Guided bone regeneration in periodontology: review

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ABSTRACT
Alveolar bone loss caused by periodontal diseases is one of complication in periodontology. In some cases, alveolar bone loss is often followed by extraction as the treatment choice and resulting in large bone defects. Deficiency of bone volume and dimension can make difficulties on implant placement in the future. Guided bone regeneration is one of treatment modalities to create bone regeneration usually in edentulous area. The success of bone regeneration in large bone defects needs bone graft and barrier membrane material. There are various types of bone graft that can be used such as autograft, xenograft, allograft, alloplast, and bioglass. The rationale of GBR advocates mechanical exclusion of undesirable soft tissues from growing into the osseous defect, therefore barrier membrane plays an important role in GBR. Various types of materials have been developed, which can be grouped together as either non-resorbable or resorbable membranes. This paper reviews the uses of GBR especially in periodontology as one of therapeutic treatment choices for bone regeneration.
Key words: guided bone regeneration, alveolar bone loss, bone graft, barrier membrane

INTRODUCTION

Bone is a component of skeletal system that provides supporting structure for body including alveolar bone that supports teeth.[1] Bone has a complex morphology, and is known as special connective tissue that consist of calcified and organic matrix.[1] Alveolar processus is considered as part of mandibula and maxilla that developed and supporting tooth socket.[2]

Alveolar bone losses caused by periodontal diseases was one of complications in periodontology. Inadequate bone volume can be caused by congenital defect, post trauma, defect post surgery or another pathologic progress including periodontal diseases.[3–5] Extraction often became the choice of treatment in severe bone loss, resulting in large bony defects. The use of implants to provide support for replacement of missing teeth has become an important component of modern dentistry. For successful placing implant, a sufficient amount and quality of bone is essential around the site of insertion, hence large bony defects can become a difficulty factor.

Alveolar bone regeneration has become one of the objectives in periodontal treatment. According to the American Academy of Periodontology, guided bone regeneration (GBR) in oral cavity is defined as procedures attempting to regenerate lost periodontal structures through different tissue responses, typically referring to ridge augmentation or bone regeneration procedures.[5,6] Guided bone regeneration is usually used in edentulous area and also benefit for implant placement at an ideal location in oral cavity, thus improving esthetics and function. For a successful bone regeneration to happen, large bony defects need an underlying grafting material and a cell occlusive membrane.[7] Dahlin, et al., was the first researcher who investigated GBR for constructing large defect in maxilla or mandibular treatment via the use of barrier membranes.[4–6,8]

In daily clinical practise we frequently encounter situations in which the bone volume is insufficient for an ideal implant placement, and large bony defects because of periodontal diseases.[9] Bone regeneration can provide a good structural support for treating cases like that. This paper reviews about the use and current technique of GBR, especially in periodontology field.

Biology of bone

Bone is a connective tissue that consists of cells and extracellular matrix, acts as supporting structural for the body, including alveolar bone for teeth.[1,10] There are three different cell types in bone structures, i.e osteoblast, osteocyte and osteoclast.[1–3] Osteoblast is a mononuclear cell that come from mesenchymal stem cell.[3] This cell is responsible for osteogenesis and new bone matrix development.[3,11] Osteocyte is a mature osteoblast inside the bone matrix and also contribute to bone production.[2] Osteoclast is a giant multinuclear cell that is responsible for the bone resorption.[2,3]

Bone constantly undergoes remodeling, which is a complex process that involves bone resorption followed by bone formatting (Fig 1) through activities of osteoblastic and osteoclastic.[1] It has an unique potential to return into the original structure, but there are some considerations for a successful bone regeneration such as adequate blood supply and mechanical stability.[6]

Definition of guided bone regeneration (GBR)

Guided bone regeneration has the same basic concept with guided tissue regeneration (GTR).[4,6,8] According to American Academy of Periodontology, GBR is a set of procedures attempting to regenerate lost periodontal structures through different tissue responses, typically referring to ridge augmentation or bone regeneration procedures.[5] Retzepi et al and

