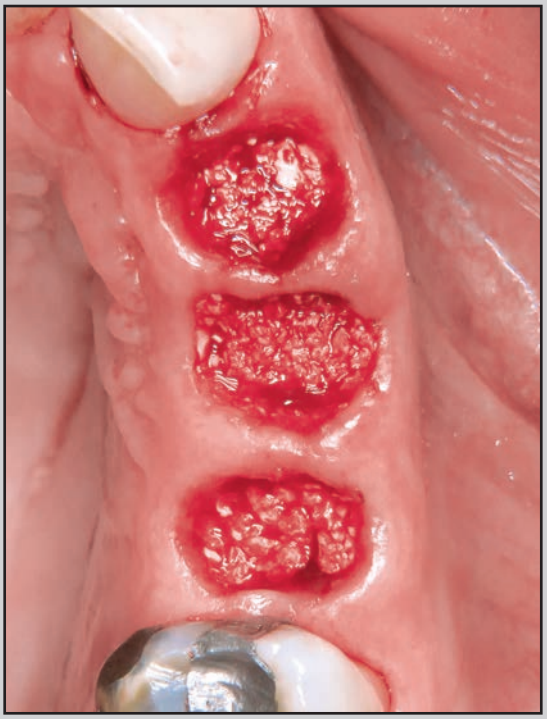
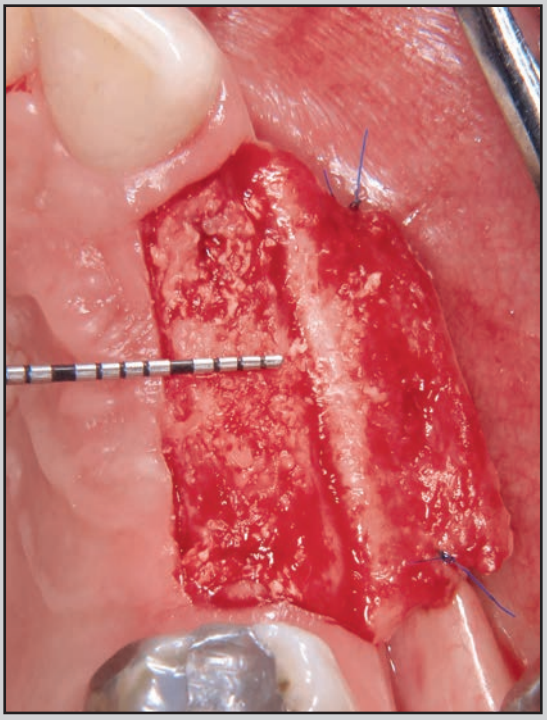
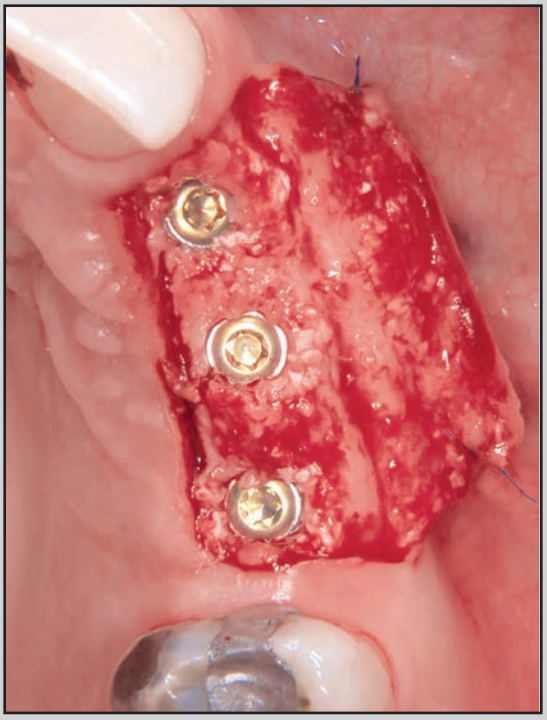
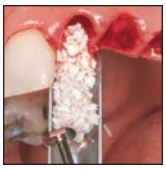





Effectiveness of Two Differently Processed Bovine-Derived Xenografts for Alveolar Ridge Preservation with a Minimally Invasive Tooth Extraction Approach: A Feasibility Clinical Trial



Behnam Shakibaie, DDS[1]
Markus B. Blatz, PhD[2]
Hamoun Sabri, DMD[3]
Ebrahim Dastouri Jamnani, DMD[3]
Shayan Barootchi, DMD[3]

