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The Evolution Bone Grafts In Periodontal Surgery

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Abstract
The health of teeth and supporting structures is object central to the modern day periodontics. To replace the diseased alveolar bone, a variety of bone replacement materials are used. These can be further categorized into : bone graft substitutes and non bone graft substitutes. We in this particular review will focus on bone graft substitutes, their types, evolution, processing and biological response towards them.

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I. Introduction

Periodontal pocket formation is the result of inflammation of supporting tissues of tooth caused by specific microorganisms present in the dental plaque. It often leads to the formation of periodontal bone defects. These bone defects formed in periodontal disease are not uniform. They are either 'horizontal' or 'vertical' or 'most commonly combination of both'.

The successful periodontal treatment mainly focus on two aspects, one is prevention of the disease and other is restoration of the lost periodontal tissue. The disease progression is prevented by performing scaling and root planing and the hard tissue destruction is treated either by surgical resection or by regenerative procedures. However, regeneration of the periodontium reduced by periodontitis is an object central to periodontal treatment. Reconstructive techniques can be subdivided into, non bone graft-associated and bone graft-associated new attachment or combination of these two methods can be used. Various bone materials such as autografts, allografts, xenografts, and alloplasts have demonstrated regenerative potential and have been successfully used in the treatment of osseous defects.

This article is aimed towards discussing various bone graft materials, their evolution, processing, biological response of the tissue towards graft and factors that lead to successful graft incorporation.

II. Bone grafts can be classified based on: 93

Based on source of donor.
1. Autogenous bone graft
2. Allogenic bone graft
3. Isogenic bone graft
4. Xenografts
5. Composite grafts

Based on nature/structure of bone:
1. Cancellous bone grafts
2. Cortical bone grafts
3. Corticocancellous grafts- Blocks

Based on form
1. Blocks
2. Cortical
3. Corticocancellous
4. Particulate
5. Cortical
6. Corticocancellous
7. Mixture of both

Based on the vascularity
1. Non vascularised bone graft

2. Vascularised bone graft
3. Pedicled
4. Microvascular free transfer

Based on function
1. Bridging graft or inlay graft
2. Reconstruction graft Contour graft- onlay graft

Laurencin *et al* (2006) classification of grafts and graft substitutes:
1. Harvested bone grafts and graft substitutes
2. Autogenous bone grafts
3. Allogenic bone grafts
4. Growth factor-based bone graft substitutes
5. TGF-β, PDGF, FGF, BMP
6. Cell-based bone graft substitutes
7. Mesenchymal stem cells
8. Ceramic-based bone graft substitutes
9. Calcium hydroxyapatite (HA)
10. Tri-calcium phosphate (TCP)
11. Bioactive glass
12. Calcium phosphate cement
13. Calcium Sulfate
14. Polymer-based bone graft substitutes
15. Open porosity polylactic acid polymer
16. Miscellaneous
17. Coral
18. Chitosan and Sponge skeleton

III. History And Evolution Of Bone Graft

The use of bone grafts in periodontal therapy can be traced to the work of **Hegedus (1923)**.[67] He used autogenous bone from the tibia to the jaws to treat bone defects caused by periodontal disease. Followed by work of Hegedus, the evaluation of bone grafts from other sources became the main focus of attention. **Buebe FE and Silvers HF (1936)**[110] used boiled cow bone powder to treat the intrabony defects successfully in humans. Later **Forsberg H (1956)**[39] used **Os purum** material (i.e ox bone that is treated with potassium hydroxide, acetone and salt solution) in 11 human intrabony defects.

Melcher AH (1962)[77] grafted 187 bone defects in 163 patients with anorganic bone. This is a bovine bone from which the organic material is extracted by means of ethylenediamine and autoclaved. He found that the long term sequestration of the graft material and slow resorption were reduced with the use of anorganic bone. **Patur B and Glickman I (1962)**[98] got similar results with use of anorganic bone. Boplant was graft procured from bovine bone in late 1960s. It was prepared by detergent extraction of the bone from the soft tissue, immersion of the bone in chloroform methanol solution to reduce lipid content, sterilization of the processed bone in propiolactone, and then it was freeze dried. In 77 intraosseous defects in 56 patients, **Scopp IW et al (1966)**[117] reported that the use of boplant resulted in pocket depth reduction of 3 mm at 6 months and 4mm after one year. But the results noted in widespread clinical use of boplant followed by these reports were not coherent with the studies. They basically resulted in routine rejection and failure of the graft. Boplant was subsequently withdrawn from the market.

