Vertical and Horizontal Augmentation Using Guided Bone Regeneration

Ph.D. Thesis

Dr. med. dent. et univ. Istvan Urban

Supervisor: Prof. Dr. Katalin Nagy, DDS, PhD
Faculty of Dentistry, University of Szeged

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1. Introduction

Bone augmentation procedures are often necessary for the successful placement of endosseous dental implants. Several treatment modalities have been developed for bone growth, including distraction osteogenesis, onlay bone grafting, and guided bone regeneration (GBR). Guided bone regeneration may be used for either vertical augmentation or horizontal augmentation, and clinical studies will be presented that demonstrate the clinical significance of these types of procedures.

1.1 Vertical Augmentation with GBR

Supracrestal or vertical bone augmentation presents one of the greatest challenges of bone regeneration in implant dentistry. This is primarily due to the difficulty of the surgical procedure and its potential complications. Supracrestal augmentation aims to achieve bone regeneration in a direction without bony walls to support the stability of the bone graft. It is demanding biologically, because bone regeneration and angiogenesis has to reach a distance from the existing bone. In addition, the soft tissue has to be advanced to provide a closed healing environment for the increased dimension of the healing bone graft. Several treatment modalities have been developed for vertical bone growth, including distraction osteogenesis, onlay bone grafting, and vertical guided bone regeneration (GBR).

The application of GBR for supracrestal regeneration was introduced and the surgical technique described (Tinti and Parma-Benfenati 1998). There are few reports of vertical GBR, and they present conflicting results and relatively high complication rates. The first animal and human histologic studies demonstrated successful vertical bone augmentation (Jovanovic et al. 1995; Simion et al. 1994). Complications reported with vertical augmentation involved membrane exposure and/or subsequent infection, with rates ranging between 12.5% and 17% (Tinti and Parma-Benfenati 1998; Simion et al. 1994, 1998).

The long-term results of vertical GBR following 1 to 5 years of prosthetic loading were examined in a retrospective multicenter study evaluating 123 implants (Simion et al. 2001). Three treatment modalities (non-resorbable regenerative membranes in

combination with blood clot only, demineralized freeze-dried bone allograft (DFDBA), or autogenous bone chips) were studied and the results from this investigation revealed that vertical bone regeneration superior to 4 mm could only be achieved with the use of autogenous bone chips. These authors reported an overall success rate of 97.5%, leading them to conclude that vertically augmented bone using GBR techniques responds to implant placement in a fashion similar to native, non-regenerated bone. In another study, the GBR technique for vertical augmentation was used in combination with a sinus lift procedure for posterior maxillary reconstruction (Simion et al 2004). However, the implant survival and success rates were 92.1% and 76.3%, respectively, which conflicted with previously reported results on vertical and horizontal GBR (Buser et al 2002; Simion et al 2001). All these studies utilized non-resorbable, titanium reinforced, expanded polytetrafluoroethylene (e-PTFE) membranes (GORE-TEX® Regenerative Material Titanium Reinforced or GTRM-TR, W.L. Gore & Associates, Flagstaff, AZ). These membranes have been associated with a high incidence of soft tissue problems, such as exposure (Zitzmann 1997). Other authors have reported a similar soft tissue response of e-PTFE membranes when compared to resorbable membranes (Simion 1997). Titanium osteosyntheis plates covered with a collagen resorbable membrane was compared to e-PTFE membranes in a randomized clinical trial for vetical GBR, and there were no statistically significant differences in terms of complications between the two techniques (Merli et al 2006). In addition, more sites achieved a complete regenerative outcome when the e-PTFE membrane was used. No long-term results were reported of implants placed into vertically regenerated bone when particulated bone graft materials was covered with titanium osteosntheis plates and a resorbable membrane. Hence, the utilization of e-PTFE membranes represents the current state of the science in vertical GBR.

1.2 Horizontal Augmentation with GBR

Augmentation utilizing guided bone regeneration (GBR) has become a major treatment option to provide optimal bone support for osseointegrated dental implants. Simple defects were initially treated with GBR, including dehiscence and fenestration defects (Aghaloo & Moy 2007; Esposito et al 2006a; Hämmerle et al 1998, 2002; Dahlin

et al 1991; Jovanovic et al 1992; Lorenzoni 1998; Zitzmann et al 2001a; Moses et al 2005). In addition, GBR has been utilized for horizontal and vertical ridge augmentations(Hämmerle et al 1998; Dahlin et al 1991; Jovanovic et al 1992; Lorenzoni 1998; Zitzmann et al 2001a; Moses et al 2005; Simion et al 2001; Buser et al 2002; Urban et al 2009 a, b) and has demonstrated reproducible outcomes with high implant survival rates and low complication rates (Esposito et al 2006b).

The so called "knife-edge" ridges, or Cawood and Howell Class IV edentulous jaw (Cawood & Howell 1988), present a unique problem for horizontal augmentation. The necessary height of the ridge is adequate on the lingual/palatal side, but the width is insufficient making implant placement often impossible without prior treatment (Proussaefs & Lozada 2003). However, there is a good prognosis for this treatment as the residual ridge can be used to stabilize the bone graft, making it less subject to movement, one of the factors that may lead to a failure. To avoid movement of the bone graft, autogenous bone blocks are often screwed onto the ridge to ensure stability and subsequent new bone formation (von Arx & Buser 2006; Cordaro et al 2002; Schenk et al 1994; Buser et al 1996). Bone blocks (also referred to as "onlay bone graft") can be fixated onto the residual ridge, providing a limited number of additional bone forming cells into the augmentation site, and may eliminate the use of a non-resorbable titanium reinforced membranes (Chiapasco et al 1999). Studies of onlay bone grafting have reported 60% to 100% implant survival rates, with the majority of reported survival rates > 90% (Aghaloo & Moy 2007; Chiapasco et al 2006). However, block bone grafts are associated with varying morbidity depending on the harvest site (Nkenke et al 2001, 2004; Raghoebar et al 2001) and early resorption that could compromise clinical outcome (von Arx & Buser 2002; Maiorana et al 2005). Thus for partially edentulous patients it has been recommended that the utilization of GBR may be an alternative grafting procedure for patients presenting with advanced ridge atrophies (Chiapasco et al 2006).

Clinical studies utilizing GBR for the treatment of knife-edge ridges used both non-resorbable and resorbable membranes (Buser et al 2002; Hämmerle et al 2008). To obtain the anticipated volume of the ridge, utilizing GBR, autogenous bone or bone substitutes are placed under the barrier membrane to prevent collapse of the augmentation volume (Lindhe et al 2003).

Resorbable membranes have shown better soft tissue compatibility, compared to non-resorbable membranes (Friedmann et al 2002; Zitzmann et al 1997, 2001a). Reports of clinical and preclinical animal studies have demonstrated that a resorbable membrane in combination with particulated bone or bone substitute can be used for the treatment of knife-edge ridges. Friedmann et al. (2002) reported on a clinical study using a slowly resorbing collagen membrane in combination with anorganic bovine-derived bone mineral (ABBM) for the augmentation of horizontally deficient ridges. Good results were obtained, but the handling of the collagen membrane was technique sensitive as has been observed with non-resorbable membranes (Chiapasco et al 1999). Hämmerle et al. (2008) have used ABBM in combination with a collagen membrane, and concluded this was an effective treatment for horizontal ridge augmentation. Similarly, Zitzmann et al. (2001b) have performed a histologic analysis in defects that had been filled with ABBM and covered with a collagen membrane. Their results indicated that ABBM may be a suitable material for staged localized ridge augmentation. As an additional osteogenic component, particulated autogenous bone can be mixed with bone substitutes to add more osteogenic factors and a limited number of osteogenic cells to the augmentation site.

The potential advantages of this treatment modality compared to autogenous bone block application are an increased exposure of osteoinductive growth factors and greater osteconductive surface. Autogenous bone can be mixed with ABBM: harvesting less autogenous bone may result in a decreased morbidity from this procedure.
Traditional synthetic membranes have demonstrated therapeutic problems using traditional polymers like polylactic acid because of their inflammatory and foreign body reaction upon degradation (von Arx et al 2005). More recent experimental results with a newly developed synthetic resorbable membrane made of polyglycolic acid (PGA) and trimethylene carbonate (TMC) have yielded positive results. Recent studies in an animal model with this membrane have demonstrated no histologic foreign body or inflammatory reaction (Stavropoulos et al 2004). This synthetic resorbable membrane has been designed to slowly resorb over 4-6 months, providing a prolonged barrier function to ensure that the newly formed bone has sufficient time to mature before soft tissue can grow into it.

In vitro and preclinical animal studies with native collagen membranes have shown excellent biocompatibility and demonstrated equivalent bone formation in dehiscence-type defects when this more rapidly resorbing native collagen membrane was compared to non-resorbable and slowly resorbing membranes (Rothamel et al 2004; Schwarz et al 2008). These nonclinical results and the case series using the native collagen membrane (Hämmerle et al 2008) may indicate that a slowly resorbing membrane is not necessary for horizontal augmentation.

2. AIM OF THE STUDIES

Three studies will be presented: a retrospective study that utilized vertical augmentation; a horizontal augmentation study that utilized a new synthetic membrane (this study is referred to as "HA/1"); and a horizontal augmentation study that utilized a native, bilayer collagen membrane (this study is referred to as "HA/2").

2.1 Study on Vertical Augmentation

The aims of this retrospective study were to: (1) evaluate results of vertical GBR with particulated, autogenous bone grafts; (2) determine clinical and radiographic success and survival rates of implants placed in surgical sites after prosthetic loading; and (3) compare success and survival rates of implants placed in defects treated simultaneously with sinus augmentation and vertical GBR to other areas treated with vertical GBR only.

2.2 Horizontal Augmentation Utilizing a New Synthetic Membrane (HA/1).

The purpose of this clinical series was to evaluate clinically and histologically the possibility of using a new synthetic resorbable membrane in combination with a mixture of anorganic bovine bone mineral (ABBM) and autogenous particulated bone in horizontal augmentation of knife-edge ridges.

