ISSN: 2581-5989
PubMed - National Library of Medicine - ID: 101738774

International Journal of Dental Science and Innovative Research (IJDSIR)

IJDSIR : Dental Publication Service

Available Online at: www.ijdsir.com

Volume – 6, Issue – 2, April - 2023, Page No. : 160 – 174

Current status of bone grafts in periodontal therapy

[1]Dr. Chaganti Siri Sravani, [2]Dr. Mounika Basavaraju, [2]Dr. Sitamahalakshmi K, [2]Dr. Satya Kurada, [3]Dr. Suryakanth Malgikar

[1] Consultant Dentist, Prasidh Hospital, Hyderabad, Telangana, India.

[2] Senior Lecturer, Department of Periodontology, Kamineni Institute of Dental Sciences, Narketpally, Nalgonda (Dist.), Telangana, India.

[3]Associate Professor, Department of Periodontology, Kamineni Institute of Dental Sciences, Narketpally, Telangana, India.

Corresponding Author: Dr. Suryakanth Malgikar, Associate Professor, Department of Periodontology, Kamineni Institute of Dental Sciences, Narketpally, Nalgonda (Dist.) Telangana – 508 254.

Citation of this Article: Dr. Chaganti Siri Sravani, Dr. Mounika Basavaraju, Dr. Sitamahalakshmi K, Dr. Satya Kurada, Dr. Suryakanth Malgikar, "Current status of bone grafts in periodontal therapy", IJDSIR- April - 2023, Volume – 6, Issue - 2, P. No. 160 – 174.

Type of Publication: Review Article

Conflicts of Interest: Nil

Abstract

Bone replacement grafts are widely used to promote bone formation and periodontal regeneration. Bone grafting, placing bone or bone substitutes into defects created by the disease process, acts like a scaffold upon which the body generates new bone. A wide range of bone grafting materials, including bone grafts and bone graft substitutes, have been applied and evaluated clinically, including autografts, allografts, xenografts, and alloplasts. To Date, histologic evidence in humans indicates that bone grafting is the only treatment that leads to the regeneration of bone, cementum, and a functionally oriented new periodontal ligament coronal to the base of a previous osseous defect.

Keywords: Periodontal Regeneration, Autograft, Allograft, Xenograft

Introduction

Bone replacement grafts are widely used to promote new bone formation and periodontal regeneration therapy, especially in intrabony defects. Bone grafting materials function, in part, as structural scaffolds and matrices for the attachment and proliferation of anchorage-dependent osteoblasts. Various types of grafting materials have been introduced in reconstructive periodontal treatment based on their ability to facilitate the reconstruction of the lost supporting apparatus through the following mechanisms.[1]

1. Osteogenesis (contain bone-forming cells)

2. Osteoconduction (serves as a scaffold and space provision for bone formation)
3. Osteoinduction (contain bone-inducing substances).

Historical Background

The use of bone grafts for reconstructing intra-osseous defects produced by a periodontal disease dates back to Hegedus in 1923. He reported success in six cases by transplanting autogenous bone from the tibia to the jaws to treat "advanced pyorrhea". After Hegedus, it was revived in 1965 by Nabers and O'leary, they used shavings of cortical bone removed by hand chisels during osteoplasty and ostectomy and they were used to treat one, two-wall defect.[2] Schallhorn et al.[3] used Allografts of iliac bone and marrow. Rivault et al in 1971 laid down the requirements of successful grafting. Froum et al in 1975 reported a 73% fill with osseous coagulum and 60.7% fill with hip marrow. Richardson et al in 1999 used **Bio-Oss** a bovine bone from which all inorganic components are removed and used for regeneration.

The objective of Bone Graft Therapy

The objectives of bone graft therapy as stated by Schallhorn et al.[3] in 1970 include:

- Probing depth reduction
- Clinical attachment gain
- Bone fill of the osseous defect
- Regeneration of new bone, cementum, and periodontal ligament.

Criteria for evaluation of Graft Success for Periodontal Regeneration[4]

For any graft material to be considered a successful regenerative material, it should have clear histological, clinical, and radiographic evidence of the following criteria:

1. **Biologic acceptability:** The graft should not have any side effects or cause any unwanted tissue reaction.
2. **Resorbability:** The graft should resorb slowly and be replaced by the patient's bone.
3. **Regeneration:** The graft should have evidence of regenerative ability with the formation of new bone, cementum, and periodontal ligament fibers.
4. **Defect fill:** The graft should have evidence of bone fill.
5. **Stability:** Treatment should be stable at re-evaluation visits.

Classification of bone graft materials

Autogenous Bone Grafts

It is harvested from the patient's own body which is an ideal material because of its osteoconductive and osteoinductive properties as it contains a source of osteoprogenitor cells. The autogenous bone can be derived from both intraoral and extraoral sites. It is still considered the "Gold Standard" by which other grafting materials are compared.[5]

Sources of Autogenous Grafts

Autogenous bone can be harvested from intraoral donor sites (mandibular symphysis and ramus, maxillary tuberosity, edentulous areas, tori) or extraoral sites (iliac crest, tibia, calvaria). (Figure 1) represents the sources of autogenous grafts.[6] Several types of autogenous grafts have been proposed in the literature. They include cortical bone chips, osseous coagulum, bone blend, intraoral and extraoral cancellous bone, and marrow.

1. **Cortical Bone Chips:** Nabers and O'Leary (1965) reported that shavings of cortical bone were removed by hand chisels during osteoplasty and osteotomy.

