



Bone Grafts and Bone Substitutes for Periodontal Reconstruction-A Review

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I. INTRODUCTION

Bacterially induced periodontitis leads to the destruction of tooth-supporting tissues, culminating in tooth loss. Disease reversal with regeneration of new bone, cementum, and periodontal ligament about a root surface previously contaminated by bacterial plaque is the ultimate goal of periodontal therapy. Bone grafts, both autogenous and allogeneic, are felt by some to be essential if restoration of lost bone accompanied by a functional attachment apparatus is to be achieved. "Bone grafting materials will enhance regeneration of a new attachment apparatus" (Bowers et al, 1989c).

"Osseous grafting therapy has been shown to be clinically successful for time intervals exceeding 20 years when encompassed in a comprehensive care program based on effective daily plaque control by the patient and a professionally supervised periodontal maintenance program" (Schallhorn, 1980).

A bone graft is a piece of bone or particles of bone taken from the patient or some other person or some other source and used to replace lost bone or fill a bony defect.

Bone grafts have been employed for repair for more than a hundred years. It is a dynamic process and is extensively used in reconstructive surgery. During the last 20 yrs it has undergone numerous advances.

Bone, which has been lost as a result of excision, resorption or sequestration, will not repair by normal process of healing. So they are to be replaced by means of alloplast, bone grafts or its substitutes, bone transport.

For a successful regeneration, bone graft when applied should heal, become incorporated, revascularise and eventually assume the desired form.

History:

1) 1668 – Job Van Meekern (Dutch surgeon) 1st attempt to use bone graft and to do publication.

2) 1809 – Merrem 1st successful bone implant. It is the 2nd most frequently transplanted tissue in USA more than 20,000 procedures performed annually.

3) 1908 – Ledor used allograft.

4) 1975 – Taylor used first clinically successful vascularized bone graft.

5) 1867 – Olter – reviewed literature and reported his own experiment, concluding that the transplanted periosteum and bone remained alive and could under proper circumstance, become osteogenic.

6) 1893 – 1898 – Barth – claimed that all transplanted periosteum and bone will die and are replaced by surrounding tissue. He and Morchand were the 1st tissue the term "Creeping substitution". Invasion of old bone by bone like tissue without previous resorption of bone.

7) 1907, 1909 – Axhausen formulated his principles stating that periosteum has high degree of survival and osteogenic activity in autografts, markedly less in homografts and practically none in heterografts. He believed that all transplanted bone will die, but most of the periosteum survives.

8) Urist M R elaborated the concept of bone induction in 1965 with the identification of bone morphogenic proteins.

Uses of bone grafts:

1. To repair congenital defects.
2. To augment bone in congenital deformities like hemifacial atrophy, micrognathia, nasal deformities, etc. in these cases advancement osteotomies are done followed by bone grafting in the deficiency site.
3. To encourage healing of non united fractures.
4. To reconstruct posttraumatic deformity. Bone graft is used to restore facial projections, vertical stress pillars, continuity of mandible etc.
5. To spread union and restore continuity of bone at osteotomy sites following orthognathic surgery.



6. To fill cavities following cyst and tumor enucleation.
7. To restore continuity of bone following tumour ablation. The defect following oncologic resection can vary from small segments or cavities to entire size of mandible or maxilla. In these situations bone grafts have two functions – mechanical and biological.
8. Mechanically it maintains the contour of soft tissue act as a porous matrix on which host tissues can deposit bone, it provides site for fixation of plates and screws; and implants to serve function.
9. Biologically, it provides bone cells, bone morphogenic protein and various growth factors, which stimulate bone formation.

Principles of bone grafting:

Mutaz B Habal (1994) gave certain principles based on his experience and literature review. These include,

1. Harvest bone from areas you are familiar,
2. Contour bone graft to fit the defect,
3. Fix the bone graft to the defect in a tension free manner,
4. Ensure absolute immobilization – static VS dynamic zones,
5. Differentiate between child and adult grafts,
6. Avoid contaminated sites,
7. Do not have graft exposed,
8. Ensure adequate blood supply to the graft,
9. Do not compromise,
10. Assess “graft take” periodically.

Types of bone graft

Bone grafts can be classified.

1. Based on nature of bone (Graft anatomy).
2. Based on source of donor.
3. Based on vascularity.
4. Based on donor site.
5. Based on function.

Based on nature of bone:

- Cancellous bone graft
- Cortical bone graft
- Corticocancellous grafts

. Blocks

. Chips

. Powder

- Marrow graft

Depending on source of donor:

- A. Autogenous bone graft – from same individual
- B. Allogenic – allograft – from another individual of same species

- C. Isogenic bone graft – from genetically related individual
- D. Xenografts - from different species
- E. Composite grafts: Partly allograft & Autograft

Depending on the vascularity autografts:

- A. Non vascularised
- B. Vascularised bone Pedicled

Microvascular free transfer.

Depending on donor site:

- Iliac crest graft
- from anterior ileum
- posterior ileum
- trephine grafts
- Rib graft
- Full thickness
- Split rib graft
- Calvarial graft
- Full
- Split
- Fibula
- Others

Depending on function:

- Bridging graft or inlay graft
- Reconstruction graft
- Contour graft – onlay graft.

Biology and healing of bone and bone grafts

The osseous healing process is dynamic and unique, in that the skeleton is one of the few organ systems capable of regenerating without the formation of scar tissue.

Wolff in 1892 postulated that " a given bone is organized to create a particular functional circumstances, ----- and that if a particular circumstances are altered, then the bone structure will be also altered."

The three mechanism of bone regeneration after bone transplantation.

1. Osteogenesis.
2. Osteoconduction.
3. Osteoinduction.

Osteogenesis: It involves new bone formation by surviving pre-osteoblasts within the graft. Healing by this mechanism is seen in vascularised bone grafts and to some extent in cancellous bone grafts due to rapid revascularization.

Osteoconduction: It is a prolonged process. Here the bone graft functions as a nonviable scaffold for the gradual in growth of blood vessels and osteo-progenitor cells from the recipient site, with



gradual resorption and deposition of new bone. This is called creeping substitution. It is seen predominantly in cortical grafts.

Osteoinduction: It involves transformation of local mesenchymal cells into bone-forming cells in the presence of an appropriate inductive stimulus. Insoluble polypeptide moieties and specific enzymes known as 'bone morphogenic proteins' regulate it. Demineralization of bone prior to implantation is required for osteoinduction to occur.