Xenogeneic-derived biomaterials are among the most routinely employed bone substitutes for immediate grafting of extraction sites as a modality of alveolar ridge preservation (ARP). The deproteinized bovine bone material is widely used and documented around the world. The present pilot clinical trial evaluated and compared the clinical and morphologic alterations of extraction sites after ARP using two commercially available yet differently processed bovine bone grafts. A total of 20 adjacent extraction sites in 10 patients were included. All sites received the exact same ARP therapy except for the type of bovine bone graft, which was randomly assigned between two adjacent extraction sockets in 10 patients (Group A received Bio-Oss particles and Group B received Cerabone particles). At all sites, healing was monitored at the time of surgery and at 1, 2, 3, and 4 months postoperative. All of the augmented extraction sites achieved successful implant therapy regardless of the bone graft material used for ARP. Six weeks after implant placement, second-stage/uncovering procedures were performed without complications. Intergroup comparisons of the crestal gingival healing process (CGHP), mean transversal crestal ridge resorption (MTRR), and mean implant primary stability (MIPS) were in favor of Group A sites (treatment with Bio-Oss particles). Int J Periodontics Restorative Dent 2023;43:541–549. doi: 10.11607/prd.6128

[1]Specialized Clinic in Microscopic Dentistry, Tehran, Iran.
[2]Department of Preventive and Restorative Science, School of Dental Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA.
[3]Department of Periodontics & Oral Medicine, University of Michigan School of Dentistry, Ann Arbor, Michigan, USA.

Correspondence to: Dr Behnam Shakibaie, Specialized Clinic in Microscopic Dentistry, Unit 23, No 122, West Soleimani Street, Andarzgou Blvd, Farmanieh, 1938764381 Tehran, Iran. Email: drbshakibaie@yahoo.com

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Upon tooth extraction, the alveolar socket undergoes a significant amount of physiologic remodeling that leads to ridge atrophy.[1–3] This morphologic change in hard and soft tissue dimensions could compromise esthetics and the optimum placement of dental implants.[4–7] Thus, there was a rise in routine application of alveolar ridge preservation (ARP) therapies with the aim of attenuating this remodeling process.[8] While the effectiveness of ARP for reducing postextraction bone loss has been well documented,[9] few studies have focused on other factors, such as morphologic changes in the ridge contour[10] or sequela of the healing process and the reaction of local soft tissues (texture, quality, thickness, etc).[11–13]

Among the available approaches for ARP, xenogeneic-derived biomaterials are among the most routinely employed due to their accessibility.[14–17] Deproteinized bovine bone material is an example that is widely documented by clinicians and researchers due to its availability, biocompatibility, and osteoconductive priorities.[14,16,18–20] This study aims to evaluate the healing processes and the morphologic changes of the alveolar ridge after ARP treated with two differently processed bovine particulate grafts in adjacent extraction sockets.