2.3 Horizontal Augmentation Utilizing a Native, Bilayer Collagen Membrane (HA/2)

The use of a more rapidly resorbing native collagen membrane and 1:1 mixture of autogenous particulated bone/ABBM as grafting material for horizontal augmentation has not yet been investigated. Accordingly, the purpose of this clinical series was to evaluate clinically and histologically the use of a more rapidly resorbing native collagen membrane in combination with a mixture of ABBM and autogenous particulated bone in horizontal augmentation of knife-edge ridges to confirm the acceptability of the osteoconductive material in the procedure and to limit the amount of harvested autogenous bone required for the procedure.

3. MATERIALS AND METHODS

3.1 Vertical Augmentation

This retrospective study reported on patients who were consecutively treated with vertical augmentation using GBR and particulated autografts from June 1999 to Oct 2004. All patients were treated at either the Center for Implant Dentistry (Loma Linda University School of Dentistry, Loma Linda, CA, USA) or in a private clinic (Budapest, Hungary). All surgical procedures were performed by the same practitioner (I.U.) with over 15 years of experience in oral surgery and implant therapies, and the prosthetic treatments were performed by residents in the Loma Linda University Implant Dentistry program or private practitioners.

Inclusion criteria: Cases were selected that required vertical bone regeneration (1) to achieve the necessary bone levels in order to place dental implants, and (2) to improve the crown/implant ratio and esthetics. Patients were required to have good oral hygiene prior to treatment.

Exclusion criteria: Patients were excluded if they were current smokers; engaged in excessive alcohol consumption; or had uncontrolled systemic conditions or uncontrolled periodontal disease.

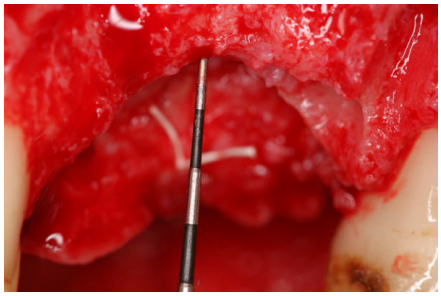
Clinical Procedures: Briefly, all patients were treated with vertical ridge augmentation utilizing titanium reinforced, non-resorbable, expanded polytetrafluoroethylene (e-PTFE) membranes (GORE-TEX® Regenerative Membrane Titanium Reinforced or GTRM-TR, W.L. Gore & Associates, Flagstaff, AZ, USA) and particulated autografts.

Defects were measured during the grafting procedures with a calibrated periodontal probe. Vertical bone defects were measured from the most apical portion of the bony defect to a line connecting the interproximal bone height between neighboring teeth, or to the original bone crest of the edentulous area.

The surgical technique has been described previously (Tinti et al 1998). Briefly, a remote full-thickness flap was elevated in the edentulous area and the residual bone ridge was prepared carefully to receive an autogenous bone graft and a GTRM-TR membrane. The autografts were harvested from the mandible, particulated in a bone mill (R. Quétin Bone-Mill, Roswitha Quétin Dental Products, Leimen, Germany), and applied to the defect. The bone graft was immobilized and covered with a GTRM-TR membrane that was stabilized with titanium bone tacks. When implants were placed simultaneously, the fixtures protruded from the base of the defect to the desired vertical position, and were covered with the graft and membranes.

In posterior maxillary cases with both severe vertical crestal bone atrophy and enlarged maxillary sinus, a combined procedure of vertical GBR and a simultaneous maxillary sinus graft was used. The sinus grafts utilized the lateral window approach and the grafting material consisted of autogenous particulated bone with anorganic bovine spongiosa bone mineral (Bio-Oss®, Geistlich Pharma AG, Wolhusen, Switzerland). The classification and rationale for this procedure with posterior maxillary alveolar defects that combines GBR and sinus bone grafts have been described previously (Jovanovic & Altman 1998; Simion et al 2004). Bone harvest sites were selected based on the amount of bone required versus available bone and anatomic limitations. Clinical photographs were taken during the procedures. See **Figure 1** (a and b graphically present parts of the surgical procedure).

Figure 1. Vertical Augmentation Study: Measurement of representative defect before and after treatment. **(a)** A 7-mm vertical defect involving 3 teeth. **(b)** Buccal view of the autogenous bone graft and membrane in place. **(c)** and **(d)** Regenerated bone crest at membrane removal after 9 months of healing.



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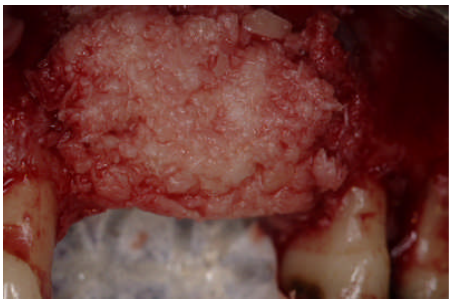

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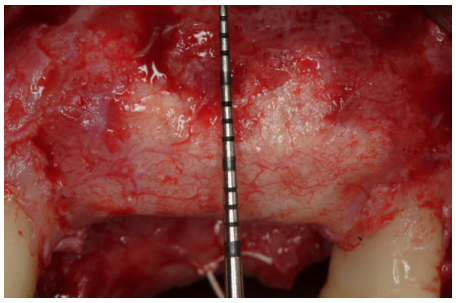

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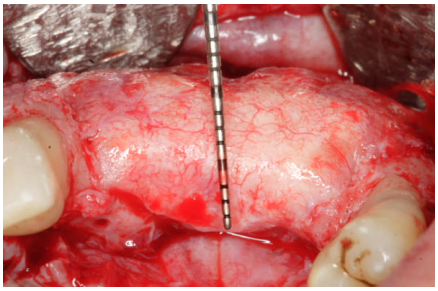


(d)

The surgical site was allowed to heal for 6 to 9 months. Then, the GTRM-TR membranes were removed, and implants were placed or uncovered. At the time of membrane removal, bone regeneration was evaluated (see **Figures 1c** and **1d**). At implant placement, a collagen membrane (Bio-Gide® Resorbable Bilayer Membrane, Geistlich Pharma AG, Wolhusen, Switzerland) was placed over the newly formed crestal bone to protect the graft from early resorption. The objective was to place the implant platform to crestal bone level, leave in submerged healing for 6 months, then uncover the implants.

All patients were to receive a provisional prosthesis during the healing phase of the bone grafts and the implants in order to provide function and esthetics, and no

pressure to the site. Final restorations were to occur within a few weeks after the implants were uncovered. Patients received fixed implant-supported restorations and entered into a scheduled maintenance program that included a clinical examination every six months and annual radiographic examination.

Clinical examination: Peri-implant mucosal conditions were assessed for redness, hyperplasia, suppuration, swelling, and presence of plaque. Probing depths were recorded according to established methods (Buser et al 1990, 2002; Van Steenberghe et al 1990).

Radiographic examination: Periapical radiographs were taken at the abutment connection and then every 12 months thereafter with a long cone parallelling technique. Crestal bone levels were measured up to 0.01 mm using NIH image software, with the implant abutment junction as the baseline reference (Wyatt et al 2001).

Complications: Complications in bone graft healing, such as membrane exposure and/or subsequent infection, were recorded.

Implant Success Criteria: Success was evaluated according to established methods that evaluated the following : absence of pain, foreign body sensation, dyesthesia, mobility, or peri-implant radiolucency. Following the first year of function, there could be $\leq$ 0.2mm crestal bone remodeling annually (Albrektsson et al 1986), and $\leq$ 2.0 mm total crestal bone remodeling by the end of the fifth year was considered acceptable (Wennstrom & Palmer 1999).

Statistical Analysis:

Recorded data were used for calculations of mean values and standard deviations (SD). Cumulative Success Rates (CSR) were evaluated using life table analysis (Colton 1974). Significant differences in marginal bone level changes between three groups were assessed by t-tests, employing a critical p-value of 0.0167 to account for multiple comparisons.

3.2 Horizontal Augmentation Utilizing a New Synthetic Membrane (HA/1).

This case series reported on patients who were consecutively treated in the posterior mandible or maxilla with horizontal augmentation using GBR and particulated autografts from January 2003 through May 2006. All patients required augmentation of a “knife-edge” ridge for subsequent implant placement, including some patients (17 out of

22 maxillary cases) who also required a sinus floor elevation. All patients were treated in a private practice (Budapest, Hungary), and all surgical procedures were performed by the same practitioner (I.U.) with over 15 years of experience in oral surgery and implant therapies. The prosthetic treatments were performed and restored by the author (I.U.) and other private practitioners.

Patients in good physical health and the ability to maintain good oral hygiene were treated with the new resorbable membrane and bone graft. All patients were fully informed about the whole treatment prior to the first surgical procedure and gave written consent for the procedure. Patients were not eligible for this treatment if they were current smokers, engaged in excessive alcohol consumption, or had uncontrolled systemic conditions or uncontrolled periodontal disease.

All patients were treated with horizontal ridge augmentation using a recently developed synthetic barrier membrane composed of a microporous structure of synthetic bioabsorbable glycolide and trimethylene carbonate copolymer fiber (GORE RESOLUT® ADAPT® LT Regenerative Membrane, W.L. Gore & Associates, Inc., Flagstaff, AZ). This membrane was developed with a new chemical composition and ratio of the components with the aim of a longer resorption time of 4 to 6 months. Either autogenous bone or a combination of autogenous bone and anorganic bovine bone-derived mineral (ABBM, Bio-Oss®, Geistlich Pharma AG, Wolhusen, Switzerland). The first 7 patients were treated with autogenous bone alone to confirm the technique and use of the new membrane. Subsequent patients were treated with a combination of autogenous bone and ABBM to confirm the acceptability of a new osteoconductive material in the procedure and to limit the amount of harvested autogenous bone required for the procedure.

Patients were pre-medicated with amoxicillin 2 g one hour before surgery and 500 mg penicillin three times a day for one week following the surgery. In the event of a penicillin allergy, clindamycin 600 mg was used for premedication and 300 mg four times a day for one week following surgery. Oral sedation, usually Triazolam 0.50 mg (Halcion), was also frequently administered one hour prior surgery. Patients were instructed to rinse with 0.2% chlorhexidine solution (e.g., Corsodyl) for one minute to disinfect the surgical site and a sterile surgical drape was applied to minimize the

potential contamination from extraoral sources. A local anesthetic (Septanest with adrenaline 1/100,000) was applied.

