Guided Bone Regeneration: Evidence & Limits

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ABSTRACT
Dental implants are considered nowadays by most of patients and clinicians as the first line of treatment in restoring missing teeth. Over the last fifty years, advances in technology and pressure from media, made dental implant patients nowadays, not content with mere survival, but expecting high aesthetic and long term functional durability. In some clinical scenarios, when teeth were lost due to trauma, infection or advanced gum disease, insufficient bone can be found at the missing teeth area which can influence the aesthetics, and long term prognosis of the dental implants and their prosthetic super structure. In such cases, dental implant therapy would not be an option without horizontal and/or vertical bone augmentation. (Esposito et al. 2009) In this mini review, the authors will firstly define the guided bone regeneration (GBR) concept and identify different used materials. Secondly, and after performing a literature reviews on the application of GBR in different clinical situations, some hints and tips concurring to attain optimal results will be suggested. Finally, this paper will test the level of available evidence when using Guided Bone Regeneration.

KEYWORDS
Guided Bone Regeneration, Membrane, Implant placement, Staged approach, Simultaneous approach.

INTRODUCTION
A variety of techniques and materials have been used to restore the necessary volume of bony tissue for supporting dental implants. The most commonly described methods in the dental literature are: Guided Bone Regeneration (GBR), onlay veneer grafting, interpositional inlay grafting, ridge splitting technique and distraction osteogenesis (*Aghaloo et Moy 2007*).

Guided bone regeneration is a frequently used procedure for hard tissue reconstruction (*Esposito et al. 2006, Hämmerle et al. 2008, Buser et al. 2011*). The treatment concept advocates that regeneration of osseous defects is predictably attainable via the application of occlusive membranes, which mechanically exclude non-osteogenic cell populations from the surrounding soft tissues, thereby allowing osteogenic cell populations originating from the parent bone to inhabit the osseous wound (*Retzepi et Donos 2010, Donos et al. 2002a, 2002b, 2002c*).

Indeed, successful results in the craniofacial region have been reported following the placement of mechanical barriers over jawbone defects in rabbits (*Kahnberg 1979*) and over cranial defects in rats (*Melcher 1969*). To the same extent, a well conducted split mouth design random controlled trial on sinus grafting indicated that a graft is not needed to obtain new bone in the sinus cavity, if it is possible to keep sufficient space using a resorbable rigid barrier. (*Felice 2009*). These studies suggest that bone regeneration is significantly enhanced when the invasion of soft tissue into osseous defects is mechanically impeded.

Thus, Guided bone regeneration (GBR) was introduced as a therapeutic modality aiming to achieve bone regeneration, via the use of barrier membranes (*Dahlin et al. 1988*).

Clinical applications and materials used in GBR
Various non-resorbable and resorbable membrane materials have been used in experimental and clinical studies in the context of GBR treatment. However, before choosing the membrane type, some prerequisites are essential. These include: **(1)** Biocompatibility, i.e. no interaction between material and tissue, **(2)** Cell occlusion properties, i.e. to prevent fibrous connective tissue invasion, **(3)** Integration by the host tissues, **(4)** Clinical manageability and space making ability (*Karring et al., 1993*).

Expanded polytetrafluorothylene (e-PTFE) has been the most frequently used material for periodontal and bone regeneration. e-PTFE is a chemically stable and biologically inert polymer, featuring a porous structure and flexible form. Their use has shown to lead to successful GBR treatments in many clinical reports. (*Hämmerle & Jung 2003*).

Titanium-reinforced e-PTFE membrane can also used in GBR (*Urban et al. 2009, Simon et al. 1994, 2007*). It consists of a double layer of e-PTFE and a titanium framework interposed, making of it a shapeable one

with a stable form to allow the reconstruction of the geometry of the lost bone. Its main indications are for three dimensional bone reconstruction.

Non-resorbable membranes do not undergo the enzymatic degradation when placed in the living body as in the case of the resorbable membranes. Hence, they require a second surgical intervention in order to be removed. Moreover, the exposure of these membranes may lead to total failure of the regeneration process (*Rochietta et al. 2008*). These disadvantages led to the development of resorbable membrane devices.

Several resorbable membranes have been tested showing various degrees of successful bone regeneration, including collagen type I, polyurethane, polyglactin 910, polylactic acid, polyglycolic acid, and different copolymers of polylactic and polygalactic acid (*Sandberg et al. 1993, Zellin et al. 1995, Brunel et al. 1998*).

Absorbable collagen membranes are used more and more frequently in dentistry for guided bone regeneration (GBR). The great advantage of using absorbable membranes is that a second procedure to remove the membrane is not necessary.

However, resorbable membranes have some drawbacks such as uncontrolled duration of barrier function (resorption time can ranges from four to sixteen weeks) and the need of membrane supporting material to minimize membrane collapse. In some cases, adding to the fact that the resorption process can interfere with wound healing and may also have a negative influence on the bone regeneration. That's why a cross-linking of the resorbable membrane was proposed (*Bronstein et al. 2009*). Artificial cross-linking of collagen is an attempt to increase the barrier function of collagen membranes. However, recent results from clinical and pre-clinical studies have shown that this is unnecessary (*Becker et al. 2009, Scwharz et al. 2006*).