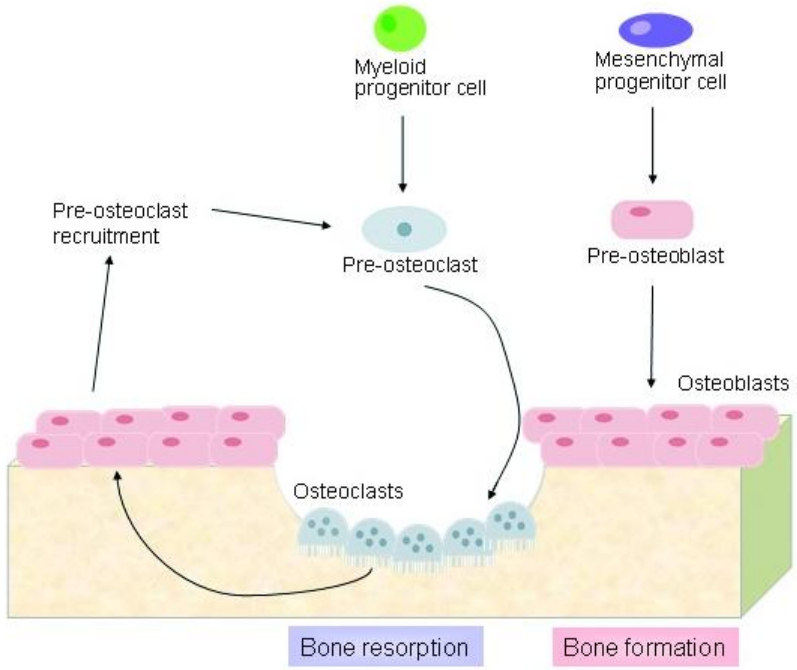

Fig 1 Bone remodelling (cited from: http://GBR.restorativemedicine.org/books/fundamentals-of-naturopathic-endocrinology/professionals/adrenal-metabolism-disorders/disorders-similar-to-hypothyroidism/)

Manesh et al, explained that the concept of GBR treatment is to regenerate osseous defect using barrier membrane to prevent the population of non-osteogenic cell from soft tissue, thus allow the population of osteogenic cells from adjacent bone to cover osseous injury.[7,8] Guided bone regeneration is usually used in edentulous area and also benefit for placing implant at ideal location in oral cavity, thus improving esthetic and function.

In GTR we are dealing with epithelial and connective tissue exclusion and space creation to allow for the cells of periodontal ligament to repopulate the root surface and allow bone cell to grow into area defect.[4] Thus, in GTR there are five compartments, which are the epithelium, connective tissue, cells of periodontal ligament, cementum, and bone.[4] While in GBR, there are two compartments, the connective tissue and the bone.[4] The connective tissue exclusion, which is achieved with the barrier membrane, allowed for the bone regeneration to occur.[4] Murray in 1957 stated that three things were necessary for the new growth of bone: the presence of a blood clot, preserved osteoblast, and contact with living tissue.[4]

The biological basis for guided boner regeneration involved fulfillment of bone growth requirement are establishing stable immobile base, allow for release of growth factors and finally preserving the blood supply to the area of defects.[7] Guided bone regeneration have been recommended for isolated bone defects or defects connected to implant placement such as dehiscence, residual intraosseous, fenestration, and socket post extraction.[4,5]

There is a principle of the fundamental rationale and stages for successful regeneration, both for bone and other tissues, called PASS and is a guide to the physiological processes central in tissue regeneration.[7] The PASS are 1) primary wound closure to ensure undisturbed and uninterrupted wound healing, 2) angiogenesis to provide mesenchymal cells which undifferentiated, space maintenance/creation to facilitate adequate space for bone in growth and necessary blood supply, 3) space maintenance in the bone grafting procedure functions as space holder by its very nature while acting as scaffold for new bone formation, and also initiating osteogenesis through its osteoinductive ability, and 4) stability of the wound and implant to induce blood clot formation and uneventful healing events.

