PRACTICAL APPLICATIONS

How to Select Replacement Grafts for Various Periodontal and Implant Indications

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Focused Clinical Question: How are bone replacement grafts for various periodontal and implant indications properly selected?

Summary: The purpose of this paper is to review the properties of available bone replacement materials and provide guidelines of how to choose certain graft materials for different clinical indications (e.g., periodontal defects, peri-implant defects, socket augmentation, ridge augmentation, and sinus augmentation).

Conclusion: Full understanding of material properties and meticulous case selection may help to maximize the benefit of bone replacement grafts in tooth- and implant-related regeneration. *Clin Adv Periodontics* 2013;3:167-179.

Key Words: Alveolar ridge augmentation; bone substitutes; guided tissue regeneration; peri-implantitis; sinus augmentation therapy; socket graft.

Background

Alveolar bone, as a part of periodontium, plays a primary role in the maintenance of both the natural dentition and dental implants. Resulting from periodontal disease or trauma, bony destruction leads not only to functional concerns but also esthetic impairment. To regain lost bone tissue, the use of bone replacement grafts has been introduced and widely applied in periodontal and implant therapy.

Early researchers, Dr. Gerald Bowers and Dr. Robert Schallhorn, established the fecundated principles of osseous grafting by conducting a series of research projects over the past decades. In a landmark article published in 1977, the advantages of osseous grafting procedures was suggested, including reconstruction of lost periodontium, cessation of disease progression, and improvements in both function and esthetics.[1] Indeed, the efficacy of osseous grafting has been demonstrated in histologic assessments,[2-6] which become the rationale for the use of bone substitutes in modern dentistry.

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Bone replacement materials have been used in several situations, such as infrabony defects,[7] furcation defects,[8] ridge augmentation,[9] socket preservation,[10] peri-implant defects,[11] and sinus augmentation.[12] To achieve desirable outcomes and maximal effectiveness, the selection of osseous grafting materials should be based on their unique features, therapeutic objectives, and indications.[1] This paper aims to provide guidelines for clinicians to select osseous grafts for periodontal or implant indications. In addition, the characteristics of bone substitutes used are reviewed.

Properties of Bone Replacement Grafts

An ideal bone replacement material should possess certain features. Biocompatibility and non-toxicity are prerequisite, as well as resistance to infection. In addition to reasonable cost, the ideal bone grafting materials should be easy to manipulate and readily obtainable. They should also possess some properties of regenerative potential or supportability, i.e., osteogenesis, osteoinduction, and osteoconduction.[1,13-15] In other words, osteogenic grafts have the potential to trigger bone formation by transplantation of osteoblasts and precursor osteoblasts. Osteoinductive grafts provide a stimulus for the differentiations of bone-forming cells, whereas osteoconductive materials only serve as a scaffold for the migration and ingrowth of bone cells.[13,16]

Based on graft sources, bone replacement materials are classified into four categories with their unique characteristics. The properties of each bone graft category is summarized in Table 1. Table 2 summarizes the characteristics of commercially available bone replacement grafts.

Autografts

Autogenous bone replacement grafts, transplanted within the same individual, are obtained from either extraoral or intraoral sites. In general, autografts are considered as the gold standard in most clinical situations because of the capacity of osteogenesis and no risk of disease transmission. With various harvesting techniques, characteristics of autografts may represent minor differences with regard to donor sites. For example, cancellous bone and marrow grafts possess the greatest induction potential of osteogenesis.[17,18] Compared to the osseous coagulum techniques, the bone blend technique yields the mixture of cortical and cancellous graft of a larger particle size with clinically manageable and predictable properties. However, osseous coagulum and bone blend techniques can only procure a limited amount of bone, whereas cancellous bone and marrow grafts lead to additional surgical insult and

TABLE 1 Properties, Advantages, and Disadvantages of Bone Replacement Grafts

Bone Replacement Graft	Properties	Advantages	Disadvantages	Indications
Autografts (obtained from the same individuals)	Osteogenesis/ osteoinduction/ osteoconduction	Capacity of osteogenesis	Limited availability	Class II furcation defect
		Elimination of the potential complications of histocompatibility	Additional surgical intervention	2-wall periodontal defects
		No risk of disease transmission	Possible complications: root resorption, ankylosis	2-wall or circumferential peri-implant defects
				Intact, thick-walled extraction sockets
				Horizontal ridge augmentation: OBG, ridge split/expansion, GBR
				Sinus augmentation
Allografts (obtained from different individuals of the same species)	Osteoinduction/ osteoconduction	Possible osteogenesis	Possible disease transmission	Class II furcation defect
		No need for additional surgical intervention		2-wall periodontal defects
				2-wall or circumferential peri-implant defects
				2-wall or 3-wall extraction sockets
				Horizontal ridge augmentation: OBG, ridge split/expansion, GBR
				Sinus augmentation
Xenografts (obtained from different species)	Osteoinduction (?)/ osteoconduction	No need for additional surgical intervention	Possible disease transmission	2-wall or circumferential peri-implant defects
			Slow resorption rate	2-wall or 3-wall extraction sockets
				Horizontal ridge augmentation: ridge split/expansion, GBR
				Sinus augmentation
Alloplasts (synthetic grafts)	Osteoconduction	No risk of disease transmission	Slow resorption rate	2-wall or circumferential peri-implant defects
		No need for additional surgical intervention		2-wall or 3-wall extraction sockets
				Horizontal ridge augmentation: ridge split/expansion, GBR
				Sinus augmentation

? = not enough evidence.

TABLE 2 Characteristics of Commercially Available Bone Replacement Grafts

Characteristics	Commercial Name(s)
Allografts	
DFDBA	DBX Putty Demineralized Bone Matrix,* Grafton DBM,† OsteoDemin,‡ Regenaform§
FDBA	MinerOss,† NonDemin,‡ CurOss,‡ CancellOss,‡ enCore Mineralized Allograft,‖ Puros Cancellous,¶ Puros Cortical Bone¶
Mixture of DFDBA and FDBA	DynaBlast,# enCore Combination Allograft‖
Xenograft	
Bovine bone	OsteoGraf/N,* Bio-Oss,** NuOss XC Sinus/Socket Forms,†† NuOss††
Alloplasts	
Non-resorbable HA	OsteoGraf/D*
Resorbable HA	OsteoGraf/LD,* OsteoGen‡
TCP	chronOS Granules and Preforms‡‡
Mixture of HA and β-TCP	OSTEON II,§§ 4Bone,‖‖ OSTEON (sinus, orthopedic)§§
Calcium sulfate	BondBone,‖‖ CaSO4 Calcium Sulfate Hemihydrate,†† SynOss††
Calcium phosphosilicate	NovaBone Dental Putty¶¶
Collagen-coated bone grafts	
Type I collagen-coated bovine bone	PepGen P-15/PepGen P-15 FLOW,* Bio-Oss Collagen,** NuOss Collagen††
Type I collagen-coated alloplasts	OSTEON Collagen§§
Combination of growth factor and bone grafts	
Recombinant platelet-derived growth factor-BB and β-TCP	GEM-21**

* DENTSPLY International, York, PA.
† BioHorizons, Birmingham, AL.
‡ Exactech, Gainesville, FL.
§ Impladent, Holliswood, NY.
‖ Osteogenics Biomedical, Lubbock, TX.
¶ Zimmer Dental, Carlsbad, CA.
# ACE Surgical Supply, Brockton, MA.
** Dentium, Cypress, CA.
†† Keystone Dental, Burlington, MA.
‡‡ Synthes, West Chester, PA.
§§ Osteohealth, Shirley, NY.
‖‖ MIS Implant Technologies, Shlomi, Israel.
¶¶ NovaBone, Jacksonville, FL.

expense.[1,19,20] Additionally, root resorption is a common concern when fresh iliac grafts are used.[21,22]

Allografts

Because of limited availability of autogenous bone grafts, allografts have been introduced as alternative bone replacement grafts in extensive bony defects. Allografts are harvested from different individuals of the same species, and they possess osteoconductive and osteoinductive properties and eliminate the need for a second surgical site. The main alternative is autografts, but the main concern with allografts is the possible antigenicity and potential for disease transmission, although the frequency is rare.[23,24] To prevent disease transmission, fresh-frozen grafts are no longer used.[25] Instead, freeze-dried bone allografts (FDBAs) and decalcified FDBAs (DFDBAs) are widely available from tissue banks. Despite harvesting from similar sources, minor differences of properties are presented. Compared to DFDBA, FDBA tends to be more slowly resorbed and thus is better for space maintenance. DFDBA has the potential for osteoinduction with more expression of bone morphogenetic protein.[26-28] Therefore, DFDBA is indicated for periodontal regeneration, whereas FDBA is more suitable for augmentation procedures.[29] In addition, allografts can be classified as cortical, cancellous, and mixed based on the location of the donor site. It is believed that cancellous bone shows better bone incorporation and more rapid revascularization compared to cortical bone.[30,31] However,

