

Guided Bone Regeneration

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Introduction:

Improper or no bone healing is a significant clinical problem within orthopedics, oral and maxillofacial surgery, plastic surgery, as well as periodontology. A main obstacle for successful bone healing and the formation of new bone is that, in contrast to osteogenesis, connective tissue formation occurs rapidly, thus, ingrowth of soft tissue may disturb or totally prevent osteogenesis from taking place in a defect or wound area.

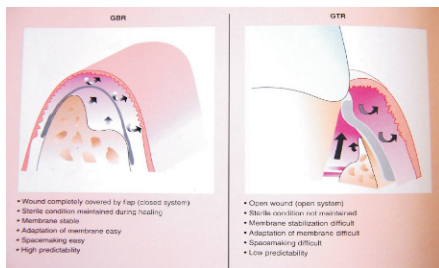
A variety of suggestions have been presented with the purpose of solving these problems. One possibility is to graft fresh autogenic bone samples. Other methods use bone chips and powder, various commercially available allografts, or different synthetic calcium phosphate products.

Four methods have been described to increase the rate of bone formation and to augment bone volume: osteoinduction (Reddi 1981; Urist 1965); osteoconduction (Buch et al. 1986; Reddi et al. 1987); distraction osteogenesis, (Ilizarov 1989); and finally, guided tissue regeneration (GTR), (Dahlin et al. 1988, 1991a; Kostopoulos&Karring 1994; Nyman & Lang 1994).

Periodontal studies during the last several decades have led to new techniques and a new treatment approach referred to as guided tissue regeneration (GTR). Briefly, this concept is based on the principle that specific cells contribute to the formation of specific tissues. **What Is Guided Bone Regeneration (GBR)?**

Guided bone regeneration (GBR) is a surgical procedure involving the placement of a cell-occlusive physical barrier between the connective tissue and the alveolar bone defect.

Guided bone regeneration (GBR) is a technique of bone regeneration that evolved from guided tissue regeneration (GTR) which is a procedure performed for the regeneration of lost periodontium. While GTR is for the regeneration of periodontal tissue of natural teeth (root cementum, periodontal ligament, and alveolar bone), GBR is for the regeneration of supporting bone.



Implant therapy, based on the principles of osseointegration, has become highly predictable. Implant success depends on establishing an

environment in which bone remodeling can occur, with close contact of the fixture surface and bone. For this reason, optimizing the condition of the recipient site is sought following the principles of guided bone regeneration. Guided bone regeneration (GBR) is a reconstructive surgical procedure that evolved from the guided tissue regeneration (GTR) technique. At one time, the terms GTR and GBR were used interchangeably. GBR term was used specifically to denote the reconstruction of alveolar bone defects prior to or in association with the placement of dental implants.

In GBR, the osseous defects are covered with a barrier membrane, which is adapted closely to the surrounding bone surface, creating a protected space for the organizing blood clot and to prevent collapse caused by pressure from the tissue flap. Nonosseous cells (epithelial cells and fibroblasts) are inhibited and space is preserved between the bone surface and membrane. Osteoblasts derived from the periosteum and bone is selectively induced on the osseous defect area, facilitating new bone formation.

Besides providing space, the physical barrier protects the blood clot by diverting mechanical stress that acts on the tissue flap during the critical early stages of wound healing.

Besides space creation and wound stabilization, several other factors seem to influence the predictability of GBR (Nevins et al, 1995):

1. A barrier material of sufficient stiffness and/or barrier support to ensure the desired volume of the compartment.
2. A healthy vascularized bone bed.
3. Retention of the barrier in its submerged position.
4. An appropriate amount of healing time, usually a minimum of 3 months of wound healing in the mandible and 6 months in the maxilla.

Guided bone regeneration in implant therapy is especially useful for fixture placement with dehiscence defects or fenestration defects. In alveolar ridges with marked facial/buccal depressions or in knife-edge alveolar crests, the position and direction of fixture placement is restricted. Improvement of alveolar ridge morphology becomes possible with GBR.

