



**Review Article**

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## **Bone Grafts and Bone Graft Substitutes in Periodontal Regeneration: A Review**

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### **Abstract**

Periodontal disease is one of the most prevalent afflictions worldwide. The most serious consequence is the loss of the periodontal supporting structures, which includes the periodontal ligament, alveolar bone and cementum resulting in the early loss of teeth. Bone replacement grafts are widely used to promote new bone formation and periodontal regeneration in periodontal therapy especially in intrabony defects. Conventional surgical approaches like as open flap debridement (OFD), provide critical access to evaluate and detoxify root surfaces as well as establish improved periodontal form and architecture. Advances in material sciences, however, have increasingly blurred such boundaries between types of bone replacement grafts used.

**Keywords:** Bone Grafts, Bone Graft Substitutes, Periodontal Regeneration.

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### **Introduction**

Today, Bone replacement grafts are widely used to promote new bone formation and periodontal regeneration in periodontal therapy especially in intrabony defects. Conventional surgical approaches like as open flap debridement (OFD), provide critical access to evaluate and detoxify root surfaces as well as establish improved periodontal form and architecture. However, these surgical techniques offer only limited

potential in restoring or reconstituting components of periodontium. Bone grafts, functions as structural scaffolds and matrices for attachment and proliferation of osteoblasts. Many classification systems have been used to organize bone grafts. Advances in material sciences, however, have increasingly blurred such boundaries between types of bone replacement grafts used.<sup>1</sup> (Table.1)

- It should be nontoxic.
- It should be nonantigenic.
- It should be resistant to infection.
- Should not cause any root resorption or ankylosis.
- Strong and resilient.
- Easily adaptable and available.
- Should require minimal surgical intervention.
- Should stimulate new attachment and be able to trigger osteogenesis, cementogenesis and formation of a functional periodontal ligament.

**Materials and Methods**

Osteogenic grafting materials, such as cancellous bone/bone marrow, contain living cells that are capable of differentiation and formation of bone. Osteo-inductive grafting materials, such as demineralized bone matrix (DBM), provide a biologic stimulus (proteins and growth factors)

that induces the progression of mesenchymal stem cells and other osteo-progenitor cells toward the osteoblast lineage. Osteo-conduction defines the process that permits osteogenesis when cells already committed to bone formation are present in a closed environment.