   Cortical chips, due to their relatively large particle size (1,559.6×183μm) and higher potential for

sequestration, were replaced by autogenous osseous coagulum and bone blend.[7]

2. **Osseous Coagulum:** Intra-oral bone, when obtained with high- or low-speed round burs and mixed with blood, becomes a coagulum.[8,9] A number 6 or 8 round carbide bur, rotating at 25000 to 30000 rpm, without irrigation, produces bone dust which when coated with blood makes an osseous coagulum.
3. **Bone Blend:** Bone blend is cortical or cancellous bone that is procured with a trephine or rongeurs, placed in an amalgam capsule, and triturated to the consistency of a slushy osseous mass. The resultant particle size is in the range of 210 x 105µm. Froum et al.[10] reported the osseous coagulum-bone-blend type of grafts provided 2.98 mm coronal growth of alveolar bone, compared with 0.66 mm obtained when open flap debridement alone was used.
4. **Intraoral Cancellous Bone and Marrow:** Healing bony wounds, healing extraction sockets, edentulous ridges, Mandibular Retromolar areas, and the Maxillary tuberosity have all been used as sources of intraoral cancellous bone and marrow.[11]
5. **Extra-oral Cancellous Bone and Marrow:** Extraoral autogenous grafts can be harvested from the iliac crest (Anterior or Posterior), rib, and calvarium. Schallhorn in 1968, described the first autogenous Iliac bone graft in one case report where a bone marrow biopsy was immediately implanted into interproximal bony craters between both lower canines and lateral incisors. At 5 months of re-entry, the defects appeared filled. The main disadvantages of iliac crest bone graft are sequestration, the need for general anesthesia, prolonged postoperative recovery, root resorption, ankylosis, morbidity and/or limping.[12,13,14,15,16]

Allografts

The most commonly used forms of allografts in Periodontal Practice are:

1. **Fresh-frozen bone allografts (FFB):** Fresh frozen cancellous bone provides the highest osteoconductive and osteoinductive potential among all allograft materials available for use. However, due to the risk of disease transmission, antigenicity and extensive cross-matching fresh-frozen allografts are not used anymore.[17,18]
2. **Freeze-dried bone allografts (FDBA):** Undemineralized FDBA was introduced to periodontal therapy in 1976.[19] Freeze drying removes approximately 95% of the water from bone by a process of sublimation in a vacuum. Although freeze drying kills all cells, the morphology, solubility, and chemical integrity of the original specimen are maintained relatively intact.[20,21] Freeze drying also markedly reduces the antigenicity of a periodontal bone allograft.[22,23] Cortical FDBA demonstrates greater osteoinductive potential due to the growth factors stored in the matrix.[24]

Esthetic ridge preservation procedures utilizing freeze-dried bone allograft (FDBA) and rhPDGF-BB (platelet-derived growth factor-BB) demonstrate that growth factor along with enhanced bone matrix significantly induces bone and soft tissue healing. FDBA used in combination with absorbable barrier membranes has been used as a replacement for autograft blocks for ridge augmentation.[25]

Disadvantages: Cost, Slow revascularization, and lack of patient acceptance due to fear of transfer of disease from the donor.[26]

3. **Demineralized freeze-dried bone allograft (DFDBA):** Urist and co-workers showed through numerous animal experiments that demineralization

of a cortical bone graft induces new bone formation and greatly enhances its osteogenic potential.[27,28] This graft material induces the host undifferentiated mesenchymal cells to differentiate into osteoblasts with the subsequent formation of new bone. The demineralization of the allograft with HCl induces the bone-inducing agent, which has been called the bone morphogenic proteins.[29] DFDBA has been used extensively in the treatment of periodontal osseous defects. Controlled clinical studies documented considerable bone fill-in sites treated with DFDBA as compared to nongrafted sites.[30,31]

In a study platelet-rich plasma was combined with decalcified freeze-dried bone allograft for the treatment of non-contained human intrabony periodontal defects, and results revealed that in non-contained defects addition of PRP to DFDBA significantly enhanced the regenerative output obtained compared with bone graft alone.[32] Histological evidence of complete regeneration in humans with new cementum, periodontal ligament, and bone amounting to 80% of the original defect depth was reported at sites treated with DFDBA.[33] DFDBA is the only bone graft proven to result in periodontal regeneration in controlled human histological studies and is recognized in the consensus report of the 1996 World Workshop in Periodontics to fulfill all criteria for promotion of periodontal regeneration.[34]

Disadvantages: Cost, lack of patient acceptance due to fear of disease transfer from the donor, and radiolucency of the material.

Xenografts

A xenograft is a tissue transferred between genetically dissimilar members of different species. It is osteoconductive, biocompatible, and structurally similar to human bone. There are two sources of xenografts used for bone replacement in periodontics: Bovine bone and Natural coral.[35,36]

1. **Bovine-derived bone replacement graft:** The xenograft most commonly used in periodontal regeneration procedures is the deproteinized bovine bone mineral, commercially known as Bio-Oss®, with 75-80% porosity and crystal size of approximately 10 mm in the form of cortical granules which is processed to yield natural bone mineral without the organic elements.[37] Bovine bone is processed for the elimination of its organic part leaving a hydroxyapatite ‘‘skeleton” of a microporous structure of cortical and cancellous bone, similar to that of the human body. It has been suggested that this type of graft acts as an osteoconductive scaffold and enables bone growth with subsequent integration with the host’s bone.[38]