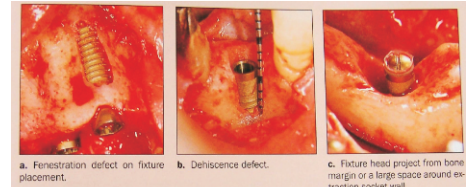
GBR using a barrier membrane has become widely used for bone regeneration of osseous dehiscences and fenestrations and for localized ridge augmentation and immediate implant placement.

Approaches Of GBR:

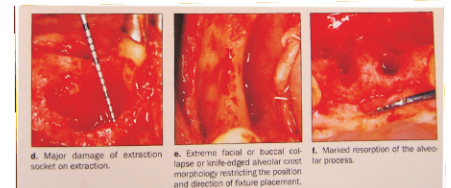
Simultaneous approach and staged approach

There are two approaches to GBR in implant therapy:

1. Simultaneous approach – Fixture placement and GBR are performed simultaneous to create increased bone around the fixture.



2. Staged approach – GBR is used to increase the alveolar ridge or improve ridge morphology before fixture placement. The fixture is placed after healing



Indications of th simultaneous approach:

Facial or buccal collapse may occur in the extraction sockets of anterior teeth, dehiscence or fenestration defects may result. In the simultaneous approach, bone is regenerated using a barrier membrane in the osseous defect around the fixture.

Indications for staged approach:

1. Insufficient vertical and buccolingual bone for fixture placement and stabilization.
2. Bone resorption extending to one third of the root apex of the extracted tooth due to a severe osseous defect.
3. A large and flat osseous defect with insufficient bone width (less than 5.0mm) such that fixture placement cannot be achieved in the proper prosthetic position and angle.
4. Maxillary anterior ridge morphology leading to an unpredictable esthetic result after fixture placement.
5. Extreme loss of facial bone plate with gingival recession.
6. Severe circumferential osseous defect and vertical osseous defect.
7. Simultaneous fixture placement with barrier membrane difficult due to a large osseous defect around the fixture.

Advantages of the staged approach:

In the staged approach, the bone regeneration mechanism is activated on GBR surgery and on fixture placement. Additionally, compared to the simultaneous approach, larger bone surface can contribute to the formation of new bone. A more favorable bone bond is expected because osteoblasts need travel a lesser distance to the fixture surfaces after bone augmentation.

Guided Bone Regeneration In Immediate Extraction Socket:

The experimental and clinical investigation

of Brånemark and coworkers have provided periodontists, oral surgeons, and restorative dentists the biologic and clinical knowledge to predictably restore patients to proper function, comfort, and esthetics with implant-supported restorations. These restorations can be used to rehabilitate fully and partially edentulous patients as well as those requiring single-tooth replacements.

The traditional approach was to remove hopeless teeth and wait for 4 months to 1 year to allow sufficient time for alveolar bone healing prior to implant placement. But with the recent concepts of GBR it has been proved that bone promotion can be done around implants placed in immediate extraction sockets also.

Indications and contraindications of immediate implant placement:

Dental conditions that might be good indications for immediate implant placement are root fractures, failed endodontic therapy, and advanced periodontal disease. Teeth with unrestorable carious lesions or poor crown-to-root ratios might also be good candidates for immediate implant placement.

According to Salama et al, extracted sites suited for an immediate implant are:

1. Four-wall socket
2. Three-wall dehiscence type defect (5mm or less in the apicocornal direction)
3. The osseous crest lies in the coronal one third of the root to be extracted.
4. Sufficient bone (4-6mm) beyond the apex for primary stability of the implant and the optimum distance between the CEJ of the adjacent teeth and the top of the fixture top is 3-5mm. Sufficient buccal bone wall of the extraction socket is necessary for an esthetically favorable result.

Contraindications for immediate implants include, areas of insufficient depth due to proximity of the maxillary sinus or inferior alveolar canal and the bottom of the extraction socket or width of the extraction socket is less than 4-5mm, or the site depth is not more than 10 mm. Others include areas of periodontal disease with acute inflammation or where complete curettage of the extraction socket is not possible.

The successful treatment outcome depends on proper diagnosis and treatment planning. Possible factors that must be taken into consideration for immediate implant placement are lip and smile line, gingival thickness, presence or absence of periodontal disease adjacent to the tooth to be removed and bone quality and quantity.

