GUIDED BONE REGENERATION IN IMPLANT DENTISTRY– A REVIEW THE PAST PRESENT & FUTURE

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ABSTRACT

Post-extraction crestal bone resorption and periodontal disease are common and unavoidable which can lead to significant ridge dimensional changes. To regenerate enough bone for successful implant placement, Guided Bone Regeneration has emerged as a predictable method to enhance the bone volume in deficient recipient sites prior to implant placement. It provides sufficient bone volume and adequate soft tissue thickness to enable implants to be placed at the most optimal position from a prosthetic point of view. In the past, non-absorbable membranes with basic functions such as space maintenance were used with bone graft materials. Due to several limitations of the non-absorbable membranes, membranes of the second and third generation equipped with controlled absorbability, and a functional layer releasing growth factors or antimicrobials were introduced. Moreover, tissue engineering using biomaterials enabled faster and more stable tissue regeneration. The scaffold with three-dimensional structures manufactured by computer-aided design and manufacturing (CAD/CAM) showed high biocompatibility, and promoted cell infiltration and revascularization.

Key words: Platelet Rich fibrin, RBC, HB, Densenetwork, loose network.

INTRODUCTION

Dental Implants are now an integral part of periodontal and restorative dentistry. They present a reliable way to restore function and aesthetics in fully or partially edentulous patients. The process of osseointegration [12] is the basis for dental implant success i.e. the direct anchorage of implant to bone without intervening fibrous connective tissue. Successful implant placement requires adequate alveolar ridge dimensions, which are essential to house the implant. Periodontal bone loss, gingival recession, tooth loss, and long-term use of removable appliances etc. results in alveolar defects that prevent the placement of implants in an optimal prosthetic position.

In these situations, the clinician is obligated to perform augmentation procedures to reconstruct lost bone and place implants in a prosthetically driven position. So considerable research has been conducted to promote bone growth and regeneration and many predictable treatment protocols and biomaterials are recently introduced in implant dentistry for bone regeneration, including distraction osteogenesis, onlay bone grafting, and guided bone regeneration (GBR).

The aim of the present review is to highlight and discuss guided bone regeneration (GBR) in detail along with exploration of its past researches, current applications and future perspectives.

GUIDED BONE REGENERATION:

Guided bone regeneration is based on the biologic principles of guided tissue regeneration. Osseous regeneration by GBR depends on the migration of pluripotential and osteogenic cells (e.g. osteoblasts derived from the periosteum and/or adjacent bone and/or bone marrow) to the bone defect site and exclusion of cells impeding bone formation (e.g. epithelial cells and fibroblasts).

The following principles are needed for a successful GBR technique. [20]

Exclusion of epithelium and connective tissue,
Space maintenance, stability of the fibrin clot, and
Primary wound closure.

HISTORICAL PERSPECTIVE: The principle of using barrier membranes were first evaluated in the late 1950s and early 1960s by the research teams of Bassett et al., [2] and Boyne et al., [4] for the healing of cortical defects in long bones and osseous facial reconstruction. However, these studies had no impact on the development of new surgical techniques to regenerate localized defects in the jaws because the potential of this membrane application probably was not recognized.

The utilization of barrier membranes for implant patients was certainly triggered by the clinical application of barrier membranes for periodontal regeneration, called Guided Tissue Regeneration (GTR) was first developed in the early 1980s by Nyman et al [16] .The use of PTFE membranes for bone regeneration was initiated in the mid-1980s by the group led by Nyman and Dahlin,[7] who performed a series of experimental studies. These studies were performed with expanded polytetrafluoroethylene (PTFE), which is a bioinert membrane. [3] The barrier membrane creates a secluded space and facilitates the proliferation of angiogenic and osteogenic cells from the marrow space into that defect without interference by fibroblasts.

Schank et al demonstrated the principle of GTR in his landmark experimental study in foxhounds. The utilization of ePTFE membranes for GBR procedures in patients started in the late 1980s.