This concept was first described by Urist in 1965. Huggins, Urist and Reddi have shown that a group of insoluble polypeptide morphogens, enzymes and enzyme inhibitors from endochondral bone stimulated bone formation when implanted intramuscularly or subcutaneously.

There are 8 factors, which induce bone formation called bone morphogenic proteins (BMP). These factors are BMP 2 (BMP 2a), BMP 3 (Osteogenin), BMP 4 (BMP2b), BMP 5, BMP 6, BMP 7 (Osteogenic protein 1), BMP 8 (Osteogenic protein 2) and Transforming growth factor.

Terminology:

The definitions provided here are adapted from the American Academy of Periodontology's Glossary of Periodontic Terms.

Regeneration: is the reproduction or reconstitution of a lost or injured part. As applied to periodontics, it means the formation of new bone, cementum, and periodontal ligament on a previously diseased root surface.

At one time the terms **regeneration and new attachment were synonymous**. Today, **new attachment** means the reunion of connective tissue with a root surface that has been deprived of its periodontal ligament. This reunion occurs by the formation of new cementum with inserting collagen fibers. The formation of new bone is not necessarily a condition of new attachment. In addition, new attachment to a root surface may be mediated through epithelial adhesion (junctional epithelium) or connective tissue adhesion. Likewise, in the past, the terms new attachment and reattachment were often used interchangeably.

Reattachment: means to attach again, the reunion of connective tissue with a root surface on which viable periodontal tissue is present. The area of reattachment is not affected by bacterial contamination. Attachment apparatus refers to the cementum, the alveolar bone, and the periodontal ligament.

Repair: is the healing of a wound by tissue that does not fully restore the architecture or function of the part. Bone fill is the presence of hard tissue in a periodontal osseous defect, as determined by clinical re-entry of the original defect site. This term does not indicate the nature of the histologic attachment to the tooth. The amount of bone fill is usually determined by surgical reentry procedures.

Bone grafts, both autogenous and allogenic, are felt by some to be essential if restoration of lost bone accompanied by a functional attachment apparatus is to be achieved. "Bone grafting materials will enhance regeneration of a new attachment apparatus" (Bowers et al, 1989c). "Osseous grafting therapy has been shown to be clinically successful for time intervals exceeding 20 years when encompassed in a comprehensive care program based on effective daily plaque control by the patient and a professionally supervised periodontal maintenance program." (Schallhorn, 1980)

History of periodontal bone grafts:

The use of bone grafts in periodontal therapy can be traced to the work of Hegedus (1923). He reported success in six cases by transplanting autogenous bone from the tibia to the jaws to treat "advanced pyorrhea". Subsequent to this report and for the next several decades, the evaluation of xenografts of various types became the main focus of attention. Buebe and Silvers (1936) used boiled cow bone powder to successfully repair intrabony defects in humans. Studies in dogs (Beube, 1934 and 1942) suggested that surgically created periodontal defects had an accelerated rate of healing after placement of boiled cow bone powder, with bone and cementum being deposited more rapidly in grafted defects. Os purum is ox bone that is soaked in potassium hydroxide to remove collagen, in acetone to remove lipid, and in a salt solution to remove proteins. Forsberg (1956) used this material in 11 human intrabony defects. One showed excellent results, seven were satisfactory, and three were unsatisfactory. Anorganic bone is bovine bone from which the organic material is extracted by means of ethylenediamine and autoclaved.

Melcher (1962) grafted 187 bone defects in 163 patients with a minimum follow-up of 3 years. He felt that protracted sequestration and slow resorption mitigated against the use of anorganic bone. Patur and Glickman (1962) found similar results. Bioplant is bovine bone that is prepared by detergent extraction, chloroform methanol extraction to reduce lipid content, sterilization in propiolactone, and freeze drying. In



77 intraosseous defects in 56 patients, Scopp et al (1966) reported pocket depth reduction of 3 mm at 6 months and an additional millimeter after 1 year. Older (1967) reported good results in four cases, fair results in three, and unsuccessful results in two, as measured by probing depth reduction and increasing radiographic density. The widespread clinical use that followed these reports resulted in routine rejection and failure (Emmings, 1974). Bopplant was subsequently withdrawn from the market (Emmings, 1974).

Rationale of bone grafting:

Moderate to severe periodontal osseous defects are often not amenable to osseous resection without further compromising the support of the involved and adjacent teeth. Instead, therapy is directed not only at pocket reduction, but also correction of the bony defect. Regeneration of lost bone and attachment apparatus improves the support of the tooth, and it is hoped, its long-term prognosis. Bone replacement grafts have been used successfully to this end. Histological reports confirm the ability to gain new attachment in the apical position of bony defects (Caton et al. 1990, Dragoo et al. 1993).

Clinical objectives of bone grafting :(Schallhorn 1988).

- Probing depth reduction.
- Clinical attachment gain.
- Bones fill of osseous defect.
- Regeneration of new bone, cementum, and periodontal ligament as determined by histological analysis.

Ideal characteristics of a bone graft :(Edwin Rosenberg et al. 1998),

1. Nontoxic
2. Non antigenic
3. Resistant to infection
4. No root resorption or ankylosis.
5. Strong and resilient.
6. Easily adaptable.
7. Readily and sufficiently available.
8. Minimal surgical procedure.
9. Stimulates new attachment.

Carranza FA Jr (1990) described different types of bone and nonbone graft materials and classified them as follows.

A. Autogenous bone grafts:

- 1) Bone from the intra oral site:
 - Osseous coagulum
 - Bone blend
 - Intraoral cancellous bone marrow transplant

-Bone swaging

2) Bone from extra oral site:

-Iliac autograft

B. Allograft:

-Iliac marrow allograft

-Decalcified freeze dried bone allograft.

C. Xenografts.

-Keil bone

-Calf bone (bioplant)

-Anorganic bone

D). Non bone graft materials:

-Sclera

-Cartilage

-Plaster of paris.

- Calcium phosphate biomaterials

a) Hydroxyapatite.

b) Tricalcium phosphate.

c) Coral derived materials.

A. Autogenous Bone Grafts:

There are several types of autogenous bone grafts that have been or are being used clinically. They include cortical bone chips, osseous coagulum, bone blend, intraoral and extraoral cancellous bone, and marrow.