The flap design was chosen to ensure primary tension-free closure after the bone grafting procedure despite the increased dimension of the ridge. A remote flap was performed including crestal and vertical releasing incisions. A full thickness, mid-crestal incision into the keratinized gingiva was performed with a surgical scalpel. The two divergent vertical incisions were placed at least one tooth away from the surgical site. In edentulous areas, the vertical incisions were placed at least 5 mm away from the augmentation site. After primary incisions, periosteal elevators were used to reflect a full thickness flap beyond the mucogingival junction and at least 5 mm beyond the bone defect. In the posterior mandible, the lingual flap was elevated beyond the linea milohyoidea and anatomical locations, like the mental and the infra-orbital nerves, were protected.

Grafting: After flap elevation and evaluation of the defect size, autogenous bone was harvested from the retromolar regions using a trephine burr. For posterior mandibular sites, the bone harvest was performed on the same side and the harvest site preparation was included in the flap design. For maxillary sites, an additional flap was created in the posterior mandible for bone harvesting.

The harvested graft was particulated in a bone mill (R. Quétin Bone-Mill, Roswitha Quétin Dental Products, Leimen, Germany) and then either applied alone or after preparing a 1:1 mixture with ABBM (the combination is referred to as “composite bone graft”). The bone of the exposed augmentation site was cleaned of all soft tissue remnants prior to grafting. Ridge measurements were taken and are described in a section below. The recipient bone bed was prepared with multiple decorticalization holes using a small round burr.

The new synthetic membrane was trimmed to the volume of the graft, and care was taken to avoid contact with the edges of the adjacent teeth. The membrane was fixed to at least at two points on the lingual/palatal sides with titanium pins. The autogenous particulated bone graft or composite bone graft was placed into the defect, and the membrane was folded over and fixed in place with additional titanium pins on the vestibular side.

Additional grafting: For maxillary cases with a sinus proximity (17 of the 21 maxillary cases), additional sinus floor augmentation was performed. No other combination grafting procedures were performed.

Soft tissue management: Once the membrane was completely secured, the flap was mobilized to permit tension free, primary closure. A periosteal releasing incision connecting the two vertical incisions was performed to achieve elasticity of the flap. The flap was than sutured in two layers: first horizontal mattress sutures (GORE-TEX® CV-5 Suture, W.L. Gore & Associates, Inc., Flagstaff, AZ) were placed 4 mm from the incision line; then, single interrupted sutures with the same ePTFE suture were placed to close the edges of the flap, leaving at least a 4 mm thick connective tissue layer between the membrane and the oral epithelium. This intimate connective tissue-to-connective tissue contact provides a barrier preventing exposure of the membrane. Vertical incisions were closed with single interrupting sutures.

The single interrupted sutures were removed between 10 to 14 days post surgery, and mattress sutures were removed after two to three weeks.

Measurements of the alveolar ridge width were taken intra-surgically, at the original surgery and then after the healing phase before preparation of the implant bed. The same calliper was used to take all measurements 2 mm apically from the top of the crest.

Complications in bone graft healing, such as membrane exposure, subsequent infection, and/or morbidity associated with the harvest site, were recorded,

Periapical radiographs were taken at the abutment connection and then every 12 months thereafter with a long cone parallelling technique.

Functionally loaded implants were monitored to evaluate the following: Absence of pain, foreign body sensation, dyesthesia; Radiological contact between the host bone and the implant surface.

Figures 2 and **3** present the surgical methods utilized in this study.

Figure 2: **HA/1 Study**: Representative case of autogenous bone only as grafting material. (a) Occlusal view of posterior maxillary area presents thin bone crest. (b) Buccal view of the defected area presents elevated maxillary sinus and the recipient bone bed is prepared with multiple decorticalization holes. (c) Autogenous particulated bone is in place. (d) Membrane is fixated with titanium pins. (e, f) After 6 months of uneventful healing, occlusal view of the augmented bone crest. Two implants are in position. (g) Final prosthetic reconstruction. (h) Peri-apical radiograph after 5 years of function.

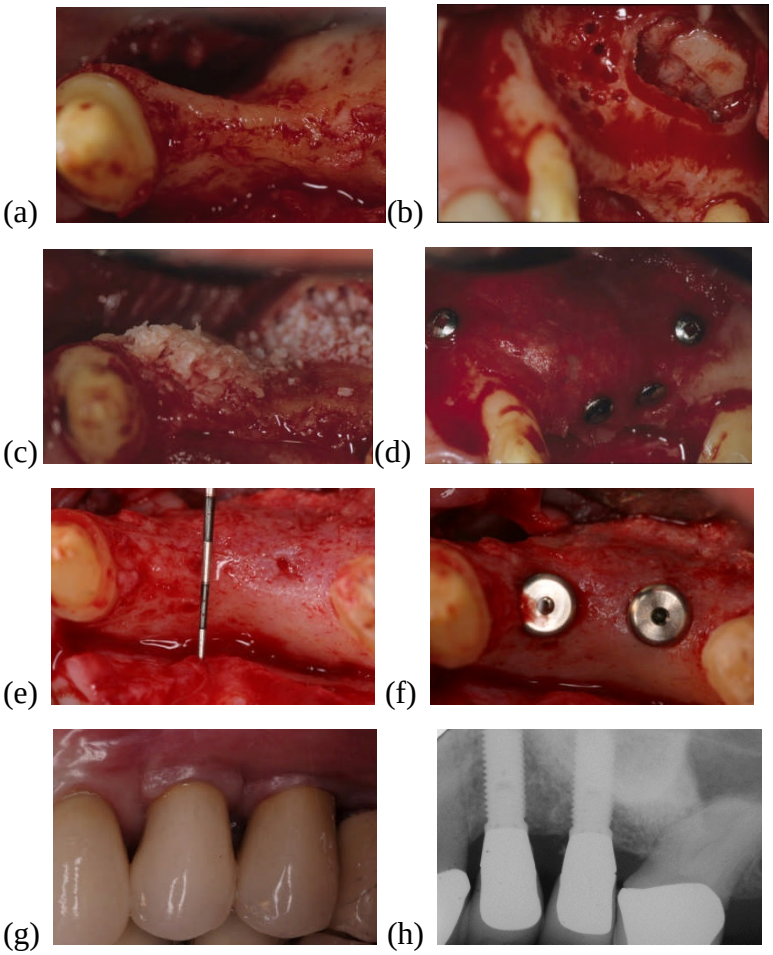
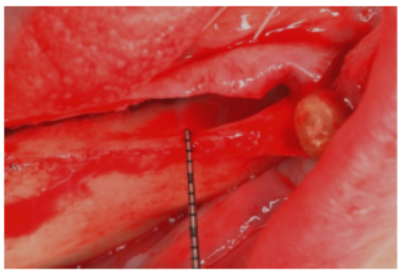
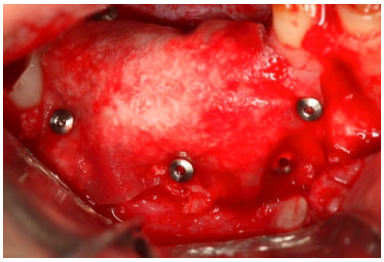
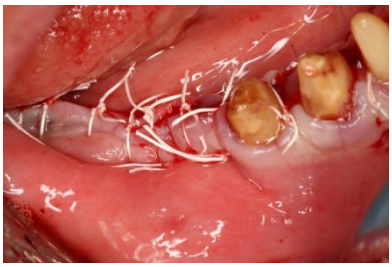
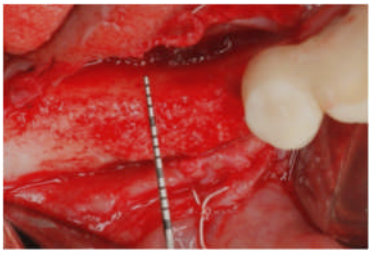
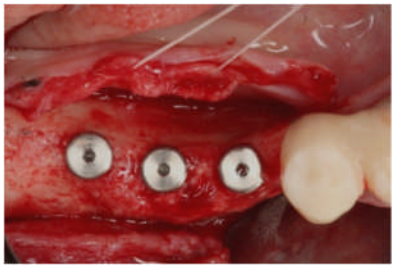
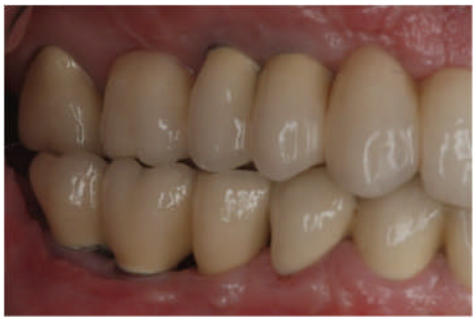


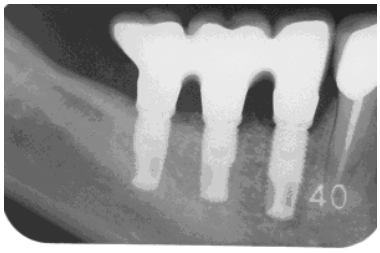
Figure 3: HA/1 Study: Representative case of 1:1 mixture of autogenous particulated bone and ABBM as grafting material: Posterior mandibular site. (a) Occlusal view of the site showing the knife edge ridge. (b) Buccal view after application of a mixture of autogenous particulated bone and ABBM granules, the synthetic resorbable membrane is secured over the graft with titanium pins. (c) Sutured defect ensuring primary tension free wound closure. (d) Re-entry surgery after 8 months revealing sufficient bone width to

place dental implants. (e) Implant placed into the augmented ridge. (f) Final prosthetic reconstruction. (g) Radiographs after 12 months of loading

(a)  (b) 

(c)  (d) 

(e)  (f) 

(g) 

At the time of implant placement, cylindrical biopsies were obtained from selected healed and augmented surgical sites using a trephine burr with an inner diameter of 2.0 mm.

Specimens were fixated in 4 percent formaldehyde. Before processing they were rinsed in water and dehydrated in alcohol (70%, 80%, 90%, 100%) for 3 days in each concentration and then defatted for 1 day in Xylol (Merck, Darmstadt, Germany). Specimens were transferred for 2 weeks in a mixture of methyl methacrylate (MMA,

Methylmetacrylat, Merck, Darmstadt, Germany) and 15% Dibuthylphthalat (Fluka, Steinheim, Germany) and then placed for one day in a mixture of MMA, 15% Dibuthylphthalat, and 1.5% dried Benzolperoxid (Merck, Darmstadt, Germany). Infiltration took place in an airproof sealed glass envelope for 2 weeks in a polymerization mixture of MMA (Methylmetacrylat, Merck, Darmstadt, Germany), 15% Dibuthylphthalat and 3% dried Benzoyl peroxide at room temperature. Sections were then ground to a thickness of 80 µm on a rotating grinding plate (Stuers, Ballerup, Denmark).

