TRABAJO DE FIN DE GRADO

Grado en Odontología

REGENERATIVE MATERIALS IN PERIODONTOLOGY: TYPES, USES AND INDICATIONS

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ABSTRACT:

Introduction: Regenerative dentistry has as main purpose to find new therapeutic approaches for edentulism, bone defects, periodontitis and other tissue loss-related pathologies.

The periodontal disease and bone defects are explained with their updated classification.

The main materials developed for periodontal regeneration are the autografts, allografts and xenografts besides the platelet-derived-growth factor (PDGF) and the enamel matrix derivatives (EMD) which provide additional stimuli necessary to enhance it. Finally, barrier membranes are introduced among which the non-resorbable and resorbable membranes.

Objectives: this work will focus in highlightening the main materials used for the regeneration of the periodontium and their indications depending on different clinical situations.

Methodology: research through scientific articles found in MEDLINE, PUBMED and Google Scholar. Supportive clinical trials and systematic reviews have been found also by looking through the bibliography of the main chosen articles.

Discussion: comparisons between the scaffold materials have been made, in particular between cortical DFDBA and cancellous DFDBA, then FDBA and DFDBA. Also between non resorbable and resorbable membranes. Finally different clinical cases have been presented in order to understand the different materials to use for each clinical situation and bone defect.

Conclusion: For periodontal regeneration to occur regenerative dentistry uses autografts, allografts or xenografts used alone or together with the growth factors PDGF or EMD and/or with non-resorbable or resorbable membranes.

Currently there is not an ideal grafting material since they all present advantages and limitations. There is not a better choice between non-resorbable and resorbable membranes, the final considerations are different according to the surgical site in question.

For the regeneration of intraosseous defects clinical studies failed to demonstrate more efficacy of EMD over GTR but the use of EMD is safer.

In the case of critical-size defects relevant are the GBR and/or conservative surgical techniques.

RESUMEN:

Introducción: La odontología regenerativa tiene como objetivo principal encontrar nuevos enfoques terapéuticos para el edentulismo, los defectos óseos, la periodontitis y otras patologías relacionadas con la pérdida de tejido. La enfermedad periodontal y los defectos óseos se explican con su clasificación actualizada. Los principales materiales desarrollados para la regeneración periodontal son los autoinjertos, aloinjertos y xenoinjertos, además del factor de crecimiento derivado de las plaquetas (PDGF) y los derivados de la matriz del esmalte (EMD), que proporcionan los estímulos adicionales necesarios para mejorarla. Por último, se presentan las membranas de barrera, entre las que se encuentran las no reabsorbibles y las reabsorbibles.

Objetivos: este trabajo se centrará en destacar los principales materiales utilizados para la regeneración del periodonto y sus indicaciones en función de las diferentes situaciones clínicas.

Metodología: investigación a través de artículos científicos encontrados en MEDLINE, PUBMED y Google Scholar. También se han encontrado ensayos clínicos de apoyo y revisiones sistemáticas buscando en la bibliografía de los principales artículos elegidos.

Discusión: se han realizado comparaciones entre los materiales de los andamios, en particular entre el DFDBA cortical y el DFDBA esponjoso, y luego entre el FDBA y el DFDBA. También entre las membranas no reabsorbibles y las reabsorbibles. Por último, se han presentado diferentes casos clínicos con el fin de comprender los diferentes materiales a utilizar para cada situación clínica y defecto óseo.

Conclusiones: Para que se produzca la regeneración periodontal la odontología regenerativa utiliza autoinjertos, aloinjertos o xenoinjertos utilizados solos o junto con los factores de crecimiento PDGF o EMD y/o con membranas no reabsorbibles o membranas reabsorbibles. Actualmente no existe un material de injerto ideal ya que todos presentan ventajas y limitaciones. No existe una mejor elección

entre las membranas no reabsorbibles y las reabsorbibles, las consideraciones finales son diferentes según la zona quirúrgica de que se trate.

Para la regeneración de defectos intraóseos, los estudios clínicos no han podido demostrar una mayor eficacia de la EMD sobre la GTR, pero el uso de la EMD es más seguro.

En el caso de los defectos de tamaño crítico son relevantes la RGC y/o la técnica quirúrgica conservadora.

INTRODUCTION

Regenerative dentistry and tissue engineering are a developing field that in the last century has made considerable improvements and that is still in an important developing era.

Dental Tissue Engineering and Regenerative Dental Medicine have evolved from the more advanced field of Tissue Engineering and Regenerative Medicine (TERM), based on the principle that cells, biocompatible scaffolds and growth factors can develop into new regenerated functional tissues and organs (1).

The main purpose of regenerative dentistry is to find new therapeutic approaches for edentulism, bone defects, periodontitis and other tissue loss-related pathologies. In order to do so biomedical engineers, scientist researchers, doctors and dentists are gathering together their knowledges with the purpose of creating bioengineered replacement tissues that can re-establish the initial lost function and morphology (1).

“Tissue regeneration” means in fact a healing that leads to a complete restoration of function and morphology of the issued tissue or organ, which differs from the repair that is the mere healing of the damaged tissue with the formation of new one other than the original in terms of morphology or function.

Dental tissue engineering and regenerative dental medicine extend their researches and work in a multiple of fields: embryonic tooth bud-based strategies have been developed in order to regenerate a whole dental organ. Another field is the regenerative endodontic that uses endogenous stem cells obtained from an induced periapical bleeding, scaffolds using blood clots and platelet-rich plasma in order to obtain the further root maturation in immature teeth with pulp necrosis (1).

The periodontal disease

The periodontal disease is defined as a "chronic inflammatory condition" (2) that leads to the irreversible destruction of those structures that surround and stabilize the tooth. These affected structures are those that constitute the periodontium, an organ consisting on two soft connective tissues, the gingiva and the periodontal ligament, and two hard connective tissues, the supporting alveolar bone and the root lining cementum. Their progressive destruction will eventually lead to a compromised dentition from both a functional and an aesthetic point of view with as ultimate consequence the loss of the tooth itself (2).

The pathophysiology of the periodontal disease is characterized by the activation of a series of molecular pathways that will eventually induce the activation of proteinases that would cause the degradation of the periodontal ligament fibers. The consequence of the progressive loss of the periodontal ligament favors the colonization of pathogens along the root surface of the teeth leading to bone loss and apical migration of the junctional epithelium with periodontal pocket formation and gingival recession (3).

The pathogenesis of the periodontal disease is multifactorial and includes mainly:

- pathogen microorganisms of the subgingival biofilm that colonize the periodontal attachment;
- genetic factors as alterations in the polymorphonucleates leukocytes or hereditary anomalies leading to immunosuppression;
- acquired, modifying host factors, including social and behavioral factors as smoking, dietary habits, stress, medicaments, systemic diseases as HIV, diabetes and cardiovascular diseases;
- dental local factors as plaque accumulation, dental position, radicular proximity or external reabsorption, morphologic alterations and occlusal discrepancies.

The diagnosis of the periodontal disease is based mainly on the clinical exploration of the patient, in the detection of the inflammatory process and the extension and distribution of the insertion loss. The

clinical evidences are characterized by alterations in the morphology, consistency, volume, adaptation to the gingival margin, color changes and presence of hemorrhage and exudate.

The periodontal disease can be classified into different stages based on the severity of the condition. The first stage is the gingivitis which is an inflammatory process of the gingiva characterized clinically by bleeding gums, puffy in appearance and darker in color and no apical migration of the junctional epithelium nor destruction of the surrounding supporting structures. This condition is reversible and it does not always progress into periodontitis.

If not reversed through a good oral hygiene and a professional plaque removal, the gingivitis can, on the other hand, progress into periodontitis which is an irreversible inflammatory process that extends to the supporting structures of the tooth. The periodontitis is characterized by apical migration of the junctional epithelium and a progressive destruction of the periodontal ligament and alveolar bone leading to the formation of periodontal pockets from 3 and up to 6 or more mm of depth. This stage can worsen until a severe loss of the supporting structures of the tooth and so to the loss of it. The periodontitis is in fact one of the leading causes for tooth loss and it is a condition present in most adult population.

A new classification was made on November 2017 in Chicago by the American Academy of Periodontology (AAP) and the European federation of Periodontology (EEP) comprehending participants from all over the world that gathered in order to update the previous classification in use since 1999 (4).

Chart 1 (4)

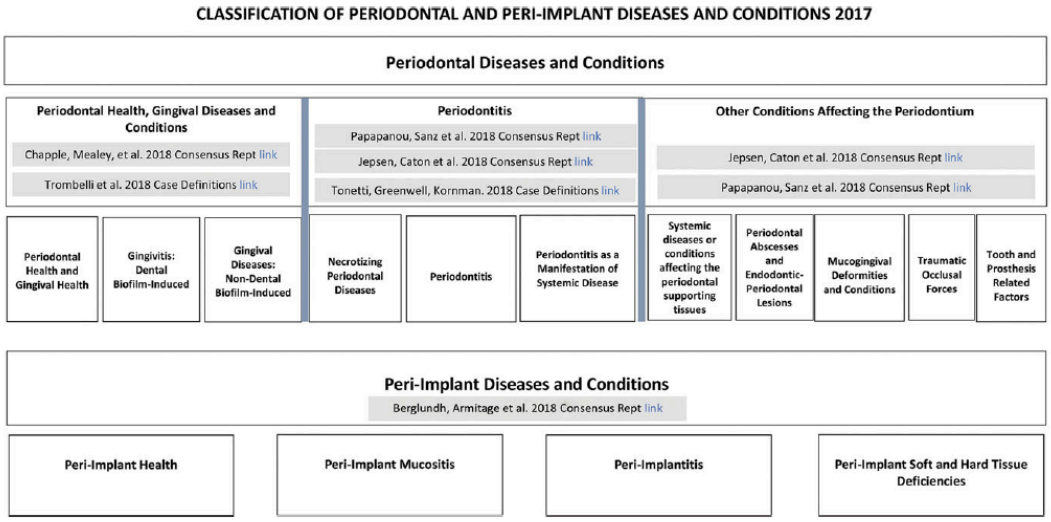


Chart 2 (4)

Periodontitis Consensus Report
Papapanou, Sanz et al. 2018
Active link to consensus report

Staging and Grading of Periodontitis:
Framework and Proposal of a New Classification and Case Definition
Tonetti, Greenwell, Kornman 2018
Active link to case definitions

FORMS OF PERIODONTITIS

1. **Necrotizing Periodontal Diseases**
   Herrera et al. 2018 link
   a. Necrotizing Gingivitis
   b. Necrotizing Periodontitis
   c. Necrotizing Stomatitis

2. **Periodontitis as Manifestation of Systemic Diseases**
   Jepsen, Caton et al. 2018 Consensus Rept link Albandar et al. 2018 link
   Classification of these conditions should be based on the primary systemic disease according to the International Statistical Classification of Diseases and Related Health Problems (ICD) codes

3. **Periodontitis**
   Fine et al. 2018 link Needleman et al. 2018 link Billings et al. 2018 link
   a. **Stages:** Based on Severity[1] and Complexity of Management[2]
      Stage I: Initial Periodontitis
      Stage II: Moderate Periodontitis
      Stage III: Severe Periodontitis with potential for additional tooth loss
      Stage IV: Severe Periodontitis with potential for loss of the dentition
   b. Extent and distribution[3]: localized; generalized; molar-incisor distribution
   c. **Grades:** Evidence or risk of rapid progression[4], anticipated treatment response[5]
      i. Grade A: Slow rate of progression
      ii. Grade B: Moderate rate of progression
      iii. Grade C: Rapid rate of progression

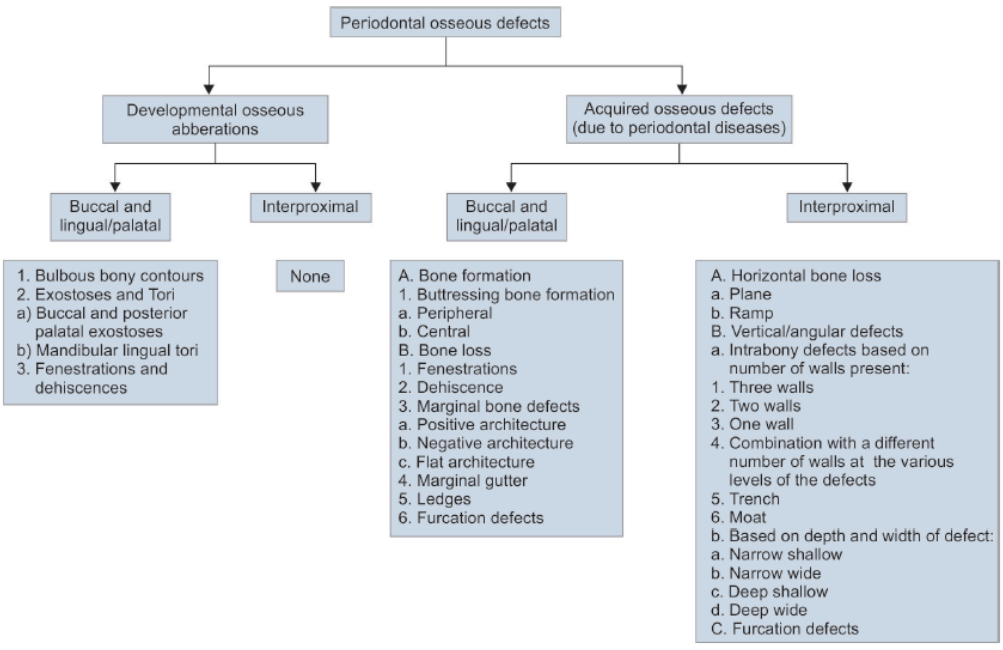
[1] Severity: Interdental clinical attachment level (CAL) at site with greatest loss; Radiographic bone loss & tooth loss
[2] Complexity of management: Probing depths, pattern of bone loss, furcation lesions, number of remaining teeth, tooth mobility, ridge defects, masticatory dysfunction
[3] Add to Stage as descriptor: localized <30% teeth, generalized ≥ 30% teeth
[4] Risk of progression: direct evidence by PA radiographs or CAL loss, or indirect (bone loss/age ratio)
[5] Anticipated treatment response: case phenotype, smoking, hyperglycemia

It is important to specify though that the periodontal disease is not the only cause responsible for bone loss, inflammation of the tissues and the loss of support to the tooth. Dental trauma from occlusion is another of the leading causes of this condition, due to the increase of the tension and compression of the periodontal ligament. It is possible to recognize whenever the actual cause is the occlusal trauma because of the resulting specific bone defect morphology that has to adapt to the new occluding force: a funnel-shaped widening of the crestal portion of the periodontal ligament and an angular shaped bone defect (5).

The bone defects morphology varies a lot according to different factors: the physiologic variations of the alveolar bone, the crestal angulation of the interdental septa, the width and thickness of the vestibular and lingual alveolar plates, the presence of fenestrations and dehiscences, the alignment of the teeth, the root anatomy and position within the alveolar process and the proximity with another tooth surface (6).

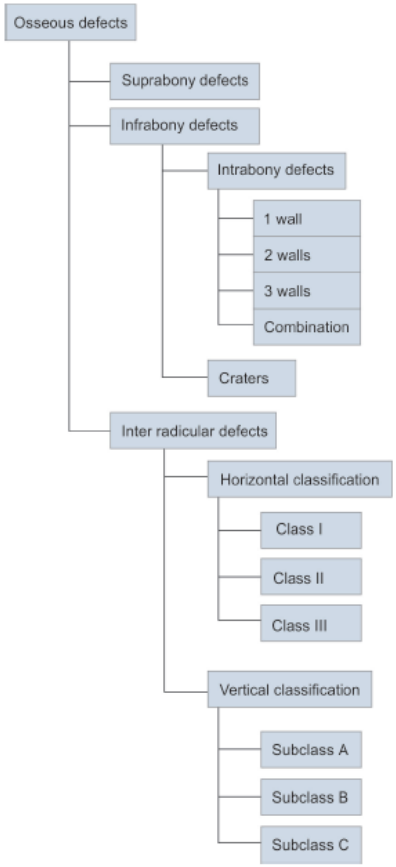
Bone defects have been differently classified by many clinicians and researchers as to mention Goldman and Cohen (7), Pritchard (8), Clarke (9) and lastly, as shown below, by Vandana and Bharath (10).

Chart 3: newly classification of POD by Vandana and Bharath (10)



In order to simplify this though we can mention the three main categories into which osseous defects have been classified by Papapanou and Tonetti: suprabony defects, infrabony defects and inter radicular defects (11).

Chart 4: Papanou's and Tinetti's classification



In suprabony defects, also called horizontal defects, the base of the pocket is found coronal to the residual alveolar crest. The horizontal bone loss pattern is the most common in the periodontal disease and presents a homogeneous reduction of bone height maintaining the bone crest perpendicular to the axis of the teeth (5).

Suprabony defects, differently to intrabony and angular defects, are not amenable to periodontal regeneration so far (12).

In infrabony defects, or vertical defects, the base of the pocket is found apical to the residual alveolar crest. They can be divided into intrabony and crater-like defects. The intrabony defects affect mainly one tooth and are classified according to the residual bone walls, width and extension of the defect

around the tooth. In particular, regarding the number of residual bone walls, they classify in one wall defect, two walls defect a three walls defect (7). The number refers to the walls left in the bone defect, not to those that have been lost.

Crater-like defects affect two adjacent teeth in a similar proportion.

Infrabony defects are furtherly divided into deep or shallow defects and wide or narrow defects according to the angle formed by the bone wall of the defect and the long axis of the tooth.

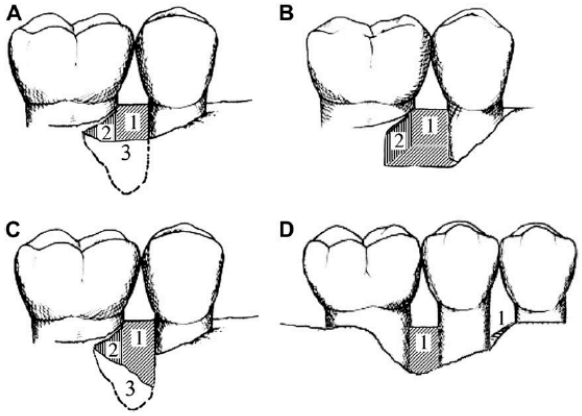


Fig. 5. Schematic illustration of intraosseous defects classified according to the number of bony walls present. (*A*) Three-wall defect; (*B*) 2-wall defect; (*C*) combination defect; (*D*) 1-wall defect. One-wall defects typically do not respond well to regenerative therapy. (12)

The inter-radicular defects, or furcation defects, are classified according to the amount of horizontal bone loss within the root furcation. Class I inter-radicular defects do not extend to the furcation but are rather limited to the furcation flute of the tooth and they are considered being reversible with a nonsurgical-therapeutic approach and oral hygiene maintenance.

Class II inter-radicular defects extend to the furcation of the tooth but still not completely through it.

Class III inter-radicular defects extend completely throughout the furcation of the tooth. These two most severe bone defects need a surgical therapeutic approach in order to improve and reobtain a better tooth support.

The correct diagnosis of the bone defect is of great importance in order to choose the most appropriate therapy for the specific situation. Periodontal probing and radiographies are the main diagnostic tools for this purpose.

Periodontal treatment and bone regeneration

The periodontal treatment aims to arrest the progressing of the disease by reducing the inflammation of the periodontium and the level of microbials present in order to obtain the complete restoration of the supporting structures of the tooth "to their original architecture and function" (2) and to the formation of a strong connection between the tooth and its surrounding structures. The main objectives of the periodontal therapy are then control of the inflammation, periodontal attachment gain, decrease of deep probing depth and reduction of furcation lesions.

The current conventional therapeutic techniques, as to mention the non-surgical subgingival debridement and the surgical open flap debridement, focus on arresting the spread and action of pathogens in the periodontal ligament and reversing the inflammation by modifying the local environment leading to a process of repair, which, as previously explained, is different from regeneration, resulting in fact in an attachment with a long junctional epithelium (2). This epithelial attachment though is non-physiological and does not properly connect the cementum of the tooth to the adjacent gingival connective tissue.

Besides the limitations in terms of regeneration, this therapeutic approach can often cause gingival recession which can eventually lead to sensibility and predisposition to root caries. These conventional techniques resulted finally being more effective in the prevention of the progression of the pathology rather than being effectively therapeutic.

In the last fifty years on the other hand, regenerative surgical techniques have been developed with the objective of promoting a proper and predictable regeneration of the periodontium with a new physiologic functional attachment, including the regeneration of alveolar bone, periodontal ligament and cementum. A successful regenerative therapy clinical outcome would then include a reduction of the probing depth, an increasing in the clinical attachment level and providing a radiographically evidenced bone filling.

One of the effects of the advanced periodontal disease is the alteration of bone morphology and the destruction of the surrounding tooth-supporting tissues and eventually tooth loss. The loss of a tooth would increase the rate of alveolar ridge reabsorption itself as well.

As stipulated by Wolff's Law, physiologically this is induced because of the changes in the mechanical loadings that occur with modifications in the distribution of the forces to the bone occurring during mastication leading to continuous bone remodeling (14).

In order to prevent further alveolar bone alteration and preserve and regenerate the surrounding supporting tissues, techniques of bone regeneration and tissue engineering using cells and/or gene delivery and scaffolds alone or together with grow factors, have been developed.

Bone regeneration, both the physiologic one that occurs along the whole life, and the reparative one that follows a damage, is characterized by three major processes: osteogenesis, osteoinduction and osteoconduction.

Osteogenesis is the formation of new bone by vital cells, mainly osteoblasts, promoted by every vital bone graft that is transplanted from a donor graft or from an autologous bone. The cells transplanted will then be able to differentiate and synthesize new bone at the recipient site. An example of an osteogenic grafting material is the cancellous bone or the bone marrow.

Osteoinduction is the process by which osteogenesis is induced. It is initiated by the growth factors within the graft and it enables the proliferation and migration of the undifferentiated and pluripotent cells into the damaged site to be regenerated. It works by promoting the stimulation of these osteoprogenitor cells of the surrounding tissues to differentiate into preosteoblasts that then begin new bone formation. Osteoinduction can be promoted by autologous bone, by the same purified osteoinductive factors extracted from autologous, homologous or heterologous material, or by recombinant factors, and finally by demineralized bank bone such as the demineralized bone matrix (DBM).

Osteoconduction, or guided bone formation, is the apposition of new bone starting from existing bone. This means that an osteoconductive material has the ability to operate as scaffold to guide tissue regeneration and it allows bone growth to occur on its surface or inside its pores and channels (15). This material will then be integrated or partially substituted by the newly formed bone.

The improved understanding of the last years of these processes necessary for the repair and regeneration of the bone has helped in the development of regenerative medicine and tissue engineering. The three major components for tissue regeneration are in fact the cells, a degradable support or scaffold material that can offer a guide and support for the different cell types, and finally bioactive factors such as growth factors needed for further cell proliferation and differentiation (15,16).

Materials used in periodontal regeneration

The definition of a biomaterial refers to a natural or synthetic material that can be placed into different living tissues as part of a medical device or implant without developing "any adverse immune rejection reactions" (17). The biomaterial has the ability, once placed into a specific tissue, to initiate a series of event that will eventually lead to cell proliferation and interaction. The interaction between the biomaterial and the surrounding cells will result in the charging of the biomaterial surface energy that will further become an adequate matrix for biomolecule adhesion.

The biomaterials used in tissue engineering have recently developed and improved a lot but they all have the same basic fundamental characteristics such as biocompatibility, resistance to corrosion, physical and mechanical strength, non-carcinogenic and non-toxic properties (16).

Scaffold materials: bone grafts

As already mentioned, focusing in bone regeneration in the surgical therapeutic approach of the periodontal disease, tissue engineering approaches using biomaterials that have an osteogenesis, osteoconductive and an osteoinductive capacity.

By introducing a variety of biomaterials in bone tissue engineering, a wide category of scaffolds has recently developed.

With the term "scaffold" we refer to a biomaterial that has as main purpose the stimulation of osteogenesis by acting as a support surface that serves as a template for cell infiltration, attachment and interaction and "the formation of bone extra cellular matrix to provide structural support to the newly formed tissue" (15).

This means that, by introducing a solid scaffold acting as artificial extracellular matrix (ECM) that supports and guides the cells, tissue regeneration is induced at the defective site.

As the new tissue forms, the scaffold degrades providing the adequate environment for matrix deposition and tissue regeneration (15).

The peculiarities of the scaffolds such as its surface, fiber architecture, high hydrophilicity and porosity, have great relevance in enhancing cell adhesion potential, inducing the further tissue development and the formation of a proper vascular system. With their specific configuration they in fact promote adhesion of the cells in the damaged site and their following proliferation and differentiation (16).

With this objective, scaffolds also provide the suitable environment for nutrients and growth factors necessary for initiating the cascade of mediator signals for cell differentiation in the surrounding tissue.

Moreover scaffolds must not generate inflammatory reactions as well as have a degradability rate long enough for assuring tissue regeneration (16).

As already mentioned these biomaterials must have all the same main characteristics:

Table 5: Main characteristics of biomaterial scaffolds used in regenerative medicine (18)

Properties	Importance
Biocompatibility	The scaffolds should not determine rejection responses from the body
Non-toxic/Non-carcinogenic	Their components or degradation products should not cause biological responses
Chemical stability	Chemical alterations should not occur, at least during the regenerative process
Mechanical properties	Mechanical properties must complete tissue requirements; resistance and weight should also be similar
Adequate chemical surface	The surface characteristics should favor cell adhesion, differentiation and proliferation
Shape, dimension and design	They should fit in the targeted tissue, stimulating the regenerative process
Absorbability and degradability	Absorbable, with an adequate degradability rate in concordance with the tissue regenerative/repair process

Scaffolds can be classify into different groups based on their nature:

- *Organic*: Autograft (recipient and donor are the same individual); allograft (recipient and donor are two different individuals but of the same specie); xenograft (recipient and donor from two different species).
- *Synthetic organic*: hydroxyapatite and osteoinductive factors such as platelet-derived growth factors (PDGF), enamel matrix derivative (EMD) and bone morphogenic proteins (BMP).
- *Inorganic biomaterials*: silicone, methylmethacrylate, polyethylene, bioactive glass and others (19).

Autogenous bone graft

The autogenous bone graft, also called autograft, is bone tissue harvested from the patient itself, both from extraoral or intraoral donor sites.

Depending on the size of the graft needed, the harvest sites are typically chosen between chin, jaw, tibia, fibula, iliac crest, ribs or the cranium.

Differently from allografts (grafts harvested from a genetically different donor of the same species) and xenografts (donor from another species), autografts do not have the risk to be rejected from the recipient and so to develop immunological reactions as well as to transmit any disease to it.

Another important characteristic is that the tissue harvested from the patient itself is already complete with the living cellular elements needed to enhance bone growth, this means that osteogenesis occurs by using the same pre-existing cellular lineage and growth factors which will be compatible with the recipient tissue site. Once implanted, the graft will easily become vascularized and will osseointegrate with the surrounding bone starting the osteogenesis process (19).

Autografts then, being made of living cells, have the fundamental osteogenesis, osteoinduction and osteoconduction properties. Because of these biological characteristics, besides the impossibility of developing an immune reaction and host rejection or pathological transmission, autograft is considered to be the "gold standard" as a graft material.

About the donor site, previous systematic reviews have reported that in engineering dentistry the intraoral graft are the most favorable compared with extraoral locations because of the convenient surgical access and proximity to the recipient sites, avoidance of cutaneous scarring and because the harvesting process can be performed under local anesthesia avoiding postoperative hospitalization besides having lower morbidity and lower operatory cost (20, 21).

On the other hand though autogenous bone graft implies a donor site morbidity since a second surgery site and procedure is needed for graft harvest, adding operative time and pain for the patient which is the most common complication. Less frequent complications include nerve injury, hematoma, infection, graft resorption and fracture at the donor site. Besides the possible sequelae that could arise with the harvest procedure, another limitation of autograft is that there could be limited availability in instances where the patient's overall bone quality and/or density is poor, or when a large volume of graft material is required (especially in pediatric patients) (19).

In order to overcome these limitations, very often the bone graft is taken from the site of a tooth extraction or by collecting bone chips during the drilling for implant placement.

Clinically, in periodontal therapy there have been using several types of autogenic bone graft materials: cortical bone chips, bone blend, osseous coagulum, intraoral and extraoral cancellous bone and marrow (22).

Also, because of some of the mentioned limitations, alternatives to autograft biomaterials have been proposed along the years of tissue engineering development, all of these sharing the characteristics of being limitless in supply and not requiring any donor site. Even though these nonautogenous materials can offer different advantages, the feature though that differences the autologous bone graft from these is its osteogenic property and this is what still makes it the gold standard for regenerative medicine (19).

Allograft

An allograft material, also known as allogeneic graft or homograft, is harvested from an individual other than the one receiving it, being of the same species but with a different genotype. Allografts are then still deriving from humans, from living related or unrelated donors, by cadaveric donors or even from artificial bone which derives from ceramics (ex. hydroxyapatite).

The tissue used to perform an allograft is usually given by Tissues Banks and does not have any osteogenic property. It can though go through tissue processing including decellularization, cleansing, sterilization, dehydration and preservation for clinical use that would give them osteoinductive and osteoconductive properties. This tissue processing includes pulverization and the extraction of the viable mineralized cells from the originating bone tissue of the donor leaving a framework called extracellular matrix (ECM). Demineralized bone matrix is then processed resulting in a composite of growth factors, non-collagenous proteins and collagen. Freezing or freeze-drying these biomaterials, especially through the process of sterilization under exposition to ethylene oxide and gamma radiations, is essential also for minimizing the risk of inducing an immune response from the host but at the same time it does also decrease significantly its osteoinductive properties (23).

This processed tissue is made primarily of proteins and minerals which will serve as scaffold guiding the osteoblasts from the defected bone, in which the bone graft is placed, inducing bone regeneration. For this reason allograft are defined as grafting materials with osteoconductive and some osteoinductive capacity (23).

There are different types of bone allografts according to their preparation: they are available as fresh/fresh-frozen (FFBA), freeze-dried (FDBA), or demineralized and freeze-dried bone allograft (DFDBA).

As mentioned, allograft are said being osteoconductive because, as scaffolds, they provide a structural framework enhancing the host tissue to grow (12, 24).

The maximum osteoinductive potential has been demonstrated through in vivo studies occurring in scaffolds demineralized around to 2% residual calcium" (30). Moreover its ability in inducing new bone formation in soft and osseous tissues is believed being explained by the presence in the material of bone morphogenic proteins (BMPs) (25).

These proteins together with cytokines and growth factors interact with the host tissue osteogenic undifferentiated precursors, the mesenchymal stem cells, initiating the process of undifferentiation and bone regeneration (24).

Has been demonstrated though that the osteoinductive ability of demineralized freeze-dried bone allografts depends on different factors among which the age of the donor and the acquisition and processing mechanism (26).

DFDBA have been studied and developed even for overcoming the disadvantages of autografts and being an alternative to it. Differently from autografts, allogenic bone grafts are in fact abundantly and easily available and do not cause any morbidity at the harvest site; although these advantages, it is not frequently chosen as regenerative material in insolation for segmental defects since, as previously explained, it does not provide osteogenic inputs as well as being weakly osteoinductive and potentially infective (22).

Another limitation to take into account of allografts is the cost which, especially for DBM, is high. As to mention, single-use allograft materials has been shown having a cost ranging from $376-$2230, not to mention the single aliquot DBM. Even though not all the allograft materials are as expensive as DBM, they still represent a quite substantial financial effort (22).

Freeze-Dried Bone Allograft

FDBA was introduced in dentistry for periodontal regeneration from J T Mellonig et al. in 1976 and prepared for its use through a process of vacuum that removes from the bone approximately 95% of water killing all its cells but leaving its original morphology and chemical integrity plus reducing its antigenicity which otherwise could induce an immune rejection reaction from the host (21).

The capability of FDBAs of being osteoconductive depends on how much the graft integrates in the defected area: this is the graft material that serves as a framework for osteoblasts.

Several studies have been carried out getting to the conclusion that the use of FDBA in the periodontal treatment, especially that of furcation defects, is more effective if combined together with autogenous bone rather than FDBA used alone. An example is the comparative study carried out from Mellonig in 1991 that, together with eighty-nine clinicians, selected a total of 1521 defective sites among which 991 were treated with FDBA alone, whereas 524 with FDBA combined together with autograft. After a follow up of 6 months results have been collected and analyzed: more than 50% or even up to 100% of bone fill was achieved in 220 (67%) defects treated with FDBA and in 137 (78%) defects treated with FDBA + A. The probing depth was significantly reduced in 69 and 79% of the defects, respectively (21).

Decalcified Freeze-Dried Bone Allografts

DFDBA, thanks to its osteoinductive properties, is now considered being the graft material of choice when compared to other allografts such as FDBA and to xenografts. Its inductive ability is given from

its demineralization process with hydrochloric acid that exposes its BMP's, the bone morphogenic proteins found in the bone matrix (21).

The difference from an undemineralized allograft, given as said from the decalcification process of DFDBA, is that the demineralized graft is able to induce bone regeneration by enhancing host progenitor cells to differentiate into osteoblasts and so being osteoinductive, whereas FDBA can only be considered osteoconductive as it only function as scaffold for the new bone to regenerate (21).

This material, because of the protein factors contained in its structure, turned out being able to well regenerate the periodontal ligament (Bowers, 1985). The neoformation of a new attachment in its three components the bone, the cement and the periodontal ligament is also confirmed by Mellonig (1996), whose histomorphometric investigations evidenced the regenerative potential of DFDBA on bone, cement and periodontal ligament at the level of exposed roots; the author moreover hypothesizes better results by adding to the DFDBA a portion of mineralized bone matrix, especially useful in larger osseous defects (21).

We can distinguish between cortical DFDBA and cancellous DFDBA.

Xenograft

Xenotransplantation refers to nonhuman cells, tissue or organs transplanted from a donor of a different specie, into a human recipient.

Xenografts, in regenerative medicine, have developed in order to overcome some limitations of the already mentioned autografts and allografts. Xenografts are in fact considered the most indicated choice for children which might be physically too small to receive transplantations from an adult donor. Moreover organs transplanted from animal donors can be implanted into patients that are not yet in the human organ transplantation list, potentially saving life-threatening situations.

In regenerative dentistry there are different types of xenograft sources among which as to mention the bovine-derived xenograft (BDX), commercially known as Bio-Oss®, the equine-derived xenograft, the porcine-derived xenograft and the natural coral xenograft (12, 27).

The most commonly used xenograft is the deproteinized bovine bone mineral which, because of its preparation process that removes all the osteogenic organic components, results in natural bone mineral mainly consisting of hydroxyapatite (HA) retaining a porous architecture (27). Because of this process of extraction mechanism, the Bio-Oss® becomes completely devoid of antigenicity (28). It is in fact reported from Cohen et al. (29) that the implantation of the BDX does not cause any subsequent systemic or local immune response and it has been calculated that the risk of pathologic transmission is 1 in 10 (28).

This biomaterial has developed as a bone replacement graft because very similar to the human bone in many of its features: its inner surface area, crystalline size, porosity and calcium-to-phosphate ratio (30). Moreover it is assessed that BDX is able to integrate very well with the new bone and to become vascularized (28).

In the treatment of human vertical intraosseous defects it has been demonstrated a statistically relevant probing depth reduction and clinical attachment gain with the use of BDX in comparison with a non-graft control treatment (30).

A similar amount of results plus bone fill and defects resolution were also observed in comparison with the use of demineralized freeze-dried bone allograft (31).

Another therapeutic situation of particular interest when using Bio-Oss as a graft material is the direct sub-antral augmentation procedure where dental implants that were placed in grafts with Bio-Oss resulted having a similar or even better survival rate than autogenous grafts (32).

Even though bovine-derived bone grafts have many advantages over other grafting materials besides being demonstrated having an high osteoconductive potential, they are reported being fragile. Because of this limitation they could risk to fail during the fixation of the screw of the implant or after the clinical procedure (27).

Even though bone grafts have been demonstrated being efficacious in the regeneration of periodontal osseous defects, irrespectively of the type of the chosen bone graft material, the mean of attachment gain and bone fill is of around of 3.00 mm (21).

The ultimate goal of the periodontal treatment though is both to reverse the advancement process of disease and to achieve the complete regeneration of the periodontium. It is then clear the need of additional enhancing stimuli. Among these polypeptide growth factors have been introduced. This group of natural biologic response modifiers includes factors such as the platelet-derived-growth factor (PDGF), the enamel matrix derivatives (EMD), insulin-like growth factor (IGF), bone morphogenic proteins (BMPs) and the osteogenin (21).

Synthetic organic biologically active grafts

In order to achieve the best results in terms of bone fill and gain in clinical attachment in the periodontal regeneration, newer strategies of cellular tissue engineering have developed and continuous researches and studies are being carrying on looking for new therapeutic alternatives, materials and techniques.

In the last decades it has been researched a way to boost the regenerative potential of the periodontal cells by introducing modified genetic materials and increasing the concentration and production of growth factors and differentiation factors (27). In order to enhance the regenerative potential of bone, in vitro experiments have been carried out by increasing the growth of osteoprogenitors and osteoblasts on 3D constructs. Moreover with the same purpose, the use of platelet-derived growth factors (PDGF), enamel matrix derivatives (EMD) and bone morphogenic proteins (BMPs) has been investigated (27).

PDGF: Platelet-Derived Growth Factor

The bone remodeling cycle is the physiologic activity that allows the bone to continuously remodel and repair if fractured and to the bone graft to integrate in the defected site. This process is regulated by a complex system of cytokines and growth factors that are responsible for the recruitment, proliferation and activity coordination of osteoblasts and osteoclasts (33). Among these biological factors, the platelet-derived growth factor (PDGF) is one of the most essential in the regulation of bone reparative activity. More in detail, PDGF is a protein abundantly found in the bone matrix that, consequently to hard- or soft-tissue injury, during the process of clotting is locally released by the blood platelets. Once released, the PDGF is able to stimulate the migration and proliferation of the pool of osteogenic cells into the injury site populating the scaffold, by acting as both a chemotactic and mitogen agent (27, 33). Subsequently these progenitor cells differentiate into osteoblasts and/or chondrocytes under direction of the bone morphogenic proteins (BMP) (27).

Is then evident the relevant role of PDGF in the periodontal regeneration, in the whole process that includes the regeneration of the periodontal ligament, the cement and the bone. Its importance was firstly discovered in 1980s from Lynch and co-workers with an animal study (34). The use of this biomaterial in regenerative therapies from that moment on has increasingly acquired attention and developed overcoming different limitations. At first in fact the biomaterial was administered in form of a platelet concentrate gel used alone or combined with a variety of osteoconductive matrices, but had as main disadvantage the need of obtaining blood samples from the patients as well as lack of predictability in the outcome (35). Then finally, advances in recombinant engineering led to the production of the proteins in big amounts, being it controlled in concentration and purification.

Thanks to these improvements, most recent bioengineered materials are now prepared with the growing factors already incorporated into the scaffold material and the release of them is controlled over a period of time previously determined. This emerging new trend is of relevant importance because it offers to the clinician an already available biomaterial for a controlled and predictable periodontal regeneration, optimizing the clinical outcomes.

Enamel-matrix derivative (Emdogain®)

EMD refers to "the purified fraction derived from the enamel layer of developing porcine teeth" (36) and it is composed by different proteins among which the amelogenins which constitute the 90% of the total content, the enamelin, ameloblastin, amelotin and a series of proteinases (36).

From a generic biologic point of view, it has been evidenced that EMD play a relevant role in wound healing mediating bone remodeling and favoring angiogenic activity and soft tissue regeneration. This happens because EMD has been shown to regulate many cells activity as migration, proliferation, differentiation and attachment as well as to mediate the expression of growth and transcription factors, ECM constitutes, cytokines and others (36).

In the last twenty years its relevant role in the periodontal regeneration has been investigated: the researches started on the basic knowledge that certain enamel matrix proteins were found on the surface of developing roots of non- yet erupted teeth, prior to the formation of the cementum, hence hypothesizing a role of EMP in the cementogenesis (36).

Because of this finding, further studies have been carried on the assumption that EMP might be relevant on the periodontal formation prior to cementogenesis getting to the demonstration that EMPs are effectively proteins secerned by the Hertwig's epithelial root sheet able of enhancing periodontal regeneration (37).

Osteoconductive materials: barrier membranes

In periodontology we can identify two main surgical techniques for achieving periodontal regeneration: the guided tissue regeneration (GTR) and the guided bone regeneration (GBR). These techniques, as their name suggest, guide the migration and proliferation of the different cell populations of the periodontium in their right position into the defected site in order to obtain a regenerated physiologically and morphologically correct new periodontium.

With the GTR this is obtained with the surgical placement of membranes that act as physical barriers between the different healing tissues of the periodontium separating the gingival epithelium and connective tissue to one side and the alveolar bone tissue and periodontal ligament to the other (27). GTR is based on the principle that the different periodontal tissues regenerate with distinct speeds: the use of the membranes prevents the soft tissue, which has a faster turnover, to invade the space intended for bone and periodontal tissue, which are slower in their regeneration. Besides, they selectively guide the migration of PDL cells into the defected site (27). More in detail, based on the so called "cell-occlusivity" property, membranes prevent epithelial cells, granulation end fibrous tissue from entering into the intended bone- and PDL-regenerating space, as well as allowing the osteoprogenitor bone cells, osteoblastic cells and cells responsible for the new vascularization, to enter the defected site, mediating at the same time the diffusion of growth factors, nutrients, cytokines and other bioactive elements.

Besides this main purpose, these membranes are often used together with bone graft with the intention of sustaining and preserving it, moreover they serve for slowing down its reabsorption rate (38).

The indications for GTR are:

- two-/three- walled narrow vertical defects;
- circumferential defects;
- class II molar furcation;
- class I/II gingival recession;
- thick gingiva;
- defects without tooth mobility (38).

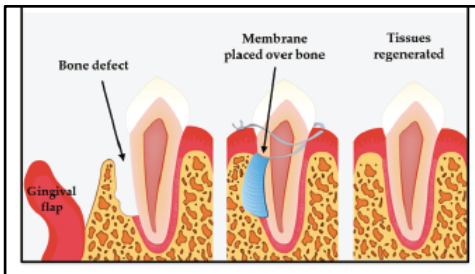


Illustration showing periodontal guided tissue regeneration (GTR) technique using a barrier membrane. Courtesy of Ms. Esraa Khalil, Graphic Designer, Amman, Jordan. (38)

The GBR aims to obtain bone regeneration in post extraction sites or in those sites where an implant is needed and the alveolar ridge is insufficient. In GBR the membrane is located in order to prevent the fibroblasts from colonizing the intraosseous defect while it is healing, allowing at the same time the osteoblasts to migrate into the bone wound filling it, thus initiating the bone regeneration (38).