Bone graft

Muschler defined bone graft as any individual implanted material or its combination with other materials, which promotes bone healing response by providing osteogenic, osteoinductive or properties of osteoconductives.[6,9] An osteogenic material can be defined as one that is inherent capacity to form bone, which implies that it contains living cells that are capable of differentiation into bone cells.[9] An osteoinductive material provides biologic signals

capable to induce local cells to enter pathway of differentiation.[9] While, an osteconductive material provides a 3-dimensional interconnected scaffolds where local bone tissue may regenerate new living bone, but unable to form bone or to induce its formation.[9]

There are some types of bone graft, such as the autograft, the allograft, the xenograft, the alloplast, and the bioglass.[2,9,12] Autogenous bone grafts or autograft are still considered to be the gold standard because of the lack of mechanism of immunologic rejection and the presence of stem cells and growth factors, both with osteoinductive and osteoconductive properties, and this graft is also the only graft that able to do osteogenesis.[9,13] Autografts are subdivided in two groups; cancellous autografts and cortical autografts.[9] Cancellous bone is revascularized more rapidly than cortical bone, owing to its porous nature, therefore permitting more complete incorporation and perhaps even total replacement.[6,14] It is also believed that new bone formation on transplanted trabecular surfaces precedes resorptive activity.[14]

Allograft is defined as tissue that has been harvested from one individual and implanted into another individual of the same species.[2,9] The use of cadaver bone for grafting is considered as the best available alternative to autografts.[9] Despite the superiority of autografts, allografts are preferred by patients as bone grafting materials because they don't need donor site surgery.[9] Allografts are obtained from cadaver tissue banks for mineralized freeze-dried (FDBA) or decalcified freeze-dried (DFDBA) bone.[9] Mineralized FDBA are mineralized bone matrix that has no active bone morphogenetic proteins (BMPs) and it lacks osteoinductive properties, although it has osteoconductive properties.[9] Graft incorporation is qualitatively similar to autograft, but occur more slowly. Decalcified freeze-dried are processed by hydrolic acid demineralization so that it preserves the BMP in bone; therefore it maintains some of inherent osteoinductive properties.[9] BMP are associated with the organic matrix of bone and embedded within mineral content, so demineralized process increases its bioavailability.[9]

Bone xenograft is defined as a bone tissue harvested from one species and implanted into a different species. One of the most commonly used xenografts is anorganic bovine bone.[9] Xenograft of bovine has an ultrastructural composition similar to human bone. Bovine xenograft is composed of almost pure hydroxyapatite, and it is chemically treated to remove all organic components so it can be used as a graft material that without causing host immune response.[9]

Synthetic biomaterial that consists calcium phosphate chemically resemble the bone mineral.[9] Calcium phosphate are selected to regenerate bone tissue due to their biocompatibility, osteointegration and osteoconductivity.[9] Another synthetic biomaterial for bone regeneration is bioglass which is the first calcium substituted silicon oxide.[9] One of the unique characteristics of bioglass is bioactivity that allowed this material to a quick integration to bone tissue.[9] Bioglass is suitable for bone regeneration in dental implant surgery; moreover, it is purely synthetic therefore it does not present problems regarding transmission of infectious diseases.[9]

Barrier membrane

Dahlin, et al was the first to introduce GBR as a therapeutic modality aiming to achieve regeneration of bone via the use of barrier membranes.[4–8] The rationale of GBR advocate mechanical exclusion of undesirable soft tissues from growing into the osseous defect, thereby allowing only osteogenic cell population in the site of osseous wound. According to Dahlin, et al., the GBR therapeutic protocol involves surgical placement of a cell occlusive membrane facing the bone surface in order to physically seal off the skeletal site in need for regeneration.[5,6] (Fig 2)

