Review Article

Bone Grafts in Periodontics

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Abstract

Bone replacement in materials had been used in a wide variety of surgical approaches. The use of such bone grafts for reconstructing osseous defects is the choice of periodontist, which significantly improves the clinical outcome in regeneration procedures. It increases the bone formation and quality of vital bone. A wide range of bone grafting materials, have been applied and evaluated clinically, including autografts, allografts, xenografts, and alloplasts. It substitutes as a basic building block for the periodontal reconstruction, by providing clinical application with its biological functions. This review insight various use of bone graft materials and its characteristic features in promoting its bone formation and emphasis on recent advances in this field.

Keywords: Graft, regeneration, scaffold

Introduction

Maintaining the health of teeth and their supporting structures is the goal of modern periodontics. Most periodontal practices focus on the prevention of disease, initial therapy, and corrective surgical treatment to eliminate deep periodontal pockets. However, restoring supporting tissues to their healthy level is a critical area that offers a much more appealing, and in fact, a more desired outcome for the patients.[1] Periodontal regeneration has become one of the primary objectives of periodontal therapy. Regeneration can be defined as the reproduction or reformation of organs or tissue that have been lost or injured as a result of a wound or infection. Periodontal regeneration refers to the restoration of supporting tissues of the teeth such as bone, cementum, and periodontal ligament to their original healthy levels before damage from periodontal bacteria has occurred. Regeneration of supporting tooth structures is a huge step up in managing advanced periodontal disease and preventing tooth loss.[1]

Bone grafting is a dynamic phenomenon. A successful bone graft is applied, heals, becomes incorporated, revascularizes, and eventually assumes the form desired. In their early application, bone grafts were considered a mere strap lattice, and the results were measured primarily by the graft's ability to withstand the mechanical stresses that surround them. Today, bone grafts are viewed as biological structures. Of course, mechanical stress, shear stress (extrinsic and intrinsic), contouring, and remodelling are also important in the long term and are part of the healing process of a bone graft.

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Bone Regenerating Grafts

The use of bone grafts for reconstructing intra-osseous defects produced by periodontal disease dates back to Hegedus in 1923.[2] It was then revived in 1965 by Nabers and O'Leary.[3] Buebe and Silvers (1936) used boiled cow bone powder to successfully repair intra-bony defects in humans. Force berg (1956) used Ox purum in 11 human intra-bony defects. Melcher and Dent[4] used an organic bone in bovine bone in bone defects, which showed sequestration and slow resorption militated against the use of organic bone. Scopp *et al*.,[5] used Boplant bovine bone and reported pocket depth reduction at 6 months. Now, with the introduction of advanced bone grafting techniques, it is possible to increase the volume, width, and height of bone in deficient areas.

Bone graft can aid in bone regeneration by three different methods, which include:

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i. Osteogenesis
ii. Osteoconduction, and
iii. Osteoinduction.

- Osteogenesis is the formation of new bone by the cells contained within the graft materials such as cancellous bone/bone marrow that contain living cells that are capable of differentiation and formation of bone[3]
- Osteoinduction is a chemical process in which molecules contained within the grafts such as DBM (bone morphogenetic proteins [BMPs]), that provide a biologic stimulus which induces the progression of mesenchymal stem cells and other osteoprogenitor cells toward the osteoblast lineage convert[3]
- Osteoconduction is a physical effect by which the matrix of the graft forms a scaffold on which cells in the recipient site can form new bone (osteogenesis) in a closed environment.[6]

Classification of Bone Graft

Based on the type of graft used

- Particulate
- Putty
- Block.

These are available as large or small particles, a combination of porosities, and from specific locations of origin (e.g. cortical, cancellous) [Figure 1].

Based on the Source

- Autograft
- Allograft
- Xenograft
- Alloplast

Based on Bone Graft Substitutes (Laurencin)

- Allograft based
- Factor based
- Cell based
- Ceramic based
- Polymer based.