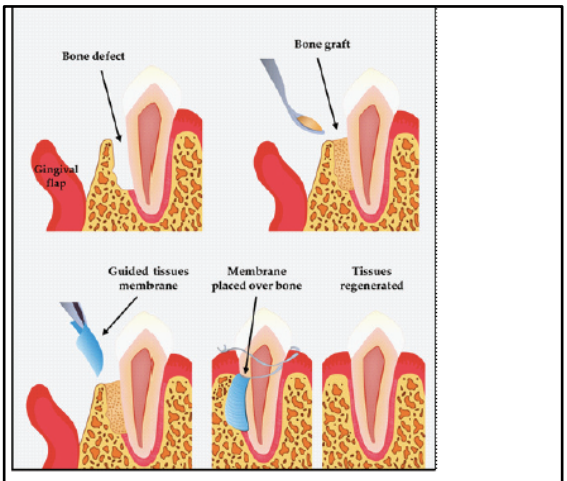


Illustration showing guided bone regeneration (GBR) technique using bone graft and a barrier membrane. Courtesy of Ms. Esraa Khalil, Graphic Designer, Amman, Jordan. (38)

The indications for GBR are:

- class II/III molar furcation;
- post extraction socket previous to implant placement;
- apicectomy consequent to a periapical pathology;
- fenestration and dehiscence bone defects in sites with implants;
- sinus lift or sinus repair if perforated;

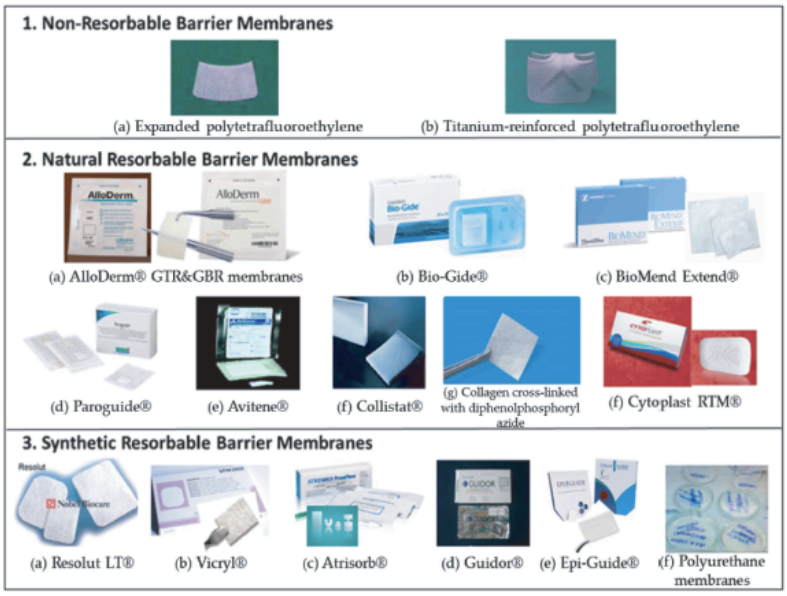
- horizontal or limited vertical alveolar ridge augmentation (39).

The contraindications for GBR are:

- comorbidities that contraindicate surgery;
- poor oral hygiene;
- active infection in the surgical site;
- inflammation of the soft tissue;
- smokers;
- generalized horizontal bone loss: very compromised remaining bone (39).

The membranes used for periodontal regeneration must all share some important characteristics: biocompatibility, occlusivity and selective cell-permeability, space creation and maintenance, mechanical features, tissue integration and clinical manageability (37,38).

We can distinguish two categories of membranes used for GTR and GBR: non-resorbable membranes and resorbable membranes.



Nonresorbable and resorbable barrier membranes available for periodontal GTR and GBR therapy. (38)

Non-resorbable membranes:

Non-resorbable membranes are made of materials that do not degenerate with time and maintaining their structural integrity they assure their efficiency until needed. Once their function has been completed they are surgically removed (38).

Their effectiveness and safety in the system has been investigated and their role in the periodontal regeneration proven with evidence (40).

Many materials have been used for GTR and GBR, first of which the cellulose acetate (Millipore®) that then was substituted with a non-porous biocompatible fluorocarbon polymer, the Polytetrafluoroethylene (PTFE). Among these, the most used in the guided regeneration of periodontal ligament and bone are the expanded-polytetrafluoroethylene (e-PTFE) and the high density polytetrafluoroethylene (d-PTFE) that can also be find reinforced with titanium (Ti-d-PTFE). Besides these, titanium membranes are used.

The e-PTFE, also known as Gore-Tex®, is a biocompatible and highly stable polymer in the system, does not elicit any immunologic reaction in the host and it is resistant to degradation (40).

Its effectiveness and limitations has been investigated and as major complication after its application the premature membrane exposition has been reported in 30-40% of the cases. The membrane exposition then can possibly lead to infection by bacteria contamination, besides the invasion of fibrous tissue with a consequent reduction in the regeneration rate (41). At the first sign of inflammation the membrane must be immediately removed.

In order to reduce this risk, the suturing techniques are of crucial interest for obtaining a primary closure over the e-PTFE membrane but this might be arduous in wider defects.

In order to overcome the limitations of e-PTFE membranes, further researches have been carried on and the d-PTFE has been proposed as a possible substitute. The dense-PTFE is higher in density and has as main difference to the e-PTFE that its surface has smaller pores, reducing the amount of

bacteria able to penetrate and to possibly infect the surgical site. Moreover these membranes are characterized by small indentations facing the inner side of the flap that strengthen their connection. Because of this, primary closure is not essential and if membrane exposition occurs the epithelial ingrowth is limited as well as the bacterial contamination, reducing the risk of infection and fail. We can then assess that even if membrane exposition occurs (in the case in which no edges are visible), it is not needed to prematurely remove the membrane. It is important though to keep it controlled in order to avoid any inflammatory processes to occur in the first month (41).

An occasional complication that can be observed 2-3 months after d-PTFE implantation is the swelling of the tissues that can come along with a fistula as well. In this case the membrane can be easily removed but by that time bone regeneration has already occurred (41).

In the clinical application, in order to test the performance of e-PTFE in comparison to d-PTFE, a prospective randomized controlled trial was performed (65). A group of 23 patients undergoing GBR surgery for implants placement in an atrophic posterior alveolar ridge of the mandible was selected. The GBR was performed using both an autologous bone graft and an allogenic bone graft covered with either the e-PTFE membrane in the control group and with d-PTFE in the case group. 6 months later the membrane was removed and the results examined: 4.91 mm (SD ±1.78) of bone fill was obtained in the control sites and 5.49 mm (SD±1.58) in the case sites. The results did not evidence statistically relevant differences between the election of e-PTFE and the d-PTFE so it can be assessed that in the treatment of vertical bone defects around implants there is not a preferable GBR material to use (42).

Considering though all the advantages of d-PTFE and the fact that it is easier to remove than e-PTFE, we can finally assess that this membrane can become the new golden standard material for GTR and GBR (41).

Polytetrafluoroethylene membranes used alone without any reinforcement and/or graft material, showed being more susceptible to collapse into the wide defected site because of the compression of

the mucosa overlying it. Because of this limitation, for the treatment of more complicated situations of deep vertical defects or in supracrestal areas, more rigid materials have developed as to mention the titanium-reinforced e-PTFE (Ti-e-PTFE) or the titanium mesh.

Titanium was discovered being a perfect material to use in regenerative surgery because of its rigidity, strength, light weight and resistance to corrosion (27) besides being less susceptible to bacterial contamination thanks to its smooth surface and, because of its elasticity, being able to provide enough space for bone to regenerate in big defects of the alveolar process (43). On the other hand the limitations of titanium mesh are related to the difficulty of its removal and to the possible mucosal irritation and membrane exposure due to its sharp edges and rigidity (43).

Since non-resorbable membranes do not degrade and maintain their integral structure until needed, once their function is achieved and the periodontal regeneration has occurred, they need to be removed with a second surgery. This helps the clinician to have complete control over the treatment and obtaining a much more predictable result. Contrarily the need of a second surgery is increases the patient morbidity and stress, the risk of infection of the surgical site and an increase in time and costs. Also, the new regenerated tissues might suffer from the surgical trauma or even being contaminated leading to a post-operative infection (44). In order to overcome these disadvantages researchers and clinicians worked together to find an alternative to non-resorbable membranes and come up with the bioresorbable barriers.

Resorbable membranes:

Resorbable membranes resulted being a good solution to overcome many limitations of the non-resorbable membranes and since 1990s they have been used as the material of choice in many clinical situations (45).

As deducible, resorbable membranes offer the main advantage of being degraded by the organism avoiding the need of a second surgery to remove it. This lowers drastically the risk of morbidity and

infection besides being time and cost saving. For what concerns the clinical outcome it has been evidenced a similar degree of bone regeneration when compared to non-resorbable barriers (46).
On the other hand though this same characteristic might be a disadvantage if considered the fact that reabsorbing the membrane does not allow a predictable result in terms of amount of bone regeneration which risks to be insufficient by the time of reabsorption of the barrier (47).
A lack in sufficient bone regeneration might also occur whenever the membrane gets associated to an inflammatory reaction of the adjacent tissues being the neutrophils and macrophages responsible for accelerating the barrier degradation thus altering its structural support and function. This could even lead to implant loss if the membrane is associated to it. Another disadvantage of resorbable membranes is their lack of rigidity and progressive loss of strength which causes them to have the tendency to collapse and invade the space intended for regeneration. Because of this, that would determine fibrous tissue ingrowth, inflammation and possible bacterial contamination thus the failure of the treatment, resorbable membranes are now frequently used in association with autografts or allografts, together with additional reinforcements (48).

These barriers can be found as natural or synthetic barriers. The first group comprehend membranes of bovine collagen, porcine collagen or chitosan origin and the second one membranes fabricated from organic aliphatic polyesters. Thanks to the numerous sources from which to obtain collagen and polyglycolic or polylactic acid, many different types of resorbable membranes are now available for GTR/GBR and each of them present its own suitable characteristic for the clinical situation (49).

Natural resorbable membranes are fabricated from human or animal collagen which is a very appropriate material for guiding regeneration thanks to its biological properties: it has low immunogenicity, it is hemostatic, well-tolerated and being chemotactic it is able to attract and activate PDL and gingival fibroblasts, hence induce fibroblast DNA synthesis (45) potentially increasing tissue thickness. Besides, osteoblasts showed to better adhere to collagen membranes than any other

membrane surface (49). Because of all these properties, collagen has demonstrated being a great biomaterial for the fabrication of bioresorbable barriers which are now used a lot for guiding regeneration applications. Many in fact are the collagen membranes currently available and they can be classified according to the collagen type they are made of and their resorption time.

Table 6: most currently used collagen membranes (27)

Membrane	Constitution	Method of cross-linking	Tissue sources	Resorption time
BioGide	Types I & III collagen	None	Porcine (dermis)	24 weeks
BioMend	Type I collagen	Formaldehyde	Bovine (tendon)	6–8 weeks
BioMend-Extend	Type I collagen	Formaldehyde	Bovine (tendon)	18 weeks
Tissue Guide	Atelocollagen + tendon collagen	HMDIC[a]	Bovine (tendon + dermis)	4–8 weeks
BioBar	Type I collagen	N/A	Bovine (tendon)	24–32 weeks
Paroguide	Type I collagen (96%) & Chondroitin-4 sulfate (4%)	DPPA[b]	Calf skin	4–8 weeks
Biostite	Type I collagen (9.5%), Chondroitin-4 sulfate (2.5%) & HA[c] (88%)	DPPA[b]	Calf skin	4–8 weeks
Periogen	Types I & III collagen	Gluteraldehyde	Bovine (dermis)	4–8 weeks
AlloDerm Regenerative Tissue Matrix (RTM)	Type I collagen	None	Human cadavers (skin)	28–36 weeks
Cytoplast RTM	Type I collagen	N/A	Bovine (tendon)	26–38 weeks

HMDIC[a] Hexamethylenediiscyanate
DPPA[b] Diphenylphosphorylazide
HA[c] Hydroxypatite

The synthetic resorbable membranes are mostly composed of poly-hydroxy acids, as to mention the poly-lactic acid (PLA) and the polyglycolic acid (PGA) (50). According to their polymers ratio, synthetic resorbable barriers are available in a wide spectrum of tensile strength that ranges from 40 to140 MPa for PLA and PGA (48) which is lower than non-resorbable membranes (100 MPa for e-PFTE membranes) but higher than natural resorbable membranes (4-5 MPa for porcine membranes). Synthetic resorbable membranes have the advantage to be degraded from the organism hence they do not need a second surgery for their removal. They are in fact completely hydrolyzed into water and carbon dioxide from proteolytic enzymes (50) with a degradation rate varying depending on the presence or not of glycolic and lactide acid in their composition (49).

Table 7: Currently available synthetic resorbable membranes (50)

Product (Company)	Material	Resorption Period (months)
Guidor® (Sunstar)	PLA (Polylactic Acid)	1.5 - 2
Resorb X® (KLS Martin)	PDLLA (Poly-DL-Lactic Acid)	1.5 - 2
Cytoflex Resorb® (Unicare Biomedical)	PLGA (Poly-Lactic-Glycolic Acid)	4
Resolute® (Gore®)	PGA-TMC (Polyglycolic Acid Trimethylene Carbonate)	4 - 6
Epi-Guide® (Curasan, Inc.)	PDLLA (Poly-DL-Lactic Acid)	6 - 12
Atrisorb (Tolmar)	P(DL)LA – NMP (Poly-DL-Lactic Acid)	9 - 12
Inion™ GTR (Inion)	PLDLGA-TMC (Poly-LD-Lactic-Glycolic Acid Trimethylene Carbonate)	12 - 24
Vivosorb® (Polyganics)	PDLLCL (Poly-DL-Caprolactone)	16

OBJECTIVES

Principal objective: to understand which are the main biomaterials to use in order to achieve periodontal regeneration.

Secondary objectives:

1) to understand which is the best option among scaffold grafting materials;
2) to understand which is the best option between non-resorbable and resorbable membranes;
3) to understand which is the best surgical approach and what materials to use depending on the morphology of the defected site: vertical intra-bony defect, critical-size non contentive defect, post-extraction site for alveolar preservation.

MATERIALS AND METHODS

The research has been developed through the use of the web by looking for journal scientific articles in the web sites MEDLINE, PUBMED and Google Scholar. Another method used in order to find specific articles was by looking through the bibliography of the most relevant articles that have been selected for the research.

In order to find the appropriate bibliography for this research mainly articles from 2000 have been selected.

The key words used are “regenerative dentistry”, “bone graft”, “osteogenesis, osteoinduction, osteoconduction”, “stem cells in the periodontium”, “periodontal regeneration”, “allograft materials”, “xenograft materials”, “platelet-derived growth factors”, “enamel matrix derivative”, “periodontal defects”.

Different comparative controlled trial studies have been selected and compared and a systematic review of several materials and surgical techniques in the therapeutic approach of the periodontium have been made.

Moreover some clinical cases have been introduced in order to highlight some of the most appropriate therapeutic approaches for the most relevant bone defects, as well as the materials chosen for each of them. The clinical cases have been personally followed throughout the last six months, since the diagnosis until the post-operative follow-up, together with dr. Enrico Gomiero, the periodontist that performed the surgeries.

A bibliography with the corresponding references has been made with the use of MENDELEY, the Vancouver style has been chosen for referencing.

DISCUSSION

From the knowledge of the most important and used materials for periodontal regeneration, it is fundamental to understand which one to use in order to obtain the best outcome achievable in every specific situation. Many comparative analytical studies and clinical trials have been carried on in order to obtain scientific evidence that suggest the clinicians which surgical approach to adopt with as ultimate goal the regeneration of the periodontium.

With this objective, first of all some materials have been compared in order to have a general idea of which ones are now considered to be the best in terms of results, generally speaking.

Talking about the grafting materials and in particular about the Decalcified Freeze-Dried Bone Allografts, as mentioned, we can distinguish between cortical DFDBA and cancellous DFDBA. Analyzing the results of comparative analytical studies carried out in the years it has been assessed that the use of cortical bone as grafting material would lead to a bigger bone fill in comparison to the cancellous DFDBA.

In a clinical study a bone filling with a range of 75-95% was described with the use cortical DFDBA (34). In another one that selected 27 intraosseous defects, 2,4 mm of bone fill of the original bone defect resulted from the use cortical DFDBA, better result in comparison to the use of cancellous DFDBA that in a study of a treatment of 16 patients showed a result of a mean of 1,38 mm of bone fill and even only 0,33 mm in 6 control sites (27,51).

Moreover, in order to understand whereas to choose to use FDBA or DFDBA as grafting material, direct comparison studies have been carried out: in 1989 Rummelhart et al clinically compared 11 defective sites after treatment reporting no statistically relevant difference in clinical attachment gain, probing depth and bone fill (27).

Another comparative trial aimed to enlighten the radiographic and clinical outcomes when FDBA is used compared to DFDBA with chlorine membrane associated (52). Nine patients were recruited and eighteen deep intra bony defect sites treated and followed for 12 months of observational period. The mobility rate of the teeth was reported being of grade I-II.

Also in this case though the radiographic evaluation showed no statistically significant results: important bone fill was observed in both groups with an increase of 4.78 ± 0.25 mm in sites treated with FDBA and 4.28 ± 0.44 mm in sites treated with DFDBA (52).

In general though, if needed to choose between FDBA or DFDBA, it is important to remember the main difference between these biomaterials: FDBA serves as a scaffold favorizing an osteoconductive

surface whereas DFDBA, besides this, it is also considered being osteoinductive since it even provides a source of osteoinductive factors.
Said this, in the decision of the therapeutic approach to use, it can be assessed that FDBAs have better physical characteristics if the tissue is still mineralized, although even DFDBAs can be used. On the other hand DFDBAs are certainly recommended in sites where the regeneration may be more problematic and need an additional osteoinductive support.

In 1993 Mellonig and Brunsvold carried out a controlled histologic study in animals and humans using bone autologous grafts and allografts for the treatment of periodontal osseous defects (51).
This study wanted to demonstrate the possibility of the periodontium to regenerate with the use of bone graft, moreover it looks for the differences in therapeutic outcomes depending on the different types of bone defects and the regenerative bone graft material chosen, both in animals and in humans.

As result of the study it could be possible to assess the effectiveness of the use of bone graft materials in the periodontal treatment of defective bone sites in animals and humans. It was evidenced that not a complete regeneration of the periodontium was achieved by only using these regenerative techniques. In fact it has been achieved a mean of 60% of bone fill of the original defect and a mean of 2,68 mm of clinical attachment gain (51).

As previously mentioned, we can finally assess that currently there is not an ideal graft material for periodontal regeneration, they all have advantages and limitations.
Autograft is so far defined as the material of choice followed by allografts and xenografts (51).

Together with scaffold materials, also the introduction of the Enamel Matrix Derivative allowed big improvements in the dental tissue engineering. In order to give evidence to the EMD's clinical importance in each possible situation, many controlled clinical trials and systematic reviews have been carried on. A systematic review reports significant results after evaluating the outcomes of 27

studies with the use of EMD in the treatment of 20 intra-bony defects, 6 recessions and one furcation (53).

For intra-bony defects it was assessed that the clinical outcome if used the EDM was significantly better compared with the results with traditional control treatments, with an additional gain in clinical attachment level of 1,30 mm. No significant differences were shown when compared with resorbable membranes which resulted as effective as EDM.

For recession coverage the coronally advanced flap combined with EDM gave much better root coverage compared with the flap alone but resulted being no more effective than the connective tissue graft.

Regarding the treatment of furcations, in the horizontal defects the use of EDM gave improved results in depth reduction (2.6 ± 1.8 mm) compared with the use of resorbable membranes (1.9 ± 1.4 mm) (53).

Another important issue is whether to use the non-resorbable membranes versus the resorbable membranes in the clinical application.

Many systematic reviews, meta-analysis and clinical trials have been analyzed and compared in order to get to a conclusion on whether it is most favorable to use non resorbable barriers or resorbable barriers in the guided periodontal regeneration.

The final considerations are different according to the surgical site in question.

For class II furcation defects many comparative studies (54-56) got to the conclusion that there are no statistically relevant differences in periodontal regeneration between the two membranes and that both of them give satisfactory clinical outcomes. However in 1995 Hugoson et al. carried out a study in 35 patients and actually affirmed that the improvement in clinical attachment was achieved both towards vertical and horizontal direction in the resorbable membrane group, but only in the vertical direction in the non-resorbable membrane one which presented remarkable higher gingival recession (57).

Class III furcation defects did not positively respond to GTR and both the membrane types did not result being effective in the periodontal regeneration and clinical attachment gain (58).

For the treatment of intrabony periodontal defects no statistically relevant differences were found in the study carried out in 2011 by Corinaldesi G, Lizio G, Badiali G, et al. on eleven patients comparing the healing of periodontal intrabony defects distal to the mandibular second molars related to the impactation of the third molar (59).

Besides, it has been assessed that the choice between non-resorbable membranes and resorbable membranes does not influence the clinical outcome also in the ridge preservation procedures (60) nor in vertical ridge augmentation associated to implant placement (61) or in peri-implant bony defects (62), all of them resulted in similar outcomes.

We can finally assess that the selection of the materials to use, besides the surgical technique, is widely influenced by the morphology of the bone defect. Not only, the surgical approach and the prognosis of a regenerative procedure will depend on the patient factors, the bone defect factors and the dental factors.

Among the patient factors we can consider being the most relevant its periodontal status, life style, stress and habits and its oral hygiene. Besides we have to consider its age, genetic and systemic pathologies. In order to start a regenerative procedure it is in fact fundamental that the patient does not smoke, that has perfect control and awareness over his oral hygiene and systemic conditions and that will follow the recommendations of the dentist. A regenerative procedure will have a poor prognosis in the case of a poor oral hygiene with plaque accumulation, bleeding on probing and bacterial proliferation, in a smoking patient or in a patient with systemic conditions not under control.

As previously explained, in the surgical planning crucial are also the bone defect factors. Different will be the materials to be chosen in each case and the consequent prognosis.

As bone defect factor we consider the morphology or defect angle of the affected bone and its influence in the clinical outcome after the regenerative surgery. To wider defects has been associated a reduced amount of clinical attachment gain and bone fill after a regenerative procedure and one year follow-up (63).

A clinical study has been carried on aiming to predict the healing potential of the bone sites according to their morphology (64). The results showed statistically relevant differences among the defects: those with an angulation of less than 45° showed after regenerative treatment a mean filling of 1.22 mm, much more than in angles between 45° and 90° that gained only 0.05 mm or than those greater than 90° that even showed a further bone loss of 0.05 mm in apical direction.

The same result was assessed from another study on 242 intra-bony defects that showed that angular defects shallower than 25° could gain up to 1.5 mm in comparison to wider defects of 37° or more that did not gain as much as clinical attachment (65).

On the other hand, for what concern the circumference of the defect or the number of its residual bone walls, no statistically relevant differences have be found in the results and so we can assess that there is a lack of association in the residual bony walls and the clinical outcomes after periodontal regeneration (63).

Besides the angular bone morphology and the residual osseous walls of the defects, the overall bone loss pattern and its severity have to be taken into account. The bone defects that are considered being not predictable with GTR are the horizontal supra-bony defects, the furcation defects class III and the interdental crater-like defects while those with a predictable result are the vertical intra-bony defects and the furcation defects class II.

As said, different is the surgical approach for each situation and bone defect morphology and recent clinical studies have been carried on in order to understand which one might be the best for grater results.

The narrow vertical intra-bony defects are the most predictable defects in terms of periodontal regeneration. The surgical techniques used for the formation of a physiological new clinical attachment and bone fill of these vertical intra-bony defects use mainly Enamel Matrix Derivative (Emdogain®) alone or together with bone graft or rather barrier membranes.

Many clinical trials have been considered in order to understand which surgical approach would be the safest and with better results in this type of osseous defect.

First of all we want to understand whether to use EMD or rather a barrier membrane.

With this purpose a multicenter practice-based clinical trial has been carried on selecting seventy-five patients with chronic periodontitis with ≥ 3 mm osseous defects and treating them with EMD or GTR randomly (66). After one year of follow up the clinical attachment level (CAL), probing depth (PD), gingival recession (REC) and bleeding on probing (BOP) were measured and compared: in patients treated with EMD the mean CAL gained and probing depth reduction were of 3.1 ± 1.8 mm and 3.8 ± 1.5 respectively whereas for the GTR patients 2.5 ± 1.9 and 3.3 ± 1.5. The analysis of the results lead to the conclusion that there are no statistically relevant differences between EMD and GTR use in terms of attachment gains. What has to be considered though is the frequency of surgical complication appearance: all the surgical cases treated with GTR presented at least one complication, mainly due to membrane exposure, while this happened only in 6% of the EMD cases. As result we can say that this clinical trial failed to demonstrate more efficacy of one biomaterial over the other in this type of bone defect but for sure the surgical management and appearance of complications resulted being indicative in the choice of the material to use leading to the conclusion that the use of EMD in the regeneration of vertical intra-osseous defects is the safest option (66).

The same conclusion was given in a study carried out in 2009 in Manchester that evaluated the results after a follow up of 1.5 and 10 years (67).

Another review analyzed 28 studies with a total of 955 intra-bony defects treated with EMD or GTR giving as result in the EMD cases a mean of 3.6 ± 0.04 mm of PD reduction in defects with an initial

mean of probing depth of 7.95 ± 0.05 mm and a CAL gain mean of 5.82 ± 0.07 from a 9.4 ± 0.04 mm defect mean. This review then concluded assessing that the use of EMD gave significantly better results compared to those given by using a GTR technique besides being safer (68).

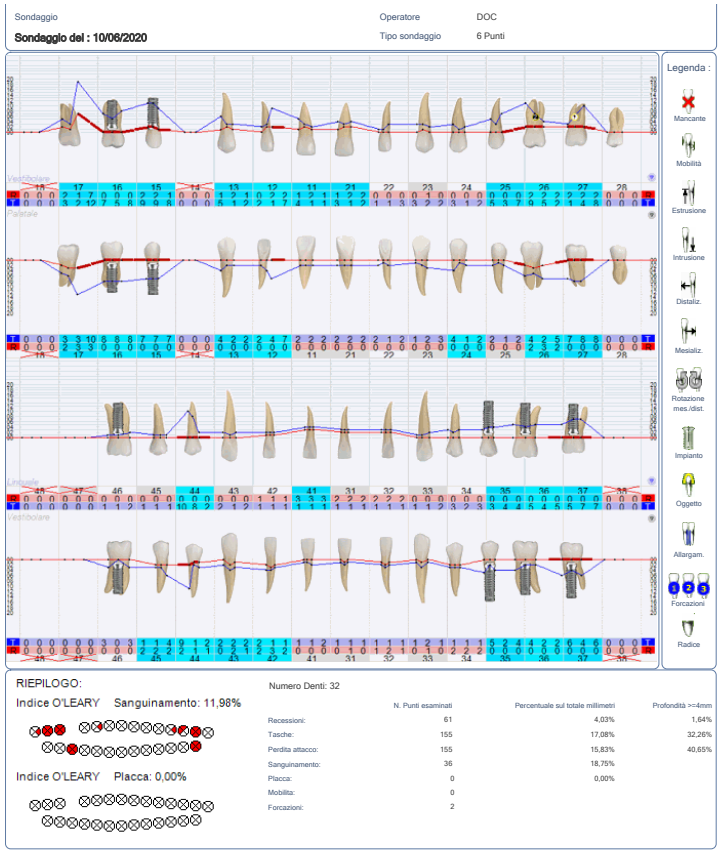
We can finally asses that in intra-osseous defects the use of Enamel Matrix Derivative is a better choice over the use of GTR. What is known though is that without the use of a barrier membrane there is the risk of the collapse of the mucoperiosteal flap, mainly in deep one- or two- walled defects. To overcome this complication then a further investigation is about the use of a grafting material together with the EMD in order to obtain the inhibition of the epithelial downgrowth at the same time as the release of the growing factors from the EMD.

With this purpose other systematic reviews aimed to understand whether to use EMD alone or together with bone graft have been analyzed (69 - 71).

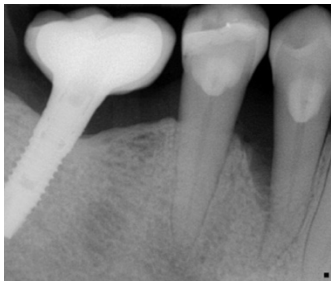
A study (69) selected 434 patients and 548 intra-bony defects obtaining the following data: the mean CAL gained in defects treated with EMD combined with bone graft was of 3.76 ± 1.07 mm whereas it resulted being of 3.32 ± 1.04 mm in defects treated with EMD alone. The mean PD reduction and REC increase measured 4.22 ± 1.20 mm and 0.76 ± 0.42 mm respectively at the defects treated with the combination of the two biomaterials and 4.12 ± 1.07 mm of PD reduction and 0.91 ± 0.26 mm of REC increase at defects treated with EMD alone. The results of the study then indicate a better clinical outcome in terms of CAL gain and PD and REC reduction when combining EMD together with bone graft rather than using the EMD alone.

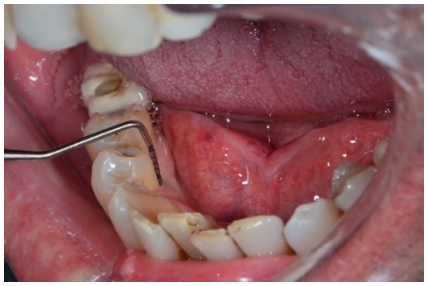
With this knowledge, together with the periodontist Enrico Gomiero, some clinical cases have been studied and, starting from the diagnosis, the proper surgical approach has been planned taking into consideration evidences based on the bibliographic literature.

CASE 1: intra-osseous one-walled-vertical defect on a 44 distal



The periodontogram was performed in June 2020 on a 57 years old patient, non-smoking, with good oral hygiene, BOP of 18,75% and without any systemic condition.





The clinical evaluation was performed with intraoral examination with CP12 and radiographically with periapical x-rays.

The defected site in consideration is distal to the 44 and had a PD of 10 mm in disto-vestibular and 9 mm disto-lingual with a REC of 2 mm.


The surgery was performed in November 2020 and aimed to the regeneration of the periodontal site together with the preservation of the papilla. The technique used for the flap design and opening was the Modified Minimally Invasive Surgical Technique (M-MIST) designed from Tonetti and Cortellini in 2009 with the purpose of reducing the surgical trauma and postoperative discomfort by opening just a small buccal flap ensuring a proper blood supply and primary closure (72).

Once raised the full-thickness flap the granulation tissue was removed and the root scaling of the roots has been performed ensuring a perfect debridement of the cement.

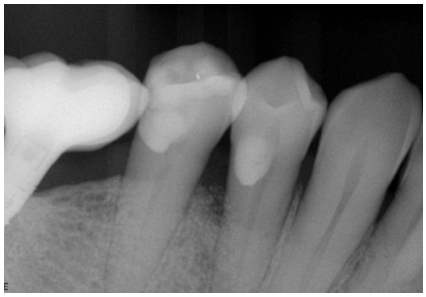


The root surface was treated with a chelating agent, the EDTA, for four minutes, by dissociating the calcium and making the surface suitable for the use of the Enamel Matrix Derivative (Emdogain ®). After the application of the EMD the scaffold material of choice was the bovine-derivative xenograft (BDX), commercially called Bio-Oss®, because of its osteoconductive properties and since completely devoid of antigenicity and risk of developing pathological infections. Moreover BDX is able to integrate very well with the new bone and to become vascularized (28).


A primary closure was achieved with two suspended stitches on the two adjacent teeth 44 and 45 to the defected site and a central single stitch in the preserved papilla over it. The suture used is a 6-0 absorbable braded and coated wire of polyglactin with atraumatic triangular cutting edge.

The suture was removed after three weeks and the correct healing of the surgical site was assured.

The patient was then scheduled once a month for the following three months.




In March 2021, after four months from the surgery, it was reported the last check-up that evidences a great periodontal regeneration and CAL gain of 6 mm (starting from a CAL of 12 mm) and periodontal probing depth reduction of 6 mm obtaining a residual probing depth of 4 mm.

The patient will follow the maintaining program scheduled every three month for the following year.

The two following clinical cases present the same osseous defect morphology and surgical approach based on the same criteria.

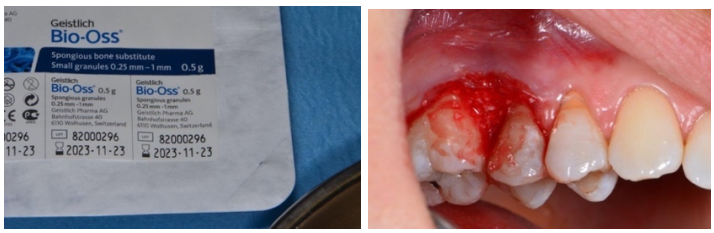
CASE 2: intra-osseous one-walled-vertical defect on a 15 distal

43 years old patient, non-smoking, with good oral hygiene, BOP of 13,15% and without any systemic condition.


One walled-intra-bony defect of PD of 8 mm disto-vestibular and 7 mm disto-palatal of the 15.

M-MIST flap design with papilla preservation.

Chelating agent EDTA for 4 minutes and Enamel Matrix Derivative (Emdogain ®)



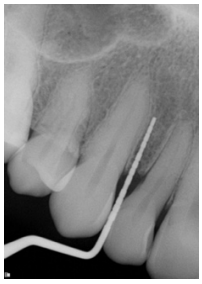
Bovine-derivative xenograft (Bio-Oss ®)

Suture with two suspended stitches on the two adjacent teeth 16 and 15 and a central single stitch in the preserved papilla. The suture used is a 6-0 absorbable braded and coated wire of polyglactin with atraumatic triangular cutting edge. The suture was removed after three weeks.

Six months after the surgery the results significantly evidence a great periodontal regeneration with a PD reduction of 5 mm and a CAL gain of 6 mm.

CASE 3: intra-osseous three-walled-vertical defect on a 13 mesial

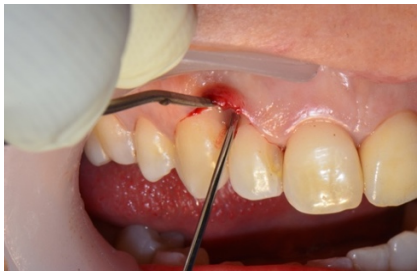
26 years old patient, non-smoking, with good oral hygiene, BOP of 12,38% and without any systemic condition.



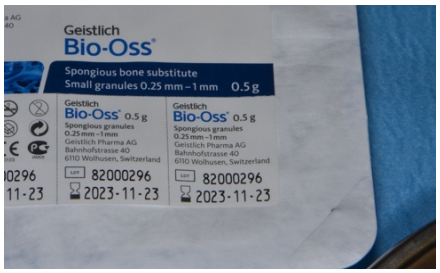

Three walled-intra-bony defect of PD of 9 mm mesio-vestibular and 5 mm mesio-palatal of the 13.

M-MIST flap design with papilla preservation.





Chelating agent EDTA for 4 minutes and Enamel Matrix Derivative (Emdogain ®)



Bovine-derivative xenograft (Bio-Oss ®)



Suture with two stitches in the preserved papilla. The suture used is a 6-0 absorbable braded and coated wire of polyglactin with atraumatic triangular cutting edge. The suture was removed after three weeks.

Six months later a perfect periodontal regeneration can be noticed with a PD reduction of 7 mm.

For non-contained intra-bony defects the surgical approach and chosen materials are going to be different since the bone defects have another morphology. Lacking of the supportive bony walls, the materials to be chosen need to have a structure and a stability themselves. The EMD, because of its consistency, does not maintain the space itself needing as consequence another material to be associated with in order to give better clinical outcomes. A 12-months randomized controlled clinical trial suggested the use of EMD combined together with a biphasic calcium phosphate bone graft (73). Based on the same principle that highlights the unsuitability of EMD for the periodontal defects that lack of a self-contained morphology, another randomized, controlled clinical trial compared the regeneration potential of EMD used alone or together with the ePTFE membrane in 40 deep non-contained intra-bony defects after a follow-up of 12 months (74). The results evidenced more CAL gain and PD reduction in those sites treated with EMD combined with GTR compared to those treated with EMD alone.

Another clinical trial that has been taken into account aimed to study the effect of GBR used in combination with Deproteinized Bovine Bone Mineral and/or EMD on the regeneration of wide non-contained bone defects (75). The study was performed on forty rats that were subdivided into 4 groups depending on the biomaterials used, resulting, after four months, in quite different outcomes. In Group A that left one site untreated and in the contralateral with a resorbable membrane alone an insufficient bone regeneration occurred. In group B one site was filled with EMD and the contralateral was treated with GBR together with EMD; the completed bone regeneration occurred where the two materials were combined. In group C one site was treated with DBBM (Bio-Oss ®) and the

contralateral with GBR and DBBM together. In group D one site was treated with DBBM mixed with EMD while the contralateral with GBR covering the DBBM combined with EMD. Significantly higher rates of bone regeneration resulted in these groups in which sites the DBBM was placed.

Table 10: number of sites with incomplete or complete bone healing depending on the materials used (75)

Treatment	Incomplete healing	Complete healing	Total defects
Control – no treatment	5	0	5
GBR	0	5	5
EMD	5	0	5
GBR + EMD	0	5	5
DBBM	3	1	4
GBR + DBBM	0	4	4
DBBM + EMD	4	1	5
GBR + DBBM + EMD	0	5	5

The results evidence that in those sites in which no GBR was placed no predictable bone healing occurred.

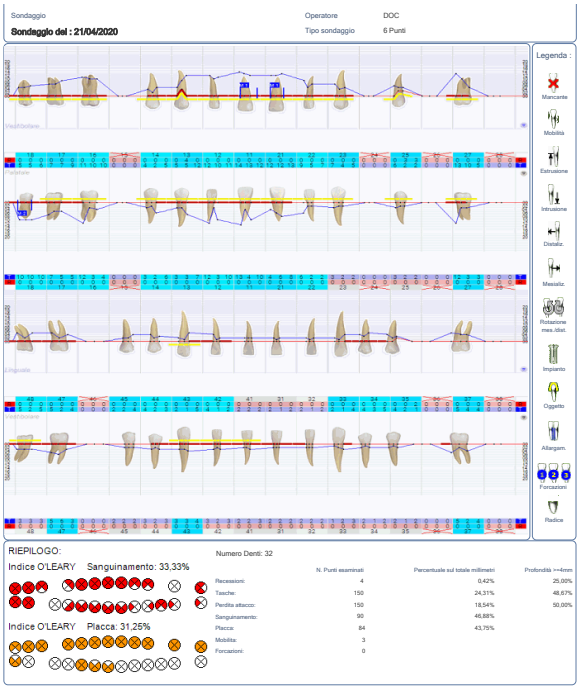
The study concludes assessing that in deep non contained defects the predictability of bone regeneration mainly depends on the presence of barrier membranes while the combination of DBBM and/or EMD did not specifically influenced the regeneration provided by the GBR.

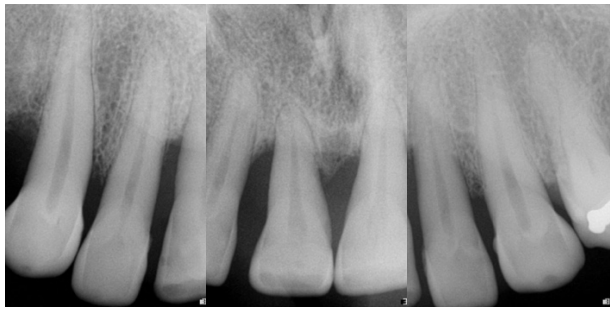
From these studies is then evident the important role of the barrier membrane for the regeneration of critical-size defects. What has to be mentioned though is the high morbidity of the GTR that, as already repeated several times, have high incidence of postoperative complication and clinical fail.

The recent studies in fact are now focusing on the importance of the clot stability inside the defected site and the papilla preservation in order to obtain a favorable and stable environment where the periodontal regeneration and tissue healing are enhanced (72). We can finally assess that a more conservative surgical approach is then acquiring more and more relevance over the use of a barrier membrane.

The following clinical case with critical-size defects presents this second surgical approach.

CASE 4:

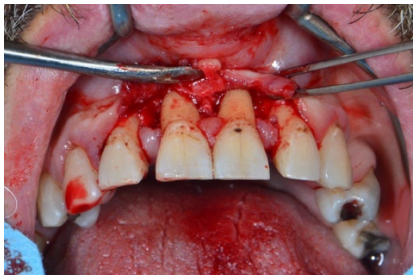




Patient of 52 years old, he came to the first visit with a very bad oral hygiene, accumulation of plaque and chronic periodontitis with generalized increased PD, BOP and swelling and suppuration of the gingival tissues. The patient started an educational protocol of three months during which he has had prophylaxis treatments with ultrasound every 20 days and a full mouth non-surgical treatment with scaling and root planning. He was taught to follow the basic hygiene techniques at home besides the use of mouthwashes, dental floss and chlorhexidine. The improvement obtained was notable.

Once educated the patient, he was finally considered a good candidate for regenerative surgery. Its PD were still of 12-14 mm and the recessions of the superior incisal area of 3 and 4 mm.

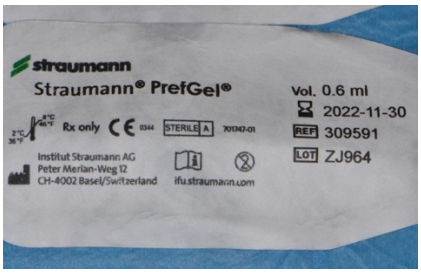
The purpose of this case was, besides reducing the periodontal depth and obtain bone fill, to significantly reduce the gingival recessions, improving the esthetic of his smile. This was very important for the decision and planning of the surgical approach.

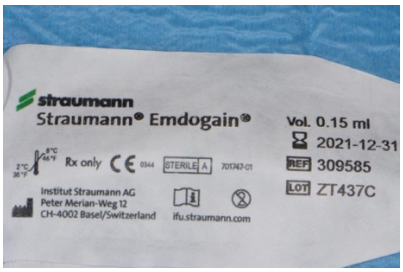


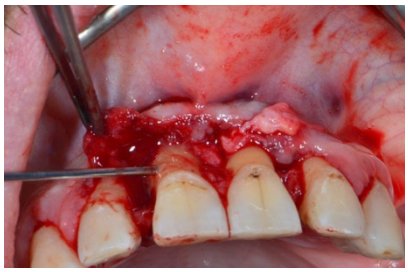

A vestibular full-thickness flap with preservation of the papillae was performed and raised allowing the access for the debridement of the roots surfaces and removal of the granulation tissue.

The surgical approach in this case was very different to the previous one mainly because of the purpose of the coronal repositioning of the flap in order to reduce the gingival recession.

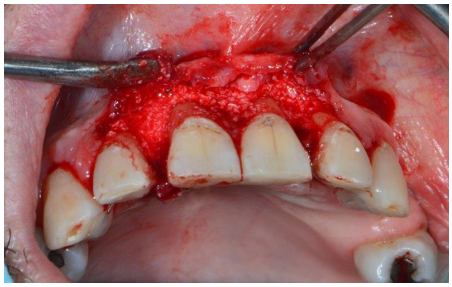
Because of this, no barrier membrane was used since it would have prevented from the flap stabilization in its correct position.







The papillae got deepithelialized and the roots surfaces treated with EDTA. As regenerative materials the EMD was used for enhancing the osteoinduction and the BMX as scaffold material.