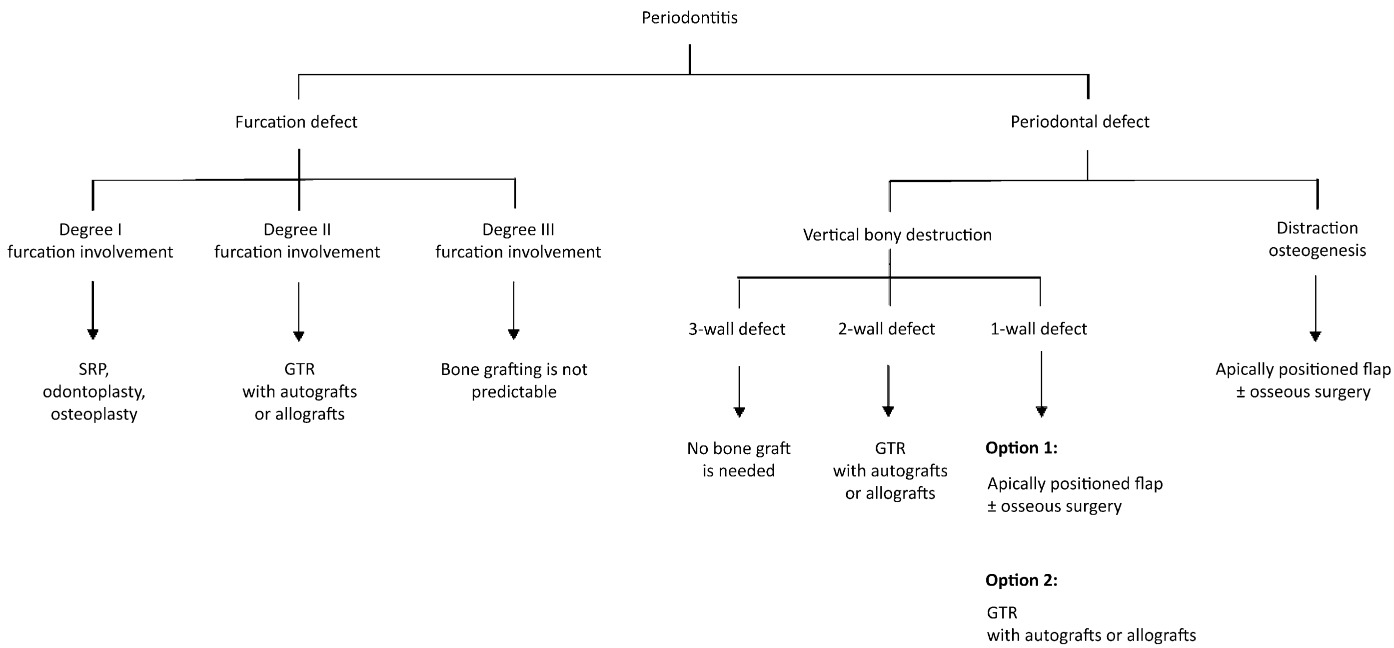

FIGURE 1 Disease-related indications: periodontitis. SRP = scaling and root planing.

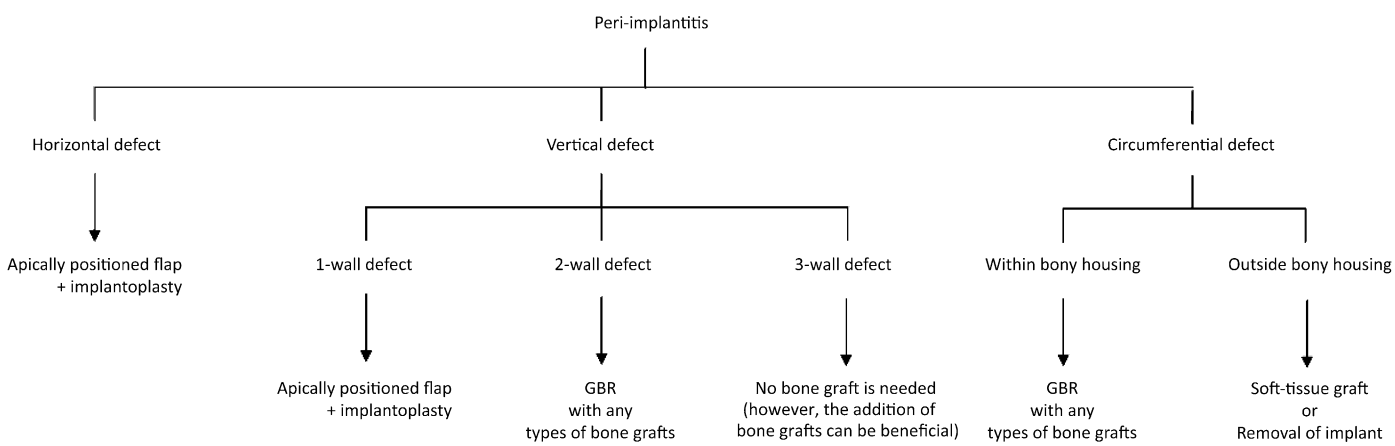

FIGURE 2 Disease-related indications: peri-implantitis.

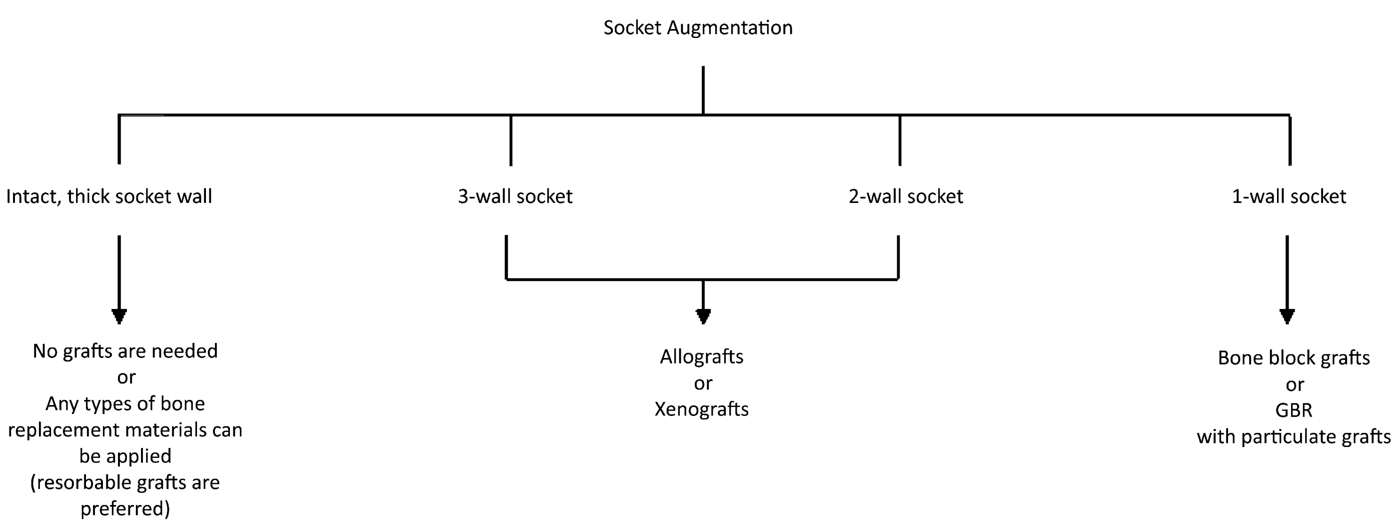

FIGURE 3 Implant-related indications: socket augmentation.