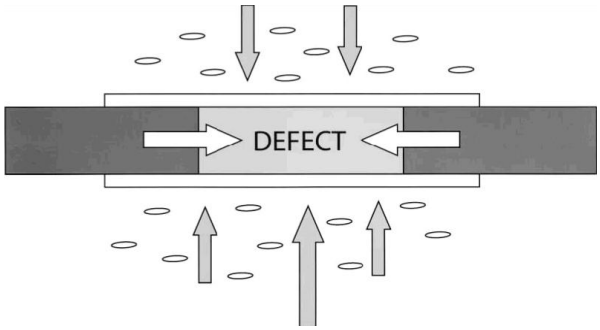

Fig 2 Principle of osteopromotion using barrier membrane[5,6]

There are five important criteria in the design of barrier membranes;[5] cell-occlusiveness, space making, biocompatibility, tissue integration and clinical manageability.[5] Various types of materials have been developed, which can be grouped together as either non-resorbable or resorbable membranes.[5]

Expanded polytetra-fluorothylene (e-PTFE) is a non-resorbable membrane that has been used frequently for periodontal and bone regeneration.[4–6,8] Expanded polytetra-fluorothylene (e-PTFE)is a chemically stable and biologically inert polymer, featuring a porous structure and flexible form. It resists enzymatic and microbiological degradation and and does not elicit immunologic reactions. Hammerle and Jung were documented that their use

predictably leads to successful the guided bone regeneration treatment results.

The non-degradable barrier membranes do not undergo solubilisation when placed in the living body, hence they require a second surgical intervention in order to be removed.[8] This disadvantage led to the development of biodegradable membrane devices.[8]

Collagen membranes are one type of resorbable membranes that is often the choice in bone regeneration treatment.[5] Collagen is the principal component of connective tissue and provides structural support for tissues throughout the body.[5,12] Some properties of collagen membranes that are advantageous for bone regeneration are well tolerated, bioresorbable, absorbed slow (about 6-8 weeks, so they give the cells time to regenerate at the wound site), easy to manipulate and adapt, act as chemotactic agent for fibroblasts so they could enhance cell migration, and also they act as hemostatic agent, which may facilitate initial clot formation and stabilization.[5]

DISCUSSION

Guided bone regeneration (GBR) using barrier membranes with or without bone graft material has been used widely in periodontal bone regeneration

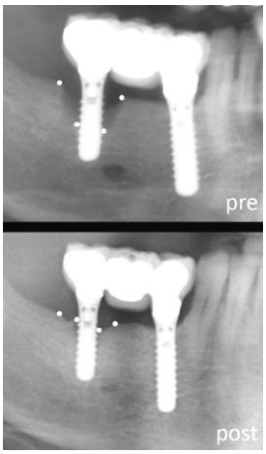

Fig 3 Magnification of a section of panoramic x-rays before (pre) and 12 months after (post) surgical intervention. The points indicate the surrounding bone level, the medial ones the deepest point of the pockets beside the implant.

treatment. There have been many researches on the effectiveness of this therapy.

Wiltfang studied the combination of autogenous graft with demineralized xenograft on 36 peri-implantitis with bone loss (depth ≥4 mm), controlled for 1 year.[15] This combination showed average defect reduction 3.5 mm radiographically, and pocket depths reduction from 7.5 mm to 3.5 mm (Fig 3).[15]

Macedo et al., studied the used of fresh-frozen human bone allograft (FHBAs) on vertical ridge augmentation, clinically and computed tomography (CT).[16] After 7 months, there were significantly differences on bone reformation compared to its initial condition (4.03 ± 1.69 mm). Bone graft resorption occurred 20% (1.0 ± 0.82 mm). This study concluded FHBA showed satisfaction vertical bone formation with low ratio of resorption, good density, besides this study primary stabilization for implant placement.[16]

Keith *et al.*, studied 82 bone reconstruction with allogenic graft in 73 patients, who underwent implant placement at 4-6 weeks after the grafting. They were controlled until 36 months post prostheses insertion.[17] They reported that no resorption occurred on 69% of allograft blocks, and 2 mm resorption was seen only on 31% blocks.[17] Wood et al., reported significant new bone formatting inside the preserved socket with demineralized allograft compared with socket preserved with mineralized allograft.