The GBR technique has been used either as a simultaneous or a staged approach. During earlier stages of research several complications were noted in both approaches and one such complication which occurred frequently was the collapse of PTFE membranes, thus leading to reduced volume of regenerated tissue underneath the membrane.

Therefore, in order to prevent the collapse and also to provide support to the membranes, bone fillers such as autografts or allografts were recommended by various group of researchers, which led to enhanced new bone formation through the osteogenic potential of autogenous bone grafts.

However the GBR technique based on the utilization of ePTFE membranes in combination with bone grafts or bone substitutes had the following disadvantages:

1. Significant rate of membrane exposures arising from soft tissue dehiscence, often leading to local infection underneath the membrane and subsequently to a compromised treatment outcome of the GBR procedure.
2. Difficult handling of the membrane during surgery because of its hydrophobic properties, requiring stabilization of the membrane with mini screws and tacks.
3. The need for a second surgical procedure to remove the bioinert, non-resorbable membrane.

These shortcomings could only be corrected with the utilization of a bioresorbable membrane. This trend was again initiated in the field of GTR, with the introduction of the first bioresorbable membranes in the early 1990s. This led to, numerous researches which examined different biomaterials for GBR on animal models.

The first published clinical reports were predominantly studies with collagen membranes. Today, collagen membranes are routinely used in daily practice for GBR procedures. A systematic review by Aghaloo and Moy [1] demonstrated that implants placed with the GBR procedure have favourable survival rates and that the GBR procedure is the only well-documented surgical technique among various surgical techniques used for localized ridge augmentation.

Designing of the implant abutment is done with the fusion software initially. Using laser melting system, metals like nickel, steel, titanium, cobaltchromium, aluminium is used for fabrication. The abutment is built by melting and fusing layers of metallic powder .Once a single layer is established, build plate is lowered to reintroduce the powder and subsequent layers is printed.Post processing is done by removal of witness marks and grit blasting, manual creation of threads etc.

CURRENT APPLICATIONS

GBR has become the more predictable and Successful option for bone regeneration. Bone regeneration can be accomplished through three different mechanisms: osteogenesis, osteoinduction, and osteoconduction.

Osteogenesis is the formation and development of bone, even in the absence of local undifferentiated mesenchymal stem cells.

Osteoinduction is the transformation of undifferentiated mesenchymal stem cells into osteoblasts or chondroblasts through growth factors that exist only in living bone.

Osteoconduction is the process that provides a bio-inert scaffold, or physical matrix, suitable for the deposition of new bone from the surrounding bone or encourage differentiated mesenchymal cells to grow along the graft surface.

VERTICAL AUGMENTATION WITH GBR

Supracrestal or vertical bone augmentation presents one of the greatest challenges of bone regeneration in implant dentistry, due to the difficulty of the surgical procedure and its potential complications. Vertical augmentation aims to achieve bone regeneration in a direction without bony walls to support the stability of the bone graft. Bone regeneration and angiogenesis has to reach a distance from the existing bone, so that this is a biologically demanding procedure. The soft tissue has to be advanced to provide a closed healing environment. The application of GBR technique for supracrestal regeneration was introduced and described by Tinti and Parma-Benfenati in 1998. [19] Complications such as membrane exposure and/or subsequent infection, with rates ranging between 12.5% and 17% have been reported.

HORIZONTAL AUGMENTATION WITH GBR

Guided bone regeneration has become a major treatment option to provide optimal bone support for implants. Knife-edge ridges, or Cawood and Howell Class IV edentulous jaw [5] with adequate height on the lingual/palatal side, and with insufficient width, present a unique problem for horizontal augmentation. Implant placement are often impossible in these conditions. However, prognosis of GBR procedure is good for this condition as the residual ridge stabilizes the bone graft. Both non-resorbable and resorbable membranes can be used and bone grafts are placed under the barrier membrane to prevent collapse. [13] Autogenous bone blocks can often be screwed onto the ridge for stability. Bone blocks (onlay bone graft) fixation may eliminate the use of a non-resorbable titanium reinforced membranes. [6]
The increase in the success rate of the GBR procedure is because of the availability of various Bone grafts and Membranes.
Various biomaterials available for use in GBR include:
1. Bone grafts[8]
2. Barrier membranes[17]