Allograft Based

- Allograft bone used alone or in combination
- For example: allegro, orthoblast, graft-on
- Action: osteoconductive, osteoinductive

Factor Based

- Natural and recombinant growth factor used alone or in combination
- For example: Transforming growth factor-beta, platelet-derived growth factor, fibroblast growth factor, BMP
- Action: Osteoinductive, osteoinductive, and osteoconductive with carrier materials.

Cell Based

- Cells used to generate new tissue alone or seeded onto a support matrix
- For example: Mesenchymal stem cells
- Action: osteogenic, both osteogenic and osteoconductive with carrier materials.

Ceramic Based

- Includes calcium phosphates, calcium sulfate, and bioactive glass used alone or in combination
- For example: Osteograft, osteoset, Novabone
- Action: Osteoconductive, limited osteoinductive when mixed bone marrow.

Polymer Based

- Includes degradable and nondegradable polymers used
- For example: Cortoss, OPLA, Immix
- Action: Osteoconductive, bioresorbable in the degradable polymer.

Indications of Bone Grafts

1. Deep intraosseous defects-two-walled and three-walled defects
2. Tooth retention
3. Support for critical teeth-abutment tooth
4. Bone defects associated with juvenile periodontitis
5. Esthetics (shallow intraosseous defects)
6. Furcation defects-Grade II, III furcation
7. Ridge augmentation
8. Sinus lifting procedure
9. Regeneration around implants
10. Filling donor site bone defects.

Ideal Requisites of Bone Grafts

- Osteoinductive property
- Non-toxic
- Resistant to infection
- No root resorption or ankylosis
- Non-antigenic and biologic compatibility
- Easily adaptable and available
- Predictability
- Strong and resilient
- Require minimal surgical intervention
- Rapid vascularization
- Should stimulate new attachment and be able to trigger osteogenesis.

Ideal Bone Graft Substitutes

- Should be biocompatible
- Bioresorbable
- Osteoconductive
- Structurally similar to bone
- Easy to use and cost effective.

Specific Characteristic of Each Graft

There may be varying degrees of mineralization, material composition and formation, and restorability.[7] Also to be considered is whether the material is osteoconductive or osteoinductive and how quickly or slowly, or if at all the graft will resorption.

Autogenous Grafts

Autogenous bone graft, which is harvested from the patient's own body, is considered ideal because of its osteoconductive and osteoinductive properties and because it contains a source of osteoprogenitor cells. It is still considered the gold standard by which other grafting materials are compared.[8] There are several types of bone graft that have been or are being used clinically. Intra-oral autogenous bone grafts harvested from the maxillary tuberosity, edentulous alveolar areas, healing bony wound, extraction sites, and mental and retro-molar areas. Extra-oral autografts from iliac cancellous bone and marrow provide a great osteogenic potential, Inducing cementogensis, bone regeneration and fibres reattachment. These grafts also include cortical bone chips ,osseous coagulam,bone bend,intra oral and extra oral cancellous bone and marrow. The use of cortical bone removed during osteoplasty and ostectomy from sites when the surgical areas could use successfully to increase in bone height (O' Heary 1965). The cortical chips due to their 5 relative large particle size and potential for sequestration were 6 replaced by osseous coagulum and bone blend. The bone blend is the combination of cortical and cancellous bone that is procured with a trephine or rongeurs. They are osteogenic, osteoconductive, and osteoinductive. There is no risk of host rejection or disease transmission.[9] There is a minimal inflammatory reaction. There is rapid revascularization around the graft particles. There is a potential release of growth and differentiation factors sequestered within the grafts (Marx 1994, Kim *et al*. 2005). However, its major disadvantages are procurement morbidity, limited availability and high cost. Schallhorn,[10] Hiatt and Boyce considered the fill of crestal facial and furcation defects to be more clinically predictable using iliac autografts than with intraoral cancellous bone.