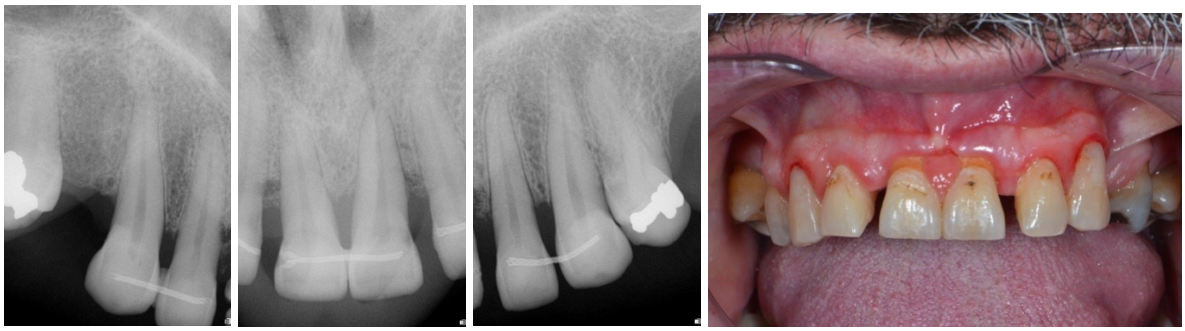


Crucial was then the coronal flap repositioning since it had to perfectly enclosure the regenerative materials inside the defected sites and reduce the gingival recession.

The flap was sutured to the deepithelialized papillae with five suspended stitches to the adjacent teeth of each defected sites ensuring a perfect primary suture. The suture used is a 6-0 absorbable braded and coated wire of polyglactin with atraumatic triangular cutting edge.

The incisors got finally stabilized with a fiberglass splinting.

The stitches were then removed after three weeks post-operative. It was noticed that a great tissue healing was occurring but a premature stitch fall caused a little dehiscence and gingival retraction in the central papilla.



Three month after the surgery a perfect primary closure was achieved except for a less visible defect in the central papilla. A residual PD of 4 mm was achieved and minimal bleeding on probing was assessed (1,56%). The recessions improved a lot resulting being of 1 and 2 mm. The patient will follow the periodontal maintaining program scheduled every three month for the following year besides having performed a prophylaxis with ultrasound every month in order to control his oral hygiene and behaviour.

Regenerative dental medicine extends its application with great importance also in the alveolar ridge preservation after teeth extraction developing what is called the Alveolar Ridge Preservation technique (ARP). As explained, the loss of a tooth would increase the rate of alveolar ridge reabsorption which, as stipulated by Wolff's Law, it is caused by the changes in the mechanical loadings that occur with modifications in the distribution of the forces to the bone occurring during mastication leading to continuous bone remodeling (14). It is then very important to preserve the alveolar ridge as soon as possible after tooth extraction.

During the years many ARP techniques with different regenerative materials have been studied and proposed: the main ones are the autogenous graft, the DFDBA, FDBA, DBBM and alloplastic polymers. Among these the most recent studies assess that the deproteinized bovine bone mineral (DBBM) is currently the most efficacious and used biomaterial for this purpose (76).

Moreover in other clinical trials on the anterior sector it was studied that if used together with collagen it would have prevented from ridge resorption (77).

Another randomized controlled clinical trial on the posterior sector evidenced a big difference in terms of alveolar bone regeneration in those post extraction sites treated with DBBM with 10% collagen (DBBM-C) covered with a native bilayer collagen membrane (NBCM) in comparison to the control group left with spontaneous healing (78).

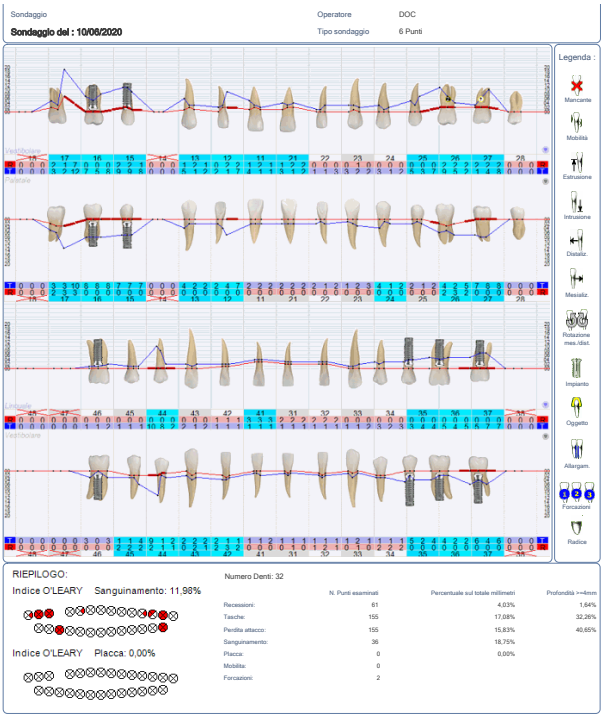
In 2017 a randomized clinical study was performed with the objective of quantitatively determine the amount of alveolar ridge regeneration resulting from the use of different ARP techniques (79).

The study was performed in 40 patients providing 35 post-extraction sites. These were randomly assigned to four different regenerative technique: Tx1 were treated with the use of DBBM covered with soft tissue harvested from the palate; Tx2 were treated with DBBM alone; Tx3 were treated with DBBM covered with an absorbable collagen membrane and Tx4 were left untreated without any regenerative procedure. After 6 months of follow-up Tx1 and Tx3 that were treated with DBBM covered with a graft tissue or membrane presented a much bigger rate of bone regeneration than Tx2 group and the control group. The trial then concluded that alveolar preservation occurs more

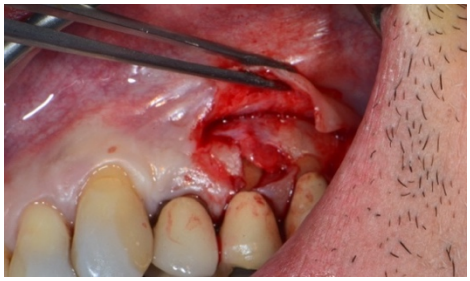
favorably where the bone graft material, the deproteinized bovine bone mineral, is covered by a contentive graft, as a soft tissue graft or a collagen barrier membrane.

CASE 5:

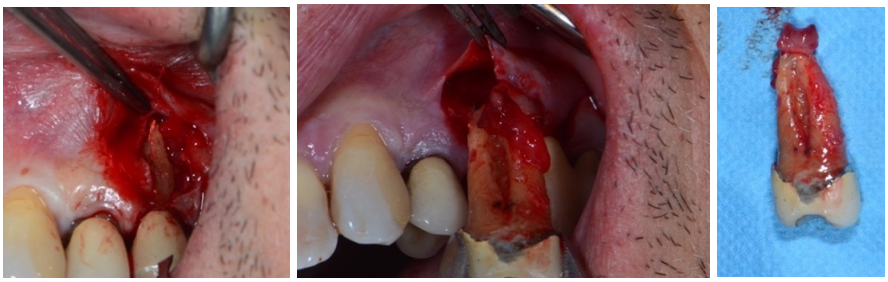
Same patient of case 1. 57 years old, non-smoking, with good oral hygiene, BOP of 18,75% and without any systemic condition.



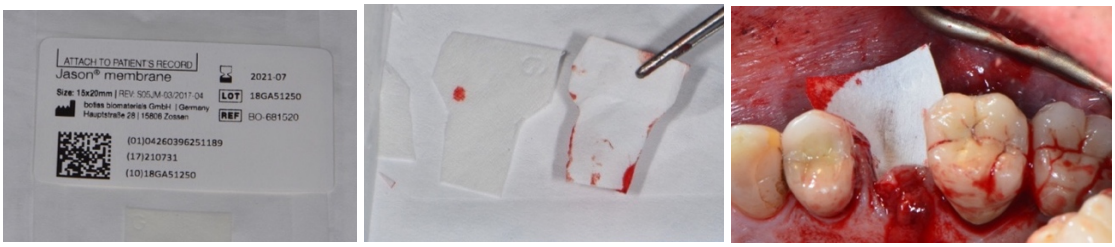
The patient presented a disto-vestibular PD of the 25 of 7 mm and a mesio-vestibular PD of the 26 of 9 mm.



Once the flap was raised it was very clear that the vestibular osseous defect was to big to regenerate assuring as well a good stability of the tooth so it was decided to extract the 25.

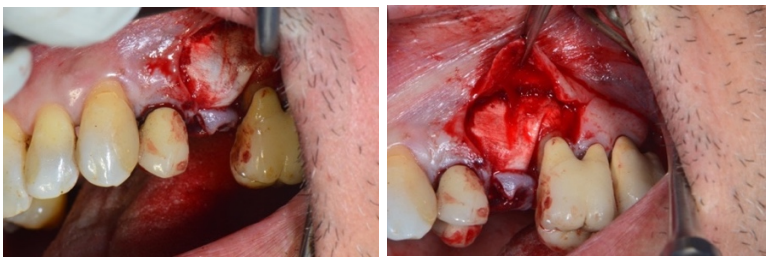


The surgical approach then aimed to the alveolar preservation. Once extracted the 25 a perfect cleaning of the alveolus was performed removing all the granulation tissue.



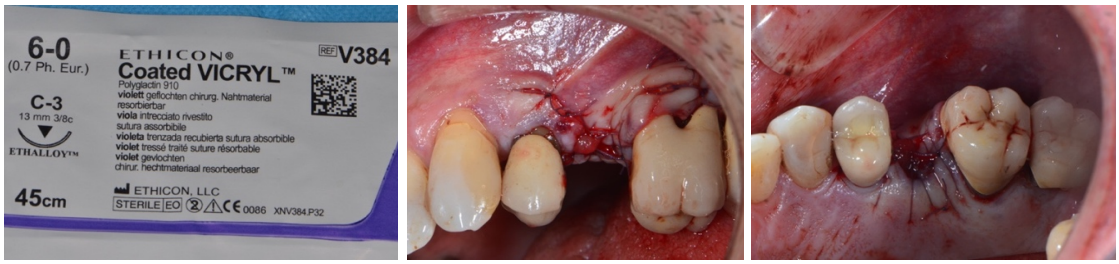
A resorbable collagen membrane was prepared in its shape in order to fit the defected site and positioned adhering to the elevated vestibular flap.

As grafting material the deproteinate bovine bone mineral was placed inside the alveolus.



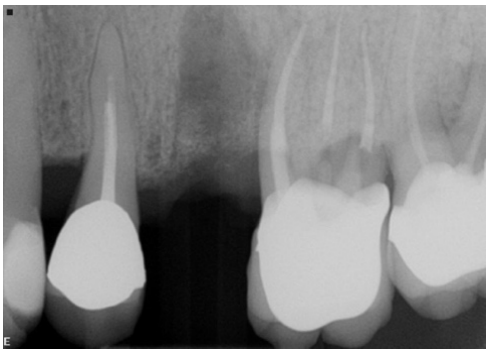
The barrier membrane was then perfectly repositioned over the grafting material assuring a perfect sealing and adherence to the defect. The precision of this step was crucial. Because of the big defected site, in order to obtain the stability of the used biomaterials, the resorbable membrane was positioned under the papillae and over the scaffold material. In GBR the membrane is in fact located in order to prevent the fibroblasts from colonizing the intraosseous defect while it is healing, allowing at the same time the osteoblasts to migrate into the bone wound filling it, thus initiating the bone

regeneration. The scaffold material under it, besides acting as osteoconductive element, prevented the membrane from collapsing leading to the failure of the regeneration. A collagen membrane was chosen because of it optimal properties: it has low immunogenicity, it is hemostatic, well-tolerated and being chemotactic it is able to attract and activate PDL and gingival fibroblasts, hence induce fibroblast DNA synthesis (45) potentially increasing tissue thickness. Besides, osteoblasts showed to better adhere to collagen membranes than any other membrane surface (49).



Of great importance was also the suturing procedure since an accurate sealing of the wound is needed in order to avoid membrane exposure and contamination with the consequent infection of the site and failure of the regeneration. The suture used is a 6-0 absorbable braded and coated wire of polyglactin with atraumatic triangular cutting edge.

After three weeks from the surgery the stitches were removed and the primary closure assessed.

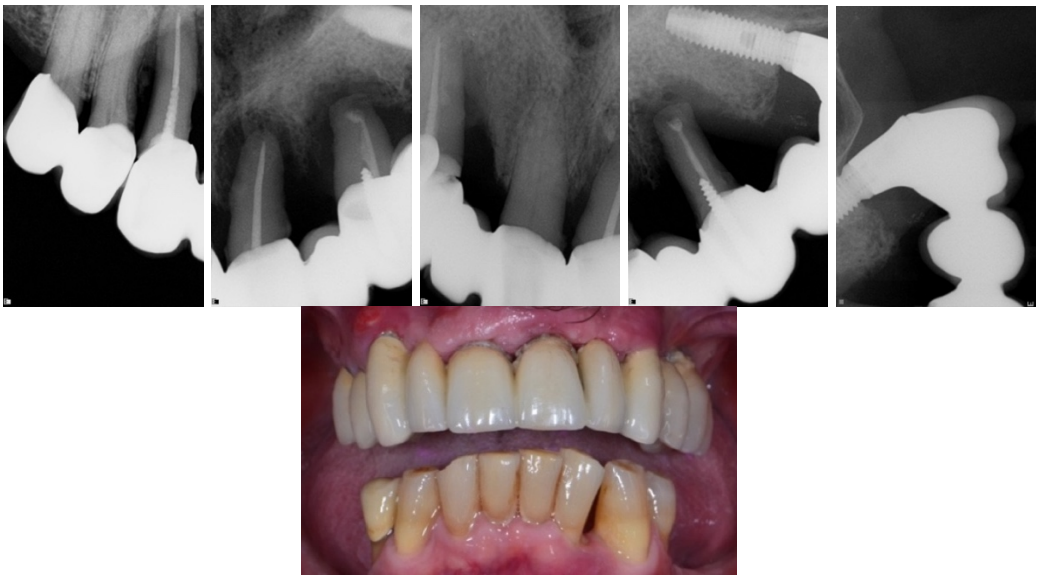


One month post-operative it is already visible the regenerative process occurring inside the post extraction site. In other five to seven months a further surgery with implant insertion is going to be considered.

Still talking about alveolar ridge preservation with DBBM (Bio-Oss ®) and resorbable collagen membrane, very interesting is the study performed on 30 patients with the aim of confirming and evidencing the efficacy of these biomaterials in the bone regeneration after dental extraction (80). This trial in fact concluded that an important difference was noticed in alveolar ridge bone height and width when comparing the group treated with DBBM and the resorbable collagen membrane and the control group left without any additional regenerative materials. These results suggest that the use of DBBM and the collagen membrane positively influence the alveolar regeneration.

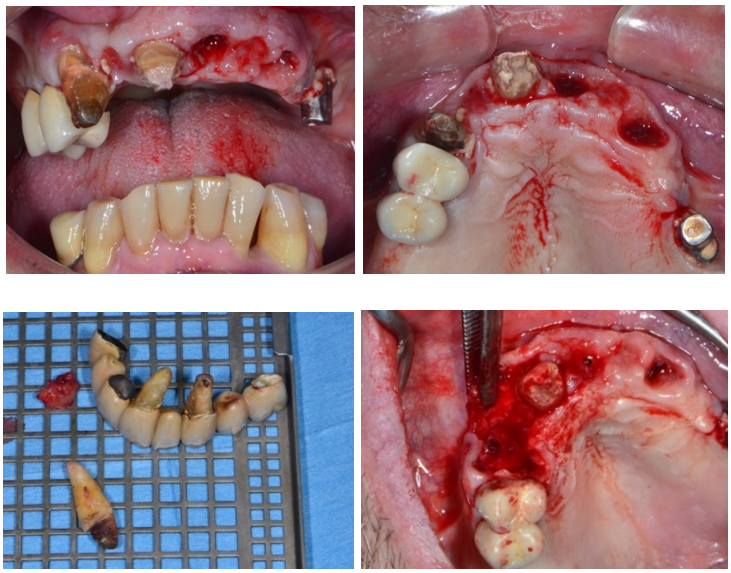
CASE 6:

64 years old patient, came to the first visit with vary bad oral hygiene, swelling of the gingival tissues and generalized bleeding on probing, grade III mobility of 13-12-21-23. He presented an old bridge from 13 to 26, having as pillars the 13-12-21-23 and the implant on the 25. Splinted crowns on the 15-14. 3-4 mm PD of the 15 and distal to the 14, 9 mm PD mesial to the 14. Physiologic PD of the implant.



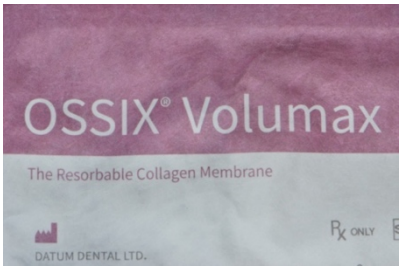
Because of the high mobility of the anterior teeth and the lack of periodontal support, once the active infection and inflammation of the soft tissues were stabilized, it was performed the removal of the bridge and the extraction of 13-12-21 and 23.

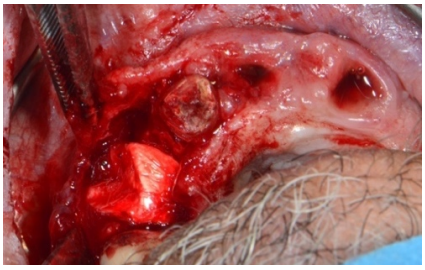
The regenerative surgery in order to preserve the upper alveolar ridge could then get started.



Once the alveoli got perfectly inspected and cleaned from any radicular rest, bony chip and inflammatory tissue, an horizontal transversal cut was performed in order to create a unique big space where to introduce the regenerative materials and start the alveolar ridge preservation.

As grafting material squares of compacted deproteinate bovine bone mineral were introduced with the multiple function of being a scaffold for osteoconduction, give structure to the ridge and sustain the barrier membrane. It was mainly used in the first quadrant being it the most compromised.

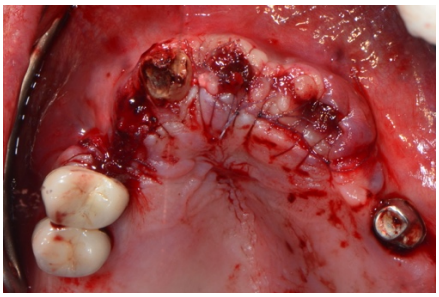
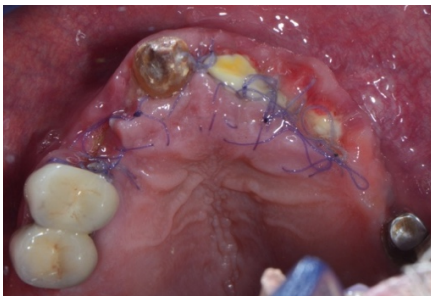
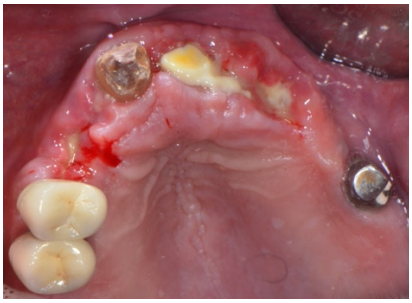




The barrier material chosen was a resorbable collagen membrane. A first portion was positioned over the grafting material and stabilized with three stitches.

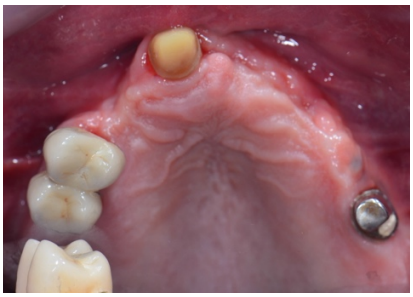


The rest of the alveolar ridge was filled with Bio-Oss, the same DBBM grafting material but in powder form. Another resorbable collagen membrane was positioned over it assuring the sealing.

A perfect primary closure was then of fundamental importance. The suture used for it is a 6-0 absorbable braded and coated wire of polyglactin with atraumatic triangular cutting edge.

Three weeks post-operative the stitches got removed but a little portion of membrane got exposed. Perfect hygiene control was taught to the patient that had to keep it controlled, beside weekly check-ups have been scheduled in order to assure that no infection could occur.



Three months post-operative the primary closure was completely achieved and the alveolar ridge perfectly preserved presenting a good bone width and height. The 11 achieved a good periodontal regeneration with a residual PD of 3 mm and it was reconstructed with composite and prepared for a future PFM crown. Meanwhile a provisory bridge was placed, using as pillars the reconstructed 11 and the implant on the 25.

CONCLUSION

This work focused on highlighting the importance of the regenerative dental medicine, presenting the main biomaterials used in its application in order to achieve periodontal regeneration, together with their indications in different clinical situations.

- For periodontal regeneration to occur regenerative dentistry uses scaffolds alone or together with growth factors and/or barrier membranes.

  Regarding the autograft, it has the fundamental osteogenesis, osteoinduction and osteoconduction properties, besides it does not have the risk to be rejected from the recipient and so to develop immunological reactions as well as to transmit any disease to it. For this reason autograft is considered the gold standard for regenerative medicine.

  About allografts, they are available as fresh/fresh-frozen (FFBA), freeze-dried (FDBA), or demineralized and freeze-dried bone allograft (DFDBA). Differently from autografts, allogenic bone grafts are abundantly and easily available and do not cause any morbidity at the harvest site. Although these advantages, they are not frequently chosen as regenerative material since they do not provide osteogenic inputs as well as being weakly osteoinductive, potentially infective and expensive.

  Xenografts developed in order to overcome many of the disadvantages of autografts and allografts. They are considered the most indicated choice for children which might be

physically too small to receive transplantations from an adult donor. Moreover they do not cause any systemic or local immune response and it has been calculated that the risk of pathologic transmission is 1 in 10.

Beside the use of scaffold materials, it was also concluded that in order to achieve an higher rate of periodontal regeneration there is the need of additional enhancing stimuli. Among these polypeptide growth factors have been introduced: the platelet-derived-growth factor (PDGF), the enamel matrix derivatives (EMD), insulin-like growth factor (IGF), bone morphogenic proteins (BMPs) and the osteogenin.

PDGF is able to stimulate the migration and proliferation of the pool of osteogenic cells into the injury site populating the scaffold, by acting both as chemotactic and mitogen agent. Subsequently these progenitor cells differentiate into osteoblasts and/or chondrocytes under direction of the BMP.

EMD play a relevant role in wound healing mediating bone remodeling and favoring angiogenic activity and soft tissue regeneration. This happens because EMD has been shown to regulate many cells activity as well as to mediate the expression of growth and transcription factors, ECM components, cytokines and others.

The third category of regenerative biomaterials considered being of fundamental importance are the barrier membranes. During the regenerative process in fact, membranes prevent epithelial cells, granulation end fibrous tissue from entering into the intended bone- and PDL-regenerating space, as well as allowing the osteoprogenitor bone cells, osteoblastic cells and cells responsible for the new vascularization, to enter the defected site, mediating at the same time the diffusion of growth factors, nutrients, cytokines and other bioactive elements.

- As scaffold materials are used autogenous bone grafts, allografts and xenografts and we can conclude that currently there is not an ideal graft material for periodontal regeneration, they all have advantages and limitations. It can be assessed though that autograft is so far defined as the material of choice followed by allografts and xenografts. Among the allografts we can mainly distinguish between FDBA and DFDBA and their main difference is that FDBA serves as a scaffold favorizing an osteoconductive surface whereas DFDBA, besides this, is also considered osteoinductive since it even provides a source of osteoinductive factors.

  Moreover it can be concluded that the use of FDBA in the periodontal treatment, especially that of furcation defects, is more effective if combined together with autogenous bone rather than FDBA used alone. In addition, DFDBA, thanks to its osteoinductive properties, is now considered being the grafting material of choice when compared to other allografts such as FDBA and to xenografts. Finally it can be assessed that the use of cortical DFDBA would lead to a bigger bone fill in comparison to the cancellous DFDBA.

- We can distinguish among non-resorbable membranes and resorbable membranes.

  Non-resorbable membranes have the disadvantage of a second surgery, besides they have the risk of being contaminated if a perfect primary closure over it is not provided. To facilitate its removal in case of infection, besides being safer thanks to is surface structure, dense-PTFE has been introduced as substitute of the e-PTFE. It was also concluded that in order to avoid the membrane to collapse inward the defect site, the solution was the combination together with a grafting material; moreover the more rigid titanium-reinforced e-PTFE (Ti-e-PTFE) or the titanium mesh have been introduced.

  Resorbable membranes, natural and synthetic, overcame the limitations given from the need of a second surgery but have the disadvantage of being unpredictable since they can be reabsorbed previously than needed limiting the regeneration rate.

It was then concluded that there is not a better choice between non-resorbable and resorbable membranes, the final considerations are in fact different according to the surgical site in question.

For class II furcation defects and for the treatment of intrabony periodontal defects there are no statistically relevant differences in periodontal regeneration between the two membranes, both of them give satisfactory clinical outcomes. Same conclusion also for the ridge preservation procedures.

Class III furcation defects did not positively respond to GTR and both the membrane types failed in its regeneration.

- The final conclusions of this work are about the choice of the biomaterials to use with respect to the specific bone defect morphology and extension. Besides these general indications, it was assessed that each clinical situation has to be taken into account as a single case and be customized as needed.

  Regarding the use of EDM, it may be inferred that for intra-bony defects and for recession coverage the clinical outcomes when using EDM are significantly better than the results with traditional control treatments, but similar to the use of resorbable GTR.

  Regarding the treatment of furcations, in the horizontal defects the use of EDM give improved results in depth reduction compared with the use of resorbable membranes.

For vertical intrabony defects the first question was whether to use EMD or rather a barrier membrane. Clinical studies failed to demonstrate more efficacy of one biomaterial over the other in this type of bone defect but for sure the surgical management and the risk of appearance of complications with GTR resulted being indicative in the choice of the material. One may conclude then that the use of EMD in the regeneration of vertical intra-osseous defects is the safest option. Moreover, a better clinical outcome in terms of CAL gain and PD

and REC reduction is obtained when combining EMD together with bone graft rather than using the EMD alone.

For non-contained intra-bony defects it was concluded that EMD is not the best choice because of its lack of self-structure. If used, better results are obtained if combined with GTR. For these types of defects then, it can be concluded that the predictability of bone regeneration mainly depends on the presence of barrier membranes while the combination of DBBM and/or EMD do not specifically influence the regeneration provided by the GBR. This point is actually still a matter of debate since new regenerative surgical approaches are currently focusing their attention on the technique rather than the chosen materials. We can finally assess that a more conservative surgical approach is acquiring increasing relevance over the use of a barrier membrane.

Regarding the alveolar ridge preservation, many grafting materials have been studied and used and it can be now concluded that the deproteinized bovine bone mineral (DBBM) is currently the most efficacious and used biomaterial for ARP.

Moreover we can assess that alveolar preservation occurs more favorably where the bone graft material, the deproteinized bovine bone mineral, is covered by a contentive graft as a soft tissue graft or a collagen barrier membrane.

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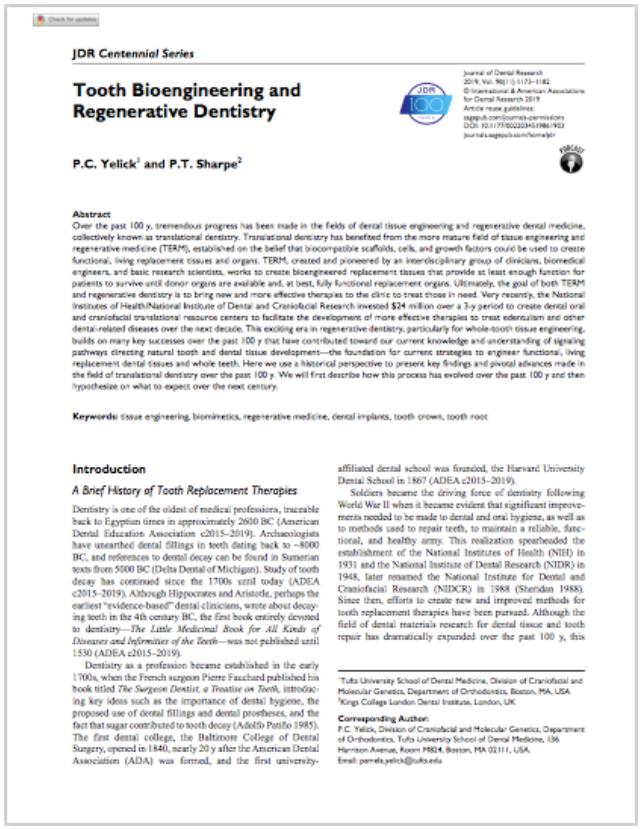
ANNEXES

Article 1



JDR Centennial Series

Tooth Bioengineering and Regenerative Dentistry

P.C. Yelick[1] and P.T. Sharpe[2]

Abstract

Over the past 100 y, tremendous progress has been made in the fields of dental tissue engineering and regenerative dental medicine, collectively known as translational dentistry. Translational dentistry has benefited from the more mature field of tissue engineering and regenerative medicine (TERM), established on the belief that biocompatible scaffolds, cells, and growth factors could be used to create functional, living replacement tissues and organs. TERM, created and pioneered by an interdisciplinary group of clinicians, biomedical engineers, and basic research scientists, works to create bioengineered replacement tissues that provide at least enough function for patients to survive until donor organs are available and, at best, fully functional replacement organs. Ultimately, the goal of both TERM and regenerative dentistry is to bring new and more effective therapies to the clinic to treat those in need. Very recently, the National Institutes of Health/National Institute of Dental and Craniofacial Research invested $24 million over a 3-y period to create dental oral and craniofacial translational research centers to facilitate the development of more effective therapies to treat edentulism and other dental-related diseases over the next decade. This exciting era in regenerative dentistry, particularly for whole-tooth tissue engineering, builds on many key successes over the past 100 y that have contributed toward our current knowledge and understanding of signaling pathways directing natural tooth and dental tissue development—the foundation for current strategies to engineer functional, living replacement dental tissues and whole teeth. Here we use a historical perspective to present key findings and pivotal advances made in the field of translational dentistry over the past 100 y. We will first describe how this process has evolved over the past 100 y and then hypothesize on what to expect over the next century.

Keywords: tissue engineering, biomimetics, regenerative medicine, dental implants, tooth crown, tooth root

Introduction

A Brief History of Tooth Replacement Therapies

Dentistry is one of the oldest of medical professions, traceable back to Egyptian times in approximately 2600 BC (American Dental Education Association c2015–2019). Archaeologists have unearthed dental fillings in teeth dating back to ~8000 BC, and references to dental decay can be found in Sumerian texts from 5000 BC (Delta Dental of Michigan). Study of tooth decay has continued since the 1700s until today (ADEA c2015–2019). Although Hippocrates and Aristotle, perhaps the earliest "evidence-based" dental clinicians, wrote about decaying teeth in the 4th century BC, the first book entirely devoted to dentistry—*The Little Medicinal Book for All Kinds of Diseases and Infirmities of the Teeth*—was not published until 1530 (ADEA c2015–2019).

Dentistry as a profession became established in the early 1700s, when the French surgeon Pierre Fauchard published his book titled *The Surgeon Dentist, a Treatise on Teeth*, introducing key ideas such as the importance of dental hygiene, the proposed use of dental fillings and dental prostheses, and the fact that sugar contributed to tooth decay (Adolfo Potito 1985). The first dental college, the Baltimore College of Dental Surgery, opened in 1840, nearly 20 y after the American Dental Association (ADA) was formed, and the first university-affiliated dental school was founded, the Harvard University Dental School in 1867 (ADEA c2015–2019).

Soldiers became the driving force of dentistry following World War II when it became evident that significant improvements needed to be made to dental and oral hygiene, as well as to methods used to repair teeth, to maintain a reliable, functional, and healthy army. This realization spearheaded the establishment of the National Institutes of Health (NIH) in 1931 and the National Institute of Dental Research (NIDR) in 1948, later renamed the National Institute for Dental and Craniofacial Research (NIDCR) in 1988 (Sheridan 1988). Since then, efforts to create new and improved methods for tooth replacement therapies have been pursued. Although the field of dental materials research for dental tissue and tooth repair has dramatically expanded over the past 100 y, this

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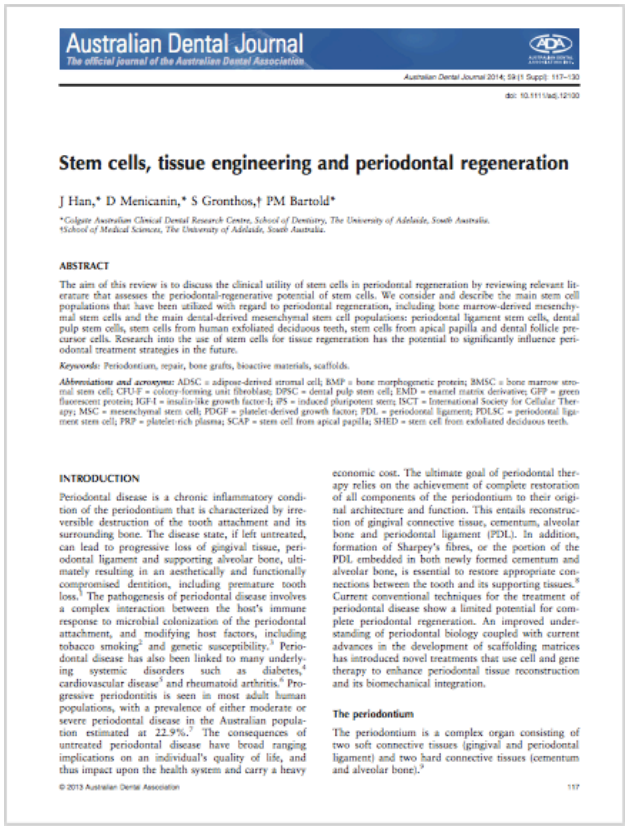
Article 2



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Stem cells, tissue engineering and periodontal regeneration

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ABSTRACT

The aim of this review is to discuss the clinical utility of stem cells in periodontal regeneration by reviewing relevant literature that assesses the periodontal-regenerative potential of stem cells. We consider and describe the main stem cell populations that have been utilized with regard to periodontal regeneration, including bone marrow-derived mesenchymal stem cells and the main dental-derived mesenchymal stem cell populations: periodontal ligament stem cells, dental pulp stem cells, stem cells from human exfoliated deciduous teeth, stem cells from apical papilla and dental follicle precursor cells. Research into the use of stem cells for tissue regeneration has the potential to significantly influence periodontal treatment strategies in the future.

Keywords: Periodontium, repair, bone grafts, bioactive materials, scaffolds.

Abbreviations and acronyms: ADSC = adipose-derived stromal cell; BMP = bone morphogenetic protein; BMSC = bone marrow stromal stem cell; CFU-F = colony-forming unit fibroblast; DPSC = dental pulp stem cell; EMD = enamel matrix derivative; GFP = green fluorescent protein; IGF-I = insulin-like growth factor-I; iPS = induced pluripotent stem; ISCT = International Society for Cellular Therapy; MSC = mesenchymal stem cell; PDGF = platelet-derived growth factor; PDL = periodontal ligament; PDLSC = periodontal ligament stem cell; PRP = platelet-rich plasma; SCAP = stem cell from apical papilla; SHED = stem cell from exfoliated deciduous teeth.

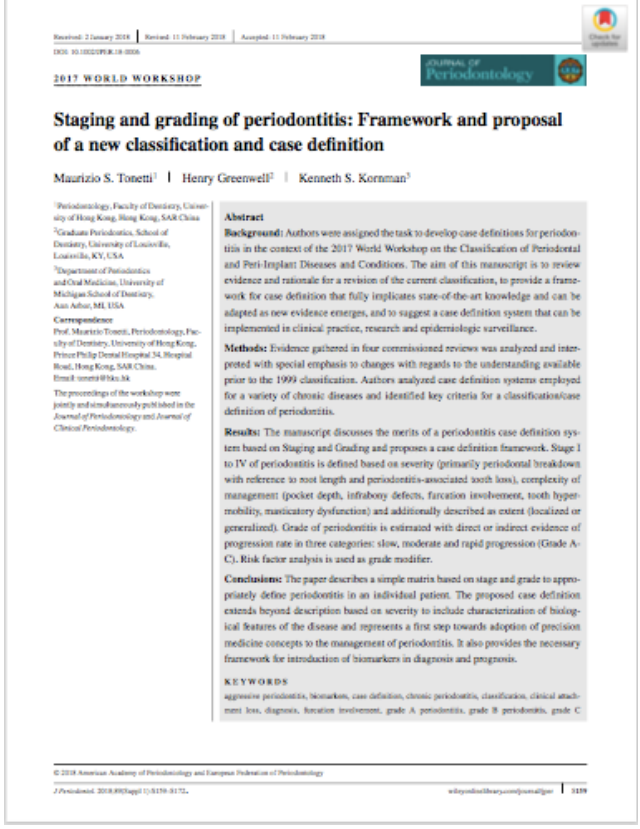
INTRODUCTION

Periodontal disease is a chronic inflammatory condition of the periodontium that is characterized by irreversible destruction of the tooth attachment and its surrounding bone. The disease state, if left untreated, can lead to progressive loss of gingival tissue, periodontal ligament and supporting alveolar bone, ultimately resulting in an aesthetically and functionally compromised dentition, including premature tooth loss.[1] The pathogenesis of periodontal disease involves a complex interaction between the host's immune response to microbial colonization of the periodontal attachment, and modifying host factors, including tobacco smoking[2] and genetic susceptibility.[3] Periodontal disease has also been linked to many underlying systemic disorders such as diabetes,[4] cardiovascular disease[5] and rheumatoid arthritis.[6] Progressive periodontitis is seen in most adult human populations, with a prevalence of either moderate or severe periodontal disease in the Australian population estimated at 22.9%.[7] The consequences of untreated periodontal disease have broad ranging implications on an individual's quality of life, and thus impact upon the health system and carry a heavy economic cost. The ultimate goal of periodontal therapy relies on the achievement of complete restoration of all components of the periodontium to their original architecture and function. This entails reconstruction of gingival connective tissue, cementum, alveolar bone and periodontal ligament (PDL). In addition, formation of Sharpey's fibres, or the portion of the PDL embedded in both newly formed cementum and alveolar bone, is essential to restore appropriate connections between the tooth and its supporting tissues.[8] Current conventional techniques for the treatment of periodontal disease show a limited potential for complete periodontal regeneration. An improved understanding of periodontal biology coupled with current advances in the development of scaffolding matrices has introduced novel treatments that use cell and gene therapy to enhance periodontal tissue reconstruction and its biomechanical integration.

The periodontium

The periodontium is a complex organ consisting of two soft connective tissues (gingival and periodontal ligament) and two hard connective tissues (cementum and alveolar bone).[9]

Article 3



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2017 WORLD WORKSHOP

JOURNAL OF Periodontology

Staging and grading of periodontitis: Framework and proposal of a new classification and case definition

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The proceedings of the workshop were jointly and simultaneously published in the *Journal of Periodontology* and *Journal of Clinical Periodontology*.

Abstract

Background: Authors were assigned the task to develop case definitions for periodontitis in the context of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. The aim of this manuscript is to review evidence and rationale for a revision of the current classification, to provide a framework for case definition that fully implicates state-of-the-art knowledge and can be adapted as new evidence emerges, and to suggest a case definition system that can be implemented in clinical practice, research and epidemiologic surveillance.

Methods: Evidence gathered in four commissioned reviews was analyzed and interpreted with special emphasis to changes with regards to the understanding available prior to the 1999 classification. Authors analyzed case definition systems employed for a variety of chronic diseases and identified key criteria for a classification/case definition of periodontitis.

Results: The manuscript discusses the merits of a periodontitis case definition system based on Staging and Grading and proposes a case definition framework. Stage I to IV of periodontitis is defined based on severity (primarily periodontal breakdown with reference to root length and periodontitis-associated tooth loss), complexity of management (pocket depth, infrabony defects, furcation involvement, tooth hypermobility, masticatory dysfunction) and additionally described as extent (localized or generalized). Grade of periodontitis is estimated with direct or indirect evidence of progression rate in three categories: slow, moderate and rapid progression (Grade A-C). Risk factor analysis is used as grade modifier.

Conclusions: The paper describes a simple matrix based on stage and grade to appropriately define periodontitis in an individual patient. The proposed case definition extends beyond description based on severity to include characterization of biological features of the disease and represents a first step towards adoption of precision medicine concepts to the management of periodontitis. It also provides the necessary framework for introduction of biomarkers in diagnosis and prognosis.

KEYWORDS
aggressive periodontitis, biomarkers, case definition, chronic periodontitis, classification, clinical attachment loss, diagnosis, furcation involvement, grade A periodontitis, grade B periodontitis, grade C

Article 4

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2017 WORLD WORKSHOP

JOURNAL OF Periodontology

A new classification scheme for periodontal and peri-implant diseases and conditions – Introduction and key changes from the 1999 classification

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The proceedings of the workshop were jointly and simultaneously published in the *Journal of Periodontology* and *Journal of Clinical Periodontology*.

Abstract

A classification scheme for periodontal and peri-implant diseases and conditions is necessary for clinicians to properly diagnose and treat patients as well as for scientists to investigate etiology, pathogenesis, natural history, and treatment of the diseases and conditions. This paper summarizes the proceedings of the World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. The workshop was co-sponsored by the American Academy of Periodontology (AAP) and the European Federation of Periodontology (EFP) and included expert participants from all over the world. Planning for the conference, which was held in Chicago on November 9 to 11, 2017, began in early 2015.

An organizing committee from the AAP and EFP commissioned 19 review papers and four consensus reports covering relevant areas in periodontology and implant dentistry. The authors were charged with updating the 1999 classification of periodontal diseases and conditions[1] and developing a similar scheme for peri-implant diseases and conditions. Reviewers and workgroups were also asked to establish pertinent case definitions and to provide diagnostic criteria to aid clinicians in the use of the new classification. All findings and recommendations of the workshop were agreed to by consensus.

Article 5

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REVIEW ARTICLE

WILEY Periodontology 2000

Role of occlusion in periodontal disease

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1 | INTRODUCTION

Although more than a century has elapsed since the first publication of Karolyi,[1] which implicated the forces of occlusion in the behavior of periodontal tissues, deep-rooted controversy about the role of occlusion in the development/progression of marginal inflammatory infectious periodontal disease—gingivitis and periodontitis—still remains. Some studies propose that traumatogenic occlusal forces are related to the initiation and/or progression of periodontal disease.[2-8] Conversely, other studies find no association between trauma from occlusion and periodontal disease.[9,10] These contradictory arguments have led to widespread disagreement in the literature in relation to the role of occlusion in the pathogenesis of periodontal disease, inspiring much Latin American research.[3,8,11-20] Accordingly, a detailed and comprehensive presentation of important clinical and scientific evidence to shed light on the role of occlusion in chronic periodontal disease is required.

2 | A HISTORICAL PERSPECTIVE

The role of trauma from occlusion in the etiology of periodontal disease has been discussed since the early 1900s. Historically, the first evidence for a role of trauma from occlusion in periodontal disease came from research performed in animals[21] and human cadavers.[5] These studies suggested that trauma from occlusion was related to the development of infrabony pockets, possibly consequent to ischemia of periodontal ligament and depletion in gingival blood supply.[21]

Further research[2] suggested that trauma from occlusion resulted in disorganization of periodontal tissues, impairing their normal repair function. Besides that, the alterations produced by trauma from occlusion might contribute to the deepening of periodontal pockets, favoring the spread of inflammation to neighboring tissues.[2,22]

By this time, other studies performed in animals showed no causative association between trauma from occlusion and periodontal disease, indicating little to no correlation between trauma from occlusion and periodontal disease.[23-25] Bhaskar and Orban[26] failed to observe the development of gingivitis or periodontitis in animals subjected to trauma from occlusion but not affected by plaque-related chronic periodontitis. Polson[27] and coworkers[9,28] did not find a positive correlation between occlusal trauma and gingival inflammation or pocket development.