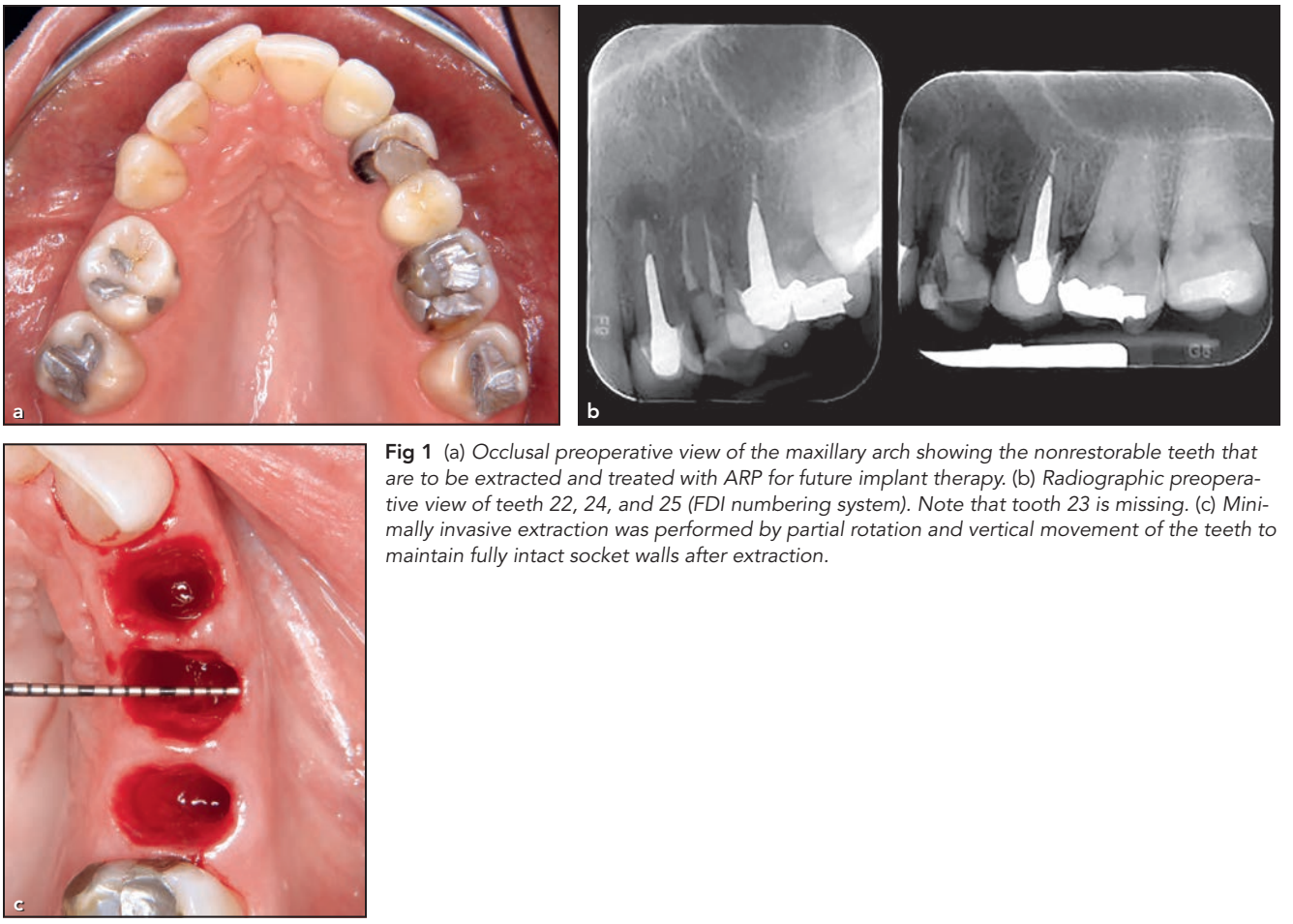


Fig 1 (a) *Occlusal preoperative view of the maxillary arch showing the nonrestorable teeth that are to be extracted and treated with ARP for future implant therapy.* (b) *Radiographic preoperative view of teeth 22, 24, and 25 (FDI numbering system). Note that tooth 23 is missing.* (c) *Minimally invasive extraction was performed by partial rotation and vertical movement of the teeth to maintain fully intact socket walls after extraction.*

Materials and Methods

Study Design and Patient Recruitment

This study was designed as a preliminary controlled clinical trial to obtain a side-by-side comparison of two commercially available large-particle bovine-derived bone grafts with different fabrication processes. To eliminate interpatient systemic and local variability, the comparison of the two bone grafts occurred within the same individual and in adjacent extraction sites. From September 2017 to January 2020, patients from a specialty practice (Tehran, Iran) were recruited to participate. For eligibility, each patient must have had at least two adjacent nonmolar nonrestorable teeth requiring implant therapy. Causes for extraction could comprise nonrestorable decay and/or failure/unsuccessful endodontic therapy. Extractions due to periodontal disease were not allowed due to the likelihood of bone/attachment loss. Extraction sockets presenting with compromised buccal bone (≥ 50% loss of buccal plate after extraction) or a dehiscence were excluded. Patients were excluded if they had a smoking habit, compromised health/immune system, or pregnancy. Details of the study protocol were explained to all interested participants, and all recruited patients provided their written informed consent prior to research commencement.

Study Protocol and ARP

After administration of local anesthesia, a minimally invasive extraction was performed, as previously described.[21,22] Careful attention was paid to maintain intact socket walls with delicate manipulation of local soft tissues. After extraction, all sites

were carefully examined using a dental microscope (OPMI PROergo, Zeiss) to confirm intact socket walls prior to inclusion (Fig 1). Next, for each patient, both adjacent extraction sites received ARP therapy using a particulate bovine bone graft, which was lightly packed to fill the socket up to the alveolar crest, followed by coverage using a tailored piece of gelatin sponge (Stypro, Curasan) and sutured with a monofilament material (Seralon 6-0, Serag-Wiessner). The only difference between the two adjacent extraction sites was the type of large-particle bovine-derived bone graft, which was randomly assigned: Sockets in Group A received Bio-Oss xenograft material (particle size 1 to 2 mm, Geistlich Pharma) while sites in Group B received Cerabone (particle size 1 to 2 mm, Botiss Medical; Fig 2). If a patient had more than two adjacent teeth that required extraction and ARP, only the two most anterior sockets were included in the study, and the choice of biomaterial for the other site(s) was left to the patient, or selected randomly if the patient was indifferent (Fig 3).

All patients received provisional restorations to cover the extraction sites. The base of all prostheses was carefully relieved to avoid any pressure on the treated sites. Patients were provided with postoperative instructions consisting of antibiotics (500 mg amoxicillin tid for 3 days or, in case of allergies, 300 mg clindamycin tid for 3 days) and anti-inflammatory medication (as indicated). Patients were also asked to rinse with 0.2% chlorhexidine gluconate solution for 3 days. All sutures were removed at 10 days postsurgery (Figs 4a and 4b).

