

From Our Office to Yours...

In the past decade, the regeneration of bone defects for the placement of dental implants has become both more predictable and successful, largely due to the adjunctive use of biologic modifiers.

As periodontal specialists, we initially focused on regeneration of the bone around compromised teeth. Newer materials and techniques now allow us to provide an improved bone ridge foundation to support your prosthodontic procedures, and improve the long-term esthetic outcome for our patients.

*This issue of **The PerioDontaLetter** describes the current, improved biomaterials we use, and discusses the advances in tissue engineering, and potential use of 3-D printing for bone scaffold design.*

We hope you find this information helpful.

As always, we welcome your comments and suggestions on these significant advancements in the regeneration of bone defects for dental implant placement.

New Bone Grafting Technologies Utilizing Biologic Modifiers

Several methods are available to augment the deficient ridge, including bone grafting, guided tissue/bone regeneration (GTR/GBR), bone block grafting, and ridge expansion, with or without the application of biologic modifiers.

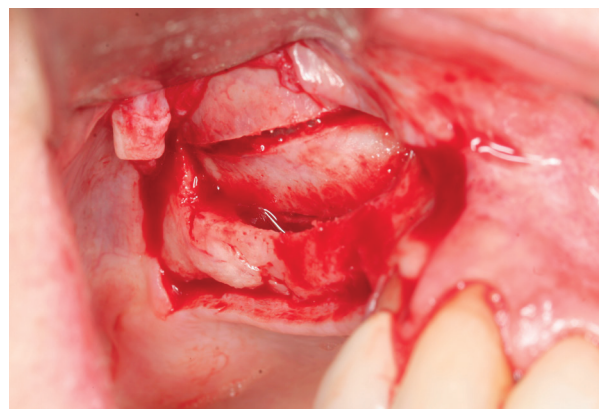
The choice of graft materials and augmentation techniques will depend on several factors, including the degree of atrophy, the morphology of the osseous defect, anticipated type of prosthesis, and clinician or patient preferences.

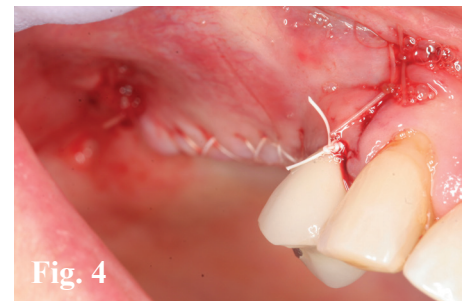
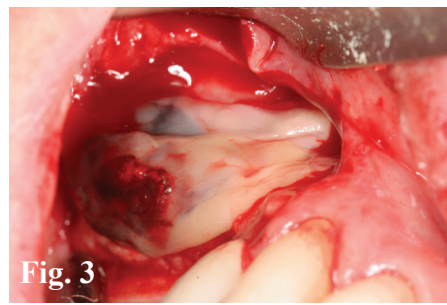
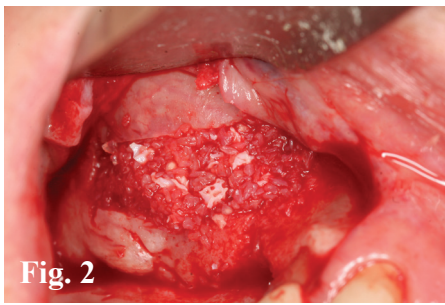
Bone Grafting Materials

Four major bone graft materials are commonly used for periodontal regeneration: autogenous grafts or autografts, allografts, xenografts and alloplasts (synthetics). These graft materials may function as osteogenic, osteoinductive and/or osteoconductive scaffolds.

Autografts — bone obtained from the patient — are still regarded as the

Figure 1.
*Surgical entry
was performed
for a sinus lift.
(See Figures 2,
3 and 4 on page
2.)*





Figures 2, 3 and 4. A bone graft was placed to increase vertical height. The graft was covered by platelet-rich fibrin (PRF) to regenerate a greater amount and higher quality of bone, and to act as a barrier to soft tissue ingrowth. Primary closure of the wound was achieved to promote rapid healing.

“gold standard” in bone grafting because of superior osteoinduction and osteoconduction properties. However, there are potential disadvantages, including donor site morbidity, the limited volume of bone which can usually be acquired, increased surgical time, costs, and the unpredictability of the replacement rate of cortical autografts. On the other hand, cancellous, autogenous bone from specific regions produces a greater amount of osteogenic cells.