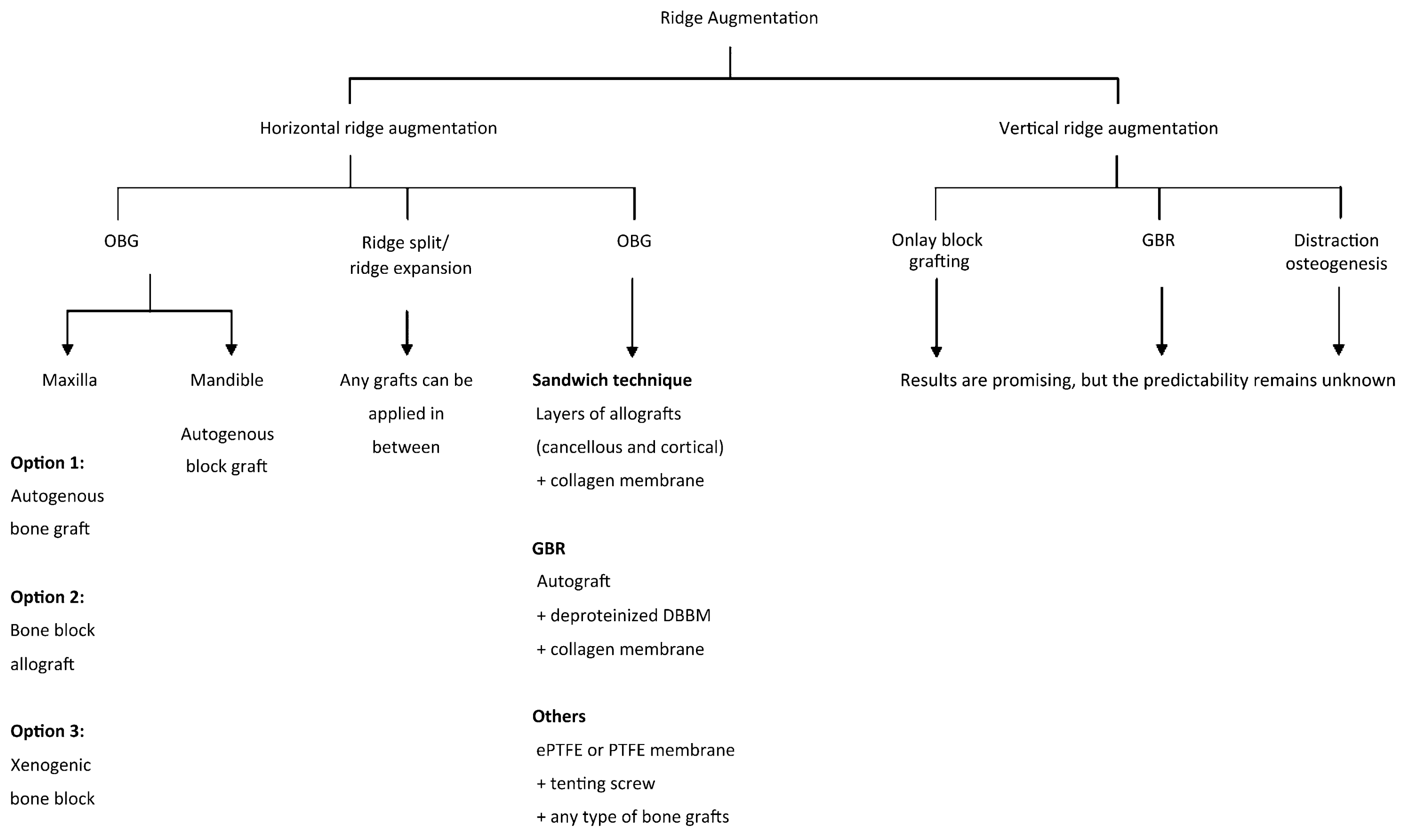

FIGURE 4 Implant-related indications: ridge augmentation. DBBM = deproteinized bovine bone mineral; ePTFE = expanded polytetrafluoroethylene; PTFE = polytetrafluoroethylene.

FIGURE 5 Clinical scenario 1. Pretreatment view of mandibular second molar. An infrabony defect was noted on the distal aspect of tooth #31.

limited evidence is available to clarify the differences and the primary indications for these allografts.

Xenografts and Alloplasts

Osteoconductive bone replacement grafts include xenografts and alloplasts. Serving as the scaffold of bone regeneration, xenografts are obtained from species other than human, such as bovine, porcine, and coral.[15] Similar to allografts, xenografts avoid additional surgical insult in regenerative procedures, leading to less patient discomfort. Despite osteoconduction, osteoinductibility of xenografts has also been demonstrated in an animal study.[32] Nevertheless, iatrogenic transmission of prion-related diseases is the main concern with the use of bovine products, although the risk has declined as a result of appropriate preventive measures.[33] Synthetic bone substitutes are alternatives as an osteoconductive scaffold in regenerative procedures and have no risk of disease transmission and no need of second surgical sites. The types of alloplasts used in periodontal and implant indications include absorbable/non-resorbable hydroxyapatite (HA) products, β-tricalcium phosphate (β-TCP), polymethylmethacrylate and hydroxylethylmethacrylate calcium-layered polymer, polyactic acid polymer, and bioglass materials. Instead of formation of new attachment, it appears that alloplasts act as non-irritating fillers that support periodontal repair.[29,34]

Additional Options

Recently, a revolution in properties of materials has been generated with the use of tissue engineering, the combination of different bone materials, and the changes in processing techniques. To improve the regenerative outcomes, the use of synthetic collagen or growth factors in conjunction with osteoconductive materials has been proposed to promote both bone formation and to speed wound healing.[8,35-37] Moreover, the combination of mineralized and demineralized allografts has been introduced in addition to a mixture

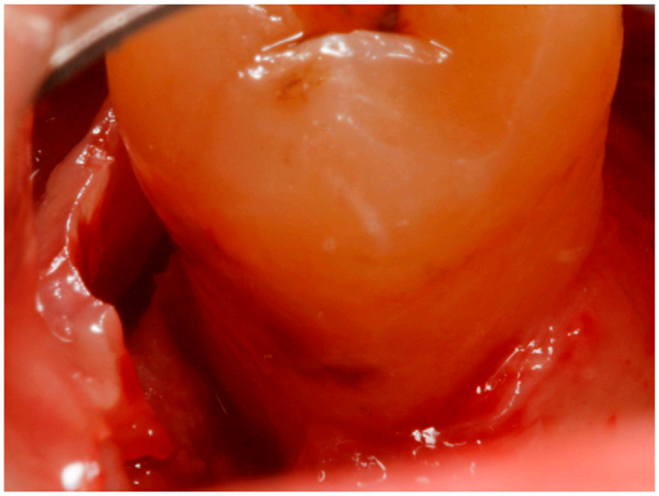

FIGURE 6 Clinical scenario 1. After full-thickness flap reflection and debridement, a 3-wall infrabony defect was seen on the distal aspect of tooth #31.

of cortical and cancellous allografts. At present, there is limited evidence supporting the superiority of any of these combinations compared to a conventional formula.

To date, there is no ideal bone replacement graft that is suitable for all regenerative procedures. Selection of bone grafts should be based on properties of materials, indications/clinical scenarios, and the purpose of the grafting procedures.

Decision Process and Clinical Scenarios: Bone Grafts for Periodontal and Implant Indications

The main indications of bone grafting procedures can be divided into both periodontal and peri-implant disease-related sites and implant site development applications. They include regenerative procedures for destruction caused by periodontal or peri-implant diseases and bone augmentation procedures for implant site preparation. In addition to defect morphology, selection of bone replacement grafts should be based on their properties corresponding to indications. Decision trees regarding disease-related and implant-related indications are proposed in Figures 1 through 4.

FIGURE 7 Clinical scenario 1. Postoperative radiograph taken 4 years after GTR.

Disease-Related Indications

Periodontal defects (clinical scenario 1). Bone replacement grafts have been widely used in conjunction with membrane barrier technique in guided tissue regeneration (GTR) procedures. Intrabony defects and Class II furcation defects are the main indications for bone grafting.[38] In addition to formation of new attachment, favorable results in terms of probing depth reduction and clinical attachment gain have been reported with the use of all types of bone grafts.[8,39-48] The additional benefits of GTR in combination with bone grafts and growth factor–releasing devices, such as peptide coating, platelet-rich plasma, and enamel matrix derivative protein, have been evaluated and remain controversial.[48-53] Compared to allografts, limited evidence is available to support the superiority of the use of xenografts or alloplasts in the treatment of periodontal defects.[54-57] In addition to the concerns of disease transmission with xenografts, there are few human trials with large sample sizes demonstrating the efficacy of alloplasts on periodontal regeneration. Therefore, autologous bone grafts and allografts are recommended because of the capacity of osteoconduction, osteoinduction, and osteogenesis (Fig. 1).

In Figure 5, a periodontal defect is shown on the distal aspect of the mandibular second molar. After debridement, an intrabony defect was noticed and treated with a GTR procedure using mineralized allograft (Fig. 6). Promising results with complete bone fill were achieved 4 years after treatment (Fig. 7).

Peri-implant defects. Regenerative procedures have been evaluated in the treatment of peri-implantitis.[58,59] Regarding defect morphology of peri-implant lesions, guided bone regeneration (GBR) is indicated in 2-wall or 3-wall intrabony defects and circumferential defects (Fig. 2).[60,61] In human models, various bone replacement grafts have been applied to manage peri-implant bone loss with positive outcomes. They include autologous,[62-64] allogeneic,[11,58] xenogenic,[63,65-67] and synthetic[59,65,68,69] bone substitutes. In a recent systematic review, the results suggested that complete bone fill was achieved in ≤10.4% of GBR-treated peri-implant lesions, whereas 85.5% of peri-implant defects showed bone gain.[70] Because of the heterogeneity of experimental design, to date, limited evidence is available to make a conclusion to suggest any specific types of bone replacement materials. Additional research is expected to address the regenerative procedures in peri-implant lesions.

Implant-Related Indications

Socket augmentation (clinical scenario 2). To prevent ridge resorption after tooth extraction, socket augmentation is necessary for future implant site development. The use of bone replacement grafts allows better space creation and maintenance by preventing potential collapse of membranes. Compared to non-grafted sites or collagen-grafted sites, desirable results in grafted sites have been shown in previous studies, including less dimensional changes,

FIGURE 8 Clinical scenario 2. Preoperative view of a fractured maxillary premolar that was recommended for extraction.

