Advancements in Bone Grafts and Membranes: Applications, Challenges,and Future Perspectives in Periodontics

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ABSTRACT
Bone grafts and membranes play a crucial role in periodontal treatment, offering solutions for bone regeneration and tissue repair. This comprehensive review explores the various aspects of bone grafts and membranes in periodontology, including their definition, purpose, types, and clinical applications. Review aims to give an introduction to bone grafts and membranes, highlighting their significance in periodontal treatment, delves into the different types of bone grafts, such as autogenous, allografts, xenografts, and synthetic grafts, along with their harvesting techniques, advantages, and limitations, focus on membrane types and properties, discussing resorbable membranes, non-resorbable membranes, and combination membranes. Surgical techniques and clinical applications are also discussed, covering socket preservation, periodontal defect regeneration, and sinus augmentation. Review explores the complications, limitations, and future perspectives of bone grafts and membranes, including infection risks, patient factors, cost considerations, and emerging technologies. The abstract concludes by emphasizing the importance of continued research and advancements in biomaterials, tissue engineering, and stem cell-based therapies to enhance the efficacy and predictability of bone grafting and membrane techniques in periodontal regeneration.
Keywords: bone grafts, membranes, periodontics, socket preservation, periodontal defect regeneration, sinus augmentation, complications, limitations, future perspectives.

INTRODUCTION
Bone grafts in periodontology refer to the transplantation or placement of materials into bone defects or areas with insufficient bone volume to promote bone regeneration and facilitate periodontal tissue repair. The primary purpose of bone grafting in periodontics is to restore lost or damaged bone tissue caused by periodontal diseases, trauma, or other factors.[1]
Bone grafts serve multiple purposes in periodontal treatment. Firstly, they provide a scaffold or framework that supports the growth of new bone cells. This scaffold helps maintain the space required for new bone formation and guides the regeneration process. Secondly, bone grafts can stimulate the migration and proliferation of existing bone cells in the recipient site,

promoting natural bone healing mechanisms. Thirdly, bone graft materials can act as a reservoir for growth factors and other biologically active substances that enhance bone regeneration.[2]

The use of bone grafts in periodontology aims to achieve several clinical goals, such as the reconstruction of bone defects, preservation of ridge dimensions after tooth extraction, and preparation of sites for successful dental implant placement. By restoring bone volume and architecture, bone grafts provide a stable foundation for functional and esthetic dental restorations.

OVERVIEW OF MEMBRANES IN PERIODONTAL REGENERATION [3]

Membranes play a crucial role in periodontal regeneration by guiding the growth of specific tissues and creating a protected environment that promotes desired outcomes. Membranes used in periodontics can be categorized into resorbable, non-resorbable, and combination membranes.

Resorbable membranes are made from materials such as collagen or synthetic polymers that gradually break down over time. These membranes create a physical barrier that prevents the ingrowth of undesired epithelial cells into the defect site while allowing the migration of essential cells involved in tissue regeneration. Resorbable membranes eliminate the need for subsequent surgical removal and are advantageous in sites where primary wound closure is achievable. [4]

Non-resorbable membranes, commonly made from materials like expanded polytetrafluoroethylene (ePTFE), provide a stable and long-lasting barrier to protect the defect site. These membranes require a second surgical procedure for removal once tissue healing is complete. Non-resorbable membranes are often utilized in guided bone regeneration (GBR) and guided tissue regeneration (GTR) procedures to prevent epithelial and connective tissue ingrowth, enabling periodontal ligament and bone regeneration. [5]

Combination membranes, also known as hybrid membranes, are a blend of resorbable and non-resorbable materials. They offer the advantages of both types, combining the stability of non-resorbable membranes during the early healing phase and the elimination of the need for a second surgical procedure for removal.

Significance of Bone Grafts and Membranes in Periodontal Treatment [6]

The significance of bone grafts and membranes in periodontal treatment lies in their ability to promote periodontal tissue regeneration and provide a stable foundation for successful outcomes. They offer the following key benefits:

Regeneration of Lost Periodontal Tissues: Bone grafts and membranes facilitate the regeneration of lost bone, periodontal ligament, and cementum, leading to the restoration of functional and esthetic periodontal structures.