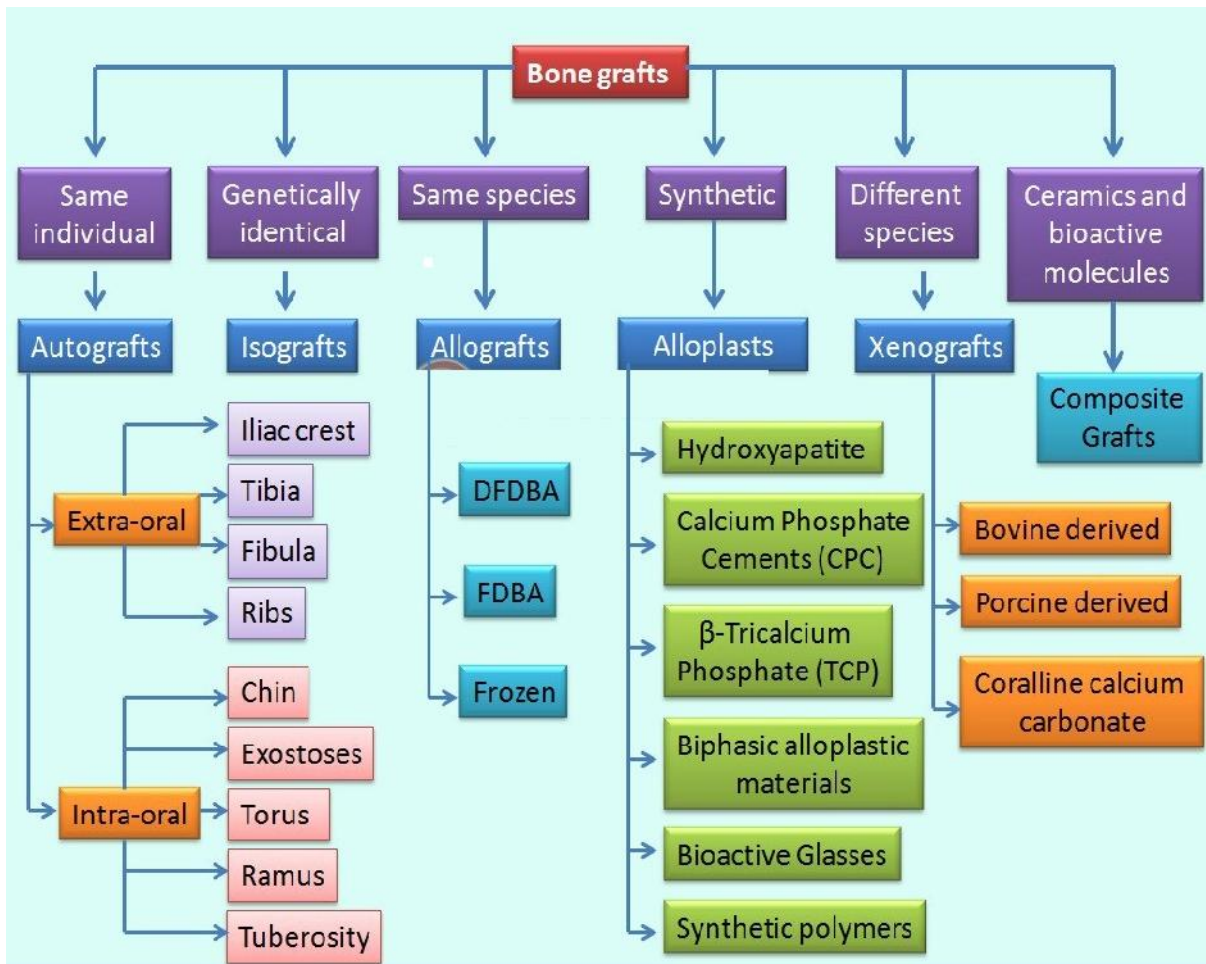


Fig.1: Classification of Bone Grafts:

In general, bone replacement grafts can be categorized into following depending upon source. (Fig.1)

- a. Autogenous
- b. Allograft
- c. Alloplast
- d. Xeno- Graft

**Autogenous Grafts:** Autogenous bone graft, which is harvested from the patient's own body, is considered ideal because of its osteo-conductive and osteo-inductive properties and because it contains a source of osteo-progenitor cells. It is still considered the gold standard by which other grafting materials are compared (Rosenberg and Rose1998) (Table.2).<sup>8,9</sup>

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Table.2: Autogenous bone has been adopted as the gold standard because:<sup>8,9</sup>

- Autograft bone includes cells participating in osteogenesis,
  - A tissue reaction is induced without inducing immunological reactions.
  - There is a minimal inflammatory reaction.
  - There is rapid revascularization around the graft particles
  - A potential, release of growth and differentiation factors sequestered within the grafts
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Depending upon sites Autogenous grafts were further classified into:

**A: Intra-oral Autografts:** Intra-oral autogenous bone grafts harvested from the maxillary tuberosity, edentulous alveolar areas, healing bony wound, extraction sites and mental and retro-molar areas.

Several types of autogenous bone grafts can be used:<sup>4</sup>

**(a) Cortical bone chips:** These are not used today because they are generally much longer particles  $1,559.6 \times 183$  mm and have a higher potential for sequestration.<sup>5</sup>

**(b) Osseous coagulum:** This is made by harvesting intraoral bone with round burns, and then mixing it with blood.<sup>6</sup>

**(c) Blend of cortical and cancellous intraoral bone:** Bone blend is the combination of cortical and 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 final particle size is about  $210 \times 105$  mm.<sup>5</sup>

**B. Extra-oral Autografts:** Extra-oral autografts from iliac cancellous bone and marrow provide a great osteogenic potential, being able to induce cementogenesis, bone regeneration and Sharpey's fibers reattachment.<sup>7</sup> Although autograft procedures fulfill many of the characteristics of an ideal bone graft material, autografts are more invasive due to the additional surgical

manipulations required to obtain donor tissue, and are limited by the relatively small quantity of bone that can be obtained from such techniques. These procedures also have been associated with postoperative root resorption. As a result, autografts may not be routinely practical in severe periodontitis cases involving multiple teeth and severe defects.<sup>8</sup>

**Allografts:** The allografts are obtained from other individuals of the same species but disparate genotype. They include freeze-dried bone allografts (FDBA) and demineralized freeze-dried bone allograft (DFDBA). The two types of allografts work by different mechanisms. FDBA provides an osteo-conductive scaffold and elicits resorption when implanted in mesenchymal tissues. DFDBA also provides an osteo-conductive surface. In addition, it provides a source of osteo-inductive factors. Therefore, it elicits mesenchymal cell migration, attachment and osteogenesis when implanted in well-vascularized bone, and it induces endochondral bone formation when implanted in tissues that would otherwise not form bone.<sup>9</sup> Both FDBA and DFDBA materials are widely used in periodontal therapy and there are no reports of disease transmission during the 30-year history of using freeze-dried bone allografts. Most bone banks adhere to the guidelines of the American Association of Tissue Banks (AATB) with respect to procurement, processing and sterilization of bone grafts (Centers for Disease Control and Prevention 2010). **Xenografts:** Xenografts are

grafts shared between different species. Currently, there are two available sources of xenografts used as bone replacement grafts in periodontics: bovine bone and natural coral. Both sources, through different processing techniques, provide products which are biocompatible and structurally similar to human bone. The Bovine Derived Xenograft (BDX) is a xenograft consisting of deproteinized, sterilized bovine bone with 75-80% porosity and a crystal size of approximately 10 mm in the form of cortical granules.