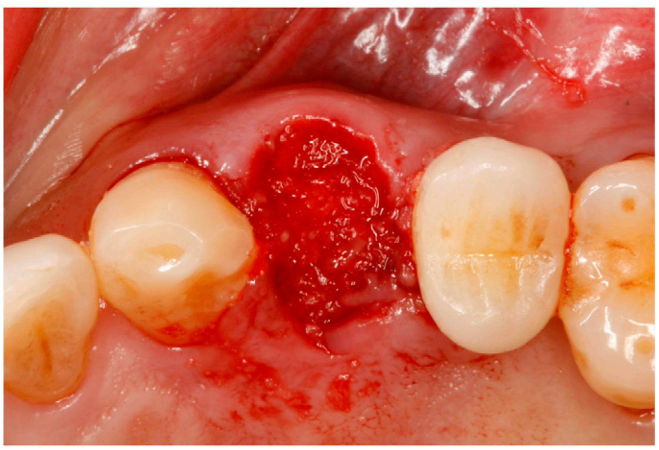

FIGURE 9 Clinical scenario 2. Extraction socket was augmented using mineralized bone putty and collagen dressing.

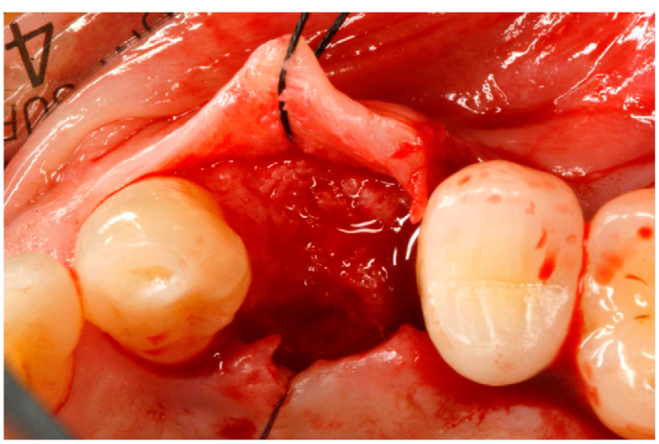

FIGURE 10 Clinical scenario 2. Reentry at 6 months after socket augmentation for implant placement.

greater mineralized component, and better organization of bone structures.[10,71-73]

In socket augmentation, it has been suggested that the use of bone replacement grafts should be selected based on the remaining walls of extraction sockets.[74] However, autologous bone failed to prevent ridge resorption despite its osteogenic properties. Indeed, 25% of reduction was shown on the coronal portion of the ridge.[75] Histologically, allografts were replaced by newly formed bone, whereas the extraction sockets grafted with xenografts exhibited a delayed healing pattern.[75-79] Up to 61% of vital bone fill was reported in an allograft group compared to only 26% in a xenograft group,[79] although xenografts may have benefits in minimizing dimensional changes.[72,75] In addition, fibrous encapsulation surrounding the residual bone particles has been observed when xenografts and alloplasts were used as the grafting materials,[76,80,81] leading to reduction of bone-to-implant contact after implant placement.

In short, any type of a resorbable osseous graft is recommended for placement in a socket with intact and thick walls. For 2-wall or 3-wall sockets, both allografts and xenografts are effective for socket augmentation. In a socket with one bony wall remaining, a bone block graft or GBR with particulate grafts might be a better option (Fig. 3).

Figures 8 through 10 show a socket augmentation procedure using mineralized bone putty that was applied immediately after extraction of a fractured maxillary premolar. Six months later, a full-thickness flap in the same region was reflected for implant placement. Minimal dimensional changes were visualized, which provided a good foundation for implant placement and restoration.

Ridge augmentation (clinical scenario 3). With the advent of implant dentistry, techniques, such as onlay bone grafting (OBG), ridge split/expansion, or GBR with particulate bone grafts,[82] were proposed for horizontal bone augmentation. Techniques used to gain vertical height included onlay block grafting, distraction osteogenesis, and GBR.

For OBG, allogenic[9,83] and xenogenic [84] bone blocks as well as chin or ramus autografts[85,86] have been used for horizontal ridge augmentation. Although there is no need for donor site, greater graft resorption has been reported in the patients treated with allograft blocks compared to autologous block grafts.[87] With a 7% to 8% failure rate, complications associated with cancellous block allografts were significantly greater in the mandible than in the maxilla.[88] In addition, the efficacy of xenogenic block grafts was also evaluated in recent years. A feasibility study was conducted by Schwarz et al.[84] to compare equine- and bovine-derived cancellous bone blocks in lateral ridge augmentation in a dog model. Minimal bone formation and grafting integration was shown in bovine grafts, although no adverse events were reported. Thus, it is suggested that block autografts can be effective in both jaws, whereas block allografts may be more predictable for the maxilla. Block xenografts may be a feasible option, but the efficacy remains unknown.

Ridge split in combination with different particulate graft has shown promising results in most studies.[89-91] However, limited evidence is available, especially when compared to other treatment modalities. Regarding GBR, several techniques and different graft materials have been used with satisfactory results.[92] With non-resorbable barrier membranes plus tenting screws, promising outcomes have been achieved with the majority of bone replacement grafts.[93-96] In an animal study, Fiorellini et al.[95] demonstrated that implant osseointegration can be successfully achieved after GBR using expanded polytetrafluoroethylene membranes regardless of the types of osseous grafts used. Using absorbable barrier membranes, ridge augmentation can be applied along with simultaneous implant placement (Fig. 11), which is known as the sandwich bone augmentation technique. A combination of various bone grafts is preferred. They include layers of cancellous and cortical allografts[97,98] (Fig. 12) and the mixture of autogenous grafts and deproteinized bovine bone mineral.[99,100] This combination of bone replacement grafts is advantageous because of the capacity of space maintenance with low-turnover-rate bone grafts and the property of osteogenesis/osteoinduction/osteoconduction of autografts/cancellous allografts. Compared to baseline, marked bone formation was noticed after treatment (Fig. 13).

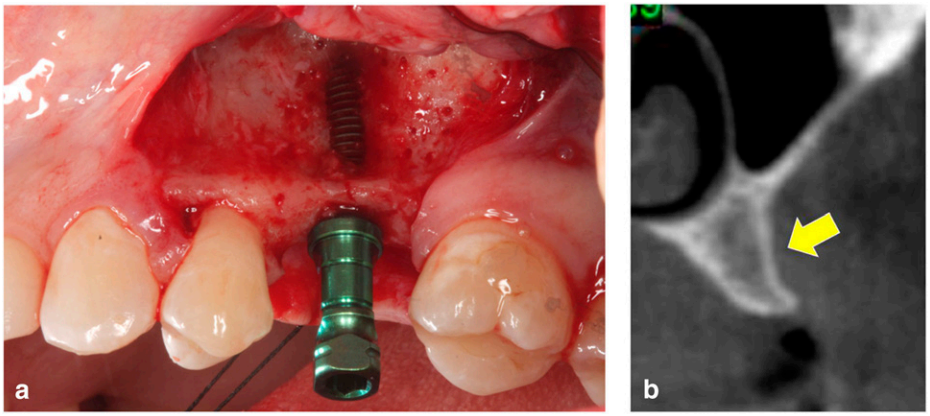

FIGURE 11 Clinical scenario 3. **11a** Preoperative view showing ridge deficiency and fenestration on the buccal aspect of the implant. **11b** Radiograph taken at baseline. Ridge deficiency was noted on the buccal aspect of the edentulous ridge. Yellow arrow indicates the ridge deformity noted on the buccal aspect of the edentulous ridge.

Vertical ridge augmentation is one of the greatest challenges in implant dentistry. Despite high long-term implant survival rate (92.1% to 100%), varying implant success rates (76.3% to 97.5%) and vertical bone gain (2 to 8 mm) were discussed in a systemic review.[101] Complications were also demonstrated in various studies.[91,102,103] Although desired results have been suggested with the application of various types of bone grafts,[104-107] the predictability remains unclear. A proposed decision tree is shown in Figure 4.

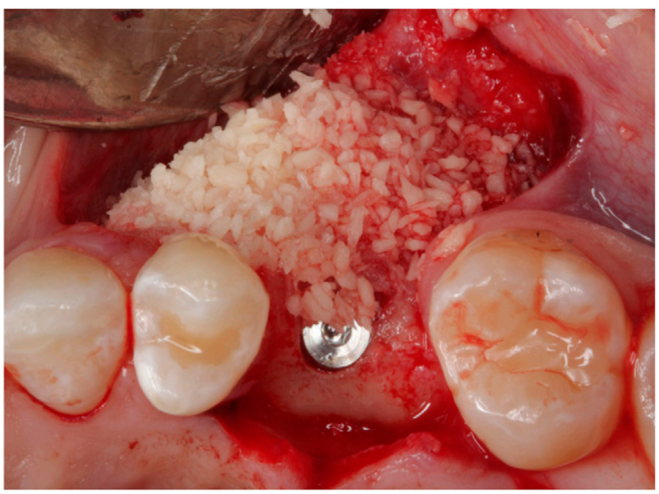

FIGURE 12 Clinical scenario 3. GBR with sandwich technique. Ridge augmentation was performed using cancellous allografts as the inner layer and cortical allografts as the outer layer.