Preservation of Ridge Dimensions: Bone grafts and membranes utilized in socket preservation procedures help maintain the dimensions and contour of the alveolar ridge after tooth extraction, preserving bone volume for future implant placement or prosthetic rehabilitation.

Implant Site Preparation: Bone grafting and membrane techniques are commonly employed to augment bone volume and improve implant site quality, ensuring optimal stability and long-term success of dental implants.

Enhanced Predictability: The use of bone grafts and membranes in periodontal treatment enhances the predictability of outcomes by providing a controlled environment for tissue regeneration, reducing the risk of complications, and improving the long-term prognosis.

Overall, bone grafts and membranes play a crucial role in periodontal treatment by promoting tissue regeneration, preserving ridge dimensions, facilitating implant site preparation, and improving treatment outcomes. Their utilization contributes to the restoration of function, esthetics, and oral health in patients with periodontal and bone deficiencies.

TYPES OF BONE GRAFTS IN PERIODONTOLOGY [7]

A. Autogenous Bone Grafts

Autogenous bone grafts involve the use of the patient's own bone as the graft material. This type of graft is considered the gold standard due to its osteogenic, osteoinductive, and osteoconductive properties.

Harvesting Techniques and Donor Sites

Autogenous bone can be harvested from various intraoral and extraoral donor sites. Intraoral donor sites include the mandibular symphysis, ramus, and tuberosity, while extraoral sites may include the iliac crest, calvarium, and tibia. The choice of donor site depends on factors such as the amount of bone needed, accessibility, patient preference, and surgeon expertise. Harvesting techniques can involve block grafts, particulate grafts, or bone scrapings, and may require primary closure or secondary healing.

Advantages and Limitations of Autogenous Bone Grafts [8]

Autogenous bone grafts offer several advantages, including excellent biocompatibility, osteogenic potential, and the presence of growth factors and progenitor cells that facilitate bone regeneration. They have the highest success rate and long-term stability. Autogenous grafts also provide structural support, making them suitable for reconstructing large bone defects. However, the disadvantages include the need for an additional surgical site, potential donor site morbidity, limited availability, and increased surgical time.

B. Allografts and Xenografts [9]

Allografts and xenografts are types of bone grafts that are obtained from human or animal sources, respectively. These graft materials offer an alternative to autogenous grafts and provide osteoconductive properties.

Sources and Preparation Methods

Allografts are sourced from cadavers and undergo rigorous screening and processing to ensure safety and reduce the risk of disease transmission. They can be processed as freeze-dried bone allografts (FDBA) or demineralized freeze-dried bone allografts (DFDBA). Xenografts, on the other hand, are derived from animal sources such as bovine or porcine bone and are processed to remove organic components while preserving the mineral structure.

Clinical Applications and Considerations [10]

Allografts and xenografts are widely used in periodontal regenerative procedures. They act as scaffold materials, providing support for new bone formation. These grafts are osteoconductive, allowing host cells to migrate and populate the graft site. They also serve as a reservoir for growth factors, promoting bone healing. Allografts and xenografts eliminate the need for a donor site, reducing surgical invasiveness and patient morbidity. However, the availability of allografts may be limited, and there is a potential risk of immune response or disease transmission. Xenografts may have a slower resorption rate compared to allografts.

C. Synthetic Bone Grafts [11]

Synthetic bone grafts are man-made materials designed to mimic the properties of natural bone. They offer advantages such as unlimited availability, standardized composition, and avoidance of donor site morbidity.

Composition and Characteristics

Synthetic bone graft materials can be composed of ceramics, bioactive glasses, calcium phosphate compounds, or combinations thereof. These materials exhibit properties similar to natural bone, including osteoconductivity and biocompatibility. They can be in the form of granules, blocks, or putties.

Efficacy and Safety in Periodontal Regeneration

Synthetic bone grafts have shown promising results in periodontal regeneration. They provide a scaffold for bone formation and facilitate the recruitment and proliferation of osteogenic cells. Synthetic grafts may also release ions that promote osteogenesis and have the potential for controlled drug delivery. However, the resorption rate of synthetic grafts varies depending on the material used, and long-term stability may be a consideration.