However, these studies, although performed under controlled experimental conditions, used animal models, which do not deliver reliable data on the role of occlusion in humans because teeth in animals are designed for defense and attack, as well as for mastication, and respond very well to different occlusal stimuli. In addition, the envelope of mandibular motion in animals is quite different from that in humans, with no opposing directions resulting from the lateral distribution of occlusal forces. This is probably one of the reasons why jiggling forces are needed in animals to achieve a periodontal injury compatible with that induced by traumatogenic occlusion in humans, with a particular exception for primates.[4,9,28-60]

During the 1960s and early 1970s, Glickman[7,61] and coworkers[9,9,17,18,62-65] proposed that occlusal trauma acted as a co-destructive zone, influencing the spread of inflammatory gingival exudate directly to the periodontal ligament, eliciting a combined lesion of trauma from occlusion and periodontitis. The final result could be the development of infrabony periodontal pockets, as suggested by other studies,[15,22,25] indicating an association of trauma from occlusion with periodontitis.

However, the possible coexistence of trauma from occlusion and inflammation without the formation of infrabony pockets cannot be ruled out, meaning that these conditions are not pathognomonic of trauma from occlusion.[5] Moreover, suprabony pockets and horizontal bone loss could result from the association between trauma from occlusion and inflammation, under certain circumstances yet to be determined.

The type of periodontal pocket that develops in response to the association between trauma from occlusion and chronic periodontitis

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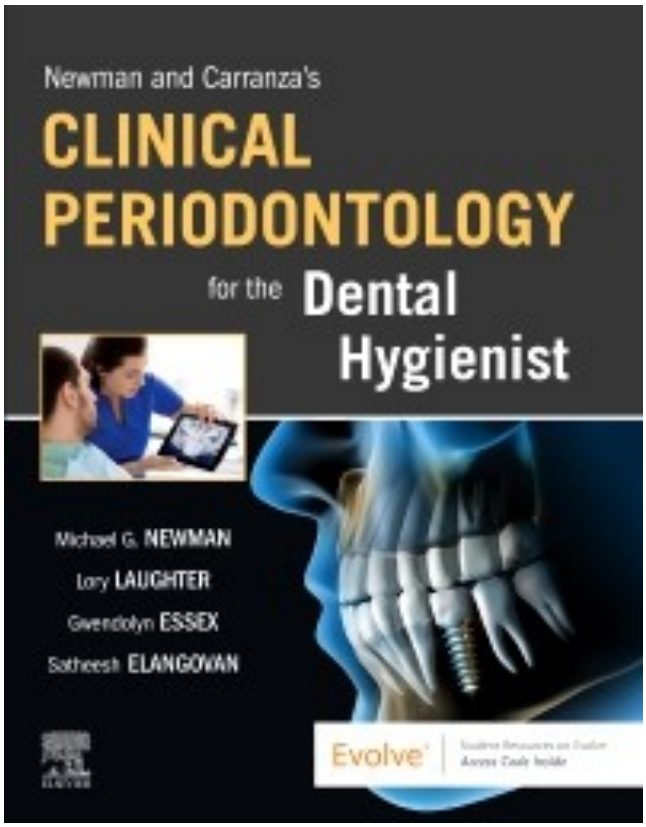
Article 6



Article 7

The Infrabony Pocket: Classification and Treatment†

by HENRY M. GOLDMAN, D.M.D.* AND D. WALTER COHEN, D.D.S.**

IN recent years, the principal clinical lesion of periodontal disease, the pocket, has been studied clinically, radiographically, and histopathologically. As a result of these investigations it became apparent that the pocket had to be classified on the basis of the location of the bottom of the pocket in its relationship to the alveolar crest. Arising from these studies came the classification of pockets: (1) suprabony or supracrestal and (2) infrabony or subcrestal. The suprabony pocket is defined as a pathological sulcus where the base of the pocket is coronal or occlusal to the alveolar crest, while the infrabony is defined as a pathological sulcus where the bottom of the pocket is apical to the alveolar crest. The suprabony pocket was further subdivided into the gingival or pseudopocket and the periodontal pocket. This classification had merit not only from a teaching standpoint but also on a therapeutic basis.

Much attention has been focused on the infrabony type of pocket in recent publications and this lesion has been described as amenable to either the new attachment procedure or osseous surgery for its eradication. It became obvious to us from our observations of clinical as well as human skull material that a classification of the infrabony pocket was necessary not only for academic purposes but also to serve as a rational basis for the selection of a method of treatment.

The proposed classification of the infrabony pocket is on a morphologic basis and is dependent on the location and number of osseous walls remaining about the pocket. Much of this material studied was from human skulls where the gingivae and other soft tissues were intact. The location of the bottom of the pocket was established, the material radiographed, and then the soft tissue was removed. The remainder of the material was taken from clinical cases under treatment.

The first group of infrabony pockets described have three osseous walls. These trough-like defects are commonly observed in the interdental areas where one finds an intact proximal wall as well as the buccal and lingual walls of the alveolar process. Some of these lesions may be shallow with a broad orifice to the osseous part of the pocket while others may be narrow and deep. Three wall infrabony pockets are occasionally observed on the lingual surfaces of maxillary and mandibular teeth where the lingual plate is intact as well as both proximal walls. Less frequently noted are infrabony pockets located on the buccal surfaces of maxillary and mandibular posterior teeth. It is not uncommon to find them extending around the tooth to involve 2 or sometimes 3 surfaces. When the infrabony pocket is circumferential and involves the four surfaces of the tooth, it actually has four osseous walls (buccal, lingual, mesial, distal). This occurs infrequently.

The determination of the position as well as the number of osseous walls is of concern to the clinician during his examination procedures.

The radiograph can be of great aid in demonstrating the presence of buccal and lingual and proximal walls in a pocket occurring in the interdental area. Placing a radiopaque object such as a gutta percha point, a periodontal probe, or Hirschfeld

†Presented at the Academy of Periodontology Meeting in Miami, Fla. on October 31, 1957.

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Article 8

The Diagnosis and Management of Vertical Bony Defects

John F. Prichard

Accepted for publication 28 April 1982

MARGINAL PERIODONTITIS and pulpal disease often cause similar-appearing lesions in the periodontium. Successful therapy depends on correct diagnosis, which is sometimes difficult. Some bony defects caused by pulpal disease require surgical debridement in addition to standard endodontic therapy.

With one exception three-walled intrabony periodontal defects discussed in this report were managed by surgical debridement without any type of implant or graft. Long-term observation is required to determine the value of techniques used in the treatment of intrabony periodontal defects.

The diagnosis and management of discrete areas of advanced vertical bone resorption often pose problems. Vertical bony defects are caused by both periodontal and pulpal infection, and the radiographic image does not always distinguish between the two disease processes. The objective of treatment is the formation of new cementum and a new connective tissue attachment. Failure to accomplish this goal will usually result in loss of the affected teeth. There is evidence that bone will repair a defect with a long junctional epithelial adhesion instead of a connective tissue attachment, but there is no evidence that this provides a stable long-term result.

THE PERIODONTAL-PULPAL QUANDARY

Lesions in the periodontium often present difficult diagnostic problems, and what is called "combined periodontal-pulpal disease" may be the most difficult diagnostic problem in dentistry. The physical appearance and symptoms of inflammation, swelling, and suppuration are similar for infections of both periodontal and pulpal origin (Fig. 1). The radiographic appearance of bone resorption in the marginal and furcal region can be caused by infection originating in either the periodontium or the pulp (Fig. 2).[1] When there is pain and swelling in the periodontium, pulpal disease is seldom suspected as the cause unless there is an obvious open cavity in a tooth or radiographic evidence of periapical pathosis. However, there is also the possibility that marginal periodontitis and pulpal inflammation are both present. Historically, periodontal disease has always been prevalent. However, the widespread incidence of pulpal disease is a recent development. Today the use of modern high-speed handpieces and full coverage coronal restorations has been added to accidental trauma and dental caries as common causes of pulpal disease.

Most periodontists and endodontists call any pulpal lesion "combined periodontal-pulpal disease" if bone resorption is evident radiographically in either the furcal or crestal region. They also apply the combined disease designation to cases in which bone resorption from a periodontal lesion reaches the apical region of the affected tooth. However, the pulpal lesion does not change its character and become marginal periodontitis when it forms a sinus tract through the gingival crevice (Fig. 3) and the pulp does not immediately or inevitably become infected when bone resorption from marginal periodontitis reaches the apex (Figs. 4–6). Failure to understand this has caused great confusion along with frequent incorrect diagnosis and treatment. Pulpal lesions sometimes require surgical intervention, and the operation is sometimes performed by a periodontist. However, this does not change the character of the lesion to marginal periodontitis. Root resection is a combination procedure of exodontia and endodontia; it may be carried out because of either periodontal or pulpal disease.[2]

The Effect of Pulpal Lesions on the Periodontium

Inflamed or necrotic pulps elaborate noxious products that can invade the periodontium through either apical, lateral, or accessory canals and cause resorption of contiguous bone and drainage of an exudate. Bone resorption may be in the furcal and intraradicular region, or it may occur along the lateral surface of the root (Fig. 7). Drainage may be through the gingival crevice, which simulates periodontitis. A sinus tract may open in the gingival crevice, the attached gingiva, a gingival papilla, or the alveolar mucosa. Abnormal tooth mobility may

Article 9

Anatomical Considerations in Periodontal Surgery

by

MICHAEL A. CLARKE, D.D.S., M.S.
KENNETH W. BUELTMANN, D.D.S., M.S.

A VARIETY OF SURGICAL PROCEDURES have been devised for the treatment of periodontal disease and associated abnormalities. Such procedures may be accompanied by certain operative hazards related to the presence and location of important anatomic structures. Limits may be imposed on the scope of periodontal therapy by local and individual anatomical features. Effective planning and execution of surgical therapy is based on a clear knowledge of the anatomy of the superficial and deep structures encountered during surgical intervention.

Surgical anatomy may be defined in part as the knowledge of anatomical facts which have local significance in relation to surgical therapy. Primary emphasis is placed on an understanding and awareness of important structures that may be encountered during surgery or which place limits on the nature of the planned surgery, rather than on a detailed and precise knowledge of systematic anatomy.

It is the purpose of this paper to discuss anatomical considerations pertinent to periodontal surgery. A systematic descriptive review of structures that may be encountered by periodontal surgeons will be presented. This will be followed by a detailed description of surgical anatomy in relation to periodontal therapy. Illustrations of important anatomic structures as displayed by conventional periodontal surgical entry procedures will be provided. The significance of such structures in relation to treatment planning, surgical techniques, and the avoidance of operative hazards will be discussed.

REVIEW OF THE LITERATURE

Very few articles concerning surgical anatomy in relation to periodontal therapy are available in the literature. Rosenberg[1] discussed vestibular alterations in periodontics, including a brief consideration of the muscles of facial expression which might be encountered by the periodontal surgeon. Precautions and hazards in periodontal surgery were described by Bradin.[2] Key anatomical features and their significance were listed, though the bulk of the article was concerned with therapeutic techniques and general patient management. Veal[3] discussed exposure of neurovascular bundles during periodontal surgery, including a clinical photograph illustrating surgical exposure of the mental foramen and nerve.

Heslop[4] discussed surgical anatomy of the jaws in relation to injury, particular diseases, and surgical intervention. Though written for the oral or maxillofacial surgeon, the article contained much useful information for the periodontist.

Articles concerning the pathways by which dental infections may spread are useful in their descriptions of anatomic spaces. Anatomic considerations in diagnosis and treatment of odontogenic infections were listed by Laskin[5] who emphasized the importance of an understanding of regional anatomy in proper diagnosis and treatment planning. He indicated that, from the standpoint of the clinician, certain surgical spaces could be described that were different from the fascial spaces described by anatomists. Spilka[6] described pathways of dental infections, including discussions of pertinent anatomic spaces.

Clinical textbooks provide varying degrees of anatomical information. Prichard[7] includes a concise description of normal and pathologic osseous anatomy related to periodontal surgery. Goldman and Cohen[8] briefly consider surgical anatomy in relation to periodontics. Kruger,[9] in his *Textbook of Oral Surgery*, discusses fascial planes and anatomic spaces as pathways for the spread of infection. Anatomical considerations are well illustrated in his descriptions of surgical techniques employed in the correction of hard and soft tissue abnormalities.

MATERIALS AND METHODS

Basic information concerning systematic anatomy was obtained by a review of standard textbooks of anatomy (Gray,[10] Netter,[11] Pernkopf,[12] Cunningham/Romanes[13]). Similar information concerning surgical anatomy in the head and neck regions was obtained by a review of appropriate textbooks (Hollinshead,[14] Shapiro,[15] Sicher and DuBrul[16]). Material discussed in the preceding review of the literature provided additional background information. Original anatomic drawings were prepared by the authors to illustrate important structural relationships.

Surgical dissections to display anatomic features of significance were performed on fresh and prepared specimens. Surgical entries, utilizing conventional periodontal surgical techniques, were employed wherever possible. Photographic documentation was accomplished with a clinical intraoral camera system.

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Article 10

10.5005/jp-journals-10063-0028

REVIEW ARTICLE

Periodontal Osseous Defects: A Review

[1]Bharath Chandra GNR, [2]KL Vandana

ABSTRACT

Periodontitis is an inflammatory process affecting the periodontal tissues caused by multi-factorial origin. Among all the characteristic signs of periodontal disease, loss of support from alveolar boneis the one which usually represents theanatomical sequela to the progression of periodontitis apically.The bone loss which is induced by periodontitis occur either single or in different combination forms. The identification of these osseous defects on surgical exposure of bone is clinically challenging as the osseous and it becomes imperative for a clinician to understand these defects and categorize them well to have better therapeutic approaches. Intimate knowledge of all these periodontal osseous defects associated with periodontal disease is essential. So this review is aimed at classification and deep insight which will be helpful for proper diagnosis and treatment of periodontal osseous defects.

Keywords: Alveolar process, Bone resorption, Periodontitis.

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INTRODUCTION

Periodontium is composed of both soft and hard tissues in which alveolar bone is the part which forms and also supports the teeth in both maxilla and mandible. Alveolar bone formation occurs as the eruption of tooth takes place in order to facilitate the osseous attachments to the periodontal ligament and disappears once the tooth is lost.[1]

Alveolar bone has its embryological origin from the initial condensation of ecto-mesenchyme around the early tooth germ. The alveolar process house the teeth and exist as long as teeth are present in it. The sharpey's fibres are embedded in the alveolar bone proper which is the compact bone, compromised of oral and buccal cortical plates and the cancellous bone located between them.[1]

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The bone loss in periodontal disease occurs at local sites, but it is regulated by both systemic and local factors. Bone resorption is probably the most critical factor in periodontal attachment loss leading to eventual tooth loss.[2] Radiographically it is diagnosed by evidence of "bone loss" around the tooth. Normally the crest of alveolar bone is situated between 0.4 to 1.97 mm approximately apically to the cemento-enamel junction (CEJ) of thatparticular tooth.[3]

The bone loss which is induced by periodontitis ie osseous defects occur either single or in different combination forms. The identification of these osseous defects on surgical bone exposure is clinically challenging as the osseous surgeries are based on this diagnosis. It becomes imperative for a clinician to understand these defects and categorize them well to have better periodontic therapeutic approaches.

Periodontal osseous defects (POD) is an important clinical reality, however, it's classification and description are not being dealt in regular universally accepted text books. Hence, an attempt is made in this review paper to revisit, modify and describe various aspects of POD for the first time in literature.

Incidence and Prevalence

The changes which are observed in the alveolar process architecture may differ in form, distribution and degree within same individual at different sites as well as between individuals.

The prevalence of vertical defect was higher in male patients (14.95%) when compared to female patients (8.2%) and also it was rare in patients with dental awareness (de Toledo et al 2012).[4] Vertical defects are commonly associated with posterior teeth (Baljoon et al.),[5] with the higher prevalence in mandibular posterior teeth (33.8%) (Vrotsos et al., Kasaj et al.).[6,7]

Vertical defects are commonly associated with molars with higher prevalence of crater formation (26.5%), followed by circumferential defects (23.4%) and 3 wall defects (20.08%) (Wu et al.).[8]

Osseous Defects

Definition: Osseous defects are defined as the alterations in the morphology of the alveolar bone (GPT). These occur normally (anatomic variations) and disease induced. As these defects act a crucial role either in initiating or

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Diagnosis and epidemiology of periodontal osseous lesions

PANOS N. PAPAPANOU & MAURIZIO S. TONETTI

Loss of alveolar bone support is one of the characteristic signs of destructive periodontal disease and is generally considered to represent the anatomical sequela to the apical spread of periodontitis. The extent and the severity of alveolar bone loss in the dentition are usually assessed by a combination of radiographic and clinical means and are important adjuncts to the clinician in the diagnosis, treatment planning, and assessment of prognosis of the periodontal patient. The presence of periodontal osseous lesions is clinically significant in many ways. It relates to the associated loss of tooth support, to the site specificity of periodontal destruction, and to the possibility that ecological niches (deep pockets and furcation involvement) associated with some osseous lesions may represent site-specific risk factors or indicators for disease progression.

Etiology

A variety of factors have been associated with the formation of intrabony defects: among these, trauma from occlusion and food impaction have been extensively discussed in the older literature (9, 10). Anatomic factors such as plaque-retaining local elements and the distance between adjacent root surfaces have also been proposed to play a role (47, 50, 52). The latter argument is based on the observation that a close proximity between neighboring roots results in involvement of the whole interdental septum in the inflammatory, resorptive process which, in turn, results in destruction of the entire interdental alveolar bone and precludes the formation of an infrabony defect.

The development of a furcation invasion has been mainly associated with the special anatomical niche that is formed following the exposure of the furcation fornix (51), while the presence of enamel pearls or projections has also been named as predisposing to breakdown (29). Variations in the morphology of multirooted teeth are also of importance in determining at what stage in the periodontal breakdown process a furcation will become involved. The length of the common root trunk, the presence of developmental depressions, the root morphology and the presence of accessory pulp canals have received considerable attention (23).

Irrespective of the number and nature of the contributing factors involved, the formation of an osseous periodontal lesion is today considered to be the result of an apical downgrowth of subgingival plaque with a concomitant resorption of bone within a 2-mm radius from the root surface (17, 50–52). The more remotely located bone structures and the root surface retain their integrity and form the anatomical boundaries of the osseous lesion.

Classification

Since periodontal osseous lesions represent the anatomical sequelae to the apical spread of periodontitis, and in particular to the interplay between site specific progression and the local anatomy, their morphology is determined by a variety of factors which include: location of the causative microorganisms on the root surface, root and root trunk anatomy, thickness of the alveolar bone, root position within the alveolar process, and the steric relationship with adjacent periodontal lesions (that is, proximity with another involved root surface). Each individual defect affecting a specific tooth in the dentition of a certain patient, therefore, presents a unique anatomy. Many attempts, however, have been made to classify periodontal osseous defects. Classifications are generally based upon specific morphological criteria and are aimed at guiding clinicians with their diagnosis, treatment and prognosis. A first level of classification differentiates between suprabony defects, infrabony defects, and interradicular or furcation defects (Fig. 1).

Article 12

Regeneration of Periodontal Tissue: Bone Replacement Grafts

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KEYWORDS

- Bone grafts • Periodontal • Intrabony • Scaffold
- Regeneration • Bone substitutes

Bone replacement grafts are widely used to promote bone formation and periodontal regeneration. Conventional surgical approaches, such as open flap debridement, provide critical access to evaluate and detoxify root surfaces as well as establish improved periodontal form and architecture; however, these surgical techniques offer only limited potential in restoring or reconstituting component periodontal tissues. Bone grafting materials function, in part, as structural scaffolds and matrices for attachment and proliferation of anchorage-dependent osteoblasts (**Fig. 1**). A wide range of bone grafting materials, including bone grafts and bone graft substitutes, have been applied and evaluated clinically, including autografts, allografts, xenografts, and alloplasts (synthetic/semisynthetic materials). Although not all bone grafting materials support the formation of a new periodontal attachment apparatus, there is conclusive evidence that periodontal regeneration is achievable with bone replacement grafts in humans.[1]

The purpose of this review is to provide an overview of the biologic function and clinical application of bone replacement grafts for periodontal regeneration. Emphasis is placed on the clinical and biologic goals of periodontal regeneration as well as evidence-based treatment outcomes.

PERIODONTAL REGENERATION: CLINICAL AND BIOLOGIC GOALS

The biologic goal of periodontal regeneration is restoration of the periodontium to its original form and function. Periodontal *repair* is healing of the periodontium by tissue

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Article 14

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Tissue engineering for bone regeneration and osseointegration in the oral cavity☆

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ABSTRACT

Objective. The focus of this review is to summarize recent advances on regenerative technologies (scaffolding matrices, cell/gene therapy and biologic drug delivery) to promote reconstruction of tooth and dental implant-associated bone defects.
Methods. An overview of scaffolds developed for application in bone regeneration is presented with an emphasis on identifying the primary criteria required for optimized scaffold design for the purpose of regenerating physiologically functional osseous tissues. Growth factors and other biologics with clinical potential for osteogenesis are examined, with a comprehensive assessment of pre-clinical and clinical studies. Potential novel improvements to current matrix-based delivery platforms for increased control of growth factor spatiotemporal release kinetics are highlighting including recent advancements in stem cell and gene therapy.
Results. An analysis of existing scaffold materials, their strategic design for tissue regeneration, and use of growth factors for improved bone formation in oral regenerative therapies results in the identification of current limitations and required improvements to continue moving the field of bone tissue engineering forward into the clinical arena.
Significance. Development of optimized scaffolding matrices for the predictable regeneration of structurally and physiologically functional osseous tissues is still an elusive goal. The introduction of growth factor biologics and cells has the potential to improve the biomimetic properties and regenerative potential of scaffold-based delivery platforms for next-generation patient-specific treatments with greater clinical outcome predictability.

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Article 15

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Review Article

An Osteoconductive, Osteoinductive, and Osteogenic Tissue-Engineered Product for Trauma and Orthopaedic Surgery: How Far Are We?

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The management of large bone defects due to trauma, degenerative disease, congenital deformities, and tumor resection remains a complex issue for the orthopaedic reconstructive surgeons. The requirement is for an ideal bone replacement which is osteoconductive, osteoinductive, and osteogenic. Autologous bone grafts are still considered the gold standard for reconstruction of bone defects, but donor site morbidity and size limitations are major concern. The use of bioartificial bone tissues may help to overcome these problems. The reconstruction of large volume defects remains a challenge despite the success of reconstruction of small-to-moderate-sized bone defects using engineered bone tissues. The aim of this paper is to understand the principles of tissue engineering of bone and its clinical applications in reconstructive surgery.

1. Introduction

Bone is a highly vascularised tissue that constantly undergoes remodelling as a result of the balance between the activities of the osteoclasts and the osteoblasts, which allows adaptation to mechanical stresses, maintenance of bone health, and repair of small injuries. A recent study demonstrated that the coupling between osteoclastic bone resorption and osteoblastic bone formation is needed for bone homeostasis [1]. Because of the potential of bone to spontaneously regenerate, most small bone lesions, such as fractures, heal well with conventional therapy or surgery. During bone repair, the osteogenic process, under the influence of bone-derived bioactive factors, commences after the inflammatory phase and is initiated by precursor cells from the periosteum adjacent to the fracture site. This generates hard callus by intramembranous bone formation. An autologous bone graft or bone substitute is often required to assist in the healing of an extensive traumatic or postsurgical bone defect and of osseous congenital deformities. The majority of bone formation, however, is by enchondral ossification of the soft callus that appears after infiltrated mesenchymal cells are induced to chondrogenesis. This improved understanding of repair, and regeneration has helped with the development of orthopaedic tissue engineering [2].

Historically, a variety of substitutes like celluloid, aluminium, gold, vitallium, tantalum, stainless steel, titanium, methyl methacrylate resins, polyethylene, silicone elastomers, and hydroxyapatite ceramics have been tried [3]. The main concerns with the use of these synthetic materials for bone reconstruction were their inability to vascularise, integrate, and undergo remodelling. This may result in structural failure of the implant under load or pathological changes in the surrounding bone, as seen in stress shielding [4]. The other issues are inflammatory scarring, neoproliferative reaction in the adjacent tissues and infection [5]. Because of their high osteoinductive potential and remodelling characteristics, bioactive substitutes such as demineralized bone matrix (allogeneic or xenogeneic) have shown promise, despite risk of disease transmission, as well as cost and availability [6]. This led to the evolution of tissue engineering techniques (biologically enhanced allografts, cell-based therapies, and gene-based therapies) to treat bone defects.

Article 16

SPECIAL FOCUS REVIEW

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Biomaterials and bioengineering tomorrow's healthcare

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Keywords: biomaterials, nanomaterials, diagnostics, healthcare, three-dimensional matrices

Biomaterials are being used for the healthcare applications from ancient times. But subsequent evolution has made them more versatile and has increased their utility. Biomaterials have revolutionized the areas like bioengineering and tissue engineering for the development of novel strategies to combat life threatening diseases. Together with biomaterials, stem cell technology is also being used to improve the existing healthcare facilities. These concepts and technologies are being used for the treatment of different diseases like cardiac failure, fractures, deep skin injuries, etc. Introduction of nanomaterials on the other hand is becoming a big hope for a better and an affordable healthcare. Technological advancements are underway for the development of continuous monitoring and regulating glucose levels by the implantation of sensor chips. Lab-on-a-chip technology is expected to modernize the diagnostics and make it more easy and regulated. Other area which can improve the tomorrow's healthcare is drug delivery. Micro-needles have the potential to overcome the limitations of conventional needles and are being studied for the delivery of drugs at different location in human body. There is a huge advancement in the area of scaffold fabrication which has improved the potentiality of tissue engineering. Most emerging scaffolds for tissue engineering are hydrogels and cryogels. Dynamic hydrogels have huge application in tissue engineering and drug delivery. Furthermore, cryogels being supermacroporous allow the attachment and proliferation of most of the mammalian cell types and have shown application in tissue engineering and bioseparation. With further developments we expect these technologies to hit the market in near future which can immensely improve the healthcare facilities.

Introduction

Biomaterial in medical terminology is "any natural or synthetic material (which includes polymer or metal) that is intended for introduction into living tissue especially as part of a medical device or implant" (for example artificial heart valve or joint). Biomaterials from healthcare perspective can be defined as "materials those possess some novel properties that makes them appropriate to come in immediate contact with the living tissue without eliciting any adverse immune rejection reactions." Definition of biomaterials when intended for implant device purpose in accordance to Food, Drug, and Cosmetic Act (1976) is "an instrument, apparatus, machine, implant or other similar or related article, including any component, part or accessory which is intended for use in diagnosis of disease or in cure or prevention in man or other animals, and which does not achieve any of its principal intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its principal intended purposes. These devices or any type of biomaterial is used to physically replace any hard or soft tissue which has undergone any accidental damage or destruction through some pathological processes. In addition to use of biomaterials as implant devices they have also shown applicability in other healthcare related areas like disposable medical devices, diagnostic kits, polymeric therapeutics, etc. So in general biomaterials are the devices those are used to improve the general healthcare of society and are fabricated by the process that employs or mimics biological phenomenon. Over the time biomaterials have played an imperative role in the area of bioengineering or biomedical engineering to improve the overall healthcare of society. Area of bioengineering encompasses two closely related areas of interest i.e., (1) it applies the principles of engineering science to understand how living organisms function and (2) it applies engineering technologies to design and develop new devices like diagnostic or therapeutic instruments or formulation of novel biomaterials for medical applications, design of artificial tissues or organs and development of new delivery systems. Overall bioengineering focuses on the uses of biomaterials or similar types of materials or principles to improve the healthcare services. With the advent of bioengineering concepts there has been a technological evolution in two key aspects of healthcare i.e. in diagnostic imaging and implanted therapeutic devices. Diagnostic imaging technologies have developed as novel methods to non-invasively view the abnormalities in living system or during the developmental state (in womb). Additional improvement with these technologies have revolutionized the healthcare and made the early treatment of diseases possible. Such imaging techniques like computed axial tomography (CAT), magnetic resonance imaging (MRI) or diagnostic ultrasound has substantially reduced the patient morbidity, so improving the healthcare.[1] Implantable medical devices e.g. cardiac rhythm management stimulator, prosthetic heart

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Article 17

New Frontiers in Biomaterials

R. Gilbert Triplett, DDS, PhD[a,b,*], Oksana Budinskaya, DDS[c]

KEYWORDS

• Tissue engineering • Regenerative medicine • Biomaterials • Angiogenesis
• Nanophase biomaterial • Atmospheric cold plasma

KEY POINTS

- Tissue loss due to trauma or pathology or for congenital purposes necessitates the replacement of form and function, and this has led to the development of tissue engineering and regenerative medicine.
- Grafting materials and techniques have undergone a rapid evolution from simply replacing tissues to stimulating a response from the host.
- These developments are promising in that previously unattainable results in skin, nerve, muscle, and specialized tissue bioengineering are within reach.

INTRODUCTION

A biomaterial in medical terminology is "any natural or synthetic material (which includes polymer or metal) that is intended for introduction into living tissues as part of a medical device or implant" (for example artificial heart or temporomandibular joint). Biomaterials from a health care perspective can be defined as "materials that possess some novel properties that makes them appropriate to come into immediate contact with the living tissue without eliciting an adverse immune rejection reaction."[1]

Tissue loss in the craniomaxillofacial region occurs frequently from disease, trauma, and congenital abnormalities. This loss induces serious physiologic and psychological consequences for patients and their families.[2] Reconstruction of this area to an esthetic and functional state is the goal of the reconstructive surgeon.

Historically, tissue replacement with biomaterials in the craniomaxillofacial region focused on the physical properties of the material itself, such as inertness, malleability, and strength. Over the past 35 years, both the science and funding of biomaterials have seen incredible growth. Biomaterial science has evolved through the research, clinical experience, and collaboration between researchers and surgeons. Recently research has redirected its focus on the biologic interactions of implant materials with the surrounding tissue and cells.[3]

In the past, removable or implanted prostheses used to obturate and replace tissues in this region were fabricated with metals and ceramics. Although they provided an improved esthetic and functional state, they had their limitations. These materials were believed "inert" and, therefore, incapable of eliciting an unfavorable reaction from the host tissue. It is now recognized that various "inert" materials can change physically and chemically after implantation and, from a biological perspective, no material should be considered truly inert.[4]

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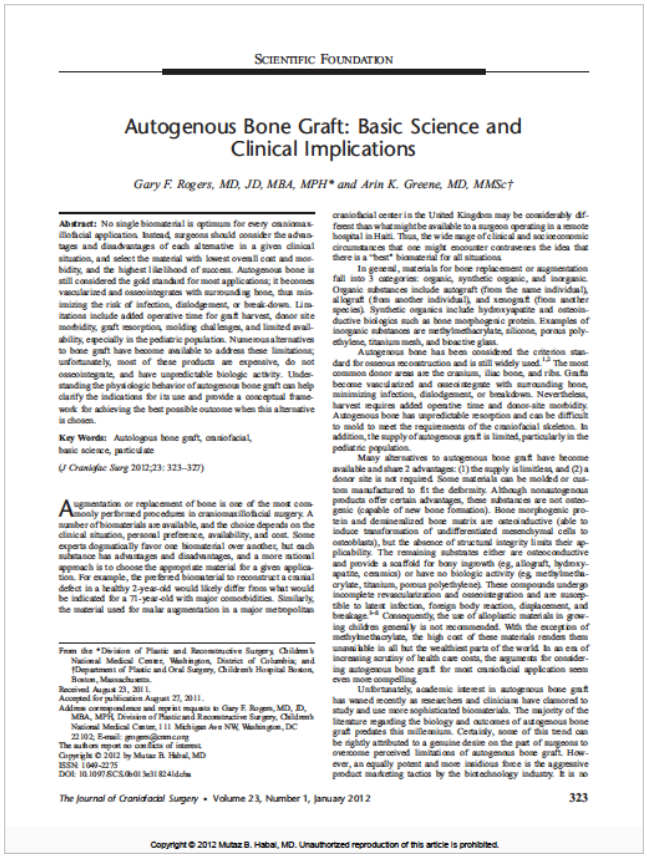
Article 18



SCIENTIFIC FOUNDATION

Autogenous Bone Graft: Basic Science and Clinical Implications

Gary F. Rogers, MD, JD, MBA, MPH and Arin K. Greene, MD, MMSc†*

Abstract: No single biomaterial is optimum for every craniomaxillofacial application. Instead, surgeons should consider the advantages and disadvantages of each alternative in a given clinical situation, and select the material with lowest overall cost and morbidity, and the highest likelihood of success. Autogenous bone is still considered the gold standard for most applications; it becomes vascularized and osseointegrates with surrounding bone, thus minimizing the risk of infection, dislodgement, or break-down. Limitations include added operative time for graft harvest, donor site morbidity, graft resorption, molding challenges, and limited availability, especially in the pediatric population. Numerous alternatives to bone graft have become available to address these limitations; unfortunately, most of these products are expensive, do not osseointegrate, and have unpredictable biologic activity. Understanding the physiologic behavior of autogenous bone graft can help clarify the indications for its use and provide a conceptual framework for achieving the best possible outcome when this alternative is chosen.

Key Words: Autologous bone graft, craniofacial, basic science, particulate

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Augmentation or replacement of bone is one of the most commonly performed procedures in craniomaxillofacial surgery. A number of biomaterials are available, and the choice depends on the clinical situation, personal preference, availability, and cost. Some experts dogmatically favor one biomaterial over another, but each substance has advantages and disadvantages, and a more rational approach is to choose the appropriate material for a given application. For example, the preferred biomaterial to reconstruct a cranial defect in a healthy 2-year-old would likely differ from what would be indicated for a 71-year-old with major comorbidities. Similarly, the material used for malar augmentation in a major metropolitan craniofacial center in the United Kingdom may be considerably different than what might be available to a surgeon operating in a remote hospital in Haiti. Thus, the wide range of clinical and socioeconomic circumstances that one might encounter contravenes the idea that there is a "best" biomaterial for all situations.

In general, materials for bone replacement or augmentation fall into 3 categories: organic, synthetic organic, and inorganic. Organic substances include autograft (from the same individual), allograft (from another individual), and xenograft (from another species). Synthetic organics include hydroxyapatite and osteoinductive biologics such as bone morphogenic protein. Examples of inorganic substances are methylmethacrylate, silicone, porous polyethylene, titanium mesh, and bioactive glass.

Autogenous bone has been considered the criterion standard for osseous reconstruction and is still widely used.[1,2] The most common donor areas are the cranium, iliac bone, and ribs. Grafts become vascularized and osseointegrate with surrounding bone, minimizing infection, dislodgement, or breakdown. Nevertheless, harvest requires added operative time and donor-site morbidity. Autogenous bone has unpredictable resorption and can be difficult to mold to meet the requirements of the craniofacial skeleton. In addition, the supply of autogenous graft is limited, particularly in the pediatric population.

Many alternatives to autogenous bone graft have become available and share 2 advantages: (1) the supply is limitless, and (2) a donor site is not required. Some materials can be molded or custom manufactured to fit the deformity. Although nonautogenous products offer certain advantages, these substances are not osteogenic (capable of new bone formation). Bone morphogenic protein and demineralized bone matrix are osteoinductive (able to induce transformation of undifferentiated mesenchymal cells to osteoblasts), but the absence of structural integrity limits their applicability. The remaining substrates either are osteoconductive and provide a scaffold for bony ingrowth (eg, allograft, hydroxyapatite, ceramics) or have no biologic activity (eg, methylmethacrylate, titanium, porous polyethylene). These compounds undergo incomplete revascularization and osseointegration and are susceptible to latent infection, foreign body reaction, displacement, and breakage.[3–6] Consequently, the use of alloplastic materials in growing children generally is not recommended. With the exception of methylmethacrylate, the high cost of these materials renders them unavailable in all but the wealthiest parts of the world. In an era of increasing scrutiny of health care costs, the arguments for considering autogenous bone graft for most craniofacial application seem even more compelling.

Unfortunately, academic interest in autogenous bone graft has waned recently as researchers and clinicians have clamored to study and use more sophisticated biomaterials. The majority of the literature regarding the biology and outcomes of autogenous bone graft predates this millennium. Certainly, some of this trend can be rightly attributed to a genuine desire on the part of surgeons to overcome perceived limitations of autogenous bone graft. However, an equally potent and more insidious force is the aggressive product marketing tactics by the biotechnology industry. It is no

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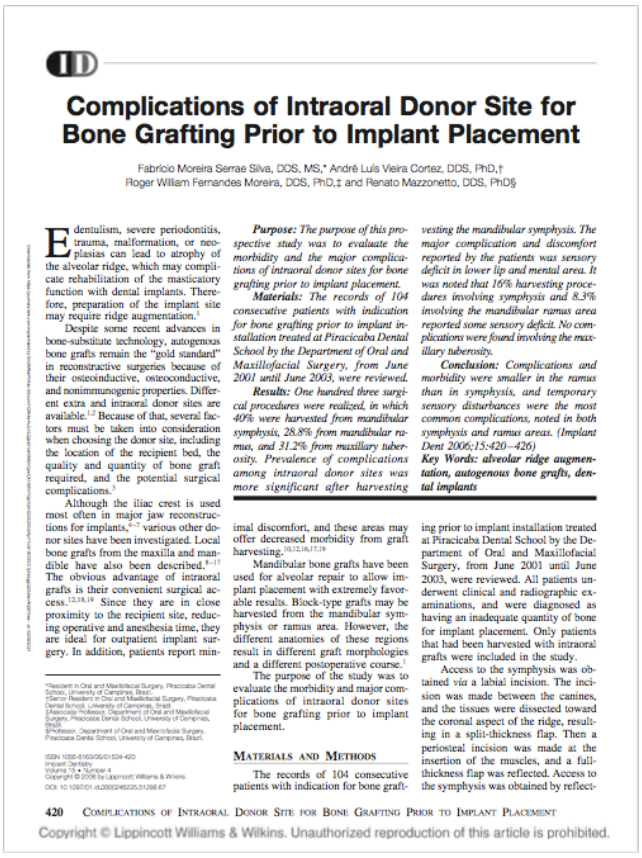
Article 19



Complications of Intraoral Donor Site for Bone Grafting Prior to Implant Placement

Fabrício Moreira Serrae Silva, DDS, MS,* André Luís Vieira Cortez, DDS, PhD,† Roger William Fernandes Moreira, DDS, PhD,‡ and Renato Mazzonetto, DDS, PhD§

Purpose: *The purpose of this prospective study was to evaluate the morbidity and the major complications of intraoral donor sites for bone grafting prior to implant placement.*

Materials: *The records of 104 consecutive patients with indication for bone grafting prior to implant installation treated at Piracicaba Dental School by the Department of Oral and Maxillofacial Surgery, from June 2001 until June 2003, were reviewed.*

Results: *One hundred three surgical procedures were realized, in which 40% were harvested from mandibular symphysis, 28.8% from mandibular ramus, and 31.2% from maxillary tuberosity. Prevalence of complications among intraoral donor sites was more significant after harvesting the mandibular symphysis. The major complication and discomfort reported by the patients was sensory deficit in lower lip and mental area. It was noted that 16% harvesting procedures involving symphysis and 8.3% involving the mandibular ramus area reported some sensory deficit. No complications were found involving the maxillary tuberosity.*

Conclusion: *Complications and morbidity were smaller in the ramus than in symphysis, and temporary sensory disturbances were the most common complications, noted in both symphysis and ramus areas. (Implant Dent 2006;15:420–426)*

Key Words: ***alveolar ridge augmentation, autogenous bone grafts, dental implants***

Edentulism, severe periodontitis, trauma, malformation, or neoplasias can lead to atrophy of the alveolar ridge, which may complicate rehabilitation of the masticatory function with dental implants. Therefore, preparation of the implant site may require ridge augmentation.[1]

Despite some recent advances in bone-substitute technology, autogenous bone grafts remain the "gold standard" in reconstructive surgeries because of their osteoinductive, osteoconductive, and nonimmunogenic properties. Different extra and intraoral donor sites are available.[2] Because of that, several factors must be taken into consideration when choosing the donor site, including the location of the recipient bed, the quality and quantity of bone graft required, and the potential surgical complications.[3]

Although the iliac crest is used most often in major jaw reconstructions for implants,[4–7] various other donor sites have been investigated. Local bone grafts from the maxilla and mandible have also been described.[8–17] The obvious advantage of intraoral grafts is their convenient surgical access.[12,18,19] Since they are in close proximity to the recipient site, reducing operative and anesthesia time, they are ideal for outpatient implant surgery. In addition, patients report minimal discomfort, and these areas may offer decreased morbidity from graft harvesting.[10,12,16,17,19]

Mandibular bone grafts have been used for alveolar repair to allow implant placement with extremely favorable results. Block-type grafts may be harvested from the mandibular symphysis or ramus area. However, the different anatomies of these regions result in different graft morphologies and a different postoperative course.[1]

The purpose of the study was to evaluate the morbidity and major complications of intraoral donor sites for bone grafting prior to implant placement.

Materials and Methods

The records of 104 consecutive patients with indication for bone grafting prior to implant installation treated at Piracicaba Dental School by the Department of Oral and Maxillofacial Surgery, from June 2001 until June 2003, were reviewed. All patients underwent clinical and radiographic examinations, and were diagnosed as having an inadequate quantity of bone for implant placement. Only patients that had been harvested with intraoral grafts were included in the study.

Access to the symphysis was obtained via a labial incision. The incision was made between the canines, and the tissues were dissected toward the coronal aspect of the ridge, resulting in a split-thickness flap. Then a periosteal incision was made at the insertion of the muscles, and a full-thickness flap was reflected. Access to the symphysis was obtained by reflect-

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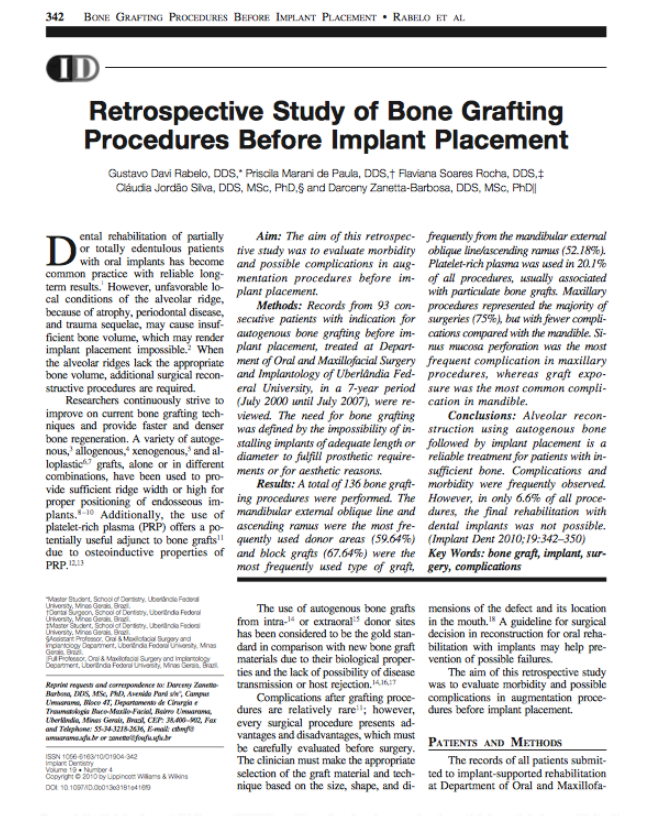
Article 20



Retrospective Study of Bone Grafting Procedures Before Implant Placement

Gustavo Davi Rabelo, DDS,* Priscila Marani de Paula, DDS,† Flaviana Soares Rocha, DDS,‡ Cláudia Jordão Silva, DDS, MSc, PhD,§ and Darceny Zanetta-Barbosa, DDS, MSc, PhD‖

Aim: *The aim of this retrospective study was to evaluate morbidity and possible complications in augmentation procedures before implant placement.*

Methods: *Records from 93 consecutive patients with indication for autogenous bone grafting before implant placement, treated at Department of Oral and Maxillofacial Surgery and Implantology of Uberlândia Federal University, in a 7-year period (July 2000 until July 2007), were reviewed. The need for bone grafting was defined by the impossibility of installing implants of adequate length or diameter to fulfill prosthetic requirements or for aesthetic reasons.*

Results: *A total of 136 bone grafting procedures were performed. The mandibular external oblique line and ascending ramus were the most frequently used donor areas (59.64%) and block grafts (67.64%) were the most frequently used type of graft, frequently from the mandibular external oblique line/ascending ramus (52.18%). Platelet-rich plasma was used in 20.1% of all procedures, usually associated with particulate bone grafts. Maxillary procedures represented the majority of surgeries (75%), but with fewer complications compared with the mandible. Sinus mucosa perforation was the most frequent complication in maxillary procedures, whereas graft exposure was the most common complication in mandible.*

Conclusions: *Alveolar reconstruction using autogenous bone followed by implant placement is a reliable treatment for patients with insufficient bone. Complications and morbidity were frequently observed. However, in only 6.6% of all procedures, the final rehabilitation with dental implants was not possible. (Implant Dent 2010;19:342–350)*

Key Words: bone graft, implant, surgery, complications

Dental rehabilitation of partially or totally edentulous patients with oral implants has become common practice with reliable long-term results.[1] However, unfavorable local conditions of the alveolar ridge, because of atrophy, periodontal disease, and trauma sequelae, may cause insufficient bone volume, which may render implant placement impossible.[2] When the alveolar ridges lack the appropriate bone volume, additional surgical reconstructive procedures are required.