Sinus augmentation (clinical scenario 4). In the maxillary posterior region, a common ridge deficiency preventing success implant placement is insufficient ridge height. To increase vertical dimension, sinus augmentation procedures have been widely applied in modern implant therapy, resulting in high implant survival rates and a low incidence of complications.[108] Although the potential of bone formation in sinus without the use of bone substitutes has been proposed,[109] the results remain controversial, and the stability of the blood clot with sinus lifting is questionable.[110-113] From previous studies, comparable clinical outcomes and a similar histologic appearance have been suggested regarding the efficacy of different types of bone replacement materials[12,114-116] as long as the membranes were not exposed. To date, no association has been found between the type of grafts used in sinus augmentation and surgical outcomes in terms of implant survival rates and occurrence of complications.[117] Despite the ability of osteogenesis of autografts, resorbable bone grafts with slow resorption may also be suitable in sinus augmentation procedures for dimension maintenance.[118] Therefore, all types of bone replacement grafts are suitable in sinus augmentation procedures. Indeed, sinus elevation

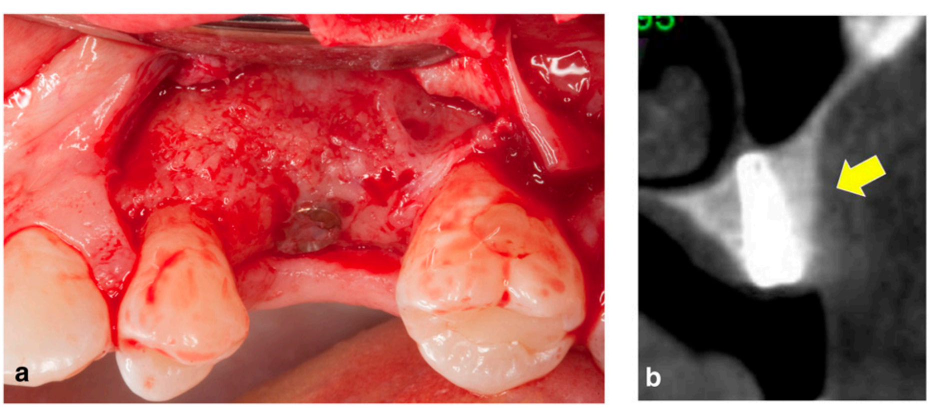

FIGURE 13 Clinical scenario 3. **13a** Reentry at 6 months postoperatively. Predominant bone formation and complete bone coverage were observed at the buccal aspect of the implant. **13b** Radiograph taken 6 months postoperatively. Predominant bone formation on the buccal aspect of the implant was seen. Yellow arrow indicates predominant bone formation on the buccal aspect of the ridge after GBR.

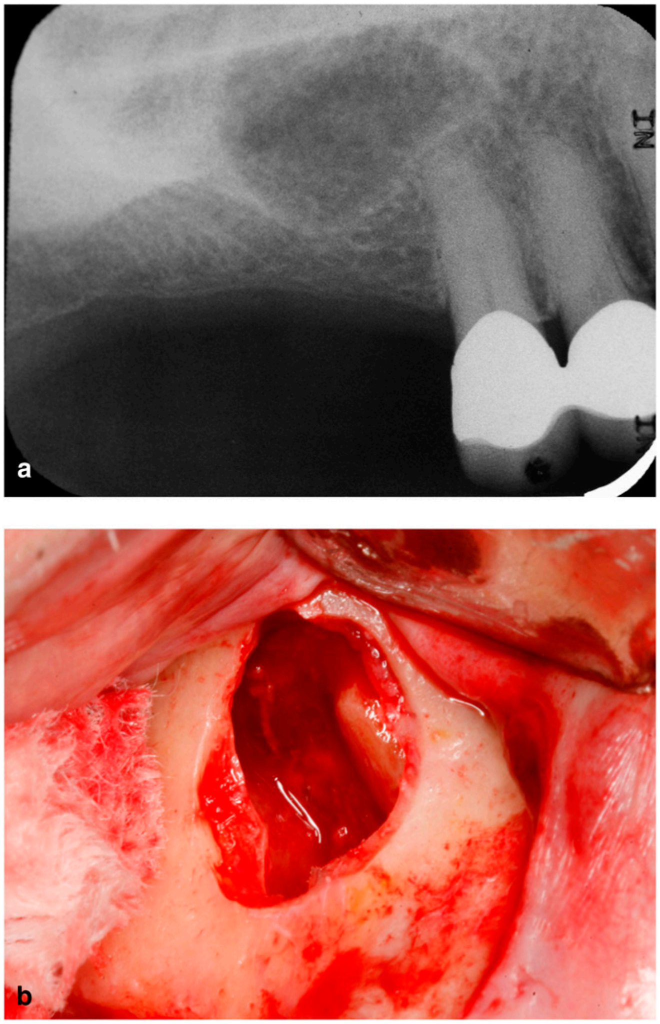

FIGURE 14 Clinical scenario 4. **14a** Preoperative radiograph. Residual ridge height was insufficient for implant placement. **14b** Sinus elevation was performed in a 65-year-old patient.

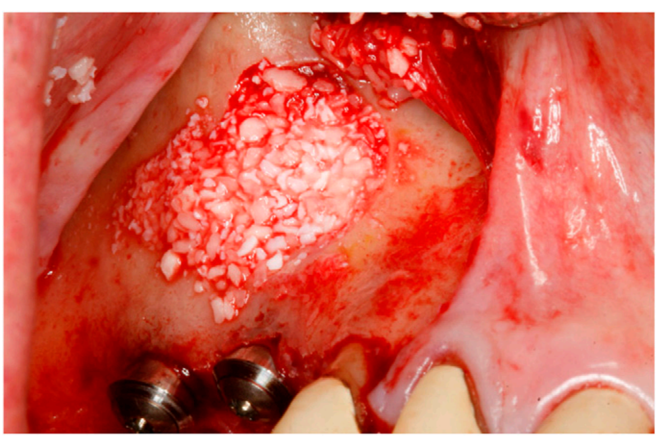

FIGURE 15 Clinical scenario 4. Sinus elevation with a collagen membrane and layered approach using autografts (at the bottom), a mixture of cortical and cancellous allografts (in the middle portion), and a mixture of xenografts and allografts (as the top layer). Implants were placed simultaneously with sinus elevation.

using a layered approach with various types of bone grafts may be effective in achieving promising outcomes.

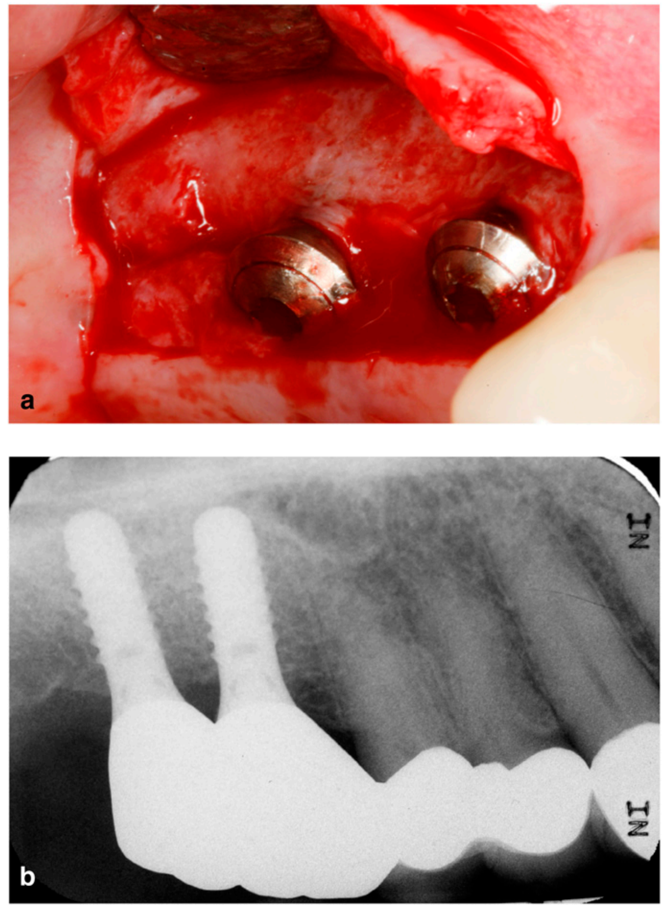

FIGURE 16 Clinical scenario 4. **16a** Reentry at 2 years postoperatively. **16b** Postoperative radiograph taken 2 years after sinus elevation.

In Figures 14 through 16, a case of implant placement with simultaneous sinus lifting is reported. A layered approach was performed in a 65-year-old patient who had insufficient ridge height on the right maxillary posterior region. With a lateral window technique, autogenous grafts were placed in the apical portion ($\approx$5-mm height). The middle portion consisted of cortical and cancellous allografts, whereas the coronal portion was filled with the combination of xenograft and allografts, which have a slower resorption rate. A collagen membrane was applied to cover the bone grafts on the outside of lateral window. Two years after surgery, both clinical and radiographic examination displayed consistent and favorable results (Fig. 16).