Bone fillers which can be Autogenous bone chips, allograft (same species), xenograft (another species), or alloplast (synthetic), are commonly used in the GBR process. Their aim is to promote osseous ingrowth and bone healing through osteoconduction, provide mechanical support of the membrane and stabilize the blood clot (*Buser et al. 2008, Jensen et al. 2006*).

Guided bone regeneration (GBR) with simultaneous implant placement

GBR with simultaneous implant placement is recommended only if the implant could be placed in an optimal three dimensional position with satisfactory primary stability from the existing natural bone (*Chen et al. 2009*). However, the success of the procedure does not rely only on implant's stability, but also on the stability of the grafting material.

Park et al. (2008) in their random controlled trial which included 22 patients wanted to check the importance of using a barrier when GBR is carried to cover exposed threads of dental implants. Patients were divided into 3 groups; In group 1, the allograft was covered with a collagen membrane. In group 2, the allograft was protected with an acellular dermal matrix. In group 3, no membrane was used. Six months later, a 48 % loss of the graft was observed in group 1 in comparison with a 42 % loss in group 2 and a 66% loss in group 3. Based on this study as well as on others papers (*Donos 2005 b, Chen et al. 2009*), we can suggest that the application of an occlusive membrane minimizes the resorption rate of the graft.

The main indication of GBR use as simultaneous approach is to treat dehiscence- and fenestration-type defects. The majority of studies used combinations of bone grafts and barrier membranes to promote bone regeneration in peri-implant defects. The most commonly used augmentation material was deproteinized bovine bone mineral (DBBM), in conjunction with e-PTFE membranes or collagen membranes.(*Zitzmann et al. 1999, Schropp et al. 2003, Nemcovsky et Artzi 2002, Covani et al. 2007, Nemcovsky et al. 2000, Chen 2005, 2007*).

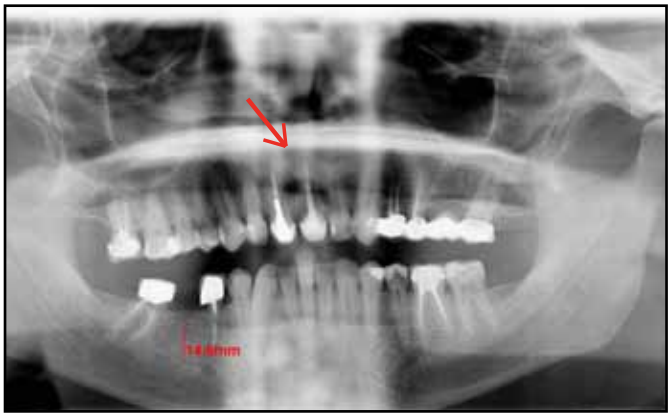
Many studies (*Parma-Benfenati et al. 1999, Tinti et Parma-Benfenati 1998, Simion et al. 1994, 2007*) had shown that GBR could be used for vertical bone augmentation in combination with implant placement. In this technique implants were inserted protruding 2 to 7mm from the bone level and the augmentation procedures is performed, mainly with non resorbable membrane with bone chips and/or bone substitutes. However, a significant rate of complications was observed. (*Esposito et al. 2009*).

GBR use as a staged approach

When the ridge anatomy does not allow for an ideal three-dimensional implant placement, a two-step procedure is recommended where the implant placement will be the second step after hard tissue reconstruction. Many studies (*Seibert and Nyman 1990, Smukler 1995, Buser et al. 1995*) had shown that GBR using membranes and bone substitutes could regenerate bone before implant placement. The implant placement could be planned for after five to nine months from performing GBR procedures. Thus, in classes III and IV of Cawood classification, GBR could achieve predictable results (*Cawood 1988*).

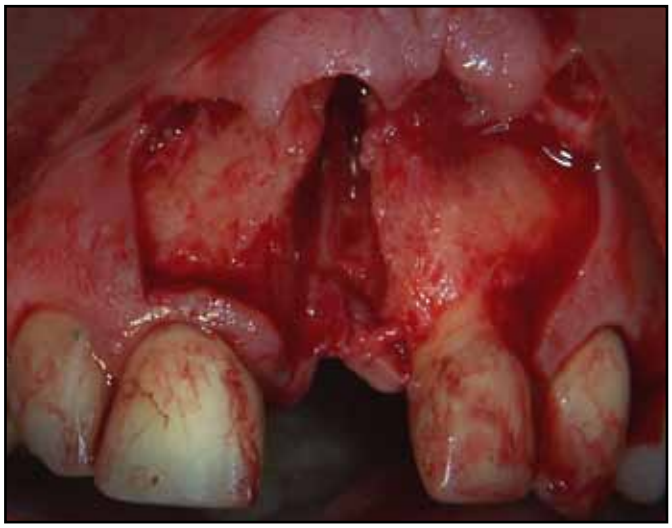
For vertical bone augmentation before implant placement, *Jovanovic et al. (1995*), *Urban et al. (2009)*, *Fontana et al. (2008)* and *Todisco (2010)* described the use non resorbable e-PTFE membrane with DFDBA (demineralized freeze-dried bone allograft) or DBBM (deproteinized bovine bone mineral) alone or mixed with autogeneous chips. The two main problems in this reconstruction are: membrane exposure and soft tissue collapse. That is why a tension free flap closure is a must, with appropriate suturing techniques. Also, the use of tenting screws have been found useful in minimize the soft tissue collapse. (*Le et al. 2010*).

