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RESEARCH ARTICLE

GUIDED BONE REGENERATION: RATIONALE AND PREDICTABILITY IN IMPLANT DENTISTRY

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ABSTRACT

Guided Bone Regeneration (GBR) is a technique for bone reconstruction of alveolar ridge achieved with help of non resorbable or resorbable membranes. Bone grafts can be used in combination with membranes to further enhance the results. It may be used in conjunction with dental implants, in socket preservation, or in a staged manner. GBR procedures have been utilized for localized ridge augmentation as well as in reconstruction of larger areas. Both vertical and horizontal augmentation can be achieved although the predictability is not same for both. This literature review discusses the rationale, flap designs and predictability of GBR.

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INTRODUCTION

One of the most important prerequisites for achieving and maintaining successful osseointegration of dental implants is that sufficient volume of healthy bone should be present at the recipient site. This includes bone of sufficient height to allow the insertion of an implant of appropriate length and also a ridge of sufficient crest width. (Schenk, 1994) Bone loss can occur because of advanced periodontal disease, periapical pathology or trauma to teeth and bone. (Farzad, 2012) Various methods such as Guided Bone Regeneration (GBR), use of appropriate growth factors, different graft materials and distraction osteogenesis have been described in literature to increase the rate of bone formation and to augment the deficient bone. However, the success rate and predictability of these procedures are yet to be established completely. GBR is based on principles of specific tissue exclusion and it aims at regenerating only the bone tissue. The treatment concept advocates that regeneration of osseous defects is predictableand easily attainable by the application of occlusive membranes. It mechanically excludes non-osteogenic cells from the surrounding soft tissues and allows osteogenic cell populations originating from the parent bone to inhabit the osseous wound. (Nyman *et al*., 1987) One of the earliest research papers on guided bone regeneration was published by Murray *et al.* (1957) where they suggested that soft tissue grows at a faster rate than bone, thus hinders bone formation in the healing area and therefore soft tissue growth should be prevented to promote bone formation. Further, they stated that only three conditions necessary for the new growth of bone were: presence of a blood clot, preserved osteoblasts, and contact with living tissue. Research work (Dieter *et al*., 2009) done by team of Karrig and Nyman highlighted the concepts of guided tissue regeneration which became the foundation for guided bone regeneration. The evolution of guided bone regeneration can be divided into: *Development phase-* In the first phase the concept of GBR was developed from the techniques of Guided Tissue Regeneration. (Dieter *et al*., 2009; Nyman *et al*., 1982; Schenk *et al*., 1994) and in the second phase various techniques for GBR were developed. (Dieter *et al*., 2009; Buser *et al*., 1990) *Phase of routine application-* Following various experimental and animal studies various authors reported bone augmentation in clinical trials using GBR concept. The use of ePTFE membranes for bone regeneration was initiated in the mid-1980s by the group led by Nyman and Dahlin. (Bosshardt, *et al*., 2009; Nyman *et al*., 1982; Nyman *et al*., 1982; Schenk *et al*., 1994) The first published clinical reports were

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predominantly studies with collagen membranes. (Hammerle and Lang, 2001) The aim of the present article is to give a brief overview about the concept of GBR, various techniques, predictability and its significance in field of periodontics.

Biology of bone regeneration

Regeneration is commonly understood as replacement of vanishing or lost components in the body by elements of equally high structural organization so that the function and structure are completely restored. It is defined as reconstruction or reproduction of a lost or injured part. (Glossary of periodontal terms, 2004) Reparative regeneration takes place when the tissues are lost because of injury or disease. Bone has unique potential to completely restore its original architecture. (Dieter *et al*., 2009) The reconstruction of the original level of tissue architecture occurs sequentially and closely resembles the pattern of bone formation occurring during the development and growth. (Schenk, 1987) Any bone lesion (fracture, defect, insertion of an implant, or disturbance of blood supply) activates local bone regeneration by the release and local production of growth factors and other signaling molecules. Heterotopic/ectopic osteoinduction is the bone formation occurring at sites where bone physiologically does not exist. If this ossification occurs in contact with existing bone, it is known as orthotropic osteoinduction. (Christoffersen and Landis, 1991)

Rationale behind guided bone regeneration (Sissons and Kember, 1977; Dieter *et al*., 2009)

Guided bone regeneration, usually in combination with grafting material is a routine dental practice to augment the bone. Bone is usually slow growing tissue (35µm/day). Both fibroblasts and the epithelial cells have the opportunity to occupy the available space more efficiently and build up the connective tissue much faster than the bone is able to grow.

