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Review Article

Guided bone regeneration: A literature review

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Abstract

Guided bone regeneration (GBR) is a reconstructive procedure of alveolar ridge using membranes. This procedure is indicated when there is no sufficient bone for implantation, or in the case of optimal implant installation for esthetic or functional needs. GBR can be performed before implant placement, when there is not enough bone for initial stability of implants and less predictable outcomes (staged approach), or performed simultaneously with implantation (combined approach). GBR techniques have been used for vertical and horizontal ridge augmentations with acceptable results. This literature review discusses the background, principles of GBR, the materials used in GBR (types of membranes and bone grafts), success criteria and long term results of GBR.

KEY WORDS: Guided bone regeneration, graft materials, dental implants, alveolar ridge augmentation.

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Predictable formation of a direct bone-to-implant interface is a treatment goal in implant dentistry. For this purpose, the existence of appropriate bone quality and quantity is necessary and important.[1]

Loss of alveolar bone may occur prior to tooth extraction because of periodontal disease, periapical pathology, or trauma to teeth and bone. Damage to the bone tissues during tooth extraction procedures may also result in bone loss. Finally, alveolar bone atrophy after tooth extraction is a well-known phenomenon. Sufficient alveolar bone volume and favorable architecture of the alveolar ridge are essential to obtain ideal functional and esthetic prosthetic reconstruction following implant therapy.[1] Four methods have been described to increase the rate of bone formation and to augment bone volume: osteoinduction using appropriate growth factors,[2] osteoconduction where a grafting material serves as a scaffold for new bone growth,[3] distraction osteogenesis by which a fracture is surgically induced and the two fragments are then slowly pulled apart[4] and finally, guided bone regeneration (GBR) which allows spaces maintained by barrier membranes to be filled with new bone.[5]

GBR is based on principles of guided tissue regeneration (GTR).[6] GTR was first developed in the early 1980s by Nyman et al.[6] This concept is based on the principle that specific cells contribute to the formation of specific tissues.[7] Melcher described the concept of selective cell repopulation of defects to enhance healing.[7] Exclusion of fast-growing epithelium and connective tissue from a periodontal wound for 6-8 weeks allows the slower growing tissues including osteoblasts, cementoblasts, and periodontal ligament cells, occupy the space adjacent to the tooth.[6,8] GBR concept employed the same principles of specific tissue exclusion but was not associated with teeth. Thus the term applied to this technique was guided bone regeneration (GBR).

Dahlin and colleagues spearheaded early research on GBR in an attempt to solve the confounding problem of reconstructing large osseous defects in the jaws and for the treatment of the atrophic maxilla or mandible. It is known that to accomplish the repair of a bone

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defect, the rate of osteogenesis extending inward from the adjacent bone ends must exceed the rate of fibrogenesis growing in from the surrounding muscle or connective tissue.[5,9,10]

In 1988, Dahlin et al.[5] published the results of animal experimentation on the healing of bone defects. Bilaterally, a through-and-through defect was surgically created in the ramus of 30 Sprague-Dawley rats. On one side of the jaw, the defect was covered with a porous polytetrafluoroethylene (PTFE) membrane (Gore-Tex®). The other side served as the control, without a membrane covering. After 3, 6 and 9 weeks of healing, the specimens were evaluated macroscopically and histologically by light microscope. Statistical analysis of the healed sites demonstrated a highly significant increase in bone regeneration on the membrane side as compared to the control.

Dahlin et al.[10] evaluated the principle of GTR to generate bone at the exposed parts of titanium implants. Thirty ''commercially pure'' 10 mm titanium implants were placed in the tibia of 15 adult rabbits, each with three to four exposed threads per implant. A PTFE membrane was placed over the test fixtures, covering the threads and 5 to 8 mm of the adjacent bone. The muscle and periosteum were replaced, adapted and sutured. The control fixtures were not covered with a membrane. After healing periods of 6, 9 and 15 weeks, the specimens were removed and evaluated grossly and histologically. The results showed that all exposed threads of the titanium implants were covered with newly formed bone at a uniform thickness, even as early as 6 weeks. New bone formation also was seen in the control areas, although to a much lesser extent than the test areas. It was shown that by placing an inert membrane with an appropriate pore size that hindered the penetration of undesirable cells, a space was created that permitted the entrance of osteogenic and angiogenic cells from the adjacent bone marrow to populate the area and proliferate. It was also recognized that the amount of new bone formation was contingent upon the amount of space created by the membrane.

Schenk et al.[11] histologically demonstrated that bone regeneration in membrane-protected defects healed in a sequence of steps that simulated bone formation of woven bone initially along new blood vasculature at the periphery of the defect. The new vascular supply emanated from surgically created perforations in the cortical bone. The woven bone was subsequently replaced by lamellar bone, which resulted in mature bone anatomy. Ultimately, bone remodeling occurred with the new secondary osteons being formed.

Because the objective of GBR is to regenerate a single tissue namely bone, it is theoretically easier to accomplish it compared to GTR that requires the regeneration of bone, periodontal ligament (PDL) and cementum to form a new periodontal apparatus.[5] More than two decades have passed from the introduction of GBR into clinical practice. Today, the general understanding of the mechanisms leading to regeneration of desired tissues still agrees with the initially published statements.[6]

Principles of guided bone regeneration

To achieve better clinical outcomes, the GBR barrier should possess the following properties:[12]

Cell exclusion: In GBR, the barrier membrane is used to prevent gingival fibroblasts and/or epithelial cells from gaining access to the wound site and forming fibrous connective tissue.