Guided Bone Regeneration Using Nucleoss Dental Implants

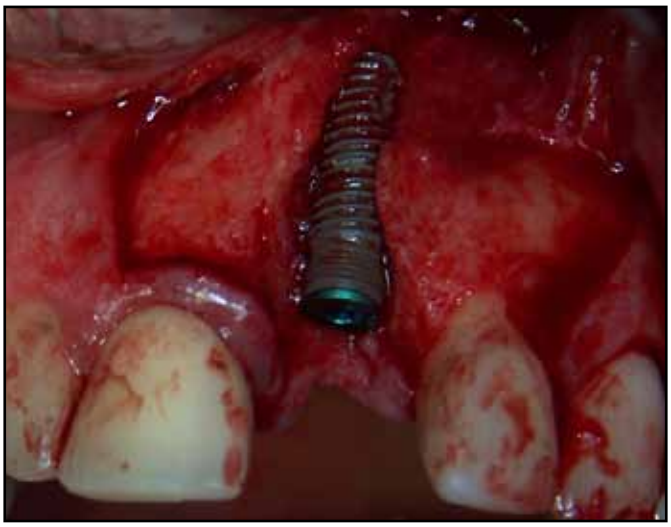


(Fig 1) *Hopeless upper left incisor due to failed root canal treatment, with a deep probing depth buccaly*

(Fig 2) *Panoramic X-ray one month after the extraction*

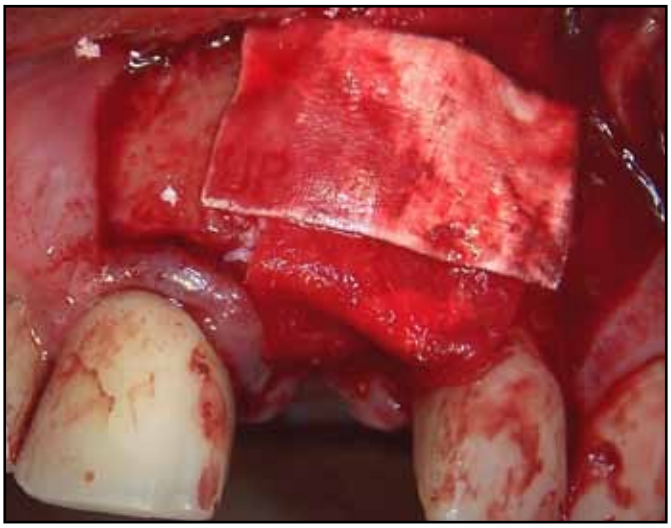


(Fig 3) *Clinical situation one month after the extraction, the extension of the defect is obvious*



(Fig 4) *Implant placement in an ideal 3 dimensional position, the whole implant threads are exposed*

(Fig 5) *DBBM mixed with autogenous bone chips collected from the site, covering the defect*



(Fig 6) *Double layer collagen membrane: well adapted and extended 3-4mm apically beyond the defect*

(Fig 7) *Tension free flap closure*

(Fig 8) *Meanwhile the patient had a Maryland bridge*

Enhancing our GBR practice (Tips and hints to achieve optimal results)
Some tips and hints can be useful to the GBR success. They are a sum-up of many publications as well as from the authors personal experience.

In the following surgical procedures, **(1)** Flap designing, **(2)** Membrane stabilization, and **(3)** Flap closure, some key techniques are essential to achieve success in GBR:

1. Flap designing
Due to an avascular zone located over the edentulous ridge about 1 to 2mm wide, (*Kleinheinz 2005*), midline incisions with vertical discharge at the anterior border of the alveolar ridge are favorable for healing. (*Norton et al. 2007*).

Whether an overlapped flap design, a coronally positioned flap, or a pedicle flap technique is used, an effective primary closure during the regenerative period is a must (*Langer and Langer 1990, Buser et al. 1995, Tinti and Parma-Benfenati 1995, Fugazzotto 1999, 2006*)

2. Membrane fixation
The membrane should overlap the defect by 3-4mm, be protected by the flap and achieve good stability (*Hämmerle et Jung 2008*).

(Fig 9) *Soft tissue healing: Mesial and distal papilla regeneration*

(Fig 10) *Clinical situation after crown cementation: Prosthetic part Dr. Belal Mohssen*

(Fig 11) *X-ray: 1 year after cementation*

Two main procedures can be implemented for membrane stabilisation:

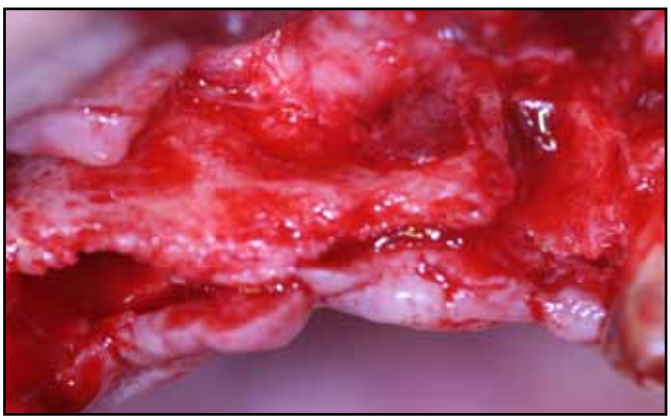
1. Adapting the membrane to the defect. It is noted that collagen membranes possess an inherent adaptation capacity. (*Buser, 2011*)
2. Fixation of the membrane by using:
   a. Resorbable and non resorbable mini screws
   b. Cover screw or healing abutment