Optical microscopy specimens were stained according to the procedure described by Richardson et al (1960). Azur II (Merck, Darmstadt, Germany) was used for the exposition of the soft tissue and Pararosalin (Sigma-Aldrich, Deisenhofen, Germany) for the differentiation of native and new bone. Imaging was performed with a microscope (Carl Zeiss, Göttingen, Germany) and a digital camera (CC-12, Soft Imaging System, Münster, Germany). Images were optimized and evaluated with the program Analysis (Soft Imaging System, Münster, Germany).

Statistical Analysis:

All data were analyzed by descriptive methods, and means, standard deviations, medians, and interquartile ranges were calculated using SAS statistical software (version 9.1.3, Cary, North Carolina). Implant survival was estimated using life table analysis.

3.2 Horizontal Augmentation Utilizing a Native, Bilayer Collagen Membrane (HA/2).

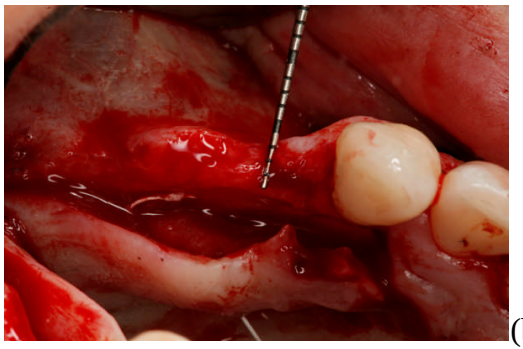
This case series reports on patients who were consecutively treated in the posterior mandible or maxilla with horizontal augmentation using GBR and particulated autografts from March 2007 through February 2010. All patients required augmentation of a “knife-edge” ridge for subsequent implant placement (Cawood-Howell class IV), including some patients who also required a sinus floor elevation. All patients were treated in a private practice (Budapest, Hungary), and all surgical procedures were performed by the same practitioner (I.U.) with over 15 years of experience in oral surgery and implant therapies. The prosthetic treatments were performed and restored by the author (I.U.) and other private practitioners.

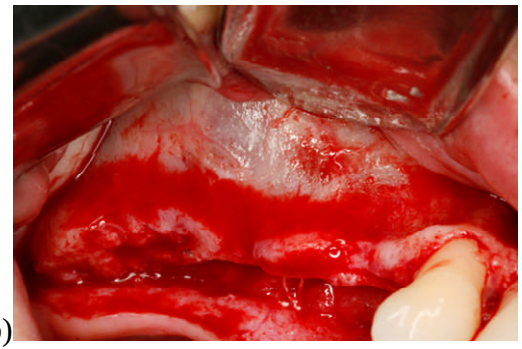
Patients in good physical health and the ability to maintain good oral hygiene were treated with the new resorbable membrane and bone graft. All patients were fully informed about the whole treatment prior to the first surgical procedure and gave written consent for the procedure. Patients were not eligible for this treatment if they were current smokers, engaged in excessive alcohol consumption, or had uncontrolled systemic conditions or uncontrolled periodontal disease.

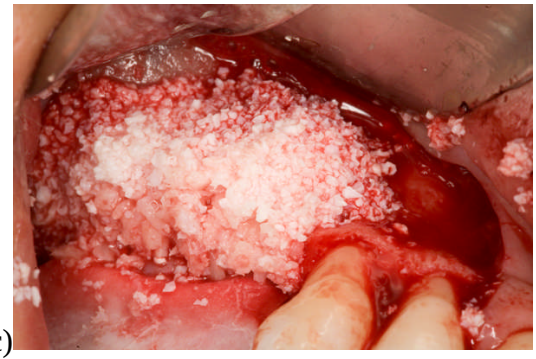
All patients were treated with horizontal ridge augmentation using a bilayer resorbable membrane derived from native collagen (Bio-Gide® Resorbable Bilayer Membrane, Geistlich Pharma AG, Wolhusen, Switzerland) and a combination of autogenous bone and anorganic bovine bone-derived mineral (ABBM, Bio-Oss®, Geistlich Pharma AG, Wolhusen, Switzerland). See **Figures 4** and **5** (below) for a graphic presentation of the surgical procedure.

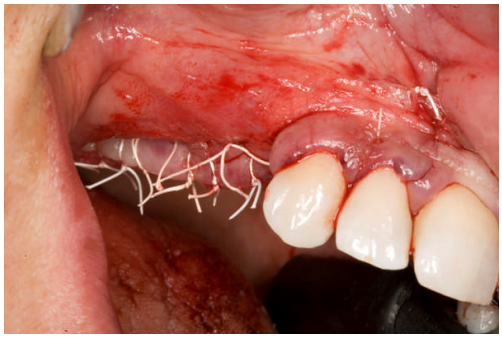
Patients were pre-medicated with amoxicillin 2 g one hour before surgery and 500 mg penicillin three times a day for one week following the surgery. In the event of a penicillin allergy, clindamycin 600 mg was used for premedication and 300 mg four times a day for one week following surgery. Oral sedation, usually Triazolam 0.50 mg (Halcion), was also frequently administered one hour prior to surgery. Patients were instructed to rinse with 0.2% chlorhexidine solution (e.g., Corsodyl) for one minute to disinfect the surgical site and a sterile surgical drape was applied to minimize the potential contamination from extraoral sources. A local anesthetic (articaine hydrochloride 4% with epinephrine bitartrate 1/100,000) was applied.

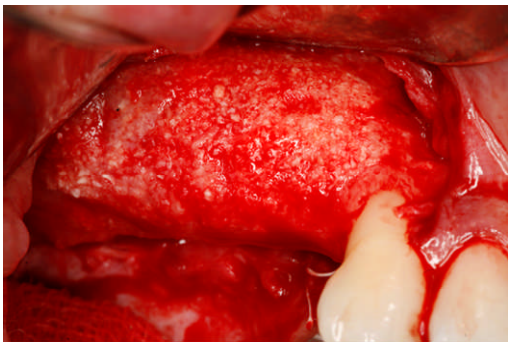
Figure 4: **HA/2 Study**: Treatment scheme of a representative case of horizontal augmentation in the posterior maxilla. (a, b) Occlusal and buccal views of posterior maxillary area presents thin bone crest. (c) The collagen membrane is fixated on the palatal area. Autogenous particulated bone mixed with ABBM in place. (d) Tension free flap closure with double-layer suturing. (e,f) Buccal and occlusal views of regenerated bone crest. (g) Periapical radiograph demonstrates stable crestal bone level after loading.

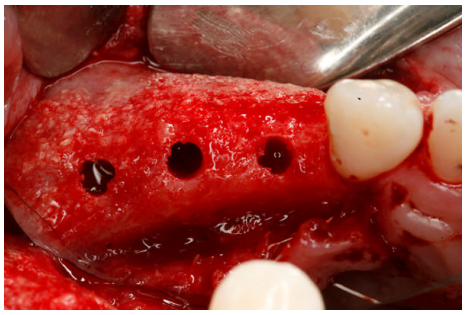
(a) 

(b) 

(c) 

(d) 

(e) 

(f) 

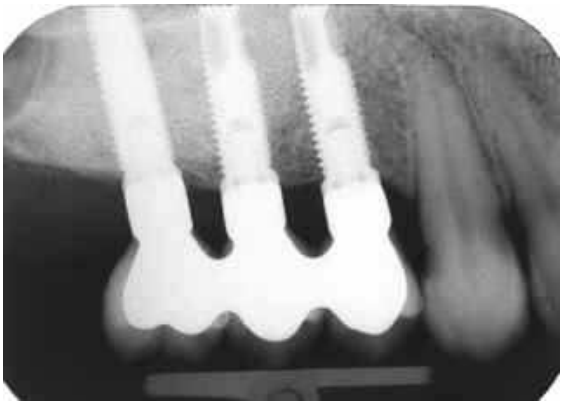
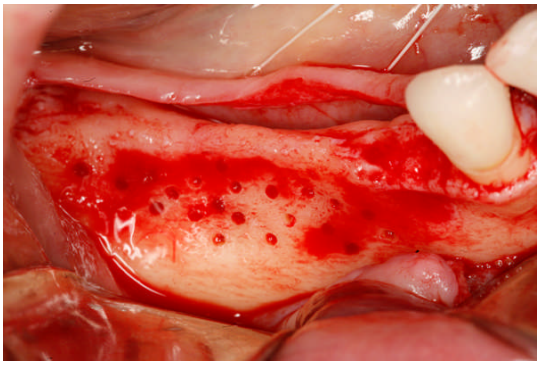
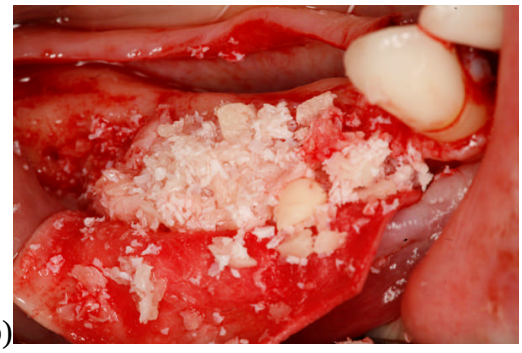
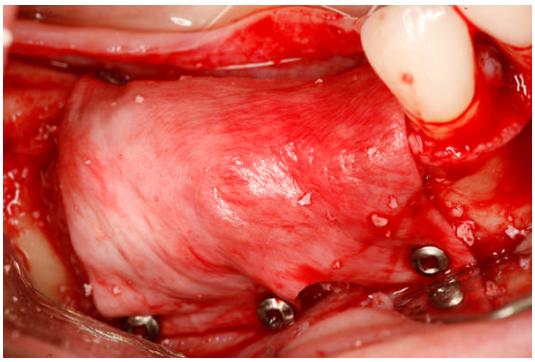
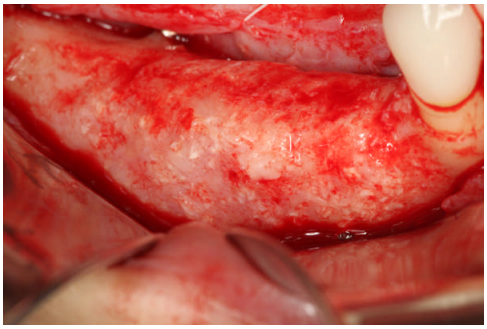
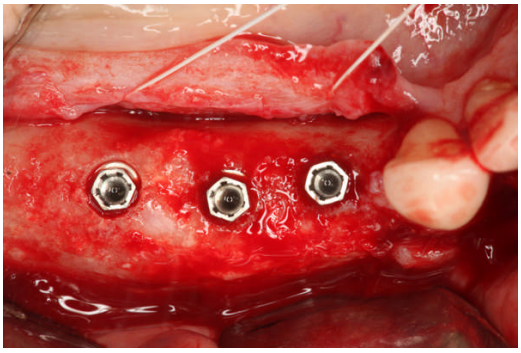
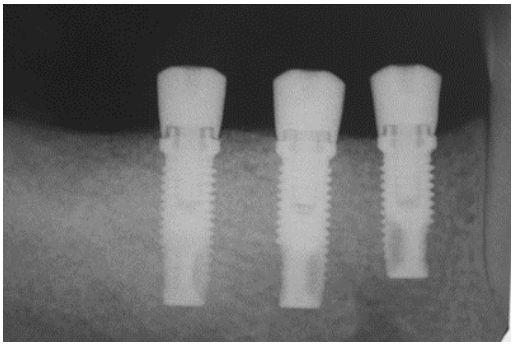
(g) 