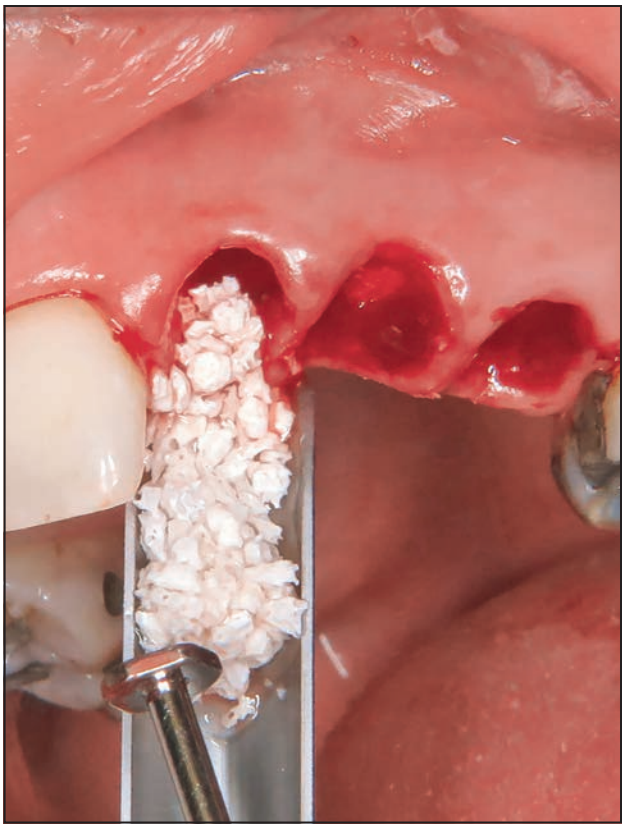


Fig 2 *ARP therapy was performed, and the mesial socket was grafted with Cerabone granules (patient allocated to treatment Group B). Note that the patient had more than two adjacent extraction sites. All were treated, but per the study protocol, only the two mesial sockets were included in the study.*

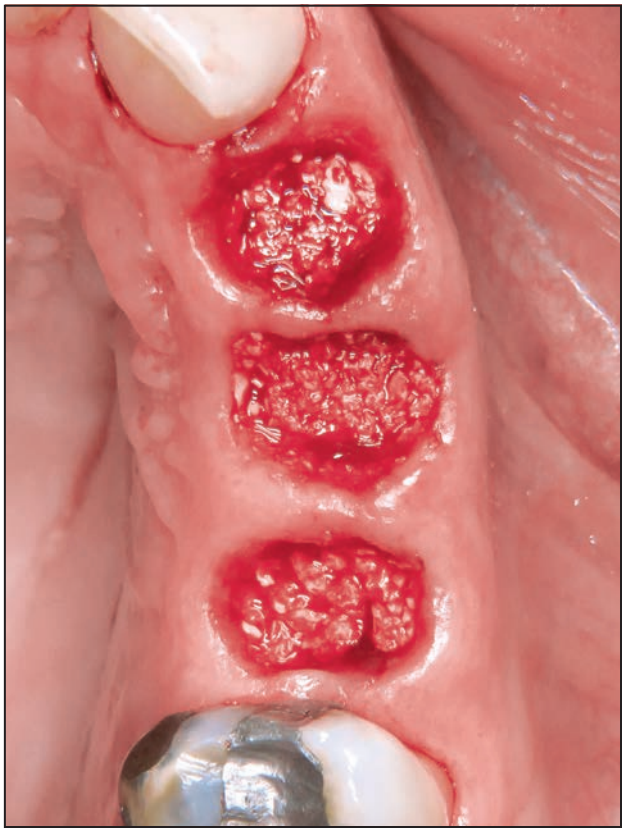


Fig 3 *Occlusal view of the same treated sockets after filling with bone substitute. Note that the most mesial extraction socket was allocated to Group B (Cerabone) and the middle socket was allocated to Group A (Bio-Oss), and both were part of the study. The third extraction socket (most distal) was also treated with Cerabone particles (randomly assigned, as the patient had no preference), but this site was not included in the study.*