3. Flap closure
Periosteal fenestrations allow some flap elasticity. If vertical incisions do not facilitate optimal tissue advancement, hold the flap under tension with a tissue forceps (e.g. Adson tissue forceps), and score the periosteum close to the base of the flap from the distal to mesial aspect across the whole flap. To attain further tissue advancement, insert a closed blunted scissor or

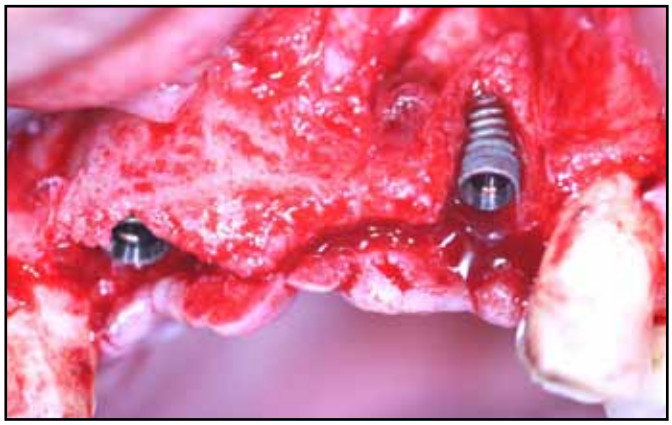
Guided Bone Regeneration
Case 2

(Fig 12) *Pre-operative clinical photo: Metal-ceramic bridge from upper right central incisor or to upper left lateral incisor. The patient consults for bridge mobility and fistula apical to the lateral incisor*

(Fig 13) *Panoramic X-ray: Wide-diameter post, weak dental structure and periapical radiolucency*



(Fig 14) *Clinical situation 3 weeks after the extraction of the 2 incisors. Intact buccal plate on the central incisor, and no buccal wall on the lateral incisor*

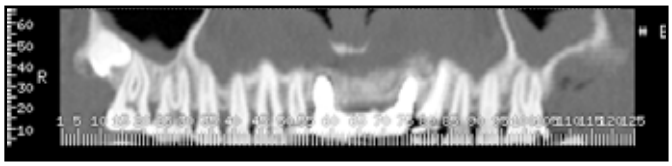


(Fig 15) *Implant placement. On the lateral incisor, almost half of the implant threads were exposed*

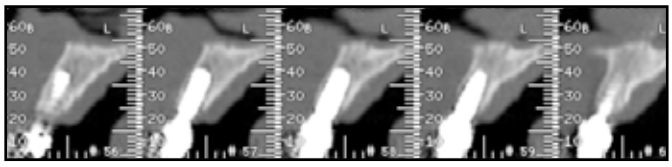
(Fig 16) *DBBM covering the implant threads and the pontic area*

(Fig 17) *Collagen membrane covering the defect. On the lateral incisor area, three layers of this membrane were used*

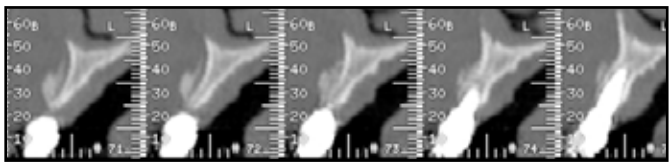
(Fig 18) *X-rays 2 months after implant placement*



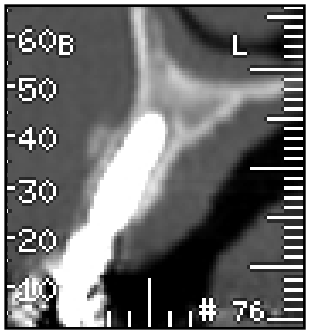
(Fig 19) *Frontal view of CBCT taken 6 months after crown cementation*



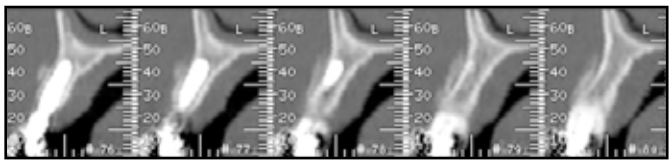
(Fig 20) *Sagittal view on the central incisor area. The buccal plate was intact*



(Fig 21) *Sagittal view on the pontic area. Note the presence of DBBM*



(Fig 22) *Sagittal view on the lateral incisor area where the patient had absence of buccal plate, note the complete regeneration of bone buccaly*



a hemostat into the incision line. The instrument is held vertically, thereby stretching apart the two sides of the incision line (*Fugazzotto 2006, Greenstein et al. 2009*).

Flap advancement around the mental foramen is often compromised (*Mraiwa et al. 2003*). A practical technique to advance a flap in the posterior mandible that avoids dissecting apical to the mental foramen is to perform a dome-shaped incision distal to where the nerve emerges around the foramen (*Greenstein et al. 2009*).