Regarding both the chemical and physical features, BDX is considered identical to the human bone.<sup>10</sup> BDX has several characteristics and advantages when compared with freeze-dried demineralized bone: no donor site is required from the patients; unlimited supplies of the material 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 as recommended by the manufacturer.<sup>11</sup> The Anorganic Porcine-Derived Bone Xenograft is 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 material showed good clinical results when used for augmentation of the alveolar crest and maxillary sinus. No studies are presently available for the treatment of periodontal bony defects. The Coralline Calcium Carbonate, Natural coral graft substitutes are derived from the exoskeleton of marine madreporic corals. 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.

**Alloplasts:** An alloplast is a biocompatible, inorganic synthetic bone grafting material. At present, alloplasts marketed for periodontal regeneration fall into two broad classes: ceramics and polymers. The fate of an alloplastic bone grafting material is dependent primarily on its chemical composition, structure and physical properties.(Table.3)<sup>12</sup>

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Table.3: An ideal synthetic bone material should be:<sup>12</sup>

- Biocompatible and readily available.
  - Able to serve as a framework for new bone formation.
  - Resorbable in the long term and have 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
  - 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)
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### **1.Polymethylmethacrylate and Polyhydroxyl ethylmethacrylate (PMMA-PHEMA)**

**Polymers:** A biocompatible microporous polymer containing polymethylmethacrylate (PMMA), polyhydroxylethylmethacrylate (PHEMA) and calcium hydroxide is available as a bone grafting material for the treatment of periodontal defects

(HTRTM Synthetic Bone-Bioplant, Norwalk, CT). This composite is prepared from a core of PMMA and PHEMA with a coating of calcium hydroxide. It forms calcium carbonate apatite when introduced into the body and interfaces with bleeding marrow.<sup>13</sup>



**2. Demineralized Dentin Matrix (DDM):** The organic component of dentin, which accounts for approximately 20% of dentin weight, is mainly type I collagen, a component of bone. Dentin also contains bone morphogenetic proteins (BMPs), which promote the differentiation of mesenchymal stem cells into chondrocytes, and thus enhance bone formation, non-collagen proteins such as osteocalcin and osteonectin, which have been implicated in calcification and dentin-specific proteins including dentin phosphoprotein, also known as phosphophoryn, and dentin sialoprotein.<sup>14,15</sup>

**3. Hydroxylapatite (HA):** Synthetic hydroxylapatite,  $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ , has been available for more than 30 years. It is the primary mineral found in bone. Synthetic hydroxylapatite can be found as porous or nonporous and in ceramic or non-ceramic forms.<sup>16</sup> The advantages of using hydroxylapatite 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 hydroxylapatite, if any, is slight and slow and is replaced by bone; and (4) cement fixation performed on a layer of hydroxylapatite particles prevents the harmful influence of polyethylene wear particles of cement interface. The clinical disadvantages hydroxylapatite 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 assemblage of particles.<sup>17</sup> The polycrystalline ceramic form of pure densely sintered HA is non-resorbable, osteo-conductive, has a low microporosity and act primarily as inert biocompatible fillers. There are several available forms of hydroxylapatite:

*a.* The coralline porous non-resorbable hydroxylapatite is a replica of a marine coral skeleton, Porites.

*b.* The resorbable non-ceramic hydroxylapatite is highly microporous, non-sintered (non-ceramic), composed of small particles measuring 300-400 nm (35-60 mesh), with a controlled, predictable rate of resorption.

*c.* Nano-crystalline hydroxylapatite (NHA). Nanoparticulate hydroxylapatite not only provides

the benefits of traditional hydroxylapatites, but also resorbs.

*d.* (FHA) biomaterial. The natural architecture of some calcified algae offers a surface that is similar to that of bone.

**4. Calcium Phosphate Cement (CPC):** Among the materials used for bone and tissue regeneration, calcium phosphate cements are gaining special interest due to their biomimetic nature and potential use as controlled release systems.