To achieve implant stability there should be a minimum of 3 to 5 mm of bone apical to the root apex. Both periapical and panoramic radiographs will be helpful in evaluating sufficient bone for implant placement without traumatizing the neurovascular bundle, maxillary sinus or adjacent teeth.

Materials For Gbr: Barrier Membranes

As the use of an occlusive or semi-occlusive membrane to provide a protected, blood clot-filled space adjacent to a bony surface results in predictable bone tissue formation, there is an increasing demand for membranes in regenerative therapy.

The GBR procedure performed in the alveolar process pose specific challenges that

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must be addressed in membrane design if the membrane is to function at the optimal level in clinical use. If the only requirement of a membrane material used for GBR procedures were to provide a barrier to the proliferation of fibrous connective tissue, any suitably biocompatible material in the form of a cell-occlusive film could be utilized in clinical practice. However, a membrane that is utilized for alveolar ridge GBR must meet a number of requirements in addition to acting as a passive physical barrier.

The physical barrier membrane which are used for GBR should satisfy the five basic criteria, i.e.,

1. Biocompatibility
2. Cell occlusivity
3. Tissue integration
4. Space making
5. Clinical manageability.

Nonresorbable barrier membrane:

Various nonresorbable materials have been used as barrier membranes, including latex and Teflon. Teflon, an expanded polytetra fluoroethylene membrane (e-PTFE, Gore-Tex Periodontal and Bone Regenerative Membranes, Gore and Associates, Flagstaff, AZ), has been used extensively as a barrier membrane in both GTR and GBR procedures. A variety of shapes and sizes have been designed to custom fit around teeth and osseous defects. These barrier membranes are nonresorbable and thus require a subsequent surgical procedure to remove them. The advantage of a nonresorbable barrier membrane is its ability to maintain separation of tissues over an extended time. Unless the barrier is exposed, it can remain in place for several months to year. Typically, GBR membranes are removed after 6 to 12 months.

The disadvantage of a nonresorbable barrier membrane is that if it becomes exposed, it will not heal spontaneously.

Resorbable Barrier Membranes:

There has been a recent surge of interest regarding the used of resorbable membranes. Copolymers of polylactide and polyglycolide (PLA/PGA) or collagen have been used to construct biodegradable membrane is the elimination of a surgical reentry for a membranes removal. A possible disadvantages is that most resorbable membranes degrade before bone formation is completed and the degrade process is associated with varying degrees of inflammation. Another disadvantage is that resorbable membranes are quite pliable. The lack in stiffness results in a collapse of the membrane into the defect area.

Bone Grafts:

Bone grafting materials for GBR procedures may be classified as to the mode of action of the material or the origin of the grafting material being used.

The mode of action is one of three phenomena:

1. Osteoconduction is defined as an implantable matrix that provides channels for bone growth at the interface.
2. Osteoinduction is defined as an implantable matrix that provides natural stimulation of bone formation throughout the implantable material, not just at the interface.
3. Osteogenetic

Bone grafting material is generally classified as autografts, allografts, xenografts or alloplast.

Source	Osteoconductive	Osteoinductive	Osteogenic
Alloplast	Yes	No	No
Xenograft	Yes	No	No
Alloplast	Yes	Yes/No	No
Autograft	Yes	Yes	Yes

Guided Bone Regeneration in

- Ridge preservation
- Extraction wounds (Class 0)
- Fenestrations (Class I)
- Dehiscence (Class II and III)
- Horizontal ridge deficiency (Class IV)
- Vertical ridge deficiency (Class V)

GBR In Extraction Sockets:

Maxillary and mandibular premolars, canines, and incisors are ideal candidates for extraction and immediate implant placement when severe periodontal breakdown, root fractures, or endodontic failures are evident. There are four prerequisites:

1. After tooth extraction, the socket must present sufficient residual walls.
2. The extraction socket must be free of pathosis.
3. The available soft tissue should allow primary closure.
4. Apical to the apex of the socket, a sufficient volume of healthy jawbone must be available to assure good initial stabilization of the implant.