1. Cortical Bone Chips:

The impetus for the modern-day use of periodontal bone grafts can be traced to the work of Nabers and O'Leary (1965). They reported that shavings of cortical bone removed by hand chisels during osteoplasty and ostectomy from sites within the surgical area could be used successfully to affect a coronal increase in bone height.

The intraosseous defects so treated were primarily one- and two-walled and not felt by the authors to be amenable to other methods of treatment. Subsequently, Nabers reported long-term success with 18- to 24-month posttreatment clinical documentation for six cases (Nabers, 1984). Although there is a paucity of information with respect to cortical bone chips, a more recent publication suggests that this type of graft is still in use and may result in bone fill with decreased probing depth (Langer et al, 1986). Cortical chips, due to their relatively large particle size — 1,559.6 x 183 μm (Zayer and Yukna, 1983) — and potential for sequestration, were replaced by autogenous osseous coagulum and bone blend.

2. Osseous Coagulum and Bone Blend:

It first described by Robinson in 1969.



The rationale for the use of osseous coagulum is the belief that the smaller the particle size of the donor bone, the more certain its resorption and replacement with host bone.

Bone is removed with a carbide bur No. 6 or No. 8 at speeds between 5000 and 30000 rpm. The coagulum formed by mixing the bone particles and blood is placed in a sterile dappen dish or amalgam cloth. The coagulum is placed in the defect a little at a time. The sources include lingual ridge of mandible, exostoses, edentulous ridges, bone distal to terminal tooth. The obvious **advantage** is the ease of obtaining bone from already exposed surgical site. The technique is also quick to accomplish and can be performed without great preparation. The **disadvantage** is relatively low predictability.

Bone blend:

The bone blend technique was designed to overcome some of the disadvantages of osseous coagulum, including

- 1) Inability to aspirate during the collection process,
- 2) Unknown quantity and quality of collected bone fragments, and
- 3) Fluidity of the material (Diem et al, 1972).

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 $210 \times 105 \mu\text{m}$ (Zayer and Yukna, 1983). Case reports indicate that intraosseous defects can be successfully managed with this graft material (Robinson, 1969). A mean bone fill of 73% was obtained in 25 defects (Froum et al, 1975). Froum et al (1976) 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 tuberosities have all been used as sources of intraoral cancellous bone and marrow (Hiatt and Schallhorn, 1973; Ross and Cohen, 1968; Soehren and Von Swol, 1979; Halliday, 1969; Rosenberg, 1971).

Ellegaard and Loe (1971) reported that grafts of intraoral cancellous bone and marrow did not

appear to influence the clinical outcome when compared with surgical curettage. Likewise, Renvert et al. (1985) found limited differences between grafted and nongrafted sites. They did, however, note significant differences in favor of grafted sites when only the deepest defects were compared and suggested that intraoral grafts be limited to treating deep lesions. As determined by probing depth measurements, Carraro et al. (1976) found no difference in the response between grafted and nongrafted one-walled defects. Two-walled defects responded more favorably when grafted than ungrafted controls.

5. Extra-oral Cancellous Bone and Marrow:

It is generally agreed that the extraoral cancellous bone and marrow offer the greatest potential for new bone growth (Cushing, 1969; Sottosanti and Bierly, 1975; Amler, 1984). This material is obtained from either the anterior or the posterior iliac crest (Schallhorn, 1968; Drago and Irwin, 1972). Schallhorn's reports of complete eradication of furcation and interproximal crater defects spurred interest in this material (Schallhorn, 1967 and 1968).

Schallhorn (1975) has been documented that mean clinical bone fill of 3.33mm in 182 defects and 4.36mm in seven defects, mean bone apposition of 2.54mm in crestal or zero wall defect.

Patur (1974) the effect of iliac crest marrow and intraoral Cancellous bone grafts in 1 wall, 2 wall, and 3 wall bony defects in humans was evaluated. The amount of bone fill in one wall bony defects was larger with iliac crest marrow than with Cancellous bone or when no grafts were used.

Histological evidence of periodontal regeneration in humans following the use of iliac crest marrow grafts was provided by **Dragoo and Sullivan (1973)**. At 8 months following therapy a mature periodontal ligament was present at the grafted sites and about 2mm supracrestal new attachment had also formed.

Disadvantages:

Root resorption and ankylosis.

Pedicle grafts

Bone swaging:

This technique requires the existence of an edentulous area adjacent to the defect from which bone is pushed into contact with the root surface without fracturing the bone at its base.

This technique is complicated by varying degrees of elasticity of bone. It is technically difficult and usefulness is limited.



Healing sequence of Autogenous bone grafts:

- Initiation of new bone formation at 7 days
- Cementogenesis at 21 days
- New periodontal at 3 months
- By 8 months a graft should be fully incorporated into the host with functionally oriented fibers coursing between bone and cementum.
- Maturation may take 2 years.

Cellular changes occurring in autografts:

The fate of autograft depends upon, the recipient, infection and other factors also etc. In autograft few osteoblasts survive in initial weeks to produce new bone. In allograft no viable osteoblasts survives.

After transplantation of autografts the mechanism of graft incorporation as follows.

- Necrosis
- Mitosis
- Revascularization
- Osteogenesis
- Remodeling

Sources of new woven bone in autografts:

1. Osteoblasts lying on the trabeculae of cancellous bone of recipient site may migrate and deposit new bone.
2. Haemopoietic marrow contained in fresh graft also contributes to osteogenesis.
3. Osteoprogenitor cells from connective tissue.

Why are autografts considered as a gold standard among graft materials?

1. Because they are superior at retaining cell viability.
2. They contain osteoblasts and osteoprogenitor stem cells and heal by osteogenesis.
3. They avoid the potential problems of histocompatibility differences and risk of disease transfer.

Shortcomings of autogenous bone grafts:

Obtaining donor material for autograft purposes necessitates inflicting surgical trauma on another part of the patient's body.

Often sufficient autogenous bone is not available and increased chair-side time is deemed unacceptable to the patient.

Allografts:

Allografts are used for bone grafting with the availability of bone banks. The modern era of allograft transplantation was inaugurated by Lexer in 1920. Bonfiglio et al 1950 demonstrated that the

immunogenicity of the allograft could be reduced by freezing. Parrish 1973 demonstrated that these grafts are clinically sound and the grafts are partially replaced by host bone in time. Mankin et al 1983 defined the ideal behaviour of allograft implantation. These include.