Holtzcaw reported a case series on the use of a new allograft bone product composed of a 70:30 ratio of mineralized to demineralized the cortical bone particles to preserve the alveolar ridge dimensions of patients requiring tooth extraction with plans for future dental implant placement. The ten patients received atraiunatic tooth extractions with subsequent placement of the blended bone allograft. All sites were covered with a single layer of amnion-chorion, which was intentionally left exposed. The results of this case series suggest that blended bone allograft containing a 70:30 ratio of mineralized to demineralized cortical bone particles can be successfully used to facilitate future placement of dental implants with as little as 14 weeks of healing (Fig 4).[18]

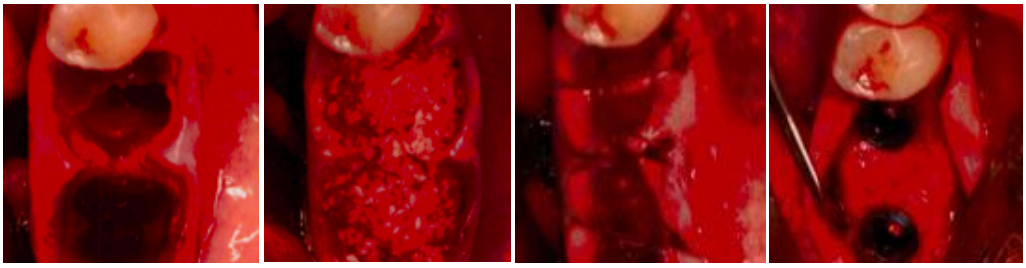

Fig 4 Atraumatic extraction followed by socket filling using allograft and covered by amnion-chorion. Implant placement after 14 weeks

Fig 5 left to right. The maxillary left lateral incisor was missing, and a deficit of tissue and an unfavorable contour were present. After elevating a full-thickness flap, the implant was placed but not completely embedded in bone. A large buccal dehiscence is visible. The bone defect filled with mineralized collagen bone substitute (MCBS) in combination with a titanium-reinforced expanded polytetrafluoroethylene membrane.

Grunder *et al*., reported a case series from eight patients free of periodontal disease, to evaluate the clinical and histologic outcome of guided bone regeneration around simultaneously placed implants in sites with missing buccal bone walls.[19] At the time of reentry at 6 months after augmentation, an adequate bone volume had formed. On average, the horizontal bone gain was 3.75 ± 0.47 mm (baseline defect width 3.88 ± 0.44 mm) and the vertical gain was 6.50 ± 0.81 mm (baseline defect height 5.88 ± 0.73 mm). No implant was lost. The clinical procedure and outcome are presented in Fig 5-8.[19]

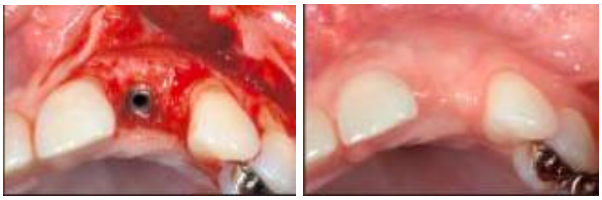

Fig 6 Left to right. After 6 months, the healed site presented a healthy soft tissue situation. At reentry, 4 mm of newly formed bone was visible buccal to the implant after removing the membrane.

