Osseous Grafting Part I: Autografts and Allografts for Periodontal Regeneration - A Literature Review

Ali Saad AlGhamdi[1], Othman Shibly[2] and Sebastian G. Ciancio[2]

[1]Department of Oral Basic & Clinical Sciences, Faculty of Dentistry, King Abdulaziz University, Jeddah, Saudi Arabia; [2]Department of Periodontics and Endodontics, School of Dental Medicine, State University of New York at Buffalo, Buffalo, NY, USA

Abstract

Osseous grafting represents one mode of therapy to manage periodontal osseous defects. Materials for osseous grafting can be obtained from the same person (autografts), from a different person of the same species (allografts), from a different species (xenografts), or from synthetic materials (alloplasts). The two types of grafts most frequently used in periodontal therapy are autogenous grafts and allografts. Both types can be obtained either intraorally or extraorally. They may be cancellous bone, cortical bone, or combinations of these. There has been a recent increase in interest in using xenografts and alloplasts. Bone graft materials are generally evaluated based on their osteogenic, osteoinductive, or osteoconductive potential. Selection of graft material is based on operator preference, type and size of the defect, resorbability of graft material, cost and patient acceptance. In this review we discuss criteria for selection of graft material, factors influencing bone graft success, autografts and allografts.

Key words: Osseous graft, periodontal regeneration, autograft, allograft.

Introduction

Regeneration has been defined as the reproduction or reconstitution of a lost or injured part to restore the architecture and function of the periodontium (Periodontology, 1992). A material or technique must demonstrate histologically that bone, cementum and a functional periodontal ligament (a new attachment apparatus) can be formed on a previously diseased root surface to be considered a regenerative modality. Osseous grafts have been used in an attempt to gain this therapeutic endpoint (Rosen *et al*., 2000).

Osseous grafting techniques represent one mode of therapy to manage combination pocket-osseous defects. They have their greatest applicability in intrabony defects, although encouraging results have been noted in furcation and suprabony sites. As with all treatment modalities, their usage is dictated by the therapeutic objectives for specific problems and whether their respective advantages and limitations outweigh other management techniques (Schallhorn, 1977). The interest in osseous grafting has emerged from the desire to fill an intrabony defect rather than radically resect surrounding intact bone tissue (Nasr *et al*., 1999). Due to the variable physical and chemical nature of bone replacement grafts, the goal of reproduction or reconstitution of lost periodontal structure has been met with varying success or with failure (Nasr *et al*., 1999).

Selection of graft material

Selection of graft material is guided by:

1. Biologic acceptability (Schallhorn, 1977; Nasr *et al*., 1999)
2. Predictability (Schallhorn, 1977)
3. Resorbability (Nasr *et al*., 1999)
4. Clinical feasibility (Schallhorn, 1977; Nasr *et al*., 1999)
5. Minimal operative hazards (Schallhorn, 1977)
6. Minimal postoperative sequelae (Schallhorn, 1977)
7. Patient acceptance (Schallhorn, 1977; Nasr *et al*., 1999)

Criteria for evaluation of graft success for periodontal regeneration

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

Correspondence to: Ali Saad AlGhamdi BDS, MS, FRCD(C), Department of Oral Basic & Clinical Sciences, Faculty of Dentistry, King Abdulaziz University, P. O. Box 109725, Jeddah 21351, Saudi Arabia E-mail: dr_thafeed@hotmail.com, asalghamdi2@kau.edu