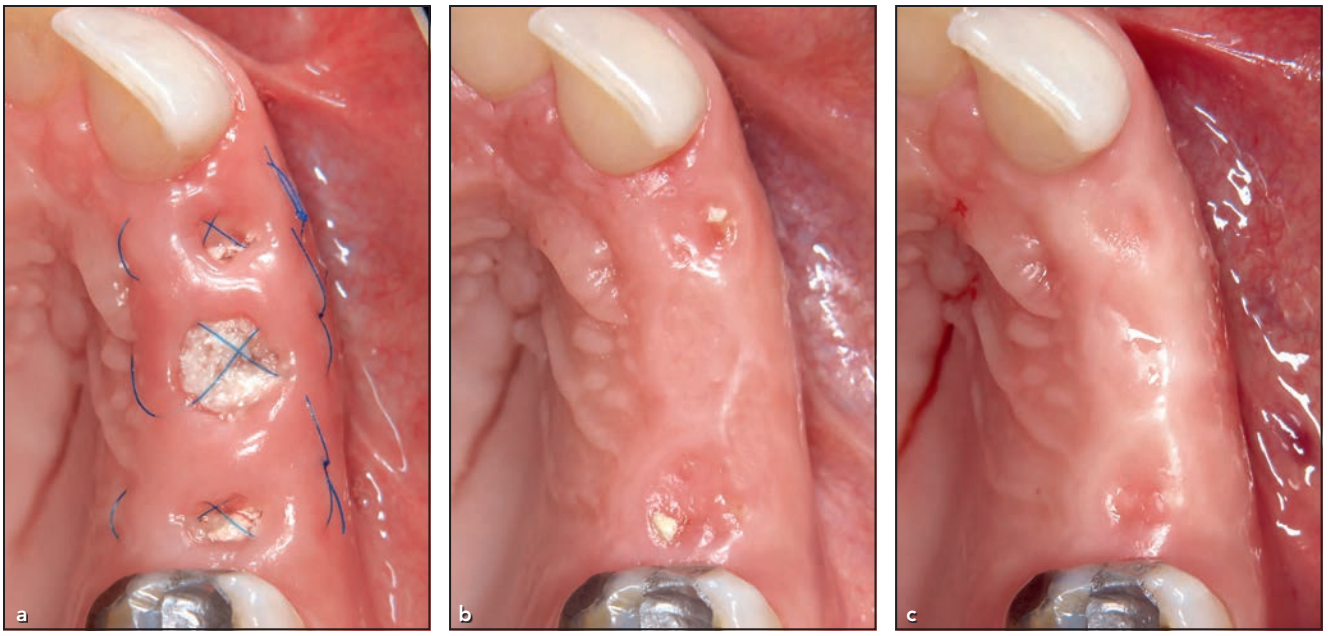
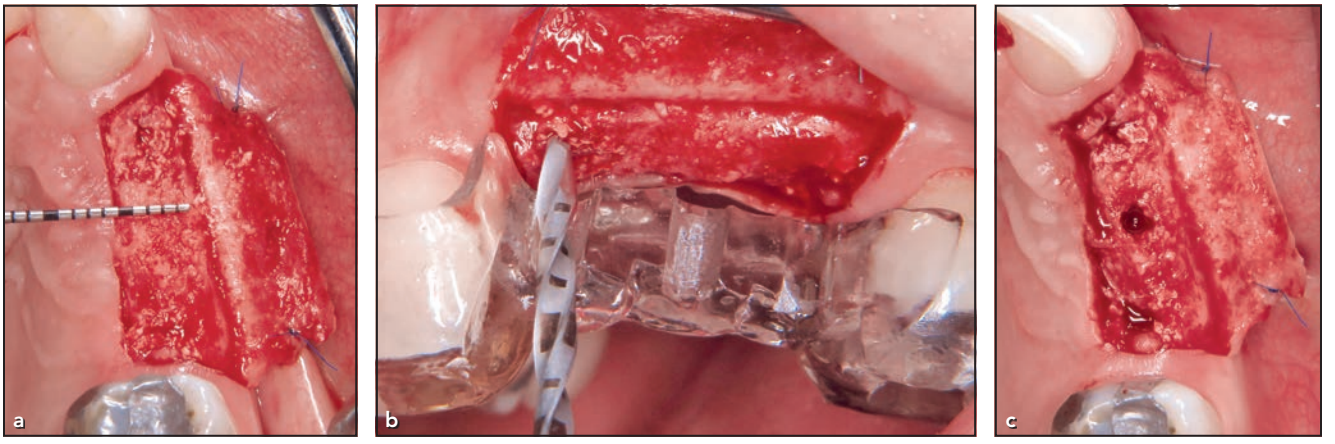


Fig 4 (a) *The occlusal view at 1 week postoperative shows a relatively quicker crestal soft tissue healing in sites treated with Cerabone granules.* (b) *After 8 weeks of healing, complete crestal soft tissue closure was seen in the middle extraction site (Group A, Bio-Oss), whereas the Group B site (mesial socket) still was not fully covered by soft tissues.* (c) *At 16 weeks postoperative, complete healing and closure of crestal soft tissues was seen in all groups and extraction sites.*



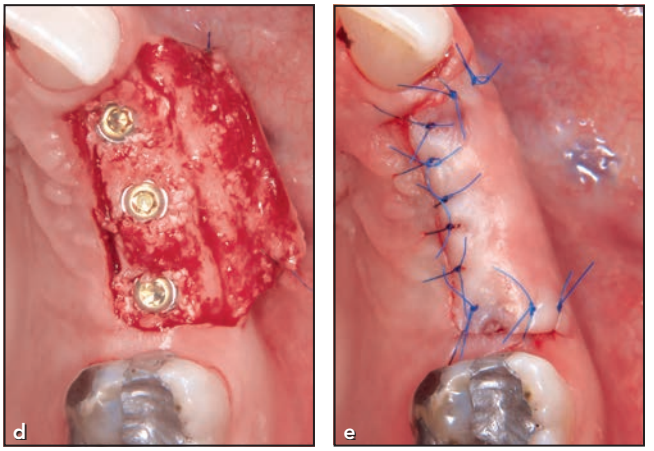


Fig 5 *Implant placement after 4 months of healing.* (a) *A papilla-sparing flap design was adopted, extending the width of the flap from the crestopalatal soft tissue edge to 1 mm higher than the cresto-vestibular edge, with a clear distance to the vestibular mucogingival border. The mucosal flap was fixated to the buccal aspect with two 6/0 Seralon sutures, showing satisfactory horizontal ridge preservation of all sites after 4 months. Note the relatively larger amount of mineralized firm crestal bone in the area, which was allocated to Group A (Bio-Oss), while Group B sites (Cerabone) did not present as fully healed and integrated.* (b) *Guided implant surgery was initiated with the pilot drill. Note the less-dense bone in the Group B site (Cerabone) relative to the Group A area (Bio-Oss).* (c) *Occlusal view of the ridge after implant site preparation.* (d) *Three bone-level implants (3.3-mm diameter, Straumann) were placed in the prosthetically planned positions, maintaining an optimal amount of bone on the facial aspect.* (e) *The flap adapted to the site, using additional interrupted sutures to obtain tension-free wound closure.*