Researchers continuously strive to improve on current bone grafting techniques and provide faster and denser bone regeneration. A variety of autogenous,[3] allogenous,[4] xenogenous,[5] and alloplastic[6,7] grafts, alone or in different combinations, have been used to provide sufficient ridge width or high for proper positioning of endosseous implants.[8–10] Additionally, the use of platelet-rich plasma (PRP) offers a potentially useful adjunct to bone grafts[11] due to osteoinductive properties of PRP.[12,13]

The use of autogenous bone grafts from intra-[14] or extraoral[15] donor sites has been considered to be the gold standard in comparison with new bone graft materials due to their biological properties and the lack of possibility of disease transmission or host rejection.[14,16,17]

Complications after grafting procedures are relatively rare[11]; however, every surgical procedure presents advantages and disadvantages, which must be carefully evaluated before surgery. The clinician must make the appropriate selection of the graft material and technique based on the size, shape, and dimensions of the defect and its location in the mouth.[18] A guideline for surgical decision in reconstruction for oral rehabilitation with implants may help prevention of possible failures.

The aim of this retrospective study was to evaluate morbidity and possible complications in augmentation procedures before implant placement.

Patients and Methods

The records of all patients submitted to implant-supported rehabilitation at Department of Oral and Maxillofa-

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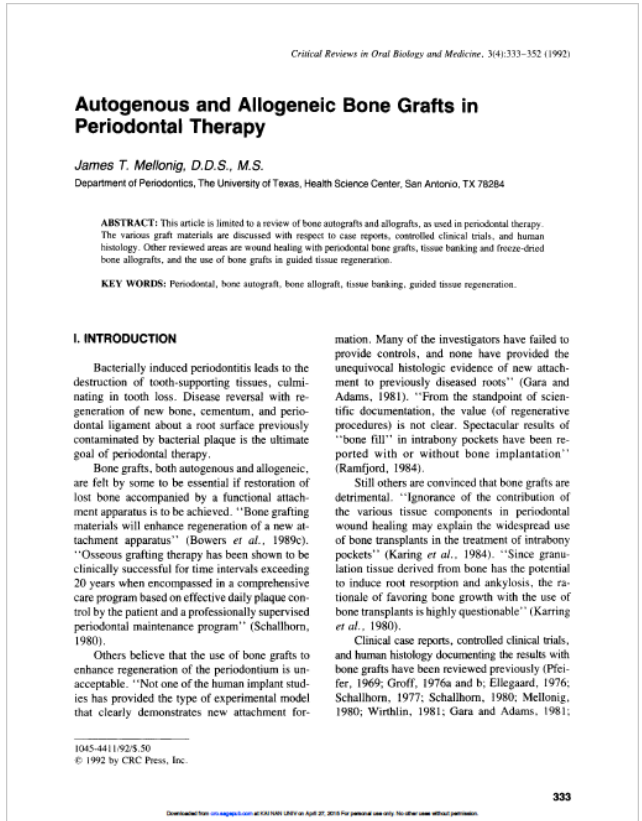
Article 21



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Autogenous and Allogeneic Bone Grafts in Periodontal Therapy

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ABSTRACT: This article is limited to a review of bone autografts and allografts, as used in periodontal therapy. The various graft materials are discussed with respect to case reports, controlled clinical trials, and human histology. Other reviewed areas are wound healing with periodontal bone grafts, tissue banking and freeze-dried bone allografts, and the use of bone grafts in guided tissue regeneration.

KEY WORDS: Periodontal, bone autograft, bone allograft, tissue banking, guided tissue regeneration.

I. INTRODUCTION

Bacterially induced periodontitis leads to the destruction of tooth-supporting tissues, culminating in tooth loss. Disease reversal with regeneration of new bone, cementum, and periodontal ligament about a root surface previously contaminated by bacterial plaque is the ultimate goal of periodontal therapy.

Bone grafts, both autogenous and allogeneic, are felt by some to be essential if restoration of lost bone accompanied by a functional attachment apparatus is to be achieved. "Bone grafting materials will enhance regeneration of a new attachment apparatus" (Bowers *et al.*, 1989c). "Osseous grafting therapy has been shown to be clinically successful for time intervals exceeding 20 years when encompassed in a comprehensive care program based on effective daily plaque control by the patient and a professionally supervised periodontal maintenance program" (Schallhorn, 1980).

Others believe that the use of bone grafts to enhance regeneration of the periodontium is unacceptable. "Not one of the human implant studies has provided the type of experimental model that clearly demonstrates new attachment formation. Many of the investigators have failed to provide controls, and none have provided the unequivocal histologic evidence of new attachment to previously diseased roots" (Gara and Adams, 1981). "From the standpoint of scientific documentation, the value (of regenerative procedures) is not clear. Spectacular results of "bone fill" in intrabony pockets have been reported with or without bone implantation" (Ramford, 1984).

Still others are convinced that bone grafts are detrimental. "Ignorance of the contribution of the various tissue components in periodontal wound healing may explain the widespread use of bone transplants in the treatment of intrabony pockets" (Karing *et al.*, 1984). "Since granulation tissue derived from bone has the potential to induce root resorption and ankylosis, the rationale of favoring bone growth with the use of bone transplants is highly questionable" (Karring *et al.*, 1980).

Clinical case reports, controlled clinical trials, and human histology documenting the results with bone grafts have been reviewed previously (Pfeifer, 1969; Groff, 1976a and b; Ellegaard, 1976; Schallhorn, 1977; Schallhorn, 1980; Mellonig, 1980; Wirthlin, 1981; Gara and Adams, 1981;

1045-44 | 1/92/$.50

Article 22

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ORIGINAL ARTICLE

The Clinical Use of Allografts, Demineralized Bone Matrices, Synthetic Bone Graft Substitutes and Osteoinductive Growth Factors: A Survey Study

Mathias P. G. Bostrom, MD · Daniel A. Seigerman

Abstract The emergence of new bone grafting options and alternatives has led to significant uncertainty when determining the most appropriate product for surgical procedures requiring bone graft in orthopedics. Allografts, demineralized bone matrices, synthetic bone graft substitutes, and osteoinductive growth factors are all viable options, yet there is a lack of data reporting clinical usage of these products. This correspondence reports on the use of bone grafting products at the Hospital for Special Surgery for a 27-month period and makes recommendations based on surgical usage, safety, and cost. Approximately half (48.6%) of all bone graft substitutes were implanted during spinal surgery. Arthroplasty, trauma, and foot/hand cases all used considerable amounts of bone grafting products as well (20.1%, 19.0%, 12.1%, respectively). Considerable differences were noticed in usage of bone grafting products among each orthopedic discipline. Of all bone graft substitutes used in arthroplasty, 14.4% were demineralized bone matrices, whereas 56.8% were allografts. Demineralized bone matrix grafts were used in 82% of trauma surgery and 89% of foot/hand cases. An increase in synthetic bone graft alternatives was noticed near the end of our investigation period.

Key words Bone Graft · DBM · Allograft · Bonegraft substitutes

Introduction

The past decade has brought forth significant advances in bone grafting options for orthopedic surgeons. The overwhelming emergence of new bone graft materials and alternatives has led to uncertainty as to which product to use for specific procedures. It is estimated that more than 500,000 bone grafting procedures are completed each year in the United States [8]. Currently, there are no available data or consensus as to the specific type of graft to be used in particular surgical indications.

Autogenous bone still remains the "gold standard" of bone graft material in all facets of orthopedic surgery. The use of autografts diminishes the risk of infectious disease transmission, whereas osteoconductive, osteoinductive, and osteogenic properties of the graft are optimal. Moreover, there is no immune response after implantation, enhancing its ability to incorporate into its new site [23, 28]. As a graft, autogenous bone is ideal, but the harvest of autografts may be associated with severe donor site pain and morbidity even with new trapdoor harvesting techniques [3, 19]. In procedures requiring large amounts of graft, there may not be adequate quantities of autogenous bone available [19]. Because of the significant shortcomings of autogenous bone graft, a current understanding of available grafting alternatives is necessary.

An allograft, by definition, is any tissue harvested from one individual and implanted into another of the same species [3]. In a search for an adequate substitute for autogenous bone, cadaveric allograft has been a viable option. Structural and morselized forms are available and prepared as either fresh-frozen or freeze-dried [19]. These grafts provide a structural framework or scaffold for host tissue to grow, hence making allograft osteoconductive. Conversely, its osteoinductive properties are mediocre at best. Upon implantation, the host is expected to experience an intricate immune response [19, 20]. Freezing or freeze-drying the allograft is crucial in minimizing this reaction; however, the fundamental properties of the material may be altered.

Although the risk of disease transmission through implantation of allograft is rare, its existence is not inconsequential. According to the American Association of Tissue Banks, no cases of HIV transmission have been reported in more than 2 million cases using allograft bone in the past

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Article 23

Effect(s) of the Demineralization Process on the Osteoinductivity of Demineralized Bone Matrix

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THE RELATIONSHIPS BETWEEN RESIDUAL calcium levels and particle size of ground demineralized bone matrix and its osteoinductive potential were investigated using in vitro and in vivo assays. The effects of variable residual calcium levels, variable particle sizes, and donor age and gender were studied using a tissue culture-based bioassay (in vitro) as well as an athymic mouse (in vivo) bioassay. The osteoinductive potential of the bone-derived biomaterial was assessed by measuring the degree of new bone formation (change in percent calcium content after 4 weeks of implantation) in the in vivo assay and levels of alkaline phosphatase activity associated with cultures of human periosteal cells (HPO cells) in the in vitro assay, respectively. Slightly demineralized bone matrix and overly demineralized bone matrix possessed a degree of osteoinductive potential whereas bone demineralized to levels of approximately 2% residual calcium provided for maximum osteoinductive potential in both assay systems. The osteoinductive potential of ground demineralized bone varied relative to the particle size such that DBM particles ranging from 500 to 710 microns provided for the highest level of calcium deposition (increase of 8.1 weight percent calcium) after 4 weeks of implantation in muscle pouches of an athymic mouse, whereas explanted particles less than 250 microns showed the lowest level of calcium deposition (increase of only 2.8 weight percent calcium). In the donor age and gender study, DBM from different donors were divided into 5 age groups for both female and male donor derived bone: less than 20, 21 to 30, 31 to 40, 41 to 50, and 51 to 60 year old age groups. This study indicated that DBM from female donors in the 31 to 40 years old age group and male donors in the 41 to 50 year age group possess the highest osteoinductive potential, whereas DBM derived from donor bone from both female and male donors in the 51 to 60 year age group presented the lowest osteoinductive potential. DBM derived from male and female donors did not in general show significant differences in osteoinductive potential. *J Periodontol 1997;68:1085–1092.*

Key Words: Biological assay; bone regeneration; bone matrix; alkaline phosphatase; osteogenesis; periodontal diseases/physiopathology.

As early as 1889, Senn[1] reported using demineralized bovine bone as a vehicle for delivery of antiseptics (iodoform) in patients with osteomyelitis. In the twentieth century Leriche and Policard,[2] LaCroix,[3] Levander,[4] Urist,[5] and Huggins et al.,[6] as pioneers, studied induced bone formation. The first unequivocal demonstration of matrix induced bone formation was by Urist[5] in 1965 in a report describing specific preparations of allogeneic bone matrix implanted in muscle.

Due to its remarkable regenerative ability, bone is one of the most frequently transplanted tissues in humans and is routinely used for the repair of skeletal defects caused by trauma, neoplasia, and infection. Three mechanisms may contribute to the deposition of bone after bone grafting: osteogenesis, osteoinduction, and osteoconduction. Osteogenesis is the formation of new bone from bone-forming cells (osteoblasts) that are transplanted as a viable cellular component in autogenous bone grafts. Osteoinduction is the formation of new bone by recipient mesenchymal cells that differentiate into bone-forming cells under the stimulation of matrix and associated protein factors present in demineralized bone. Osteoconduction is a process in which host bone-forming cells infil-

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Article 24

Arch Orthop Trauma Surg (2001) 121: 583–590

ORIGINAL ARTICLE

**C. H. Lohmann · D. Andreacchio · G. Köster
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B. D. Boyan · Z. Schwartz**

Tissue response and osteoinduction of human bone grafts in vivo

Received: 8 December 2000

Abstract Freeze-dried human bone allograft is used clinically as an adjunct to autologous bone graft. When freeze-dried human bone allograft is demineralized, the allograft is osteoinductive, since it causes bone to form heterotopically. Both types of allograft are also used alone, such as in spinal fusions, critical size defects, and periodontal therapy. The purpose of this study was to determine the effect of demineralization on the osteoinductive potential of human bone grafts obtained from two different groups of patients. One group consisted of six patients younger than 42 years of age, while the other group consisted of six patients who were older than 70 years of age. The harvested material was lyophilized and divided into two portions, one of which was used directly while the other was demineralized. Osteoinductive ability was established using an in vivo assay for heterotopic bone formation. Activity in these bone grafts was compared with a batch of commercially prepared demineralized, freeze-dried human bone grafts that had been previously shown to be active and another batch that had been shown to display low ('inactive') osteoinductive ability. A bone induction score was determined for each group of grafts based on the number and size of any ossicles formed. In addition, the area of new bone formation and area of residual particles were determined histomorphometrically. Tissue response to the bone grafts varied with donor age and whether the samples had been demineralized or not. Only demineralized, freeze-dried bone graft from patients younger than 42 years of age was osteoinductive; all other batches displayed little or no osteoinductive activity. In the demineralized, freeze-dried bone from donors younger than 42 years of age, the bone induction score and new bone area were significantly higher than in the other batches of bone graft, and the area of residual particles was reduced. Both demineralized and nondemineralized bone graft from patients older than 70 years of age were encapsulated in dense, fibrous connective tissue. These results may help explain the observed differences in clinical outcome when demineralized, freeze-dried bone graft or nondemineralized, freeze-dried bone graft from different donors is used in bone regeneration applications.

Keywords Freeze-dried human bone allograft · Demineralized bone · Osteoinduction

Introduction

The current use of demineralized, freeze-dried bone allografts (DFDBA) in orthopedics, periodontics, oral and maxillofacial surgery, and plastic and reconstructive surgery is based on the osteoinductive ability of these preparations [25, 32]. In addition to their ability to induce bone when implanted heterotopically, they provide a space-filling osteoconductive matrix, facilitating the formation of bone orthotopically as well. The ability of demineralized bone to induce new bone formation in soft tissues and to enhance bone formation in osseous tissues is believed to be due to the content and diffusibility of bone morphogenetic proteins (BMPs) present in the material. The BMPs and other growth factors and cytokines interact

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Article 25

Bone Morphogenetic Protein Induced Bone Formation and the Bone – Bone Marrow Consortium *

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A low molecular weight component named bone morphogenetic protein (BMP), chemically isolated from the organic matrix of bone, induces postfetal connective tissue cells (pericytes) surrounding small blood vessels to differentiate into cartilage and bone. The sequence of biochemical and morphological pre-, para-, and postdifferentiated events indicate that BMP initiates an organized process of diverse means to an end. The end product is a spherical ossicle of lamellar bone filled with red bone marrow. The process is morphogenetic because a preliminary phase of 24 h of hyaluronate accumulation followed by 24 h of hyaluronidase activity, characteristic of embryonic skeletal tissue anlagen formation, precedes the cytodifferentiation phase of development. Cytodifferentiation culminates in the formation of a complete ossicle (Figs. 1, 2). It is not known whether BMP is endocytosed and transferred to the nucleus to derepress one key gene, or a tandem-linked chain of genes, regulating the biosynthesis of various skeletal products.

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Fig. 1. Roentgenogram of an ossicle (*arrow*) developed in response to bovine BMP as associated bone matrix noncollagenous proteins shown in Figs. 2, 3, 4

Bone Transplantation
Eds.: M. Aebi, P. Regazzoni

Article 26

Perspectives

Building better bone: the weaving of biologic and engineering strategies for managing bone loss†

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Running Title – Building Better Bone

Author Contributions – AS, MS, JA, and NJW all authored equivalent portions of the manuscript. AS managed tables and figures. MS was the chief editor for the manuscript. JA and NJW analyzed survey results. All authors reviewed the final manuscript.

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Article 27

Sheikh et al. Biomaterials Research (2017) 21:9
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Biomaterials Research

REVIEW Open Access

Natural graft tissues and synthetic biomaterials for periodontal and alveolar bone reconstructive applications: a review

Zeeshan Sheikh[1,2*†], Nader Hamdan[3†], Yuichi Ikeda[1,4], Marc Grynpas[2], Bernhard Ganss[1] and Michael Glogauer[1]

Abstract

Periodontal disease is categorized by the destruction of periodontal tissues. Over the years, there have been several clinical techniques and material options that been investigated for periodontal defect repair/regeneration. The development of improved biomaterials for periodontal tissue engineering has significantly improved the available treatment options and their clinical results. Bone replacement graft materials, barrier membranes, various growth factors and combination of these have been used. The available bone tissue replacement materials commonly used include autografts, allografts, xenografts and alloplasts. These graft materials mostly function as osteogenic, osteoinductive and/or osteoconductive scaffolds. Polymers (natural and synthetic) are more widely used as a barrier material in guided tissue regeneration (GTR) and guided bone regeneration (GBR) applications. They work on the principle of epithelial cell exclusion to allow periodontal ligament and alveolar bone cells to repopulate the defect before
the normally faster epithelial cells. However, in an attempt to overcome complications related to the epithelial down-growth and/or collapse of the non-rigid barrier membrane and to maintain space, clinicians commonly use a combination of membranes with hard tissue grafts. This article aims to review various available natural tissues and biomaterial based bone replacement graft and membrane options used in periodontal regeneration applications.

Background

It has been estimated that the global economic cost incurred due to dental diseases amounted to $442 Billion in 2010, of which $298 Billion can be attributed to direct treatment costs and $144 Billion to indirect costs in terms of productivity losses due to periodontal disease, caries and tooth loss [1]. Chronic periodontitis is a disease that affects approximately half of the adult population in the United States [2], of those, it is estimated that 2 to 6 million people could require professional treatment. Since the average cost for full mouth periodontal surgery is about $4000 to $5000, and if 300,000 people only actually received treatment, the projected cost could be more than one billion dollars. This would be an overwhelming liability for insurance companies and health care plans to cover. This out-of-pocket cost to the individual would contribute in discouraging some individuals from seeking treatment [3]. The chronic untreated loss of periodontal tissues: gingiva, alveolar bone, periodontal ligament and cementum, ultimately results in tooth loss leading to functional and aesthetic repercussions. Various treatment modalities (surgical and non-surgical) have been investigated to try repair/regenerate periodontal tissues damaged or lost due to disease. In an attempt to achieve periodontal regeneration, soft and hard tissue replacement grafts, guided tissue/bone regeneration (GTR/GBR), root surface biomodifications, and delivery of growth factors have been developed [4]. Four major hard tissue replacement graft materials are commonly used for periodontal regenerative applications. These are the autogenous or autografts, allografts, xenografts and alloplasts. Autografts are graft materials obtained from the same individual and have been historically thought to be the "gold standard" [5]. However, there are

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Article 28

Scientific Foundation

Repair of Experimental Calvarial Defects with Bio-Oss Particles and Collagen Sponges in a Rabbit Model

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Various materials have been used for reconstruction of both acquired and congenital calvarial defects. Unfortunately, each has its limitations. Autologous bone grafts have irregular rates of resorption that may require secondary corrective surgery, and individual harvest sites have limited stores that can necessitate additional donor locations. Alloplastic materials have unlimited quantities and volume stability but they may not become incorporated and are associated with a higher incidence of infection. The optimal bone substitute should stimulate new bone formation and permanently supplant the temporary space filler, thereby reconstituting the surgical defect. We evaluated 2 newly available bone substitutes, resorbable natural bone mineral (Bio-Oss particles) and a combination of collagen and natural bone mineral collagen combination (Bio-Oss sponges), to repair calvarial defects in an adult, male, New Zealand white rabbit model. We found that the particulate Bio-Oss material resorbed and then underwent the normal physiological stages of bone remodeling. The collagen and Bio-Oss combination was replaced by new bone ingrowth. These materials may have potential for use in the reconstruction of skull defects.

Key Words: Calvarial defects, Bio-Oss, Bio-Oss collagen sponge, alloplastic, bone substitute

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A variety of autogenous and alloplastic materials have been proposed for use in craniofacial reconstruction. Autologous bone grafts have been harvested from a number of sites, including rib, ileum, or cranium. Unfortunately, these grafts have exhibited uneven resorption, often requiring secondary surgical correction [1]. Many of the alloplastic replacement materials, except for hydroxyapatite, have caused foreign body reaction and eventual encapsulation [2,3]. The definitive bone substitute should eventually resorb and then encourage new bone formation, thus permanently replenishing the defect.

We investigated the possible use, biocompatibility, and ultimate fate of 2 newer bone substitutes—(1) resorbable Bio-Oss particles and a collagen and (2) Bio-Oss sponge—for reconstruction of surgically created, critical-size skull defects in an adult, male, New Zealand white rabbit model.

Materials and Methods

Forty-four adult, male, New Zealand white rabbits ranging in age from 9 to 12 months and weighing an average of 475 gm (±65 gm) served as the experimental model. National Institutes of Health guidelines for the care and use of laboratory animals (NIH publication 85-23, Rev. 1985) were observed. The animals were housed at the University of California, Davis, animal quarters at 20°C (40% humidity) in standard cages and received 16 hours of light and 8 hours of darkness. They were fed standard pellets and tap water *ad libitum*.

Bio-Oss is natural bone derived from a bovine source that is similar to human bony tissue, both clinically and physiologically. It is a calcium-deficient carbonate apatite. Bio-Oss is then completely deorganified through a proprietary extraction mechanism to make it completely devoid of antigenicity. The Bio-Oss collagen sponge is an anorganic bone substitute supplemented with 10% collagen

Article 29

Phenotypic Characterization of Mononuclear Cells Following Anorganic Bovine Bone Implantation in Rats

Robert E. Cohen, Richard H. Mullarky,† Bernice Noble,‡ Robin L. Comeau,§ and Mirdza E. Neiders‖*

THE PURPOSE OF THIS STUDY was to measure inflammatory changes associated with implantation of anorganic bovine bone and bovine bone/collagen composite grafts, and to compare the response to that obtained following grafting with hydroxyapatite. Anorganic bovine bone, either with or without bovine collagen, as well as granular and block forms of synthetic hydroxyapatite, were implanted subcutaneously in Wistar rats. Saline and turpentine oil were used as controls. Biopsies were obtained after 3 days and at 1, 2, 4, 6, and 8 weeks. A panel of 6 monoclonal antibodies was used to detect monocytes, several distinct macrophage subsets, Ia-antigen expression, and T- and B-lymphocytes. Cells identified by each antibody were counted after immunocytochemical staining, and sera obtained 6 weeks after grafting were used in immunoblotting assays to detect antibodies to bovine serum proteins and collagen. Anorganic bovine bone, bovine bone/collagen, and hydroxyapatite all produced a transient macrophage infiltrate that was maximum 3 days after implantation, but resolved to normal levels within 6 to 8 weeks. Lymphocyte infiltration was not elicited by any bovine graft material, and antibodies to bovine serum proteins or type I collagen were not detected in any of the animals examined. These data indicate that a systemic or local immune response does not develop following implantation with anorganic bovine bone or with anorganic bovine bone/collagen materials. It appears appropriate to explore further the merits of these materials for periodontal regenerative procedures. *J Periodontol 1994; 65:1008–1015.*

Key Words: Collagen; dental implants; bone and bones; grafts, bone; inflammation/etiology; lymphocytes, B cell; lymphocytes, T cell; hydroxyapatite; macrophages.

The ultimate goal of periodontal therapy is regeneration of a functional attachment apparatus destroyed by periodontitis.[1] Well-controlled clinical studies have generally demonstrated a greater extent of bone fill in grafted periodontal defects compared to ungrafted sites.[2-6] Currently, techniques used for periodontal regeneration include osseous autografts, allografts, and alloplastic materials, as well as guided tissue techniques with and without osseous grafting. Although autograft procedures fulfill many of the characteristics of an ideal bone graft material as described by Boyne,[7] autografts are more invasive due to the additional surgical manipulations required to obtain donor tissue, and are limited by the relatively small quantity of bone that can be obtained from such techniques.[2] These procedures also have been associated with postoperative root resorption.[8] As a result, autografts may not be routinely practical in severe periodontitis cases involving multiple teeth and severe defects.

The use of freeze-dried, demineralized human bone allografts overcomes many of the problems associated with autografts, since these materials are usually derived from bone harvested at autopsy.[4,5] Since these materials are human products procured from bone banks, there is a small but measurable risk of disease transmission, estimated at 1 in 1 million to 1 in 8 million.[9] Although the risk of disease is low if materials are processed correctly, many patients are reluctant to provide consent due to fear of disease. Osseous grafts derived from synthetic or natural hydroxyapatite also are used in periodontal regenerative therapy, but

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Article 30

Human Histologic Evaluation of a Bovine-Derived Bone Xenograft in the Treatment of Periodontal Osseous Defects

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This study evaluated a bovine-derived bone xenograft (Bio-Oss) in the treatment of human periodontal osseous defects. Four patients with at least one tooth that had been recommended for extraction because of interproximal advanced periodontal disease volunteered to participate. The surgical procedure consisted of flap reflection, soft tissue debridement, placing a notch in calculus as a histologic reference point, root planing, placement of the bovine-derived xenograft and a bioresorbable physical barrier, and flap closure. Patients were seen every 2 weeks for plaque control and any necessary adjunctive treatment. At 4 to 6 months postsurgery, 6 teeth, along with the adjacent graft site, were removed en bloc. Histologic observations demonstrated new bone, new cementum, and new periodontal ligament coronal to the reference notch in 3 of the 4 specimens. This study indicates that periodontal regeneration is possible following grafting with a bovine-derived xenograft. (Int J Periodontics Restorative Dent 2000;20:19–29.)

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Periodontal regeneration composed of new bone, cementum, and a periodontal ligament about a root surface previously contaminated by bacterial plaque is the ultimate goal of periodontal therapy. Numerous histologic studies have attempted to demonstrate periodontal regeneration following placement of various graft materials by using the apical extent of root planing, a naturally occurring root notch, a root notch at the base of the defect, or a root notch at the level of the alveolar crest.[1–8] While periodontal regeneration may certainly have been the outcome, these studies did not demonstrate that the root surface was biologically contaminated and devoid of a connective tissue attachment. Since the publication of the work of Cole et al,[9] a notch placed through the apical extent of calculus into the root surface has been the standard histologic reference marker for establishing a contaminated root surface. Using this criterion, periodontal regeneration has been documented for autogenous intraoral osseous-coagulum bone blend, demineralized freeze-dried bone

Article 31

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Clinical evaluation of Bio-Oss®: a bovine-derived xenograft for the treatment of periodontal osseous defects in humans

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Abstract. The purpose of this study was to compare the bovine derived xenograft (BDX) Bio-Oss® to demineralized freeze dried bone allograft (DFDBA) in human intrabony defects. 17 healthy patients with no systemic disease with moderate-severe periodontitis (7 males, 10 females; aged 34–67), were treated. Surgically, defects were included only if the intraosseous defect depth was >3.0 mm. Final selection included 30 defects. The sites were randomly assigned treatment with DFDBA or BDX. Soft tissue and osseous defect measurements were taken the day of surgery and 6 months post-operatively at re-entry. Average baseline PD, CAL, and surgical defect depth for the DFDBA group were not statistically different from the BDX group. No adverse healing response occurred. The results showed a statistically significant improvement in PD and AL for both materials at 6 months in 26 defects (4 defects did not respond to therapy). Soft tissue measurements for the DFDBA group included PD reduction of 2.0±1.3 mm, and AL gain of 2.6±1.6 mm, while the BDX group showed a PD reduction of 3.0±1.7 mm, and AL gain of 3.6±1.8 mm. Osseous measurements showed bone fill of 2.4 mm (46.8%) for the DFDBA group and 3.0 mm (55.8%) for the BDX group. Defect resolution was 59.4% for the DFDBA group and 77.6% for the BDX group. Statistical analysis revealed there was no statistical difference between the 2 materials in all measurements.

Key words: Bio-Oss®; intrabony defect; DFDBA; periodontal surgery; regeneration; bone grafts; re-entry

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Regeneration of new bone, cementum, and periodontal ligament is considered one of the primary objectives of periodontal therapy and has been demonstrated utilizing intraoral (Froum et al. 1975) and extraoral autografts (Schallhorn & Hiatt 1972, Dragoo & Sullivan 1973), and demineralized freeze dried bone allograft (DFDBA) (Bowers et al. 1989a, Bowers et al. 1989b). Clinical investigations into alloplastic materials have revealed acceptable soft tissue clinical responses (Meffert 1985, Barnett et al. 1989, Bowen et al. 1989, Oreamuno et al. 1989), but histologic evaluation indicates these grafts heal almost exclusively with connective tissue encapsulation (Froum et al. 1982, Stahl & Froum 1987, Stahl et al. 1990).

Recently, a bovine derived xenograft has been introduced into periodontics. This material, Bio-Oss®, has an unlimited supply, no additional donor site, and proven safety (Schlickewei & Paul 1991; Schlickewei & Kuner 1991, Paul et al. 1993, Cohen et al. 1994). Bio-Oss® undergoes a low heat (300°C) chemical extraction process by which all organic components are removed, but maintains the natural architecture of bone (Gross 1997). When evaluating parameters such as inner surface area, porosity, crystallite size, and calcium to phosphorous ratio, Bio-Oss® most closely resembles human cancellous bone as compared to DFDBA and synthetic hydroxylapatite (Giovanoli 1994, Valdre et al. 1995).

Bio-Oss® has been tested extensively in vitro and in vivo by both the medical and dental communities. Bio-Oss® was evaluated by Chen et al. 1996, with regards to its osteogenic potential and was found to support bone ingrowth when implanted into the muscle of rabbits. With regards to graft activity following placement, Thaller et al. (1994), found that Bio-Oss® resorbed and

Article 32

The Piezoelectric Bony Window Osteotomy and Sinus Membrane Elevation: Introduction of a New Technique for Simplification of the Sinus Augmentation Procedure

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All of the surgical techniques to elevate the maxillary sinus present the possibility of perforating the schneiderian membrane. This complication can occur during the osteotomy, which is performed with burs, or during the elevation of the membrane using manual elevators. The purpose of this article is to present a new surgical technique that radically simplifies maxillary sinus surgery, thus avoiding perforating the membrane. The piezoelectric bony window osteotomy easily cuts mineralized tissue without damaging the soft tissue, and the piezoelectric sinus membrane elevation separates the schneiderian membrane without causing perforations. The elevation of the membrane from the sinus floor is performed using both piezoelectric elevators and the force of a physiologic solution subjected to piezoelectric cavitation. Twenty-one piezoelectric bony window osteotomy and piezoelectric sinus membrane elevations were performed on 15 patients using the appropriate surgical device (Mectron Piezosurgery System). Only one perforation occurred during the osteotomy at the site of an underwood septa, resulting in a 95% success rate. The average length of the window was 14 mm; its height was 6 mm, and its thickness was 1.4 mm. The average time necessary for the piezoelectric bony window osteotomy was approximately 3 minutes, while the piezoelectric sinus membrane elevation required approximately 5 minutes. (Int J Periodontics Restorative Dent 2001;21:561–567.)

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Various studies prove the high success rate of prosthetic rehabilitation with implants of the upper posterior maxilla. In the presence of normal bone volume and density,[1–3] the standard surgical technique consists of a simple preparation of the implant site and results in a success rate of almost 100%, with rare and easily solved postsurgical complications.[4,5]

However, when the upper maxilla is atrophied in the posterior area, the residual crest is insufficient to serve as an implant site.[6,7] The most effective surgical method to solve these anatomically unfavorable conditions is therefore found in an advanced surgical technique that elevates the floor of the maxillary sinus by means of a bone sinus graft to obtain a properly sized implant site in the cavity (the sinus augmentation procedure).[8] The most common surgical technique to access the maxillary sinus opens a bony window in the lateroposterior wall using a modified version of the Caldwell-Luc osteotomy technique.[9–13] The most important factor is to keep the schneiderian membrane intact so

Article 33

Recombinant Human Platelet-Derived Growth Factor: Biology and Clinical Applications

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The abilities of bone to remodel, fractures to repair, and bone grafts to incorporate are all fundamental reflections of the bone remodeling cycle. This process is characterized by the recruitment and differentiation of osteoblastic and osteoclastic cell populations, whose cellular activities are coordinated and regulated by an elaborate system of growth factors and cytokines. One of the crucial biological factors responsible for reparative osseous activity is platelet-derived growth factor (PDGF). The potent stimulatory effects of PDGF as a chemoattractant and mitogen for mesenchymal cells (including osteogenic cells), along with its ability to promote angiogenesis, have been demonstrated in a variety of preclinical models predicting maxillofacial, spine and appendicular skeletal, and soft-tissue applications. The biological profile of PDGF, including its ability to recruit osteoprogenitor cells, makes it particularly suited to address the skeletal defects that are seen with comorbid conditions such as osteoporosis, diabetes, and the effects of smoking. The clinical success and safety that have been demonstrated with use of recombinant human PDGF (rhPDGF) in the repair of periodontal defects have led to U.S. Food and Drug Administration (FDA) approval of rhPDGF for this indication. Ongoing pilot and pivotal trials in the United States and internationally will continue to clarify the promising role of PDGF in the treatment of challenging skeletal disorders.

PDGF and the Bone Remodeling Cycle

The skeleton has a robust, intrinsic capacity to regenerate during homeostasis and following injury. This remarkable regenerative process is characterized by the remodeling cycle, in which cell populations are recruited and differentiated for the purposes of bone resorption or bone formation. These activities are coordinated and regulated by an elaborate system of growth factors and cytokines, several of which are either now available or in promising stages of development for clinical application through recombinant technology. One of the crucial biological factors responsible for reparative osseous activity is PDGF. PDGF works by binding to cell-surface receptors on most cells of mesenchymal origin, and it stimulates the reparative processes in multiple tissue types. The potent stimulatory effects of PDGF as a chemoattractant and a mitogen, along with its ability to promote angiogenesis, position it as a key mediator in tissue repair. As a consequence of the recognized importance of PDGF in wound-healing and its orthopaedic therapeutic potential, a review on PDGF is timely. This article will highlight the biology behind PDGF, the preclinical history of PDGF in dentistry and orthopaedics, and the compelling dental and clinical orthopaedic studies of PDGF that have appeared in the literature.

Biology

PDGF Expression and Function in Bone-Healing

The family of PDGF polypeptide growth factors includes PDGF-A, B, C, and D, encoded by four genes located on different chromosomes. PDGF-A and PDGF-B can form both homodimers and heterodimers, whereas PDGF-C and PDGF-D exist as homodimers[1]. PDGF has a half-life of approximately thirty minutes when circulating in the blood[2–4], suggesting that local delivery of the growth factor will be critical to achieving clinical success.

Following injury and hemorrhage, bone repair is characterized by activation of the coagulation cascade and formation of a blood clot at the site of trauma (Fig. 1). Platelets aggregate and release their cytokine-laden granules, including varying amounts of PDGF-AB, PDGF-AA, PDGF-BB, and PDGF-CC, into the developing blood clot[4–6]. The PDGFs act early in the wound-healing cascade by initially attracting and activating neutrophils and macrophages[4–6], which are key cell

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Article 34

The combination of platelet-derived growth factor-BB and insulin-like growth factor-I stimulates bone repair in adult Yucatan miniature pigs

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The combination of insulin-like growth factor-I and platelet-derived growth factor-BB has previously been shown to stimulate healing of soft tissue wounds and the formation of bone and ligament around teeth. The purpose of the present study was to evaluate the effects of platelet-derived growth factor-BB and insulin-like growth factor-I individually and in combination on the healing of osseous wounds. Four standardized cortical wounds were created in each tibia of 11 adult Yucatan miniature pigs. The wounds in one tibia per animal were treated with either purified recombinant human insulin-like growth factor-I, platelet-derived growth factor-BB, or both in a methylcellulose gel. The wounds in each contralateral tibia received placebo gel alone. Coded serial sections of each wound were evaluated by computer-aided histomorphometry 21 days after surgery. The area and perimeter of the newly formed mineralized callus, the thickness of the total callus, and the percentage of mineralized tissue within the callus were significantly increased compared with the values of matched controls only in wounds treated with a combination of insulin-like growth factor-I and platelet-derived growth factor-BB. No significant differences in the measured parameters of callus formation were found in wounds treated with either insulin-like growth factor-I or platelet-derived growth factor-BB alone. Cartilage was present only in sites treated with insulin-like growth factor-I alone. These results suggest that the combination of platelet-derived growth factor-BB and insulin-like growth factor-I stimulates bone formation in wounds in long bones of adult animals and that these growth factors act via different pathways during the repair process. **(WOUND REP REG 1994;2:-182-90.)**

Numerous polypeptide growth factors have been shown to enhance the healing of cutaneous wounds,[1,2] but differences and synergistic interactions among factors may exist. For example, the combination of natural or recombinant platelet-derived growth factor (PDGF-AB or -BB) and insulin-like growth factor-I (IGF-I) has been shown to be more potent in stimulating the repair of cutaneous wounds than individual growth factors PDGF, IGF-I, epidermal growth factor, acidic and basic fibroblast growth factor, or transforming growth factor (TGF)-α.[3] The PDGF/IGF-I combination and TGF-β_1 were equally potent simulators of connective tissue repair, although TGF-β_1 reduced epithelial volume.[3]

IGF-I	Insulin-like growth factor-I
PDGF	Platelet-derived growth factor
TGF	Transforming growth factor

Many growth factors, including IGF-I and PDGF, have been isolated in abundance from bone matrix, which suggests a role for these growth factors in bone formation.[4] IGF-I[5] and PDGF[6] have been shown to be produced by bone cells and to have a number of effects on bone cells. Both PDGF and IGF-I promote the

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Article 35

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The Biology of Platelet-Rich Plasma and Its Application in Oral Surgery: Literature Review

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ABSTRACT

Platelet-rich plasma (PRP) is a new approach in tissue regeneration and a developing area for clinicians and researchers. It is used in various surgical fields, including oral and maxillofacial surgery. PRP is prepared from the patient's own blood and contains growth factors that influence wound healing. Of these growth factors, platelet-derived growth factor, transforming growth factor, insulin-like growth factor, and epidermal growth factor play a pivotal role in tissue repair mechanisms. Although the growth factors and mechanisms involved are still poorly understood, the easy application of PRP in the clinic and its possible beneficial outcome, including reduction of bleeding, rapid soft tissue healing, and bone regeneration, hold promise for new treatment approaches. However, animal studies and human trials demonstrate conflicting results regarding the application of PRP. Therefore the aim of this literature review is to evaluate the scientific evidence regarding the use of PRP in dentistry, to describe the different bioactive substances included in PRP and their participation in the healing process, to elucidate the different techniques and available technology for PRP preparation, to review animal and human studies, to clarify risks, and to provide guidance for future research.

INTRODUCTION

PLATELET-RICH PLASMA (PRP) is a new approach in tissue regeneration and a developing area for clinicians and researchers (Fig. 1). It is used in various surgical fields, including head and neck surgery, otolaryngology, cardiovascular surgery, and oral and maxillofacial surgery.[1] Although the growth factors and mechanisms involved are still poorly understood, the easy application of PRP in clinical practice and its possible beneficial outcome, including bone regeneration, reduction of bleeding, and rapid wound healing, hold promise for new treatment approaches. An important feature of PRP is that this autologous product, which is prepared from the patient's own blood, eliminates concerns about immunogenic reactions and disease transmission.

Although basic clinical research has focused on the application of growth factors, the short shelf life and inefficient delivery to target cells are major concerns associated with local administration of recombinant human growth factors. Additionally, they are expensive, and high doses may be required to achieve any therapeutic effect. An alternative, easy, cost-effective way to obtain high concentrations of growth factors for tissue healing and regeneration may be autologous platelet concentrates. In 1990, Gibble and Ness introduced fibrin gel, a biomaterial that includes hemostatic agents and has adhesive properties.[2] PRP is an autologous modification of fibrin glue that has been used in various applications with promising clinical success.[3,4] Different bioactive substances are released from platelets upon activation. Of them, platelet-derived growth factor (PDGF), transforming growth factor (TGF), insulin-like growth factor (IGF), and epidermal growth factor (EGF) play a pivotal role in initiating and sustaining wound healing and tissue repair mechanisms.[5]

The aim of this literature review was to discuss the scientific evidence regarding the use of PRP in dentistry and to describe the different bioactive substances present in PRP and their participation in the healing process. This review was also intended to elucidate the different techniques and

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Article 36

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Systematic Review

Twenty years of enamel matrix derivative: the past, the present and the future

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Abstract

Background: On June 5th, 2015 at Europerio 8, a group of leading experts were gathered to discuss what has now been 20 years of documented evidence supporting the clinical use of enamel matrix derivative (EMD). Original experiments led by Lars Hammarström demonstrated that enamel matrix proteins could serve as key regenerative proteins capable of promoting periodontal regeneration including new cementum, with functionally oriented inserting new periodontal ligament fibres, and new alveolar bone formation. This pioneering work and vision by Lars Hammarström has paved the way to an enormous amount of publications related to its biological basis and clinical use. Twenty years later, it is clear that all these studies have greatly contributed to our understanding of how biologics can act as mediators for periodontal regeneration and have provided additional clinical means to support tissue regeneration of the periodontium.