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

Factors influencing graft success

Local factors

1. Absence of infection: Bone and graft materials rapidly resorb through solution-mediated resorption in conditions of low pH. Therefore, before bone grafting, all evidence or potential causes of infection should be eliminated.
2. Soft tissue closure: Primary soft tissue closure is a mandatory condition for the success of grafting procedures. Incision line opening during initial healing is the most common postoperative complication in intraoral bone grafting (Tolman, 1995). As a result, the graft is contaminated, vascularization is delayed and/or eliminated, and loss of graft material results.
3. Defect size and topography: The predictability of regeneration is generally believed to increase as the number of remaining bony walls increases: three-wall defect > two-wall defect > one-wall defect (Cortellini and Bowers, 1995; Rosen *et al.*, 2000; Polimeni *et al.*, 2006). A deep and narrow defect is more favorable and predictable for regeneration than a shallow and wide defect (Carraro *et al.*, 1976; Cortellini and Bowers, 1995; Polimeni *et al.*, 2006).
4. Space maintenance: Space maintenance is paramount to bone formation. If the graft material resorbs too rapidly, compared with the time required for bone formation, the site may fill with connective tissue rather than bone. Therefore the space or contour and size of the augmentation should be maintained until the graft has formed enough bone to maintain the space itself (Misch, 1999; Polimeni *et al.*, 2006).
5. Healing time: Adequate healing time must be provided to allow regeneration of the new bone volume. The amount of time required is variable and depends on local factors such as the number of remaining walls of bone, the amount of autogenous bone in the graft, and the size of the defect. Larger grafts, less autogenous bone in the graft, and fewer bony walls increase the amount of healing time (Misch and Dietsh, 1993; Misch, 1999).
6. Graft immobilization: Absolute graft immobility is paramount to its union to the recipient bone. If pieces of bone graft are mobile, they cannot receive a blood supply, become encapsulated in fibrous tissue, and often sequestrate (Lin *et al.*, 1990).
7. Blood vessels: They arise from two primary sources. The host cortical bone contains very few arterioles, whereas cancellous bone has an intensely vascular network. A second source of blood vessels for transplanted bone cells is introduced into the graft site from the soft tissues (Melcher and Accursi, 1971; Misch and Dietsh, 1993).
8. Regional acceleratory phenomenon (RAP) (Misch and Dietsh, 1993): This is the local response to a noxious stimulus and describes a process by which tissue forms faster than the normal regional regeneration process. After injury, the concentration of growth factors increases significantly at the injured site, enhancing the various healing stages and causing healing to occur two to 10 times faster than normal physiologic healing (Frost, 1983). The RAP begins within a few days of injury, typically peaks at one to two months, usually lasts four months in bone, and may take six to more than 24 months to subside (Frost, 1983; Misch, 1999).
9. Growth factors: Growth factors important for bone regeneration can be placed in four groups: platelet-derived growth factors (PDGF), fibroblast growth factor (FGF), transforming growth factors beta 1 & 2 (TGF-β1 & TGF-β2), and insulin-like growth factor (IGF) (Graves *et al.*, 1994). The presence of growth factors in the graft material will enhance its osteoinductive ability and accelerate healing.
10. Particle size: A range of 125-1000 μm is acceptable with 250-750 μm most commonly available. A minimal pore size of 100 μm is needed between particles to allow vascularization and bone formation. Particles less than 100 μm in size elicit a macrophage response and are rapidly resorbed with little or no new bone formation (Zaner and Yukna, 1984).

Systemic factors

1. Conditions such as diabetes, hyperparathyroidism, thyrotoxicosis, osteomalacia, osteoporosis, Paget's disease, and some medications may all affect the healing process.
2. Habits such smoking and drinking alcohol.

Patient selection

1. Physical health
2. Oral hygiene
3. Compliance and motivation

Graft sources

1. Autografts
2. Allografts
3. Xenografts

4. Alloplasts
   Autografts and allografts will be reviewed in this paper; xenografts and alloplasts will be the topic of a separate review (Part II).

Autografts

An autograft is tissue transferred from one position to another within the same individual. It is osteogenic (able to form or develop new bone), osteoinductive (contains bone morphogenetic proteins, or BMPs, that convert the neighboring cells into osteoblasts, which in turn form bone), and osteoconductive (the matrix of the graft forms a scaffold that encourages outside cells to penetrate the graft and form new bone). The autograft is the gold standard of bone grafting procedures. It is cortical, cancellous bone and marrow, or a mixture of these tissues, harvested from intraoral or extraoral donor sites.