A.Cell exclusion

Exclusion of the undesirable cells from the wound environment enables cells from the bone tissue to proliferate into the coagulum filled space below the barrier membrane.

B.Repopulation of selected cells

The barrier membrane used creates a secluded space that allows the bone to use its great natural healing capacity in an undisturbed or protected manner.

C.Inhibition of epithelial migration

By excluding fast-growing epithelium and connective tissue from a periodontal wound for 6-8 weeks, slower growing tissues including osteoblasts, cementoblasts, and periodontal ligament cells are allowed more time to occupy the space adjacent to the tooth.

"Pass" principles for predictable bone regeneration (Hom-Lay Wang and Lakshmi Boyapati, 2006)

P: *Primary wound closure*:
Tension free primary closure helps to promote wound healing, especially if the wound margins are everted such that the internal connective tissue aspects of the flap approximate about each other, impeding epithelial exposure. Exposure of a membrane especially non-absorbable one and subsequent infection reduces the quantity of new bone growth by GBR by 6 times. Exposure in general allows epithelial infiltration into the wound site, defeating the purpose of procedure.

A: *Angiogenesis*:

The oxygen and nutrient exchange afforded by pervasive vascularization guarantees the development and the viability of regenerated tissue in addition to the speed at which it arises. Because angiogenesis stems from the existing vascular network, the clinician should take steps to make an intimate contact between the existing supply and the area of GBR.

S: *Space maintenance*:

Bone cannot grow into a space that does not exist. Naturally a slow resorbing graft material coupled with a rigid membrane is able to sustain a space with greater security than a material with faster turnover. This gives more drawn out healing period during which new bone encapsulates and ultimately replaces the non-native matter. Tenting apparatus in the form of pins, screws and posts helps to ensure the patency of the created void. These devices buttress the membrane, giving a sort of regenerative canopy. It is highly useful in cases where the desired regeneration is completely out of the envelope of the bone, a precarious situation.

S: *Stability of wound*:

Mobility of the wound (membrane, graft, adjunct fixation), whether caused by the prosthetic pressure, patients habit, or overzealous mastication disrupts the clot formation and subsequent granulation tissue- woven bone- lamellar bone maturation. Furthermore, micro-movement undermines the cell exclusion function of the membrane; this breach of the barrier invites the fibroblasts into the area and so gives rise to the fibrous malunion instead of regenerated bone.

Timing of GBR

GBR procedures can be carried out at the time of tooth extraction as socket preservation. Also in cases of atrophic edentulous ridges, GBR can be done in conjunction with implant placement or as staged approach with delayed implant placement. The decision criteria for implant placement according to ITI consensus (Stuttgart, Germany, August 2008) was (Chen and Buser, 2009): Type 1- immediate implant (at time of tooth extraction).Type 2- Early implant placement following soft tissue healing (4-8 weeks). Type 3- Early implant placement following partial hard tissue healing (12-16 weeks) and Type 4- late implant placement (>6months).

Flap design for optimal esthetics and predictability (Forum *et al*., 2012)

The incisions are designed in accordance with the following five goals:

A. Access to the bone defect.

B. Maintenance of adequate blood supply of the elevated flap and surrounding tissues.
C. Preserving the interdental/implant papilla.
D. Sufficient advancement of the flap.
E. Allowing tension-free primary closure.

Various flap designs for GBR have been described in literature. Flap design requires the covering of the membrane by thick soft tissue with sufficient blood supply and avoiding membrane exposure. Therefore, the flap must include sufficient keratinized mucosa and should beextended more than one tooth mesio-distally.

Flap designs (Buser *et al*., 1993)

In the Conventional technique a midcrestal incision is made which extends mesiodistally and a full thickness flap is raised. The flap is made as thick as possible. The envelope flap should be made without a vertical incision, if possible, to maintain blood supply. The vertical incision if placed should extend at least one tooth (5mm) from the proposed membrane margin. Flap design should emphasize on a large base of flap. Divergent vertical relieving incision should be given. Conventional technique is used when sufficient keratinized mucosa is present in the edentulous ridge. A mid-crestal incision or para-crestal incision can be given depending upon the thickness of keratinized gingiva. Various authors have proposed modifications in the flap design depending upon the thickness of the keratinized gingiva available such as Lateral incision technique (Buser *et al*., 1996) in which a partial-thickness bevel incision is made to obtain a wide junctional surface. A second incision is made 4-5 mm toward the palatal side of the maxillary crest or 4 mm below the buccal mucogingival junction of the mandibular crest to prepare a partial-thickness flap. A full-thickness flap is reflected where the bevel incision reaches the bone surface. The wide junctional surfaces obtained by this technique overlap each other, yielding favorable wound closure. Various other flap designs have also been advocated such as coronally advanced flap, overlapped flap, double flap incision designs and minimally invasive designs.