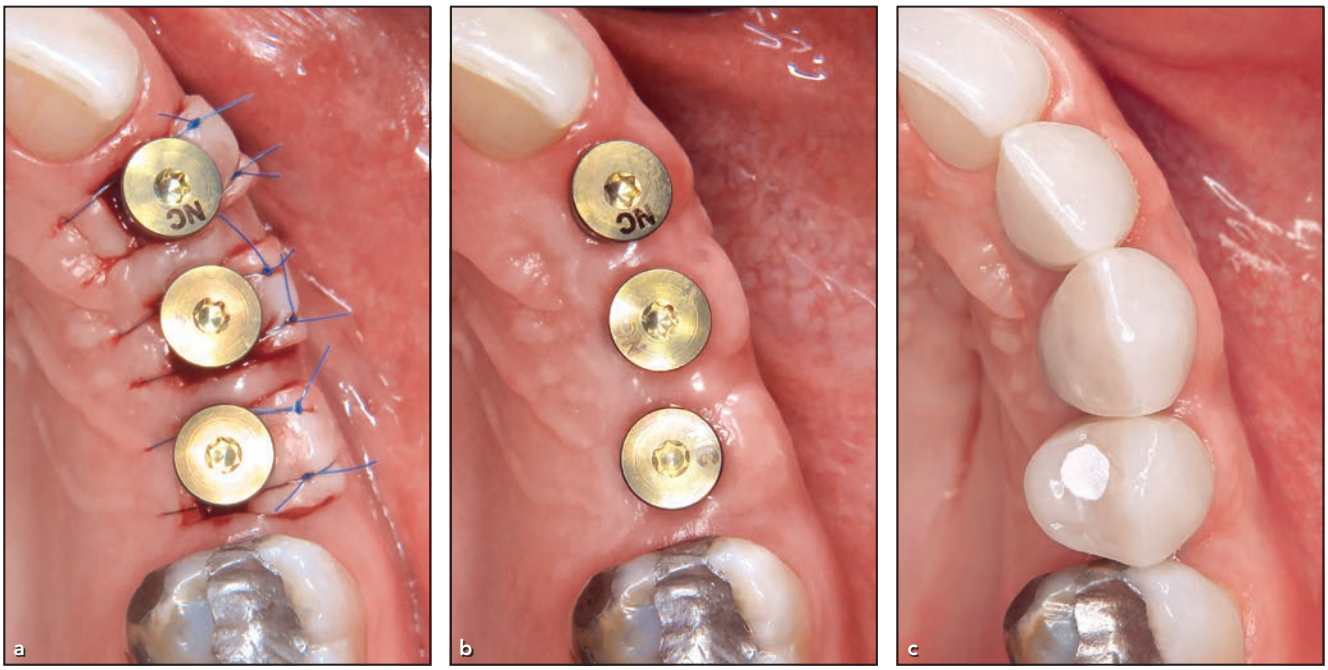


Fig 6 *Second stage uncovering procedure 6 weeks after implant placement.* (a) *Three mini VSRFs were performed, sparing all papilla structures and using wide-neck healing abutments.* (b) *Optimal soft tissue healing, especially on the buccal aspect, was seen 4 weeks after surgical implant exposure.* (c) *Clinical view of the implant sites 6 months after placing the final suprastructures with three full-ceramic single crowns.*

Surgical Protocol for Implant Therapy

After approximately 4 months of healing (16 to 18 weeks), patients returned for implant therapy (Fig 4c). All implant surgeries were 3D digitally planned using a commercially available software (3Shape), to produce patient-specific CAD/CAM–fabricated surgical guides.

The flap design for implant therapy was as minimally invasive as possible. Split-thickness flaps were elevated, leaving the periosteum intact on the crestal surface of the bone to prevent the potential removal of bone substitute particles that were not fully mineralized (Fig 5a). Fabricated surgical guides were used to achieve the planned implant position, followed by implant placement according to manufacturer's instructions and primary wound closure (Figs 5b to 5e).

Second-stage implant surgery was performed 6 weeks after implant insertion, using the vestibular split rolling flap (VSRF) technique to obtain an optimal ridge contour before the prosthetic phase (Figs 6a and 6b). Ceramic single crowns were delivered as final restorations (Fig 6c).