Tenting: The membrane is carefully fitted and applied in such a manner that a space is created beneath the membrane, completely isolating the defect to be regenerated from the overlying soft tissue. It is important that the membrane be trimmed so that it extends 2 to 3 mm beyond the margins of the defect in all directions. The corners of the membrane should be also rounded to prevent inadvertent flap perforation.

Scaffolding: This tented space initially becomes occupied by a fibrin clot, which serves as a scaffold for the in-growth of progenitor cells. In GBR, the cells will come from adjacent bone or bone marrow.

Stabilization: The membrane must also protect the clot from being disturbed by movement of the overlying flap during healing. It is therefore often, but not always, fixed into position with sutures, mini bone screws, or bone tacks. Sometimes, the edges of the membrane are simply tucked beneath the margins of the flaps at the time of closure, providing stabilization.

Framework: Where necessary, as in non-space maintaining defects such as dehiscences or fenestrations, the membrane must be supported to prevent collapse.

Bone-replacement grafts are often used for this purpose. They serve as a sort of internal framework to provide a measure of support to the graft. Stiffer membranes such as titanium-reinforced membranes have also been used for this purpose.

Wang and Boyapati[13] proposed the PASS principles for predictable bone regeneration in 2006. To attain horizontal and/or vertical bone augmentation beyond the envelope of skeletal bone, four principles are needed to be met: exclusion of epithelium and connective tissue, space maintenance, stability of the blood clot, and primary wound closure.

Barrier membranes

There are five criteria considered important in the design of barrier membranes used for GTR.[14,15] These include biocompatibility, cell-occlusiveness, space making, tissue integration and clinical manageability. Various types of materials have been developed, which can be grouped together as either non-resorbable or resorbable membranes.

Non-resorbable membranes

The first membranes used experimentally by Nyman's group in their initial work were constructed from Millipore® (cellulose acetate) filters. As this technique became more prevalent, the first commercial membrane was produced from Teflon® (e-PTFE). This membrane consisted of 2 parts: a collar portion, having open pores to allow in-growth of connective tissue and to prevent epithelial migration; and an occlusive portion, preventing the flap tissues from coming into contact with the root surface.[16] This membrane is the gold standard of GTR and GBR treatments.[16]

PTFE is a synthetic fluoropolymer that relies on an extremely strong bond between carbon and fluorine for its nondegradable, biologically inert properties. There is no known enzyme in the body capable of cleaving carbon-fluorine bonds. Added rigidity of the material, PTFE, can be achieved by reinforcement with fluorinated ethylene propylene, resulting in ePTFE.[17] Study by Buser et al.[18] was one of the first to report successful ridge augmentation with GBR in humans using an e-PTFE membrane and tenting pins. The gain in new bone formation ranged from 1.5 to 5.5 mm.

Creation and maintenance of sufficient space underneath the barrier is an important factor for a successful result. Therefore, titanium-reinforced polytetrafluoroethylene membranes (PTFE, Gore-Tex, WL Gore, Flagstaff, AZ, USA) and titanium membranes (Figure 1) were introduced to increase the stability of barrier membranes [15,19,20]

Lundgren et al. compared guided bone regeneration by PTFE membranes with titanium foils. The most regeneration was seen in defects underneath the titanium foils, particularly if they had perforations. The authors suggested the possibility that cells and fluids necessary for nourishment had passed through the perforated foils and aided regeneration.[21]

Since 1995, titanium membranes with microperforations (FRIOS BoneShield, Friatec, Mannheim, Germany) have been used for guided bone regeneration. The membranes are either triangular or oval. The mechanical properties of the membrane prevent collapse of the membrane and provide a constant volume underneath it and areas of microporosity that are small enough to prevent soft tissue penetration through the membrane permit diffusion of interstitial fluid.[22]

High surface roughness of ePTFE membranes facilitates adhesion of bacteria. Thus, primary closure over the membrane needs to be achieved to avoid exposure to the oral environment and resulting bacterial colonization