A study evaluated the treatment of intrabony defects with Bovine-Derived Xenograft alone and in combination with Platelet-Rich Plasma, and concluded that the addition of a high concentration of autologous platelets to a bovine-derived xenograft to treat intrabony defects significantly improved clinical periodontal response in terms of PPD reduction and CAL gain.[39]

2. **Coralline calcium carbonate:** Bicoral (Inoteb, Saint Gonnery, France) is calcium carbonate obtained from natural coral, Genus **PORITES,** and is composed primarily of aragonite (> 98% calcium carbonate). It is biocompatible and resorbable with a pore size of 100 to 200 μm, similar to the porosity of spongy bone.[40,41,42] Coralline calcium carbonate grafts have high osteoconductive potential allowing for new bone deposition to occur rapidly after implantation.[43] Coralline calcium carbonate was associated with a significant gain in the periodontal ligament (PDL) clinical attachment, reduction of

probing depths, and greater defect fill in periodontal regeneration applications.[44,45,46]

Drawbacks: Major drawbacks associated with Xenografts include- Risk of Disease transmission, and Graft Rejection.[47]

Alloplastic materials:

In addition to bone graft materials, many alloplastic materials have been tried for the restoration of the periodontium. These include plaster of Paris, Polymers, ceramics, Calcium carbonate, Calcium Phosphates, Hydroxyapatite, and Bioactive Glass. Figure. 1 represents various types of commercially available alloplastic grafts. Alloplastic materials can be manufactured in various forms and with varying physicochemical properties. They can be made available in both resorbable and non-resorbable forms and can be customized with varying levels of porosity and pore sizes.[48,49,50]

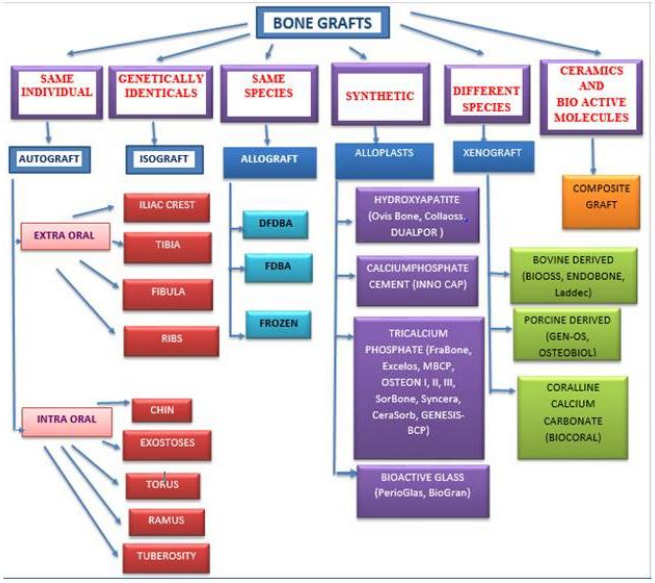

Figure 1: Classification of Bone graft Materials with their trade names.

Hydroxyapatite

Hydroxyapatite (HA) is one of the most widely used CaP graft biomaterials in both the research and clinical fields. HA has a similar composition and structure to natural bone minerals. Synthetic HA ($Ca_{10}(PO_4)_6(OH)_2$), is available and used in various forms: (Table 1).[51]

1) Porous non-resorbable

2) Solid non-resorbable

3) Resorbable (non-ceramic, porous)

PRODUCT NAME	DELIVERY	COMPOSITION
OSSABASE-HA	GRANULES	HA
OVIS BONE-HA	GRANULES	HA
COLLAOSS (BLOCK), OOSSBONE COLLAGEN	PLUG	HA (90%±5%) & collagen (10%±5%)
COLLAOSS (PUTTY)	GRANULE	HA (90%±5%) & collagen (10%±5%)
COLLAOSS (SYRINGE)	INJECTABLE	HA (90%±5%) & collagen (10%±5%)
DUALPOR COLLAGEN D-PUTTY	BLOCK	HA (60%) +bovine collagen (0.3%) & distilled water (39.7%)
DUALPOR COLLAGEN D	INJECTABLE	HA (60%) +bovine collagen (0.3%) & distilled water (39.7%)

Table 1: Commercially available HA-based Biomaterials

HA is non-osteogenic, not conclusively osteoinductive, but rather functions as an osteophilic and osteoconductive graft material. The resorptive potential of HA is dependent upon the temperature at which it is

processed. When prepared at higher temperatures the HA produced is dense, non-resorbable, and has a larger crystal size.[52]

Other forms of Hydroxyapatite available include: -

A) The coralline porous non-resorbable hydroxyapatite is a replica of a marine coral skeleton, **Porites.** After the organic components of the coral have been removed, the aragonite of the coral skeleton is converted to HA by treatment with an ammonium phosphate at elevated temperature and pressure

B) The resorbable non-ceramic hydroxyapatite is highly microporous, non-sintered (non-ceramic), composed of small particles measuring 300-400 mm (35-60 mesh), with a controlled, predictable rate of resorption. As the material resorbs, it acts as a mineral reservoir and predictably induces new bone formation via osteoconductive mechanisms. The material appears to be very biocompatible in both hard and soft tissues

C) **Nano-crystalline hydroxyapatite (NHA):** Nano-particular hydroxyapatite not only provides the benefits of traditional hydroxyapatites but also resorbs. The particle size was reported to be 18ηm on average, which allows for an accelerated substitution by vital bone**.** Nano-HA offers a new approach for inducing periodontal cell differentiation. Many studies have shown that nano-HA increases the protein synthesis of PDL cells, improves the activity of alkaline phosphatase, induces cell differentiation, effectively promotes periodontal tissue regeneration and formation of new teeth attachments, and affects teeth phenotypic differentiation.[53,54,55]