**5.  $\beta$ -Tricalcium Phosphate (TCP):** Tricalcium phosphate is a porous calcium phosphate compounds. Alpha and beta tricalcium phosphate are produced similarly, although they display different resorption properties. The crystal structure of alpha tricalcium phosphate ( $\alpha$ - $\text{Ca}_3(\text{PO}_4)_2$ ) is monoclinic and consists of columns of cations, while the beta tricalcium phosphate has a rhombohedral structure. The former is formed by heating the latter above 1,180°C and quenching in air to retain its structure. Alpha form is less stable than beta and forms the stiffer material calcium-deficient hydroxylapatite when mixed with water.<sup>18</sup>

**6. Calcium Sulfate:** Calcium sulfate, generally known as plaster of Paris, or gypsum, is perhaps, the oldest ceramic bone substitute material. Given the relatively simple chemistry of calcium sulfate, there is less latitude for formulation variation than is the case in the calcium phosphate domain. Traditionally, calcium sulfate hemihydrate ( $\text{CaSO}_4 \times 1/2\text{H}_2\text{O}$ ) powder is hydrated to form calcium sulfate dihydrate ( $\text{CaSO}_4 \times 2\text{H}_2\text{O}$ ), undergoing a slight exothermic reaction to set to a solid form.<sup>19</sup>

**7. Bioactive Glasses (BG):** Among the different alloplastic materials used in periodontal therapy, hydroxylapatite, calcium phosphates and bioactive glass ceramics share a common factor, which is their capacity to form a carbonated hydroxylapatite 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 et al (1971) bioactive glasses have clinically gained wide acceptance in restorative orthopaedics and

dentistry. The original composition of bioactive glass approved by the FDA, designated 45 S5, was composed of 46.1 mol% SiO<sub>2</sub>, 26.9 mol% CaO, 24.4 mol% Na<sub>2</sub>O, and 2.5 mol% P<sub>2</sub>O<sub>5</sub>. The original composition and fine structure has been extensively modified in an attempt to further enhance bioactive glass as a bone replacement graft.<sup>20</sup>

**8. Oily CaOH<sub>2</sub> Suspension:** Recently, a non-setting oily CaOH<sub>2</sub> suspension (OCHS; OsteoinductalR, Osteoinductal GmbH, Munich, Germany) has been introduced into the market for application in jawbone surgery. This formulation contains, apart from CaOH<sub>2</sub>, liquid and solid carbohydrate chains and various fatty acids (e.g., oleic, palmitoleinic, gadoleinic, margarine, pentadecane, myristic, linolenic, stearic, arachidic, lauric) esterified with glycerol, while the oily part consists of a natural product of porcine origin, oleum pedum and vaselinum album.<sup>21</sup>

**9. Porous Titanium Granules:** Tigran™ PTG (Natix, Tigran Technologies AB, Malmo, Sweden) is irregularly shaped and porous granules manufactured using commercially pure titanium. The granules are between 0.7 mm and 1.0 mm. When they are mixed with the patient's blood or with a saline solution, the granules attach to each other due to the capillary force. The titanium surface is very thrombogenic, which facilitates the formation of stabilizing blood clots around the granules. The granules that have a porosity of about 80% and an osteo-conductive surface structure, imitate properties of human bone, and create a scaffolding for bone generation that stimulates osteoblast colonization and osseo-integration. The granules are non-resorbable and keep their volume during the operation and the entire healing period which ensures mechanical stability and a desired aesthetic result. Tigran™ PTG is easy to use. No special tools are needed. When osseo-integration is completed, common drilling techniques are used when an implant has to be placed in the treated area.

**Composite Grafts:** One of the most promising emerging surgical options may be the use of a "composite graft" that contains osteogenic cells and osteo-inductive growth factors along with a

synthetic osteo-conductive matrix. Composite materials being tested in preclinical and clinical trials may exhibit functionality comparable to autograft and allograft. Composite synthetic grafts offer an alternative that can potentially unite the three essential bone-forming properties in more controlled and effective combinations without the disadvantages found with autograft. A composite graft combines an osteo-conductive matrix with bioactive agents that provide osteo-inductive and osteogenic properties, potentially replicating autograft functionality. The osteo-conductive matrix becomes a delivery system for bioactive agents, requiring less chemotaxis and less migration of osteoblast progenitor cells to the graft site. The direct infusion of progenitor cells should lead to more rapid and consistent bone recovery. When an osteo-conductive scaffold is seeded with bone morphogenetic proteins, for example, the composite graft may become both osteogenic and osteo-inductive, providing a competitive alternative to autograft). Such potential composite grafts are: bone marrow/synthetic composites, ultraporous b-TCP/BMA composite, osteo-inductive growth factors and synthetic composites, BMP/polyglycolic acid polymer composites and BMA/BMP/polyglycolic acid polymercomposite.<sup>22</sup> In addition to these materials, research is continuing to modify the products with hopes of creating a graft that incorporates faster, resorbs and yields a bony union that resembles natural form and structure (Kuo et al, 2007).

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