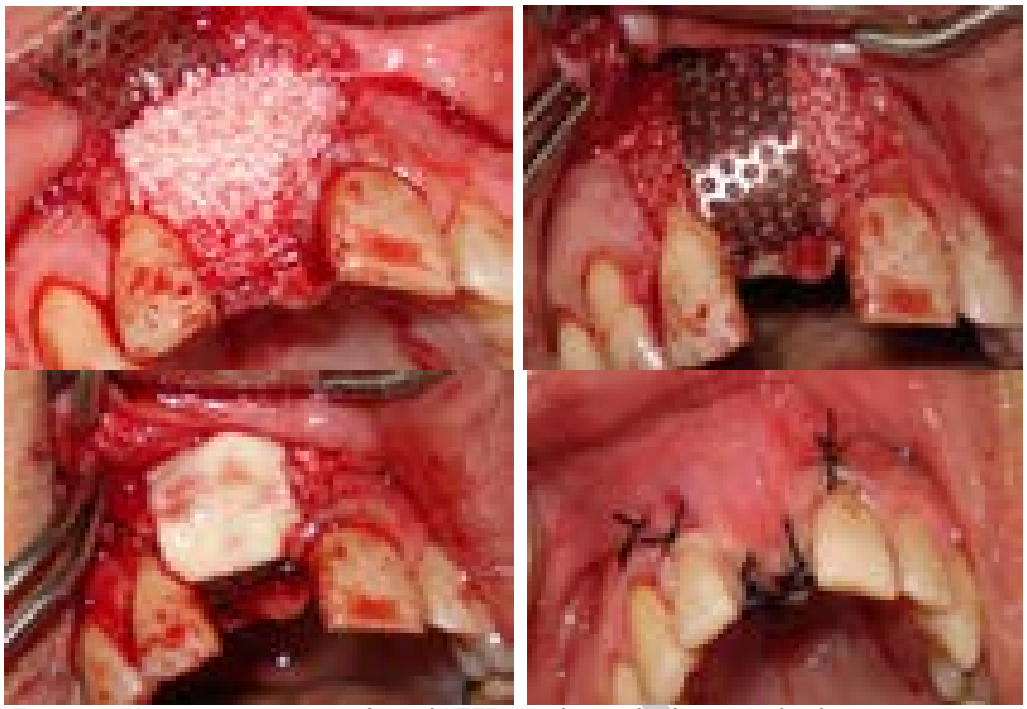

Figure 1. Using a titanium-reinforced PTFE membrane for horizontal ridge augmentation

because the resulting inflammation can impair the treatment outcome. Furthermore, the removal of ePTFE membranes often necessitates a second surgical procedure.[23] For these reasons, Aa membrane made of high-density polytetrafluoroethylene (dPTFE), designed specially for use in socket grafting, which does not require primary closure, was introduced by Barry Bartee (Figure 2).[24] For usage of this membrane, no primary coverage is necessary and there is no need for releasing incisions or additional freeing of the flap; thereby facilitating the surgical procedure and enhancing the esthetic outcome by not changing the mucogingival junction. In addition, because of the comparatively smooth surface, dPTFE membranes can usually be removed without an additional surgical procedure.[23] Significant advantage of dPTFE membranes is impenetrable for bacteria because of its surface characteristics.[23] The successful use of this membrane was shown in animal and clinical studies.[23-25]

Resorbable membranes

There are two types of biologically resorbable membranes: 1) polyglycoside synthetic