To maintain flap orientation, it is advantageous to place a stitch at the midpoint of the flap (a horizontal mattress suture).

Polyglactin 910 suture or E-PTFE sutures seem to maintain prolonged tensile strength (*Greenstein et al. 2009*). After suturing, apply pressure for 10 minutes to obtain a fibrin clot; this prevents pooling of blood under the flap.

Discussion (Levels of evidence upon using GBR)

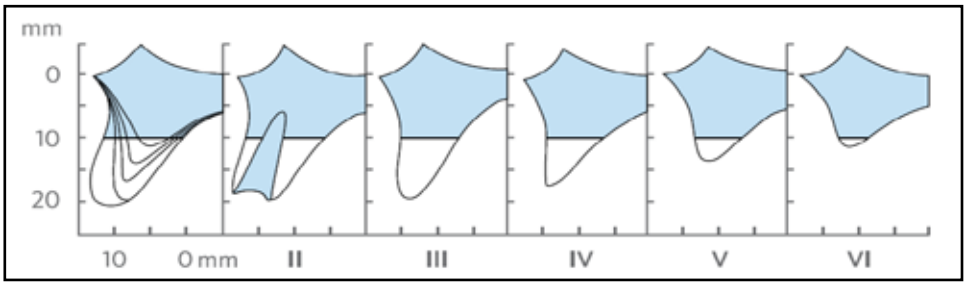
The past two decades of clinical and scientific investigation have established the use of guided bone regeneration (GBR) as a proven method to regain a diminished alveolar ridge (*Zitzmann et al. 1999*) or for socket preservation (*Wang et al. 2004*). The dental literature is full of systematic reviews, clinical trials and consensus statements supporting the use of GBR a reliable procedure in treating dehiscence and fenestration-type defects (*Chen et al. 2009, Esposito 2008*).

With respect to horizontal bone augmentation before implant placement, in cases of extreme horizontal bone resorption, we are still unable 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". However, for other authors, GBR seems to give comparable results to autogenous bone block which, up till now, is considered the gold standard in bone reconstruction (*Meijndert 2007*).

On the other hand, *Meijndert et al.* performed an RCT study in 2007 which had a large sample size of 93 patients divided into 3 equal groups. They used three different techniques to horizontally augment local ridge maxillary defects (from 1st to 1st premolars) for allowing placement of single implants **(1)** bone blocks from the chin, combined to particulate autogeneous chips; **(2)** bone graft from the chin with a resorbable barrier; and **(3)** 100% bovine anorganic bone with a resorbable barrier. Implants were placed 3 months after autogenous bone grafting and 6 months after augmenting sites with DBBM. Patients in the first 2 groups were treated according to the first 2 techniques respectively, i.e. with blocks of bone, whereas in the third group, the defects were reconstructed with 100% bone substitute and a resorbable barrier. Despite these relatively high numbers, the authors confirmed that no complication occurred. Only two implants failed early in the bone substitute group. However, they were successfully replaced. It is true that the healing period for the bone substitute group was three months longer, but on the other hand, no autogenous bone was needed to complete the procedure.

Esposito's systematic review in 2009 concluded that there is early evidence that GBR can be used as a staged approach to allow for vertical bone augmentation. While the random controlled trials included in his Cochrane review confirmed this proposition. The evaluated techniques, however, were associated with high complication rates ranging from 60% (*Bianchi 2008*) to 20% (*Felice 2008*).

The ITI fourth consensus (*Chen et al. 2009*) concerning the predictability of vertical bone augmentation declared that "Vertical ridge augmentation procedures most



(Table 1) *Classification of the edentulous jaws, according to Cawood JI & Howell RA (Int J Oral Maxillofac Surg 1988 Aug;17(4):232-6)*

(Table 2) *Advantages and disadvantages of different membrane types. (+ favorable point; - unfavorable point)*

	ePTFE	Collagen	PLA/PGA
Handling, Adaptation	-	++	+
Exposure, Site Infection	-	++	?
Collapse	+	-	-/+
Barrier Function	++	+	+
Breakdown, Bone Resorption	++	++	-
Re-entry	-	+	+

(Table 3) *Levels of evidence upon using GBR*

GBR used for dehiscence and fenestration type defects	High level
GBR used for socket preservation	High level
GBR used as a 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

often required the use of autogenous block graft, which may be combined with a membrane and/or a particulate autograft, allograft, or xenograft. Despite the use of an autogenous block graft, elevated rate of complications and a need for additional grafting have to be anticipated." The common point between *Esposito*'s review and the ITI consensus statement is the high percentage of complications with vertical bone augmentation.

CONCLUSION

Within the limits of this mini-review which aimed to analyze the outcome of the use of GBR for hard tissue reconstruction, it is concluded that GBR can be successful treatment modality for dehiscence-and fenestration-type defects around dental implants. 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 less complications.

Thus, a moderate level of evidence in the staged approach is found and more clinical trials are required to test the validity of GBR in vertical and horizontal bone augmentation.