In delayed extraction socket treatment, after all diagnostic procedures are carefully evaluated the tooth is planned for extraction. The tooth is extracted atraumatically, while preserving the surrounding bone walls. The socket is debrided of granulation tissue with curettes and excavators. The flaps are released and soft tissue closure is achieved with horizontal mattress and interrupted sutures.

In situations where the extraction socket is appropriate for implant placement, the patient is evaluated approximately 8 weeks following extraction for complete soft tissue coverage of the extraction site. In such situations where the extraction socket is inappropriate to place an implant, the original protocol of a 6- to 12-month healing period to allow complete ossification of the extraction socket or a staged approach utilizing the GBR technique for localized ridge augmentation is recommended.

GBR In Fenestrations:

Treatment of Fenestration defects:

They can be corrected by two approaches:

- (1) A staged event, with the implant placed after regeneration (GBR) takes place; or
- (2) Implant positioning associated with a guided bone regeneration (GBR) technique, using autogenous bone chips and a barrier membrane, in a one-stage approach.

GBR In Horizontal Ridge Deficiency

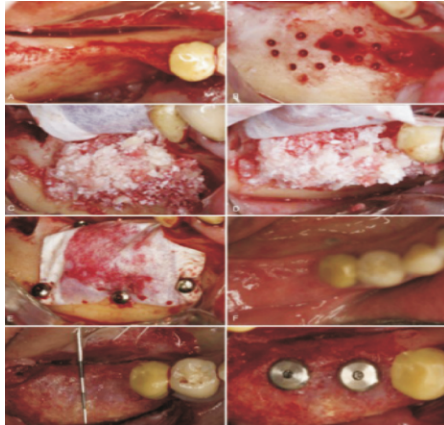
Horizontal ridge augmentation is necessary when the presurgical evaluation reveals that the width of the alveolar ridge is insufficient for adequate implant placement.

Two different applications of GBR are possible:

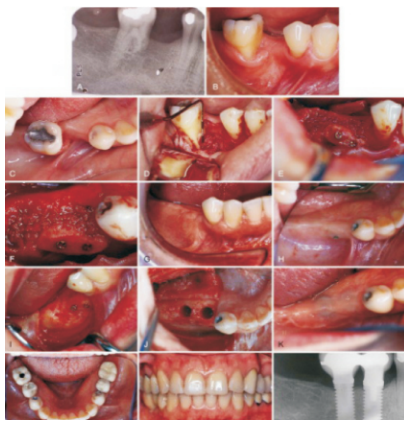
- a) Simultaneous approach, utilizing membranes to regenerate the bone defect (dehiscence or fenestrations) around an inserted implant.
- b) Staged approach, utilizing membranes for localized ridge augmentation and subsequent implant placement into the newly regenerated alveolar ridge in a second surgical procedure.



Particulate bone graft: Advantages of particulate bone grafts or bone chips are that the smaller pieces of bone demonstrate more rapid ingrowth of blood vessels, larger osteoconduction surface, more exposure of osteoconductive growth factors, and easier biologic remodeling when compared with a bone block. However, they lack a rigid structure and are easily displaced than block



a) Monocortical block graft: Cortical block of bone harvested from a remote site are used to increase the width of the bone. The block graft taken from an intraoral (e.g., mandibular symphysis or ramus) or extraoral (e.g., iliac crest or tibia) site is fixated to the prepared recipient site with screws. The graft can be separated from overlying soft tissues with a barrier membrane or simply covered by mucoperiosteal flap. The disadvantage of this technique is the biologic limitation of revascularizing large bone blocks.



GBR In Vertical Ridge Deficiency:

Vertical ridge augmentation is indicated when the bone height is insufficient for long term implant stability, or when prosthetic rehabilitation will result in excessively long crowns and an unfavorable implant/crown ratio.

Surgical aspects for achieving predictable results with the GBR technique for ridge augmentation:

1. Use of systemic and meticulous low-trauma surgical technique to minimize insult to the bone and soft tissue flap.
2. Use of a lateral incision technique with a combined split-thickness/full-thickness flap design.
3. Use of an appropriate e-PTFE membrane.
4. Creation and maintenance of a space

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underneath the membrane using autogenous corticocancellous bone grafts stabilized with supporting screws.