Aims: This review article aims to: (1) provide the biological background necessary to understand the rational for the use of EMD for periodontal regeneration, (2) present animal and human histological evidence of periodontal regeneration following EMD application, (3) provide clinically relevant indications for the use of EMD and (4) discuss future avenues of research including key early findings leading to the development of Osteogain, a new carrier system for EMD specifically developed with better protein adsorption to bone grafting materials.

Conflict of interest and source of funding statement
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Article 37

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Formulation of enamel matrix derivative for surface coating

Kinetics and cell colonization

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Gestrelius S, Andersson C, Johansson A-C, Persson E, Brodin A, Rydhag L, Hammarström L: Formulation of enamel matrix derivative for surface coating. Kinetics and cell colonization. J Clin Periodontol 1997; 24: 678–684.

Abstract. Enamel Matrix Derivative (EMD) contains a protein complex belonging to the amelogenin family. Enamel matrix as well as EMD have been found to promote periodontal regeneration when applied onto denuded root surfaces in dehiscence models. In the present studies it is shown that propylene glycol alginate (PGA) is a suitable vehicle for EMD for its local application. EMD can be dissolved in PGA at an acidic pH, resulting in a highly viscous solution. At neutral pH and body temperature the viscosity decreases and EMD precipitates. Multilayers of EMD on mineral or protein surfaces have been analysed using ellipsometry, total internal reflection fluorescence (TIRF) and biospecific interaction analysis (BIA). The studies show that EMD adsorbs both to hydroxyapatite and collagen and to denuded dental roots. It forms insoluble spherical complexes, and detectable amounts remain at the site of application on the root surface for two weeks, as shown with radiolabelled protein in rats and pigs. Scanning electron micrograph (SEM) studies on monkey teeth further indicate that EMD in PGA may promote repopulation of fibroblast-like cells during the first weeks after application.

Key words: propyleneglycol alginate (PGA); adsorption; hydroxyapatite; collagen; dentin; kinetics; scanning electron microscopy; histomorphometry

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In order to facilitate use of enamel matrix derivative (EMD) as a matrix for regenerative periodontal treatment, a suitable formulation for its application onto affected dental root surfaces is required. EMD contains proteins belonging to the amelogenin family, which is the hydrophobic constituent of the enamel matrix proteins (Fischer & Termine 1985, Aoba et al. 1987). The characteristic of such proteins is that they aggregate and become practically insoluble at physiological pH and body temperature. The solubility increases at acid or alkaline pH and low temperature. A suitable liquid formulation should thus have a non-neutral pH and allow gradual reprecipitation of the matrix when physiological conditions are reestablished. With this in mind, the usefulness of a number of different vehicles, including alginates, dextrans and celluloses, were compared in a dehiscence model in monkeys (Hammarström et al. 1997). From the tests carried out, measuring regeneration of cementum and alveolar bone after 8 weeks, *propylene glycol alginate* (PGA) was found to be the most suitable vehicle for EMD. PGA is a propylene glycol ester of alginic acid, which is commonly used in food and pharmaceuticals as a thickening agent. The esterification of carboxyl groups in alginic acid results in macromolecules giving high viscosity, even at a low pH and in the presence of ions such as calcium. In this paper, the behaviour and kinetics of EMD in PGA vehicle solution will be described, including its effect on periodontal ligament cells over time in vivo.

Material and Methods

Chemicals

Freeze dried pellets of EMD (BIORA AB) were dissolved in refrigerated propyleneglycol alginate, PGA (6% w/w, Kelco International) solutions or in 10 mM acetic acid. Porous hydroxyapatite particles were obtained from Asahi Optical Co (HAP 2: 2 μ, 8 square meter surface area per g; HAP 40: 40 μ, 22 square meter per g). Type I collagen from human placenta was obtained from Sigma (C-7521). *o*-phosphoric acid (37% in distilled water, Merck Suprapur®) was used for etching teeth. Other chemicals are described together

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Chapter 19

Barrier Membranes for Periodontal Guided Tissue Regeneration Applications

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Strategies for periodontal therapy are aimed toward elimination of etiological factors, prevention of spread and elimination of symptoms of disease, correction of anatomical defects, and regeneration of periodontal tissues. Various regenerative surgical techniques are frequently utilized for the augmentation of deficient ridges with decreased bone height prior to placement of dental

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Article 39

Implant Dentistry

Guided bone regeneration using bone grafts and collagen membranes

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When nonabsorbable membranes are used for guided bone regeneration (GBR), second surgeries are required for membrane retrieval. In addition, these types of membranes show a high incidence of flap sloughing and membrane exposure that often lead to infection and unfavorable results. Absorbable barriers such as collagen membranes were developed to overcome these drawbacks. This article presents the principles and the clinical procedure of using barrier membranes composed of absorbable collagen in GBR aimed at the repair and regeneration of ridge dehiscence defects around implants. The unique properties of collagen membranes that make them ideally suited to GBR procedures are reviewed. In addition, the indications and contraindications for using collagen membranes for GBR procedures are examined. Finally, cases are presented to demonstrate details of surgical principles and techniques. *(Quintessence Int 2001;32:504–515)*

Key words: barrier materials, bone-replacement grafts, collagen membranes, guided bone regeneration, guided tissue regeneration, implants

Prostheses fabricated on implants have increased stability and retention compared to traditional removable partial dentures and are more conservative of tooth structure than fixed appliances. In addition, numerous studies have documented long-term success rates for implants.[1,2] It is no wonder that in the last 10 years the use of implants in the United States has increased dramatically. Alveolar bone loss created by disuse atrophy, disease, trauma, residual bone defects, or sinus pneumatization can limit the amount of bone available both in height and width. This restricts the ability to place implants in the appropriate positions. Furthermore, it creates difficulties for clinicians who restore implant prostheses as well as causes improper occlusal loads on implants, which could result in bone loss or implant failure in some cases. Placing implants into less-than-adequate bone, but with optimal prosthetic position, may also lead to disappointment when bony dehiscences and fenestrations are discovered at the time of second-stage surgery. Unfortunately, even under the best of circumstances where implants osseointegrate well into correct prosthetic position, periimplantitis can subsequently develop and damage implant-supporting bone.

A reasonable solution to the prosthetic dilemma created by lack of available bone would be to augment ridge deficiencies prior to or during implant placement. Such an approach could enhance the prognosis of implant prosthesis cases. Guided bone regeneration (GBR) is a surgical technique used to regenerate alveolar bone defects prior to, in conjunction with, or subsequent to the placement of implants. The principles of GBR were derived from knowledge generated by the development of guided tissue regeneration (GTR) technology, which had as its goal the regeneration of periodontal tissues damaged by disease.

PRINCIPLES OF GBR

Guided bone regeneration shares in common with GTR the use of barrier membranes to achieve regeneration. To achieve better clinical outcomes, the GBR barrier should possess the following properties.[3,4]

- *Cell exclusion:* Certain cells must be excluded from the area targeted for bone regeneration. In GBR, the barrier membrane is used to prevent gingival fibroblasts and/or epithelial cells from gaining access to the wound site and forming fibrous connective tissue.

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Article 40

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Bone augmentation by means of barrier membranes

CHRISTOPH H. F. HÄMMERLE & RONALD E. JUNG

The development of guided bone regeneration (GBR) has substantially influenced the possibilities for using implants. The use of bone augmentation procedures has extended the use of endosseous implants to jaw bone areas with insufficient bone volume. Lack of bone volume may be due to congenital, post-traumatic, or post-surgical defects or the result of disease processes. The recently achieved predictability and success of this procedure can change the treatment of a compromised patient into a nearly normal challenge.

Based on pioneer experiments investigating healing of periodontal tissues following surgical therapy, a principle of tissue healing was discovered by Nyman & Karring in the early 1980's (60, 62, 87, 88). It was found that cells which have access to and migrate into a given wound space determine the type of tissue regenerating in that space. Both the exclusion of undesired cells from the wound area and the formation of a wound space into which desired cells are allowed to migrate were initially achieved by the placement of barrier membranes (61). The present understanding of the mechanisms leading to regeneration of desired tissues is still in accordance with these initial concepts.

The aim of the present chapter was to review the techniques and membrane materials applied for GBR in conjunction with implant based oral rehabilitation.

Types of membranes

General aspects

A wide range of membrane materials have been used in experimental and clinical studies to achieve GBR including polytetrafluoroethylene (PTFE), expanded PTFE (ePTFE), collagen, freeze-dried fascia lata, freeze-dried dura mater allografts, polyglactin 910, polylactic acid, polyglycolic acid, polyorthoester, polyurethane, polyhydroxybutyrate, calcium sulfate, micro titanium mesh, and titanium foils. Devices used for GBR in conjunction with endosseous implants should be safe and effective. Since no life-threatening diseases or deficiencies are treated, possible adverse effects emerging from the implanted devices should be kept to a minimum. At the same time, documentation of the effectiveness of the procedures and materials should be available. Certain critical criteria regarding membranes used for guided tissue regeneration have been postulated (47): biocompatibility, cell occlusiveness, integration by the host tissues, clinical manageability, and the space making function. For bioresorbable and biodegradable membranes, additional criteria need to be fulfilled. Tissue reactions resulting from the resorption of the membrane should be minimal, these reactions should be reversible, and they should not negatively influence regeneration of the desired tissues (38).

Although GBR is a quite successful procedure, a better understanding of the factors critical for success or failure is mandatory. This understanding will lead to more refined clinical protocols and to the manufacture of membrane materials with improved performance for a given indication. Some of these factors include the ideal size of membrane perforations, membrane stability, duration of barrier function, enhanced access of bone and bone-marrow-derived cells to the area for regeneration, ample blood fill of the space, and prevention of soft tissue dehiscence.

Non-resorbable membranes

Polytetrafluoroethylene

With the presentation of the first successful GBR procedures and the subsequent wide and successful application of ePTFE membranes, this material became a standard for bone regeneration. Expanded PTFE is characterized as a polymer with high stability

Article 41

NEW GENERATION PTFE-MEMBRANES

Non-resorbable membranes

In the eighties and nineties various regenerative materials have been introduced in the fields of periodontics and implantology. Many of these materials make use of the principle of guided tissue regeneration (GTR), which also includes guided bone regeneration (GBR). The then used non-resorbable membranes could lead to good results. A considerable disadvantage, however, was that during exposure of a non-resorbable membrane infections often arose and so this led to a (partial) failure. The introduction of a "new" non-resorbable membrane will eliminate this disadvantage. Melle Vroom and Lodewijk Gründemann give a report below of their experiences regarding the use of these membranes.

The principle of the GTR/GBR roughly means that due to sealing off a cavity with the help of a regenerative material the epithelial cells and connective tissue cells can be shut out and bone regeneration is made possible from the inside out. This gives more time to the process of bone regeneration. One of these regenerative materials is the material which has as its base polytetrafluoroethylene (PTFE), which has various applications in medical disciplines such as in cardiovascular surgery where it has been used for over thirty years. Within the fields of periodontics and implantology a form of PTFE which was treated by means of heating and applying pressures, was introduced in the eighties. This resulted in an expanded form (e-PTFE).

This form, with or without titanium reinforcement, was manufactured by the Gore company and has gained a lot of renown within the field of dentistry. Various studies have shown that the use of this material can lead to good (sometimes even spectacular) results.[1]

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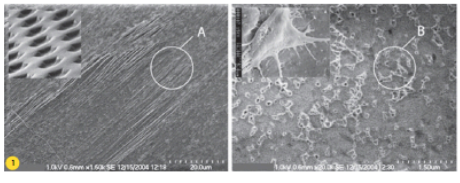
Fig. 1 EM-image of the d-PTFE-membrane. The left figure shows an enlargement of the surface at point A. The right figure shows the fibroblasts that attach to the d-PTFE membrane. *(Photographs are used by courtesy of Osteogenics Biomedical, Inc.)*



Article 42

CLINICAL ORAL IMPLANTS RESEARCH

Marco Ronda
Alberto Rebaudi
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Expanded vs. dense polytetrafluoroethylene membranes in vertical ridge augmentation around dental implants: a prospective randomized controlled clinical trial

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Key words: biomaterials, bone regeneration, clinical research, clinical trials, guided tissue regeneration

Abstract

Objective: This prospective randomized controlled trial was designed to test the performance of titanium-reinforced dense polytetrafluoroethylene (d-PTFE) membrane vs. titanium-reinforced expanded polytetrafluoroethylene (e-PTFE) membrane in achieving vertical bone regeneration, both associated with a composite grafting material.

Material and methods: The study enrolled 23 patients requiring bone augmentation with guided bone regeneration (GBR) procedures for placing implants in atrophic posterior mandibles (available bone height <7 mm). Implants were inserted and left to protrude from the bone level to achieve the programmed amount of vertical regeneration. Defects were filled with a composite bone graft (50% autologous bone and 50% mineralized bone allograft) and randomly covered with either an e-PTFE membrane (control) or a d-PTFE membrane (test). Membrane removal was performed after 6 months, and changes in bone height were recorded.

Results: Seventy-eight implants were inserted in 26 mandibular sites contextually to vertical ridge augmentation procedures. The healing period was uneventful in all sites, and the vertical defects were satisfactorily filled with a newly formed hard tissue. Mean defect fill after 6 months was 5.49 mm (SD ± 1.58) at test sites and 4.91 mm (SD ± 1.78) at control sites. The normalized data (percentage changes against baseline) did not show any statistically significant difference between test and control groups (P = NS).

Conclusions: Based on the data from this study, both d-PTFE and e-PTFE membranes showed identical clinical results in the treatment of vertical bone defects around implants, using the GBR technique. The membrane removal procedure was easier to perform in the d-PTFE group than in the e-PTFE group.

The effectiveness of guided bone regeneration (GBR) with non-resorbable membranes in obtaining vertical regeneration of the alveolar crest has been clinically and histologically documented in many studies (Simion et al. 1994a, 1998; Tinti et al. 1996; Parma-Benfenati et al. 1999). Moreover, the stability of the bone vertically regenerated around dental implants and its favorable response under functional loading have been demonstrated in human subjects (Tinti & Parma-Benfenati 1998; Simion et al. 2001; Zitzmann et al. 2001; Aghaloo & Moy 2008).

In the GBR technique, a membrane is used as a mechanical barrier to create a protected space around the bone defect: The blood clot fills the space, and osteogenic cells are allowed to colonize the augmentation area without the competition of the overlying soft tissue cells. The fundamental characteristics of barrier membranes in regenerative therapy were defined by Karring et al. [1993] and include biocompatibility, cell occlusion properties, integration by the host tissues, clinical manageability and space-making ability. These requisites are fulfilled by polytetrafluoroethylene (PTFE), a polymer consisting of a carbon backbone covalently bonded to a uniform sheath of fluorine atoms, which can be manipulated and engineered into a variety of forms.

For years, research has been focused mainly on the applications of expanded

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Article 43

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Guided bone regeneration with titanium membranes: a clinical study

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SUMMARY **Guided bone regeneration using barrier membranes is useful in bone augmentation. Because the commonly used polytetrafluoroethylene (PTFE, Gore-Tex®, WL Gore, Flagstaff, AZ, USA) membranes or resorbable membranes tend to collapse, more stable membranes are desirable. A titanium membrane (FRIOS® BoneShield, Friatec, Mannheim, Germany) was evaluated in a clinical study of 52 patients. Most of them had particulate bone grafts or phycogene hydroxyapatite (Algipore®, Friatec, Mannheim, Germany) or both stabilized with titanium membranes. In 78 procedures, 23 membranes (29%) became exposed, but only seven of these (9%) led to failure of the graft with a considerable loss of augmented material. The time interval between operation and possibly exposure was responsible for the result. Early exposures (within a few weeks) led to poor formation of new bone within the grafts, whereas if exposure was later, results were as good as in procedures in which the membranes did not become exposed.**

INTRODUCTION

An adequate supply of bone is one of the prerequisites of good long-term prognosis in implant dentistry. The volume of bone is often not sufficient because of trauma, advanced periodontal disease, or atrophy of the alveolar ridge.[1] Bone grafts, augmentation of the maxillary sinus floor, and guided bone regeneration have been used to ensure sufficient bone at the implant sites. Biological principles of guided tissue regeneration to gain new bone have been tested in experimental animal studies,[2–4] and the principle of guided bone regeneration is the creation and maintenance of secluded spaces.[5,6] The ingrowth of osteogenic cells is therefore undisturbed by competing non-osteogenetic soft tissue cells. Dahlin *et al.* published a controlled clinical study in which fixture fenestrations treated with guided bone regeneration showed significantly more new bone formation than control sites of fenestration defects. As well as the coverage of exposed implant surfaces by newly formed bone,[7–10] the goal was to increase the volume of bone on the alveolar ridge.[2] In the first studies of guided bone regeneration, flexible membranes were applied. But the creation and maintenance of sufficient space underneath the barrier is an important factor for a successful result.[3,11] Therefore titanium-reinforced[12] polytetrafluoroethylene membranes (PTFE, Gore-Tex, WL Gore, Flagstaff, AZ, USA) and titanium membranes[11,13] were introduced to increase the stability of barrier membranes. The aim of this study is to present first clinical results of a microperforated titanium membrane used for guided bone regeneration and to evaluate the results of different augmentation techniques.

MATERIALS AND PATIENTS

Since 1995, we have used titanium membranes with microperforations (FRIOS BoneShield, Friatec, Mannheim, Germany) for guided bone regeneration. The membranes are either triangular or oval (Fig. 1). The mechanical properties of the membrane prevent collapse of the membrane and provide a constant volume underneath it and areas of microporosity that are small enough to prevent soft tissue penetration through the membrane permit diffusion of interstitial fluid. The membrane has to be preshaped according to the size of the defect. Lateral slits allow fixation with titanium pins to the bone surrounding the defect and make the membrane able to be molded. It can therefore be adapted to fit passively according to the shape of the augmented site.

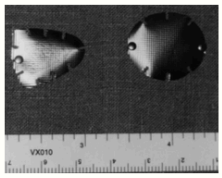

Fig. 1 – Various titanium membranes.

Article 44

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Devices for periodontal regeneration

DIMITRIS N. TATAKIS, ANANYA PROMSUDTHI & ULF M. E. WIKESJÖ

The use of devices in periodontal regenerative therapy has been associated with the concept of guided tissue regeneration. The hypothesis originated by Melcher (95) and established by Karring et al. (59, 108, 109) suggests that selected cell populations residing in the periodontium can produce new cementum, alveolar bone and periodontal ligament, provided that these populations are given the opportunity to occupy a periodontal wound. Such opportunity arises when other cell populations, such as epithelial cells or gingival fibroblasts, which also would invade the wound space are effectively excluded. This provision to exclude specific tissues during the healing phase of a periodontal defect wound has generated an impetus for the development of periodontal devices, commonly called barriers or membranes, for guided tissue regeneration.

The first clinical device used in periodontal surgery which allowed regeneration of cementum, periodontal ligament and alveolar bone was a cellulose acetate (paper) laboratory filter (108, 109). The use of the paper filter provided the first human histological evidence of periodontal regeneration in response to guided tissue regeneration (109). This barrier, however, lacked several characteristics deemed necessary for guided tissue regeneration. Since then, several barriers made out of a variety of materials have been introduced. This chapter reviews properties of the various barriers used for guided tissue regeneration from a biomaterial perspective.

General concepts

A biomaterial is defined as a nonviable material used in a medical device, intended to interact with biological systems (16). Any device introduced into the body to address a particular need has to fulfill two major requirements: safety and efficacy. Safety is assessed through a wide selection of *in vitro* and *in vivo* assays designed to address specific aspects of biocompatibility. By definition, biocompatibility is the ability of a material to perform with an appropriate host response in a specific situation, which means that neither the material adversely and significantly affects the body nor the physiological tissue environment adversely and significantly affects the material (16, 159). Cell culture cytotoxicity, skin irritation, subcutaneous implantation, blood compatibility, hemolysis, carcinogenesis, mutagenicity, pyrogenicity, sensitization and short- and long-term histological tissue reaction are some of the assays used to evaluate biocompatibility. Besides general biocompatibility testing, particular tests need to be considered, depending on the end-use of the device (16, 64, 65).

For a device to be effective, it has to meet certain criteria based on organ and tissue properties and specific goals (64, 110). Characteristics, or design criteria, for guided tissue regeneration devices have been proposed and discussed by Scantlebury (125), Gottlow (60), and Hardwick et al. (65) and are summarized in Table 1. An additional characteristic, biological activity, should be considered for future generation devices. The reason a barrier fails to provide positive results when used for guided tissue regeneration within a proper experimental or clinical protocol is believed to be failure to meet one or more of the characteristics outlined in the paragraphs below.

Besides biocompatibility, the first design criteria for a guided tissue regeneration device is its ability

Table 1. Design criteria for periodontal guided tissue regeneration devices

Biocompatibility
Cell exclusion
Space maintenance
Tissue integration
Ease of use
Biological activity

Article 45

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CLINICAL ORAL IMPLANTS RESEARCH
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Case report

The use of a new bioresorbable barrier for guided bone regeneration in connection with implant installation

Case reports

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Lundgren D, Sennerby L, Falk H, Friberg B, Nyman S. The use of a new bioresorbable barrier for guided bone regeneration in connection with implant installation. Case reports.
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This report presents 4 cases with 6 implant exposures after the installation of Brånemark System® implants which called for treatment applying the guided bone regeneration technique. A bioresorbable barrier (GUIDOR® Matrix Barrier) was used to cover the defects, 4 defects with and 2 without the support of autologous bone chips. Complete bone filling was found in 4 (2 without and 2 with bone chips) and partial filling in 2 (with bone chips) of the treated defects, as registered at the abutment connection 6–7 months after surgery. Besides its ability to serve as a barrier for guided bone regeneration, it was found that the matrix barrier had the following properties; biocompatibility observed as uneventful tissue healing, malleability facilitating the clinical handling and ability to be resorbed within 6 to 7 months, as evaluated by clinical inspection. The observations of the present case reports indicate that the tested barrier may be used for guided bone regeneration in connection with implant installation. It is advisable, however, to use a supporting material to prevent barrier collapse, although bone regeneration can be achieved in certain situations without such material if the defect morphology is favourable.

Key words: bioresorption – guided bone regeneration – guided tissue regeneration – oral implant

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A prerequisite for the successful installation of oral implants is the availability of sufficient jawbone volume. Installation of endosseous implants in areas where the dimensions of the jawbone are equal to or less than those of the implant results in parts of the implant surfaces not being covered by bone. This may lead to recession of the soft tissue with denudation of the implant surface, which in turn will mechanically irritate the soft tissue and prevent proper cleaning. It is also preferable to strive for full bone coverage to increase the retention of the implants, thereby improving the prognosis for the prosthetic reconstruction. In such situations, ridge enlargement based on the guided tissue regeneration concept could be carried out either before or in connection with implant installation, as demonstrated in previous animal experiments (Dahlin et al. 1989; Becker et al. 1990; Seibert & Nyman 1990) and clinical studies (Becker & Becker, 1990; Buser et al. 1990; Nyman et al. 1990; Dahlin et al. 1991a, b; Buser et al. 1993). In the studies referred to, nonbioresorbable expanded polytetrafluoroethylene membranes were used (Gore-Tex™, Gore Inc., Flagstaff, AZ, USA). However, an advantage of a bioresorbable barrier would be that the second surgical procedure can be limited to implant installation or abutment connection when a two-stage implant system is used, thus avoiding elevation of large flaps for barrier removal. Also, when a one-stage implant system is used, only one surgical procedure needs to be carried out.

Article 46

Matteo Chiapasco
Marco Zaniboni

Clinical outcomes of GBR procedures to correct peri-implant dehiscences and fenestrations: a systematic review

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Conflicts of interest:
The authors declare no conflicts of interest.

Key words: bone regeneration, dehiscence, fenestration, implant

Abstract

Objective: To analyze the clinical outcomes of endosseous implants following guided bone regeneration (GBR) procedures to correct dehiscence/fenestration defects associated with implant placement.

Methods/Search strategy: A Medline search was performed for human studies published in English focusing on GBR procedures for the correction of dehiscence/fenestration defects associated with the placement of screw-shaped titanium implants. The selected studies had to include at least 10 consecutively treated patients with a minimum follow-up of 12 months after the start of prosthetic loading. The clinical outcomes in terms of the complication rate of the GBR procedure, implant survival, and stability of marginal soft tissues around implants were evaluated.

Results: Seven publications were included in this review. A total of 238 patients received 374 implants. Defects were treated with resorbable or non-resorbable membranes, in association with or without graft materials. Patients were followed for 1–10 years after the start of prosthetic loading. In the postoperative period, 20% of the non-resorbable membranes and 5% of the resorbable ones underwent exposure/infection. However, in the majority of cases, a complete or an almost complete coverage of the initial defect was obtained. The overall survival rate of implants, irrespective of the type of membrane and grafting materials, was 95.7% (range: 84.7–100%). No significant modifications of probing depth and/or variation of clinical attachment level around implants were observed during the follow-up period.

Conclusion: Despite the favorable results obtained, it was difficult to draw a significant conclusion as far as the more reliable grafting material and membrane barrier for the correction of dehiscence/fenestration defects are concerned, due to the limited sample of patients and the wide variety of grafting materials and membranes, used alone or in combination. Moreover, due to the lack of randomized clinical trials, it was impossible to demonstrate that such augmentation procedures are actually needed to allow the long-term survival of implants.

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Dental rehabilitation of partially or totally edentulous patients with oral implants has become a routine treatment modality in the last decades, with reliable long-term results (Albrektsson et al. 1986; van Steenberghe 1989; van Steenberghe et al. 1990; Lindquist et al. 1996; Buser et al. 1997; Arvidson et al. 1998; Lekholm et al. 1999; Brocard et al. 2000; Weber et al. 2000; Leonhardt et al. 2002; Bedktor et al. 2004; Esposito et al. 2004). However, unfavorable local conditions of the alveolar ridge, due to atrophy, periodontal disease, and trauma sequelae, may provide insufficient bone volume, which may potentially compromise the long-term survival

Article 47

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

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Affiliations — collapse

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PMID: 19587874

Abstract

Purpose: The aims of the current study were to: (1) evaluate the results of vertical guided bone regeneration (GBR) with particulate autogenous bone grafts, (2) determine clinically and radiographically the success and survival rates of 82 implants placed in such surgical sites after prosthetic loading for 12 to 72 months, and (3) compare defects that were treated simultaneously with sinus augmentation and vertical GBR to other areas of the jaw treated with vertical GBR only.

Materials and methods: Eighty-two implants were inserted in 35 patients with 36 three-dimensional vertical bone defects. The patients were divided into three groups: single missing teeth (group A), multiple missing teeth (group B), and vertical defects in the posterior maxilla only (group C). All group C subjects were treated simultaneously with sinus and vertical augmentations. All patients were treated with vertical ridge augmentation utilizing titanium-reinforced polytetrafluoroethylene (e-PTFE) membranes and particulated autografts. After removal of the e-PTFE membrane, all sites received a collagen membrane.

Results: At membrane removal, mean vertical augmentation was 5.5 mm (+/-2.29 mm). Mean combined crestal remodeling was 1.01 mm (+/-0.57 mm) at 12 months, which remained stable through the 6-year follow-up period. There were no statistically significant differences between the three groups in mean marginal bone remodeling. One defect had a bone graft complication (2.78%, 95% CI: 0.00%, 8.15%). The overall implant survival rate was 100% with a cumulative success rate of 94.7%.

Conclusions: (1) Vertical augmentation with e-PTFE membranes and particulated autografts is a safe and predictable treatment; (2) success and survival rates of implants placed in vertically augmented bone with the GBR technique appear similar to implants placed in native bone under loading conditions; (3) success and failure rates of implants placed into bone regenerated simultaneously with sinus and vertical augmentation techniques compare favorably to those requiring only vertical augmentation.

Article 48

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Bio-absorbable polymers in implantation-An overview

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Poly-α-hydroxy aliphatic esters are novel bio-absorbable polymers (BAPs), which are being used extensively as implantation products (orthopaedics, drug delivery, scaffolds and sutures). Polylactic acid (PLA), polyglycolic acid (PGA) and polydioxanone (PDO) are approved from food and drug administration agency (FDA) for human clinical uses. This review presents available synthetic routes for making bio-absorbable polymers, their properties and end use applications.

Keywords: Bio-absorbable polymer, Polylactic acid, Polyglycolic acid

Introduction

Orthopaedic surgeons have been repairing serious bone fractures by binding fractures with screws, pins, and other fixation-type devices using metals made up of highly sophisticated metal alloys of cobalt[1-4], titanium[5-7], zirconium[8-10], and tantalum[11-13]. However, these metal alloys are hard and stiffer than bone and possibly interfere with regenerating bones. Search for more compatible materials with the human body led to consider bio-absorbable polymers (BAPs). In 1960s, Kulkarni *et al*[14,15] implanted BAP as sutures and rod for repairing mandibular fractures in dog. Poly-α-hydroxyaliphatic esters are developed *in vivo* biomedical applications of orthopaedics, drug delivery systems, scaffolds, sutures and staplers. BAPs over alloys can eventually be resorbed or excreted by human metabolism without any side effects and exhibit more bone-like properties. Poylactic acid (PLA), polyglycolic acid (PGA) and polydioxanone (PDO) are some of the implant dominant BAPs (Scheme 1). Under ideal conditions, a BAP could encourage bone healing while body slowly metabolizes it, thus eliminating need for a second surgery that may be required when a metal alloy is implanted[15-20]. Polymeric drug delivery devices prevent drug degradation and may also provide management of drug release by varying drug-to-polymer ratio, molecular weight and composition of polymer[21,22]. Bio-absorbable implants can be designed for fracture fixation, drug delivery, or ligament repair and other clinical use.

This review presents current issues on methods of preparation of bio-absorbable materials using various catalysts and initiators for making high molecular weight and functional BAPs, besides structure-property correlations of polymers prepared under various conditions and their end use applipl:cations.

Preparation of Bio-absorbable Polymers (BAPs)

Polycondensation

Under polymerization of lactic acid and glycolic acid via direct condensation, hydroxyl group present in ±-position reduces reactivity of monomer and thereby increases reaction time. High purity is important to undergo effective reaction although commercially available monomer in the market is 85-90% pure[23-25]. Regular polycondensation method produces low molar mass products. Low molar mass oilgo (lactic acid) (OLA), oilgo (glycolic acid) (OGA) and combination of copolymers with functional monomers can be used to develop spherical microspheres for drug delivery systems and high molar mass polymers are also used for load bearing applications in biomedical implants[26-28]. Effect of catalytic action and method of polymerization plays an important role in synthesizing high molar mass polymers. Sn (II) and Ni (II) compounds show efficiency in synthesis of high molar weight polymers[29,30]. Stannous octoate and tetraphenyltin catalysts have been approved by Food and

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Article 49

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REVIEW ARTICLE

Jan Behring · Rüdiger Junker · X. Frank Walboomers Betsy Chessnut · John A. Jansen

Toward guided tissue and bone regeneration: morphology, attachment, proliferation, and migration of cells cultured on collagen barrier membranes. A systematic review

Received: January 20, 2008 / Accepted: April 23, 2008

Abstract Collagen barrier membranes are frequently used in both guided tissue regeneration (GTR) and guided bone regeneration (GBR). Collagen used for these devices is available from different species and is often processed to alter the properties of the final product. This is necessary because unprocessed collagen is rapidly resorbed in vivo and demands for barrier membranes are different in GTR and GBR. This systematic literature review attempts to evaluate possible effects of collagen origin and mode of cross-linking on the potential of different cells to attach to, proliferate on, and migrate over barrier membranes in vitro. Seventeen original studies, selected by a systematic process, are included in this review. The results show that fibroblasts of different species and originating tissues as well as bone-forming cells are able to attach to collagen membranes irrespective of collagen origin or mode of processing. Different cell types behave differently on identical membranes. Many pieces of evidence are currently available, and we attempted to elucidate the effects of collagen origin and mode of processing on cellular behavior, but further research will be required before it will be possible to predict for certain the effect a specific procedure will have with a given product.

Key words Guided tissue regeneration · Guided bone regeneration · Collagen · In vitro · Membrane

Introduction

In guided tissue regeneration (GTR) and guided bone regeneration (GBR), barrier membranes are used to separate the area of the defect into two compartments.

An ideal resorbable membrane for these techniques should facilitate the attachment, proliferation, and migration of cells on its surface in order to seal the underlying defect off from the oral flora, even in the case of membrane exposure. The adherence of connective tissue cells to the inside of a membrane promotes periodontal regeneration, and an attachment can help to stabilize the blood clot and integrate the membrane into the tissue.

Collagen is the main structural macromolecule of the human body and can easily be reconstituted into the different shapes needed in medicine, including occlusive membranes. However, native collagen is degraded within a few days, and untreated collagen membranes lack stability to maintain space if bony support is missing.

To overcome these problems, various cross-linking techniques have been developed. Cross-linking involves the multiplication of naturally occurring links between collagen molecules. This leads to stiffer collagen membranes and slows down enzymatic degradation. Both properties seem to be dose- or time-dependent, depending on the mode of cross-linking. This means that the number of collagen cross-links is proportional to both the stiffness of the membrane and the degradation time. The most frequently used cross-linking method is to tan the collagen with glutaraldehyde (GA), which, although an effective cross-linking agent, has been shown in vitro and in vivo to increase the cytotoxicity of collagen membranes. GA is released during collagen degradation, and a constant release of remnant (nonreacted) GA has been shown to inhibit cell proliferation. Therefore, several other techniques to cross-link collagen have been described.

Many different collagen barrier devices are on the market or under development today (Table 1). In addition to the effects of cross-linking, it has been shown that the surface topography of a membrane and the origin of the collagen used may affect the properties of a GTR or GBR membrane.

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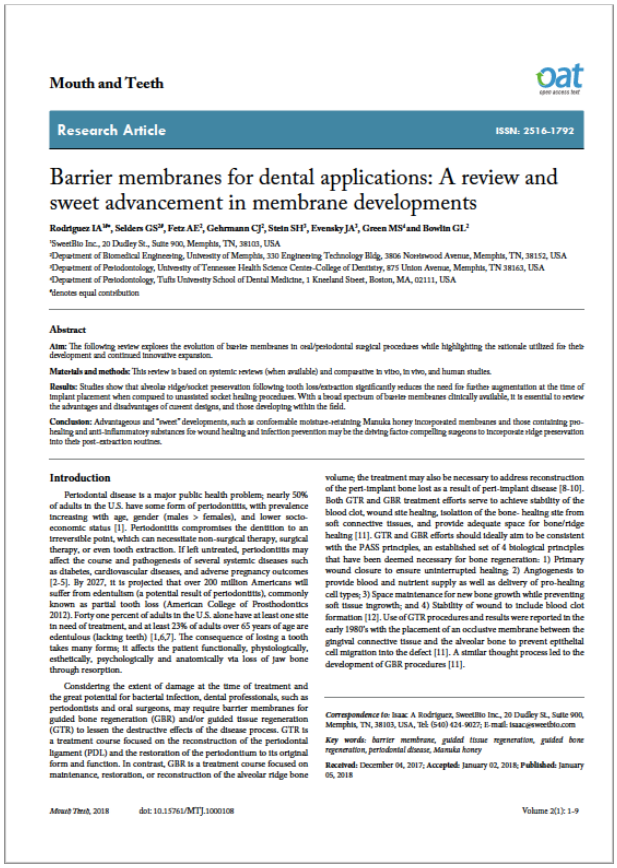

Mouth and Teeth

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Research Article ISSN: 2516-1792

Barrier membranes for dental applications: A review and sweet advancement in membrane developments

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Abstract

Aim: The following review explores the evolution of barrier membranes in oral/periodontal surgical procedures while highlighting the rationale utilized for their development and continued innovative expansion.

Materials and methods: This review is based on systemic reviews (when available) and comparative in vitro, in vivo, and human studies.

Results: Studies show that alveolar ridge/socket preservation following tooth loss/extraction significantly reduces the need for further augmentation at the time of implant placement when compared to unassisted socket healing procedures. With a broad spectrum of barrier membranes clinically available, it is essential to review the advantages and disadvantages of current designs, and those developing within the field.

Conclusion: Advantageous and "sweet" developments, such as conformable moisture-retaining Manuka honey incorporated membranes and those containing pro-healing and anti-inflammatory substances for wound healing and infection prevention may be the driving factor compelling surgeons to incorporate ridge preservation into their post-extraction routines.

Introduction

Periodontal disease is a major public health problem; nearly 50% of adults in the U.S. have some form of periodontitis, with prevalence increasing with age, gender (males > females), and lower socio-economic status [1]. Periodontitis compromises the dentition to an irreversible point, which can necessitate non-surgical therapy, surgical therapy, or even tooth extraction. If left untreated, periodontitis may affect the course and pathogenesis of several systemic diseases such as diabetes, cardiovascular diseases, and adverse pregnancy outcomes [2-5]. By 2027, it is projected that over 200 million Americans will suffer from edentulism (a potential result of periodontitis), commonly known as partial tooth loss (American College of Prosthodontics 2012). Forty one percent of adults in the U.S. alone have at least one site in need of treatment, and at least 23% for adults over 65 years of age are edentulous (lacking teeth) [1,6,7]. The consequence of losing a tooth takes many forms; it affects the patient functionally, physiologically, esthetically, psychologically and anatomically via loss of jaw bone through resorption.

Considering the extent of damage at the time of treatment and the great potential for bacterial infection, dental professionals, such as periodontists and oral surgeons, may require barrier membranes for guided bone regeneration (GBR) and/or guided tissue regeneration (GTR) to lessen the destructive effects of the disease process. GTR is a treatment course focused on the reconstruction of the periodontal ligament (PDL) and the restoration of the periodontium to its original form and function. In contrast, GBR is a treatment course focused on maintenance, restoration, or reconstruction of the alveolar ridge bone volume; the treatment may also be necessary to address reconstruction of the peri-implant bone lost as a result of peri-implant disease [8-10]. Both GTR and GBR treatment efforts serve to achieve stability of the blood clot, wound site healing, isolation of the bone- healing site from soft connective tissues, and provide adequate space for bone/ridge healing [11]. GTR and GBR efforts should ideally aim to be consistent with the PASS principles, an established set of 4 biological principles that have been deemed necessary for bone regeneration: 1) Primary wound closure to ensure uninterrupted healing; 2) Angiogenesis to provide blood and nutrient supply as well as delivery of pro-healing cell types; 3) Space maintenance for new bone growth while preventing soft tissue ingrowth; and 4) Stability of wound to include blood clot formation [12]. Use of GTR procedures and results were reported in the early 1980's with the placement of an occlusive membrane between the gingival connective tissue and the alveolar bone to prevent epithelial cell migration into the defect [11]. A similar thought process led to the development of GBR procedures [11].

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Key words: barrier membrane, guided tissue regeneration, guided bone regeneration, periodontal disease, Manuka honey

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Article 51

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Bone grafts and periodontal regeneration

MICHAEL A. BRUNSVOLD & JAMES T. MELLONIG

One of the biggest challenges remaining in dentistry is to predictably regenerate the alveolar bone destroyed by periodontitis. It is exciting to consider how many more dentitions could be restored to optimum health, aesthetics and function if this were possible. Great strides are being made to achieve this goal using the method of bone grafting and other regeneration procedures. Recent advances in bone grafting include: 1) improved procurement and availability of bone graft material, 2) improved methods for complete detoxification of diseased root surfaces, 3) better understanding of the cell kinetics of wound healing, 4) application of the principles of guided tissue regeneration and 5) the use of growth factors to enhance healing.

Periodontal bone grafting in the past has been controversial and unpredictable. Strong proponents of bone grafting argue that the majority of healing studies show better success using grafting materials than open flap debridement in managing severe osseous defects. Others argue that the amount of bone regeneration possible with current techniques is too limited and unpredictable to be useful.

This review attempts to clarify the role of bone grafting in the present era of regeneration. The information discussed includes a definition of terms, objectives of bone grafting, types of bone grafts, surgical procedure and bone banking.

Terminology

Some of the controversy regarding periodontal reconstruction stems from confusion of terminology. The term regeneration is often used inappropriately to describe the healing process of repair.

In this review, periodontal regeneration is defined as the process by which the architecture and function of the periodontium is completely restored. Repair of the periodontium is defined as re-establishment of continuity without full restoration of architecture and function.

Two other related terms are also commonly confused. New attachment is the reunion of connective tissue with a root surface that has been deprived of its periodontal ligament; reunion occurs by the formation of new cementum with inserting collagen fibers. Reattachment is the reunion of connective tissue with a root surface on which viable periodontal tissue is present. The types of grafts are defined separately in another section of this review.

Objectives of bone grafts

The objectives of periodontal bone grafts are: 1) probing depth reduction, 2) clinical attachment gain, 3) bone fill of the osseous defect and 4) regeneration of new bone, cementum and periodontal ligament (90). Clinical studies and case reports supply valuable information concerning the first 3 objectives. The last objective requires histologic analysis to verify (Fig. 1).

Animal studies are of value to indicate the potential of graft materials to produce favorable results. The results must be viewed with caution, however, and should not be directly applied to humans. Animal studies compare graft and nongraft procedures in artificially created defects (Table 1). The majority of these reports indicate a superior result obtained following the placement of a graft. Nongraft control sites were never found to be superior to grafted sites.

Human histologic analysis is the gold standard for determining the true potential of any graft material to regenerate the periodontium. Histologic evaluation of 159 human periodontal grafts has been reported (Table 2). A critical step in these trials is documentation on the root surface of where bacterial contamination occurred prior to treatment. The methods for this documentation have varied a great

Citing Literature

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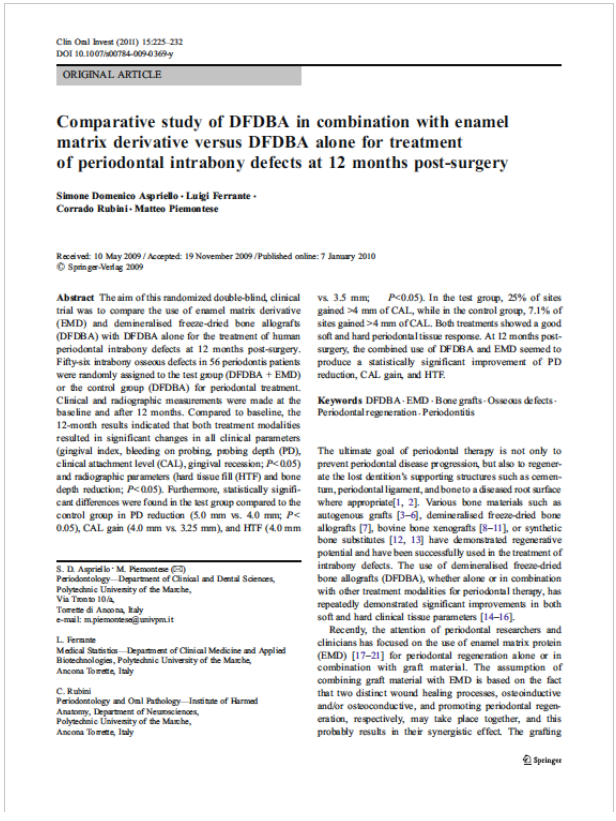

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ORIGINAL ARTICLE

Comparative study of DFDBA in combination with enamel matrix derivative versus DFDBA alone for treatment of periodontal intrabony defects at 12 months post-surgery

Simone Domenico Aspriello · Luigi Ferrante · Corrado Rubini · Matteo Piemontese

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Abstract The aim of this randomized double-blind, clinical trial was to compare the use of enamel matrix derivative (EMD) and demineralised freeze-dried bone allograft (DFDBA) with DFDBA alone for the treatment of human periodontal intrabony defects at 12 months post-surgery. Fifty-six intrabony osseous defects in 56 periodontis patients were randomly assigned to the test group (DFDBA + EMD) or the control group (DFDBA) for periodontal treatment. Clinical and radiographic measurements were made at the baseline and after 12 months. Compared to baseline, the 12-month results indicated that both treatment modalities resulted in significant changes in all clinical parameters (gingival index, bleeding on probing, probing depth (PD), clinical attachment level (CAL), gingival recession; $P<0.05$) and radiographic parameters (hard tissue fill (HTF) and bone depth reduction; $P<0.05$). Furthermore, statistically significant differences were found in the test group compared to the control group in PD reduction (5.0 mm vs. 4.0 mm; $P<0.05$), CAL gain (4.0 mm vs. 3.25 mm), and HTF (4.0 mm vs. 3.5 mm; $P<0.05$). In the test group, 25% of sites gained >4 mm of CAL, while in the control group, 7.1% of sites gained >4 mm of CAL. Both treatments showed a good soft and hard periodontal tissue response. At 12 months post-surgery, the combined use of DFDBA and EMD seemed to produce a statistically significant improvement of PD reduction, CAL gain, and HTF.