Allografts

The allografts are obtained from other individuals of the same species but disparate genotype, are used widely. There are three main divisions:

- Frozen
- Freeze-dried
- Freeze-dried demineralized.

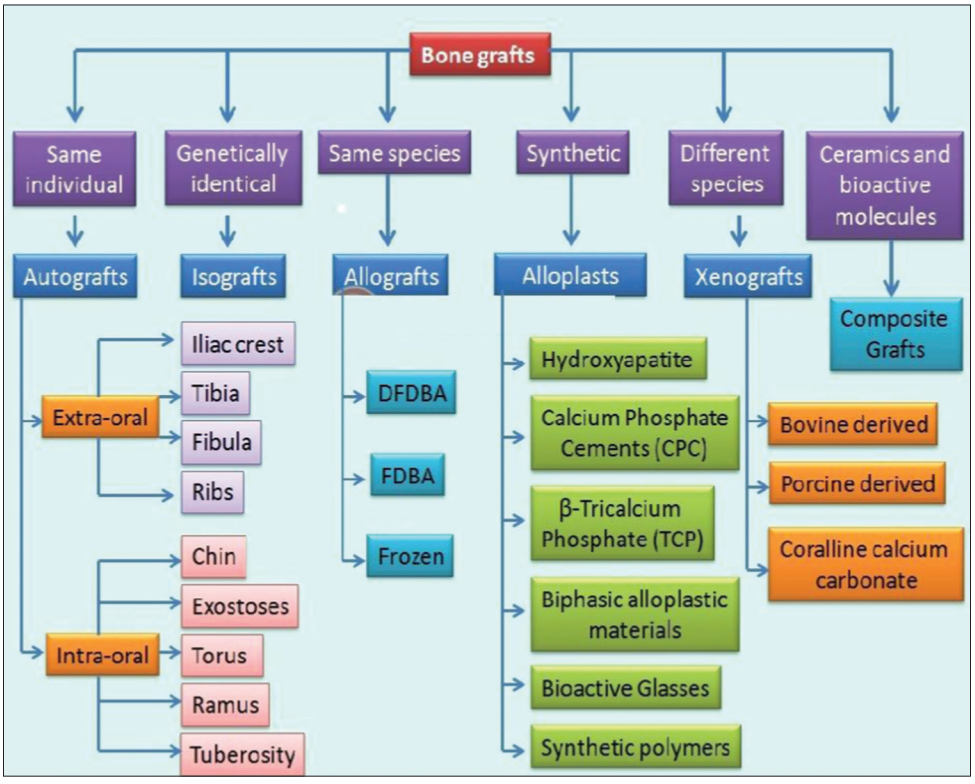

Figure 1: Classification of bone grafts[13]

Bone allografts are the most frequently used alternative to the autogenous bone for bone grafting procedures in the USA (Reynolds *et al*. 2010). The allograft induced bone formation in nonorthotropic sites, presumable due to the influence of bone-inductive proteins called BMPs.[1]

The possibility of disease transfer, antigenicity, and the need for extensive cross-matching has disallowed the use of fresh frozen bone in modern periodontics. The evidence that freeze-drying markedly reduces the antigenicity and other health risks associated with fresh frozen bone, as well as the favorable results obtained in the field trials with freeze-dried bone allografts, have led to the extensive use of freeze-dried bone allografts in the treatment of periodontal osseous defects. The use of cortical bone is recommended rather than cancellous bone allografts since cancellous bone is more antigenic, and there are more bone matrix and consequently more osteo-inductive components in cortical bone. Freeze-dried bone allograft is regarded as osteoconductive scaffold and has shown clinical efficacy by Mellonig.[11] Demineralized freeze-dried bone allograft provides a source of osteoconductive surface and osteoinductive factors by the pioneering work of Urist *et al*. Therefore, it elicits mesenchymal cell migration, attachment, and osteogenesis. It induces endochondral bone formation. Clinical results after using frozen iliac allograft are favorable the need for extensive cross-matching to decrease the likelihood of the graft rejection and disease transmission. Borghetti *et al*.[12] reported on the results using cryopreserved allografts from femur heads to treat intra-bony lesions. Safety is always a concern when an allograft material is used. The risk of disease transmission for freeze-dried bone allograft and demineralized freeze-dried bone allograft has been reviewed. Freeze-drying the material further reduces the risk to one in eight million.