1. The bone should be dead as a result of freezing.
2. It could be stored for long period
3. It should have enough strength to provide structural stability.
4. It should be replaced by host bone at a slow but steady rate.

Recently the techniques of bone acquisition, preparation and storage have been refined. The allografts are harvested in an aseptic manner and sterilized secondarily with ethylene oxide or gamma irradiation. To reduce immunogenicity these are either frozen, freeze dried, demineralized or autoclaved.

Advantages:

1. It reduces additional surgery and the resultant morbidity.
2. Operating time is reduced.
3. All the bone required is readily available which is valuable especially when large bone grafts are required.

Disadvantages:

1. There are chances for disease transmission.
2. Difficult preparation of the graft.
3. Difficult storage of certain types of graft.
4. Loss of viable osteo-progenitor cells.
5. Graft rejection due to immune reaction.

The bone must be harvested in a sterile environment within 24 hours after death with minimal mechanical or thermal damage. Frequent culturing is done throughout the processing of bone and any contaminated bone is discarded. The harvested bone is cleaned of soft tissue and stripped of periosteum. Bone marrow is removed to reduce immune reaction. Then the bone is processed using gamma radiation or chemicals.

Excessive processing results in loss of inductive potential of the graft. Gamma rays and ethylene oxide vapours are potent sterilizing agents effective against most of the pathogens.

In order to speed up revascularization, Bur Well et al 1968 advocated addition of autograft cancellous bone and bone marrow to allografts. This enhances the inductive properties and gives living osteogenic cells.

De Fries et al 1971 & Canfrell 1974 suggested drilling of multiple holes in a block of



large allograft for permitting ingrowth of granulation and spread of revascularization.

Types of Allografts:

Based on the preparation allografts are divided into:

1. Fresh allogenic bone.
2. Frozen bone
3. Freeze dried bone
4. Demineralised bone grafts
5. Autolysed, Antigen-extracted Allogenic (AAA) bone graft.

Fresh allogenic bone:

It has not found any clinical application due to time required for screening, sterilization and transportation.

Frozen bone:



FIGURE 1: Photograph of a sample of tricortical fresh-frozen bone.

It is harvested and processed by storing the bone at temperature varying from -20°C to -170°C . If a specimen is composite graft of bone and cartilage, it is treated with glycerol prior to freezing to protect the chondrocytes from the effects of freezing.

The frozen bones of humerus, rib, vertebral bodies, femur, tibia, and fibula are available as corticocancellous granules, cancellous granules, cortical chips, chips and as blocks.

The frozen bone heals by Osteoconduction and Osteoinduction.

The main **advantage** is simplicity in preparing the bone for storage.

The **disadvantages** are

1. Need to keep the graft frozen
2. Temperature to be monitored to avoid inadvertent thawing and spoilage of the graft.
3. To keep the graft frozen during transportation
4. Freezing the bone does not kill all viruses and pathogens.

Freeze dried bone graft:



This is prepared by freezing drying process of the bone. This involves freezing the bone and then sublimating (purify/refine) the solid ice directly to a vapour by forming a vacuum around the specimen within a vacuum chamber. The processing cycle takes 7 – 14 days. This kills all human cells and lessens antigenicity but some organisms can survive. This graft can survive 5 to 7 yrs.

It is available in various forms. It has to be reconstituted before either with saline or antibiotic solutions. Larger blocks might require up to 24 hrs while smaller chips are usually soaked for 45 to 60 minutes.

The advantages are

1. Easy to store
2. Adequate strength
3. Available in many forms
4. Less antigenicity.

The disadvantages are

1. Freeze-dried bone tends to be more brittle than fresh bone. Fracture of the bone when manipulated.
2. Resorption of the graft.

Demineralized bone:

Bone allografts are commercially available from tissue banks. They are obtained from cortical bone within 12-24 hrs of death of the donor, and lyophilized after a series of physical and chemical processing steps, according to the guidelines of the American association of Tissue Banks.

The main processing steps according to **Pearson et al 1981** include

1. Bone procurement from human donor



2. Bone stored at -70°
3. Bone cut into 2-3mm cubes
4. Bone fragments decalcified in 0.6N HCL for 4 days at 4° C
5. Prolonged washing in cold autoclaved triple distilled water.
6. Bone defatted with cold 100% ethanol for 24 hrs
7. Washed in cold, autoclaved triple distilled water.
8. Fragment sealed into sterile vials.
9. Freeze dried for 2weeks.

This is mainly used in the form of sheaths or as onlays. Because of its high BMP content it shows osteoinductive property. It can be used along with other graft materials to increase the osteoinductive property.

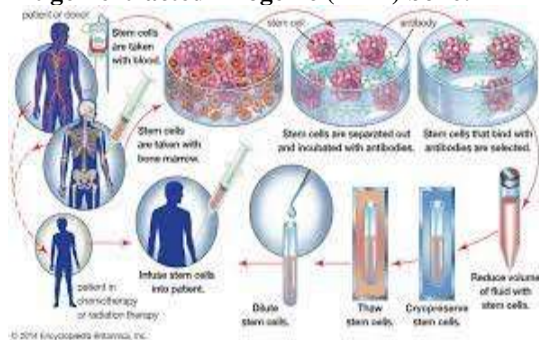
The advantages are:

1. This is soft so it can be easily shaped and contoured.
2. It contains more amounts of Bone morphogenic proteins.

The disadvantages are:

1. High rate of resorption as it has no mineral content.
2. Infection rate is high.
3. It cannot be used in stress bearing areas as it lacks strength.

Antigen-extracted Allogenic (AAA) bone:



It is the antigen extracted autolyzed allogenic chemosterilized bone. It was described by Urist in 1975. The cadaver bone is harvested as soon as possible after death and processed so that the BMP is preserved while all the stainable intralacunar material is enzymatically digested. By this immunological reaction has been reduced. This is then freeze dried

Freeze-Dried Bone Allograft:

- Undemineralized FDBA was introduced to periodontal therapy in 1976 (Mellonig et al., 1976).