Conclusions

With the advent of technology, autologous bone grafts remain the best choice in most situations but are no longer the only option in modern dentistry. Various bone replacement grafts from other sources are available, and they display different properties. With various available grafts and regenerative techniques, full awareness of their features and indications is the cornerstone of successful regeneration. Using these guidelines, careful case and material selection corresponding to different indications can be beneficial to achieve predictable and consistent treatment outcomes. ■

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References

1. Schallhorn RG. Present status of osseous grafting procedures. *J Periodontol* 1977;48:570-576.
2. Bowers GM, Granet M, Stevens M, et al. Histologic evaluation of new attachment in humans. A preliminary report. *J Periodontol* 1985;56: 381-396.
3. Bowers GM, Schallhorn RG, Mellonig JT. Histologic evaluation of new attachment in human intrabony defects. A literature review. *J Periodontol* 1982;53:509-514.
4. Bowers GM, Chadroff B, Carnevale R, et al. Histologic evaluation of new attachment apparatus formation in humans. Part III. *J Periodontol* 1989;60:683-693.
5. Bowers GM, Chadroff B, Carnevale R, et al. Histologic evaluation of new attachment apparatus formation in humans. Part II. *J Periodontol* 1989;60:675-682.
6. Bowers GM, Chadroff B, Carnevale R, et al. Histologic evaluation of new attachment apparatus formation in humans. Part I. *J Periodontol* 1989;60:664-674.
7. Cortellini P, Tonetti MS. Focus on intrabony defects: Guided tissue regeneration. *Periodontol 2000* 2000;22:104-132.
8. Suaid FA, Macedo GO, Novaes AB, et al. The bone formation capabilities of the anorganic bone matrix-synthetic cell-binding peptide 15 grafts in an animal periodontal model: A histologic and histomorphometric study in dogs. *J Periodontol* 2010;81:594-603.
9. Wallowy P, Dorow A. Lateral augmentation of the maxilla and mandible using framework technique with allogeneic bone grafts. *J Oral Implantol* 2012;38:661-667.
10. Iasella JM, Greenwell H, Miller RL, et al. Ridge preservation with freeze-dried bone allograft and a collagen membrane compared to extraction alone for implant site development: A clinical and histologic study in humans. *J Periodontol* 2003;74:990-999.
11. Mellonig JT, Griffiths G, Mathys E, Spitznagel J Jr. Treatment of the failing implant: Case reports. *Int J Periodontics Restorative Dent* 1995; 15:384-395.
12. Froum SJ, Wallace SS, Elian N, Cho SC, Tarnow DP. Comparison of mineralized cancellous bone allograft (Puros) and anorganic bovine bone matrix (Bio-Oss) for sinus augmentation: Histomorphometry at 26 to 32 weeks after grafting. *Int J Periodontics Restorative Dent* 2006; 26:543-551.
13. Reynolds MA, Aichelmann-Reidy ME, Branch-Mays GL. Regeneration of periodontal tissue: Bone replacement grafts. *Dent Clin North Am* 2010;54:55-71.
14. Rosenberg E, Rose LF. Biologic and clinical considerations for autografts and allografts in periodontal regeneration therapy. *Dent Clin North Am* 1998;42:467-490.
15. Nasr HF, Aichelmann-Reidy ME, Yukna RA. Bone and bone substitutes. *Periodontol 2000* 1999;19:74-86.
16 Lindhe J, Lang NP, Karring T. *Clinical Periodontology and Implant Dentistry.* Oxford, UK: Blackwell Munksgaard 2008;2:v.
17. Cushing M. Autogenous red marrow grafts: Their potential for induction of osteogenesis. *J Periodontol* 1969;40:492-497.
18. Halliday DG. The grafting of newly formed autogenous bone in the treatment of osseous defects. *J Periodontol* 1969;40:511-514.
19. Rosen PS, Reynolds MA, Bowers GM. The treatment of intrabony defects with bone grafts. *Periodontol 2000* 2000;22:88-103.
20. Brunsvold MA, Mellonig JT. Bone grafts and periodontal regeneration. *Periodontol 2000* 1993;1:80-91.
21. Dragoo MR, Sullivan HC. A clinical and histological evaluation of autogenous iliac bone grafts in humans. II. External root resorption. *J Periodontol* 1973;44:614-625.
22. Schallhorn RG. Postoperative problems associated with iliac transplants. *J Periodontol* 1972;43:3-9.
23. Simonds RJ, Holmberg SD, Hurwitz RL, et al. Transmission of human immunodeficiency virus type 1 from a seronegative organ and tissue donor. *N Engl J Med* 1992;326:726-732.
24. Buck BE, Resnick L, Shah SM, Malinin TI. Human immunodeficiency virus cultured from bone. Implications for transplantation. *Clin Orthop Relat Res* 1990;251:249-253.
25. Costain DJ, Crawford RW. Fresh-frozen vs. irradiated allograft bone in orthopaedic reconstructive surgery. *Injury* 2009;40:1260-1264.
26. Urist MR. Bone: Formation by autoinduction. *Science* 1965;150: 893-899.
27. Urist MR, Strates BS. Bone morphogenetic protein. *J Dent Res* 1971; 50:1392-1406.
28. Schwartz Z, Somers A, Mellonig JT, et al. Addition of human recombinant bone morphogenetic protein-2 to inactive commercial human demineralized freeze-dried bone allograft makes an effective composite bone inductive implant material. *J Periodontol* 1998;69: 1337-1345.
29. Wang HL, Cooke J. Periodontal regeneration techniques for treatment of periodontal diseases. *Dent Clin North Am* 2005;49:637-659, vii.
30. Abbott LC, Schottstaedt ER, Saunders JB, Bost FC. The evaluation of cortical and cancellous bone as grafting material; A clinical and experimental study. *J Bone Joint Surg Am* 1947;29:381-414.
31. Stevenson S, Emery SE, Goldberg VM. Factors affecting bone graft incorporation. *Clin Orthop Relat Res* 1996;324:66-74.
32. Torricelli P, Fini M, Rocca M, Giavaresi G, Giardino R. Xenogenic demineralized bone matrix: Osteoinduction and influence of associated skeletal defects in heterotopic bone formation in rats. *Int Orthop* 1999; 23:178-181.
33. Belay ED, Schonberger LB. The public health impact of prion diseases. *Annu Rev Public Health* 2005;26:191-212.
34. Reynolds MA, Aichelmann-Reidy ME, Branch-Mays GL, Gunsolley JC. The efficacy of bone replacement grafts in the treatment of periodontal osseous defects. A systematic review. *Ann Periodontol* 2003;8: 227-265.
35. Butz F, Bächle M, Ofer M, Marquardt K, Kohal RJ. Sinus augmentation with bovine hydroxyapatite/synthetic peptide in a sodium hyaluronate carrier (PepGen P-15 Putty): A clinical investigation of different healing times. *Int J Oral Maxillofac Implants* 2011;26:1317-1323.
36. Choo T, Marino V, Bartold PM. Effect of PDGF-BB and beta-tricalcium phosphate (β-TCP) on bone formation around dental implants: A pilot study in sheep. *Clin Oral Implants Res* 2013;24:158-166.
37. Nevins M, Nevins ML, Karimbux N, Kim SW, Schupbach P, Kim DM. The combination of purified recombinant human platelet-derived growth factor-BB and equine particulate bone graft for periodontal regeneration. *J Periodontol* 2012;83:565-573.
38. Bashutski J, Oh TJ, Chan HL, Wang HL. Guided tissue regeneration: A decision-making model. *J Int Acad Periodontol* 2011;13:48-57.
39. Shirmohammadi A, Chitsazi MT, Lafzi A. A clinical comparison of autogenous bone graft with and without autogenous periodontal ligament graft in the treatment of periodontal intrabony defects. *Clin Oral Investig* 2009;13:279-286.
40. Camelo MC, Nevins ML, Nevins M. Treatment of Class II furcations with autogenous bone grafts and e-PTFE membranes. *Int J Periodontics Restorative Dent* 2000;20:233-243.
41. Markou N, Pepelassi E, Vavouraki H, et al. Treatment of periodontal endosseous defects with platelet-rich plasma alone or in combination with demineralized freeze-dried bone allograft: A comparative clinical trial. *J Periodontol* 2009;80:1911-1919.
42. Gurinsky BS, Mills MP, Mellonig JT. Clinical evaluation of demineralized freeze-dried bone allograft and enamel matrix derivative versus enamel matrix derivative alone for the treatment of periodontal osseous defects in humans. *J Periodontol* 2004;75:1309-1318.
43. Nevins M, Camelo M, Nevins ML, Schenk RK, Lynch SE. Periodontal regeneration in humans using recombinant human platelet-derived growth factor-BB (rhPDGF-BB) and allogenic bone. *J Periodontol* 2003;74: 1282-1292.
44. Trejo PM, Weltman R, Caffesse R. Treatment of intraosseous defects with bioabsorbable barriers alone or in combination with decalcified freeze-dried bone allograft: A randomized clinical trial. *J Periodontol* 2000;71:1852-1861.
45. Tsao YP, Neiva R, Al-Shammari K, Oh TJ, Wang HL. Effects of a mineralized human cancellous bone allograft in regeneration of mandibular Class II furcation defects. *J Periodontol* 2006;77:416-425.
46. De Leonardis D, Garg AK, Pedrazzoli V, Pecora GE. Clinical evaluation of the treatment of Class II furcation involvements with bioabsorbable barriers alone or associated with demineralized freeze-dried bone allografts. *J Periodontol* 1999;70:8-12.
47. Vastardis S, Yukna RA, Mayer ET, Atkinson BL. Periodontal regeneration with peptide-enhanced anorganic bone matrix in particulate and putty form in dogs. *J Periodontol* 2005;76:1690-1696.
48. Döri F, Kovács V, Arweiler NB, et al. Effect of platelet-rich plasma on the healing of intrabony defects treated with an anorganic bovine bone mineral: A pilot study. *J Periodontol* 2009;80:1599-1605.
49. Sallum EA, Pimentel SP, Saldanha JB, et al. Enamel matrix derivative and guided tissue regeneration in the treatment of dehiscence-type defects: A histomorphometric study in dogs. *J Periodontol* 2004;75: 1357-1363.
50. Döri F, Huszár T, Nikolidakis D, Arweiler NB, Gera I, Sculean A. Effect of platelet-rich plasma on the healing of intrabony defects treated with