Type of bone grafts		
Autogenous	Extraoral	Iliac crest Tibial plateau
	Intra oral	Mandibular symphysis Maxillary tuberosity Ramus Tori Exostoses
Allografts		Demineralized freeze-dried bone allograft (DFDBA) Mineralized freeze-dried bone allograft (FDBA)
Xenografts		Deorganizied bovine bone
Alloplasts		Calcium carbonate Calcium sulphate Bioactive glass polymers Ceramic materials

Barrier membranes	
First generation or Non resorbable membranes	Expanded Polytetrafluoroethylene High-Density Polytetrafluoroethylene Titanium Mesh Titanium-Reinforced PTFE
Second or resorbable membranes	Polymeric Membranes Collagen Membranes
Third generation membranes	Membranes Releasing Antimicrobial Agent Membranes Releasing Growth Factors Platelet-Rich Fibrin (PRF) Membrane Membranes with Calcium Phosphate Cell Transferred Membrane

GBR USING TISSUE ENGINEERING

Tissue engineering (TE) is a technique which fabricates tissues outside the body and implants them into the body to regenerate the lost target tissues [15]. The classic tissue engineering includes four essential requirements: (1) scaffold, i.e., biomaterials which provide space for new cell ingrowth; (2) biological agent, i.e., appropriate regulatory signals; (3) cells, i.e., responsive progenitor cells; and (4) blood supply. The fabrication of a successful scaffold plays a crucial role in TE. Hence, these new technologies focusses on 3d scaffolds.

FUTURE DIRECTIONS

Future perspectives on GBR looks promising with new technology and new reliable biomaterials . Until now, various biomanufacturing techniques enabled the formation of more advanced scaffolds for regeneration therapy. Although many options were introduced, there are still some limitations due to the biomaterials themselves and their combination of the manufacturing process.

The phase of tissue regeneration depends on the infiltration of mesenchymal cells from surrounding tissue and their differentiation into specified cells such as osteoblasts, cementoblasts, and PDL fibroblasts. [9][11]As re-vascularization is another crucial factor of fast regeneration, seeding pro-angiogenic factors into the scaffold before implantation should be considered. More advanced regeneration targets having original biology of tissue after implantation of biomaterials is necessary. Therefore, a precise coupling of synthetic polymers with a biologic component could be the future trend of biomaterials. Bioprinting is a technology utilizing 3D printing to combine cells, growth factors, and biomaterials to imitate natural tissue. Generally, they use a layer-by-layer method to deposit materials such as bioinks [10]. Bioprinting could accomplish patient-customized tissue for ideal regeneration.

CONCLUSION

For the treatment of many patients suffering from the depletion of periodontal tissues, GBR were developed for over 30 years. At first, the bone graft materials and membranes used in GBR were studied, and the standard indications of each material were determined. Then, the studies went further to change the paradigms of GBR by using scaffolds instead of graft materials and membranes.

With the development of CAD/CAM systems and 3D printers, scaffolds can have multiphasic layers for the ideal induction of original tissue compartments. However, the newly developed scaffolds remain to be widely applied in actual clinical situations, and they still have some limitations. In the future, continuous attempts should be made to develop the optimal biomaterials for predictable patient-customized regeneration in preclinical and clinical aspects.