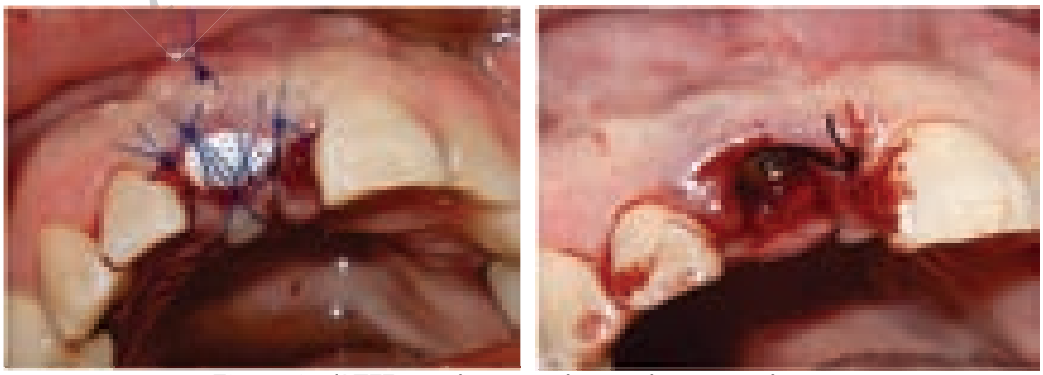

Figure 2. dPTFE membrane with open barrier technique

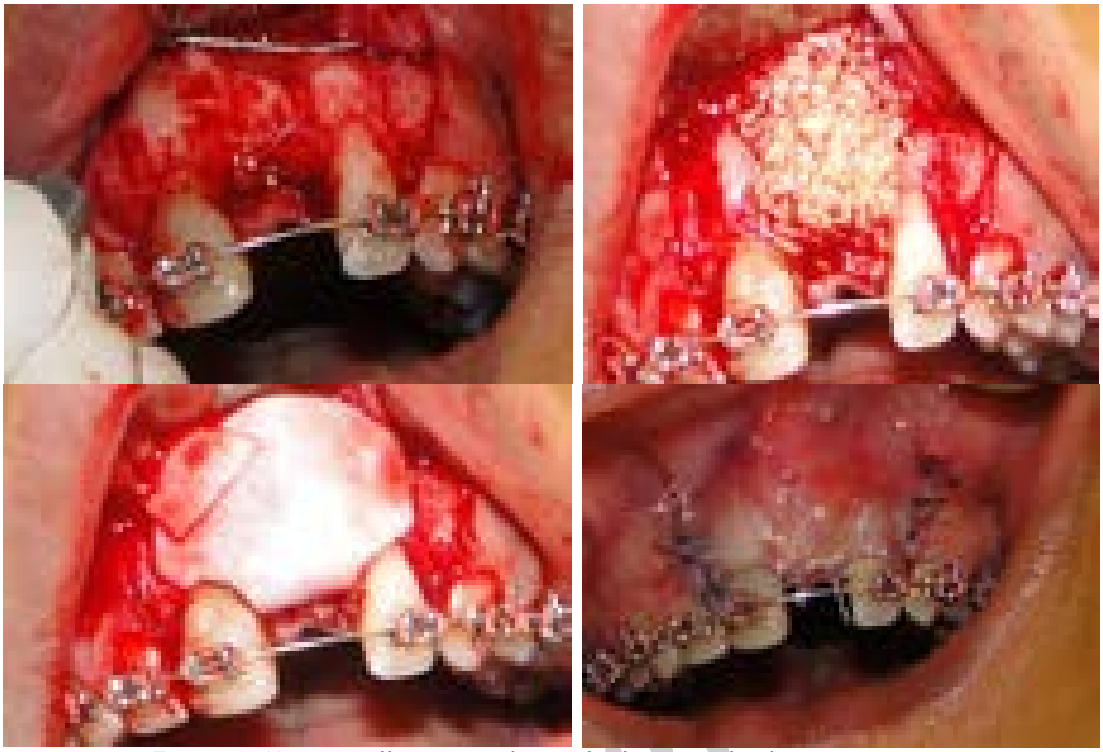

Figure 3. Using a collagen membrane for horizontal ridge augmentatio

copolymers: polylactic acid (Guidor®), polyglactide and polylactide (Resolute), polyglactin 910 (Vicryl®); 2) collagen.[17]

Collagen membranes share in common with all resorbable membranes the fact that they do not require a second surgery for retrieval.

This saves time and cost and is greatly appreciated by patients (Figure 3). Collagen is the principal component of connective tissue and provides structural support for tissues throughout the body.[12] Properties of collagen

membranes are mentioned below: Hemostasis: Collagen is hemostatic agent and possesses the ability to stimulate platelet attachment and to enhance fibrin linkage, which may facilitate initial clot formation and clot stabilization, leading to enhanced regeneration.[12]

Chemotaxis: Collagen has been shown to be chemotactic for fibroblasts in vitro. This property could enhance cell migration in vivo.[12]

Ease of manipulation: collagen can be easily manipulated and adapted.[12]

Well tolerated: Collagen has been demonstrated to be a weak immunogen and is therefore, well tolerated by patients. Membranes made of bovine collagen do not elicit an antibody response when used in GTR.[12]

Bioresorbable: Because collagen is bioresorbable, during enzymatic degradation, it will incorporate with the flap to support new connective tissue attachment.[26] This may result in augmenting tissue/flap thickness to protect further bone formation.

Slow absorption: Membranes must remain in place until cells capable of regeneration are established at the wound site. Collagen membranes cross-linked with formaldehyde have been shown by Blumenthal[27] to last 6 to 8 weeks before being absorbed, whereas non-cross linked membranes lose their structural integrity in 7 days.

Degradation of resorbable membranes is accomplished by various mechanisms present within the periodontal tissues. The primary structural component of most commercially available collagen membranes is type I collagen, which is degraded by endogenous collagenase into carbon dioxide and water. Cross-linkage of collagen fibers can affect the rate of degradation.[28] Cross-linking is a laboratory

modification of the collagenous matrix designed to stabilize the collagen fibers and maintain the integrity of the membrane after placement.[29] There are many different laboratory techniques for cross-linking collagen membranes, including ultraviolet light and glutaraldehyde, which increases the time period that the device serves as an occlusive barrier in vivo.[29]

Cross linking of collagen membranes was associated with prolonged biodegradation, decreased tissue integration and decreased vascularization.[30] Clinically, the rapid degradation of non-cross-linked collagen membranes following exposure to the oral cavity has been reported to be an advantage in horizontal ridge augmentation procedures.[31]

Acellular dermal matrix allograft (AlloDerm™) has been used in periodontal, plastic and reconstructive surgery since 1994. AlloDerm™ may be used for soft tissue augmentation procedures around dental implants without using the patient's own palate to procedure the donor tissue (Figure 4).[32]

Fowler et al. in their case report preserved the ridge with utilizing an acellular dermal matrix as a barrier membrane and a demineralized freeze-dried bone allograft. This report demonstrated an acceptable esthetic result with no loss of ridge height or width. Soft tissue dimensions were also preserved. The two graft materials were well accepted by the body and healing was rapid and without significant discomfort.[33]

In another study, Borges et al. compared the effectiveness of the acellular dermal matrix (ADM) as a membrane for guided bone regeneration (GBR), with a bioabsorbable membrane. In seven dogs, the mandibular premolars were extracted. After 8 weeks, one bone defect was surgically created bilaterally and the GBR was performed. Each side was randomly assigned to the control group (CG: bioabsorbable membrane made of glycolide and lactide copolymer) or the test group (TG: ADM as a membrane). Post-operative healing of the CG was uneventful. In the TG, membrane was exposed in two animals and one of them was excluded from the sample. There were no statistically significant differences between the groups for any histomorphometric measurement. Clinically, both groups showed an increase in the thickness of keratinized tissue and a reduction in the width of keratinized tissue. Radiographically, an image suggestive of new bone formation could be observed in both groups at 8 and 16 weeks following GBR.[34]

The use of Alloderm has several advantages because it does not contain cellular material, which eliminates the possibility of rejection because of the presence of major histocompatibility complex class I and II antigens. In addition, the unlimited supply, color match, and thickness, as well as no degradation if primary closure is not achieved, and formation of additional attached gingival makes this material a good choice for membrane barrier techniques.