Xenografts

Xenografts are grafts shared between different species. There are two available sources of Xenografts used as bone replacement grafts in periodontics: bovine bone and natural coral. Both sources are biocompatible and structurally similar to human bone.[1] The Bovine-Derived Xenograft (BDX) is a xenograft consisting of deproteinized, sterilized bovine bone with 75%–80% porosity and acrystal size of approximately 10 mm in the form of cortical granules. BDX is considered identical to the human bone. Advantages when compared with freeze-dried demineralized bone: no donor site is required from the patients; unlimited supplies of the Materials are available; the material is easily handled and used as freeze-dried demineralized bone, and the results are predictable when good surgical principles are observed, a sterile environment is maintained and tissue is handled properly. Examples are Bio-Oss® (Osteohealth Co., Shirley, NY) andOsteograf/N® (CeraMed Dental, LLC, Lakewood, CO). The Inorganic Porcine-Derived Bone Xenograftis a natural replicate of autologous bone, conserves the same intimate structures (matrix and porous form) and presents a high osteoconductive activity. It is biocompatible and bioavailable. The Coralline Calcium Carbonate, Natural coral graft substitutes are derived from the exoskeleton of such as Biocoral® (Inoteb, Saint Gonnery, France). Researchers first started evaluating corals as potential bone graft substitutes in the early 1970s in animals and in 1979 in humans. The structure of the commonly used coral, Porites, is similar to that of cancellous bone, and its initial mechanical properties resemble those of bone. The main advantages of xenografts are that they are osteoconductive and readily available. A major disadvantage of bovine-derived grafts is because it can cause disease transmission, which was evident in the case of bovine spongy form encephalopathy reported in great Britain.[13,14]

Alloplasts (Synthetic Grafts)

A number of synthetic or inorganic graft materials are available for use in the treatment of intrabony lesions. Synthetic grafts act almost exclusively as biological fillers, with scant bone fill and very limited connective tissue regeneration. The synthetic materials can be classified by their ability to be bio-absorbed. The absorbable materials include the ceramics, beta-tricalcium phosphate, hydroxyapatite (HA), calcium sulfate and calcium carbonate. The nonabsorbable materials include porous HA, dense HA, bioglass and a calcium-coated polymer of hydroxyl ethyl methacrylate and polymethyl methacrylate (PMMA).

Alloplasts are biocompatible and readily available.

- Able to serve as a framework for new bone formation
- Resorbable in the long term and have the potential for replacement by host bone
- Radiopaque
- Available in particulate and molded forms and Easy to manipulate clinically
- Not support the growth of oral pathogens
- Have surface electrical activity (i.e., be charged negatively)
- Microporous and provide added strength to the regenerating host bone matrix, and permit biological fixation[15]
- Nonallergenic
- Adapt to be effective in a broad range of medical situations (e.g., cancer, trauma, and infective bone destroying diseases)
- Have a surface that is amenable to grafting
- Act as matrix or vehicle for other materials (e.g., bone protein inducers, antibiotics, and steroids)[16]
- Clinical results are encouraging for these materials based on their biocompatibility, enhancement of clinical attachment levels, reduction of probing depths, and hard tissue fill of the intra-bony defects.