As autografts are considered to be gold standard, various researchers have developed techniques to obtain autografts for use in periodontal defects. These techniques evolved during late 1960s. **Nabers CL and O'Leary TJ (1965)**[91] reported that shavings of cortical bone collected during osteoplasty and osteotomy by the use of hand chisels could be used as graft in the bone defects. However due to large particle size of grafted bone, sequestration of the grafted bone was observed during long term follow ups. **Robinson RE** introduced the **osseous coagulam** technique in **1969**.[105] In this technique bone was collected with the use of high or slow speed round burs and was mixed with blood. This coagulum obtained was then used as graft. But it was difficult to aspirate the graft, quantity and quality of graft obtained, couldnot be measured and difficulty in the manipulation of the obtained material, due to its fluidity. Another technique, known as **bone blend** was proposed by **Diem CR, Bowers GM and Moffitt WL (1972)**[28] to overcome these shortcomings. In this technique, shavings of cortical and cancellous bone is obtained by trephine or bone ronguers, and then they are triturated in the amalgam capsule to a slushy bone mass. Healing extraction wounds, or osteotomy sites served as **intraoral donor sites** for autogenous grafts. **Schallhorn RG (1967, 1968)**[114,115] introduced the use of autogeneous hip marrow grafts (iliac

crest marrow) in the treatment of furcation and intrabony defects. As these procedures required a secondary surgical site to procure donor material, the morbidity and compliance of the patient was compromised.

This lead to development of allografts. **Hiatt WH and Schallhorn RG (1971)** were the first to use iliac and cancellous bone and marrow graft.[53] But this needed extensive cross matching of donor and recipient, and the possibility of disease transfer restrict the use of iliac cancellous bone and marrow allograft. **Mellonig JT *et al in 1976*** introduced undermineralized freeze dried bone allograft.[78]**Friedlander G (1988)**[40] and **Mellonig JT (1980 and 1991)**[79, 83] reported that freeze drying the bone graft rendered it non vital ; however the morphology, solubility, and chemical integrity of the original specimen are maintained relatively intact. It also reduced antigenicity of a periodontal bone allograft.[103, 123] A composite graft of FDBA and tetracycline in a 4:1 volume ratio had shown favourable results in the treatment of the osseous defects associated with localized juvenile periodontitis.[36, 133] **Libin BM *et al* (1975)**[68] were the first to report the use of cortical and cancellous decalcified FDBA (DFDBA) in humans. **Urist MR and co-workers** further conducted animal experiments to study the osteogenic potential of demineralized cortical bone graft.[124, 125, 126, 128] Demineralization with hydrochloric acid exposes the bone inductive proteins located in the bone matrix.[130] These proteins are collectively called bone morphogenetic protein (BMP). [130] BMP stimulates the formation of new bone by osteoinduction.[129]**Harkas (1984)**[47] studied that the demineralized graft induces host cells to differentiate into osteoblasts, whereas an undemineralized allograft is felt to function by osteoconduction as it affords a scaffold for new bone formation.[37]

During late 1980s various **synthetic materials** were developed. These are called as **alloplasts**. These function only as defect fillers and no true regeneration is seen with them. Various types of bone grafts and also their combinations are used with varying degrees of success. The future of bone grafts is likely to lie in the industrially manufactured biomaterials in combination with laboratory-grown cells developed by tissue-engineering.

Processing Of Bone Graft:

Autogenous grafts: Various autografts that have been used clinically are:

1. Cortical bone chips
2. Osseous coagulum and Bone blend
3. Intra and extraoral cancellous bone and marrow

Cortical bone chips: shavings of cortical bone removed by hand chisel during osteoplasty and osteotomy from the sites of surgical area are used in the osseous bone defects for regeneration of the lost tissue. However it is reported that due to large particle size of the graft (i.e 1,559.6×183 μm), chances of sequestration increases. So osseous coagulum and bone blend were used.

Osseous Coagulum and Bone Blend: osseous coagulum is obtained by shaving intraoral bone with high or low speed round burs and mixing it with blood. In bone blend technique the cortical or cancellous bone is procured by trephine or ronguers. The procured bone is then placed in an amalgam capsule and triturated to a consistency of a slushy osseous mass. The particle size is in the range of 210×105μm.

Intraoral Cancellous Bone and Marrow: this is procured from the healing bony wounds, healing extraction socket, mandibular retromolar pad area, maxillary tuberosity and edentulous ridges.

Extraoral cancellous bone and marrow: this graft is procured either from the anterior or posterior iliac crest. It is generally reported that this graft offers the greatest potential of bone growth.

Allografts:

As per American Association of Tissue Banks, collection of bone under the following circumstances is excluded for processing of graft [4]:

1. Donors from high-risk groups, as determined by medical testing and behavioral risk assessments.
2. Donors test positive for HIV antibody by ELISA.
3. Autopsy of donor reveals occult disease.
4. Donor bone tests positive for bacterial contamination.
5. Donor and bone test positive for hepatitis B surface antigen (HBsAG) or hepatitis C virus (HCV)
6. Donor tests positive for syphilis.

The main aim in the processing of allograft is to minimize the antigenicity and contamination of the graft material. Initially, the technician separates the bone from the soft tissue and section it into smaller and more manageable pieces of approximately 5 mm in diameter. Now these pieces are processed under various techniques to nearly eliminate the moisture content, reduce antigenicity and increase shelf life at room temperature. The bone particles after the first cut are given repetitive wash with solutions like acetone, ethanol or hydrogen peroxide, resulting in reduction of the organic matrix and antigenicity, succeeded by treatment with antimicrobials, antibacterials and antimycotic solutions. Now the processed bone particles are freezed with liquid nitrogen at a temperature of -80ºC, followed by lyophilization or treatment with solvent washes to eliminate remaining

moisture content and antigenicity. This is followed by secondary graft cutting to the size of 250-750 µm and packing in sterile containers. An additional step is done in case of demineralized bone allograft after secondary cutting. The bone graft particles are immersed into hydrochloric acid succeeded by immersion into the buffering solution. They are then washed with distilled water to remove the residues of buffering solution, then the graft is packed in sterile containers followed by low dose gamma irradiation at low temperatures.