Barrier membranes employed in GBR

Historically, the concept of GBR has been used in experimental reconstructive surgery since the mid-1950s, for spinal fusionand maxillofacial reconstruction (Boyne, 1964). Initial research hypothesized that various cellular components in the tissue have different rates of migration into a wound area during healing and that a mechanical hindrance would exclude the invasion of fibroblasts (Ogiso *et al*., 1991). Preliminary experimental studies showed that the use of a non-resorbable membrane as a mechanical barrier resulted in complete healing of the bone defect, and collagen membranes prevented the apical migration of epithelium and supported new connective tissue attachment and tissue regeneration (Pitaru *et al*., 1988). The decision to employ non-resorbable or resorbable barrier membrane is based ultimately on the required time for regeneration. Larger defects call for extended maturation time periods and therefore a longer lasting membrane. To achieve better clinical outcomes, the GBR barrier should possess the properties of Cell exclusion, Tenting, Scaffolding, Stabilization and Framework (Wang and Carroll, 2001).

Classification of membranes

Minabe (1991): classified membranes as 1) Nonabsorbable: Polytetrafluoroethylene (e-PTFE) type, Titanium reinforced polytetrafluoroethylene type. 2) Bioabsorbable: Collagen type, Synthetic polymer type (lactate-glycol compound).

Gotlow (1993): proposed the following generations of membranes: 1) First generation (nonresorbable) 2) Second generation (resorbable) 3) Third generation (resorbable with growth factors).

Predictability of GBR procedures

Esposito's systematic review in 2009 included 13 RCTs dealing with vertical and horizontal augmentation techniques and concluded that there is early evidence that GBR can be used as a staged approach to allow for vertical bone augmentation. The evaluated techniques, however, were associated with high complication rates ranging from 60% to 20%. (Esposito, 2009) With respect to horizontal bone augmentation before implant placement, in cases of extreme horizontal bone resorption, it is still difficult to confirm that GBR is a reliable procedure. In 2009, the ITI consensus statement (Chen *et al*., 2009) clarified that "horizontal ridge augmentation often requires the use of autogenous bone block, which may be combined with a membrane and/or a particulate autograft, allograft, or xenograft". (Chen and Buser, 2009) Very low level of evidence exists in literature for GBR procedures in severe vertical defects. Presently available data demonstrates GBR therapy to be a predictable and successful procedure to augment bone in a horizontal direction at sites exhibiting in sufficient bone volume for implant placement under standard conditions. For horizontal ridge augmentation, resorbable membranes have successful and predictable results same as nonresorbable membranes. Long-term results showed that survival rates of implants placed in augmented bone is high and comparable with implants placed in native bone. As for using GBR in a staged approach for horizontal and/or vertical bone augmentation, some of the studies reveal a high percentage of success. However, many of them had a short - term follow-up. Moreover, complications arise with vertical reconstructions, while in the case of horizontal augmentation, studies have shown fewer complications.

Table 1. Level of evidence available for GBR procedures in various clinical situations (Esposito, 2009)

Clinical procedure	Level of evidence
GBR used for dehiscence and fenestration type defects	High level
GBR used for socket preservation	High level
GBR used as staged approach for horizontal bone augmentation	Moderate level Low risk of complications
GBR used as a staged approach for vertical bone augmentation	Moderate level Significant risk of complications
GBR used for severe vertical bone reconstruction	Low level

With extreme bone resorption (Cawood class VI), and inmaxillo-facial surgeries, the use of GBR is not well documented. Thus, a low level of evidence can be attributed in these clinical situations.

Conclusion

With better understanding of wound healing and the biology of bone regeneration, researchers have been able to apply the concept of GBR to achieve predictable bone regeneration specially in socket preservation and dehiscence or fenestration type defects. Various authors have described the principles for successfully achieving bone regeneration. These principles if followed diligently often provide the desired results. The choice of the barrier membrane to be used resides on the clinical experience of the clinician and the duration for which it is required. Severely atrophied jaws or larger defects require longer time and non-resorbable membranes in such cases are more commonly used.

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