REFERENCES

1. Aghaloo TL, Moy PK. Which hard tissue augmentation techniques are the most successful in furnishing bony support for implant placement? [published correction appears in Int J Oral Maxillofac Implants. 2008 Jan-Feb;23(1):56]. Int J Oral Maxillofac Implants. 2007; 22 Suppl: 49-70.
2. Bassett CAL, Creighton DK & Stinchfield FE Contributions of endosteum, cortex and soft tissues to osteogenesis. Surg Gynecol Obstet 112: 145 (1961).
3. Becker W., et al. “The use of e-PTFE membranes for bone promotion around titanium implants placed into extraction sockets: a prospective multicenter study”. International Journal of Oral and Maxillofacial Implants 9.1 (1994): 31-40.
4. Boyne PJ, Mikels TE. Restoration of alveolar ridges by intramandibular transposition osseous grafting. J Oral Surg. 26(9): 569-76 (1968).
5. Cawood JI and Howell RA. “A classification of the edentulous jaws”. International Journal of Oral and Maxillofacial Implants 17.4 (1988): 232-236.
6. Chiapasco M., et al. “Clinical outcome of autogenous bone blocks or guided bone regeneration with e-PTFE membranes for the reconstruction of narrow edentulous ridges”. Clinical Oral Implants Research 10.4 (1999): 278-288.
7. Dahlin C, Sennerby L, Lekholm U, Linde A, Nyman S. Generation of new bone around titanium implants using a membrane technique: an experimental study in rabbits. Int J Oral Maxillofac Implants. 4(1): 19-25 (1989).
8. Doug Sutherland., et al. “Grafts and Bone Graft Substitutes”. Bone Regeneration and Repair: Biology and Clinical Applications.
9. Fan, H.; Zeng, X.; Wang, X.; Zhu, R.; Pei, G. Efficacy of prevascularization for segmental bone defect repair using beta-tricalcium phosphate scaffold in rhesus monkey. Biomaterials 2014, 35, 7407–7415. [CrossRef] [PubMed]
10. Groll, J.; Boland, T.; Blunk, T.; Burdick, J.A.; Cho, D.W.; Dalton, P.D.; Derby, B.; Forgacs, G.; Li, Q.; Mironov, V.A.; et al. Biofabrication: Reappraising the definition of an evolving field. Biofabrication 2016, 8, 013001. [CrossRef] [PubMed].
11. Hokugo, A.; Kubo, Y.; Takahashi, Y.; Fukuda, A.; Horiuchi, K.; Mushimoto, K.; Morita, S.; Tabata, Y. Prefabrication of vascularized bone graft using guided bone regeneration. Tissue Eng. 2004, 10, 978–986. [CrossRef] [PubMed]
12. Jayesh RS, Dhinakarsamy V. Osseointegration. J Pharm Bioallied Sci. 2015;7(Suppl

1):S226-S229. doi:10.4103/0975-7406.155917
13. Lindhe J., et al. "Clinical periodontology and implant dentistry". Oxford, UK; Malden, MA: Blackwell, (2003).
14. Misch CE, Dietsh F. Bone-grafting materials in implant dentistry. Implant Dent 1993; 2: 158-67.
15. Nakahara, T.; Nakamura, T.; Kobayashi, E.; Kuermoto, K.; Matsuno, T.; Tobata, Y.; Eto, K.; Shimizu, Y. In situ tissue engineering of periodontal tissues by seeding with periodontal ligament-derived cells. Tissue Eng. 2004, 10, 537–544. [CrossRef]
16. Nyman S, Lang NP, Buser D, Bragger U. Bone regeneration adjacent to titanium dental implants using guided tissue regeneration: A report of two cases. Int J Oral Maxillofac Implants 5: 9-14 (1990).
17. Rakhmatia YD., et al. "Current barrier membranes: Titanium mesh and other membranes for guided bone regeneration in dental applications". Journal of Prosthodontic Research 57.1 (2013): 3-14.
18. Simion Massimo., et al. "Vertical ridge augmentation using a membrane technique associated with osseointegrated implants". International Journal of Periodontics and Restorative Dentistry 14.6 (1994): 497-512.
19. Tinti Carlo and Stefano Parma-Benfenati. "Vertical ridge augmentation: Surgical protocol and retrospective evaluation of 48 consecutively inserted implants". International Journal of Periodontics and Restorative Dentistry 18.5 (1998): 435-443.
20. Wang HL, Boyapati L. "PASS" principles for predictable bone regeneration. Implant Dent 2006; 15: 8-17.