Xenografts: These are derived from species other than human species. E.g bovine or porcine. These also undergo processing techniques that include- decellularization, cross linking of scaffold and terminal sterilization.

Synthetic materials: These materials are made from hydroxyapatite, calcium carbonate, or tricalcium phosphate in combination with hydroxyapatite. Hydroxyapatite is a naturally occurring mineral (main mineral component of bone), made from bioactive glass and is better known as 'synthetic bone graft'. Grafts made of calcium carbonate, are less in usage because it is completely resorbable in short time and makes breaking of the bone easier. Alloplasts made of tricalcium phosphate in combination with hydroxyapatite give effect of both, osteoconduction and resorbability.

Biological Response To Grafts

Histological analysis of the wound healing adjacent to the post grafting root surface is needed to determine the biological response to allografts. The objectives of the clinician using bone grafts are
(1) probing depth reduction;
(2) clinical attachment gain;
(3) bone fill of the osseous defect; and
(4) regeneration of new bone, cementum, and periodontal ligament.

There are largely 4 different cell types responsible for the generation of bone: osteoprogenitor cells, osteoblasts, osteoclasts, and osteocytes. Bone reconstruction on a physiologic level is accomplished by combinations of three processes: osteogenesis, osteoconduction and osteoinduction.

Osteogenesis:

Osteogenesis is defined as the formation of new bone. It occurs when viable osteoblasts or mesenchymal stem cells are transplanted with bone graft. It is the process by which osteoblasts at the defect site express osteoid that subsequently mineralizes, yielding new bone. This occurs only with fresh autologous grafts, bone marrow transplants (autograft or allograft).

Osteoconduction:

Osteo-conduction refers to a bone graft or implant's ability to provide a structural framework on which host cells reconstitute. This scaffold enables the ingrowth of vessels, osteoblasts and stem cells so that union occurs with the host skeleton. Both viable and nonviable materials may possess osteoconductive properties. The process of osteoblastic resorption followed by osteoblastic deposition is termed "creeping substitution". Osteoconductive properties are found in cancellous autografts and allografts, demineralised bone matrix, hydroxyapatite, collagen and calcium phosphate, ceramics.

Osteoinduction:

Osteoinduction is the induction of osteoprogenitor cells (or other non-differentiated cells) to differentiate down an osteoblast lineage. There is the recruitment of stem cells from the host bed into the graft site, where they differentiate into osteoblasts. Several growth factors which influence this process are bone morphogenic proteins (bmps), platelet-derived growth factors, insulin-like growth factors, fibroblast growth factors (acidic and basic), epidermal growth factor; tgf-β (β1 and β2)and retinoic acid.

HEALING OF BONE GRAFTS

STAGE	ACTION
1. Inflammation	Vasodilation, inflammatory cells attracted by chemotaxis
2. Osteoblast differentiation	Mesenchymal cells differentiate into osteoblast
3. Osteoinduction	Osteoblasts and osteoclasts are stimulated to begin process of healing
4. Osteoconduction	Bone begins to form over scaffold of graft
5. Remodeling	Resorption and new bone formation continues for extended period of time.

REQUIREMENTS FOR A SUCCESSFUL GRAFT

The outcome from bone replacement graft procedures depends on the various parameters. These parameters can be broadly divided into:
A) Patient related factors
B) Operator related factors

C) Material related factors

Patient related factors:
1) **Patient selection:** A patient who is to be treated with bone graft procedures should be:
I) In good physical health.
2) Have good oral hygiene and cooperative for long term maintenance program.
3) Should be a non-smoker. **Heasman L et al (2006)**[50]

2) Type of bone defect present:

The success of the graft is directly proportional to the number of remaining bony walls in the defect to be treated. So, the chances of success are in order: three-wall defects > two wall defect > one wall defects. **Prichard (1968)**

3) Plaque Control: good plaque control results in favourable outcome in regenerative procedures. **Rosling B et al (1976)**.[110]

4) Underlying systemic disease:

Patient related factors such as genetics, age, various systemic conditions and stress have been proposed to adversely affect the outcome of regenerative procedures. According to **Tomar SL et al (2000)**[123] diabetics have increased risk for failure of regenerative procedure because of increased microbial challenge and delayed wound healing.

5) Tooth factors:

endodontic status of the tooth and hypermobility affect the outcome of regenerative procedures. [21, 28, 87, 88, 89, 103]According to **Fleszar TJ (1980)**[38] higher attachment gain was observed in non mobile teeth after periodontal therapy.