Various types of alloplasts are:

1. PMMA and polyhydroxyethyl-methacrylate (PHEMA) polymers: A biocompatible micro porous polymer containing PMMA, PHEMA and calcium hydroxide is available as a bone grafting material for the treatment of

periodontal defects (HTRTM Synthetic Bone-Bioplant, Norwalk, CT)[17]

2. Demineralized dentin matrix: Organic component of dentin, which accounts for approximately 20% of dentin weight, is mainly type I collagen, a component of bone. (BMPs) promote the differentiation of mesenchymal stem cells into chondrocytes, and thus enhance bone formation.[18,19]
3. HA: Synthetic HA, Ca10 (PO4) 6(OH) 2, has been available for > 30 years. It is the primary mineral found in bone. Synthetic HA can be found as porous or nonporous and in ceramic or nonceramic forms.[20] The advantages of using HA are:

(1) Immunoreactions can be ignored; (2) postoperative morphologic changes and volume decreases do not occur if small blocks and chips are adequately packed during surgery; (3) postoperative absorption of HA, if any, is slight and slow and is replaced by bone; and (4) cement fixation performed on a layer of HA particles prevents the harmful influence of polyethylene wear particles of cement interface. The clinical disadvantages HA particles are that they tend not to stay in place in a bleeding site, and there is a relatively slow restoration of bone within the particles.[21] The polycrystalline ceramic form of pure densely sintered HA is non-resorbable, osteo-conductive has low microporosity and act primarily as inert biocompatible fillers

4. Calcium phosphate cement (CPC): Calcium phosphate preparation to become available was synthetic hydroxyapatite in the 1970's. CPCs are gaining special interest due to their biomimetic nature and potential use as controlled release systems[13]
5. β-tricalcium phosphate (TCP): Tricalcium phosphate is a porous calcium phosphate compounds Alpha and beta tricalcium phosphate are produced alpha tricalcium phosphate a-Ca3(PO4) 2 is monoclinic and consists of columns of cations, while the beta TCP has a rhombohedral structure Alpha form is less stable than beta and forms the stiffer material calcium-deficient HA when mixed with water. Examples of commercially available beta tri calcium phosphate graft material are Synthograft™ (Bicon, Boston MA, USA) and Cerasorb® (Curasan Pharma GmbH, Kleinostheim, Germany)[22]
6. Calcium sulfate: Calcium sulfate, generally known as plaster of Paris, or gypsum, is perhaps, the oldest ceramic bone substitute material. Calcium sulfate or plaster of Paris was first documented as being used for fracture treatment by the Arabs in the 10th century, which would surround the affected limb Ina tub of plaster. In 1852 a Dutch army surgeon named Matheson incorporated plaster into the bandage able form which we are familiar with today. Currently, medical grade calcium sulphate impregnated with tobramycin is commercially available (Osteoset®; Wright Medical Technology, Arlington, TN, USA)[23,24]
7. Bioactive glasses (BG): it capacity to form a carbonated HA layer on their surfaces once exposed to simulated body fluids or implanted *in vivo*, hence the concept of "bioactivity." Since their invention three decades ago by Hench BG have clinically gained wide acceptance 3 in restorative orthopedics and dentistry. Examples of BG 4 commercially available are Perioglas® (Block Drug Co., 5 NJ, USA) and Biogran® (Orthovita, PA, USA)[25]
8. Oily CaOH2 Suspension: Non-setting oily CaOH2 suspension (OCHS; Osteo inductal R, Osteo inductal GmbH, Munich, Germany) has been introduced for application in jaw bone surgery[13,26]
9. Porous Titanium Granules: Tigran™ PTG (Natix, Tigran Technologies AB, Malmo, Sweden) is irregularly shaped and porous Granules. The granules that have aporosity of about 80% and an osteoconductive surface structure imitate properties of human bone, and create the scaffolding for bone generation that stimulates osteoblast colonization and osseointegration. The granules are nonresorbable[13]
10. Composite grafts: One of the most promising emerging surgical options may be the use of a "composite graft" that contains osteogenic cells and osteoinductive growth factors along with a synthetic osteoconductive matrix. Composite synthetic graft an alternative that can potentially unite the three essential bone-forming properties in more controlled and effective combinations. A composite graft combines an osteoconductive matrix with bioactive agents that provide osteo-inductive and osteo genic properties, potentially replicating autograft functionality. Potential composite grafts are bone marrow/synthetic composites, ultra porous b-TCP/BMA composite, osteoinductive growth factors, and synthetic composites, BMP/polyglycolic acid polymer composites and BMA/BMP/polyglycolic acid polymer composite.[27]