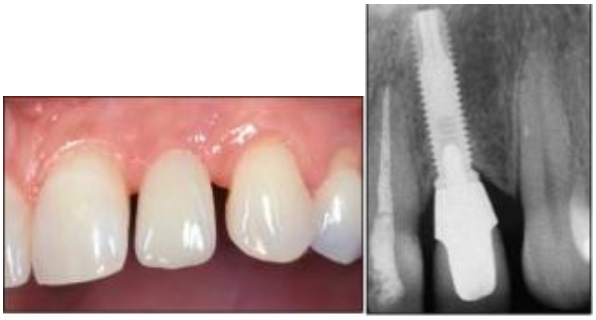

Fig 7 Final result with an implant-supported all-ceramic crown showed a very good esthetic outcome (left). Radiographic outcome on right showed successful osseointegration of the implant.

Dahlin et al., studied bone augmentation by GBR in combination with bovine hydroxyapatite (BHA) for implant placement on the 20 systemically healthy individuals who were referred to two implant centers for rehabilitation in anterior region. The cumulative implant survival rate was 97.5% corresponding to one implant failure. The radiologic evaluation of the marginal bone level (MBL) demonstrated a crestal bone height above the level of the fixture head. The bone height decreased from -3.51 to -2.38 mm (p <.001). The marginal soft tissue level (MSTL) was -1.52 mm at baseline and -1.15 mm at the 5-year follow-up (p<.04) demonstrating a stable submucosal crown margin throughout the study period. The clinical procedure and outcome are presented in Fig 9-12.[20]

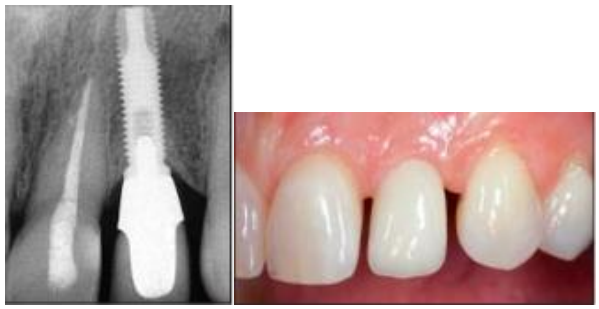

Fig 8 The 3-year follow-up showed a stable situation. Radiographic outcome at right 3 years showed stable osseointegration of the implant.

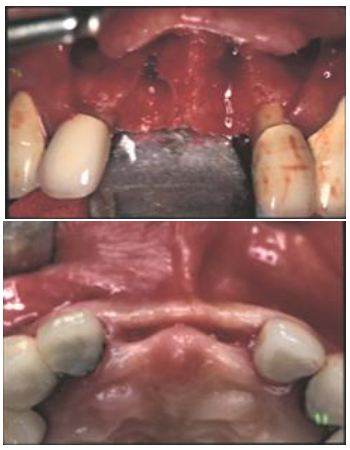

Fig 9 Upper to bottom. Note the loss of the buccal bone plate. Axial view demonstrating a narrow alveolar ridge following extraction of tooth 11 and 21

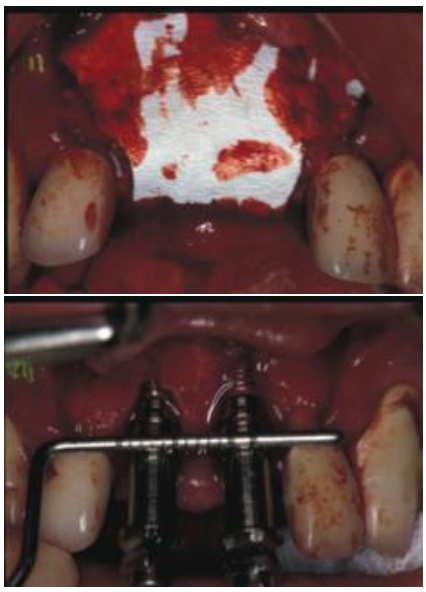

Fig 10 (above to bottom) Considerable amount of bone-filling material was placed in order to recreate in slight excess the original contour of the alveolar ridge. To prevent soft tissue ingrowth and favor bone-forming cells, a bioabsorbable membrane was applied over the reconstructed area. The implant was to be located about 2 mm apically to the border of the surgical template and the cementoenamel junction of neighboring teeth.