Nano-sized materials have a stimulatory effect on mesenchymal stem cells with an increase in protein absorption, and osteoblast adhesion and it was demonstrated that nano-HA stimulates the local alveolar osteoblasts to produce relevant bone-specific BMPs, which are known to initiate and regulate bone formation starting from the progenitor cells. Furthermore, the nano-HA is associated with a significant increase in the expression of several important markers of osteogenesis such as alkaline phosphatase, osteocalcin, and osteonectin.[56] **Advantages** of using hydroxyapatite are: - (1) Immunoreaction can be ignored (2) Postoperative morphologic changes and volume decreases do not occur if small blocks and chips are adequately packed during surgery (3) Post-operative adsorption of hydroxyapatite, if any, is slight and slow and is replaced by bone (4) Cement fixation performed on a layer of hydroxyapatite particles prevents the harmful influence of polyethylene wear particles of cement interface.

Disadvantages: - Particles don't tend to stay in place in a bleeding site, and there is a relatively slow restoration of bone within the assemblage of particles.[57]

Tricalcium phosphate (TCP): TCP is a porous form of calcium phosphate. TCP has two crystallographic forms; α-TCP and β-TCP.[58] Alpha and beta-tricalcium phosphate are produced similarly, although they display different resorption properties. β- TCP shows the characteristics of good biocompatibility and osteoconductivity. Physiochemically, β-TCP is a resorbable material with 99% phase purity, total microporosity, and a homogeneous ceramic sinter structure. Thus, the optimal matrix for the formation of new bone is available immediately after implantation.[59] β- TCP exhibits degradation kinetics comparable to the rate of new bone growth and regenerative properties similar to those of autologous bone grafts. Resorption of TCP grafts is thought to be dependent on dissolution by biological fluids in the absence of osteoclasts around the materials and by the presence of osteoclast-mediated resorption based on the osteoclast-like giant cells in defect areas in many studies.[60] TCP biomaterials have

been used in human clinical studies to repair periapical and marginal periodontal defects, alveolar bony defects, and alveolar ridge augmentation in vertical and horizontal dimensions (Table 2).[61]

PRODUCT NAME	DELIVERY	COMPOSITION	PROPERTY
Boncel-Os	Granule	β- TCP (70%) + HA (30%)	Biocompatible, Osteoconductive Excellent wettability
BoneSigma BCP	Granule	β- TCP (40%) + HA (60%)	Osteoconductive properties Long-term volume stability
DualPor COLLAGEN D-PUTTY	Block	β- TCP (40%) + HA (60%) + bovine collagen (5.5%)	Biocompatibility, Bioabsorbable Easy handling and moldable, Hemostasis and anti-adhesion effect
FRABONE	Granule	β- TCP (40%) + HA (60%)	Biocompatibility, Bioactive Osteoconductivity, Osteoinductivity Mechanical strength Structural feature reserve a stable room and is filled up with vessels and new bone material, resulting in faster regeneration
FRABONE (Inject)	Injection	β- TCP (40%±5%) + HA (60%±5%) + coated with hyaluronic acid	Highly biocompatible and bioresorbable due to hyaluronic acid Osteoconductivity, Osteoinductivity High mechanical strength Structural feature, Moldability Injectability
GENESIS-BCP	Granule	β- TCP (40%) + HA (60%)	High mechanical strength Highly biocompatible
MBCP Plus	Granule	β- TCP (80%) + HA (20%)	Permeable, Resorbable, Hydrophilic Bioactive, Osteoconductive Regeneration
NEW BONE	Granule	β- TCP (80%) + HA (20%)	Osteoconductive synthetic bone graft, highly resorbable due to 80% β-TCP, Easy manipulation
OSTEON	Granule/syringe	β- TCP (30%) + HA (70%)	Osteoconductive
OSTEON II	Granule/ syringe	β- TCP (70%) + HA (30%)	Highly resorbable due to higher β-TCP content Easy manipulation, Excellent wettability, Osteoconductive
OSTEON III	Granule/ syringe	β- TCP (40%) + HA (60%)	Biocompatible, Osteoconductive

OSTEON III Collagen	Cylinder	β- TCP (40%) + HA (60%) + type I collagen (>95% porcine tendon collagen)	Easy manipulation Excellent wettability
Ovis BONE BCP	Granule	β- TCP (80%) + HA (20%)	Osteoconductive, Excellent wettability Easy manipulation Biocompatibility and great bioactivity
TOPGEN-S	Granule	β- TCP (80%) + HA (20%)	Excellent hydrophilicity Osteoconductive

Table 2: Commercially available biphasic tricalcium phosphate grafts

Biphasic calcium phosphates

β- TCP is mostly used in association with HA (Table 3). The balance between HA and β-TCP is crucial to obtaining adequate mechanical strength, suitable degradation kinetics, and osseointegration in biphasic calcium-phosphate ceramics. The resorption of β-TCP is faster than the resorption of HA, but the mechanical properties of HA are slightly better than β- TCP's (average compressive resistances are, respectively, 160 and 100 MPa). Thus, the association of β-TCP and HA enables a faster and higher bone growth rate than using HA alone.[62,63] while offering better mechanical properties than β-TCP alone.[64] HA and β-TCP ceramics form a strong direct bond with the host bone.[65] They can be found with different HA/β-TCP ratios and can be associated with bone marrow aspirate which then provides enhanced osteogenic properties to the material.[66] HA and β-TCP ceramics form a strong direct bond with the host bone. The mechanical properties of grafting materials are controlled by the amount of β-TCP and HA of the biphasic material in particular, a material with a high percentage of β-TCP shows poor mechanical properties. Morra et al. developed a biphasic granulate bone filler with a HA/β-TCP weight ratio of 75/25; after being implanted in rabbits, this graft elicited an excellent new bone formation without any inflammatory response.