Oh et al. compared two collagen membranes, Bio-Gide ® and BioMend ExtendTM, for the treatment of implant dehiscence defects in eight mongrel dogs.[35] The results of this study indicated that: (1) GBR treatment with

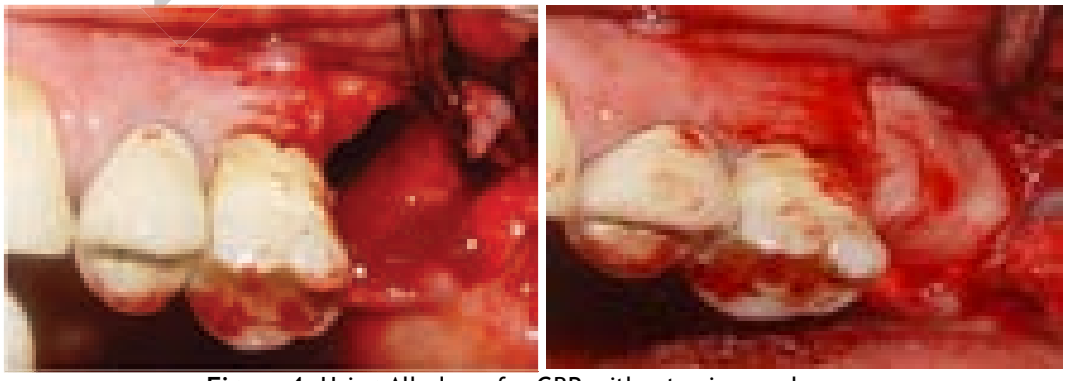

Figure 4. Using Alloderm for GBR without primary closure

collagen membranes may significantly enhance bone regeneration, manifested at late stage (16 weeks) of healing; and (2) space maintenance and membrane coverage were the two most important factors affecting GBR using bioabsorbable collagen membranes.

Synthetic polymers can be prepared reproducibly under strictly controlled conditions and can be made available in almost unlimited quantities, which are clear advantages over collagen. Another advantage is the ability of these polymers to completely biodegrade to carbon dioxide and water via the Krebs cycle.[17] Synthetic polymers used as barrier membrane materials are polyglycolides (PGAs), polylactides (PLAs), or copolymers. Polydioxanones and trimethylene carbonates are also used.[17]

The early tissue reactions to PLA membranes were analyzed by Piattelli et al. in an experimental study in the rabbit tibia. After 3 weeks, the membrane started to show signs of degradation. In some areas, bone was in direct contact with the membrane surface, while in other portions a small layer of multinucleated giant cells was interposed between the bone and the membrane.[36]

In another study, Von et al. exhibited fibrous encapsulation on both sides of the PLA membrane, with minimal signs of cell infiltration.[37] Simion et al. studied premature exposure of PLA/PGA membranes to the oral cavity. After exposure, these membranes started to resorb and after 3-4 weeks, the resorption process was completed. Simion et al. regarded this characteristic behavior as an advantage over nonresorbable barriers because it could lead to spontaneous healing and closure of the tissue.[38]

Guidor (PLA) was the first resorbable barrier to be approved by the Food and Drug Administration (FDA) for membrane techniques. The resorption process of the material is programmed to ensure barrier function for a minimum of 6 weeks, after which it slowly resorbs. Complete resorption occurs at approximately 12 months.[39]

Platelet-rich plasma (PRP) is not a barrier membrane. Barrier membranes prevent soft tissue from invading the bone graft site for at least several weeks or months. PRP does not prevent fibroblasts from invading a bone graft site over a long time. Therefore, we must not use PRP as a membrane.[40]

GBR with bone grafting

Various methods have been developed to prevent membrane collapse and to preserve and maintain the space. Placing various bone graft materials under the membrane or using mechanical support are among the methods used. Grafts are generally classified according to their original source as follows: autograft (oral or extraoral), allograft (DFDBA, FDBA, Puros cancellous), xenograft (bovine or porcine), and alloplasts (hydroxyapatite, calcium phosphate).[41-44]

Autogenous bone grafts

Autogenous bone is derived from the individual for whom the graft is intended. It has long been considered the gold standard of bone graft materials. Autogenous bone grafts form bone by the processes of osteogenesis, osteoinduction, and osteoconduction. It consists of two components. The first is a natural anatomical structure for scaffolding cellular invasion and for graft and host site support. The second offers a component of primarily type I collagen that provides pathways for vascularity and resilience.[41-43]

Allografts

Allografts are tissues taken from individuals of the same species as the hosts. There are three main divisions: (1) frozen, (2) freeze-dried, and (3) freeze-dried demineralized. They come in different forms such as particulate, gels and putties. A major advantage of their use is that the material is readily available without the requirement of a secondary surgical site. They provide a source of type I collagen, which is the sole organic component of bone. However, they do not produce the inorganic calcium or scaffolding necessary for bone regeneration. Allograft bone must be processed to guarantee safety.[45,46]

Alloplasts

Alloplasts are synthetic. They contribute to the repair of osseous defects and to the enhancement of osseous ingrowth.