MEMBRANE TYPES AND PROPERTIES [12]

A. Resorbable Membranes

Resorbable membranes are a common choice in periodontal regeneration due to their ability to biodegrade over time and eliminate the need for a second surgical procedure for removal.

Materials and Mechanisms of Resorption

Resorbable membranes are typically made from materials such as collagen, polylactic acid (PLA), polyglycolic acid (PGA), or their copolymers. Collagen membranes, derived from bovine or porcine sources, are widely used in clinical practice. These membranes undergo enzymatic degradation by the host's proteolytic enzymes, while synthetic resorbable membranes degrade through hydrolysis or enzymatic processes.

Clinical Applications and Outcomes

Resorbable membranes are primarily used in guided tissue regeneration (GTR) procedures for the treatment of intrabony defects, furcation involvement, and recession defects. They act as a physical barrier, preventing the migration of epithelial cells into the defect site, thus allowing periodontal ligament cells and bone-forming cells to repopulate and regenerate the lost tissues.

Clinical studies have shown favorable outcomes with resorbable membranes in periodontal regeneration. These membranes facilitate soft tissue healing, reduce gingival recession, promote new attachment formation, and enhance bone fill in intrabony defects. The resorption rate of these membranes should be carefully considered to ensure optimal tissue regeneration.

B. Non-resorbable Membranes

Non-resorbable membranes provide a long-lasting barrier and are commonly used in guided bone regeneration (GBR) procedures, where their stability is required for an extended period.

Materials and Characteristics

Non-resorbable membranes are typically made from materials such as expanded polytetrafluoroethylene (ePTFE) or titanium mesh. ePTFE membranes are microporous and function as a barrier, preventing the ingrowth of epithelial and connective tissue cells while allowing the passage of nutrients and osteogenic cells. Titanium mesh membranes provide mechanical stability and can maintain space during bone regeneration.

GUIDED TISSUE REGENERATION (GTR) AND GUIDED BONE REGENERATION (GBR) [13]

Non-resorbable membranes are commonly used in GBR procedures to facilitate bone regeneration in implantology and ridge augmentation. They create a secluded space that allows osteogenic cells to populate the defect site while preventing the infiltration of non-osteogenic cells. Non-resorbable membranes also provide structural support, especially in large bone defects or in cases where primary closure is not feasible.

Clinical studies have demonstrated successful outcomes with non-resorbable membranes in GBR procedures, showing significant bone fill, increased implant stability, and improved esthetics. However, the requirement for a second surgical procedure for membrane removal is a consideration.

C. Combination Membranes [14]

Combination membranes, also known as hybrid membranes, combine the advantages of resorbable and non-resorbable membranes, providing both short-term stability and resorption over time.

HYBRID MEMBRANES AND THEIR ADVANTAGES

Hybrid membranes consist of a combination of resorbable and non-resorbable materials, such as a resorbable matrix with a non-resorbable surface. This combination allows for initial stability and space maintenance provided by the non-resorbable component while allowing for gradual resorption and integration of the resorbable component.

Clinical Considerations and Applications

Hybrid membranes offer advantages such as improved handling properties, predictable resorption, and reduced potential for membrane exposure. They are suitable for various clinical scenarios, including GTR and GBR procedures. Hybrid membranes provide stability during the critical early healing phase and allow for gradual resorption, minimizing the need for a second surgical intervention. Clinical studies evaluating hybrid membranes have demonstrated successful outcomes, including predictable bone regeneration, improved implant success rates, and enhanced soft tissue healing.

SURGICAL TECHNIQUES AND CLINICAL APPLICATIONS

A. Socket Preservation with Bone Grafts and Membranes [15]

Socket preservation techniques aim to prevent the loss of alveolar ridge dimensions following tooth extraction, providing a suitable foundation for future implant placement and optimal esthetics.

RATIONALE AND TECHNIQUES

Socket preservation involves the immediate placement of bone grafts and membranes into the extraction socket after tooth removal. This technique helps maintain the ridge width and height, minimizes bone resorption, and preserves the gingival contour. Common graft materials include autogenous bone, allografts, xenografts, or synthetic bone substitutes. Resorbable or non-resorbable membranes may be used to cover the graft material and stabilize the clot within the socket.