PRODUCT NAME	DELIVERY	COMPOSITION	PROPERTY
Bone Sigma TCP	Powder	β-TCP 100%	Osteoconductive High resorption rate: Rapid osseointegration and recovery in dental implants
Excelos Inject	Injectable	β-TCP 100%	Hemostasis and injectable by poloxamer-based hydrogel High moldability Osteoconductive High resorption rate Space maintenance for new bone formation
Excelos (TCPGLD)	Powder	β-TCP 100%	Osteoconductive Faster absorption and biodegrade rate Space maintenance for new bone formation
MEGA-TCP	Powder	β-TCP 100%	Biocompatibility, Biodegradable
Sorbone	Powder	β-TCP 100%	Osteoconductive, High resorption rate, Biocompatibility, Easy handling
SynCera	Powder	β-TCP 100%	Osteoinduction >70% new bone formation
Cerasorb M	Powder	β-TCP 99%	99% resorption Optimal microenvironment for osteoblast adhesion proliferation and Subsequent bone remodeling
TCP Dental	Granule	β-TCP 99%	Osteoconductive, Early resorbable and angiogenesis

Table 3: Commercially available Tricalcium phosphate-based grafts A study comparatively evaluated the efficacy of biphasic calcium phosphate to the deproteinized bovine bone in Maxillary sinus augmentation and concluded that both graft materials demonstrated similar biocompatibility and osteoconductivity in the maxillary sinus augmentation. However, higher new bone volume fraction and new bone surface density were observed in the calcium phosphate group compared with the bovine bone group. Another study used improved biphasic calcium phosphate combined with periodontal ligament stem cells for periodontal regeneration to treat Dehiscence defects in beagle dogs, and concluded that improved BCP works as a scaffold to provide space for periodontal tissue formation, and as a barrier to obstruct epithelium invading, and thus serves a promising method for periodontal regeneration.[67]

Bioactive glass: Developed for the first time by Hench et al in the 1970s, bioactive glasses (or bioglasses) are originally silicates that are coupled to other minerals naturally found in the body (Ca, Na2O, H, and P).[68] Heat treatment of a MgO-CaO-SiO_2-P_2O_5 glass gave a glass-ceramic containing crystalline apatite [Ca_{10} (PO_4)6O, F2)] and β-wollastonite (CaO.SiO_2) in a MgO-CaO-SiO_2 glassy matrix, and this CaO, SiO_2-based glass is called bioactive glass (BG). The particle sizes of bioactive glasses (Bio-Glass®) range from 90 to 710 μm to 300–355 μm.[69,70] In bone tissue engineering, a bioactive material has been traditionally defined as a material that

undergoes specific surface reactions in vitro and in vivo, promoting the formation of an HA-like layer that allows a strong bond between host bone and grafting material to occur. This ability was also referred to as osteostimulation by Schepers & Ducheyne. Bioactive glasses are osteoinductive materials, too, as they can induce osteoprogenitor cells to migrate into the structure of the graft and can promote cell differentiation by affecting the gene expression of undifferentiated cells.[71,72] The use of bioglasses does not induce an inflammatory response, and their resorption is complete in 6 months for silica-based bioglasses.[73]

There are two forms of bioactive glass currently available: [**Perioglas & Biogran]**

A clinical study on the efficacy of hydroxyapatite - Bioactive glass composite granules in the management of periodontal bony defects, successfully showed performance of HA: BG was better compared to HAP and open flap debridement for the reconstruction of infrabony defects.[74] A study clinically and radiographically evaluate the periodontal regenerative potential of PerioGlas and it revealed a statistically significant improvement in both clinical and radiographic parameters, but (experimental) sites which received PerioGlas® material after open flap debridement showed better results when compared with (control) sites treated with only open flap debridement.[75] An in vivo study showed that BG nanoparticles induced cementoblasts to proliferate. The ionic products from BG nanoparticles increased cementoblast viability, and mitochondrial activity and induced cell proliferation, indicating that they could be a potential material for use in cement regeneration through tissue engineering.[76]

Disadvantages: - Bioactive glass undergoes no resorption, and limited true periodontal regenerative outcomes based on histological analysis have been demonstrated.[77,78]

Conclusion

Although complete periodontal regeneration is unpredictable with any regenerative therapy currently used, periodontal bone grafts show strong potential. The regeneration of supporting periodontal tissue in humans is possible in selected sites and patients with the use of autografts, allografts, or xenografts. The addition of autograft or growth factors to allograft seems to enhance the regenerative potential of these materials. The clinician should make an effort to select graft material and a technique based on scientific evidence, the type, and size of the defect, the resorbability of graft material, cost, and patient acceptance.