- 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 (Friedlaender, 1988; Mellonig, 1980 and 1991).
- Freeze drying also markedly reduces the antigenicity of a periodontal bone allograft (Turner and Mellonig, 1981; Quattlebaum et al, 1988). At no time could any donor-specific anti-HLA antibodies be detected in any human recipient who received several FDBA grafts (Quattlebaum et al, 1988).
- FDBA is the only graft material that has undergone extensive field testing in the treatment of adult periodontitis (Mellonig et al, 1976; Sepe et al, 1978; Sanders et al, 1983; Mellonig, 1991). Field test studies provide information as to efficacy and feasibility but suffer from lack of project control, erratic documentation, and equivocal investigator compliance.
- Eighty-nine clinicians implanted a total of 997 sites with FDBA alone and 524 sites with FDBA plus autogenous bone (FDBA + A), (Mellonig, 1991). Sufficient data, as determined by surgical reentry at 6 months, were collected to determine predictability in 329 sites treated with FDBA and 176 sites treated with FDBA + A. Complete or >50% bone fill was obtained in 220 (67%) sites treated with FDBA and 137 (78%) of the sites treated with FDBA + A. Significant probing depth reduction occurred in 69 and 79% of the sites, respectively (Mellonig, 1991). It can be concluded from this and other studies that FDBA in combination with autogenous bone is more efficacious than FDBA alone, especially in the treatment of furcation invasion defects (Pearson and Freeman, 1980; Sanders et al, 1983).
- Altieri et al (1979) investigated FDBA sterilized with three rads of γ -irradiation, when compared with a nongraft procedure for debridement in ten paired sites. Both graft and nongraft sites demonstrated >50% bone fill in 60% of the sites.
- A composite graft of FDBA and tetracycline in a 4:1 volume ratio has shown promise in the treatment of the osseous defects associated with localized juvenile periodontitis (Yukna and Sepe, 1981; Evans et al, 1989). A study that compared FDBA with and without tetracycline to a nongraft procedure in 12



juvenile periodontitis patients demonstrated significantly greater bone fill and resolution of osseous defects in grafted as opposed to control sites (Mabry et al, 1985).

Decalcified Freeze-Dried Bone Allograft:

- 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 (Urist, 1965; Urist et al, 1967; Urist and Dowell, 1968; Urist et al, 1968 and 1975).
- The work of Urist has been confirmed by others (Koskinen et al, 1972; Chalmers et al. 1975; Oikarinen and Korhonen, 1979; Mellonig et al. 1981a and b).
- Demineralization with hydrochloric acid exposes the bone inductive proteins located in the bone matrix (Urist and Strates, 1970).
- These proteins are collectively called bone morphogenetic protein (BMP) (Urist and Strates, 1971). They are composed of a group of acidic polypeptides that have been cloned and sequenced (Urist et al., 1983a and b; Wozney et al. 1988).
- In addition, there appears to be homology among bone inductive proteins between mammalian species (Sampath and Reddi 1987).
- BMP stimulates the formation of new bone by osteoinduction (Urist et al, 1970). That is, the demineralized graft induces host cells to differentiate into osteoblasts (Harakas, 1984), whereas an undemineralized allograft is felt to function by osteoconduction as it affords a scaffold for new bone formation (Goldberg and Stevenson, 1987).
- The sequence of bone induction with a demineralized bone graft is believed to follow a bone induction cascade (Reddi et al, 1987; Bowers and Reddi, 1991). At day 1, there is chemotaxis of fibroblasts and cell attachment to the implanted demineralized bone matrix.
- At day 5, there is continued cell proliferation and differentiation of chondroblasts.
- At day 7, chondrocytes synthesize and secrete matrix.
- From days 10 to 12, there is vascular invasion, differentiation of osteoblasts and bone formation and mineralization.
- By day 21, there is bone marrow differentiation. This cascade for the induction of endochondral bone has been shown to occur in heterotopic sites of animals grafted with demineralized bone matrix (Reddi et al. 1987).

- It has not been demonstrated to occur following implantation of this material in a periodontal osseous defect. A more likely scenario for the periodontal defect is the induction of new bone through the intermembranous route (Mellonig et al, 1981b).
- Libin et al (1975) were the first to report the use of cortical and cancellous decalcified FDBA (DFDBA) in humans.
- The three grafted sites responded with 4 to 10 mm of new bone formation. Cortical DFDBA was evaluated in 27 intraosseous periodontal defects and yielded a mean of 2.4 mm of bone fill (Quintero et al, 1982).
- In six cases, Werbitz (1987) showed bone fill ranging from 75 to 95% of the original defect.
- The results of a radiographic analysis of cancellous DFDBA in 16 patients demonstrated a mean bone fill of 1.38 mm, whereas six control sites showed 0.33 mm (Pearson et al, 1981).
- The reason for this meager bone fill after a graft of cancellous DFDBA may lie in the fact that the bone inductive proteins are located in the bone matrix (Urist and Iwata, 1973). Because the mass of bone matrix is lower in cancellous bone than that in cortical bone, the yield of new bone could be expected to be lower with cancellous than cortical bone (Urist et al, 1970).
- The processing of both preparations included multiple immersions in absolute ethanol. The DFDBA underwent further processing that included immersion in 0.6 N HCl (Mellonig, 1991). Each of these chemical processes was thought to inactivate HIV (Martin et al, 1985; Resnick et al, 1986; Quinnan et al, 1986).

Sequence of bone induction:

Day 1 - Chemotaxis of fibroblast + cell attachment to the implanted demineralized matrix.

Day 5- cell proliferation + differentiation of chondroblasts.

Day7- Chondrocytes synthesize secrete matrix synthesis.

Day 10-12 – vascular invasion, osteoblast differentiation, bone formation + mineralization.

Day 21- bone marrow differentiation.

What is the long term outcome of DFDBA – treated sites.....!

McClain 1993 – 5 years

Flemming 1998, - DFDBA V/S open debridement 3 years follow up

Alveolar bone maintained over 3 years.



Differences between autograft and allograft bone grafts:

Autologous bone graft	Allogenic bone graft
1. More osteoinductive	1. Very slow minimal osteoinduction
2. Donor site morbidity	2. No donor site morbidity
3. Increased osteoinduction but also increased resorption. So that net augmentation of ridge is decreased.	3. Tend to retain by the body for longer periods.
	4. Lack of vascularity and cellularity
	5. Minimal but immunologic response is present
	6. Minimal oral contamination.

Small particle bone grafts when compared to large particle are:

- Quicken to revascularize
- More osteoclastic activity
- Resorbed quickly
- Net gain is also ridge high is minimal

Xenografts:

Xenografts are grafts shared between different species. Currently, there are two available sources.

1. Bovine bone



2. Natural coral



Xenografts are osteoconductive and readily available. Biocompatible and structurally similar to human bone.