an anorganic bovine bone mineral and expanded polytetrafluoroethylene membranes. *J Periodontol* 2007;78:983-990.

51. Hanna R, Trejo PM, Weltman RL. Treatment of intrabony defects with bovine-derived xenograft alone and in combination with platelet-rich plasma: A randomized clinical trial. *J Periodontol* 2004;75:1668-1677.
52. Kaigler D, Avila G, Wisner-Lynch L, et al. Platelet-derived growth factor applications in periodontal and peri-implant bone regeneration. *Expert Opin Biol Ther* 2011;11:375-385.
53. Pietruska M, Pietruski J, Nagy K, Brecx M, Arweiler NB, Sculean A. Four-year results following treatment of intrabony periodontal defects with an enamel matrix derivative alone or combined with a biphasic calcium phosphate. *Clin Oral Investig* 2012;16:1191-1197.
54. Brown GD, Mealey BL, Nummikoski PV, Bifano SL, Waldrop TC. Hydroxyapatite cement implant for regeneration of periodontal osseous defects in humans. *J Periodontol* 1998;69:146-157.
55. Kothiwale SV, Anuroopa P, Gajiwala AL. A clinical and radiological evaluation of DFDBA with amniotic membrane versus bovine derived xenograft with amniotic membrane in human periodontal grade II furcation defects. *Cell Tissue Bank* 2009;10:317-326.
56. Harris RJ. A clinical evaluation of an allograft combined with a bioabsorbable membrane versus an alloplast/allograft composite graft combined with a bioabsorbable membrane. 100 consecutively treated cases. *J Periodontol* 1998;69:536-546.
57. Hall EE, Meffert RM, Hermann JS, Mellonig JT, Cochran DL. Comparison of bioactive glass to demineralized freeze-dried bone allograft in the treatment of intrabony defects around implants in the canine mandible. *J Periodontol* 1999;70:526-535.
58. Mellonig JT, Triplett RG. Guided tissue regeneration and endosseous dental implants. *Int J Periodontics Restorative Dent* 1993;13:108-119.
59. Roos-Jansåker AM, Renvert H, Lindahl C, Renvert S. Surgical treatment of peri-implantitis using a bone substitute with or without a resorbable membrane: A prospective cohort study. *J Clin Periodontol* 2007;34:625-632.
60. Aljateeli M, Fu JH, Wang HL. Managing peri-implant bone loss: Current understanding. *Clin Implant Dent Relat Res* 2012;14(Suppl. 1): e109-e118.
61. Schwarz F, Herten M, Sager M, Bieling K, Sculean A, Becker J. Comparison of naturally occurring and ligature-induced peri-implantitis bone defects in humans and dogs. *Clin Oral Implants Res* 2007;18: 161-170.
62. Khoury F, Buchmann R. Surgical therapy of peri-implant disease: A 3-year follow-up study of cases treated with 3 different techniques of bone regeneration. *J Periodontol* 2001;72:1498-1508.
63. Romanos GE, Nentwig GH. Regenerative therapy of deep peri-implant infrabony defects after CO2 laser implant surface decontamination. *Int J Periodontics Restorative Dent* 2008;28:245-255.
64. Tawil G, El-Ghoule G, Mawla M. Clinical evaluation of a bilayered collagen membrane (Bio-Gide) supported by autografts in the treatment of bone defects around implants. *Int J Oral Maxillofac Implants* 2001; 16:857-863.
65. Schwarz F, Sculean A, Bieling K, Ferrari D, Rothamel D, Becker J. Two-year clinical results following treatment of peri-implantitis lesions using a nanocrystalline hydroxyapatite or a natural bone mineral in combination with a collagen membrane. *J Clin Periodontol* 2008;35:80-87.
66. Schwarz F, Sahm N, Schwarz K, Becker J. Impact of defect configuration on the clinical outcome following surgical regenerative therapy of peri-implantitis. *J Clin Periodontol* 2010;37:449-455.
67. Lu SY, Huang CC. Resolution of an active peri-implantitis in a chronic steroid user by bone augmentation with PepGen P-15 and a barrier membrane. *J Oral Implantol* 2007;33:280-287.
68. Tözüm TF, Keçeli HG. Treatment of peri-implant defect with modified sandwich bone augmentation. Case report and follow-up. *N Y State Dent J* 2008;74:52-57.
69. Deppe H, Horch HH, Neff A. Conventional versus CO2 laser-assisted treatment of peri-implant defects with the concomitant use of pure-phase beta-tricalcium phosphate: A 5-year clinical report. *Int J Oral Maxillofac Implants* 2007;22:79-86.
70. Sahrmann P, Attin T, Schmidlin PR. Regenerative treatment of peri-implantitis using bone substitutes and membrane: A systematic review. *Clin Implant Dent Relat Res* 2011;13:46-57.
71. Kim YK, Yun PY, Lee HJ, Ahn JY, Kim SG. Ridge preservation of the molar extraction socket using collagen sponge and xenogeneic bone grafts. *Implant Dent* 2011;20:267-272.
72. Barone A, Aldini NN, Fini M, Giardino R, Calvo Guirado JL, Covani U. Xenograft versus extraction alone for ridge preservation after tooth removal: A clinical and histomorphometric study. *J Periodontol* 2008; 79:1370-1377.
73. Sisti A, Canullo L, Mottola MP, Covani U, Barone A, Botticelli D. Clinical evaluation of a ridge augmentation procedure for the severely resorbed alveolar socket: Multicenter randomized controlled trial, preliminary results. *Clin Oral Implants Res* 2012;23:526-535
74. Misch CE, Suzuki JB. Tooth extraction, socket grafting, and barrier membrane bone regeneration. In: Misch CE, ed. *Contemporary Implant Dentistry*, 3rd ed. St. Louis: Mosby; 2008:870-904.
75. Araújo MG, Lindhe J. Socket grafting with the use of autologous bone: An experimental study in the dog. *Clin Oral Implants Res* 2011;22:9-13.
76. Araújo MG, Lindhe J. Ridge preservation with the use of Bio-Oss collagen: A 6-month study in the dog. *Clin Oral Implants Res* 2009;20: 433-440.
77. Artzi Z, Weinreb M, Givol N, et al. Biomaterial resorption rate and healing site morphology of inorganic bovine bone and beta-tricalcium phosphate in the canine: A 24-month longitudinal histologic study and morphometric analysis. *Int J Oral Maxillofac Implants* 2004;19:357-368.
78. Wang HL, Tsao YP. Histologic evaluation of socket augmentation with mineralized human allograft. *Int J Periodontics Restorative Dent* 2008; 28:231-237.
79. Vance GS, Greenwell H, Miller RL, Hill M, Johnston H, Scheetz JP. Comparison of an allograft in an experimental putty carrier and a bovine-derived xenograft used in ridge preservation: A clinical and histologic study in humans. *Int J Oral Maxillofac Implants* 2004;19: 491-497.
80. Bashara H, Wohlfahrt JC, Polyzois I, Lyngstadaas SP, Renvert S, Claffey N. The effect of permanent grafting materials on the preservation of the buccal bone plate after tooth extraction: An experimental study in the dog. *Clin Oral Implants Res* 2012;23:911-917.
81. Mardas N, Chadha V, Donos N. Alveolar ridge preservation with guided bone regeneration and a synthetic bone substitute or a bovine-derived xenograft: A randomized, controlled clinical trial. *Clin Oral Implants Res* 2010;21:688-698.
82. Fu JH, Wang HL. Horizontal bone augmentation: The decision tree. *Int J Periodontics Restorative Dent* 2011;31:429-436.
83. Barone A, Varanini P, Orlando B, Tonelli P, Covani U. Deep-frozen allogeneic onlay bone grafts for reconstruction of atrophic maxillary alveolar ridges: A preliminary study. *J Oral Maxillofac Surg* 2009;67: 1300-1306.
84. Schwarz F, Ferrari D, Balic E, Buser D, Becker J, Sager M. Lateral ridge augmentation using equine- and bovine-derived cancellous bone blocks: A feasibility study in dogs. *Clin Oral Implants Res* 2010;21: 904-912.
85. Greenberg JA, Wiltz MJ, Kraut RA. Augmentation of the anterior maxilla with intraoral onlay grafts for implant placement. *Implant Dent* 2012;21:21-24.
86. Cordaro L, Amadé DS, Cordaro M. Clinical results of alveolar ridge augmentation with mandibular block bone grafts in partially edentulous patients prior to implant placement. *Clin Oral Implants Res* 2002; 13:103-111.
87. Spin-Neto R, Stavropoulos A, Dias Pereira LA, Marcantonio E Jr., Wenzel A. Fate of autologous and fresh-frozen allogeneic block bone grafts used for ridge augmentation. A CBCT-based analysis. *Clin Oral Implants Res* 2013;24:167-173.
88. Chaushu G, Mardinger O, Peleg M, Ghelfan O, Nissan J. Analysis of complications following augmentation with cancellous block allografts. *J Periodontol* 2010;81:1759-1764.
89. Demarosi F, Leghissa GC, Sardella A, Lodi G, Carrassi A. Localised maxillary ridge expansion with simultaneous implant placement: A case series. *Br J Oral Maxillofac Surg* 2009;47:535-540.
90. Sethi A, Kaus T. Maxillary ridge expansion with simultaneous implant placement: 5-year results of an ongoing clinical study. *Int J Oral Maxillofac Implants* 2000;15:491-499.
91. Chiapasco M, Casentini P, Zaniboni M. Bone augmentation procedures in implant dentistry. *Int J Oral Maxillofac Implants* 2009;24(Suppl): 237-259.
92. Esposito M, Grusovin MG, Felice P, Karatzopoulos G, Worthington HV, Coulthard P. The efficacy of horizontal and vertical bone augmentation procedures for dental implants: A Cochrane systematic review. *Eur J Oral Implantology* 2009;2:167-184.
93. Pieri F, Corinaldesi G, Fini M, Aldini NN, Giardino R, Marchetti C. Alveolar ridge augmentation with titanium mesh and a combination of autogenous bone and anorganic bovine bone: A 2-year prospective study. *J Periodontol* 2008;79:2093-2103.
94. Barboza EP, Stutz B, Ferreira VF, Carvalho W. Guided bone regeneration using nonexpanded polytetrafluoroethylene membranes in