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

REFERENCES

- Aghaloo TL, Moy PK. Which hard tissue augmentation techniques are the most successful in furnishing bony support for implant placement? Int J Oral Maxillofac Implants. 2007;22:49-70.
- Ashman A. Postextraction ridge preservation using a synthetic alloplast. Implant Dent. 2000;9:168-76.
- Bartee BK. Extraction site reconstruction for alveolar ridge preservation. Part 2: membrane-assisted surgical technique. J Oral Implantol. 2001;27(4):194-7.
- Becker W, Urist M, Becker BE *et al.* Clinical and histologic observations of sites implanted with intraoral autologous bone grafts or allografts. 15 human case reports. J Periodontol. 1996;67:1025-33.
- Becker W, Dahlin C, Lekholm U *et al.* Five-year evaluation of implants placed at extraction and with dehiscences and fenestration defects augmented with ePTFE membranes: Results from a prospective multicenter study. Clin Implant Dent Relat Res. 1999;1:27-32.
- Becker J, Al-Nawas B *et al.* Use of a new cross-linked collagen membrane for the treatment of dehiscence-type defects at titanium implants: a prospective, randomized controlled double-blinded clinical multicenter study. Clin Oral Implants Res. 2009;20:742-9.
- Bianchi A, Felice P, Lizio G, Marchetti C. Alveolar distraction osteogenesis versus inlay bone grafting in posterior mandibular atrophy: a prospective study. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontics. 2008;105(3):282-92.
- Botticelli D, Berglundh T, Lindhe J. Hard-tissue alterations following immediate implant placement in extraction sites. J Clin Periodontol. 2004;31:820-8.
- Bronstein MM, Heynen G *et al.* Effect of two bioabsorbable barrier membranes on bone regeneration of standardized defects in calvarial bone: a comparative histomorphometric study in pigs. J Periodontol. 2009;80(8):1289-99.
- Brunel G, Benque E, Elharar F, Sansac C, Duffort JF, Barthet P, Baysse E & Miller N. Guided bone regeneration for immediate non-submerged implant placement using bioabsorbable materials in beagle dogs. Clin Oral Implants Res. 1998;9:303-12.
- Buser D, Dula K, Belser UC, Hirt HP & Berthold H. Localized ridge augmentation using guided bone regeneration. II. Surgical procedure in the mandible. Int J Periodontics Restorative Dent. 1995;15:10-29.
- Buser D, Bornstein MM, Weber HP, Grütter L, Schmid B, Belser UC. Early implant placement with simultaneous guided bone regeneration following single tooth extraction in the esthetic zone: A cross-sectional, retrospective study in 45 patients with a 2-to 4-year follow-up. J Periodontol. 2008;79:1773-81.