Intraoral autogenous graft:

Multiple intraoral locations have been used to harvest bone grafts, including the maxillary tuberosity, exostosis, healing wounds and extraction sites (a substantial quantity of mature bone is present by 8 to 12 weeks that contains osteoblasts and osteoids) (Soehren and Van Swol, 1979) and edentulous ridges (Rosen *et al.*, 2000). Another source includes harvesting of bone during osteoplasty or ostectomy and mixing it with the patient's blood to form an osseous coagulum (Robinson, 1969). An apparent limitation of this technique is the difficulty in controlling bone particle size and quantity, in addition to clinical management of graft material (Diem *et al.*, 1972; Rosen *et al.*, 2000). A bone blend is formed by placement of intraoral cortical and/or cancellous bone in a sterile amalgam capsule where it is triturated for 60 seconds. This is considered to yield a clinically manageable and predictable graft material of larger particle size (100 to 200 μm) (Diem *et al.*, 1972; Sanders *et al.*, 1983). A mean increase in bone height of 3.44 mm was reported with intraoral bone grafts (Hiatt and Schallhorn, 1973). Histological evidence of new cementum, bone and periodontal ligament formation was present with this graft in animals and humans (Hiatt and Schallhorn, 1973; Hawley and Miller, 1975; Listgarten and Rosenberg, 1979; Moskow *et al.*, 1979). An autogenous bone graft can be used alone or mixed with other graft materials. Disadvantages of this graft are second site morbidity and the limited quantity available.

Extraoral autogenous graft:

Extraoral autogenous grafts can be harvested from the iliac crest (most common), rib and cavarium. Iliac crest marrow is considered the most predictable method of osseous regeneration. It may be used fresh or may be stored in minimum essential medium (MEM) at refrigeration temperature (4°C) for a maximum of seven days before sustaining a dramatic decrease in graft viability (Bierly *et al.*, 1975; Sottosanti and Bierly, 1975). A mean increase in bone height of 2.1 mm to 3.33 mm was reported with this graft material (Schallhorn *et al.*, 1970; Dragoo and Sullivan, 1973a,b). Histological evidence of new cementum, bone and periodontal ligament formation was present with this graft in humans (Schallhorn *et al.*, 1970; Dragoo and Sullivan, 1973a,b). The main disadvantages with iliac crest bone graft are sequestration, the need for general anesthesia, prolonged postoperative recovery, root resorption (2.8 %, Dragoo and Sullivan, 1973b), ankylosis, morbidity and/or limping (Schallhorn, 1972; Schallhorn and Hiatt, 1972; Dragoo and Sullivan, 1973b; Ellegaard *et al.*, 1973; Ellegaard *et al.*, 1974).

Allografts

An allograft is tissue transferred between genetically similar members of the same species. Allografts are widely used in periodontal regeneration due to the fact that the use of autogenous grafts often implies an additional surgical site.

Types of allograft

a. Fresh unprocessed
b. Frozen bone
   These two types of allograft are not used due to the high possibility of disease transfer, antigenicity, and the need for extensive cross-matching (Nasr *et al.*, 1999).
c. Freeze-dried bone allograft (FDBA)
   FDBA has been used extensively in the treatment of periodontal osseous defects. Freeze-drying markedly reduces the health risks associated with fresh frozen bone. No anti-human leukocyte antigen (HLA) antibodies were found when FDBA was used for periodontal regeneration (Quattlebaum *et al.*, 1988), and no human immunodeficiency virus (HIV) was found in FDBA obtained from an AIDS patient (Mellonig *et al.*, 1992). The American Academy of Periodontology recommends the use of cortical rather than cancellous bone allografts, because cancellous bone is more antigenic, and cortical bone has more bone matrix and consequently more inductive components in (AAP, 1994; Nasr *et al.*, 1999). FDBA resorbs slowly; its mineralized skeleton acts as the support for new bone formation. Vascularization must occur before the production of new bone. FDBA revascularizes slowly by creeping substitution, which is a lengthy process sometimes associated with an increased chance of infection when this graft material is placed in regions of low vascularity, such as the sinus. FDBA is osteoconductive, not osteoin-