References

1. Brunsvold, M.A. & Mellonig, J.T. Bone grafts and periodontal regeneration. Periodontol 2000 1993; 1: 80–91.
2. Nabers, C. L & O'Leary, T. J. Autogenous Bone Transplants in the Treatment of Osseous Defects. J Periodontol 1965; 36, 5-14.
3. Schallhorn, R. G., Hiatt, W.H., Boyce. Iliac transplants in periodontal therapy. J Periodontol 1970; 41,566-80.
4. Ali Saad, A. G., Othman, S., & Sebastian, G. C. Osseous Grafting Part I: Autografts and Allografts for Periodontal Regeneration - A Literature Review: Journal of the International Academy of Periodontology 2010, 2; 34-38.
5. Rosenberg, E., & Rose, L. F. Biologic and clinical considerations for autografts and allografts in periodontal regeneration therapy. Dent Clin North Am 1998; 42, 467-490.
6. Moskow, B.S., Karsh, F., Stein, S. D., 1. Histological assessment of autogenous bone graft: A

case report and critical evaluation. J Periodontol 1979; 50, 291-300.

7. Zaner, D. J & Yukna, R. A. Particle Size of Periodontal Bone Grafting Materials. Journal of Periodontology 1984; 55, 406-409.
8. Robinson, R. E. Osseous Coagulum for Bone Induction. J Periodontol1969; 40, 503-510.
9. Rosenberg, E., & Rose, L. F. Biologic and clinical considerations for autografts and allografts in periodontal regeneration therapy. Dent Clin North Am 1998; 42, 467-490.
10. Zaner, D. J & Yukna, R. A. Particle Size of Periodontal Bone Grafting Materials. Journal of Periodontology 1984; 55, 406-409.
11. Hiatt, W.H & Schallhorn, R.G. Intraoral Transplants of Cancellous Bone and Marrow in Periodontal Lesions. Journal of Periodontol.1973; 44, 194-208.
12. Schallhorn, R.G. Postoperative Problems Associated with Iliac Transplants. Journal of Periodontology 1972; 43, 3-9.
13. Schallhorn, R.G & Hiatt, W. H. Human Allografts of Iliac Cancellous Bone and Marrow in Periodontal Osseous Defects. II. Clinical Observations. Journal of Periodontology 1972; 43, 67-81.
14. Dragoo, M.R. & Sullivan, H.C. A Clinical and Histological Evaluation of Autogenous Iliac Bone Grafts in Humans. II. External Root Resorption. Journal of Periodontology 1973; 44, 614-625.
15. Ellegaard, B., Karring, T., Listgarten, M. & Loe, H. New Attachment after Treatment of Interradicular Lesions. Journal of Periodontology 1973; 44, 209-217
16. Ellegaard, B., Karring, T., Davies, R. & Loe, H. New Attachment after Treatment of Intrabony Defects in Monkeys. Journal of Periodontology 1974; 45, 368-377.
17. Dias, R. R., Sehn, F. P., de Santana Santos, T., Silva, E. R., Chaushu, G., Xavier, S. P. Corticocancellous fresh-frozen allograft bone blocks for augmenting atrophied posterior mandibles in humans. Clin Oral Implants Res 2014; 27, 39–46.
18. Macedo, L. G., Mazzucchelli-Cosmo, L.A., Macedo, N. L., Monteiro, A. S., Sendyk, W. R. Fresh-frozen human bone allograft in vertical ridge augmentation: clinical and tomographic evaluation of bone formation and resorption. Cell Tissue Bank 2012; 13, 577–86.
19. Mellonig, J., Bowers, G., Bright, R., Lawrence, J. Clinical Evaluation of Freeze-Dried Bone Allograft in Periodontal Osseous Defects. J Periodontol 1976; 47, 125-129.
20. Friedlaender, G. Bone Banking. Clin Orthop 1988; 225, 17-21.
21. Mellonig, J.T. Alveolar bone induction: Autografts and allografts. Dental Clinics of North America 1980; 4, 719-737.
22. Turner, D & Mellonig, J. T. Antigenicity of Freeze-Dried Bone Allograft in Periodontal Osseous Defects. J Periodont Res 1981; 16, 89-99.
23. Quattlebaum, J.B., Mellonig, J. T & Hensel, N. F. Antigenicity of Freeze-Dried Cortical Bone Allograft in Human Periodontal Osseous Defects. Journal of Periodontology 1988; 59, 394-397.
24. Sunitha, R. V & Naidu, M. Platelet-rich fibrin: evolution of a second-generation platelet concentrates. Indian J Dent Res 2018; 19-42.
25. Lyford, R. H., Mills, M. P., Knapp, C. I, Scheyer, E.T., Mellonig. J.T. Clinical evaluation of freeze-dried block allografts for alveolar ridge augmentation: a case series. Int J Periodontics Restorative Dent 2003; 23, 417–25.