- Buser D, Wittneben J, Bornstein MM, Grütter L, Chappuis V, Belser UC. Stability of contour augmentation and esthetic outcomes of implant-supported single crowns in the esthetic zone: 3-year results of a prospective study with early implant placement post-extraction. Periodontol. 2011;82(3):342-9.
- Cawood JI & Howell RA. A classification of the edentulous jaws. Int J Oral Maxillofac Surg. 1988;17(4):232-6.
- Chen ST, Darby IB, Adams GG, Reynolds EC. A prospective clinical study of bone augmentation techniques at immediate implants. Clin Oral Implants Res. 2005;16:176-84.
- Chen ST, Darby IB, Reynolds EC. A prospective clinical study of non-submerged immediate implants: Clinical outcomes and esthetic results. Clin Oral Implants Res. 2007;18:552-62.
- Chen ST, J Beagle, S Jensen, M Chiapasco, I Darby. Consensus statement and recommended clinical procedures regarding surgical techniques. Int J Oral Maxillofac Implants. 2009;24:272-8.
- Covani U, Cornelini R, Barone A. Vertical crestal bone changes around implants placed into fresh extraction sockets. J Periodontol. 2007;78:810-5.
- Dahlin C, Linde A, Gottlow J & Nyman S. Healing of bone defects by guided tissue regeneration. Plastic and Reconstructive Surgery. 1988;81:672-6.
- Dahlin C, Andersson L & Linde A Bone augmentation at fenestrated implants by an osteopromotive membrane technique. A controlled clinical study. Clinical Oral Implants Research. 1991;2:159-65.
- Donos N, Kostopoulos L & Karring T. Augmentation of the rat jaw with autogeneic cortico-cancellous bone grafts and guided tissue regeneration. Clin Oral Implants Res. 2002a;13(2):192-202.
- Donos N, Kostopoulos L & Karring T. Alveolar ridge augmentation by combining autogenous mandibular bone grafts and non-resorbable membranes. Clin Oral Implants Res. 2002b;13(2):185-91.
- Donos N, Kostopoulos L & Karring T. Alveolar ridge augmentation using a resorbable copolymermembrane and autogenous bone grafts. An experimental study in the rat. Clin Oral Implants Res. 2002c;13:203-13.
- Donos N, Kostopoulos L, Tonetti M & Karring T. Long-term stability of autogenous bone grafts following combined application with guided bone regeneration. Clin Oral Implants Res. 2005b;16:133-9.
- Esposito M, Grusovin MG, Coulthard P & Worthington HV. The efficacy of various bone augmentation procedures for dental implants: a Cochrane systematic review of randomized controlled clinical trials. Int J Oral Maxillofac Implants. 2006;21:696-710.
- Esposito M, Grusovin MG, Felice P, Karatzopoulos G, Worthington HV, Coulthard P (2009). Interventions for replacing missing teeth: horizontal and vertical bone augmentation techniques for dental implant treatment. Cochrane Database of Systematic Reviews, Issue 4.
- Felice P, Marchetti C, Piattelli A, Pellegrino G, Checchi V, Worthington H *et al.* Vertical ridge augmentation of the atrophic posterior mandible with interpositional bloc grafts: bone from the iliac crest versus bovine anorganic bone. Results up to delivery of the final prostheses from a split-mouth, randomised controlled clinical trial. Eur J Oral Implantol. 2008;1:183-7.
- Felice P, Marchetti C, Iezzi G, Piattelli A, Worthington H, Pellegrino G, Esposito M. Vertical ridge augmentation of the atrophic posterior mandible with interpositional bloc grafts: bone from the iliac crest vs. bovine anorganic bone. Clinical and histological results up to one year after loading from a randomized-controlled clinical trial. Clin Oral Implants Res. 2009;20(12):1386-93.
- Felice P, Esposito M, Scarano A, Pistilli R, Lizio G, Checchi L. A comparison of two techniques to augment maxillary sinus with the lateral approach: no grafting procedure vs anorganic bone placement. Preliminary histological and clinical outcomes of a randomized controlled clinical trial. Clinical Oral Implants Research. 2009;20:973 (Abs 261).
- Fontana F, Santoro F, Maiorana C, Iezzi G, Piattelli A, Simion M. Clinical and histologic evaluation of allogeneic bone matrix versus autogenous bone chips associated with titanium-reinforced e-PTFE membrane for vertical ridge augmentation: a prospective pilot study. Int J Oral Maxillofac Implants. 2008;23(6):1003-12.
- Fugazzotto PA. Maintenance of soft tissue closure following guided bone regeneration: Technical considerations and report of 723 cases. J Periodonto. 1999;70:1085-97.
- Fugazzotto PA. Maintaining primary closure after guided bone regeneration procedures: Introduction of a new flap design and preliminary results. J Periodontol. 2006;77:1452-57.
- Greenstein G, Greenstein B, Cavallaro J, Elian N, and Tarnow D. Flap Advancement: Practical Techniques to Attain Tension-Free Primary Closure. J Periodontol. 2009;80(1):4-15.
- Hämmerle CH & Jung, R.E. Bone augmentation by means of barrier membranes. Periodontology. 2003;33:36-53.
- Hämmerle C, Jung RE. (2008) Ridge augmentation procedures. In: Lang N. and Lindhe J. Clinical periodontology and implant dentistry, 5th ed, NY: Wiley, John & Sons, Incorporated, pp 1083-98.
- Iasella JM, Greenwell H, Miller RL, et al. Ridge preservation with freeze-dried bone allograft and a collagen membrane compared to extraction alone for implant site development: a clinical and histologic study in humans. J Periodontol. 2003;74:990-9.
- Jensen OT, Greer RO Jr., Johnson L & Kassebaum D. Vertical guided bone-graft augmentation in a new canine mandibular model. Int J Oral Maxillofac Implants. 1995;10:335-44.
- Jovanovic SA & Nevins M. Bone formation utilizing titanium-reinforced barrier membranes. Int J Periodontics Restorative Dent. 1995;15:56-69.
- Kahnberg, K.E. Restoration of mandibular jaw defects in the rabbit by subperiosteally implanted Teflon mantle leaf. Int J Oral Surg. 1979;8:449-56.
- Karring T, Nyman S, Gottlow J & Laurell L. (1993). Development of the biological concept of guided tissue regeneration–animal and human studies. Periodontology. 2000;1:26-35.
- Kleinheinz J, Büchter A, Kruse-Lösler B, Weingart D, Joos U. Incision design in implant dentistry based on vascularization of the mucosa. Clin Oral Implants Res. 2005;16:518-23.
- Langer B, Langer L. Overlapped flap: A surgical modification for implant fixture installation. Int J Periodontics Restorative Dent. 1990;10:208-15.
- Le B, MD Rohrer, and HS Prassad. Screw "Tent-Pole" Grafting Technique for Reconstruction of Large Vertical Alveolar Ridge Defects Using Human Mineralized. Allograft for Implant Site Preparation J Oral Maxillofac Surg. 2010;68:428-35.
- Lekovic V, Camargo PM, Klokkevold PR, *et al.* Preservation of alveolar bone in extraction sockets using bioabsorbable membranes. J Periodontol. 1998;69:1044-49.
- Meijndert L, Meijer HJ, Stellingsma K, Stegenga B, Raghoebar GM. Evaluation of aesthetics of implant-supported single-tooth replacements using different bone augmentation procedures: a prospective randomized clinical study. Clin Oral Implants Res. 2007;18(6):715-9.
- Melcher AH. Role of the periosteum in repair of wounds of the parietal bone of the rat. Archives of Oral Biology. 1969;14:1101-9.
- Mraiwa N, Jacobs R, Moerman P, Lambrichts I, van Steenberghe D, Quirynen M. Presence and course of the incisive canal in the human mandibular interforaminal region: Two-dimensional imaging versus anatomical observations. Surg Radiol Anat. 2003;25:416-23.
- Nemcovsky CE, Artzi Z, Moses O, Gelernter I. Healing of dehiscence defects at delayed-immediate implant sites primarily closed by a rotated palatal flap following extraction. Int J Oral Maxillofac Implants. 2000;15:550-8.
- Nemcovsky CE, Artzi Z. Comparative study of buccal dehiscence defects in immediate, delayed, and late maxillary implant placement with collagen membranes: Clinical healing between placement and second-stage surgery. J Periodontol. 2002;73:754-61.
- Norton NS (2007). Netter's Head and Neck Anatomy for Dentistry. Philadelphia: Saunders.
- Park SH, Lee KW, Oh TJ, Misch CE *et al.* Effect of absorbable membrane on sandwich bone augmentation Clin Oral Implants Res. 2008; Volume 19, Issue 1:32-41.
- Parma-Benfenati S, Tinti C, Albrektsson T & Johansson C. Histologic evaluation of guided vertical ridge augmentation around implants in humans. Int J Periodontics Restorative Dent. 1999;19:424-37.