B) Operator related factors:
1) Proper flap reflection and wound stability:

Preservation of flap tissue is important for regenerative techniques to ensure coverage and containment of the graft postsurgically. Additional care should be taken to avoid either flap perforation or loss of the papilla due to granulomatous tissue from the lesion that adheres to the inner aspect of the flap. Any granulomatous tissue that may be adherent to the inner surface of the flap or papillae from the lesion should be judiciously removed, which maximizes the space available for graft material. Excessive thinning, however, can compromise blood supply and flap survival.[25]

2) Revascularization:

The underlying bone that receives the graft material must good blood supply because prompt revascularization is crucial to ensure the survival of undifferentiated mesenchymal cells and osteoblasts at the site. **Passanezi E et al (1989)**

3) Root debridement

all hard and soft deposits and any altered cementum are completely removed from the root surface for good results.

4) Graft management

The graft is delivered to the bony defect with a (dedicated) amalgam carrier or a spatula and added in incremental fashion. Light pressure should be used to maintain space between the graft particles to allow neovascularization of the site.

. The defect should be filled or slightly overfilled to maximize regeneration while not compromising flap closure or vascular supply.[25]

5) Flap closure

The goal of flap management is to obtain tension-free primary closure over the entire graft or defect complex. A monofilament or Teflon suture using vertical mattress or an interrupted technique should be used to minimize bacterial wicking. After suturing, to minimize the clot beneath the flap, slight pressure is applied from both facial and lingual aspects of flap. It is optional to place a surgical dressing to protect the wound. .[25]

6) Postoperative management/periodontal maintenance

The administration of antibiotics beginning immediately post-surgery is thought to aid in plaque control. A systematic review by **Haffajee AD et al** (**2003)**[46] reported an additional clinical benefit in attachment level gain (weighted mean gain 0.6 mm) when systemic antibiotics were prescribed as an adjunct to surgical mechanical debridement in deep pockets.

C) Material related factors:

1) Particle size:

A minimum interparticle spacing of approximately 40µ to 200µ is necessary for the ingrowth of vascular and bony tissues. Smaller particle size will inhibit revascularization of the grafted area and consequently will retard healing process. Likewise size larger than this will have increased tendency to be exfoliated.

2) Type of material:

[65] Selection of graft material is guided by:

1. Biologic acceptability
2. Predictability
3. Resorbability
4. Clinical feasibility
5. Minimal operative hazards
6. Minimal postoperative sequelae
7. Patient acceptance [2,3]

OBJECTIVES OF BONE GRAFTING

The main reason for using bonegraft is to enhance the regenerative capability of bone and achieve a new attachment apparatus.

In a meta analysis of bone replacement grafts in the treatment of intrabony defects from **1966 to 2002**, and the **American association of Periodontology (AAP)** position paper on periodontal regeneration **(2005)** agreed that bone grafts:[4]

1. Increase the bone level.
2. Reduce crestal bone loss.
3. Increase the clinical attachment level.
4. Reduce probing depth when compared with open flap surgery.
5. Increase clinical attachment level and reduce probing depth when combined with guided tissue regeneration (GTR) compared with grafts alone.
6. Support formation of a new attachment apparatus.

IV. Summary And Conclusion

Thus, we can conclude that safety, efficacy and cost are three crucial factors when selecting the proper bone graft or bone graft substitutes in the treatment of periodontal intrabony defects. Considering these factors, one can say that allografts which provide both osteoconductive and osteoinductive properties are reasonably safe and effective and holds good promise for periodontal regeneration.

Bibliography

[1]. Alghamdi As, Shibly O, Cianco Gs. Osseous Grafting Part 1: Autograft And Allograft For Periodontal Regeneration- A Literature Review. J Int Acad Periodontol. 2010; 12(2): 34-38.
[2]. Alghamdi As, Shibly O, Cianco Gs. Osseous Grafting Part Ii: Xenograft And Alloplast For Periodontal Regeneration- A Literature Review. J Int Acad Periodontol. 2010; 12(2): 39-44.
[3]. American Association Of Tissue Banks. Http://Www.Aatb.Org. August 6, 2004.
[4]. Aspriello Sd, Ferrante L, Rubini C, Piemontese M. Comparative Study Of Dfdba In Combination With Enamel Matrix Derivative Versus Dfdba Alone For Treatment Of Periodontal Intrabony Defects At 12 Months Post-Surgery. Clin Oral Investig. 2010; 15(2):225–232.
[5]. Barnett Jd, Mellonig Jt, Gray Jl, Towle Hj. Comparison Of Freeze-Dried Bone Allograft And Porous Hydroxyapatite In Human Periodontal Defects. J Periodontol. 1989; 60(5):231-237.
[6]. Becker W, Becker Bw, Caffesse R. A Comparison Of Demineralized Freeze Dried Bone Allograft And Autologous Bone To Induce Bone Formation In Human Extraction Sockets. J Periodontol. 1994; 65(12): 1128-1133.
[7]. Beube Fe, Hf Silvers. Further Studies On Bone Regeneration With The Use Of Boiled Heterogeneous Bone. J Periodontol. 1936; 7:17-21.
[8]. Bosshardt Dd, Sculean A. Does Periodontal Tissue Regeneration Really Work. Periodontol 2000. 2009; 51: 208-219.
[9]. Bostrom Mpg, Seigerman Da. The Clinical Use Of Allografts, Demineralized Bone Matrices, Synthetic Bone Graft Substitutes And Osteoinductive Growth Factors: A Survey Study. Hss Journal. 2005; 1: 9-18.
[10]. Bowers Gm, Chadroff B, Carnevale R Et Al .Histologic Evaluation Of New Attachment Apparatus Formation In Humans. Part Iii. J Periodontol. 1989a,B; 60(12): 68.