Figure 5: **HA/2 Study**: Treatment scheme of case with thin posterior mandibular ridge. (a) Buccal view of thin posterior mandibular ridge. Recipient bone bed is prepared with multiple decortication holes. (b) Buccal view after application of a mixture of autogenous particulated bone and ABBM granules. Membrane is fixated with titanium pins. (c) The resorbable collagen membrane is secured over the graft with titanium pins. (d,e) Buccal and occlusal views of the regenerated bone. Note the good incorporation of the ABBM in the newly formed ridge. (f) Periapical radiograph at the uncovery of the implants.

(a)  (b) 

(c)  (d) 

(e)  (f) 

The flap design was chosen to ensure primary tension-free closure after the bone grafting procedure despite the increased dimension of the ridge. A remote flap was performed including crestal and vertical releasing incisions. A full thickness, mid-crestal incision into the keratinized gingiva was performed with a surgical scalpel. The two divergent vertical incisions were placed at least one tooth away from the surgical site. In edentulous areas, the vertical incisions were placed at least 5 mm away from the augmentation site. After primary incisions, periosteal elevators were used to reflect a full thickness flap beyond the mucogingival junction and at least 5 mm beyond the bone defect. In the posterior mandible, the lingual flap was elevated beyond the linea milohyoidea and anatomical locations, like the mental and the infra-orbital nerves, were protected.

After flap elevation and evaluation of the defect size, autogenous bone was harvested from the retromolar regions using a trephine burr. For posterior mandibular sites, the bone harvest was performed on the same side and the harvest site preparation was included in the flap design. For maxillary sites, an additional flap was created in the posterior mandible for bone harvesting.

The harvested graft was particulated in a bone mill (R. Quétin Bone-Mill, Roswitha Quétin Dental Products, Leimen, Germany) and then either applied alone or after preparing a 1:1 mixture with ABBM (the combination is referred to as “composite bone graft”). The bone of the exposed augmentation site was cleaned of all soft tissue remnants prior to grafting. Ridge measurements were taken and are described in a section below. The recipient bone bed was prepared with multiple decorticalization holes using a small round burr.

The collagen membrane was trimmed to the volume of the graft, and care was taken to avoid contact with the edges of the adjacent teeth. The membrane was fixed to at least at two points on the lingual/palatal sides with titanium pins. The composite bone graft was placed into the defect, and the membrane was folded over and fixed in place with additional titanium pins on the vestibular side.

For maxillary cases with a sinus proximity, additional sinus floor augmentation was performed utilizing a surgical technique that has been described previously (35). No other combination grafting procedures were performed.

Once the membrane was completely secured, the flap was mobilized to permit tension free, primary closure. A periosteal releasing incision connecting the two vertical incisions was performed to achieve elasticity of the flap. The flap was than sutured in two layers: first horizontal mattress sutures (GORE-TEX® CV-5 Suture, W.L. Gore & Associates, Inc., Flagstaff, AZ) were placed 4 mm from the incision line; then, single interrupted sutures with the same ePTFE suture were placed to close the edges of the flap, leaving at least a 4 mm thick connective tissue layer between the membrane and the oral epithelium. This intimate connective tissue-to-connective tissue contact provides a barrier preventing exposure of the membrane. Vertical incisions were closed with single interrupting sutures.

The single interrupted sutures were removed between 10 to 14 days post surgery, and mattress sutures were removed after two to three weeks.

Measurements of the alveolar ridge width were taken intra-surgically, at the original surgery and then after the healing phase before preparation of the implant bed. The same calliper was used to take all measurements 2 mm apically from the top of the crest. Periapical radiographs were taken at the abutment connection and then every 12 months thereafter with a long cone parallelling technique.

Complications in bone graft healing, such as membrane exposure, subsequent infection, and/or morbidity associated with the harvest site, were recorded. Functionally loaded implants were monitored to evaluate the following: Absence of pain, foreign body sensation, dyesthesia; Radiological contact between the host bone and the implant surface.

At the time of implant placement, cylindrical biopsies were obtained from selected healed and augmented surgical sites using a trephine burr with an inner diameter of 2.0 mm.

Specimens were fixated in 4 percent formaldehyde. Before processing they were rinsed in water and dehydrated in alcohol (70%, 80%, 90%, 100%) for 3 days in each concentration and then defatted for 1 day in Xylene (Merck, Darmstadt, Germany). Specimens were then infiltrated, embedded and polymerized in Technovit 9100 (Heraeus Kulzer, Wehrheim, Germany) according to the manufacturer's instructions. After polymerization, samples were cut in 300 µm sections using a low-speed rotary diamond

saw Microslice ™ (Metals Research, Cambrige, UK). The sections were mounted onto opac acrylic-slides (Maertin, Freiburg, Germany) and grounded to a final thickness of approximately 60 µm on a rotating grinding plate (Stuers, Ballerup, Denmark).
Optical microscopy specimens were stained according to the procedure described by Richardson et al (1960). Azur II (Merck, Darmstadt, Germany) was used for the exposition of the soft tissue and Pararosalin (Sigma-Aldrich, Deisenhofen, Germany) for the differentiation of native and new bone.

Imaging was performed with a microscope (Carl Zeiss, Göttingen, Germany) and a digital camera (AxioCam HRc, Carl Zeiss, Göttingen, Germany). Images were optimized and evaluated with the program Analysis (Soft Imaging System, Münster, Germany).

All data were analyzed by descriptive methods, and means, standard deviations, medians, ranges, and interquartile ranges were calculated using SAS statistical software (version 9.2, Cary, North Carolina). Implant survival was estimated using life table analysis.

4. RESULTS

4.1 Vertical Augmentation

This retrospective study sought to encompass the scope of clinical practice where vertical bone augmentation is required for the purpose of implant placement: 82 implants were placed in 35 patients with 36 three-dimensional ridge defects ranging from 2 mm to 12 mm. Thirty-three patients (94.3%) were partially edentulous, and 2 (5.7%) were completely edentulous. Fourteen (40%) patients were men and 21 (60%) were women, and the mean age was 44.9 years (range, 19 to 72 years). A staged approach that allowed the graft to heal uneventfully before implant placement was used in most cases.

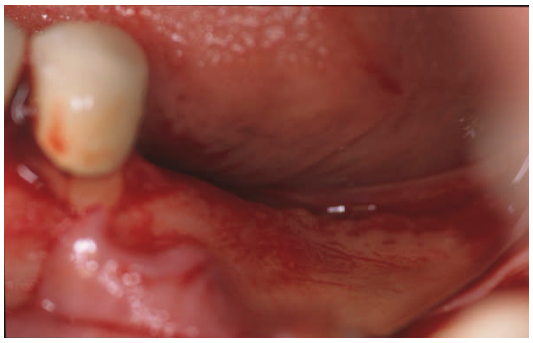
Table 1 provides treatment approaches of the patient sample. The patients treated with the simultaneous approach had less severe vertical defects, with a maximum defect size of 4 mm. With one exception, intraoral bone grafts were used; the graft was taken from the retromolar area in 21 cases (60%) and the chin in 13 cases (37.14%) (18). In 1 patient (2.8%), bone was harvested from the hip.

Table 1: Vertical Augmentation Study: Distribution and Surgical Approach in the 3 Treatment Groups

Distribution and Surgical Approach					
Treatment Groups	**# Patients**	**# Defects**	**# Implants**	**Surgical Approach (no. and %)**	
				Simultaneous	**Staged**
A	12	12	12	4 (30.8)	9 (69.2)
B	16	16	42	2 (12.5)	14 (87.5)
C	7	8	28	0 (0.0)	8 (100.0)
Total	35	36	82	6	31

The implants used in this study were all commercially available from the same manufacturer at the time of the respective surgery. Thirteen acid-etched, SteriOss (Nobel Biocare, Yorba Linda, CA), 66 anodized-surface, Branemark TiUnite (Nobel Biocare), and 3 anodized-surface, Replace TiUnite (Nobel Biocare) implants were placed in the 35 patients . All patients presented with vertical bone defects (see **Figure 6**) and were divided into 3 treatment groups: Group A (12 patients) had single missing teeth, group B (16 patients) had multiple missing teeth, and group C (7 patients/8 defects) had vertical defects in the posterior maxilla only and were treated simultaneously with sinus and vertical augmentation (see **Figure 7**).