Table 1 Characteristics of the Included Patients and Treated Sockets at Baseline

Characteristic	
Participants, n	10
Age (y), mean ± SD	48.5 ± 12.6
Men, n (%)	4 (40%)
Women, n (%)	6 (60%)
Total sockets, n (%)	20 (100%)
Location	
Maxillary sockets	12 (60%)
Mandibular sockets	8 (40%)
Tooth type	
Canines	4 (20%)
Premolars	16 (80%)

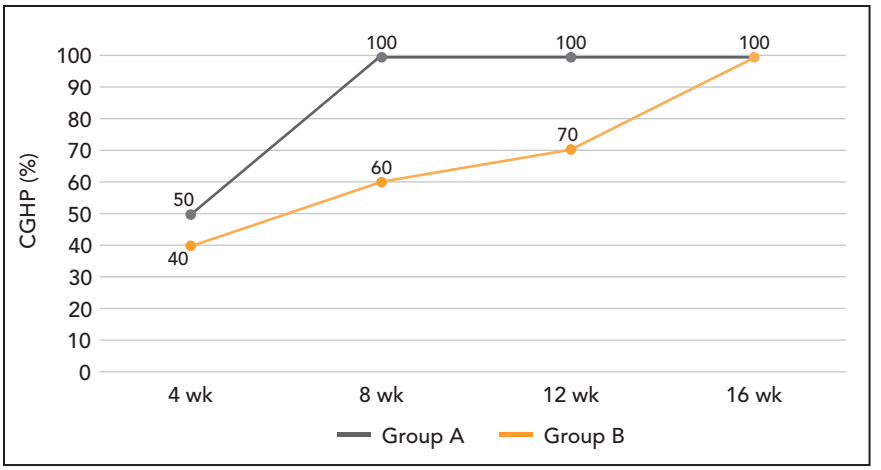


Fig 7 *Cretal gingival healing process (CGHP) in both groups over the 16-week healing period after ARP.*

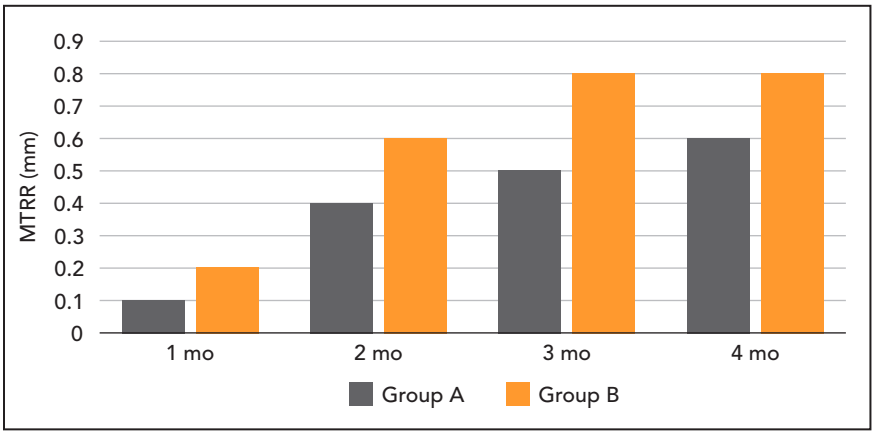


Fig 8 *Mean transversal crestal ridge resorption (MTRR) in both groups at 1, 2, 3, and 4 months after ARP.*

Study Outcomes and Time Points

The following parameters were measured by a single experienced operator (B.S.) under direct microscopic vision (OPMI PROergo) with an accuracy of 0.1 mm: mean transversal crestal ridge resorption (MTRR), crestal gingiva/soft tissue healing process (CGHP), and mean implant primary stability (MIPS).

MTRR was measured in millimeters under perpendicular vision of the microscope with a scaled periodontal probe at the time of extraction (after tooth removal) and at 1, 2, 3, and 4 months to assess the morphologic changes at the alveolar ridge crest after ARP in both groups.

CGHP percentages were obtained by clinical microscopic visual assessment of the crestal tissue healing using an optical magnification factor of 8 to 12, measured at 1, 2, 3, and 4 months after ARP. Specifically, at each follow-up, the crestal soft tissue of each extraction site was assessed for changes regarding complete closure, keratinization, presence/absence of redness, or any complications.

MIPS was measured in Ncm (using the Straumann scaled ratchet) at the time of the implant insertion and 4 months after ARP.

Results

A total of 10 patients (4 men, 6 women) with a mean age of 49 years (range: 41 to 57 years) were enrolled in the study (Table 1). All participants attended all follow-up visits without any dropouts. The study included 20 equally distributed extraction sockets. Four patients required extraction of more than two adjacent teeth (three cases in the maxilla, and one in the mandible). Per the study protocol, only the first two most mesial anterior adjacent sites were included in the study. The cause of tooth loss included unrestorable decay (15 teeth) and failure of endodontic treatment (5 teeth). For all sockets, healing was uneventful without any major complications. Second-stage procedures were uneventful, and all implants in both groups appeared to have osseointegrated.