[11]. Bowers Gm, Schallhorn Rg, Mcclain Pk, Morrison Gm, Morgan R, Reynolds Ma. Factors Influencing The Outcome Of Regenerative Therapy In Mandibular Class Ii Furcations: Part I. J Periodontol. 2003; 74(9): 1255–1268.
[12]. Boyan Bd, Weesner Tc, Lohmann Ch, Andreacchio D, Carnes Dl, Dean Dd, Cochran Dl, Schwartz Z. Porcine Fetal Enamel Matrix Derivative Enhances Bone Formation Induced By Demineralized Freeze Dried Bone Allograft In Vivo. J Periodontol. 2000; 71(8): 1278–1286.
[13]. Chalmers Jd Gray, Rush J. Observations On The Induction Of Bone In Soft Tissue. J Bone Joint Surg. 1975; 57:36-41.
[14]. Chen Cc, Wang Hl, Smith F, Glickman Gn, Shyr Y, O'neal Rb. Evaluation Of A Collagen Membrane With And Without Bone Grafts In Treating Periodontal Intrabony Defects. J Periodontol. 1995; 66(10):838–847.
[15]. Chen Sy, Wang Hl, Glickman Gn. The Influence Of Endodontic Treatment Upon Periodontal Wound Healing. J Clin Periodontol. 1997; 24(7): 449-456.
[16]. Choi Jy, Jung Uw, Lee Is, Kim Cs, Lee Yk, Choi Sh. Resolution Of Surgically Created Three-Wall Intrabony Defects In Implants Using Three Different Biomaterials: An In Vivo Study. Clin Oral Impl Res. 2011; 22(3):343–348.
[17]. Cortelleni P, Bowers Gm. Periodontal Regeneration Of Intrabony Defects: An Evidence Based Treatment Approach. Int J Periodontics Restorative Dent. 1995; 15(2): 129-145.
[18]. Cortellini P, Tonetti Ms. Evaluation Of The Effect Of Tooth Vitality On Regenerative Outcomes In Infrabony Defects. J Clin Periodontol. 2001; 28: 672-679.
[19]. Cohen Es. Chapter 10. Inductive Osseous Surgery. Atlas Of Cosmetic And Reconstructive Periodontal Surgery. Iii Edition. 2007. 129-158.
[20]. Diem Cr, Bowers Gm, Moffitt Wc. Bone Blending: A Technique For Bone Implantation. J Periodontol. 1972; 43:295-297.
[21]. Drury Gi, Yukna Ra. Histologic Evaluation Of Combining Tetracycline And Allogeneic Freeze-Dried Bone On Bone Regeneration In Experimental Defects In Baboons. J Periodontol. 1991; 62(11):652–658.
[22]. Dumitrescu Al. Bone Grafts And Bone Graft Substitutes In Periodontal Therapy. Chemicals In Surgical Periodontal Therapy. 2011. 73-144.
[23]. Duval Bt, Maynard Jg, Gunsolley Jc, Waldrop Tc. Treatment Of Human Mucogingival Defects Utilizing A Bioabsorbable Membrane With And Without A Demineralized Freeze-Dried Bone Allograft. J Periodontol 2000;71(11):1687–1692
[24]. Eagan Mj, Mcallister Dr. Biology Of Allograft Incorporation. Clin Sports Med. 2009; 28:203–214.
[25]. Ehnevid H, Janson L, Lindskog S, Blomof L. Periodontal Healing In Teeeth With Periapical Lesions. A Clinical And Retrospective Study. J Clin Periodontol. 1993; 20(4):254-258.
[26]. Evans Gm, Yukna Ra, Sepe Ww, Mabry Tw, Mayer Et. Effect Of Various Graft Materials With Tetracycline In Localized Juvenile Periodontitis. J Periodontol. 1989; 60(9):491-497.
[27]. Fagan Mc, Owens H, Smaha J, Kao Rt. Simultaneous Hard And Soft Tissue Augmentation For Implants In The Esthetic Zone: Report Of 37 Consecutive Cases. J Periodontol. 2008; 79(9):1782–1788.
[28]. Fleszar Tj, Knowles Jw, Morrison Ec, Burgett Fg, Nissle Rr, Ramfjord Sp. Tooth Mobility And Periodontal Therapy. J Clin Periodontol. 1980; 7(6):495-505.
[29]. Forsberg H. Transplantation Of Os Purum And Bone Chips In The Surgical Treatment Of Periodontal Disease (Preliminary Report). Acta Odontol. Scand. 1956; 13:235-238.
[30]. Friedlaender G. Bone Banking. Clin Orthop. 1987; 225:17-21.
[31]. Fucini Se, Quintero G, Gher Me, Black Bs, Richardson Ca. Small Versus Large Particles Of Demineralized Freeze Dried Bone Allograft In Human Intrabony Periodontal Defects. J Periodontol. 1993; 64:844-847.
[32]. Goldberg Vm And Stevenson S. Natural History Of Autografts And Allografts. Clin. Orthop.1987; 225:7-16.
[33]. Goldman Hm, Cohen Dw. Periodontal Therapy. 6th Edition. 1980; 976-977.
[34]. Grover V, Kapoor A, Malhotra R, Sachdeva S. Bone Allografts: A Review Of Safety And Efficacy. Indian J Dent Res. 2011; 22(3):532-537.
[35]. Gurinsky Bs, Mills Mp, Mellonig Jt. Clinical Evaluation Of Demineralized Freeze-Dried Bone Allograft And Enamel Matrix Derivative Versus Enamel Matrix Derivative Alone For The Treatment Of Periodontal Osseous Defects In Humans. J Periodontol. 2004; 75(10):1309–1318.
[36]. Haffajee Ad, Socransky Ss, Gunsolley Jc. Systemic Anti- Innfective Periodontal Therapy. A Systemic Review. Ann Periodontol. 2003; 8(1):115-181.
[37]. Harakas N. Demineralized Bone-Matrix-Induced Osteogenesis. Clin. Orthop. 1984; 188:239-251.
[38]. Harris Rj, Harris Le, Harris Cr, Harris Aj. Clinical Evaluation Of A Combined Regenerative Technique With Enamel Matrix Derivative, Bone Grafts, And Guided Tissue Regeneration. Int J Periodontics Restorative Dent. 2007; 27:171–179.
[39]. Hanes Pj. Bone Replacement Grafts For Treatment Of Periodontal Intrabony Defects. Oral And Maxillofac Surg Clin North Am. 2007; 19:499-512.
[40]. Heasman L, Stacey F, Preshaw Pm, Mc Cracken G, Hepburn S, Heasman Pa. The Effect Of Smoking On Periodontal Treatment Response: A Review Of Clinical Evidence. J Clin Periodontol. 2006; 33(4):241-253.
[41]. Herold Rw, Pashley Dh, Cuenin Mf, Niagro F, Hokett Sd, Peacock Me, Mailhot J, Borke J. The Effects Of Varying Degrees Of Allograft Decalcification On Cultured Porcine Osteoclast Cells. J Periodontol. 2002; 73(2):213–219.
[42]. Hiatt Wh, Schallhorn Rg. Intraoral Transplants Of Cancellous Bone And Marrow In Periodontal Lesions. J Periodontol. 1973; 44:194–208.
[43]. Holtzclaw D, Toscano N, Eisenlohr L. The Safety Of Bone Allografts Used In Dentistry: A Review. J Am Dent Assoc. 2008; 139:1192–1199.
[44]. Kassolis Jd, Rosen Ps, Reynolds Ma. Alveolar Ridge And Sinus Augmentation Utilizing Platelet-Rich Plasma In Combination With Freeze-Dried Bone Allograft: Case Series. J Periodontol. 2000; 71(10):1654–1661.
[45]. Kimble Km, Eber Rm, Soehren S, Shyr Y, Wang Hl.Treatment Of Gingival Recession Using A Collagen Membrane With Or Without The Use Of Demineralized Freeze Dried Bone Allograft For Space Maintenance. J Periodontol. 2004; 75:210–220.
[46]. Kolerman R, Tal H, Moses O. Histomorphometric Analysis Of Newly Formed Bone After Maxillary Sinus Floor Augmentation Using Ground Cortical Bone Allograft And Internal Collagen Membrane. J Periodontol. 2008; 79:2104–2111.
[47]. Koskinen Es, Ryoppy, Linkholm T. Osteoinduction And Osteogenesis In Implants Of Allogeneic Bone Matrix. Clin. Orthop.1972; 87:116-131.
[48]. Kuo Tc, Lee Bs, Kang Sh, Lin Fh, Lin Cp. Cytotoxicity Of Dp-Bioglass Paste Used For Treatment Of Dentin Hypersensitivity. J Endod. 2007; 33(4):451–454.
[49]. Laurell L, Gottlow J, Zybutz M, Persson R. Treatment Of Intrabony Defects By Different Surgical Procedures. A Literature Review. J Periodontol. 1998; 69(3):303–313.