Figure 6: Vertical Augmentation Study: Representative case with multiple missing teeth (treatment group B). **(a)** Atrophic posterior mandibular area. **(b)** Particulated chin bone graft is placed on the ridge. The cortical bone was perforated, and the membrane was secured on the lingual side before applying bone graft. **(c)** the membrane is secured over the graft with titanium pins. **(d)** Three implants are in place in the newly formed posterior mandibular ridge. Note the well-integrated bone graft. **(e)** Periapical radiograph at abutment connection. **(f)** Periapical radiograph at 3-year follow-up with implant in function. **(g)** Clinical view demonstrates healthy peri-implant mucosa.



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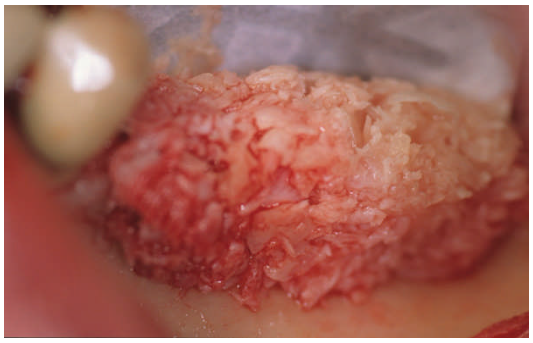

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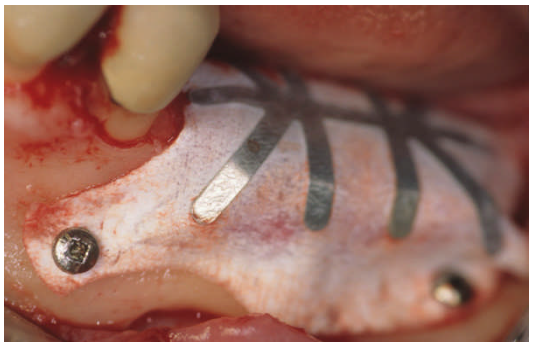

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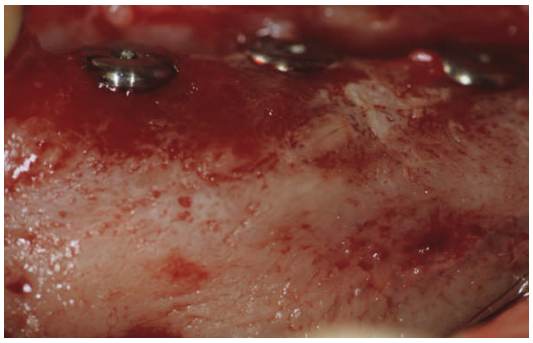

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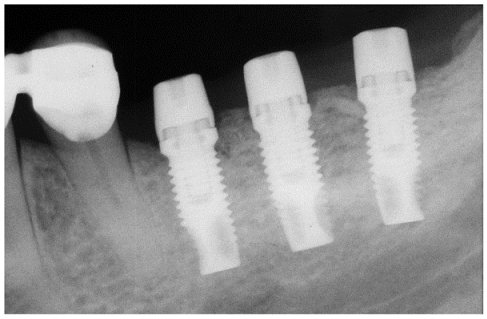

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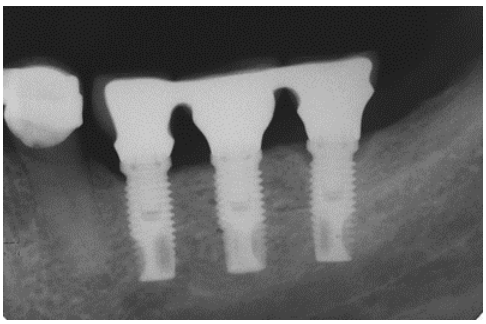

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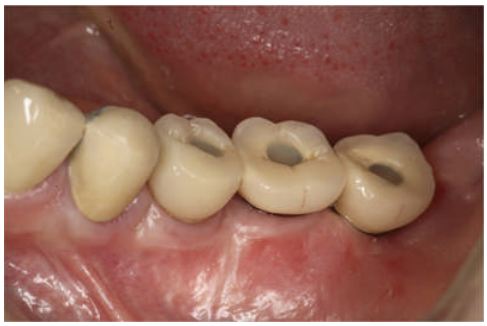
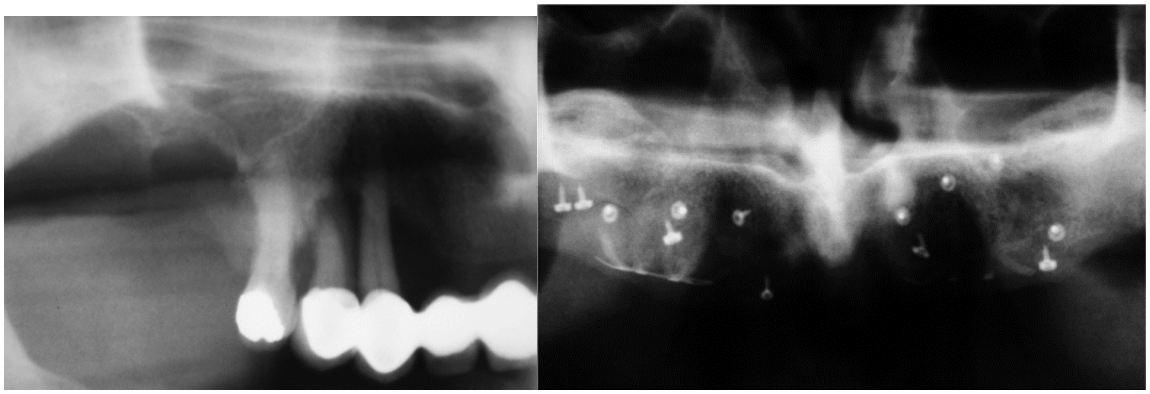
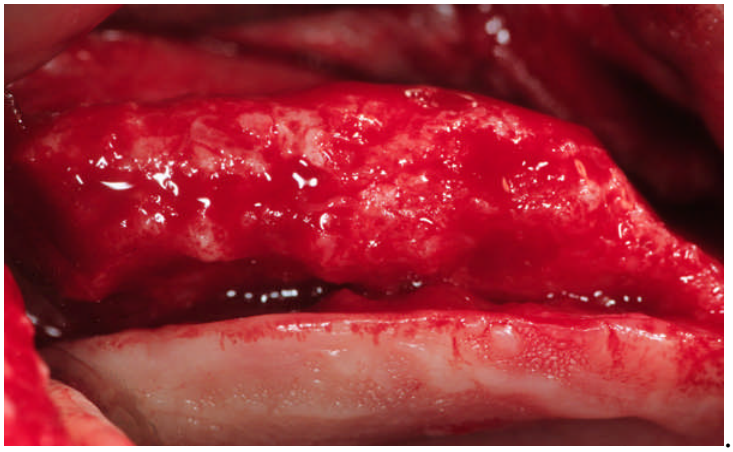


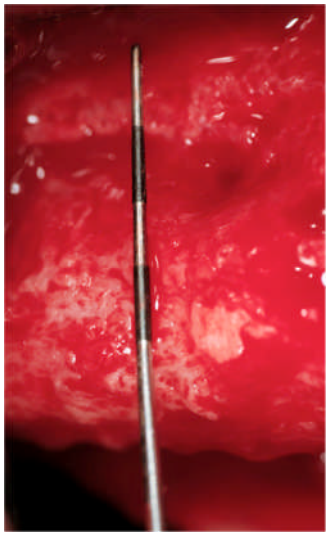
(6g)

Figure 7. Vertical Augmentation Study: Representative case requiring posterior maxillary bone regeneration (treatment group C). **(a)**. Vertical defect in the posterior maxilla. **(b)** Panoramic radiograph shows defects after treatment with sinus augmentation and vertical GBR. **(c,d)** After 9 months of uneventful healing, complete vertical bone gain is demonstrated.**(e)** Radiographs of implants at abutment connection. **(f)** Radiographs of implants after 4 years of loading. **(g**) Definitive implant-supported complete fixed prosthesis.

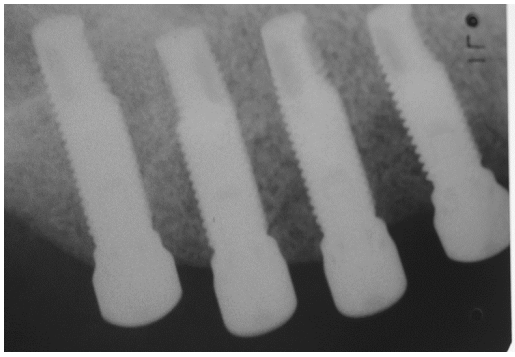


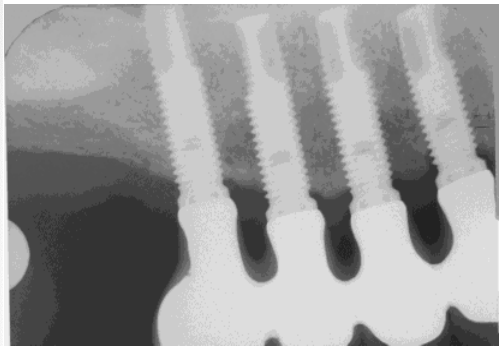
(7a) **(7b)**



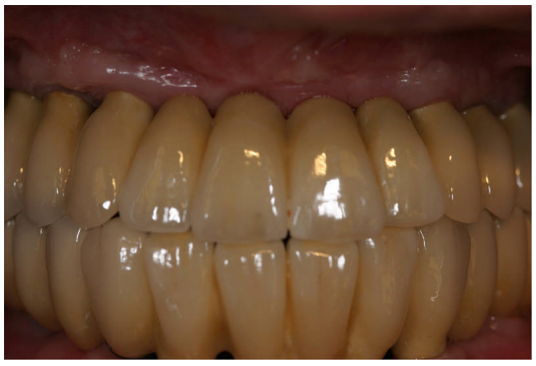


(7c) **(7d)**





(7e) **(7f)**



(7g)

Bone regeneration was evaluated clinically at the time of membrane removal. In general, all treated defect sites exhibited excellent bone formation, with an overall average of 5.5 mm (SD 2.29) of vertical augmentation (**Table 2**). None of the patients showed less bone regeneration than the space created by the membrane (**Figures 6** and **7**), with one exception. This group B patient developed a fistula on top of the membrane area 2 weeks after bone grafting. The surgical site was reopened and the membrane was removed carefully so that the graft was not disturbed. There was no visible infection of the graft. After gentle irrigation with saline, a resorbable collagen membrane (Bio-Gide) was placed over the graft, and the flap was closed and permitted to heal for an additional 7 months; at this point, implants were placed successfully. At the time of implant placement, 5 mm of the original vertical deficiency were still present, along with minimal vertical gain (2 mm).