Bovine derived bone replacement grafts:

- Commercially available bovine bone is processed to yield natural bone mineral minus the organic component.
- The advantage is that these products provide similar structural components to that of human bone with improved osteoconductive capability compared with synthetically derived materials.
- Anorganic bovine bone is the hydroxylapatite “skeleton” that retain the macroporus and microporus structure of cortical and cancellous bone remaining after chemical or low-heat extraction of the organic component.
- Currently available bovine-derived HA is deproteinated retaining its natural microporous structure, which supports cell-mediated resorption (Trachow 1991).
- Products are currently available, **Osteograft, Bio-Oss, Endobone, and Bon-Apatite**. These have been reported to have good tissue acceptance and natural osteotropic properties (Callan et al 1993, Cohen et al 1994). Histologically, no fibrous tissue or space between the hydroxyapatite and newly formed bone is found.
- A clinical study demonstrated that implantation of Bio-oss resulted in pocket reduction, gain of attachment & bone fill in periodontal defects to the same extent as that of DFDBA. (Richardson et al, 1999).
- Human histology (Camelo et al 1998) suggested a beneficial effect of placing bovine bone derived biomaterials in periodontal bone defects.



Coraline calcium carbonate:

Biocoral is calcium carbonate obtained from natural coral and is composed primarily of aragonite (>98%). Its pore size is 100 to 200 μm , which is similar to porosity of spongy bone (Guillemen et al 1987).

Its porosity at >45% provides large surface area for resorption and replacement of bone. It does not require a surface transformation into a carbonate phase, as do other bone replacement grafts to initiate bone formation. Biocoral has a high osteoconductive potential because no fibrous encapsulation has been reported (Pia Helli et al 1997).

PepGen-15:



Recently, Yunka & co-workers have used a natural, anorganic, micro porous, bovine-derived hydroxyapatite bone matrix, in combination with a cell-binding polypeptide that is a synthetic clone of the 15 amino acid sequence of type I collagen.

Anorganic Bovine Mineral (ABM) / p-15 is a synthetic, collagen-like agent that imitates autogenous bone. The inorganic / mechanical component, ABM is composed of calcium phosphate & duplicates the natural anatomic structure necessary for cellular invasion. The organic component is represented by p-15. The synthetic 15 amino acid peptide, which repeats the cell-binding domain of type 1 collagen, modulates cell binding, migrations, proliferation, & differentiation.

Alloplasts (Synthetic grafts):

POLYMERS

E.g, HTR polymer



It is biocompatible, micro porous composite co polymer Of Polymethylmethacrylate & Poly hydroxyl ethyl methacrylate coated by calcium hydroxide.

Yukna et al have reported favorable results with this material in 1990, 1994. Histological evidence of new bone has been reported by Forum et al 1996, Stahl et al 1990 and Yukna et al 1992).

Its hydrophobicity enhances clotting and its negative particle surface charge allows adherence to bone. It appears to serve as a scaffold for bone formation when in close contact with alveolar bone.

Histologically PMAA is well tolerated by the tissues. Amler and Le Geros et al in 1990 demonstrated the osteoinductive potential of PMAA in a rat model.

PMAA is not osteoinductive but has osteoconductive properties in favorable defects and it is a non-resorbable material.

Bioceramics;

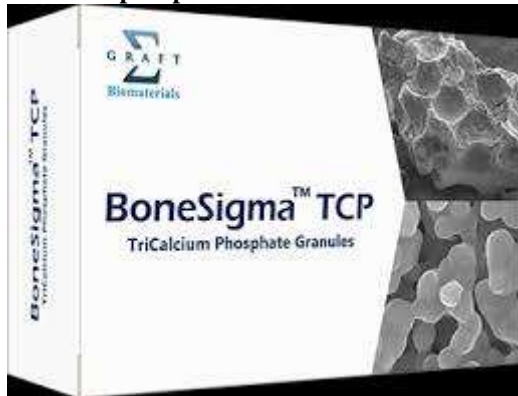


Bioceramics are comprised primarily of calcium phosphate, with the proportion of calcium and phosphate similar to that of bone. The two



most widely used forms are Tricalcium phosphate and Hydroxyapatite.

Tricalcium phosphate:



Tricalcium phosphate is a porous form of calcium phosphate, the most common form of which is β tricalcium phosphate. It serves as biological filler, which is partially resorbable and allows bone replacement. β tricalcium phosphate is powered from calcium phosphate powder mixed with naphthalene and pressed and heated at temperatures as high as 1000° C to 2000° C (Snyder et al 1984) allowing it to fuse into a solid mass. The naphthalene evaporates leaving spaces within the ceramic and giving rise to the porous structure tricalcium phosphate as a bone substitute has gained wide clinical acceptance, but the results are not always predictable. In direct comparison with allogenic cancellous grafts, the allogenic graft appears to outperform β tricalcium phosphate. The tricalcium phosphate particles generally become encapsulated by fibrous connective tissue and do not stimulate bone growth (Amler et al 1987).

Histologically, when β tricalcium phosphate is implanted into bone defects, it is rapidly resorbed by multinucleated giant cells and macrophages (Barney et al 1986, Wada 1989, Saffer et al 1990).

β -TCP (CA3 (PO4)2) has been used in a series of case reports for the treatment of periodontal osseous lesions (Nery & Lynch 1978, Strub et al.1979, Snyder et al. 1984, Baldock et al. 1985) after variable time intervals, a significant gain of bone were observed by means of re-entry or radiographs.

Histologic data from animal (Levin et al. 1974, Barney et al. 1986) and human studies (Dragoo & Kaldhal 1983, Bowers et al. 1986, Froum & Stahl 1987, Saffar et al. 1990) showed that β -TCP is rapidly resorbed or encapsulated by fibrous connective tissue, with minimal bone formation and no periodontal regeneration.

Hydroxyapatite;



Hydroxyapatite is the primary mineral content of bone.

Synthetic hydroxyapatite are marketed as A solid particulate nonresorbable form.

A porous nonresorbable form derived from exoskeleton of coral.

A resorbable nonceramic hydroxyapatite.

When sintered at high temperatures, HA is nonresorbable, nonporous, dense, and has a larger crystal size. Dense HA grafts are osteophilic, osteoconductive, and act primarily as inert biocompatible fillers.