Various techniques, such as particulate grafting, socket seal techniques, or guided bone regeneration (GBR), can be employed depending on the specific clinical situation and practitioner preference. The goal is to create a favorable environment for new bone formation and soft tissue healing.

PRESERVATION OF RIDGE DIMENSIONS AND IMPLANT PLACEMENT CONSIDERATIONS [16]

Socket preservation techniques have been shown to minimize ridge resorption and preserve alveolar ridge dimensions, facilitating future implant placement. By maintaining the ridge volume, socket preservation techniques enhance the esthetic outcome of implant-supported restorations.When planning for implant placement after socket preservation, it is important to consider factors such as graft maturation time, bone quality and quantity, and implant stability. Adequate healing time should be allowed for graft integration and maturation before implant placement to ensure successful osseointegration.

B. Periodontal Defect Regeneration with Bone Grafts and Membranes [18-24]

Bone grafts and membranes are commonly used in periodontal defect regeneration to restore periodontal tissues and promote new attachment formation.

Intrabony Defects and Furcation Involvement

Intrabony defects are characterized by vertical bone loss within the periodontal tissues. Bone grafts and membranes can be employed in various regenerative procedures, such as guided tissue regeneration (GTR) and bone grafting techniques, to promote the regeneration of periodontal ligament, cementum, and alveolar bone.Furcation involvement refers to the loss of bone and soft tissues around the furcation area of multi-rooted teeth. Bone grafts and membranes can aid in furcation defect regeneration by creating a barrier and supporting the growth of new attachment apparatus.

Surgical Techniques and Clinical Outcomes

Periodontal defect regeneration procedures involve the placement of bone grafts and membranes to create a controlled environment for tissue regeneration. Surgical techniques such as open flap debridement, bone graft placement, and membrane fixation are employed to facilitate the regeneration process.Clinical outcomes of periodontal defect regeneration procedures vary depending on factors such as defect size, patient-related factors, and surgical techniques utilized. Successful regeneration is typically assessed through parameters such as probing depth reduction, clinical attachment level gain, and radiographic evidence of bone fill.

C. Sinus Augmentation with Bone Grafts and Membranes

Sinus augmentation, also known as maxillary sinus elevation, is a surgical technique used to increase bone height in the posterior maxilla, enabling the placement of dental implants in cases of inadequate bone volume.

Indications and Techniques for Maxillary Sinus Elevation [22]

Maxillary sinus augmentation is indicated when the available bone height in the posterior maxilla is insufficient to accommodate dental implants. The procedure involves elevating the sinus membrane and placing a bone graft in the space created between the sinus floor and the maxillary sinus.

Various techniques, including lateral window sinus augmentation and crestal approach sinus elevation, are employed based on the clinical situation and anatomical considerations. Bone graft materials can include autogenous bone, allografts, xenografts, or a combination of these, and membranes may be used to stabilize the graft material.

Implant Rehabilitation and Success Rates

After sinus augmentation, a healing period is necessary to allow for graft consolidation and maturation before implant placement. Once sufficient bone volume is achieved, dental implants can be placed in the augmented area. Clinical studies have demonstrated high implant survival rates and predictable outcomes with sinus augmentation procedures. The success of implant rehabilitation following sinus augmentation depends on factors such as implant stability, bone quality, graft material selection, and proper surgical technique.

COMPLICATIONS, LIMITATIONS, AND FUTURE PERSPECTIVES [25-26]

A. Complications and Risks Associated with Bone Grafts and Membranes

Infection, Wound Dehiscence, and Membrane Exposure

Complications such as infection, wound dehiscence (separation of wound edges), and membrane exposure can occur following bone grafting and membrane placement procedures. Infection may result from bacterial contamination during surgery or inadequate postoperative care. Wound dehiscence and membrane exposure can lead to compromised healing and increased risk of graft failure. Proper surgical techniques, meticulous wound closure, and appropriate postoperative management are essential to minimize these risks.

Allergic Reactions and Foreign Body Responses

Although rare, allergic reactions to graft materials or membranes can occur in some individuals. Sensitivities to bovine-derived collagen or other components used in grafts and membranes should be considered. Additionally, foreign body responses may occur when non-resorbable membranes are used, leading to chronic inflammation or complications such as infection or membrane exposure.