5. Stabilization and close adaptation of the membrane to the surrounding bone with fixation screws.
5. Achievement of a primary soft tissue healing and a healing period of 9 months.

Future Developments:

The role of growth factors in bone augmentation:

Another adjunct to regenerative therapy is osteogenic stimulating substrates to enhance bone formation. Platelet-derived growth factor (PDGF), insulin-like growth factor (IGF-I and IGF-II), transforming growth factor beta (TGF-β), fibroblast growth factor (a-FGF and b-FGF), and bone morphogenetic proteins (BMPs 1–15). Most widely studied is BMP. BMP, by chemotaxis, triggers proliferation and differentiation of mesenchymal progenitor cells (Wozney et al. 1988). Recombinant biotechnology has enabled characterization of at least 15 BMPs and production of quantities of purified recombinant protein for therapeutic application.

Bone morphogenetic proteins (BMP) are a group of acidic polypeptides belonging to transforming growth factor- gene super family. They stimulate bone formation through osteoinduction by inducing pluripotent stem cells to differentiate into osteoblasts.

To date, 1 – 15 bone morphogenetic proteins (BMPs) have been cloned and sequenced: BMP – 1, BMP – 2 (Formerly BMP – 2A), BMP – 3 (also called osteogenin), BMP – 4 (formerly BMP – 2B), BMP – 5, BMP – 6 (human homologous of the murine Vgr – 1), BMP – 7 (also called osteogenic protein – 1 or OP – 1), BMP – 8 (OP – 2), BMP – 9, BMP – 10, BMP – 11, BMP – 12, BMP – 13, BMP – 14 and BMP – 15.

TGF-s are found in high concentrations in bone as well as in platelets (Bonewald et al, 1990) and have wide ranging effects on cell proliferation, differentiation and organization.

In bone, proposed roles of TGF-s include coupling factors, which regulate the transition from bone resorption to bone formation (Bonewald et al, 1990) and as differentiation factors regulating control over development and regeneration of mineralized tissues (Vainio et al, 1993).

Platelet-rich Plasma- A Source For Multiple Growth Factors:

A new approach to enhance the vitality of bone grafts has been introduced by using platelet-rich plasma (PRP). PRP is an autogenous source of platelet-derived growth factors and transforming growth factors that is obtained by sequestering and concentrating platelets by centrifugation. The patient's own blood is withdrawn and separated into its three basic components. The PRP is the important content, which contains a high mixture of platelets and a concentration of growth factors.

Then this PRP mixture is added to the autologous bone graft and has shown to increase the quality and reduce the time needed for bone regeneration. Clinical and experimental studies suggest that this technique holds promise for large bone defects or bone defects with low osteogenic potential.

Conclusion:

It is well known principle that nature dislikes

empty spaces. This first possible mechanism is based on the presumption, be it true or not, that non osteogenic cells, like fibroblasts in tissue compartments adjacent to the bone wound, differentiate and migrate into the bone defect more rapidly than do cells of the osteoblastic lineage. The site for bone healing or bone neogenesis thus becomes rapidly obliterated with soft tissue and therefore, the requirement to fill it with bone is not so urgent. By preventing the invasion of non bone forming cells, the membrane provides a secluded space into which bone forming cells can migrate from the adjacent bone and where osteogenesis can proceed that impeded.

The use of the membrane technique has by now developed into a valuable clinical tool to improve bone regeneration, primarily in conjunction with dental implants. Several directions for future development of this osteopromotive technique are obvious and will be commented upon: 1) the technique will be used in conjunction with bone grafting; 2) the technique will be used in reconstructive and aesthetic skeletal surgery for bone neogenesis; 3) the osteopromotion technique will be applied outside the oral cavity; 4) other membrane materials will be used for certain applications; and 5) adjuvant factors will be combined with the osteopromotion technique.

The osteopromotive membrane technique has been investigated in a relatively large number of experimental and clinical studies by us and others, providing a sound scientific basis. Even though its mechanisms of action are not fully elucidated, it is already successfully applied clinically. The technique can be expected to be further developed and refined, and in the further we will see several new applications. The use of alternative membrane materials is relatively imminent, and a combination of the osteopromotive membrane technique with various stimulatory factors may also be expected.

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