Allografts derived from another human donor are generally freeze-dried bone or demineralized freeze-dried bone. These allografts can act not only as osteoconductive scaffolds, but may also have some osteoinductive potential due to the presence of proteins, such as bone morphogenetic proteins (BMP).

Xenografts obtained from animals are widely used in clinical periodontal

regeneration and sinus grafts. Bovine, equine, and porcine-derived bone mineral are the most commonly used xenografts.

Recently, marine coral grafts have shown potential for improved defect regeneration as the coralline calcium carbonate grafts permit rapid new bone deposition, possess a porosity which allows new bone infiltration, and are not subject to fibrous encapsulation.

Bone substitutes, or alloplasts, perform well in sites with favorable osseous morphology, including socket bone grafting, sinus bone grafting, localized implant repair, and modest horizontal augmentation.

The most routinely used alloplastic bone grafting materials include hydroxyapatite, tricalcium phosphate (TCP) and bioactive glass. Calcium phosphate biomaterials are of great

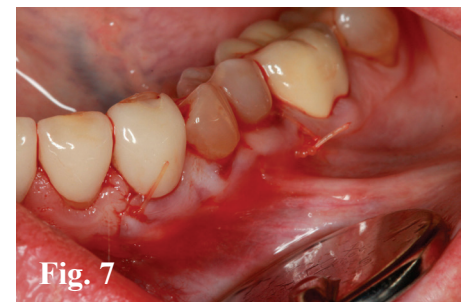
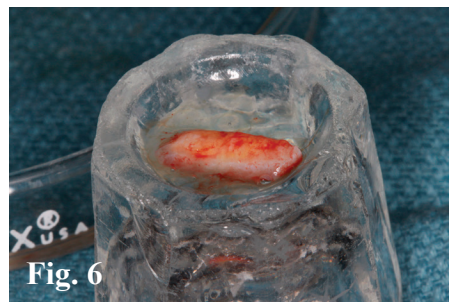
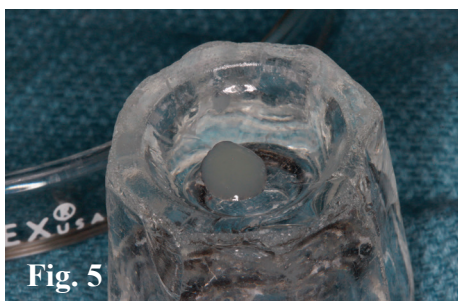
interest as bone replacement graft materials as they have a similar composition to bone mineral.

Barrier Membranes

Bone grafting materials are often used in combination with barrier membranes to prevent the down-growth of epithelial cells into the periodontal defect space, and to stabilize, contain and preserve the graft materials.

A variety of resorbable and non-resorbable barrier membranes have been synthesized for periodontal GTR/GBR applications. Currently, the most commonly used resorbable membranes are made of collagen.

Some barrier membranes need to be tacked down to to prevent movement, which might interfere with new bone formation.



Figures 5, 6 and 7. Connective tissue donor material was soaked in enamel matrix derivative (EMD, Emdogain) to promote faster reepithelialization, resolution of inflammation, accelerated blood vessel formation, wound closure, and rapid healing.

To overcome membrane compression/collapse, non resorbable membranes have been developed using stiff materials such as titanium mesh or metal reinforced expanded-polytetrafluoroethylene (ePTFE) for the treatment of complex periodontal defects.

Two of the most important responsibilities of the restorative dentist when membranes are used are to make sure there is no pressure on the wound from provisional appliances during the healing phase, and to allow the proper amount of time for bone replacement and maturation. Pressure on the wound from a provisional will cause the wound to fail, and likely compromise the bone regeneration process.

Biologic Modifiers

Growth factors are the patient's naturally-occurring, signaling proteins which can recruit cells and stimulate cell proliferation and differentiation. For many years, surgeons have used

autologous, blood-derived growth factors in combination with bone grafts to enhance bone formation, accelerate graft revascularization and enhance soft tissue healing. Various types of platelet concentrates, such as platelet-rich plasma (PRP), platelet-rich fibrin (PRF), and plasma rich in growth factors (PRGF), have been shown to be more effective at regenerating a greater amount and higher quality of bone with all types of graft materials than when bone grafts are used alone.