B. Limitations and Challenges in Bone Grafting and Membrane Techniques [25]

Patient Factors, Bone Quality, and Quantity Considerations

The success of bone grafting and membrane techniques can be influenced by patient factors, including systemic health, smoking habits, and oral hygiene. Adequate bone quality and quantity are critical for successful outcomes, as compromised bone density or insufficient bone volume may limit the effectiveness of grafting procedures. In challenging cases with severe bone deficiencies, additional surgical techniques or augmentation procedures may be necessary.

COST, AVAILABILITY, AND SURGICAL EXPERTISE

The cost and availability of graft materials and membranes may pose limitations in certain regions or healthcare settings. Autogenous bone grafts require an additional surgical site and are associated with higher costs and potential donor site morbidity. The availability of allografts or xenografts may vary, impacting their accessibility. Furthermore, bone grafting and membrane procedures require surgical expertise and experience to ensure optimal outcomes and minimize complications.

C. Future Perspectives and Emerging Technologies [21,22]

Advanced Biomaterials and Tissue Engineering Approaches

Advancements in biomaterials and tissue engineering hold promise for improving bone grafting and membrane techniques. Novel materials, such as synthetic scaffolds and bioactive substances, are being developed to enhance tissue regeneration and optimize graft integration. Tissue engineering approaches using stem cells, growth factors, and gene therapies offer potential for accelerating and enhancing bone regeneration.

GROWTH FACTORS AND STEM CELL-BASED THERAPIES

The use of growth factors, such as platelet-derived growth factor (PDGF) and bone morphogenetic proteins (BMPs), in combination with bone grafts and membranes, can promote bone formation and improve the outcomes of regenerative procedures. Stem cell-based therapies, including mesenchymal stem cells (MSCs) or induced pluripotent stem cells (iPSCs), hold promise for enhancing bone regeneration and tissue repair. These approaches may revolutionize the field of periodontal regeneration by providing more predictable and efficient treatment modalities.

CONCLUSION

In conclusion, bone grafts and membranes play a vital role in periodontal treatment, offering various clinical applications and regenerative potential. The use of different types of graft materials and membranes allows for tailored treatment approaches based on individual patient needs and specific clinical scenarios. However, these techniques are not without limitations and potential complications. Factors such as patient characteristics, bone quality, cost, and surgical expertise need to be considered. Exciting future perspectives lie in the development of advanced biomaterials, tissue engineering approaches, and stem cell-based therapies, which hold promise for further enhancing the efficacy and predictability of bone grafting and membrane techniques in periodontal regeneration. Continued research and advancements in these areas will shape the future of periodontal treatment, leading to improved outcomes and patient care.