Keywords DFDBA · EMD · Bone grafts · Osseous defects · Periodontal regeneration · Periodontitis

The ultimate goal of periodontal therapy is not only to prevent periodontal disease progression, but also to regenerate the lost dentition's supporting structures such as cementum, periodontal ligament, and bone to a diseased root surface where appropriate[1, 2]. Various bone materials such as autogenous grafts [3–6], demineralised freeze-dried bone allografts [7], bovine bone xenografts [8–11], or synthetic bone substitutes [12, 13] have demonstrated regenerative potential and have been successfully used in the treatment of intrabony defects. The use of demineralised freeze-dried bone allografts (DFDBA), whether alone or in combination with other treatment modalities for periodontal therapy, has repeatedly demonstrated significant improvements in both soft and hard clinical tissue parameters [14–16].

Recently, the attention of periodontal researchers and clinicians has focused on the use of enamel matrix protein (EMD) [17–21] for periodontal regeneration alone or in combination with graft material. The assumption of combining graft material with EMD is based on the fact that two distinct wound healing processes, osteoinductive and/or osteoconductive, and promoting periodontal regeneration, respectively, may take place together, and this probably results in their synergistic effect. The grafting

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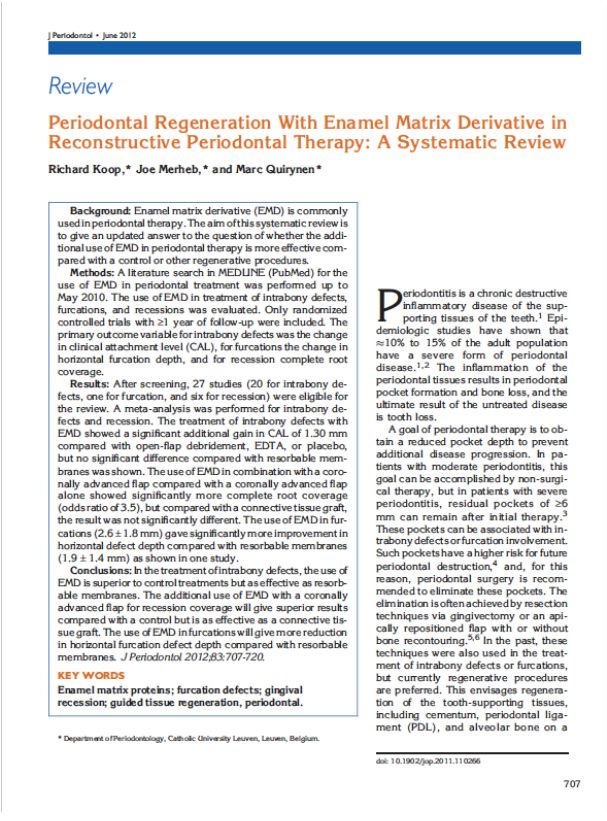
Article 53



J Periodontol • June 2012

Review

Periodontal Regeneration With Enamel Matrix Derivative in Reconstructive Periodontal Therapy: A Systematic Review

Richard Koop,* Joe Merheb,* and Marc Quirynen*

Background: Enamel matrix derivative (EMD) is commonly used in periodontal therapy. The aim of this systematic review is to give an updated answer to the question of whether the additional use of EMD in periodontal therapy is more effective compared with a control or other regenerative procedures.

Methods: A literature search in MEDLINE (PubMed) for the use of EMD in periodontal treatment was performed up to May 2010. The use of EMD in treatment of intrabony defects, furcations, and recessions was evaluated. Only randomized controlled trials with ≥1 year of follow-up were included. The primary outcome variable for intrabony defects was the change in clinical attachment level (CAL), for furcations the change in horizontal furcation depth, and for recession complete root coverage.

Results: After screening, 27 studies (20 for intrabony defects, one for furcation, and six for recession) were eligible for the review. A meta-analysis was performed for intrabony defects and recession. The treatment of intrabony defects with EMD showed a significant additional gain in CAL of 1.30 mm compared with open-flap debridement, EDTA, or placebo, but no significant difference compared with resorbable membranes was shown. The use of EMD in combination with a coronally advanced flap compared with a coronally advanced flap alone showed significantly more complete root coverage (odds ratio of 3.5), but compared with a connective tissue graft, the result was not significantly different. The use of EMD in furcations (2.6 ± 1.8 mm) gave significantly more improvement in horizontal defect depth compared with resorbable membranes (1.9 ± 1.4 mm) as shown in one study.

Conclusions: In the treatment of intrabony defects, the use of EMD is superior to control treatments but as effective as resorbable membranes. The additional use of EMD with a coronally advanced flap for recession coverage will give superior results compared with a control but is as effective as a connective tissue graft. The use of EMD in furcations will give more reduction in horizontal furcation defect depth compared with resorbable membranes. *J Periodontol 2012;83:707-720.*

KEY WORDS
Enamel matrix proteins; furcation defects; gingival recession; guided tissue regeneration, periodontal.

Periodontitis is a chronic destructive inflammatory disease of the supporting tissues of the teeth.[1] Epidemiologic studies have shown that ≈10% to 15% of the adult population have a severe form of periodontal disease.[1,2] The inflammation of the periodontal tissues results in periodontal pocket formation and bone loss, and the ultimate result of the untreated disease is tooth loss.

A goal of periodontal therapy is to obtain a reduced pocket depth to prevent additional disease progression. In patients with moderate periodontitis, this goal can be accomplished by non-surgical therapy, but in patients with severe periodontitis, residual pockets of ≥6 mm can remain after initial therapy.[3] These pockets can be associated with intrabony defects or furcation involvement. Such pockets have a higher risk for future periodontal destruction,[4] and, for this reason, periodontal surgery is recommended to eliminate these pockets. The elimination is often achieved by resection techniques via gingivectomy or an apically repositioned flap with or without bone recontouring.[5,6] In the past, these techniques were also used in the treatment of intrabony defects or furcations, but currently regenerative procedures are preferred. This envisages regeneration of the tooth-supporting tissues, including cementum, periodontal ligament (PDL), and alveolar bone on a

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Clinical comparison of resorbable and non-resorbable barriers for guided periodontal tissue regeneration

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Caffesse RG, Mota LF, Quiñones CR, Morrison EC: Clinical comparison of resorbable and non-resorbable barriers for guided periodontal tissue regeneration. J Clin Periodontol 1997; 24: 747–752. © Munksgaard, 1997.

Abstract. The purpose of this study was to compare the clinical results of guided periodontal tissue regeneration (GPTR) using a resorbable barrier manufactured from a copolymer of polylactic and polyglycolic acids (Resolut® Regenerative Material) with those of non-resorbable e-PTFE barrier (Gore-Tex® Periodontal Material). 12 subjects participated, 6 with similarly paired class II furcations and 6 with 2 similar 2, 3-wall periodontal lesions. The resorbable and non-resorbable barriers were randomly assigned to 1 defect in each subject. Non-resorbable barriers were removed in six weeks. Plaque index (PII), gingival index (GI), probing depth (PD), clinical attachment level (CAL) and gingival recession (R) were recorded at baseline, (i.e., immediately prior to surgery) and at 12 months postsurgically. The clinical healing was similar and uneventful in both groups. Intrabony pockets depicted significant changes from baseline ($p<0.05$) for probing depth reduction and gain in clinical attachment levels. No differences were found between treatments. Class II furcations showed significant improvements from baseline ($p\leq0.05$) for probing depth reduction and clinical attachment gain. No differences were detected between treatments. It is concluded that the resorbable barrier tested is as effective as the nonresorbable e-PTFE barrier for the treatment of class II furcations and intrabony defects.

Key words: guided tissue regeneration; resorbable membranes; clinical evaluation; e-PTFE; non-resorbable membranes; PLA-PGA copolymer

Accepted for publication 28 February 1997

Guided periodontal tissue regeneration(GPTR) has been successfully applied in clinical periodontal therapy since 1982 (Nyman et al. 1982, Gottlow et al. 1986, Becker et al. 1987, Nyman et al 1987). The basic principle behind the concept of GPTR is that the post-treatment clinical results achieved are dependent on the source from which the cells repopulating the exposed root surface and adjacent bony defect originate.

To date, a non-resorbable expanded polytetrafluorethylene material (e-PTFE) (i.e., Gore-Tex® Periodontal Material, W.L. Gore & Associates, Inc., Flagstaff, AZ, USA) has been widely used for periodontal regenerative procedures. This material has been shown to be safe and effective in the treatment of class II furcation and intrabony periodontal defects (Gottlow et al. 1986; Caffesse & Becker 1991; Caffesse et al. 1990b; Cortellini et al 1993b; Machtei et al. 1993). Although this material possesses the ideal characteristics of a barrier (i.e., biocompatibility, cell occlusivity, space making properties, ability to stabilize the surrounding tissues during healing, and the capacity to limit epithelial migration) (Scantlebury 1993), a second surgical procedure is necessary for its retrieval due to its non-resorbability. Due to this, a series of bioresorbable materials have been the object of intensive research during recent years (Blumenthal 1993; Chang et al. 1990; Fleischer et al. 1988; Minabe et al. 1989; Kodama et al. 1989; Pitaru et al. 1987; Blumenthal 1988; Chung et al. 1990; Hugoson et al. 1995; Van Swol et al. 1992; Blumenthal 1993b).

Recently, a bioresorbable barrier (Resolut® Regenerative Material, W.L. Gore & Associates, Inc., Flagstaff, AZ, USA) has been manufactured following the design criteria used for the non-resorbable barrier. This newly developed resorbable barrier is composed of a synthetic copolymer of polyglicolic and polylactic acids (i.e. copolymers which have a history of safe use as bioabsorbable sutures and surgical meshes). The polymer components of this barrier hydrolyze, are safely resorbed in body tissue and have been found to be inert, nonantigenic, nonpyrogenic and elicit only a mild tissue reaction during bi-

Article 55

Comparison of Bioabsorbable Laminar Bone Membrane and Non-Resorbable ePTFE Membrane in Mandibular Furcations

Tracy A. Scott, Herbert J. Towle,* Daniel A. Assad,* and Brian K. Nicoll†*

THE PURPOSE OF THIS STUDY was to compare clinical parameter changes and osseous regeneration in 12 pairs of comparable Class II mandibular molar furcation invasion defects using either a bioabsorbable demineralized laminar bone allograft membrane or a non-resorbable expanded polytetrafluoroethylene (ePTFE) membrane as a barrier in guided tissue regeneration. Measurements with calibrated periodontal probes were made to determine soft tissue recession, probing depth, and attachment levels. Defects within each pair were randomly selected for treatment with either bioabsorbable demineralized bone allograft membrane or ePTFE membrane. All defects were concurrently grafted with particulate demineralized freeze-dried bone allograft (DFDBA). Additional measurements were made at surgery to determine crestal resorption and the vertical and horizontal dimensions of the osseous defects. The temporal course and extent of membrane exposures were also recorded. The non-resorbable membrane was retrieved 6 weeks following placement. Six months following initial surgical treatment, each site was surgically re-entered and all soft and hard tissue measurements repeated. Descriptive statistical analysis revealed that both treatments resulted in significant within-group mean vertical and horizontal osseous fill, but no statistical difference emerged between the groups. As based on this pilot study, laminar bone membrane may be as effective as ePTFE when used in conjunction with DFDBA for treatment of Class II mandibular molar furcation bone defects. This pilot study of low power suggests that these two materials may be equivalent when used in conjunction with DFDBA. Further studies of much higher power and of the laminar bone alone as compared to positive and negative controls are required. Laminar bone does not require a secondary surgical procedure for removal and may undergo less frequent instances and degrees of exposure during healing. *J Periodontol 1997;68:679–686.*

Key Words: Furcation/therapy; guided tissue regeneration; membranes, artificial; membranes, barrier; polytetrafluoroethylene/therapeutic use; grafts, bone; bone, demineralized.

Melcher[1] proposed that periodontal ligament (PDL) cells play an important role in the healing of periodontal defects involving the PDL and alveolar bone. A procedure designed to inhibit the apical migration of epithelial and gingival connective tissue cells into the defect, allowing PDL cells to repopulate the root surface, would permit formation of a new attachment apparatus. Guided tissue regeneration is a surgical technique that uses a physical barrier to allow selective repopulation of the periodontal defect during healing. A non-resorbable expanded polytetrafluoroethylene (ePTFE) membrane[2] has been extensively studied in animals and humans for the treatment of vertical and molar furcation osseous defects. Human studies[2–7] using the ePTFE membrane for treatment of molar furcation defects have attained significant and predictable results. Disadvantages of a non-resorbable membrane in-

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The opinions or assertions contained herein are those of the authors and are not to be construed as official or as reflecting the views of the Department of the Navy.

[2]Gore-Tex, W. L. Gore and Associates, Inc., Flagstaff, AZ.

Article 56

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Guided tissue regeneration with non-resorbable and biodegradable barriers: 6 months results

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Eickholz P, Kim T-S, Holle F: Guided tissue regeneration with non-resorbable and biodegradable barriers: 6 months results. J Clin Periodontol 1997; 24: 92–101.
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Abstract. The aim of the present study was to compare the effects of guided tissue regeneration (GTR) with non-resorbable (cPTFE [GI) and biodegradable barriers (Polyglactin 910 (V)). In 20 patients, providing 25 pairs of symmetrical periodontal defects (7 pairs of interproximal intrabony lesions, 12 pairs of degree II and 6 pairs of degree III furcation involvement), each defect was randomly assigned to treatment with either non-resorbable (control) or biodegradable (test) devices. At baseline and 6 months after surgery, clinical measurements (GI, PPD, PAL-V, PAL-H, PII) and standardized radiographs were obtained. On the radiographs, the linear distances from the cemento-enamel junction (CEJ) to the alveolar crest (AC), and from the CEJ to bottom of the bony defect (BD) were measured using a computer-assisted analysing method (LMSRT). Both treatments revealed a significant ($p<0.05$) PPD reduction (-2.90 ± 1.33 mm (V), -2.71 ± 1.41 mm (G)), PAL-V gain (1.78 ± 1.27 mm (V), 1.46 ± 1.35 mm (G)), PAL-H gain (2.00 ± 0.82 mm (V), 1.60 ± 0.59 mm (G)), and radiographic changes (CEJ-AC: 0.48 ± 0.75 mm (V), 0.73 ± 0.92 mm (G); CEJ-BD: -0.76 ± 0.79 mm (V), -0.41 ± 0.72 mm (G)) after 6 months. The mean differences between the changes for test and control were not significant for most clinical and radiographic parameters. Similar clinical and radiographic results were found 6 months after surgical treatment using either non-resorbable or biodegradable barriers. More favorable results concerning PAL-H gain could be observed with biodegradable barriers after 6 months. Therefore, based on these results, the use of biodegradable barriers in GTR may be recommended and, thereby, a surgical re-entry to remove non-resorbable barriers can be avoided.

Key words: GTR; biodegradable barriers; non-resorbable barriers; minimal sample size

Accepted for publication 18 March 1996

From histometric studies, we know that conventional non surgical and surgical therapy of periodontal lesions is likely to result in the formation of a long epithelial attachment (Caton et al. 1980). Meticulous oral hygiene provided, this reparative healing leads to an improvement of clinical parameters, i.e., reduction of inflammation, reduction of probing pocket depths and gain of clinical probing attachment. Under the regimen of frequent recalls, including oral hygiene instruction and professional tooth cleaning, the results of conventional periodontal surgery may be maintained predictively stable. But the ultimate goal of periodontal therapy, i.e. the regeneration of lost periodontal tissues in function and architecture, is not achieved. During the last decade attempts have been made to influence periodontal healing to the effect that regeneration is possible. Animal experiments have shown that only periodontal ligament cells have the potential to form a new connective tissue attachment with new root cementum and functionally oriented collagen fibres by recolonizing debrided root surfaces (Karring et al. 1980, Nyman et al. 1980, 1982a). By using a barrier to cover the periodontal lesion after debridement, gingival connective tissue and epithelium were prevented from proliferating into the defect. This principle of guided tissue regeneration (GTR) provided the establishment of a new connective tissue attachment after periodontal surgery in man (Nyman et al. 1982b). Several clinical studies compared therapy according to the GTR-principle using non-resorbable expanded polytetrafluoroethylene (ePT-

Article 57

Treatment of Class II Furcation Involvements in Humans With Bioresorbable and Nonresorbable Guided Tissue Regeneration Barriers. A Randomized Multi-Center Study

A. Hugoson, N. Ravald,† J. Fornell,‡ G. Johard,§ A. Teiwik,† and J. Gottlow¶*

IN THIS MULTI-CENTER STUDY 38 patients with contralateral molar Class II furcation defects were treated with GTR therapy using a bioresorbable matrix barrier (test) and a nonresorbable expanded polytetrafluoroethylene (ePTFE) barrier (control). Following flap elevation, scaling, root planing, and removal of granulation tissue, each device was adjusted to cover the furcation defect. The flaps were repositioned and sutured to complete coverage of the barriers. A second surgical procedure was performed at control sites after 4 to 6 weeks to remove the nonresorbable barrier. Before treatment and 12 months postsurgery all patients were examined and probing depths, clinical attachment levels, and position of the gingival margin were recorded. The primary response variable was the change in clinical attachment level in a horizontal direction (CAL-H change). Both treatment procedures reduced the probing depths ($P \leq 0.001$). Statistically significant gain of clinical attachment level in both horizontal and vertical direction was found at the test sites. At control sites gain of attachment in horizontal direction was statistically significant. The gain of CAL-H was 2.2 mm at test sites compared to 1.4 mm at control sites ($P \leq 0.05$). At test sites, the gingival margin was maintained close to the pre-surgical level (0.3 mm), whereas at control sites gingival recession was evident (0.9 mm), the difference being statistically significant ($P \leq 0.01$). Postsurgical complications, such as swelling and pain were more frequent following the control treatment ($P \leq 0.05$). *J Periodontol 1995;66:624–634.*

Key Words: Biocompatible materials; membranes, barrier; membranes; artificial; furcation/surgery; guided tissue regeneration; polytetrafluoroethylene/therapeutic use; polylactic acid/therapeutic use.

The possibility for regeneration of lost periodontal support in Class II furcation defects following guided tissue regeneration therapy (GTR) was originally described by Gottlow et al.[1] and confirmed in case report studies by Becker et al.,[2] Schallhorn and McClain,[3] and Caffesse et al.[4] Controlled clinical studies with intra-individual comparison between GTR therapy and conventional flap surgery have been presented by Pontoriero et al.[5] and Lekovic et al.[6] Both studies showed significantly more gain of probing attachment level at GTR treated sites.

In all the studies referred to above, nonresorbable e-PTFE membrane barriers were used.[1] Recently Laurell et al.[7] reported successful treatment results using a bioresorbable barrier.[8] This device is made of amorphous polylactic acid, softened with a citric acid ester to accomplish malleability and facilitate clinical handling.

The aim of this multi-center study was to evaluate GTR therapy of Class II furcation defects with a bioresorbable matrix barrier (test) and a nonresorbable ePTFE barrier (control).

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Article 58

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Regenerative periodontal surgery with non-resorbable and biodegradable barriers: results after 24 months

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Eickholz P, Kim T-S & Holle R: Regenerative periodontal surgery with non-resorbable and biodegradable barriers: results after 24 months. J Clin Periodontol 1998; 25: 666–676. © Munksgaard, 1998.

Abstract. The aim of the present study was to compare the effects of guided tissue regeneration (GTR) with non-resorbable (ePTFE) and biodegradable barriers (Polyglactin 910). 23 patients provided 29 pairs of similar contralateral periodontal defects (12 pairs of interproximal intrabony lesions, 11 pairs of degree II and 6 pairs of degree III furcation defects). Each defect was randomly assigned to treatment with either non-resorbable (control [c]) or biodegradable (test [t]) devices. At baseline, 6, 12, 18, and 24 months after surgery, clinical measurements (PII, GI, PPD, PAL-V, PAL-H) were performed. Standardized radiographs were obtained at baseline 12 and 24 months postsurgically. On the radiographs, the linear distances from the cemento-enamel junction (CEJ) to the alveolar crest (AC) and from the CEJ to bottom of the bony defect (BD) were measured using a computer-assisted analysing method (LMSRT). Both treatments revealed a significant ($p<0.05$) PPD reduction [all defects: -2.97 ± 1.90 mm (t), -2.21 ± 1.73 mm (c); intrabony defects: -4.00 ± 1.96 mm (t), -3.00 ± 1.87 mm (c); degree II furcations: -2.67 ± 0.97 mm (t), -2.08 ± 1.54 mm (c)], PAL-V gain [all defects: 2.02 ± 1.83 mm (t), 1.18 mm±1.50 (c); intrabony defects: 3.45 ± 1.48 mm (t), 1.95 ± 1.64 mm (c); degree II furcations: 1.33 ± 0.94 mm (t), 0.92 ± 1.47 mm (c)], PAL-H gain [degree II furcations: 2.22 ± 0.94 mm (t), 1.86 ± 0.60 mm (c)], and radiographic changes [CEJ-AC: -0.56 ± 1.98 mm (t), -0.06 ± 1.19 mm (c); CEJ-BD: 2.10 ± 1.92 mm (t), 1.24 ± 2.04 mm (c)] after 24 months. For degree III furcations, neither statistically significant PPD reduction nor PAL-V gain was observed. Similar clinical and radiographic results were found 12 and 24 months after surgical treatment using either non-resorbable or biodegradable barriers. More favorable results concerning PAL-V gain in interproximal intrabony defects could be observed with biodegradable barriers after 24 months than using non-resorbable membranes. Whereas interproximal intrabony lesions and degree II furcation defects responded favorably to GTR therapy, through-and-through furcations must be looked upon as a contraindication for this regenerative technique. Based on the results of the present study, the use of biodegradable barriers in GTR may be recommended and, thereby, a surgical re-entry to remove non-resorbable barriers can be avoided.

Key words: GTR; biodegradable barriers; non-resorbable barriers; interproximal intrabony defects; degree II and III furcation lesions.

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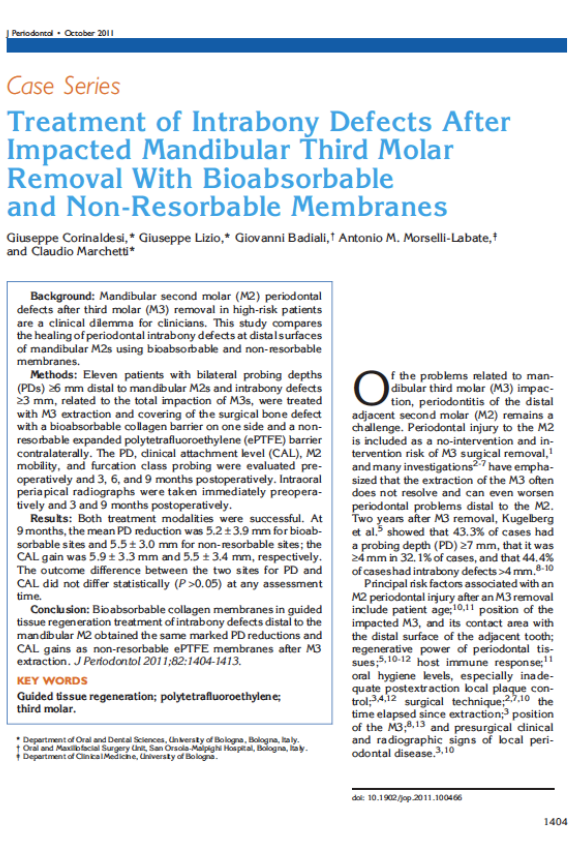
Conventional non surgical and surgical therapy of periodontal lesions is likely to result in a reparative healing with the formation of a long epithelial attachment (Listgarten & Rosenberg 1979, Caton et al. 1980). The ultimate goal of periodontal therapy, i.e. the regeneration of lost periodontal tissues in architecture and function, is not achieved. During the last 15 years attempts have been made to influence periodontal healing so that regeneration is possible. Animal experiments have shown that only periodontal ligament cells have the potential to form a new connective

Article 59



J Periodontol • October 2011

Case Series

Treatment of Intrabony Defects After Impacted Mandibular Third Molar Removal With Bioabsorbable and Non-Resorbable Membranes

Giuseppe Corinaldesi,* Giuseppe Lizio,* Giovanni Badiali,† Antonio M. Morselli-Labate,‡ and Claudio Marchetti*

Background: Mandibular second molar (M2) periodontal defects after third molar (M3) removal in high-risk patients are a clinical dilemma for clinicians. This study compares the healing of periodontal intrabony defects at distal surfaces of mandibular M2s using bioabsorbable and non-resorbable membranes.

Methods: Eleven patients with bilateral probing depths (PDs) ≥6 mm distal to mandibular M2s and intrabony defects ≥3 mm, related to the total impaction of M3s, were treated with M3 extraction and covering of the surgical bone defect with a bioabsorbable collagen barrier on one side and a non-resorbable expanded polytetrafluoroethylene (ePTFE) barrier contralaterally. The PD, clinical attachment level (CAL), M2 mobility, and furcation class probing were evaluated preoperatively and 3, 6, and 9 months postoperatively. Intraoral periapical radiographs were taken immediately preoperatively and 3 and 9 months postoperatively.

Results: Both treatment modalities were successful. At 9 months, the mean PD reduction was 5.2 ± 3.9 mm for bioabsorbable sites and 5.5 ± 3.0 mm for non-resorbable sites; the CAL gain was 5.9 ± 3.3 mm and 5.5 ± 3.4 mm, respectively. The outcome difference between the two sites for PD and CAL did not differ statistically ($P>0.05$) at any assessment time.

Conclusion: Bioabsorbable collagen membranes in guided tissue regeneration treatment of intrabony defects distal to the mandibular M2 obtained the same marked PD reductions and CAL gains as non-resorbable ePTFE membranes after M3 extraction. *J Periodontol 2011;82:1404-1413.*

KEY WORDS

Guided tissue regeneration; polytetrafluoroethylene; third molar.

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Of the problems related to mandibular third molar (M3) impaction, periodontitis of the distal adjacent second molar (M2) remains a challenge. Periodontal injury to the M2 is included as a no-intervention and intervention risk of M3 surgical removal,[1] and many investigations[2-7] have emphasized that the extraction of the M3 often does not resolve and can even worsen periodontal problems distal to the M2. Two years after M3 removal, Kugelberg et al.[5] showed that 43.3% of cases had a probing depth (PD) ≥7 mm, that it was ≥4 mm in 32.1% of cases, and that 44.4% of cases had intrabony defects >4 mm.[8-10]

Principal risk factors associated with an M2 periodontal injury after an M3 removal include patient age;[10,11] position of the impacted M3, and its contact area with the distal surface of the adjacent tooth; regenerative power of periodontal tissues;[5,10-12] host immune response;[11] oral hygiene levels, especially inadequate postextraction local plaque control;[3,4,12] surgical technique;[2,7,10] the time elapsed since extraction;[3] position of the M3;[8,13] and presurgical clinical and radiographic signs of local periodontal disease.[3,10]

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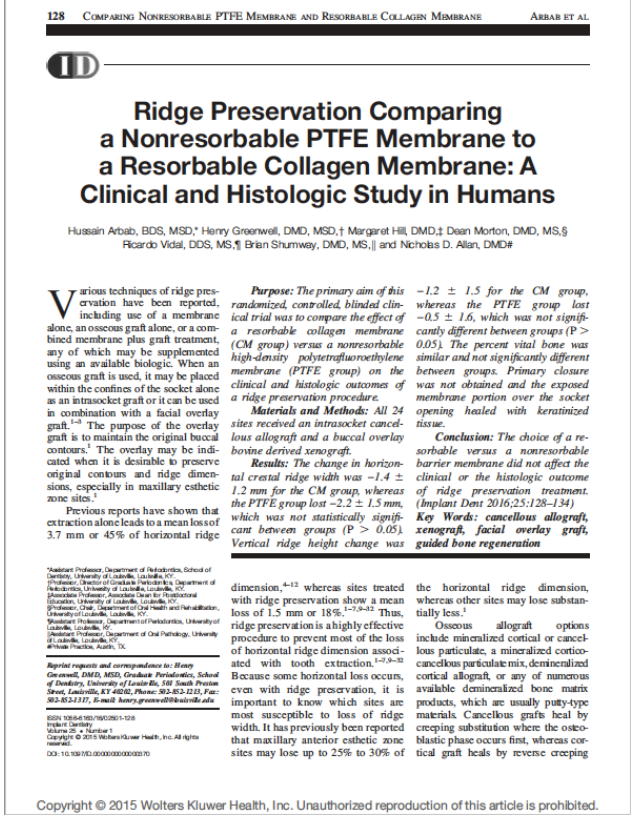
Article 60



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Ridge Preservation Comparing a Nonresorbable PTFE Membrane to a Resorbable Collagen Membrane: A Clinical and Histologic Study in Humans

Hussain Arbab, BDS, MSD,* Henry Greenwell, DMD, MSD,† Margaret Hill, DMD,‡ Dean Morton, DMD, MS,§ Ricardo Vidal, DDS, MS,¶ Brian Shumway, DMD, MS,‖ and Nicholas D. Allan, DMD#

Purpose: *The primary aim of this randomized, controlled, blinded clinical trial was to compare the effect of a resorbable collagen membrane (CM group) versus a nonresorbable high-density polytetrafluoroethylene membrane (PTFE group) on the clinical and histologic outcomes of a ridge preservation procedure.*

Materials and Methods: *All 24 sites received an intrasocket cancellous allograft and a buccal overlay bovine derived xenograft.*

Results: *The change in horizontal crestal ridge width was −1.4 ± 1.2 mm for the CM group, whereas the PTFE group lost −2.2 ± 1.5 mm, which was not statistically significant between groups (P > 0.05). Vertical ridge height change was −1.2 ± 1.5 for the CM group, whereas the PTFE group lost −0.5 ± 1.6, which was not significantly different between groups (P > 0.05). The percent vital bone was similar and not significantly different between groups. Primary closure was not obtained and the exposed membrane portion over the socket opening healed with keratinized tissue.*

Conclusion: *The choice of a resorbable versus a nonresorbable barrier membrane did not affect the clinical or the histologic outcome of ridge preservation treatment. (Implant Dent 2016;25:128–134)*

Key Words: *cancellous allograft, xenograft, facial overlay graft, guided bone regeneration*

Various techniques of ridge preservation have been reported, including use of a membrane alone, an osseous graft alone, or a combined membrane plus graft treatment, any of which may be supplemented using an available biologic. When an osseous graft is used, it may be placed within the confines of the socket alone as an intrasocket graft or it can be used in combination with a facial overlay graft.[1–3] The purpose of the overlay graft is to maintain the original buccal contours.[1] The overlay may be indicated when it is desirable to preserve original contours and ridge dimensions, especially in maxillary esthetic zone sites.[1]

Previous reports have shown that extraction alone leads to a mean loss of 3.7 mm or 45% of horizontal ridge dimension,[4–12] whereas sites treated with ridge preservation show a mean loss of 1.5 mm or 18%.[1–7,9–32] Thus, ridge preservation is a highly effective procedure to prevent most of the loss of horizontal ridge dimension associated with tooth extraction.[1–9,9–32] Because some horizontal loss occurs, even with ridge preservation, it is important to know which sites are most susceptible to loss of ridge width. It has previously been reported that maxillary anterior esthetic zone sites may lose up to 25% to 30% of the horizontal ridge dimension, whereas other sites may lose substantially less.[1]

Osseous allograft options include mineralized cortical or cancellous particulate, a mineralized corticocancellous particulate mix, demineralized cortical allograft, or any of numerous available demineralized bone matrix products, which are usually putty-type materials. Cancellous grafts heal by creeping substitution where the osteoblastic phase occurs first, whereas cortical graft heals by reverse creeping

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Article 61

Bone Level Variation After Vertical Ridge Augmentation: Resorbable Barriers Versus Titanium-Reinforced Barriers. A 6-Year Double-Blind Randomized Clinical Trial

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Purpose: *To compare the efficacy of two different techniques for vertical bone regeneration at implant placement with particulate autogenous bone at 6 years after loading by means of a double-blind, superiority, parallel-group randomized clinical trial.* ***Materials and Methods:*** *The study was conducted in a private center in Italy between April 2004 and December 2011. Patients in whom vertical bone augmentation was indicated in combination with the placement of single or multiple implants were eligible for inclusion in this trial. Patients were randomized to receive either resorbable collagen barriers supported by an osteosynthesis plate (test group) or nonresorbable titanium-reinforced expanded polytetrafluoroethylene barriers (control group). The outcome variables—radiographic bone variation at implant sites, implant failures, and complications—were evaluated 6 years after loading. Randomization was done by computer, with allocation concealed by opaque sequentially numbered sealed envelopes. The patients and the radiographic examiner were blinded to group assignment.* ***Results:*** *Twenty-two patients were randomized: 11 to the resorbable barrier group and 11 to the nonresorbable (control) group. One control group patient dropped out. The mean bone level 6 years after surgery was 1.33 mm for the resorbable group and 1.00 mm for the nonresorbable group. The adjusted difference in bone changes between groups was 0.15 mm (95% confidence interval, −0.39 to 0.69, P = .5713). No implant failures or complications occurred after loading.* **Conclusion:** *No differences were observed in this comparison of resorbable and nonresorbable barriers with simultaneous implant placement for vertical ridge augmentation.* INT J ORAL MAXILLOFAC IMPLANTS 2014;29:905–913. doi: 10.11607/jomi.3203

Key words: *alveolar ridge augmentation, bone grafting, dental implants, guided bone regeneration, randomized clinical trial*

Bone augmentation may be required for patients who lack an adequate quantity of bone for implant treatment. Augmentation procedures can be divided into two broad categories: horizontal bone augmentation, which involves increasing the width of the recipient bone, and vertical bone augmentation, which seeks an increase in the height of the recipient bone.[1]

Vertical bone defects can be treated by distraction osteogenesis, inlay and/or onlay bone grafting, guided bone regeneration (GBR), and an array of other techniques.[2–7] Reported success rates for implants placed in GBR-augmented ridges range from 61.5% to 100%.[8,9] Nevertheless, a certain number of perioperative complications associated with augmentation techniques have been reported.[1] There is a tendency, therefore, to use shorter implants, thereby eliminating the need for augmentation procedures.[10–12]

In GBR, a barrier is used to create and maintain a secluded space that allows osteoprogenitor cells to proliferate and differentiate, achieving bone regeneration.[13–15] In vertical bone augmentation, different barrier membranes in combination with various graft materials, such as autogenous bone, allografts, xenografts, and alloplastic materials, are often used.[16–21] There are two types of barrier membranes: resorbable and nonresorbable. In vertical bone augmentation, collagen resorbable barriers and nonresorbable titanium-reinforced polytetrafluoroethylene barriers are used most often.[4,18,22,23]

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Article 62

J Periodontol • November 2000

Guided Bone Regeneration Around Endosseous Implants With Anorganic Bovine Bone Mineral. A Randomized Controlled Trial Comparing Bioabsorbable Versus Non-Resorbable Barriers

Lillian Carpio,* Juan Loza,† Samuel Lynch,‡ and Robert Genco§

Background: Guided bone regeneration (GBR) is a viable treatment for osseous defects surrounding dental implants. Controversy exists regarding the choice of barrier membrane used and the method of membrane fixation to achieve GBR.

Methods: This study compared the efficacy of a porcine-derived bioabsorbable collagen membrane and an expanded polytetrafluoroethylene (ePTFE) membrane (non-resorbable) for GBR using a bovine bone xenograft/autograft bone composite in defects surrounding dental implants. The study also examined the effect of primary barrier fixation on GBR. Defect size was recorded at Stage 1 and 2 surgeries (performed 6 months apart). Forty-eight subjects (41% males, 59% females) requiring GBR were treated with either collagen (23) or ePTFE (25) barriers, respectively. Implants were titanium self-tapping screw-type. In 34 GBR sites, barrier fixation was achieved with polylactic acid resorbable pins. The remaining barriers were secured with the implant cover screw and/or embedded beneath the flaps.

Results: At 6 months, a decrease in defect width (collagen barrier 1.95 ± 0.60 mm, ePTFE barrier 2.65 ± 0.56 mm), length (collagen barrier 2.65 ± 0.61 mm, ePTFE barrier 2.26 ± 0.66 mm), and circumference (degrees) (collagen barrier 57.7 ± 18.7, ePTFE barrier 80.2 ± 19.9) was observed for both membranes. A significant number (χ^2, $P = 0.041$) of postoperative complications occurred when barrier fixation was lacking at initial surgery. Furthermore, a significant difference ($P < 0.05$) in the success of GBR with respect to defect size was observed when barrier fixation was taken into account.

Conclusions: In conclusion, both collagen and ePTFE barriers proved suitable for achieving GBR of osseous defects surrounding dental implants. The results of this study stress the importance of barrier fixation at the time of initial surgery. *J Periodontol 2000;71:1743-1749.*

KEY WORDS

Bone regeneration; osseointegration; collagen/therapeutic use; polytetrafluoroethylene/therapeutic use; dental implants, endosseous; grafts, bone; membranes, bioabsorbable; membranes, barrier.

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The concept of guided tissue regeneration (GTR) was adapted to the field of dental implants to address the lack of bone surrounding dental implants either as a result of disease or anatomic deficiencies at the time of implant placement.[1-3] In implant-related cases, we refer to the term "guided bone regeneration" (GBR), in which the tissue that will replace the osseous defect consists entirely of bone.

Different investigators have examined the efficacy of the GBR technique for treatment of osseous defects of varying sizes surrounding dental implants. Such studies have reported different degrees of success of GBR, depending upon the type of barrier selected, presence or absence of an underlying graft material, type of graft material, feasibility of technique, and clinician's preference, among other factors.[4-8]

Within the last few years, bioabsorbable membranes have been introduced for regeneration procedures.[9-11] Such membranes

Article 63

Periodontal Regeneration of Human Intrabony Defects. IV. Determinants of Healing Response

Maurizio S. Tonetti, Giovanpaolo Pini-Prato,† Pierpaolo Cortellini†*

THE PURPOSE OF THIS STUDY was to identify factors which might affect the healing response in intrabony defects treated with guided tissue regeneration. Selected sites presented with deep periodontal lesions with 1, 2, and 3 wall combination intrabony component of 6.1 ± 2.5 mm. The significance of patient, tooth, and defect characteristics and surgical parameters as predictor variables affecting the regenerative outcome before and following the removal of the barrier membrane was assessed. Outcome was measured as tissue gain under the membrane, regenerated probing attachment level (PAL), and bone fill. The total depth of the intrabony component and the radiographic defect angle significantly affected the amount of tissue gain. Seventy-five percent (75%) of the variability of regenerated PAL and bone fill was explained in terms of tissue gain under the membrane, radiographic width of the defect angle, full mouth bleeding score, and presence or absence of flap coverage of the newly formed tissue. Control of the identified predictor variables might improve the extent and predictability of guided tissue regeneration in the treatment of deep intrabony defects. *J Periodontol 1993; 64:934–940.*

Key Words: Periodontal diseases/surgery; wound healing; guided tissue regeneration; membrane/barrier.

In our previous reports we have demonstrated that treatment of intrabony defects by guided tissue regeneration (GTR) is highly effective and reproducible.[1,2] An attachment level gain of 2 mm or more was observed in 85% of treated sites. Such an observation, together with previous studies,[3,4] indicates that the application of GTR principles is a treatment of choice for deep intrabony defects. The treatment outcome, however, is reportedly dependent upon a series of factors, whose significance is largely anecdotal. The relevance of the size and the morphology of the defect, the amount of remaining periodontium, the positioning and the coverage of the barrier membrane, and recession of the marginal tissue have all been discussed following systematic clinical observations.[3,5,6]

Periodontal regeneration is a dynamic process leading to the selective cell repopulation of the root surface and neighboring areas to give rise to a granulation tissue with potential to form new cementum, periodontal ligament, and possibly bone. From a clinical standpoint this process can be divided into two different phases: the formation of new tissue under the membrane and the tissue maturation following the removal of the membrane. Each phase is characterized by unique cellular and biochemical factors which may be modulated by clinical situations and events.

The purpose of the present investigation was to identify clinical situations and events which may influence and, if controlled, further enhance the extent and predictability of the regeneration in deep intrabony defects following GTR.

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MATERIALS AND METHODS

Study Population and Experimental Design

A case series of 40 deep intrabony defects was treated by GTR in 23 patients, 14 males and 9 females, 18 to 56 years of age (mean 41.6). Fourteen subjects had 1 site; 6, 2 sites; 2, 3 sites, and 1, 4 sites. The entry criteria and experimental design have been previously reported.[1] In brief, teeth with interproximal vertical defects characterized by probing attachment level loss of at least 6 mm and radiographic evidence of an intrabony component were entered into the study. Patients underwent initial therapy consisting of scaling and root planing and oral hygiene instructions. Three months thereafter baseline clinical measurements were recorded and a periapical radiograph was taken. One week later the surgical procedure was performed and the intrasurgical clinical measurements and impressions were taken.

Article 64

Relationship Between the Radiographic Periodontal Defect Angle and Healing After Treatment

Bjorn Steffensen* and Hans–Peter Weber†

THIS STUDY RADIOGRAPHICALLY EVALUATED the correlation between the changes in alveolar bone level occurring in bony defects after periodontal therapy and the corresponding pretreatment defect angles. The defect angle was defined by the bony defect surface and the root surface. The changes were determined from identically exposed and processed radiographs obtained just prior to surgery and 15 to 18 months later.

The defect angle was clearly correlated to the radiographic changes in alveolar bone level. Most defects with an angle less than 45° showed a gain of bone while defects with the largest defect angles showed a loss. In addition, defects on root surfaces without furcations showed better healing than defects associated with furcations.

The results of healing after periodontal therapy have been evaluated clinically in longitudinal studies with different treatment modalities.[1-3] These studies have provided information about the reactions of the periodontal soft tissues, such as the clinical attachment level, and have enhanced the ability to predict the clinical outcomes of such treatments.

Other investigators have radiographically evaluated the changes of the alveolar bone level following either no treatment[4] or active treatment with or without subsequent maintenance therapy.[4-10] Such studies have demonstrated that the bone healing is related to the number of bony walls of the defect,[11] the selection of treatment modality, and the maintenance regimen.