preparation for dental implant placements — A report of 420 cases. *Implant Dent* 2010;19:2-7.

95. Fiorellini JP, Kim DM, Nakajima Y, Weber HP. Osseointegration of titanium implants following guided bone regeneration using expanded polytetrafluoroethylene membrane and various bone fillers. *Int J Periodontics Restorative Dent* 2007;27:287-294.
96. Proussaefs P, Lozada J, Kleinman A, Rohrer MD, McMillan PJ. The use of titanium mesh in conjunction with autogenous bone graft and inorganic bovine bone mineral (Bio-oss) for localized alveolar ridge augmentation: A human study. *Int J Periodontics Restorative Dent* 2003;23:185-195.
97. Lee A, Brown D, Wang HL. Sandwich bone augmentation for predictable horizontal bone augmentation. *Implant Dent* 2009;18:282-290.
98. Park SH, Lee KW, Oh TJ, Misch CE, Shotwell J, Wang HL. Effect of absorbable membranes on sandwich bone augmentation. *Clin Oral Implants Res* 2008;19:32-41.
99. Urban IA, Nagursky H, Lozada JL. Horizontal ridge augmentation with a resorbable membrane and particulated autogenous bone with or without anorganic bovine bone-derived mineral: A prospective case series in 22 patients. *Int J Oral Maxillofac Implants* 2011;26:404-414.
100. Proussaefs P, Lozada J. The use of resorbable collagen membrane in conjunction with autogenous bone graft and inorganic bovine mineral for buccal/labial alveolar ridge augmentation: A pilot study. *J Prosthet Dent* 2003;90:530-538.
101. Rocchietta I, Fontana F, Simion M. Clinical outcomes of vertical bone augmentation to enable dental implant placement: A systematic review. *J Clin Periodontol* 2008;35(Suppl. 8):203-215.
102. Fritz ME, Eke PI, Malmquist J, Hardwick R. Clinical and microbiological observations of early polytetrafluoroethylene membrane exposure in guided bone regeneration. Case reports in primates. *J Periodontol* 1996;67:245-249.
103. Lindfors LT, Tervonen EA, Sándor GK, Ylikontiola LP. Guided bone regeneration using a titanium-reinforced ePTFE membrane and particulate autogenous bone: The effect of smoking and membrane exposure. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2010;109:825-830.
104. Felice P, Marchetti C, Iezzi G, et al. Vertical ridge augmentation of the atrophic posterior mandible with interpositional bloc grafts: Bone from the iliac crest vs. bovine anorganic bone. Clinical and histological results up to one year after loading from a randomized-controlled clinical trial. *Clin Oral Implants Res* 2009;20:1386-1393.
105. Rothamel D, Schwarz F, Herten M, et al. Vertical ridge augmentation using xenogenous bone blocks: A histomorphometric study in dogs. *Int J Oral Maxillofac Implants* 2009;24:243-250.
106. Langer B, Langer L, Sullivan RM. Vertical ridge augmentation procedure using guided bone regeneration, demineralized freeze-dried bone allograft, and miniscrews: 4- to 13-year observations on loaded implants. *Int J Periodontics Restorative Dent* 2010;30:227-235.
107. Urban IA, Jovanovic SA, Lozada JL. Vertical ridge augmentation using guided bone regeneration (GBR) in three clinical scenarios prior to implant placement: A retrospective study of 35 patients 12 to 72 months after loading. *Int J Oral Maxillofac Implants* 2009;24:502-510.
108. Pjetursson BE, Tan WC, Zwahlen M, Lang NP. A systematic review of the success of sinus floor elevation and survival of implants inserted in combination with sinus floor elevation. *J Clin Periodontol* 2008;35 (Suppl. 8):216-240.
109. Lundgren S, Andersson S, Gualini F, Sennerby L. Bone reformation with sinus membrane elevation: A new surgical technique for maxillary sinus floor augmentation. *Clin Implant Dent Relat Res* 2004;6: 165-173.
110. Xu H, Shimizu Y, Ooya K. Histomorphometric study of the stability of newly formed bone after elevation of the floor of the maxillary sinus. *Br J Oral Maxillofac Surg* 2005;43:493-499.
111. Kim HR, Choi BH, Xuan F, Jeong SM. The use of autologous venous blood for maxillary sinus floor augmentation in conjunction with sinus membrane elevation: An experimental study. *Clin Oral Implants Res* 2010;21:346-349.
112. Hatano N, Sennerby L, Lundgren S. Maxillary sinus augmentation using sinus membrane elevation and peripheral venous blood for implant-supported rehabilitation of the atrophic posterior maxilla: Case series. *Clin Implant Dent Relat Res* 2007;9:150-155.
113. Cricchio G, Sennerby L, Lundgren S. Sinus bone formation and implant survival after sinus membrane elevation and implant placement: A 1- to 6-year follow-up study. *Clin Oral Implants Res* 2011;22:1200-1212.
114. Zijderveld SA, Schulten EA, Aartman IH, ten Bruggenkate CM. Long-term changes in graft height after maxillary sinus floor elevation with different grafting materials: Radiographic evaluation with a minimum follow-up of 4.5 years. *Clin Oral Implants Res* 2009;20:691-700.
115. Maiorana C, Sigurtà D, Mirandola A, Garlini G, Santoro F. Sinus elevation with alloplasts or xenogenic materials and implants: An up-to-4-year clinical and radiologic follow-up. *Int J Oral Maxillofac Implants* 2006;21:426-432.
116. Cordaro L, Bosshardt DD, Palattella P, Rao W, Serino G, Chiapasco M. Maxillary sinus grafting with Bio-Oss or Straumann Bone Ceramic: Histomorphometric results from a randomized controlled multicenter clinical trial. *Clin Oral Implants Res* 2008;19:796-803.
117. Nkenke E, Stelzle F. Clinical outcomes of sinus floor augmentation for implant placement using autogenous bone or bone substitutes: A systematic review. *Clin Oral Implants Res* 2009;20(Suppl. 4):124-133.
118. Lambert F, Léonard A, Drion P, Sourice S, Layrolle P, Rompen E. Influence of space-filling materials in subantral bone augmentation: Blood clot vs. autogenous bone chips vs. bovine hydroxyapatite. *Clin Oral Implants Res* 2011;22:538-545.