The chemical composition, physical form, and differences in surface configuration result in varying levels of bioresorbability. The varying nature of available commercial graft materials (porosity, geometries, differing solubilities and densities) will determine the resorption of these calcium phosphate–based graft materials.[47]

Xenografts

Xenografts are derived from other species. They are materials with their organic components totally removed. With their removal, concern about immunological reactions becomes nonexistent. The remaining inorganic structure provides a natural architectural matrix as well as an excellent source of calcium.[48] The inorganic material also maintains the physical dimension of the augmentation during the remodeling phases.[49]

Recombinant bone morphogenetic proteins (BMP) and tissue-derived growth factors

As a result of research on the use of recombinant bone morphogenetic proteins (BMP) and tissue-derived growth factors for osseous regeneration, these materials have been positioned as the definitive answer for future osseous regeneration. BMPs are osteoinductive compounds that encourage new bone formation. At least seven structurally unique BMPs have been identified that can induce bone formation as well as accelerate the process of bone regeneration. BMPs act as a signal in initiating and regulating specific tissue formation.[50] This activity leads to a series of developmental processes that include chemotaxis, proliferation, and differentiation, which result in the transient formation of cartilage (endochondral bone formation) and the production of living bone tissue. At this time, both the technology and the production of the material are quite expensive.[50]

Scientists and clinicians have long recognized the importance of collagen as a biomaterial because of its singular role as a major component of bone. The primary function of collagen is to act as tracks on which cells can move. Whereas collagen influences the cellular processes, the hydroxylapatite provides the structural and morphological support required for cell attachment.[51]

Detailed analyses have revealed that a 15-residue amino acid sequence within a chain of type I collagen is responsible for its cell-binding functions. This discovery led to the isolation and production of a synthetic material called P-15. As a first step, to mimic the physiological nature of bone, a composite of P-15 and natural inorganic bone mineral (ABM) was examined. ABM/P-15 is a synthetic, collagen-like agent that imitates autogenous bone.[51,52]

This material, PepGen P-15 (CeraMed, Lakewood, Colo), provides a tissue-engineered hospitable biomimetic habitat for cells and serves as a bonelike substitute for autogenous bone grafts. In clinical studies, PepGen P-15 demonstrated an increased expression of growth factors TGF, the agents associated with osteodifferentiation. PepGen P-15 has been demonstrated and clinically shown to have predictable benefits over other currently marketed bone graft replacement materials.[51,52]

Properties of graft granules

A number of studies have demonstrated that osseointegration and osteoconduction processes are influenced by physical and chemical properties of the material, including granule size, granule morphology, crystallinity and porosity, surface roughness, and ratio of calcium to phosphate (Ca:P) in the composition. Nevertheless, the requirements the best performance for these biomaterials have not been thoroughly addressed.[53]

Misiek et al. compared sharp-edged and rounded Hydroxyapatite (HA) granules and observed that although a mild inflammatory response was seen at the implant sites with both particle shapes, inflammation resolved faster in sites implanted with rounded granules.[54]

Yang et al.[55] stated that the dissolution and crystallinity of HAs were related in a negative

manner in vitro. The Ca:P ratio in the composition of HAs seems to directly affect crystallinity. Thus, highly crystalline HA—Ca10 (PO4) 6(OH)2—has a Ca:P molar ratio of 1.67, whereas less crystalline bioceramics, such as tricalcium phosphate and tetracalcium phosphate, are characterized by lower or higher ratios of 1.50 and 2.0, respectively.[56]

Takeshita et al.[57] observed that nonporous HA granules grafted into bone defects surrounding titanium implants resulted in fibrous encapsulation during the early healing stages. Deligianni et al.[58] used a bone marrow cell-culture model to demonstrate that cell adhesion, proliferation, and detachment strength increased as the roughness of HA increased.

Oonishi et al,[59] evaluated HA with granules of 1 to 3 lm, 10 lm, and 100 to 300 lm in diameter and noticed that a minimal size of 10 lm was necessary to enable a direct contact between bone and the particles. Sun et al,[60] studied the effect of different sizes of HA granules (from 0.5 to 841 lm) in osteoblast cultures and reported inhibitory effects for the 0.5 to 3 lm group. Kuroda[61] evaluated bone defects filled with HA granules of 100 to 2000 lm and observed improved osteoconductive activity in the group with granules of 100 to 300 lm. Based on the results of the Carvalho et al.'s study,[53] the scaffold structure and surface roughness, rather than the granule size itself, accounted for improved bone formation.

Horizontal and vertical ridge augmentation with GBR

A variety of surgical techniques and materials have been described to established a sufficient bony structure for supporting dental implants, including block graft augmentation, GBR, ridge splitting and horizontal distraction osteogenesis.

The first techniques used for horizontal ridge augmentation were extraoral bone block grafts and then intraoral bone block grafts. With introduction of GBR technique, combination of block grafts with bone fillers and membranes was applied. The first membrane used for horizontal ridge augmentation was ePTFE, but because of the increased risk of complications following wound dehiscence, resorbable collagen membrane introduced.[62]

The first researches about vertical ridge augmentation were animal studies in the 1990s. In the most studies, the results were significant.[62] In 1994, Simion et al. reported the first human and histologic study of vertical bone regeneration of the atrophic edentulous ridge with the GBR technique. The results showed that vertical bone regeneration was possible to an extent of 4 mm in height. The implant to bone contact was reported approximately 42% in this study.[63]

Tinti et al. performed a clinical study in this subject. They used autogenous bone chips and ePTFE membranes. Vertical ridge augmentation in this study was significant and the percentage of bone to implant contact was reported 39.1% to 63.2%.[64]

Esposito et al.[65] (2006) in a systematic review reported that both guided bone regeneration procedures and distraction osteogenesis can be used to augment bone vertically, but it is unclear which is the most efficient. It is unclear whether augmentation procedures are needed at immediate single implants placed in fresh extraction sockets; however, sites treated with barrier + Bio-Oss showed a higher position of the gingival margin than sites treated with barriers alone. More bone was regenerated around fenestrated implants with nonresorbable barriers than without barriers; however, it remains unclear whether such bone is of benefit to the patient. Bone morphogenetic-proteins may enhance bone formation around implants grafted with Bio-Oss, but there was no reliable evidence supporting the efficacy of other active agents, such as platelet-rich plasma, in conjunction with implant treatment.