Although it has been established that the clinical management of the patients and that certain clinical defect characteristics are of significance to the tissue response, the associations between radiographic morphological variables and the healing patterns of alveolar bone defects are not yet fully understood. Recent results[12] have shown that interproximal intrabony defects occur in 15% of an adult Swedish population. These findings clearly have emphasized the importance of gaining more information about the effect of treatment of such defects.

It was the aim of the present investigation to evaluate the changes which occur following treatment of bony defects with different radiographic morphology. In particular, it was a goal to determine whether the defect angle was correlated with these bone changes. If so, this would add a valuable tool for predicting the healing potential of bony defects which might be applicable in epidemiological studies as well as clinical practice.

MATERIALS AND METHODS

Pairs of radiographs covering the premolar and molar regions were obtained from 11 patients who were participating in a clinical study of periodontal treatment at the School of Dentistry, University of Michigan. After scaling and root planing and a reevaluation period for all patients, the treatment consisted of modified Widman flap surgery[13] with no osseous recontouring and complete bone coverage by the repositioned flap. All patients were followed on a regular maintenance program during which time they received prophylaxis every 3 months.

The first radiograph was taken immediately prior to periodontal surgery and served as the baseline reference. The second radiograph was obtained 15 to 18 months later. All radiographs were exposed according to a method which aimed for identical images by using individual bite blocks and identical film developing conditions.[14] The method for recording the morphological parameters of the bony defects, as well as the changes occurring in these areas, has been described in detail.[13] In summary, magnified tracings of the contours of the alveolar bone and the tooth structure were obtained from the pre– and post–treatment radiographs. These tracings were then superimposed and the morphological variables were measured by a microcomputer connected digitizing system.‡

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‡ Bit Pad Two tablet, Summagraphics, Fairfield, CT; Sigmascan 3.01 software, Jandel Scientific, Corte Madera, CA; IBM Personal Computer AT.

Article 65

J Clin Periodontol 2004; 31: 643–647 doi: 10.1111/j.1600-051X.2004.00555.x

Journal of Clinical Periodontology

Baseline radiographic defect angle of the intrabony defect as a prognostic indicator in regenerative periodontal surgery with enamel matrix derivative

Effie Tsitoura, Richard Tucker, Jean Suvan, Lars Laurell, Pierpaolo Cortellini and Maurizio Tonetti
Department of Periodontology, Eastman Dental Institute and Hospital, University College London, UK

Tsitoura E, Tucker R, Suvan J, Laurell L, Cortellini P, Tonetti M: Baseline radiographic defect angle of the intrabony defect as a prognostic indicator in regenerative periodontal surgery with enamel matrix derivative: J Clin Periodontol 2004; 31: 643–647. doi: 10.1111/j.1600-051X.2004.00555.x. © Blackwell Munksgaard, 2004.

Abstract

Introduction: The baseline radiographic defect angle has previously been correlated with the clinical outcomes of intrabony defects treated with access flap or guided tissue regeneration. The aim of this study was to investigate whether an association exists between baseline radiographic defect angle and treatment outcome when enamel matrix derivative (EMD) is used in periodontal regenerative surgery.

Materials and Methods: Baseline radiographs were collected from the test group of a previously published clinical trial using a population of 166 patients treated for chronic periodontitis. All intrabony defects were ≥3 mm for inclusion in the original study. Either modified or simplified papilla preservation technique was used to access the defect. The roots were conditioned with an EDTA gel and the primary outcome measure was clinical attachment level (CAL) change, 1 year after surgery.

Results: Sixty-seven radiographs were measurable. The probability of obtaining CAL gain >3 mm was 2.46 times higher (95% confidence interval: 1.017–5.970) when the radiographic defect angle was ≤22° than when it was ≥36°.

Conclusions: This study showed that there was a significant association between baseline radiographic defect angle and CAL gain at 1 year. The observed increased odds ratio of obtaining CAL gain of ≥4 mm after regenerative surgery with EMD is used in narrow (≤ 22°) intrabony defects, suggests that the baseline radiographic defect angle might be used as a prognostic indicator of treatment outcome.

Key words: clinical trial; enamel matrix derivative; periodontal therapy; prognosis; regeneration

Accepted for publication 26 October 2003

A correlation between radiographic changes in alveolar bone level (bone fill) occurring in intrabony defects after periodontal access flap surgery and the corresponding pre-treatment defect angles has been described, where greater potential for bone fill was found in defects with small angles (0–45°) compared with wide angles (45–90°, Steffensen & Weber 1989). Tonetti et al. (1993b) showed that, for guided tissue regeneration (GTR), the wider the radiographic defect angle, the lower the regenerated probing attachment level in intrabony defects. In a retrospective three-centre study, it was shown that clinical attachment level (CAL) gain and bone fill were positively correlated to the depth of the intrabony defect and that the less favourable results of one of these three centres were attributed to the fact that this centre had treated significantly wider defects compared with the other two centres (Falk et al. 1997).

Cortellini & Tonetti (1999) studied 242 intrabony defects treated with GTR and found a significant difference in the CAL outcomes when they compared narrow (< 25°) to wide (> 37°) defects. They concluded that the radiographic defect angle could represent a useful pre-surgical parameter to determine the potential of CAL gain in intrabony

Article 66

Volume 75 • Number 5

Treatment of Intrabony Defects With Enamel Matrix Proteins or Barrier Membranes: Results From a Multicenter Practice-Based Clinical Trial

Mariano Sanz,* Maurizio S. Tonetti,† Ion Zabalegui,‡ Alberto Sicilia,§ Juan Blanco,‖ Helena Rebelo,¶ Giulio Rasperini,# Mauro Merli,** Pierpaolo Cortellini,† and Jean E. Suvan†

Background: This prospective multicenter, randomized, controlled clinical trial compared the clinical outcomes of enamel matrix proteins (EMD) versus placement of a bioabsorbable membrane in conjunction with guided tissue regeneration (GTR).

Methods: Seventy-five patients with advanced chronic periodontitis were recruited in seven centers in three countries. All patients had at least one intrabony defect of ≥3 mm. Heavy smokers (≥20 cigarettes/day) were excluded. The surgical procedures included access for root instrumentation using the simplified papilla preservation flap and either the application of EMD or the placement of a GTR membrane. At baseline and 1 year following the interventions, clinical attachment levels (CAL), probing depths (PD), recession (REC), full-mouth plaque scores, and full-mouth bleeding scores were assessed. A total of 67 patients completed the study.

Results: At 1 year, the EMD defects gained 3.1 ± 1.8 mm of CAL, versus 2.5 ± 1.9 mm for GTR defects. Probing depth reduction was 3.8 ± 1.5 mm and 3.3 ± 1.5 mm, respectively. A multivariate analysis indicated that the differences between EMD and GTR treatments were not significant while a center effect and baseline PD significantly influenced CAL gains. No significant differences in terms of frequency distribution of the outcomes were observed. All cases treated with GTR presented at least one surgical complication, mostly membrane exposure, while only 6% of EMD treated sites displayed complications (P <0.0001).

Conclusions: The results of this trial failed to demonstrate superiority of one treatment modality over the other. GTR outcomes in this trial were lower than anticipated based on previous evidence. This was attributed to the high prevalence of post-surgical complications in the GTR group. *J Periodontol 2004;75:726-733.*

KEY WORDS

Clinical trials, controlled; clinical trials, randomized; comparison studies; guided tissue regeneration; membranes, bioabsorbable; multicenter studies; proteins, enamel matrix/therapeutic use.

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The ultimate goal of periodontal treatment is the regeneration of tissues that have been lost to periodontal disease. Considerable histological and clinical evidence gathered over the last 2 decades indicates that the regeneration of periodontal tissues lost as a result of periodontitis can be achieved in humans. In particular, two clinical approaches have been routinely employed with considerable success: bone grafting[1] and guided tissue regeneration (GTR) with barrier membranes.[2]

GTR is one of the best documented regenerative approaches. Cumulative evidence from randomized clinical trials indicates that GTR is an efficacious and predictable procedure for the treatment of intraosseous periodontal defects.[3-5] A review published in 2000, which summarized the clinical outcomes following application of GTR to the treatment of deep intrabony defects using weighted means, indicated that clinically significant attachment level gains of 3.7 ± 1.8 mm were obtained with GTR.[2] However, the weighted mean difference between GTR alone and open flap debridement was just 1.11 mm (95% confidence interval [CI] 0.63 to 1.59) when clinical trials were evaluated by a systematic review.[6] Although GTR has been proven to promote the regrowth of the destroyed periodontium, the clinical application is often difficult and several confounding factors

Article 67

Enamel matrix derivative (Emdogain®) for periodontal tissue regeneration in intrabony defects (Review)

Esposito M, Grusovin MG, Papanikolaou N, Coulthard P, Worthington HV

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WILEY

Article 68

The Use of Enamel Matrix Derivative in the Treatment of Periodontal Defects: A Literature Review and Meta-Analysis

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ABSTRACT: *Background*—Periodontal disease results in the loss of the attachment apparatus. In the last three decades, an increasing effort has been placed on seeking procedures and materials to promote the regeneration of this tissue. The aim of this paper is to evaluate the effect of enamel matrix derivative (EMD) during regenerative procedures. In addition, a meta-analysis is presented regarding the clinical results during regeneration with EMD, to gain evidence as to what can be accomplished following treatment of intrabony defects with EMD in terms of probing depth reduction, clinical attachment level gain, defect fill (using re-entry studies), and radiographic parameters. *Methods*—The review includes *in vitro* and *in vivo* studies as well as human case reports, clinical comparative trials, and histologic findings. In addition, a meta-analysis is presented regarding the regenerative clinical results. For this purpose, we used 28 studies—including 955 intrabony defects treated with EMD that presented baseline and final data on probing depth, clinical attachment level (CAL) gain, or bone gain—to calculate weighted mean changes in the different parameters. The selected studies were pooled from the MEDLINE database at the end of May, 2003. *Results*—The meta-analysis of intrabony defects treated with EMD resulted in a mean initial probing depth of 7.94 ± 0.05 mm that was reduced to 3.63 ± 0.04 mm ($p = 0.000$). The mean clinical attachment level changed from 9.4 ± 0.06 mm to 5.82 ± 0.07 mm ($p = 0.000$). These results were significantly better than the results obtained for either open-flap debridement (OFD) or guided tissue regeneration (GTR). In contrast, histologically, GTR is more predictable than EMD in terms of bone and cementum formation. No advantage was found for combining EMD and GTR. Xenograft, or EMD and xenograft, yielded inferior results compared with EMD alone, but a limited number of studies evaluated this issue. Promising results were noted for the combination of allograft materials and EMD. *Conclusions*—EMD seems to be safe, was able to regenerate lost periodontal tissues in previously diseased sites based on clinical parameters, and was better than OFD or GTR. Its combination with allograft materials may be of additional benefit but still needs to be further investigated.

Key words. Enamel matrix derivative, Emdogain®, meta-analysis, periodontal regeneration.

(I) Introduction

One goal of periodontal therapy is to provide a dentition that functions in health and comfort for the life of the patient (Zander *et al.*, 1976). Studies reporting tooth loss among patients receiving periodontal treatment show that, for the majority of these patients, this goal is a reality (Hirschfeld and Wasserman, 1978; McFall, 1982; Nabers *et al.*, 1988). The validity of this statement is enhanced in view of the contrary results observed among those who were untreated (Becker *et al.*, 1979).

Therapeutic approaches to the treatment of periodontitis generally fall into two major categories: those designed to halt the progression of periodontal attachment loss, and those designed to regenerate or reconstruct lost periodontal tissues (Pihlstrom and Ammons, 1997). Surgical procedures involving root conditioning, autografts, allografts, xenografts, and/or barrier membranes for guided tissue regeneration have been shown to contribute to a successful regenerative outcome (for review, see Garrett, 1996).

Despite the convincing histological evidence that some regeneration may occur in humans following a regenerative surgical approach (Bowers *et al.*, 1989a,b,c), complete and predictable regeneration is still a goal that is difficult to attain. In the last three decades, investigators have increased their efforts to seek procedures and materials to promote periodontal regeneration. Since growth and differentiation factors have been shown to play a key role in wound healing, it was suggested that they could enhance the regenerative process (for review, see Giannobile, 1996). Promising results have been obtained on healing and regeneration of lost attachment with application of recombinant human osteogenic protein-1 (OP-1) in surgically created critical-size class III furcation defects in dogs (Giannobile *et al.*, 1998). Moreover, periodontal regeneration has been demonstrated histologically in humans following the use of purified recombinant human platelet-derived growth factor BB (PDGF-BB) mixed with bone allograft in both Class II furcations and interproximal intrabony defects (Nevins *et al.*, 2003). Although the use of growth factors has demonstrated significant repair and/or regeneration, it is still considered experimental, since no growth factor therapy to treat periodontitis in humans has received approval by the United

Article 69

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REVIEW

Enamel matrix derivative and bone grafts for periodontal regeneration of intrabony defects. A systematic review and meta-analysis

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Abstract
Objective The aim of the present systematic review and meta-analysis was to assess the clinical efficacy of regenerative periodontal surgery of intrabony defects using a combination of enamel matrix derivative (EMD) and bone graft compared with that of EMD alone.
Materials and methods The Cochrane Oral Health Group specialist trials, MEDLINE, and EMBASE databases were searched for entries up to February 2014. The primary outcome was gain of clinical attachment (CAL). Weighted means and forest plots were calculated for CAL gain, probing depth (PD), and gingival recession (REC).
Results Twelve studies reporting on 434 patients and 548 intrabony defects were selected for the analysis. Mean CAL gain amounted to 3.76±1.07 mm (median 3.63 95 % CI 3.51–3.75) following treatment with a combination of EMD and bone graft and to 3.32± 1.04 mm (median 3.40; 95 % CI 3.28–3.52) following treatment with EMD alone. Mean PD reduction measured 4.22±1.20 mm (median 4.10; 95 % CI 3.96–4.24) at sites treated with EMD and bone graft and yielded 4.12±1.07 mm (median 4.00; 95 % CI 3.88–4.12) at sites treated with EMD alone. Mean REC increase amounted to 0.76±0.42 mm (median 0.63; 95 % CI 0.58–0.68) at sites treated with EMD and bone graft and to 0.91±0.26 mm (median 0.90; 95 % CI 0.87–0.93) at sites treated with EMD alone.
Conclusions Within their limits, the present results indicate that the combination of EMD and bone grafts may result in additional clinical improvements in terms of CAL gain and PD reduction compared with those obtained with EMD alone. The potential influence of the chosen graft material or of the surgical procedure (i.e., flap design) on the clinical outcomes is unclear.
Clinical relevance The present findings support the use of EMD and bone grafts for the treatment of intrabony periodontal defects.

Keywords Intrabony defect · Periodontal disease · Enamel matrix derivative · Bone graft · Periodontal pocket · Periodontal regeneration

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Introduction

Periodontitis is an infectious disease triggered by periodontal pathogenic bacteria and is characterized by pocket formation and attachment loss, ultimately affecting tooth survival [1]. Besides the anti-infectious therapy aiming to eliminate or reduce the periodontal pathogenic flora in order to arrest the destruction process, one important goal is to reconstruct the bone defects caused by the infectious process [2, 3]. During the last decades, various treatment modalities such as the use of different bone grafting materials, guided tissue regeneration (GTR), enamel matrix derivative (EMD), or combinations thereof have been used to predictably regenerate the lost tooth's supporting tissues including root cementum, periodontal ligament, alveolar bone, and gingiva [2, 3].

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Article 70

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Journal of Clinical Periodontology

Clinical outcomes after treatment of intra-bony defects with an EMD/synthetic bone graft or EMD alone: a multicentre randomized-controlled clinical trial

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Jepsen S, Topoll H, Rengers H, Heinz B, Teich M, Hoffmann T, Al-Machot E, Meyle J, Jervøe-Storm P-M. Clinical outcomes after treatment of intra-bony defects with an EMD/synthetic bone graft or EMD alone: a multicentre randomized-controlled clinical trial. J Clin Periodontol 2008; 35: 420–428. doi: 10.1111/j.1600-051X.2008.01217.x.

Abstract

Objectives: Comparison of the outcomes of a combination of an enamel matrix derivative and a synthetic bone graft (EMD/SBC) with EMD alone in wide intra-bony defects.

Material and Methods: Seventy-three patients with chronic periodontitis were recruited in five centres in Germany. All patients had one wide intra-bony defect of ≥4 mm. Surgical procedures involved micresurgical technique and the modified papilla preservation flap. After debridement, defects were randomly assigned to EMD/SBC (test) or EMD (control). Assessments at baseline and after 6 months included bone sounding, attachment levels, probing pocket depths, bleeding on probing and recessions. Early wound-healing, adverse effects and patients' perceptions were also recorded.

Results: Both treatment modalities led to significant clinical improvements. Change in bone fill 6 months after surgery was 2.0 mm (± 2.1) in the test group and 2.1 mm (± 1.2) in the control group. A gain in clinical attachment of 1.3 mm (± 1.8) in the test group and 1.8 mm (± 1.6) in the control group was observed. One week after surgery, primary closure was maintained in 95% of the test sites and 100% of the control sites. No differences in patients' perceptions were found.

Conclusion: The results of the present study showed similar clinical outcomes following both treatment modalities.

Key words: bone replacement graft; enamel matrix derivative; intra-bony defects; periodontal regeneration; randomized clinical trial

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Histological findings in monkeys (Hammarström et al. 1997) and observations from human case reports (Heijl 1997, Mellonig 1999, Sculean et al. 2000) have demonstrated that treatment with an enamel matrix derivative (EMD) favours the formation of a new attachment apparatus, characterized by the presence of acellular and cellular cementum with inserting collagen fibres, and of new alveolar bone.

Controlled clinical studies have shown a significantly higher gain of clinical attachment and radiographic bone gain in intra-bony periodontal defects treated with open flap debridement combined with EMD when compared with open flap debridement alone (Heijl et al. 1997, Froum et al. 2001, Tonetti et al. 2002, Giannobile & Somerman 2003, Venezia et al. 2004, Trombelli 2005). EMD has also been successfully used in Class II furcation defects to reduce the horizontal furcation depth, post-operative swelling and pain (Jepsen et al. 2004).

As the formulation of EMD does not support the flap in wider defects, attempts have been made to combine EMD with different space-maintaining products (e.g. membranes or bone

Conflict of interest and source of funding statement

The authors declare that they have no conflict of interests.

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Article 71

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Clinical evaluation of an enamel matrix protein derivative (Emdogain) combined with a bovine-derived xenograft (Bio-Oss) for the treatment of intrabony periodontal defects in humans

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Affiliations + expand

PMID: 12186348

Abstract

The purpose of the present study was to compare the treatment of deep intrabony defects with a combination of an enamel matrix protein derivative (EMD; Emdogain) and a bovine-derived xenograft (BDX; Bio-Oss) to BDX alone. Twenty-four healthy patients, each of whom displayed one intrabony defect, were randomly treated with a combination of EMD + BDX (test) or with BDX alone (control). Soft tissue measurements were made at baseline and 1 year following the therapy No differences in any of the investigated parameters were observed at baseline between the two groups. No adverse healing response was observed in any of the patients. At 1 year after therapy, the sites treated with EMD + BDX showed a reduction in probing pocket depth (PPD) from 10.0 +/- 1.5 mm to 4.3 +/- 1.4 mm and a change in clinical attachment level (CAL) from 10.9 +/- 2.0 mm to 6.2 +/- 1.9 mm (P <.0001). In the group treated with BDX, the PPD was reduced from 9.7 +/- 2.4 mm to 3.2 +/- 0.7 mm and the CAL changed from 10.1 +/- 2.3 mm to 5.2 +/- 1.2 mm (P <.0001). Hard tissue fill was observed radiographically in all defects. Both treatments resulted in significant improvements of PPD and CAL. However, no statistically significant differences in any of the investigated parameters were observed between the test and control groups. Both therapies led to significant improvements of the investigated clinical parameters.

Article 72

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Journal of Clinical Periodontology

A minimally invasive surgical technique with an enamel matrix derivative in the regenerative treatment of intra-bony defects: a novel approach to limit morbidity

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Cortellini P, Tonetti MS. A minimally invasive surgical technique with an enamel matrix derivative in the regenerative treatment of intra-bony defects: a novel approach to limit morbidity. J Clin Periodontol 2007; 34: 87–93. doi: 10.1111/j.1600-051X.2006.01020.x.

Abstract

Aims: This study was undertaken to describe a new surgical approach (minimally invasive surgical technique, MIST) and to evaluate preliminarily its clinical performance and patient perception associated with the application of enamel matrix derivative (EMD) in the treatment of isolated deep intra-bony defects.

Methods: Thirteen deep isolated intra-bony defects in 13 patients were surgically accessed with the MIST. This technique was designed to limit the mesio-distal flap extension and the corono-apical reflection in order to reduce the surgical trauma and increase flap stability. The incision of the defect-associated papilla was performed according to the principles of the papilla preservation techniques. EMD was applied on the debrided root surfaces. Stable primary closure of the flaps was obtained with internal modified mattress sutures. Surgery was performed with the aid of an operating microscope and microsurgical instruments. Clinical outcomes were collected at baseline and at 1 year. Intra-operative and post-operative patient perception was also recorded.

Results: Early wound healing was uneventful: primary wound closure was obtained and maintained in all sites with the exception of one site with a small wound dehiscence at week 1. No oedema or haematoma were noted. Patients did not report any pain. Three patients experienced slight discomfort for 2-days post-operatively. The 1-year clinical attachment level (CAL) gain was 4.8 ± 1.9 mm. The 1-year percent resolution of the defect was 88.7 ± 20.7%, and reached 100% of the baseline intra-bony component in seven sites. Residual probing depths (PD) were 2.9 ± 0.8 mm. Differences between baseline and 1-year CAL and PD were both clinically and statistically highly significant ($p<0.0001$). A minimal increase of 0.1 ± 0.9 mm in gingival recession between baseline and 1 year was recorded ($p = 0.39$).

Conclusions: This case cohort indicates that MIST associated with EMD resulted in excellent clinical improvements while limiting patient morbidity. These preliminary findings need to be confirmed in a larger study.

Key words: clinical trial; microsurgery; osseous defects; periodontal diseases; periodontal regeneration

Accepted for publication 29 September 2006

Periodontal regeneration of intra-bony defects has been achieved with different principles: these include barrier membranes (Nyman et al. 1982, Gottlow et al. 1986), demineralized freeze-dried bone allograft (DFDBA, Bowers et al. 1989), combination of barrier membranes and grafts (Camelo et al. 1998, Mellonig 2000), and enamel matrix derivative (EMD, Mellonig 1999, Yukna & Mellonig 2000). Data from controlled clinical trials and meta-analyses from systematic reviews demonstrate that the cited approaches provide added benefits in terms of clinical attachment level

Article 73

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Treatment of Non-Contained Infrabony Defects With Enamel Matrix Derivative Alone or in Combination With a Biphasic Calcium Phosphate Bone Graft: a 12-Month Randomized Controlled Clinical Trial

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Background: The use of Enamel Matrix Derivative (EMD) when dealing with non-contained defects may be limited, as EMD does not maintain a space itself. It has been proposed the use of combined therapy, using a bone graft in combination with EMD to avoid the collapse of the flap into the bony defect during the healing time. Therefore the aim of this study is to evaluate the clinical and radiological healing response of non-contained infrabony defects following treatment with a combination of EMD and Biphasic calcium phosphate (BC) or EMD alone.

Methods: Fifty-two patients with at least 1 infrabony defect ≥ 3mm in depth with a probing pocket depth ≥ 6mm were randomly treated with EMD/BC or EMD alone. Clinical and radiographic parameters were evaluated at baseline, 6 and 12 months after surgery. To standardize the procedure an acrylic stent and a millimeter radiographic grid were used. The primary outcome was the change in clinical attachment level (CAL).

Results: Analysis of the data demonstrated a statistically significant difference from baseline within each group ($p<0.05$), showing a difference in clinical and radiographic parameters at 6 and 12 months. After one year the EMD/BC group achieved a mean PPD reduction of 3.14±1.95mm (39,6%) and, 3.30±1.89mm (48,7%) in the EMD group. A mean CAL gain of 2.38±2.17mm (24,9%) in the EMD/BC group and 2.65±2.18mm (36,2%) in the EMD group was obtained. The reduction in the infrabony component was 2.71±1.79mm (57,9%) in the test group, and 2.60±2.03mm (28,5%) in the control group. However, there were no statistically significant differences between treatment groups.

Conclusions: It was concluded that the treatment of non-contained infrabony defects with EMD, with or without BC, resulted in statistically significant better results after 12 months when compared to baseline measurements. In contrast, the combined approach did not result in a statistically significant improvement.

KEY WORDS:

clinical trial, enamel matrix proteins, bone grafting.

Vertical or angular periodontal bone defects are caused when subgingival plaque continues an apical progression along the root surface.[1] If these angular defects are left untreated, a continuous progression of the lesion will occur.[1] Periodontal regeneration of the lost attachment apparatus will improve the short and long term prognosis of periodontally affected teeth.[2]

Periodontal regeneration can be defined histologically as the regeneration of the tooth supporting tissues, which involves the alveolar bone, cementum and periodontal ligament, over a previously diseased root surface.[3] Since the 1980, non-absorbable and absorbable membranes in combination with different bone grafts have been used to achieve this goal.[4]

Article 74

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Clinical Outcomes After Treatment of Non-Contained Intrabony Defects With Enamel Matrix Derivative or Guided Tissue Regeneration: A 12-Month Randomized Controlled Clinical Trial

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Background: The purpose of this study is to compare the healing of deep, non-contained intrabony defects (i.e., with a ≥80% 1-wall component and a residual 2- to 3-wall component in the most apical part) treated with either an enamel matrix derivative (EMD) or guided tissue regeneration (GTR) after 12 months.

Methods: In this randomized, controlled clinical trial, 40 subjects with 40 defects affecting single-rooted teeth were treated. The defects were treated with EMD alone or with a non-resorbable titanium-reinforced membrane. No grafting materials were used. At baseline and after 12 months, clinical parameters including probing depths (PDs) and clinical attachment levels (CAL) were recorded. The difference in CAL gain was the primary outcome.

Results: At baseline, the intrabony component of the defects amounted to 8.5 ± 2.2 mm at EMD-treated sites and 8.6 ± 1.7 mm at GTR-treated sites (P = 0.47). The mean CAL gain at sites treated with GTR was significantly greater (P <0.001) than that at sites treated with EMD (4.1 ± 1.4 mm versus 2.4 ± 2.2 mm, respectively). GTR therapy, compared to EMD application alone, significantly (P = 0.01) increased the probability of CAL gain ≥4 mm (79.2% versus 11.3%, respectively) and significantly (P= 0.01) decreased the probability of residual PDs ≥6 mm (3% versus 79.3%, respectively).

Conclusion: Although the outcomes of open-flap debridement alone were not investigated, the application of EMD alone appeared to yield less PD reduction and CAL gain compared to GTR therapy in the treatment of deep, non-contained intrabony defects. *J Periodontol 2011;82:62-71.*

KEY WORDS

Amelogenin; guided tissue regeneration; periodontal diseases; periodontitis; regeneration; wound healing.

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Periodontitis represents an inflammatory disease initiated by bacterial biofilms and, if left untreated, is one of the major causes of tooth loss. The main goal of periodontal therapy is to arrest periodontal disease progression and to avoid tooth loss. After non-surgical mechanical debridement and access flap surgery, wound healing occurs by repair mechanisms characterized by the formation of a junctional epithelium along the instrumented root surface.[1] However, the ultimate goal of periodontal therapy is the regeneration of the tooth-supporting structures, including the root cementum, periodontal ligament, and alveolar bone lost because of periodontitis.[2-4] Outcomes of histologic and clinical studies indicated that regeneration of the periodontal tissues lost as a result of periodontitis may be achieved[5,6] and maintained long-term in humans.[7-15] Numerous treatment modalities, such as the use of bone grafts,[16] guided tissue regeneration (GTR),[17] or the delivery of an enamel matrix derivative (EMD)[18] have been applied to achieve these goals with high predictability. The clinical translation of the biologic principles of GTR include the adaptation of a barrier membrane around the tooth covering the periodontal defect

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Article 75

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Effect of GBR in combination with deproteinized bovine bone mineral and/or enamel matrix proteins on the healing of critical-size defects

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Key words: guided bone regeneration, enamel matrix proteins, deproteinized bovine bone

Abstract

Objectives: To evaluate the effect of guided bone regeneration (GBR) in combination with or without deproteinized bovine bone mineral (DBBM) and/or an enamel matrix derivative (EMD) on the healing of critical-size calvarial defects.

Material and methods: Forty rats were used. In all animals, a standardized critical-size calvarial defect was created surgically. The animals were randomly allocated into 4 groups of 10 animals each. *Group A:* One calvarial defect was left untreated, while the galeal and the cerebral aspect of the contralateral defect were covered with a bioresorbable membrane (GBR). *Group B:* One calvarial defect was filled with EMD, while the contralateral defect was treated with GBR and EMD. *Group C:* One defect was filled with DBBM, while the contralateral defect was treated with combination of GBR and DBBM. *Group D:* One defect was filled with DBBM combined with EMD, while the contralateral defect was treated with combination of GBR, DBBM and EMD. The healing period was 4 months. Five specimens from each group were macerated and the length, the width and the vertical dimension (thickness) of the remaining defect were evaluated by a stereomicroscope. The remaining specimens in each group were analyzed histologically.

Results: The defects of the macerated specimens that were left untreated or were treated only by EMD, DBBM and combination of EMD and DBBM did not present predictably complete healing of the defects. All the defects where GBR was applied alone or combined with DBBM and/or EMD presented always complete healing (P<0.05). The combined use of GBR with EMD and/or DBBM did not offer any significant advantage above GBR alone in terms of healing of the length and the width of the defect. However, the vertical dimension of the defect was significantly higher (P<0.05) in the GBR-treated specimens of Groups C and D. The histological analysis supported these findings.

Conclusion: The predictability of bone formation in critical-size defects depends mainly on the presence or absence of barrier membranes (GBR). The combined use with deproteinized bovine bone mineral and/or enamel matrix proteins did not significantly enhance the potential for complete healing provided by the GBR procedure.

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In recent years, the principle of guided tissue regeneration (GTR) which was originally developed for the treatment of periodontal defects (for review see Karring et al. 1993), has also been applied successfully in the treatment of different types of bone defects (guided bone regeneration, GBR) [Dahlin et al. 1988; Dahlin et al. 1989; Dahlin et al. 1990; Kostopoulos & Karring 1994a; Hämmerle et al. 1995; Nyman et al. 1995; Matzen et al. 1996]. Furthermore, by means of the GBR principle, it is possible to produce significant amounts of bone in areas where bone has never existed before [Kostopoulos & Karring 1994b; Kostopoulos et al. 1994;

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Alveolar socket healing: what can we learn?

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In current dentistry, the healing process of the socket following tooth extraction has become an important topic of research, study and discussion. The reason for this relies mainly on the fact that after tooth extraction several changes can occur in the alveolar process, which may prevent or render difficult implant installation in a prosthetically driven position (23). In addition, the increasing demand for esthetics in dentistry highlights the importance of maintaining adequate ridge volume in order to achieve a long-term esthetically acceptable implant-support prosthesis (42). Thus, it is increasingly expected that the results of the healing process should promote the formation of an alveolar ridge with a sufficient volume of hard and soft tissues to allow an ideal implant-supported restorative outcome.

Tooth extraction was once described as a tissue amputation that may lead to functional, psychological, postural and local changes (14). Indeed, tooth extraction is initially perceived purely as tooth loss, but local changes arise and promote hard- and soft-tissue alterations. The process of local changes that take place in order to close the wound and restore tissue homeostasis is called "socket healing". Thus, the aims of the present review were two-fold: first, to describe the socket-healing process; and, second, to discuss what is to be learned from that healing process that may improve the treatment outcome.

The alveolar process

In order to understand the socket-healing process and its clinical implications, it is pivotal to know the characteristics of the tissues that comprise the alveolar process. Thus, a brief anatomic and histologic description of such tissues is provided below (for detailed review, see 7, 65).

Anatomic considerations

The alveolar process may be defined as the bone tissue that surrounds a fully erupted tooth and it is formed in harmony with the development and eruption of the teeth (Fig. 1). It is limited coronally by the bone margins of the socket walls, whilst an imaginary line that cuts the bottom of the socket in a perpendicular direction to the long axis of the root, limits it apically. Beyond such a line, the basal bone of the mandible or the maxilla can be found.

The morphologic characteristics of the alveolar process are related to: (i) the size and shape of the tooth; (ii) the site of tooth eruption; and (iii) the inclination of the erupted tooth. In general, teeth tend to erupt and incline to a position outside the center of the basal bone (62). In a recent clinical study, Januario et al. (46) described some of the morphological

Fig. 1. Cone-beam tomographic image representing the alveolar process at the maxillary lateral incisor region. The alveolar process is the bone that surrounds the root.

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Postextraction socket preservation using epithelial connective tissue graft vs porcine collagen matrix. 1-year results of a randomised controlled trial

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Key words *bone volume, porcine collagen matrix, socket preservation, soft tissue graft*

Purpose: To compare epithelial connective tissue graft vs porcine collagen matrix for sealing postextraction sockets grafted with deproteinised bovine bone.

Materials and methods: A total of 30 patients, who needed a maxillary tooth to be extracted between their premolars and required a delayed, fixed, single implant-supported restoration, had their teeth atraumatically extracted and their sockets grafted with deproteinised bovine bone. Patients were randomised according to a parallel group design into two arms: socket sealing with epithelial connective tissue graft (group A) vs porcine collagen matrix (group B). Outcome measures were: implant success and survival rate, complications, horizontal and vertical alveolar bone dimensional changes measured on Cone Beam computed tomography (CBCT) scans at three levels localised 1, 3, and 5 mm below the most coronal aspect of the bone crest (levels A, B, and C); and between the palatal and buccal wall peaks (level D); and peri-implant marginal bone level changes measured on periapical radiographs.

Results: 15 patients were randomised to group A and 15 to group B. No patients dropped out. No failed implants or complications were reported 1 year after implant placement. Five months after tooth extraction there were no statistically significant differences between the 2 groups for both horizontal and vertical alveolar bone dimensional changes. At level A the difference was 0.13 ± 0.18; 95% CI 0.04 to 0.26 mm (P = 0.34), at level B it was 0.08 ± 0.23; 95% CI -0.14 to 0.14 (P = 0.61), at level C it was 0.05 ± 0.25; 95% CI -0.01 to 0.31 mm (P = 0.55) and at level D it was 0.13 ± 0.27; 95% CI -0.02 to 0.32 mm (P = 0.67). One year after implant placement there were no statistically significant differences between the 2 groups for peri-implant marginal bone level changes (difference: 0.07 ± 0.11 mm; 95% CI -0.02 to 0.16; P = 0.41).

Conclusions: When teeth extractions were performed atraumatically and sockets were filled with deproteinised bovine bone, sealing the socket with a porcine collagen matrix or a epithelial connective tissue graft showed similar outcomes. The use of porcine collagen matrix allowed simplification of treatment because no palatal donor site was involved.

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ORIGINAL ARTICLE

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Combined use of xenogeneic bone substitute material covered with a native bilayer collagen membrane for alveolar ridge preservation: A randomized controlled clinical trial

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Abstract

Aim: The aim of this split-mouth randomized controlled study was to evaluate radiographic dimensional changes after tooth extraction in posterior sites treated with a ridge preservation technique or left for spontaneous healing.

Materials and Methods: In a total of 18 patients, tooth extraction in posterior sites of the upper and lower jaw was performed in a split-mouth design. The post-extraction sockets were randomly assigned to the following two treatment modalities: deproteinized bovine bone mineral (DBBM) with 10% collagen (DBBM-C) covered with a native bilayer collagen membrane (NBCM) (test group) and spontaneous healing (control group). Cone beam computed tomography (CBCT) scans were performed after extractions, 3 and 6 months later. The following parameters were measured: the height of the buccal bone plate (BH), height of the palatal bone plate (PH), horizontal width of the extraction socket at 1 mm, 3 mm, and 5 mm (HW-1, HW-3, HW-5), and the horizontal width (thickness) of the buccal bone plate at 1 mm, 3 mm, and 5 mm (BHP-1, BHP-3, BHP-5). Statistical analysis was performed applying a nonparametric Wilcoxon signed-rank test.

Results: The CBCT analysis showed a bone loss compared to baseline in test and control group. The measurements which have reached statistically significant differences at 6 months were BH (test: −2.31% vs control: −13.11%), PH (test: −2.07% vs control: −15.32%), HW-1 (test: −17.14% vs control: −32.47%), and HW-3 (test: −11.65% vs control: −28.47%).

Conclusions: The posterior ridge preservation technique using DBBM-C covered with a NBCM is a valid approach reducing the amount of the radiographic loss in alveolar ridge dimensions.

KEYWORDS
bone regeneration, bone substitute, cone beam computed tomography, ridge preservation

1 | INTRODUCTION

After tooth extraction, spontaneous healing process causes bone remodeling and consequently shape and volume loss of the initial socket contour (Araújo, da Silva, de Mendonça, & Lindhe, 2015; Araujo & Lindhe, 2005; Cardaropoli, Araujo, & Lindhe, 2003; Hämmerle, Araújo, & Simion, 2012) The remodeling process starts immediately after tooth extraction, and after 2 years an

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Dimensional Evaluation of Different Ridge Preservation Techniques: A Randomized Clinical Study

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The objective of this study was to quantitatively determine ridge contour changes after different alveolar ridge preservation techniques. An initial total of 40 patients provided a final total of 35 single-gap extraction sites. After tooth removal, the socket was subjected to one of four treatment modalities: placement of a deproteinized bovine bone mineral (DBBM; Endobon) covered with a soft tissue punch from the palate (Tx1); placement of DBBM without soft tissue punch (Tx2); placement of an adsorbable collagen membrane (Osseoguard) covering the DBBM (Tx3); and no additional treatment (control). Silicone impressions were obtained before and 6 months after tooth extraction for quantitative-volumetric evaluation on stone cast models. Bone quality and need for further bone augmentation were also noted. Tx1 and Tx3 resulted in significantly less bucco-oral tissue loss when compared to Tx2 and the control group. Premolar teeth and teeth extracted for traumatic reasons revealed significantly less tissue loss. Using barrier membranes or soft tissue punches in addition to placement of DBBM seems to be advantageous to limit bucco-oral tissue atrophy. The clinical benefit, however, is still questionable.
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In 2003, Schropp et al[1] evaluated 46 extraction sites in the maxillary and mandibular posterior areas and demonstrated shrinkage in the buccolingual bone width of 50% after 12 months. Remarkably, two-thirds of this change was witnessed at the buccal aspect. Furthermore, the bone height decreased by 0.8 mm 3 months after tooth extraction. A recent review article confirmed that tooth extraction leads to horizontal bone loss of 29% to 63% and vertical bone loss of 11% to 22% after 6 months.[2]

A variety of studies have evaluated the effect of ridge preservation techniques on the resorption process of the extraction socket. Among them, the present group showed in a series of preclinical and clinical studies that ridge preservation techniques are capable of reducing dimensional alterations but fail to preserve the extraction socket.[3–8] Most recently, Vignoletti et al[9] presented a review article and confirmed that alveolar ridge preservation resulted in significantly less vertical and horizontal contraction of the alveolar bone crest when compared to spontaneous healing. The subgroup analysis revealed that the use of barrier membranes, a flap surgical procedure, and a full flap closure demonstrated better results. The authors, however, stress that no clear guidelines are provided

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ORIGINAL ARTICLE

Alveolar Ridge Preservation With Deproteinized Bovine Bone Graft and Collagen Membrane and Delayed Implants

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Abstract: To evaluate clinically and radiographically an alveolar ridge, preservation technique with deproteinized bovine bone graft and absorbable collagen membrane and then restoration with delayed implants were done. The study included 30 patients. The trial group's sockets were filled with deproteinized bovine bone graft (Bio-Oss) and covered with absorbable collagen membrane (Bio-Gide). The control group's sockets healed without any treatment. Panoramic radiograph and computed tomography were taken immediately after graft and 3 and 6 months later to evaluate the height, width, and volume change of the alveolar ridge bone. Dental implants were inserted in all sockets at 6 months, and osseointegration condition was evaluated in the following 12 months. All sockets healed uneventfully. In the trial group, the mean (SD) height reduction of the alveolar ridge bone was 1.05 (0.24) mm at 3 months and 1.54 (0.25) mm at 6 months. The width reduction was 1.11 (0.13) mm at 3 months and 1.84 (0.35) mm at 6 months. Bone volume reduction was 193.79 (21.47) mm^3 at 3 months and 262.06 (33.08) mm^3 at 6 months. At the same trend, in the control group, the bone height reduction was 2.12 (0.15) mm at 3 months and 3.26 (0.29) mm at 6 months. The width reduction was 2.72 (0.19) mm at 3 months and 3.56 (0.28) mm at 6 months. Bone volume reduction was 252.19 (37.21) mm^3 at 3 months and 342.32 (36.41) mm^3 at 6 months. There was a significant difference in alveolar ridge bone height, width, and volume reduction in the 2 groups. The osseointegration condition had no significant difference between the 2 groups. This study suggested that the deproteinized bovine bone graft and absorbable collagen membrane were beneficial to preserve the alveolar ridge bone and had no influence on the osseointegration of delayed implant.

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Dental implant is more and more popular because there are no damages on the adjacent teeth. The implant inserted in the alveolar ridge bone has the same function as the natural tooth root, which can bear and transfer chewing force well.

The condition of alveolar ridge bone after tooth extraction is very important, which can influence the delayed dental implant placement. Periodontitis, bony wall fracture, or lack of intraoperative intervention usually leads to the deficiency of alveolar ridge bone volume. Dental implant placement also becomes impossible because of serious bone resorption. Buccal side lamella bone of the anterior tooth is very thin and easily causes bone resorption and gingival recession after tooth extraction, which results in esthetic risks mostly. It always needs autogenous bone graft or bone splitting technique to increase bone thickness. However, the operation procedure is difficult and causes esthetic risks easily. In the molar area, lack of alveolar ridge bone height usually results in maxillary sinus or inferior alveolar nerve damage easily. So before dental implant placement, it always needs maxillary sinus lifting or alveolar ridge augmentation, which demands high operation level of physician and results in some complications. The bone volume of alveolar ridge decides the diameter, the length of the implant that influences stability, and the bearing chewing force ability in the long run.

During the socket natural healing process, alveolar ridge bone resorption and soft tissue shrinkage are the common problems; the estimated structural loss is approximately 40% in height and 60% in width of the alveolar ridge bone[1] and continues with a rate of 0.25% to 0.5% per year.[2] Alveolar ridge bone resorption mainly happens during the first 3 months after tooth extraction, so intraoperative intervention is very important and necessary for delayed dental implant. During the last decade, efforts have been made to confirm procedures that can prevent bone resorption after extraction. The use of bone grafts aim to promote bone healing and assist bone regeneration. Various types of materials are used for socket preservation, such as autogenous bone, allograft bone,[3–5] xenograft materials,[6–8] and alloplast materials.[9] The autogenous bone graft material is recognized to be the gold standard in bone grafting because it can transfer osteogenic cells within the grafts.[10] However, the amount of bone available is limited around the socket and needs a second surgical procedure, so the development of substitutes to replace the autogenous bone should be imperative.[11,12] The deproteinized bovine bone has been tested in vitro and in vivo in the alveolar ridge preservation and plays a positive role in osteoconductive function.[13] Guided bone regeneration (GBR) procedure has been developed to counteract alveolar ridge bone resorption. Lekovic et al[14]