ductive. The efficacy of FDBA in the treatment of human periodontal defects was evaluated in many re-entry studies. Sixty to 67% of sites treated with FDBA demonstrated complete or more than 50% bone fill (Sepe *et al*., 1978; Mellonig, 1991). Mixing FDBA with autogenous bone enhances osteogenesis (Shapoff *et al*., 1980) and results in more bone fill (Sanders *et al*., 1983; Mellonig, 1991). The combination of purified recombinant human platelet-derived growth factor-BB (rhPDGF-BB) with FDBA provides excellent clinical and histological results with complete regeneration and bone fill in human periodontal defects (Nevins *et al*., 2003; Nevins *et al*., 2007). This combination seems to be promising and there is a need for more studies with larger sample size and different concentrations of rhPDGF-BB to affirm these results. Reconstitution of FDBA with tetracycline solution resulted in enhanced bone formation (Drury and Yukna, 1991). Disadvantages of FDBA are cost, slow revascularization, and lack of patient acceptance due to fear of transfer of disease from the donor.

d. Demineralized freeze-dried bone allograft (DFDBA)
Demineralized bone is bone that has had its mineral removed through acid treatment, then is washed and lyophilized until reconstituted for use. The remaining organic substrate contains bone morphogenetic proteins (BMPs). BMPs are a group of acidic polypeptides belonging to transforming growth factor-beta (TGF-β). Neighboring mesenchymal cells receive a signal from this protein complex that tells them to differentiate into bone-producing cells. Osteoinduction depends on oxygen tension, which in turn depends on the vascular status of the wound and the amount of BMP in the allograft. Osteoinduction also depends on donor age and processing methods. DFDBA from younger donors has more osteoinductive ability than DFDBA from older donors (Zhang *et al*., 1997b; Schwartz *et al*., 1998). Ethylene oxide (ETO) sterilization decreases effectiveness and resorption of the allograft (Aspenberg and Lindqvist, 1998; Tshamala *et al*., 1999). Irradiation of DFDBA reduced bone induction ability by 40% (Zhang *et al*., 1997b). Wide variation in osteoinductive ability of commercial DFDBA exists, even within the same bone bank (Zhang *et al*., 1997a; Schwartz *et al*., 1998). It is likely that more consistent and reliable results could be achieved with DFDBA if bone banks evaluated the potency of their preparations and reported this information to the clinician (Schwartz *et al*., 1996).

DFDBA has been used extensively in the treatment of periodontal osseous defects. Controlled clinical studies documented considerable bone fill in sites treated with DFDBA as compared to non-grafted sites (Mellonig, 1984; Meadows *et al*., 1993). Histological evidence of complete regeneration in humans with new cementum, periodontal ligament and bone amounting to 80% of the original defect depth was reported at sites treated with DFDBA (Bowers *et al*., 1989a,b). DFDBA is the only bone graft proven to result in periodontal regeneration in controlled human histological studies (Bowers *et al*., 1989b; Nasr *et al*., 1999) and is recognized in the consensus report of the 1996 World Workshop in Periodontics to fulfill all criteria for promotion of periodontal regeneration (Nasr *et al*., 1999). Disadvantages of DFDBA are cost, lack of patient acceptance due to fear of disease transfer from the donor, and radiolucency.

Conclusion

Regeneration has received a great deal of attention in research because of its obvious importance in improving the result of therapy. On the basis of available information, regeneration of supporting periodontal tissue in humans is possible in selected sites and patients with the use of autografts and/or allografts. The addition of autograft or growth factors to allograft seems to enhance the regenerative potential of these materials.

The clinician should make an effort to select graft material and a technique based on scientific evidence, the type and size of the defect, resorbability of graft material, cost, and patient acceptance.

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