For the clinical outcomes, the crestal soft tissue healing in Group A (Bio-Oss) appeared significantly more rapid than Group B (Cerabone). The crestal soft tissues at the sites treated with Bio-Oss seemed fully keratinized at 8 weeks, while for sites treated with Cerabone, complete soft tissue closure and keratinization seemed to require about twice as much healing time (observed mostly

at 3 or 4 months) (Fig 7). Throughout the 4-month healing period after ARP therapy, MTRR was slightly higher in the Cerabone group than in the Bio-Oss group, but all were < 1 mm (Fig 8). At the time of implant therapy, all alveolar ridges at Group A sites showed complete stability of bone graft particles into the surrounding bone, whereas in Group B, the bone graft particles did not show complete stability at the crestal region, deeming it necessary to remove some granules (to a mean depth of 4 mm) prior to or during the implant osteotomy.

All sites received bone-level implants (Bone Level Tapered, Straumann) with the same diameter (3.3 mm) and varying lengths from (10 to 14 mm). The mean primary stability at implant placement was 40 ± 5 Ncm (range: 35 to 45 Ncm) in Group A, which was significantly higher than the average of 25 ± 5 Ncm (range: 20 to 30 Ncm) in Group B. Healing after implant insertion was uneventful at all times, and implant uncovering procedures took place 6 to 7 weeks later using the VSRF approach. Prosthetic treatment of all inserted implants was also uneventful.

Discussion

Despite the lack of agreement on the best biomaterial for ARP,[8,23] due to the plethora of research,[4,24] most agree that ARP therapy is beneficial after tooth extraction and that it should be employed.[2,8] Among the varying biomaterials, particulate allogeneic and xenogeneic bone substitutes are currently the most readily employed,[8,16] followed by alloplastic and synthetically derived bone substitutes, to a lesser degree.[2,16,17] In the present study, healing was assessed in adjacent extraction sites treated with two differently processed commercially available bovine-derived bone grafts. As the literature is well-supplied with research on dimensional changes of the alveolar ridge after ARP (bone alterations),[2,8,16,25] the present study sought to explore outcomes less commonly reported in the literature, such as morphologic/contour changes of the ridge (ie, soft tissues and the underlying bone) and to evaluate the healing of the adjacent soft tissues at several equally distributed time points under direct microscopy. To reduce unwanted variability and the influence of host/systemic factors, the comparison of bone grafts was in adjacent extraction sites, as both materials were bovine in origin.

Overall, both groups led to satisfactory clinical results, as all implants could be placed without the need for additional grafting and with sufficient primary stability. Nevertheless, sites allocated to Group A (Bio-Oss), resulted in less morphologic changes in the alveolar ridge (MTRR) and accompanied a more rapid soft tissue healing. In addition, at the time of the implant surgery, these sites also presented with an enhanced stability of bone particles and led to higher primary stability values. To the present authors' knowledge, no other study on ARP has done such direct comparison of the two bone grafts, especially with a similar focus as the present study. Thus, a direct comparison of the current findings to the literature may not be feasible.

However, as the difference between the two ARP therapies merely resided in the different fabrication process of the bovine particles (sintering temperature, etc), it could be speculated that present observed differences in the healing and clinical outcomes would also be due to this phenomenon. Indeed, studies have shown that the structural characteristics and physicochemical properties of bone grafts that essentially serve as scaffolds (such as xenografts) result from their method of processing, which can directly influence their bioactivity, biodegradability, and adjacent cellular viability and proliferation.[26–29] In fact, a recent study comparing the effect on bone marrow stromal cells of bovine-derived bone grafts sintered at different temperatures found that the different groups revealed variations in surface tomography, which was related to the potential to attract stromal cells and their differentiation.[30] The same study also found significant variations in bone fraction among the groups at 6 and 12 weeks, when bone grafts were transplanted into rabbit calvarial defects.[30] A systematic review of human clinical trials also showed that different types of bone grafts inserted into the socket can lead to differences in the amount of bone remodeling.[16] Nevertheless, as the clinical understanding of extraction socket healing has increased,[4,8] it should be noted that other factors (eg, buccal plate thickness, utilization of a membrane, etc) may have an even larger role in bone remodeling.

Among the limitations of this trial, its preliminary nature is to be acknowledged, and it shaped the

qualitative assessment of the present results. Further, the study lacked a negative control group. Also, due to the lack of a histologic analysis, the true assessment of bone quality at extraction sites could not be determined. Long-term assessment of corresponding implant sites would also be beneficial to compare marginal bone levels. Lastly, readers should note that despite the intergroup differences mentioned in this report, all extraction sites healed uneventfully and successfully received implant therapy irrespective of the specific bovine bone substitute.

Conclusions

Within the limitations of this report, it can be concluded that the application of either of the utilized bovine bone grafts for ARP can render successful implant surgeries. Nevertheless, the manufacturing process of the bovine bone materials may result in different clinical outcomes throughout the healing period and at the time of implant placement.

Acknowledgments

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