Porous HA is obtained by hydrothermal conversion of calcium carbonate exoskeleton of natural coral, genus Porites. It has a pore size of 190 to 200 μ m, which allows bone in growth (West et al 1985) into the pores and ultimately into the lesion itself (Kenney et al 1985).

Another form of synthetic HA is a resorbable particulate material processed at low temperature. This resorbable form is a non-sintered. Precipitate with particles measuring 300 to 400 μ m. It has been proposed that non-sintered HA resorbs acting as a mineral reservoir at the same time acting as a scaffold for bone replacement (Ricci 1992).

Rate of resorption depends on:

- 1) The physical and chemical properties
- 2) Density
 - Larger particle Non resorbable (ridge preservation and augmentation)
 - Smaller particle Resorbable (periodontal application)
- a) **Yukna (1984)** dense HA has been shown to compare favorably with debridement in reducing pocket depth (1.3mm-2.8mm)&increase in CAL.
- b) **Forum 1982**, human histologic studies indicate that Dense HA does not induce new attachment /bone formation. Pocket reduction is primarily through fibrous encapsulation of the HA particles



in the IOD and that pocket closure is through long JE & CT attachment.

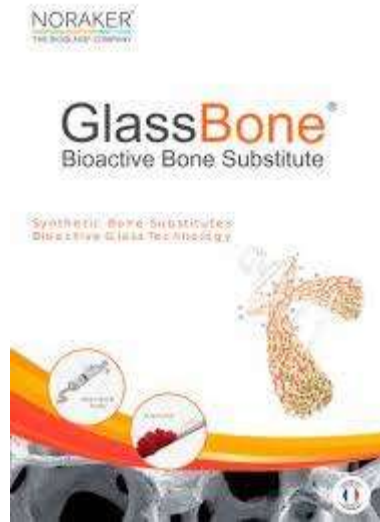
Porous HA e.g. (Interporo 200)

- Hydrothermal conversion of the CaCO_3 exoskeleton of the natural coral genus porites into the calcium phosphate Hydroxyapatite.
- Pore size: 190-200 μm .
- Resorbable, particulate material processed at a low temperature.
- osteoconductive mechanisms
- ✓ In a histological study, **Hashimoto-uoshima et al** reported that biphasic calcium phosphate supported active bone replacement from surrounding bone
- ✓ Generally, HA is not osteoinductive, but osteoconductive, a few studies demonstrate osteoinductive property associated with porous HA (**Yamasaki 1990**).
- ✓ **Takata et al** provided evidence that cementum could be deposited on porous HA in vitro.
- ✓ In controlled studies, grafting of intrabony periodontal lesions with HA resulted in a CAL-gain of 1.3-3.3 mm and also in a greater bone defect fill as compared with non-grafted surgically debrided controls (Meffert et al, 1985, Yukna et al. 1989, Galgut et al. 1992.)

GEM 21S:

Matrix is composed of two sterile components: Synthetic beta-tricalcium phosphate ($\beta\text{-TCP}$) [$\text{Ca}_3(\text{PO}_4)_2$]. $\beta\text{-TCP}$ is a highly porous, resorbable osteoconductive scaffold or matrix that provides a framework for bone ingrowth, aids in preventing the collapse of the soft tissues and promotes stabilization of the blood clot. Pore diameters of the scaffold are specifically designed for bone ingrowth and range from 1 to 500 μm . The particle size ranges from 0.25 to 1.0 mm and Highly purified, recombinant human platelet-derived growth factor-BB (rhPDGF-BB). PDGF is a native protein constituent of blood platelets. It is a tissue growth factor that is released at sites of injury during blood clotting. Extensive in vitro and in vivo studies have demonstrated its potent mitogenic (proliferative) and chemotactic (directed cell migration) effects on bone and periodontal ligament derived cells. Animal studies have shown PDGF to promote the regeneration of periodontal tissues including bone, cementum, and periodontal ligament (PDL).

Bioactive glass:



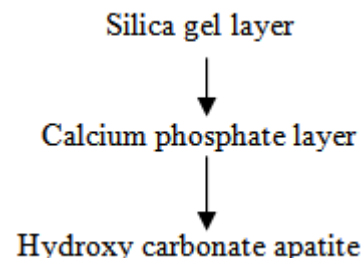
Wilson 1992 was initially introduced as an amorphous material Bioactive glass and has been demonstrated in animal studies to regenerate bone and soft tissue attachment to teeth.

- ❖ The material has subsequently been produced in particulate form.
- ❖ CaO , Na_2O , SiO_2 , P_2O_5

BAG enhances bone formation by ionic dissolution of the ceramic particles. (Ducheyne, broen 1988)

Bioactive glasses bond to bone through the development of a surface layer of carbonated hydroxyapatite (Hench 1971, 1973).

When exposed to tissue fluids, bioactive glasses are covered by a double layer composed of silica gel and a calcium phosphorus rich (apatite) layer.



The calcium phosphate rich layer promotes adsorption and concentration of proteins utilized by osteoblasts to form a mineralized extracellular matrix (El-Ghannam et al 1997).

It has been theorized that these bioactive properties guide and promote osteogenesis (Kenney et al 1996) allowing rapid formation of bone (Hench et al 1971).



Perioglas ®:



PerioGlass has a particle size ranging from 90 to 710 µm, which facilitates manageability and packing into osseous defects. In surgically created defects in non-human primates 68% defect repair was achieved in the form of new attachment (Fetner et al 1994).

Compared to β tricalcium phosphate HA and unimplanted controls Fetner et al showed that PerioGlass produced significantly greater bone and cementum repair.

Observations of the material suggest:

- Good manageability.
- Haemostatic properties.
- Osteoconductive.
- But act as a barrier retarding epithelial down growth.

King & Krieger 1997, BAG were placed in 17 IOD in 12 patients, the healing monitored over 6 months.

Mean PDD 3.4mm

Mean CAL gain..... 1.56mm

Mean radiographic fill..... 2.6mm

These clinical results remained stable over a 24 month period.

Zamet 1997 compared BAG vs OFD, there was significant increase in density and volume of bone in defects treated with perioglass.

Forum 1998 split mouth design. BAG vs OFD

Results: 12 months reentry

Mean PDR 4.26mm vs 3.44mm

Mean CAL gain... 2.96mm vs 1.54mm

Gingival recession 1.29mm vs 1.87mm

Defect fill 4.36mm vs 3.15mm.