Alloplasts can be mixed with autogenous grafts or allografts in the management of large structural defects. Some alloplastic materials are mixed together to achieve superior results. Fortoss® Vital (Biocomposites, Staffordshire, UK) is such a mixture of beta TCP and calcium sulfate.[15]

Advantages[7]

- Regeneration and reconstruction of the attachment apparatus is possible
- By reconstructing the periodontium (lost bone, cementum, and periodontal Ligament), it is possible to reverse the disease process
- Increased tooth support
- Improved function
- Enhanced aesthetics.

Disadvantages

1. Increased treatment time
2. Longer postoperative time
3. Autograft requires 2 sites

4. Increased postoperative care
5. Variability in repair and predictability
6. Greater expense
7. Availability.

Evidence-Based Literature Regarding Bone Grafts

The mechanism of periodontal regeneration till date remains a complex and elusive phenomenon. Bone grafting has become a valuable clinical procedure in today's era of dentistry in a variety of reconstructive applications. Over the last decade, different modalities of regenerative treatment have been used and clinically applied. The positive effects of bone grafts and bone substitutes on the outcome of periodontal regenerative procedures are well documented. At present, periodontist favor the bone as grafting material which has shown clinical effectiveness, functional periodontal repair, apparent bone defect fill, and pocket reduction to manageable levels.

Particulate grafts fundamentally have been used in cases of small bone defects such as dehiscence and fenestrations. The complications of particulate grafting are few, and the success rate is from 85.7% to 100%.[28] When the bone defect is moderate, and the aim is to secure vertical or horizontal increments, some authors prefer block cortico-cancellous bone in particulate form, using the Tessier osseous microtome or bone mill combination of autograft with xenograft, HA or homologous bone proved to be serving good and faster bone regeneration. The histological evaluation by Sogal and Tofe[29] confirmed good tolerance and good tissue acceptance of xenografts, with almost completely free of risk of disease transmission. Brunel *et al*.[30] and Pieri *et al*.[31] do not use grafts in the following situations: smokers of over 10 cigarettes day, severe liver or kidney disease, a history of head-and-neck radiotherapy, chemotherapy at the time of surgery, uncontrolled diabetes, active periodontal disease in the residual dentition, inflammatory or autoimmune disorders of the oral mucosa, poor oral hygiene, patient failure to cooperate, and any other disease condition contra indicating oral surgery where the anatomic factors are unfavorable.[28,32] Combination of autografts with xenograft, HA or homologous bone posed a greater rate of success rates.[33]

Conclusion

Bone grafting is now a well-recognized choice in the treatment of periodontal osseous defects, especially when used along with barrier membranes. Various types of bone grafts and also their combinations are used with varying degrees of success. Autografts have been considered to be the gold standard among bone replacement grafts as they can induce osteogenesis Complete periodontal regeneration is unpredictable with any regenerative therapy currently used, periodontal bone grafts show strong potential. A strong body of clinical evidence clearly indicates that grafts consistently lead to better bone fill than nongrafted controls. As researches progress about the biologic process of periodontal regeneration, in future perspectives, new graft materials are expected to make the task of periodontal regeneration even more predictable. New strategies such as gene therapy, poly therapy by using scaffolds, healing promotive factors and stem cells, and finally three-dimensional printing are in their preliminary stages, but may open new insights shortly.

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Conflicts of interest

There are no conflicts of interest.

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