26. Ali Saad, A. G., Othman, S., & Sebastian, G. C. Osseous Grafting Part I: Autografts and Allografts for Periodontal Regeneration - A Literature Review: Journal of the International Academy of Periodontology 2010; 2, 34-38.
27. Hiatt, W.H., Schallhorn, R., & Aaronian, A. J. The induction of new bone and cementum formation. Microscopic examination of the periodontium following human allograft, autograft, and non-graft periodontal regenerative procedures. Journal of Periodontology 1978; 49, 495-512.
28. Urist, M.R., & Dowell, T. A. Inductive substratum for osteogenesis in pellets of particulate bone matrix. Clin Orthop & Related Res 1968; 61, 61-78.
29. Urist, M. R. Bone Formation by Autoinduction. Science 1965; 150, 893-899.
30. Mellonig, J.T. Decalcified Freeze-Dried Bone Allograft as an Implant Material in Human Periodontal Defects. International Journal of Periodontics & Restorative Dentistry 1984; 4, 40-55.
31. Meadows, C.L., Gher, M.E., Quintero, G. & Lafferty, T.A. A Comparison of Polylactic Acid Granules and Decalcified Freeze-Dried Bone Allograft in Human Periodontal Osseous Defects. Journal of Periodontology 1993; 64, 103-109.
32. Agarwal, A & Gupta, N. D. Platelet-rich plasma combined with Decalcified freeze-dried bone allograft for the treatment of non-contained Human Intrabony Periodontal Defects: A randomized controlled split-mouth study 2014; 34 (5), 705-11.
33. Bowers, G.M., Chadroff. B., Carnevale, R. Histologic Evaluation of New Attachment Apparatus Formation in Humans. Part II. Journal of Periodontology 1989; 60, 675-682.
34. Nasr, H.F., Aichelmann-Reidy, M. E. & Yukna, R. A. Bone and Bone Substitutes. Periodontology 2000.1999; 19, 74-86.
35. Aichelmann-Reidy, M. E & Yukna, R. A. Bone Replacement Grafts. The Bone Substitutes. Dental Clinics of North America 1998; 42, 491-503.
36. Nasr, H.F., Aichelmann-Reidy, M. E. & Yukna, R. A. Bone and Bone Substitutes. Periodontology 2000. 1999;19, 74-86.
37. Liu, X., Li, Q., Wang, F., Wang, Z. Maxillary sinus floor augmentation and dental implant placement using dentin matrix protein-1 gene-modified bone marrow stromal cells mixed with deproteinized bovine bone: a comparative study in beagles. Arch Oral Biol 2016; 64, 102–8.
38. Nasr, H.F., Aichelmann-Reidy, M. E. & Yukna, R. A. Bone and Bone Substitutes. Periodontology 2000. 1999; 19, 74-86.
39. Hanna, R., Pedro, M. T., & Robin, L. W. Treatment of Intrabony Defects with Bovine-Derived Xenograft Alone and in Combination with Platelet-Rich Plasma: A Randomized Clinical Trial. J Periodontol 2014; 75, 1668-77.
40. Guillemin, G., Patat, J. L., Fournie, J. & Chetail, M. The Use of Coral as a Bone Graft Substitute. The Journal of Biomedical Materials Research 1987; 21, 557-567.
41. Aichelmann-Reidy, M. E & Yukna, R. A. Bone Replacement Grafts. The Bone Substitutes. Dental Clinics of North America 1998; 42, 491-503.
42. Nasr, H.F., Aichelmann-Reidy, M. E. & Yukna, R. A. Bone and Bone Substitutes. Periodontology 2000, 1999; 19, 74-86.
43. Guillemin, G., Patat, J. L., Fournie, J. & Chetail, M. The Use of Coral as a Bone Graft Substitute. The

Journal of Biomedical Materials Research 1987; 21, 557-567.

44. Gao, T.J., Tuominen, T.K., Lindholm, T.S., Kommonen, B. & Lindholm, T.C. Morphological and Biomechanical Difference in Healing in Segmental Tibial Defects Implanted with Biocoral or Tricalcium Phosphate Cylinders. Biomaterials 1997; 18, 219-223.
45. Kim, C.K., Choi, E.J., Cho, K.S., Chai, J.K. & Wikesjo, U.M. Periodontal Repair in Intrabony Defects Treated with a Calcium Carbonate Implant and Guided Tissue Regeneration. Journal of Periodontology 1996; 67, 1301-1306.
46. Mora, F., & Ouhayoun, J.P. Clinical evaluation of natural coral and porous hydroxyapatite implants in periodontal bone lesions: Results of a 1-year follow-up. J. Clin. Periodontol 1995; 22, 877–884.
47. Siaili, M., Chatzopoulou, D., Gillam, D. G. An overview of periodontal regenerative procedures for the general dental practitioner. Saudi Dental Journal 2017; 1-12.
48. Sheikh, Z.A., Javaid, M.A., Abdallah, M. N. Bone replacement graft materials in dentistry. In Dental Biomaterials (Principle and Its Application), 2nd Ed, 2013.
49. AlGhamdi, A.S., Shibly, O., & Ciancio, S.G. Osseous grafting part II: Xenografts and alloplastic for periodontal regeneration- A literature review. J. Int. Acad. Periodontol 2010; 12, 39–44.
50. Teng, F., Zhang, Q., Wu, M., Rachana, S., Ou, G. Clinical use of ridge-splitting combined with ridge expansion osteotomy, sandwich bone augmentation, and simultaneous implantation. Br. J. Oral Maxillofac. Surg 2014; 52, 703–708.
51. Tevlin, R., McArdle, A., Atashroo, D., Walmsley, G. G., Senarath-Yapa, K., Zielins, E. R. Biomaterials for craniofacial bone engineering. J Dent Res 2014; 93, 1187–95.
52. Klein, C.P., Driessen, A.A., de Groot, K. & van den Hooff, A. Biodegradation Behaviour of Various Calcium Phosphate Materials in Bone Tissue. The Journal of Biomedical Materials Research 1983; 17, 769-784.
53. Kasaj, A., Willershausen, B., & Reichert, C. Journal of oral science 2008; 50**,** 279.
54. Lu, H. Z. Wu. & Tian, Y. Chinese Journal of Conservative Dentistry 2005;1, 003.
55. Mao, Z. X., Mao, & Chu, C. Military Medical Journal of Southeast China 2008; 3, 002.
56. Andrea, P., Giorgio, P., Matteo, S. Analysis of human alveolar osteoblast behaviour on a nano-hydroxyapatite substrate: an in vitro study. BMC Oral Health 2014; 22, 1-7.
57. Oonishi, H., Kushitani, S., Yasukawa, E., Iwaki, H., Hench, L. L., Wilson, J. Particulate bioglass compared with hydroxyapatite as a bone graft substitute. Clin Orthop 1997; 334, 316-325.
58. Tamimi, F., Sheikh, Z., & Barralet, J. Dicalcium phosphate cement: brushite and monetite. Acta Biomater 2012; 8, 474–87.
59. Tadic, D., & Epple, M. A thorough physicochemical characterization of 14 calcium phosphate-based bone substitution materials in comparison to natural bone. Biomaterials 2004; 25, 987–994.
60. Lu, J. X., Gallur, A., Flautre, B., Anselme, K., Descamps, M., Thierry, B. Comparative study of tissue reactions to calcium phosphate ceramics among cancellous, cortical, and medullar bone sites in rabbits. J Biomed Mater Res 1998; 42, 357-67.
61. Nyan, M., Miyahara, T., Noritake, K., Hao, J., Rodriguez, R., Kasugai, S. Feasibility of alpha