[50]. Libin Bm, Ward H, Fishman L. Decalcified Lyophilized Bone Allografts For Use In Human Periodontal Defects. J Periodontol.1975; 45:51-56.
[51]. Lohmann Ch, Andreacchio D, Koster G, Carnes Dl Jr, Cochran Dl, Dean Dd, Boyan Bd, Schwartz Z. Tissue Response And Osteoinduction Of Human Bone Grafts In Vivo. Arch Orthop Trauma Surg. 2001; 121:583–590.
[52]. Mabry Tw, Yukna Ra, Sepe Ww. Freeze Dried Bone Allograft With Tetracycline In The Treatment Of Juvenile Periodontitis. J Periodontol. 1985; 56(2):74-81.
[53]. Mahesh J, Mahesh R, John J. Predictability Of Bone Regeneration In Periodontal Surgery- A Review. Iosar -Jdms. 2012; 2 (6):46-50.
[54]. Malinin Ti, Temple Ht, Garg Ak. Bone Allograft In Dentistry: A Review. Dentistry. 2014; 4(2):1-8.
[55]. Mao T, Kamakshi V. Bone Grafts And Bone Substitutes. Int J Pharm Sci. 2014; 6 (2):88-91.
[56]. M Bohner. Bone Substitute Materials. Reference Module In Biomedical Research. 2014; 3:1-15.
[57]. Meadows Cl, Gher Me, Quintero G, Zafferty Ta. A Comparison Of Polylactic Acid Granules And Demineralized Freeze Dried Bone Allograft In Human Periodontal Human Defects. J Periodontol. 1993; 64(2):103-109.
[58]. Mehrara Bj, Mccarthy Joseph. Repair And Grafting Of Bone. In: Mathes Sj Ed. Plastic Surgery Vol-2. Philadelphia: Wb Saunders. 2005:639-718.
[59]. Melcher Ah. The Use Of Heterogenous Anorganic Bone As An Implant Material In Oral Procedures. Oral Surg.1962; 15:996-1000.
[60]. Mellonig Jt, Bowers Gm, Bright Rw, Lawerence Jj. Clinical Evaluation Of Freeze Dried Bone Allograft In Periodontal Osseous Defects. J Periodontol. 1976; 47(3):125-131.
[61]. Mellonig Jt. Alveolar Bone Induction: Autografts And Allografts. Dent. Clin. North Am. 1980; 24:719-737.
[62]. Mellonig Jt. Bone Allografts In Periodontal Therapy. Clin. Orthop. 1996; 324:116-125.
[63]. Morris Ml. The Reattachment Of Human Periodontal Tissues Following Surgical Detachment. A
[64]. Morris Ml. Healing Of Human Periodontal Tissues Following Surgical Detachment And Extirpation Of Vital Pulps. J Periodontol. 1960; 31:23–26.
[65]. Moucha Cs, Renard Rl, Gandhiankur, Lin Ss, And Tuan Rs. Bone Allograft Safety And Performance. Engineering Of Functional Skeletal Tissues. 2007; 3:46-54.
[66]. Nabers Cl, O'leary Tj. Autogenous Bone Transplants In The Treatment Of Osseous Defects. J Periodontol.1965; 36:5-14.
[67]. Nandi Sk, Roy S, Mukherjee P, Kundu B, Dk De & D. Basu. Orthopaedic Applications Of Bone Graft & Graft Substitutes: A Review. Indian J Med Res. 2010; 132:15-30.
[68]. Nassif L, El Sabban M. Mesenchymal Stem Cells In Combination With Scaffolds For Bone Tissue Engineering. Materials. 2011; 4:1793-1804.
[69]. Nasr Hf, Aichelmann-Reidy Me, Yukna Ra. Bone And Bone Substitutes. Periodontol 2000. 1999; 19:74–86.
[70]. Nevins M, Hanratty J, Lynch Se. Clinical Results Using Recombinant Human Platelet-Derived Growth Factor And Mineralized Freeze-Dried Bone Allograft In Periodontal Defects. Int J Periodontics Restorative Dent. 2007; 27(5):421–427.
[71]. Oreamuno S, Lekovic V, Kennery Eb, Carranza Fa Jr, Takei Hh And Prokic B. Comparative Clinical Study Of Porous Hydroxyapatite And Demineralized Freeze Dried Bone Allograft In Human Periodontal Defects. J Periodontol. 1990; 61(7):399-404.
[72]. Patur B, Glickman I. Clinical And Roentgenographic Evaluation Of The Post-Treatment Healing Of Infrabony Pockets. J Periodontol. 1962; 33:164-171.
[73]. Piattelli A, Scarano A, Corigliano M, Piattelli M. Comparison Of Bone Regeneration With The Use Of Mineralized And Demineralized Freeze-Dried Bone Allografts: A Histological And Histochemical Study In Man. Biomaterials. 1996; 17:1127-1131.