Table 2: Vertical Augmentation Study: Overall Augmentation Results

Treatment Group	Mean (mm)	SD (mm)	Range (mm)
A	4.7	1.67	3.0 – 9.0
B	5.1	2.13	2.0 – 8.0
C	7.4	2.56	4.0 – 12.0
Overall	5.5	2.29	2.0 – 12.0

Regardless of which site was used for bone harvesting, there appeared to be no difference in the results in terms of bone quality and quantity at implant placement or during the follow-up period when implants were assessed clinically and radiographically. Throughout the period of the study, no early or late resorption of the newly formed bone crest was noted. The use of collagen membranes at the time of implant placement in group C sites was strictly empirical, and it was not possible to evaluate whether they were of any benefit in maintaining bone dimensions.

All implants were placed according to their predetermined optimal prosthetic positions. At the time of abutment connection, all implants were stable and were fully embedded within bone.

After the last exam for the cohort in this retrospective study, all patients had comfortable prostheses in place; all implants were still in function; and no patients reported any complaints of foreign body sensation, pain or dysesthesia. Intraoral examinations demonstrated healthy peri-implant mucosa without suppuration, swelling or redness at any implant sites. The mean probing depth was 3.03 mm (SD 0.61).

Two patients dropped out of the study after successful treatment. One patient in group A was lost to follow-up after the abutment connection, refused a radiographic exam, and consequently could not be evaluated at the 1-year evaluation. The other patient was in group B and became lost to follow-up after the 1-year evaluation.

In the 81 consecutively treated implants that were evaluated clinically and radiographically after the abutment connection, the period of functional loading in this study ranged from 1 to 6 years (mean: 40.3 months), and the mean radiographic follow-up was 34.2 months. At the 1-year examination, the mean crestal bone remodeling value for the 81 implants was 1.01mm (SD 0.57), and in most cases, the first bone-implant contact was located near the first implant thread. The mean marginal bone remodeling for the 81 implants throughout the study is provided in **Table 3**. There were no statistically significant differences between the 3 groups in mean marginal bone remodeling, and the crestal bone remained stable throughout the follow-up period.

Table 3 Mean Marginal Bone Loss Around Implants at Different Time Periods (in mm)

Time	Bone Loss							
	Group A		Group B		Group C		Overall	
	Mean (SD)	n†	Mean (SD)	n†	Mean (SD)	n†	Mean (SD)	n†
Abutment Connection	0.47 (0.61)	11	0.39 (0.47)	42	0.36 (0.58)	28	0.39 (0.53)	81
1Y	0.69 (0.55)	11	1.03 (0.53)	42	1.12 (0.58)	28	1.01 (0.57)	81
2Y	0.03 (0.17)	10	0.02 (0.32)	32	-0.15 (0.29)	25	-0.05 (0.28)	67
3Y	0.11 (0.22)	6	0.02 (0.2)	24	0.11 (0.1)	19	0.06 (0.18)	49
4Y	-0.08 (0.07)	3	-0.02 (0.14)	15	0.0 (0.14)	17	-0.02 (0.13)	35

5Y	-0.28	1	0.03 (0.1)	6	0.03 (0.12)	9	0.01 (0.13)	16
6Y			0.05 (0.0)	3	0.0 (0.12)	4	0.02 (0.1)	7

† = Number of patients who attended the respective follow up visit as a part of this retrospective study.

All of the examined 81 implants survived (**Tables 4** and **5**). Only 3 implants in group B showed increased bone remodeling (slightly more than 2 mm), and these were not considered clinically successful.

Table 4: Vertical Augmentation Study: Life Table Analysis of Implants: Overall Cumulative Success Rates

Time	Implants			Cumulative Success Rate*	Standard Error
	# Surveyed	# Failures	# Censored		
Placement to Loading	82	0	0	100.0%	0.0%
Loading to 1 Year	82	0	1	100.0%	0.0%
1 Year to 2 Years	81	1**	13	98.7%	1.3%
2 Years to 3 Years	67	1†	17	97.0%	2.1%
3 Years to 4 Years	49	1††	13	94.7%	3.1%
4 Years to 5 Years	35	0	19	94.7%	3.7%
5 Years to 6 Years	16	0	9	94.7%	5.5%
6 Years to 7 Years	7	0	7	94.7%	8.2%

* Based on implants that were evaluated in the respective follow-up period.
** Patient in Group B who became lost to follow-up after the 1-year evaluation. One of the patient's 2 treated defects exhibited 2.5 mm bone remodeling.
† There was 2.2 mm of bone remodeling in 1 implant in Group B .
†† One implant in group B had 1.62 mm bone remodeling at the 1-year evaluation, and the amount of bone remodeling had increased to 2.38 mm at the 3-year evaluation.

Table 5: Vertical Augmentation Study: Life Table Analysis of Implants

Time	Implants			Cumulative Success Rate*	Standard Error
	# of Implants	# of Failures	# Censored		
Placement to Loading					
Group A	12	0	0	100.0%	0.0%
Group B	42	0	0	100.0%	0.0%
Group C	28	0	0	100.0%	0.0%
Loading to 1 Year					
Group A	12	0	1	100.0%	0.0%
Group B	42	0	0	100.0%	0.0%
Group C	28	0	0	100.0%	0.0%
1 Year to 2 Years					
Group A	11	0	1	100.0%	0.0%
Group B	42	1	9	97.3%	2.5%
Group C	28	0	3	100.0%	0.0%
2 Years to 3 Years					
Group A	10	0	4	100.0%	0.0%
Group B	32	1	7	93.9%	4.1%
Group C	25	0	6	100.0%	0.0%
3 Years to 4 Years					
Group A	6	0	3	100.0%	0.0%
Group B	24	1	8	89.2%	6.0%
Group C	19	0	2	100.0%	0.0%
4 Years to 5 Years					
Group A	3	0	2	100.0%	0.0%
Group B	15	0	9	89.2%	7.6%
Group C	17	0	8	100.0%	0.0%
5 Years to 6 Years					
Group A	1	0	1	100.0%	0.0%
Group B	6	0	3	89.2%	12.0%
Group C	9	0	5	100.0%	0.0%
6 Years to 7 Years					
Group A	0	0	0	N/A	N/A
Group B	3	0	3	89.2%	16.9%
Group C	4	0	4	100.0%	0.0%

* Based on implants that had been evaluated in the respective follow-up period.
N/A = Not applicable.

4.2 Horizontal Augmentation Utilizing a New Synthetic Membrane (HA/1).

This case series reported on patients presenting to a clinical practice and requiring horizontal bone augmentation for the purpose of implant placement. The indication for

horizontal ridge augmentation generally resulted from a lack of horizontal bone width in the posterior maxilla or mandible.

Twenty-two (22) patients with 25 surgical sites presented posterior knife-edge ridges with an insufficient width for implant placement (Cawood-Howell class IV). All patients presented with a horizontal ridge of 4 mm or less and needed horizontal ridge augmentation prior to dental implant placement (**Table 6**). For the maxillary cases, if an additional sinus proximity was present, a sinus floor augmentation was carried out simultaneously (17 out of 21 maxillary cases).

Table 6: Horizontal Augmentation Study (HA/1): Surgical Sites Treated with Horizontal Ridge Augmentation for Subsequent Implant Placement

Patient # (Surgical Site #)	Gender	Age (years)	Maxilla / Mandible	Graft Composition	Healing Time (months)		Histology
					Graft	Implant	
1 (1)	M	50	Maxilla	Autograft	6.5	6.8	yes
2 (2)	F	52	Maxilla	Autograft	6.3	6.0	--
3 (3)	F	57	Maxilla	Autograft	6.3	5.6	yes
4 (4)	F	52	Maxilla	Autograft	10.8	5.8	yes
5 (5, 6)	F	47	Maxilla	Autograft	6.4	6.0	--
			Maxilla	Autograft + ABBM	6.3	6.0	--
6 (7)	M	59	Maxilla	Autograft	6.3	5.4	--
7 (8)	F	30	Maxilla	Autograft	6.5	6.0	--
8 (9)	F	50	Maxilla	Autograft + ABBM	11.4	7.5	--
9 (10)	F	48	Maxilla	Autograft + ABBM	6.0	8.1	--
10 (11)	F	42	Maxilla	Autograft + ABBM	6.0	5.3	--
11 (12)	F	52	Maxilla	Autograft + ABBM	6.4	5.3	yes
12 (13)	F	60	Maxilla	Autograft + ABBM	6.6	6.7	yes
13 (14)	F	38	Maxilla	Autograft + ABBM	5.8	4.9	--
14 (15, 16)	F	63	Maxilla	Autograft + ABBM	10.0	11.7	yes
			Maxilla	Autograft + ABBM	10.0	11.7	--
15 (17)	F	42	Maxilla	Autograft + ABBM	13.1	10.4	--
16 (18)	F	58	Maxilla	Autograft +	10.2	6.0	--

Patient # (Surgical Site #)	Gender	Age (years)	Maxilla / Mandible	Graft Composition	Healing Time (months)		Histology
					Graft	Implant	
				ABBM			
17 (19)	F	51	Mandible	Autograft + ABBM	6.3	6.4	--
18 (20)	M	51	Maxilla	Autograft + ABBM	7.1	8.2	--
19 (21, 22)	M	47	Mandible	Autograft + ABBM	11.3	6.0	--
			Maxilla	Autograft + ABBM	10.0	7.5	--
20 (23)	F	50	Mandible	Autograft + ABBM	7.3	5.1	--
21 (24)	F	45	Mandible	Autograft + ABBM	8.0	7.0	--
22 (25)	M	54	Maxilla	Autograft + ABBM	12.0	6.0	--
N (Data Available)		**22**			**25**	**25**	**6**
Mean (SD)	**--**	**49.91 (7.60)**	**--**	**--**	**8.12 (2.32)**	**6.86 (1.89)**	**--**
Median	**--**	**50.50**	**--**	**--**	**6.60**	**6.00**	**--**
Interquartile Range		**(47.0, 54.0)**			**(6.3, 10.0)**	**(5.8, 7.5)**	**--**
Range		**(30, 63)**			**(5.8, 13.1)**	**(4.9, 11.7)**	**--**

SD = Standard Deviation
Autograft = Autogenous Bone
ABBM = Anorganic bovine-derived bone mineral

Fifty-eight (58) implants were placed in 22 patients with 25 knife-edge ridges (17 females and 5 males with a mean age of 50 years). Intraoperative measurements indicated an average residual bone width of 2.20 mm ± 1.00 mm (range 1–4 mm) (**Table 7**).