- Pinholt EM, Bang G, Haanaes HR. Alveolar ridge augmentation by osteoinduction in rats. Scand J Dent Res. 1990;98:434-41.
- Pinholt EM, Haanaes HR, Roervik M *et al.* Alveolar ridge augmentation by osteoinductive materials in goats. Scand J Dent Res. 1992;100:361-5.
- Retzepi M, Donos N. Guided Bone Regeneration biological principle and therapeutic applications. Clin.Oral Impl. Res. 2010;21:567-76.
- Rocchietta, I., Fontana, F. & Simion, M. Clinical outcomes of vertical bone augmentation to enable dental implant placement: a systematic review. J Clin Periodontology. 2008;35(8):203-15.
- Rompen EH, Biewer R, Vanheusden A, Zahedi S & Nusgens B. The influence of cortical perforations and of space filling with peripheral blood on the kinetics of guided bone generation. A comparative histometric study in the rat. Clin Oral Implants Res. 1999;10:85-94.
- Sandberg E, Dahlin C & Linde A. Bone regeneration by the osteopromotion technique using bioabsorbable membranes: an experimental study in rats. Int J Oral Maxillofac Surgery. 1993;51:1106-14.
- Schropp L, Kostopoulos L, Wenzel A. Bone healing following immediate versus delayed placement of titanium implants into extraction sockets: A prospective clinical study. Int J Oral Maxillofac Implants. 2003;18:189-99.
- Sclar AG. Preserving alveolar ridge anatomy following tooth removal in conjunction with immediate implant placement. The Bio-Col technique. Atlas Oral Maxillofac Surg Clin North Am. 1999;7(2):39-59.
- Schwarz F, Rothamel D *et al.* Angiogenesis pattern of native and cross-linked collagen membranes: an imunohistochemical study in the rat. Clin Oral Implants Res. 2006;17(4):403-09.
- Seibert J & Nyman S. Localized ridge augmentation in dogs: a pilot study using membranes and hydroxyapatite. J Periodontology. 1990;61:157-65.
- Simion M, Trisi P & Piattelli A. Vertical ridge augmentation using a membrane technique associated with osseointegrated implants. Int J Periodontics Restorative Dent. 1994;14:496-511.
- Simion M, Fontana F, Rasperini G & Maiorana C. Vertical ridge augmentation by expanded-polytetrafluoroethylene membrane and a combination of intraoral autogenous bone graft and deproteinized anorganic bovine bone (*BioOss*). Clin Oral Implants Res. 2007;18:620-29.
- Smukler H, Barboza EP & Burliss C. A new approach to regeneration of surgically reduced alveolar ridges in dogs: a clinical and histologic study. Int J Oral Maxillofac Implants. 1995;10:537-51.
- Tinti C, Parma-Benfenati S. Coronally positioned palatal sliding flap. Int J Periodontics Restorative Dent. 1995;15:298-310.
- Tinti, C. & Parma-Benfenati, S. Vertical ridge augmentation: surgical protocol and retrospective evaluation of 48 consecutively inserted implants. Int J Periodontics Restorative Dent. 1998;18:434-43.
- Todisco M. Early loading of implants in vertically augmented bone with non-resorbable membranes and deproteinised anorganic bovine bone. An uncontrolled prospective cohort study. Eur J Oral Implantol. 2010;3(1):47-58.
- Urban IA, Jovanovic SA, Lozada JL. Vertical ridge augmentation using guided bone regeneration (GBR) in three clinical scenarios prior to implant placement: a retrospective study of 35 patients 12 to 72 months after loading. Int J Oral Maxillofac Implants. 2009;24(3):502-10.
- Wang H-L, Kiyonobu K & Neiva R F. Socket Augmentation: Rationale and Technique. Implant Dent. 2004 ;13:286-96.
- Zellin G, Gritli-Linde A & Linde A. Healing of mandibular defects with different biodegradable and non-biodegradable membranes: an experimental study in rats. Biomaterials. 1995;16:601-9.
- Zitzmann NU, Schärer P, Marinello CP. Factors influencing the success of GBR. Smoking, timing of implant placement, implant location, bone quality and provisional restoration. J Clin Periodontol. 1999;26:673-82.