Recombinant growth factors are genetically-engineered versions of platelet-derived growth factors produced in the laboratory. They are identical in structure and action to the naturally-occurring signaling protein cells.

Commercially-available growth factors which have shown promising results in ridge augmentation include recombinant platelet-derived growth factor (rhPDGF-BB, GEM 21S), and recombinant bone morphogenetic protein 2 (rhBMP-2, Infuse Bone Graft).

GEM 21S has been approved by the Food and Drug Administration (FDA) for the treatment of moderate to severe periodontal intraosseous defects. Infuse Bone Graft has FDA approval for the repair of extraction socket defects and sinus bone grafting.

BMP plays a crucial role in bone remodeling and has shown promising results for applications such as sinus augmentation and alveolar ridge preservation. The most commonly used and investigated BMPs for bone regeneration applications are BMP 2 & 7.

Enamel matrix derivative (EMD, Emdogain) has attracted increased interest in bone regeneration procedures. A recent review by the American Academy of Periodontology concluded that EMD is generally comparable with demineralized freeze-dried bone allograft and GTR in inducing faster reepithelialization, wound closure, resolution of inflammation and accelerated blood vessel formation.

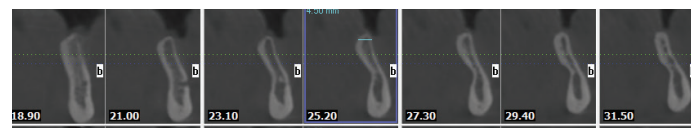
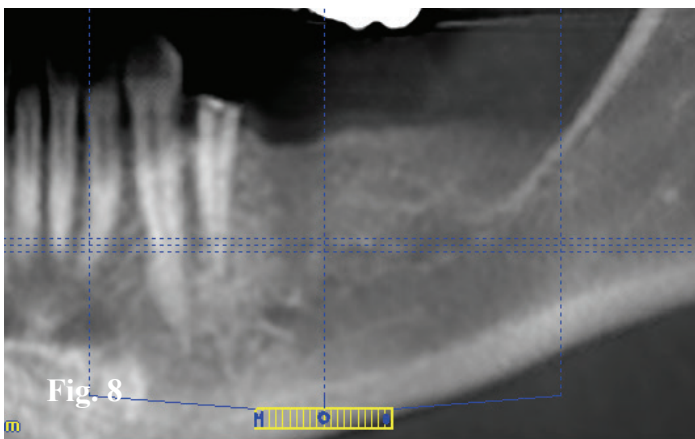


Fig. 9

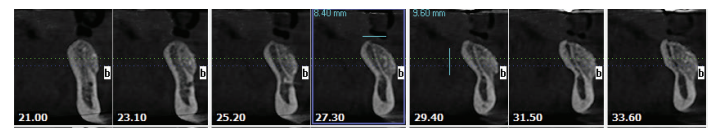
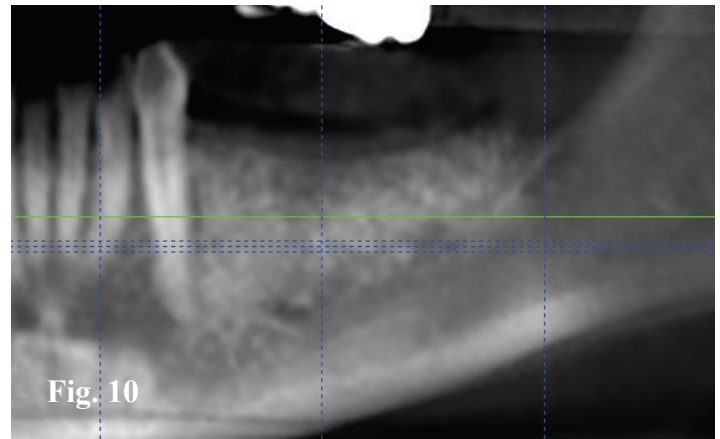
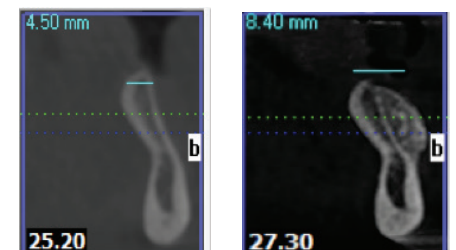
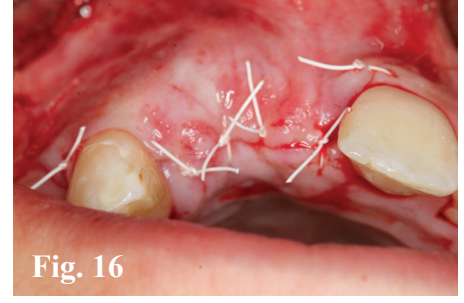
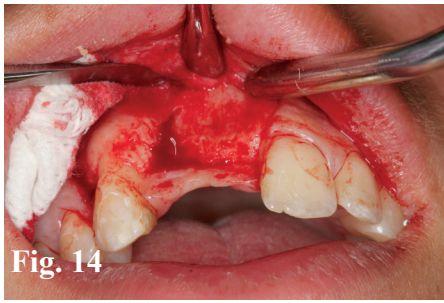