Mellonig 1998 compared perioglass vs DFDBA

Results: after 6 months

Mean PDR 3.07mm vs 2.6 mm

Mean CAL gain... 2.27mm vs 1.93mm

Mean Bone fill 2.73mm vs 2.8 mm.

(61.8% vs 62.5%)

Biogran™:



Biogran has a narrower range of particle size between 300 to 355 µm, which has been reported to be advantageous for guiding osteogenesis (Schepers et al 1991).

Formation of hollow calcium phosphate, growth chambers occurs with this particle size because phagocytosing cells can penetrate the outer silica gel by means of small cracks in the calcium phosphorus layer and partially resorbs the gel.

This resorption leads to the formation of protective pouches where osteoprogenitor cells can adhere, differentiate, and proliferate.

According to the manufacturer, larger particles do not resorb in the same manner, which slows the healing process theoretically because bony healing must progress from the bony walls of the defect (Schepers et al 1993) and smaller particles cause a transient inflammatory response which retards the stimulation of osteoprogenitor cells.

Ostim®: Ostim is synthetically manufactured and comprises nanocrystalline hydroxyapatite. Thus it is chemically similar to the inorganic bone component. In comparison to other materials it is not sintered with a very high specific surface. The small particle size facilitates resorption. Ostim is an aqueous watery paste and can be used to fill bone defects or to build up bony structures in the region of the jaws. Ostim is osteoconductive, facilitating bone growth. It will act as scaffolding for the new bone. Ostim is resorbed during the healing process, in the beginning it is osseously interweaved and finally replaced by natural bone.



NanoBone®:



Nanocrystalline hydroxyapatite (HA) as main element of autologous bone is embedded in a highly porous silica gel matrix. The silica gel stimulates the formation of collagen and bone. Autologous proteins from the blood come into the nanopores and cover the entire internal surface (> 80 m²/g) of the granules. Thus, the body recognises Nano-Bone® as a material peculiar to the body. The fluffy structure allows for the quick growth of capillaries. This process is facilitated by the change of matrix. NanoBone® is completely substituted by bone during the process. With stabilised volume, NanoBone® is resorbed to the extent to which new, autologous bone is formed (Meier et al.). Within a few days, the silica gel matrix is replaced by an organic matrix that contains important proteins for osteogenesis (BMP, osteocalcin, osteopontin etc.). Osteoclasts resorb the NanoBone® granules like bone. At the same time, osteoblasts form new natural bone. This resorption of the bone augmentation material and the formation of new,

autologous bone take place in the same way as natural remodelling.

Techniques for Periodontal Bone Grafting:

Patient Selection:

- Should be in good physical health.
- Have a positive attitude towards therapy.
- Have repeatedly demonstrated in acceptable level of plaque control.
- Be committed to a periodontal maintenance program.

Defect Selection:

- Presence of deep defect with probing depth of more than 7mm.
- Preoperative confirmation of vertical defect by radiographs.
- Minimal amount of recession for soft tissue coverage adequately over wound surface.

Tissue banking of bone allografts used in periodontal regeneration:

The possibility of disease transfer with bone allografts is unlikely if the material is procured and processed using the established tissue banking protocols of the American Association of Tissue Banks.

If exclusionary techniques such as medical and social screening, antibody testing, direct antibody tests, other serotype tests, bacterial culturing, autopsy and follow up studies of grafts from the same donor are used, the possibility of disease transfer are approximately one in 2 million (Bruk et al 1989).

Biology of Bone Healing:

Bone has an ability to regenerate itself completely rather than forming a scar tissue.

The bone repair process begins with an inflammatory response that promotes granulation tissue to proliferate in the wound site



Brings in capillaries, fibroblast and osteoprogenitor cells, osteoblasts,



Make organic matrix of woven bone and to initiate mineralization.



Healing mass of new bone is called callus



Woven bone is replaced by lamellar bone as bone-remodeling units invade the healing area.



The healing sequence of an autogenous periodontal bone graft has been identified as:

1. Initiation of new bone formation at day 7
2. Cementogenesis at day 21
3. A new PDL at 3 months (Dragoo 1972)

By 8 months, the graft should be incorporated into host bone with functionally oriented fibers between bone and cementum.

Maturation may take as long as 2 years (Dragoo 1972, Dragoo and Sullivan 1973).

Combination therapy:

Tetracycline addition to bone graft substitutes:

Tetracyclines have wide therapeutic usages not only as antimicrobial agent, but also due to their nonantimicrobial properties.

Sanders et al 1983 as a result of noncontrolled clinical study, mentioned a significant difference in osseous regeneration when antibiotics were used.

Complete or greater than 50% osseous regeneration was noted in 85% of the grafts when antibiotics were used as compared with 38% when antibiotics were omitted.

Bone grafts and GTR:

GTR involves the use of barrier membrane to seal off a defect site during healing. Varying results have been reported in studies combining nonabsorbable barrier membranes with bone grafts in treating furcation defects.

One two part study of clinical cases reported complete furcation closure in 72% of maxillary and mandibular class II furcation and in a few class II furcations when the combination of ePTFE membrane and DFDBA graft were used. Among those receiving only the membrane, only 31% of the defects were closed.

In addition, the authors note that over a 5 year follow up period, almost all of the grafted sites remained stable, where as less than half of those treated with the membrane only did (McClain et al 1993).

II. CONCLUSION

Numerous case reports and controlled clinical studies indicate that autogenous bone grafts can be used successfully in periodontal therapy. Multiple histologic reports suggest that regeneration of a new attachment apparatus is possible with different types of autogenous bone grafts. Root resorption and ankylosis may be observed only following grafts of fresh iliac cancellous bone and marrow. Iliac cancellous bone and marrow are a graft of high osteogenic

potential. Both FDBA and DFDBA have been shown to be clinically effective in the reconstruction of periodontal bone defects. Sites implanted with DFDBA demonstrate more probing depth reduction, clinical attachment gain, and bone fill than similar defects that are not grafted. Regeneration of new bone, cementum, and periodontal ligament is a frequent finding with grafts of DFDBA. Bone formation may be enhanced if guided tissue regeneration attempts are augmented with bone grafts. Bone allografts and alloplasts offer similar advantages with respect to bone fill. Regeneration is generally the result after grafts of DFDBA, whereas repair is the result after grafts of synthetic bone. Dental bone allografts are safe for human use if proper exclusionary techniques and processing are employed.

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