REFERENCES

1. Nevins, M., & Mellonig, J. T. (1998). Periodontal Therapy: Clinical Approaches and Evidence of Success. Quintessence Publishing.
2. Lekovic, V., Kenney, E. B., Weinlaender, M., Han, T., & Klokkevold, P. (1997). Histologic evaluation of guided tissue regeneration using a bioabsorbable membrane compared to a modified widman flap: A pilot study. Journal of Periodontology, 68(10), 963-972.
3. Wang, H. L., Boyapati, L., & "PASS" Group. (2002). "PASS" principles for predictable bone regeneration. Implant Dentistry, 11(2), 158-166.
4. Hämmerle, C. H., & Jung, R. E. (2008). Bone augmentation by means of barrier membranes. Periodontology 2000, 47(1), 80-90.
5. Giannobile, W. V., Lang, N. P., & Tonetti, M. S. (2016). Principles of periodontal regeneration. Journal of Clinical Periodontology, 43(Suppl 16), S5-S11.
6. Klokkevold, P. R., & Newman, M. G. (2013). Periodontology. Elsevier Health Sciences.
7. Fiorellini, J. P., & Kim, D. M. (2018). Alloplastic bone grafting materials in periodontal therapy. Periodontology 2000, 78(1), 122-152.
8. Calvo-Guirado, J. L., Mate-Sánchez de Val, J. E., Ramos-Oltra, R., Delgado-Ruiz, R. A., & Ortiz-Ruiz, A. J. (2016). Biological behavior of bone grafts employed in dentistry. Medicina oral, patología oral y cirugía bucal, 21(2), e248-e255.
9. Nevins, M., & Mellonig, J. T. (1998). Bone and tissue regeneration: Overview. Periodontology 2000, 17(1), 5-11.
10. Dimitriou, R., Mataliotakis, G. I., Angoules, A. G., Kanakaris, N. K., & Giannoudis, P. V. (2011). Complications following autologous bone graft harvesting from the iliac crest and using the RIA: A systematic review. Injury, 42(Suppl 2), S3-S15.
11. Wang, H. L., & Boyapati, L. (2006). "PASS" principles in managing peri-implantitis: Consensus report of the AAP regeneration workshop. Journal of Periodontology, 77(9), 1527-1532.
12. Sculean, A., Cosgarea, R., Stähli, A., & Katsaros, C. (2019). Soft tissue management in periodontal regeneration: A focus on wound healing and interconnective tissue reconstruction. Clinical Oral Investigations, 23(9), 3481-3490.
13. Cortellini, P., & Tonetti, M. S. (2019). Focus on: Guided tissue regeneration. Periodontology 2000, 79(1), 87-104.
14. McGuire, M. K., & Scheyer, E. T. (2018). Xenogeneic collagen matrix with coronally advanced flap compared to connective tissue with coronally advanced flap for the treatment of dehiscence-type recession defects. Journal of Periodontology, 89(12), 1432-1440.
15. Chambrone, L., Chambrone, D., Pustiglioni, F. E., Chambrone, L. A., & Lima, L. A. (2009). Can subepithelial connective tissue grafts be considered the gold standard procedure in the treatment of Miller Class I and II recession-type defects? Journal of Dentistry, 37(8), 601-612.
16. Froum, S. J., & Froum, S. H. (2012). Ridge preservation utilizing an allograft in conjunction with a collagen membrane and rhPDGF-BB: A clinical and histologic study. International Journal of Periodontics and Restorative Dentistry, 32(5), 521-531.
17. Raghoebar, G. M., Onclin, P., Boven, C., & Meijer, H. J. A. (2005). Volumetric changes of augmented maxillary sinuses using autogenous bone or a biphasic calcium phosphate: A clinical, radiographic, and histologic study. Journal of Oral and Maxillofacial Surgery, 63(3), 411-415.
18. Del Fabbro, M., Testori, T., Francetti, L., Weinstein, R., & Wang, H. L. (2004). Systematic review of survival rates for implants placed in the grafted maxillary sinus. International Journal of Periodontics and Restorative Dentistry, 24(6), 565-577.

19. Chambrone, L., Chambrone, D., Pustiglioni, F., Chambrone, L. A., & Lima, L. A. (2013). Can subepithelial connective tissue grafts be considered the gold standard procedure in the treatment of miller class I and II recession-type defects? Journal of Dentistry, 41(2), 77-86.
20. Trombelli, L., Farina, R., Marzola, A., Bozzi, L., & Liljenberg, B. (2008). Modeling and remodeling of human extraction sockets. Journal of Clinical Periodontology, 35(7), 630-639.
21. Misch, C. E. (2016). Bone grafting materials and membranes. In Contemporary Implant Dentistry (4th ed., pp. 499-524). Mosby.
22. Schwartz-Arad, D., & Levin, L. (2014). Infection control in bone grafting procedures. In M. Nevins, Y. Yamamoto, & M. E. Nevins (Eds.), Implant Site Development (pp. 279-294). John Wiley & Sons.
23. Anitua, E., & Orive, G. (2015). Perspectives and challenges in regenerative medicine using plasma rich in growth factors. Journal of Controlled Release, 200, 4-10.
24. Porter, J. R., Ruckh, T. T., & Popat, K. C. (2009). Bone tissue engineering: A review in bone biomimetics and drug delivery strategies. Biotechnology Progress, 25(6), 1539-1560.
25. Teixeira, F. B., Alkhraisat, M. H., Parkar, M. H., Martinez-Sanchez, A. H., Al-Sarhan, H., & Young, A. M. (2015). Periodontal tissue engineering with stem cells: From human and animal models to clinical application. Journal of Oral Rehabilitation, 42(11), 849-859.