Aghaloo and Moy[62] in a systematic review reported that the greatest implant survival rate (95.5%) was found for the GBR technique. In this study, the results of all techniques used for horizontal ridge augmentation were evaluated.

Esposito et al.[66] in another systematic review in 2009, evaluated 13 RCTs (Three RCTs (106 patients) dealt with horizontal and 10 trials

(218 patients) with vertical augmentation) which were suitable for inclusion. When comparing whether vertical augmentation procedures were more advantageous than short implants, a meta-analysis of two trials resulted in higher implant failures and statistically significantly more complications in the vertically augmented group. When various horizontal augmentation techniques (three trials) were compared, no statistically significant differences were observed. When various vertical bone augmentation techniques (eight trials) were compared, no statistically significant differences were observed except for three trials which showed that more vertical bone gain could be obtained with osteodistraction than with inlay autogenous grafts, and with bone substitutes rather than autogenous bone in guided bone regeneration in posterior atrophic mandibles, and that patients preferred a bone substitute block over a block of autogenous bone taken from the iliac crest.

Factors influencing the success of GBR

Factors that have been suggested to influence the outcome of GBR include patient factors (e.g., smoking), excessive swelling, passive flap tension, cortical penetration, defect morphology, defect length and defect angle, membrane fixation, and materials used.[67]

It was suggested that small to moderate horizontal bone loss of 3 to 6 mm in the HVC (horizontal, vertical and combination) classification[68] or division B (barely sufficient) bone, if the ridge width (2.5 to 5.0 mm) is barely sufficient for 4.0 mm diameter dental implants, is a good indication for GBR treatment.[69]

Park et al.[67] evaluated the morphology of the ridge on the outcomes of GBR. In this study, they reported that ridge width did not have a significant effect on the regenerative outcome and cross-sectional pre-surgical ridge angles may have prognostic value in estimating the outcome of simultaneous GBR. At 6 months, a ridge angle < 28° resulted in a statistically significantly greater percentage of defect height reduction than a ridge angle > 28°.

Due to an avascular zone located over the edentulous ridge about 1 to 2 mm wide, it may be inferred that mid-crestal incisions on the edentulous ridge with a possible vertical incision on the mesial aspect of the flap seem to yield the most anatomic potential for success.[70] Clinical human studies reported less edema, inflammation, and pain with a crestal incision compared to a vestibular or mucobuccal fold incision. This may minimize flap necrosis and further reduce the risk for membrane exposure.[67] Flap advancement is required as part of certain surgical procedures (e.g., ridge augmentation) to attain tension-free primary closure along the incision line.[71]

Romanos[72] in an article about periosteal releasing incision discussed surgical guide for this procedure which is mentioned below:

1. The flap has to be a mucoperiosteal flap, and must be raised sufficiently over the mucogingival junction in an apical direction for at least 10 mm.

2. With conventional dental forceps (surgical forceps may lead to flap perforations)

hold (but do not pull) the flap in a coronal direction to evaluate the tension during coverage of the augmentation site.

3. With a new scalpel (blade no. 15 or 15c), start at the distal part of the flap periosteum and, without stopping (that is in one shot), cut the periosteum in a depth of 1–3 mm always moving the blade in a direction from distal to mesial.

4. The blade should cut the tissue in a level apical to the mucogingival junction. To avoid flap perforation, do not cut the area of the keratinized mucosa.

5. Pull and evaluate (in a coronal direction) the flap and check for a tension-free flap advancement. In case of insufficient closure, stay at the same area and cut more deeply in the muscle layer or use a new PRI in a parallel direction to the previous one, more apically.

6. Always check the final result in such a way that the buccal flap margin covers the lingual or palatal site at least for 3–5 mm. If this overlapping does not occur, there is a lot of tension in the flap, which means the closure is insufficient. Muscle release can be performed

using dissection scissors. This is very important, especially in vertical or horizontal augmentations of the alveolar ridge with corticocancellous bone grafts or advanced applications of the GBR-technique to avoid graft exposure.

Reported methods to alleviate tension over the suture line include overlapping the flap, positioning the flap laterally, tissue grafting, or using a combination of mattress sutures and interrupted sutures.[73] Despite these surgical techniques, this procedure may still be associated with excessive tension on the suture line, which can often result in suture line opening and early membrane exposure and infection.[73] For these reasons, Kfir et al.[73] introduced minimally invasive guided bone regeneration. In this technique, a vertical incision is made mesial to the augmentation zone. The periosteum is initially elevated with a miniature chisel, and then through a series of sequential balloon inflations. This yields a tunnel with adequate space for membrane insertion, decortication, and grafting with substitute bone and platelet rich fibrin (PRF) filling. Primary closure is obtained by 2 or 3 simple interrupted sutures.Another factor that can affect the results of GBR is decortications (Figure 5). Decortication of bone prior to placing a bone graft is often performed as part of a GBR procedure. It is the intentional drilling of holes through the cortical bone into the cancellous bone or the removal of cortical bone to expose cancellous bone.[76]

Decortication is done ostensibly to enhance the healing process by promoting bleeding and allowing progenitor cells and blood vessels to reach a bone-grafted site more readily. In addition, decortication may improve the physical bond between grafted bone and a recipient site.[74,75]

Nishimura et al.[76] evaluated the Effects of cortical bone perforation on experimental guided bone regeneration in rabbits. Newly formed bone volume and ALP expression in Group B (Corticalm perforation size: 3×15 mm) were more extensive than those in Group A (Corticalm perforation size: 1×15 mm) at 6 weeks. Histomorphometric analysis showed significant differences between both groups. The authors concluded that a larger perforation was associated with prompter bone formation in the secluded space during GBR.