tricalcium phosphate for vertical bone augmentation. J. Investig Clin Dent 2014; 5, 109–116.

62. Spivak, J. M & Hasharoni, A. Use of hydroxyapatite in spine surgery. Eur Spine J 2001; 10, 197–204.
63. Bansal, R., Patil, S., Chaubey, K. K. Clinical evaluation of hydroxyapatite and β-tricalcium phosphate composite graft in the treatment of intrabony periodontal defect: a clinico-radiographic study. J Indian Soc Periodontol 2014; 5, 610–617.
64. Galois, L. & Mainard, D. Bone ingrowth into two porous ceramics with different pore sizes: an experimental study. Acta Orthop Belg 2004; 70, 598–603.
65. Schwarz, F., Herten, M., Ferrari, D. Guided bone regeneration at dehiscence-type defects using biphasic hydroxyapatite + beta-tricalcium phosphate or a collagen-coated natural bone mineral: as an immunohistochemical study in dogs. Int J Oral Maxillofac Surg 2007; 36, 1198–1206.
66. Muschik, M, Ludwig, R., Halbhubner, S. B-tricalcium phosphate as a bone substitute for dorsal spinal fusion in adolescent idiopathic scoliosis: preliminary results of a prospective clinical study. Eur Spine J 2001; 10, 178– 184.
67. Han, S., Wenyi, Z., Xiaoyu, X., Jingqia, C. Improved biphasic calcium phosphate combined with periodontal ligament stem cells may serve as a promising method for periodontal regeneration. Am J Transl Res 2018; 10, 4030-4041.
68. Krishnan, V & Lakshmi, T. Bioglass: a novel biocompatible innovation. J Adv Pharm Technol Res 2013; 4, 78-83.
69. Schepers, E., de Clercq, M., Ducheyne, P., Kempeneers, R. Bioactive Glass Particulate Material as a Filler for Bone Lesions. Journal of Oral Rehabilitation 1991; 18, 439-452
70. Schepers, E. J & Ducheyne, P. Bioactive glass particles of the narrow size range for the treatment of oral bone defects: a 1–24-month experiment with several materials and particle sizes and size ranges. J Oral Rehabil 1997; 24, 171-81.
71. Kargozar, S., Hamzehlou, S., & Francesco, B. The potential of Bioactive Glasses for Cardiac and Pulmonary Tissue Engineering. Materials 2017; 10, 1-17.
72. Kargozar, S., Francesco, B., Sepideh H. Bioactive Glasses: Where Are We and Where Are We Going? J Funct Biomater 2018; 9, 1-26.
73. Moimas, L., Biasotto, M., Di, L. Rabbit pilot study on the resorbability of three-dimensional bioactive glass fiber scaffolds. Acta Biomater 2006; 2, 191–199.
74. Debnath, T., Abhijit, C., Tamal Kanti, P. A clinical study on the efficacy of hydroxyapatite - Bioactive glass composite granules in the management of periodontal bony defects. J Indian Soc Periodontol 2014; 5, 593-600.
75. Chacko, N. L., Abraham, S., Shama, H. N., Sridhar, N., Moon, N., Barde, D. H. A Clinical and Radiographic Evaluation of Periodontal Regenerative Potential of PerioGlas®: A Synthetic, Resorbable Material in Treating Periodontal Infrabony Defects. Journal of International Oral Health 2014; 3, 20-26.
76. Carvalho, S. M., Oliveira, A. A., Jardim, C. A., Melo, C. B., Gomes, D. A., Leite, M. D. Characterization and induction of cementoblast cell proliferation by bioactive glass nanoparticles. J Tissue Eng Regen Med 2011; 6, 813-21.
77. Nevins, M. L., Camelo, M., Nevins, M., King, C. J., Oringer, R. J., Schenk, R. K. Human histologic evaluation of bioactive ceramic in the treatment of

periodontal osseous defects. Int J Periodontics Restorative Dent 2000; 20, 458-67.

78. Knapp, C. I., Frank, F., David, L. C., James, T. M. Clinical and Histologic Evaluation of Bone-Replacement Grafts in the Treatment of Localized Alveolar Ridge Defects. Part 2: Bioactive Glass Particulate. International Journal of Periodontics & Restorative Dentistry 2003; 23, 128-137.