[74]. Prichard J. The Etiology, Diagnosis And Treatment Of The Infrabony Defect. J Periodontol. 1967; 38:455.
[75]. Prichard Jf. Advanced Periodontal Disease. Surgical And Prosthetic Management. 2nd Edition. Philadelphia: Wb Saunders; 1972.
[76]. Quattlebaum J, Mellonig Jt, And Hansel N. Antigenicity Of Freeze-Dried Cortical Bone Allograft In Human Periodontal Osseous Defects. J Periodontol. 1988; 59:394-397.
[77]. Reddi Ah, Wientroub S, Muthukmuaran N. Biologic Principles Of Bone Induction. Orthop Clin North Am. 1987; 18:207-212.
[78]. Robinson Re. Osseous Coagulum For Bone Induction. J Periodontol. 1969; 40:503-510.
[79]. Rosen Sp, Reynolds Ma, Bowers Gm. The Treatment Of Intrabony Defects With Bone Grafts. Periodontol 2000. 2000; 22:88-103.
[80]. Rosen Ps, Reynolds Ma. Guided Bone Regeneration For Dehiscence And Fenestration Defects On Implants Using An Absorbable Polymer Barrier. J Periodontol. 2001; 72(2):250–256
[81]. Rosen Ps, Reynolds Ma. A Retrospective Case Series Comparing The Use Of Demineralized Freeze-Dried Bone Allograft And Freeze-Dried Bone Allograft Combined With Enamel Matrix Derivative For The Treatment Of Advanced Osseous Lesions. J Periodontol. 2002;73(8):942–949
[82]. Rosenberg E, Rose Lf. Biologic And Clinical Considerations For Autografts And Allografts In Periodontal Regeneration Therapy. Dent Clin North Am. 1998; 42:467–490
[83]. Rosling B, Nyman S, Lindhe J. The Effect Of Systematic Plaque Control On Bone Regeneration In Intrabony Pockets. J Clin Periodontol. 1976; 3(1):38-53.
[84]. Rummelhart Jm, Mellonig Jt, Gray Jl, Towle Hj. A Comparison Of Freeze Dried Bone Allograft And Demineralized Freeze Dried Bone Allograft In Human Periodontal Osseous Defects. J Periodontol. 1989; 60(12):655-663.
[85]. Sanders Jj, Sepe Ww, Bowers Gm, Koch Rw, Williams Je, Lekas Js, Mellonig Jt, Pelleu Gb Jr, Gambill V. Clinical Evaluation Of Freeze-Dried Bone Allografts In Periodontal Osseous Defects. Part Iii. Composite Freeze-Dried Bone Allografts With And Without Autogenous Bone Grafts. J Periodontol. 1983; 54(1):1–8.
[86]. Schallhorn Rg. The Use Of Autogenous Hip Marrow Biopsy Implants For Bony Crater Defects. J Periodontol. 1968; 39:145-147.
[87]. Schwartz Z, Mellonig Jt, Carnes Dl Jr, De La Fontaine J, Cochran Dl, Dean Dd, Boyan Bd. Ability Of Commercial Demineralized Freeze-Dried Bone Allograft To Induce New Bone Formation. J Periodontol. 1996; 67(9):918–926
[88]. Sculean A, Jepsen S. Biomaterials For The Reconstructive Treatment Of Periodontal Intrabony Defects. Periodantal Practice Today. 2004, 1(4). 97-109.
[89]. Shapoff Ca, Bowers Gm, Levy B, Mellonig Jt, Yukna Ra. Effect Of Particle Size On The Osteogenic Activity Of Composite Grafts Of Allogenic Freeze Dried Bone And Autogenous Marrow. J Periodontol. 1980; 51(11): 625-630.
[90]. Trejo Pm, Weltman R, Caffesse R. Treatment Of Intraosseous Defects With Bioabsorbable Barriers Alone Or In Combination With Decalcified Freeze-Dried Bone Allograft: A Randomized Clinical Trial. J Periodontol. 2000; 71(12):1852–1861.
[91]. Tomar Sl, Asma S. Smoking-Attributable Periodontitis In The United States; Findings From Nhanes Iii. National Health And Nutrition Examination Survey. Journal Of Periodontology. 2000; 71:743–75l.
[92]. Turner Dw, Mellonig Jt. Antigenicity Of Freeze Dried Bone Allograft In Periodontal Osseous Defects. J Periodont Res. 1981; 16:89-99.
[93]. Urist Mr. Bone Formation By Autoinduction. Science. 1965; 150:893-899.