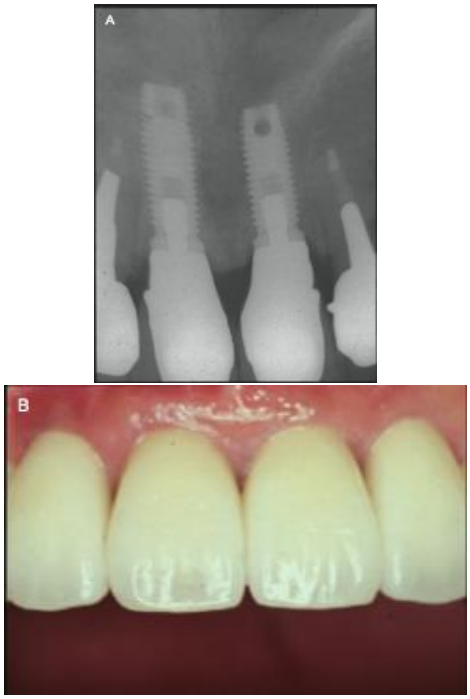

Fig 11A Intraoral radiographs at cementation of the final restorations. Note the remaining height of the newly formed interproximal bone tissue; **B** Final restorations seated in place

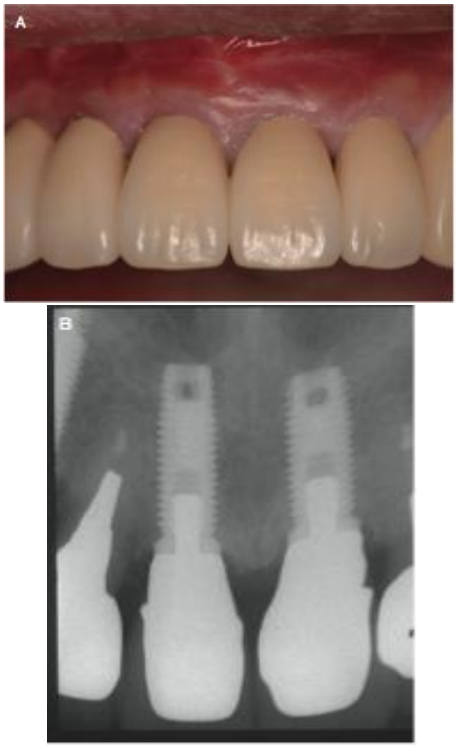

Fig 12A Five-year follow-up. Frontal view. Note the stable level of the peri-implant tissue; **B** radiograph at the 5-year follow-up. Only minor remodeling of the hard tissue is seen. Note the stable bone level well above the level of the fixture head.

It is concluded that guided bone regeneration (GBR) has been used widely in periodontal treatment to regenerate alveolar bone through various tissue responses. The guided bone regeneration treatment concept advocates that regeneration of osseous defects is predictably attainable via the application of the occlusive membranes, that mechanically exclude non-osteogenic cell populations from the surrounding soft tissues, thereby allowing osteogenic cell populations originating from the parent bone to inhabit the osseous wound.

Autografts are still considered to be the gold standard because thi graft is the only graft that is able to do osteogenesis. The necessity of secondary donor site surgery to obtain the graft still becomes a major drawback of this graft. Other graft materials such as allograft, alloplast, xenograft, and bioglass have shown promising results in many bone augmentation procedures also preferred for bone regeneration treatment. To achieve successful bone regeneration with GBR procedures, individual characteristics, indications, biomaterial properties and the surgical procedure should be considered.

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