Fig. 11

Figures 8, 9, 10, 11, 12 and 13. Pre- and post-operative CT scans of a ridge augmentation case. Recombinant bone morphogenetic protein 2 (rhBMP-2, Infuse Bone Graft) was added to xenograft particulate bone graft, resulting in significant ridge width development.



Figs. 12 & 13



Figures 14, 15 and 16. Surgical entry was obtained to expand the maxillary anterior ridge. A bone graft was placed and covered with PRF to stimulate bone growth and prevent soft tissue ingrowth, similar to a barrier membrane. Primary closure of the wound was achieved to promote rapid healing.

Tissue Engineering

Regenerating bone by combining cells from the body with growth factors and scaffold biomaterials is often referred to as the tissue engineering triad. This developing field offers an alternative strategy to the harvesting of bone from the patient.

Recently, the American Academy of Periodontology Regeneration Workshop issued a consensus report that protein and peptide therapy, cell-based therapy, genetic therapy, scaffolds, bone anabolics, and lasers are expanding the potential of regenerating periodontal tissue.

One promising technique in the future of periodontal regeneration is the release of a combination of growth factors over time to mimic the normal progression of bone formation.

Another technique which shows promise for growth factor delivery is the application of gene therapy. Genetic material is transferred into the genome of the target cells to boost their regenerative potential by increasing the production and concentration of differentiation and growth factors.

Biodegradable scaffolds to maintain space, allow vascular ingrowth, and promote cell adhesion are being researched. Custom titanium meshes have been developed to protect growth

factor-enhanced grafts to improve the results of vertical and horizontal bone augmentation.

Additionally, allogeneic and xenograft block bone grafts may be milled to custom fit an atrophic ridge. Radiographic imaging is being integrated with CAD/CAM technology to fabricate custom devices. Using dedicated software, a Cone Beam Computed Tomography (CBCT) scan of the jaw can be used to produce a stereolithographic model for reconstructive planning.

Custom-made, resorbable scaffolds are routinely fabricated using 3-dimensional printers. The use of faster resorbing polymers with a highly porous structure in these scaffolds has been shown to improve vascularization and tissue ingrowth

The printed porous scaffold may then be seeded with stem cells from bone marrow, adipose tissue, and cryopreserved umbilical cord blood to form new bone tissue.

A concentrate of stem cells from the iliac crest bone marrow may be produced to combine with bone substitutes, or to seed a porous matrix.

In-vitro amplification of osteoblasts or osteoprogenitor cells grown on 3D constructs can increase the regenerative potential of bone. Cell seeding with stem cells appears to have great future potential.

Another strategy for customized bone reconstruction is the infusion of a porous

biodegradable scaffold with osteoinductive growth factors that recruit host cells and guide bone ingrowth.

The application of biologic agents to dental implant surfaces may be another alternative for encouraging bone formation in deficient sites.

Conclusion

We clinicians are fortunate to practice implant dentistry at a time when there are numerous and innovative techniques currently available to us, and those that hold future promise, to successfully treat patients with deficient bone.

We need to continue to weigh the advantages and disadvantages of these exciting new tissue engineering techniques against the benefits of more traditional surgical approaches, which have also been shown to enhance biologic response with minimal potential for morbidity.

Clearly, utilizing these emerging technologies has the potential for predictably enhancing the results of our efforts to regenerate bone.