[94]. Urist Mr, Dowell Ta. Inductive Substratum For Osteogenesis In Pellets Of Particulate Bone Matrix. Clin. Orthop. 1968; 61:61-78.
[95]. Urist Mr And Strates B. Bone Morphogenetic Protein. J Den Res. 1971; 50:1392-1406.
[96]. Wang Hl, Kimble K, Eber R. Use Of Bone Grafts For The Enhancement Of A Gtr-Based Root Coverage Procedure: A Pilot Case Study. Int J Periodontics Restorative Dent. 2002; 22(2):119–127.
[97]. West Tl, Brustein Dd. Freeze Dried Bone And Coralline Implants Compared In The Dogs. J Periodontol. 1985; 56(6):348-351.
[98]. Yukna R, Sepe W. Clinical Evaluation Of Localized Periodontosis Defects Treated With Freeze-Dried Bone Allografts Combined With Local And Systemic Tetracyclines. Int J Periodontics Restorative Dent. 1982; 2(5):8 - 21.
[99]. Yukna Ra, Vastardis S. Comparative Evaluation Of Decalcified And Non Decalcified Freeze Dried Bone Allograft In Rhesus Monkeys. I. Histological Findings. J Periodontol. 2005; 76(1):57-65.
[100]. Zaner Dj, Yukna Ra. Particle Size Of Periodontal Bone Grafting Materials. J Periodontol. 1984; 55(7):406-409.