However, there is controversy in the dental literature with respect to the usefulness of this procedure because its ability to accelerate or increase bone regeneration has not been substantiated in human clinical trials, and there are conflicting results derived from animal studies.[75,76]

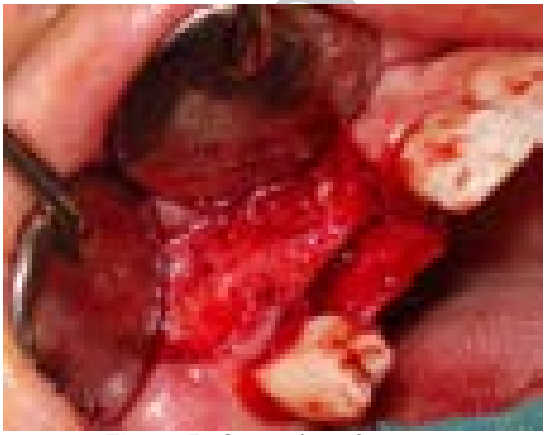

Figure 5. Cortical perforation

Decortication can have some minor negative consequences such as increased operative time, additional blood loss, potentially greater postoperative pain, and some bone loss if the GBR procedure fails.[76]

Success of GBR

The success of GBR is one of the important parts of implant dentistry. Is success to be defined merely as covering of a dehisced or fenestrated implant surface with regenerated hard tissues, or the ability to place an implant in regenerated bone without generating a fenestration or dehiscence?

The first generation definition of success was proposed by Mellonig and Triplet.[77] This definition was the ability of completely cover a dehisced or fenestrated implant surface with regenerated hard tissue.

The second-generation definition of success was the regeneration of a sufficient dimension of bone to withstand functional forces over

time.[78] However, regeneration of bone to cover an exposed implant surface, or regeneration of covering bone of sufficient thickness to withstand function forces over time are no longer adequate definitions of success following GBR therapy. In the esthetic zone, any definition of success must include regeneration or prepathologic alveolar ridge morphology, to ideally support the covering soft tissues and help maximize treatment outcomes. Such a definition represents the third –generation definition of success of GBR.[78]

Long term results of GBR

One question that must be answered is the prognosis of an implant placed in augmented ridge compared to native bone. Survival rate of implants placed into sites with regenerated bone using barrier membranes have been reported to vary between 79% and 100% with majority of studies indicating more than 90% after at least 1 year of function.[79-82]

For the first time, Fugazzotto[83] published an article on this subject in 1997. In this paper, failure and success rates of 626 implants either placed in regenerated alveolar bone or treated with guided bone regeneration to rebuild bone over implant fenestrations or dehiscences were evaluated. The cumulative success rate of implants in function in regenerated bone for 6-51 months was 93.8%.

Fugazzotto[84] Published another paper in this topic and reported the cumulative success rate of implants in function in regenerated bone for 72-133 months, was about 97.3%.

Simion et al.[85] evaluated the success rate of 123 implants inserted in vertically augmented ridges during 1-5 years of prosthetic loading. The overall success rate of 97.5% was reported according to the success criteria listed.[86]

In a 5-year prospective controlled study, implants placed into pristine bone were compared with implants associated with bone regeneration. No significant differences were found regarding the cumulative implant survival rates in the three groups: sites augmented with a collagen membrane and a deproteinized bovine bone mineral (95.4%), sites augmented with an e-PTFE membrane and a deproteinized bovine bone mineral (92.6%), and sites without augmentation (97.3%).[87]

Another study providing controls reported 38 implants in seven patients. In this study, 21 implants were placed in conjunction with GBR and 17 could be placed into the host bone without the need for regeneration therapy. A polylactic, polyglycolic acid membrane was used in all regenerated sites. After an average of 25 months following incorporation of fixed reconstructions, a 100% survival rate was found for both test and control implants and no significant difference in marginal bone levels was recorded between the two groups.[81]

Although the data are derived from a small number of studies showing an adequate design, survival rates have been documented similar to the ones generally reported for implants placed conventionally into sites without the need for bone augmentation.

Conclusion

Presently available data demonstrates GBR therapy to be a predictable and successful procedure to augment bone in a horizontal direction at sites exhibiting insufficient bone volume for implant placement under standard conditions. Among the techniques introduced for vertical ridge augmentation, GBR is a successful technique, although distraction osteogenesis allows for more vertical bone augmentation than other techniques. For horizontal ridge augmentation, resorbable membranes have successful and predictable results the same as non-resorbable membranes. Long-term results showed that survival rates of implants placed in augmented bone is high and comparable with implants placed in native bone.

Conflict of Interest

Authors have no Conflict of Interest.

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