Table 7: Horizontal Augmentation Study (HA/1): Measurements of the Ridges Before and After Augmentation

Surgical Site (#)	Ridge Width (mm)			Implants Placed (#)	Follow-up (months)
	Baseline	Re-entry	Gain		
1	2	8	6	2	66
2	4	8	6	2	66

Surgical Site (#)	Ridge Width (mm)			Implants Placed (#)	Follow-up (months)
	Baseline	Re-entry	Gain		
3	1	8	7	3	64
4	4	8	4	2	59
5	2	8	6	2	62
6	2	7	5	1	34
7	3	9	6	3	62
8	2	6	4	1	59
9	3	9	6	1	46
10	2	6	4	1	50
11	4	10	6	1	50
12	3	9	6	3	49
13	3	8	5	3	48
14	3	7	4	3	47
15	1	9	8	4	40
16	1	5	4	4	40
17	1	7	6	1	37
18	2	8	6	2	37
19	2	8	6	3	40
20	1	8	7	3	37
21	3	7	4	2	32
22	2	5	3	2	32
23	1	10	9	3	34
24	1	8	7	3	30
25	2	6	4	3	26
N (Data Available)	**25**	**25**	**25**	**25**	**25**
Mean (SD)	**2.20 (1.00)**	**7.68 (1.35)**	**5.56 (1.45)**	**2.32 (0.95)**	**45.88 (12.43)**
Median	**2.00**	**8.00**	**6.00**	**2.00**	**46.00**
Interquartile Range	**(1.0, 3.0)**	**(7.0, 8.0)**	**(4.0, 6.0)**	**(2.0, 3.0)**	**(37.0, 59.0)**
Range	**(1, 4)**	**(5, 10)**	**(3, 9)**	**(1, 4)**	**(26, 66)**

SD = Standard Deviation

All ridges were of insufficient width to place dental implants, as generally at least 6 mm are required (Esposito et al 2006a). A comparison between the baseline ridge width for the maxilla (84.0% of the surgical sites) and the mandible (16.0 % of the surgical sites) showed a mean residual ridge of 2.29 mm for the maxilla and 1.75 mm for the mandible.

After horizontal augmentation and a mean graft healing period of 8.12 months ± 2.32 months (range 5.8 – 13.1 months) the mean ridge width was 7.68 mm ± 1.35 mm ,

giving an increase of 5.56 mm ± 1.45 mm in ridge width. After the graft healing period, a total of 58 implants with an anodized TiUnite® surface (Brånemark System®, Nobel Biocare, Göteberg, Sweden) were placed. See **Table 8**.

Of the 58 implants placed, 43 implants were placed in sites augmented with the combination of ABBM and autogenous bone (74.1%), and 15 implants were placed into sites augmented only with autogenous bone (25.9%) (**Table 7**). Implants were either 3.75 mm or 4.0 mm in diameter, and implant lengths ranged from 8.5 mm to 15 mm, with the majority of implants being 13 mm or 15 mm in length (**Table 8**).

Table 8: Horizontal Augmentation Study (HA/1): Sizes of Implants Placed

Implant Length (mm)	Location of Implant Placement				Total
	Maxilla		Mandible		
	Upper Right	Upper Left	Lower Right	Lower Left	
3.75 mm Diameter					
8.5	--	--	1	2	**3**
10	--	--	3	1	**4**
11.5	2	1	2	--	**5**
13	8	11	--	--	**19**
15	--	1	--	--	**1**
4.0 mm Diameter					
8.5	--	--	--	2	**2**
13	5	7	--	--	**12**
15	7	5	--	--	**12**
Total	**22**	**25**	**6**	**5**	**58**

The graft and implant healing periods were uneventful in all cases, and no complications, such as membrane exposure, infections, or harvest site morbidity, were observed. No residual pieces of the membrane were observed at the second stage surgery. Postoperative swelling of the donor sites was remarkable in most cases with a maximum swelling at 48 hours postoperatively. Swelling gradually subsided but was still visible at one week and disappeared completely after ten days. Postoperative discomfort was primarily associated with tension from the swelling, but pain was minimal. No major complications, such as haemorrhage, postoperative infection, mandibular fracture or neurosensory disturbances, occurred in any patients in this case series.

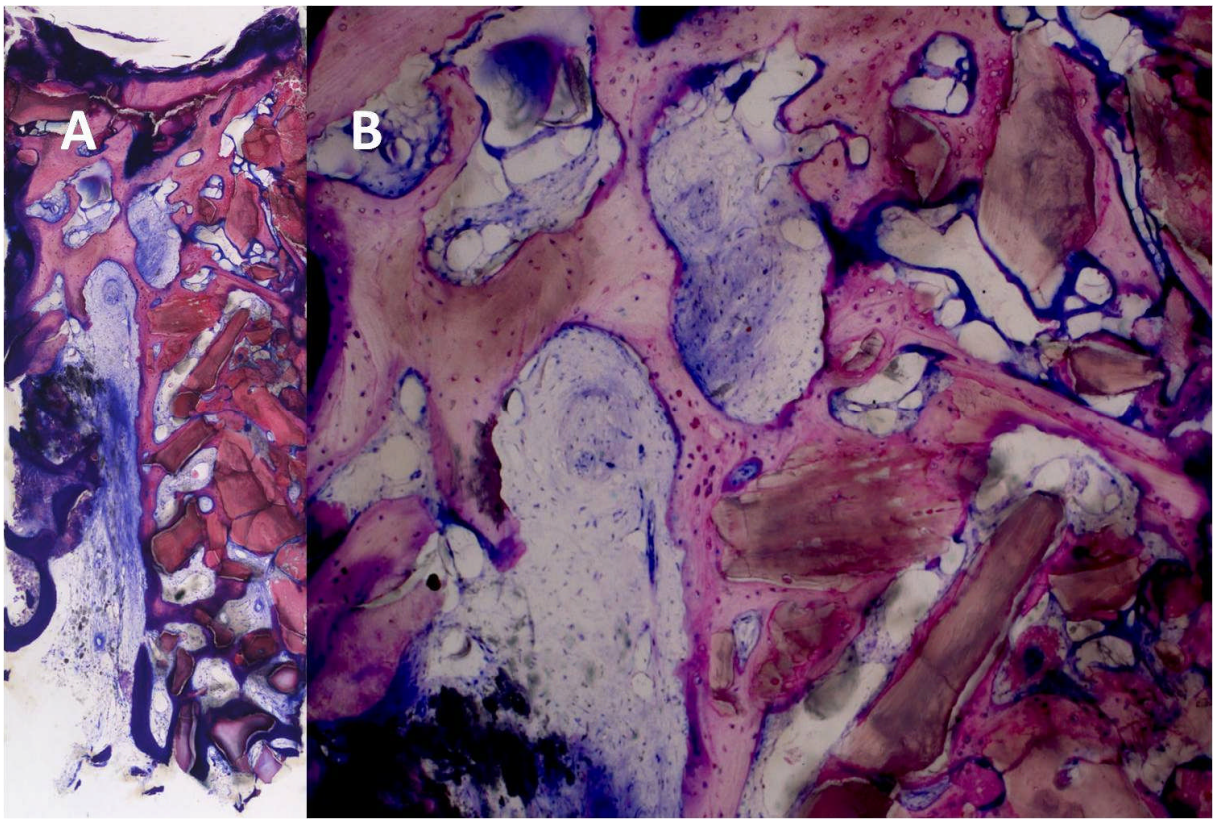
Overall the experimental membrane used in these augmentations showed no device-related side effects. Healing was similar for the mandibular and maxilliary cases as well as for the cases solely augmented with autograft or with a mixture of ABBM and autograft. Upon reopening of the surgical site at implant placement, the tissue beneath appeared healthy, with a healthy periosteal layer between the soft tissue and the bone, similar to results previously reported for non-resorbable and collagen membranes (Buser et al 1996; Hämmerle et al 2008).

After on average of 6.86 months implant healing time (SD 1.89 months, range 4.9 – 11.7 months), the healing abutments were placed in the 25 surgical sites. In three cases, primary implant stability was sufficient to place the healing abutments at implant placement. All implants appeared clinically stable upon reopening and were maintained for provisional and definitive prosthetic restoration.

All 58 implants have survived to date (100.0% at all time points; life table analysis) with an average follow-up of 45.88 months ± 12.43 months. There does not appear to be any difference in implant survival between implants placed in the mandible or the maxilla, or between sites augmented solely with autograft or with a combination of autogenous bone and ABBM.

In total, 6 biopsies were evaluated, three from surgical sites treated with autogenous bone only and three from surgical sites treated with a mixture of autogenous bone and ABBM. Representative histology is presented in **Figure 8**.

Figure 8: HA/1 Study: Histologic assessment of the regenerated area. Healing time 6.6. months; Maxilla; Surgical Site 13. (a) The local bone (knife-edge ridge) can be seen on the left side. The right side shows the mixture of autogenous bone and ABBM for ridge augmentation. ABBM particles are connected by a dense network of newly formed bone. (b) Compact augmentation with well integrated ABBM particles. The bone surrounding the particles is of variable matureness.


A
B

The original intention was to evaluate biopsy specimens from each augmented surgical site. However, due to problems with staining and storage of the specimens, only six of the specimens could be histologically evaluated to differentiate between the pre-existing bone, newly formed bone, and resorbable barrier membrane. As several of the maxillary cases also included a simultaneous sinus floor elevation, this was always evident in the augmentation and was usually observed in the biopsy specimen. In two of the sites augmented with ABBM and autogenous bone, the horizontally augmented ridge could be distinguished in the histology. Both specimens demonstrated newly mineralized bone in various degrees of maturation. In one histological specimen, the cortical plate of the former knife-edge ridge was observed, and the augmentation area showed the ABBM being connected by a dense network of newly formed bone. In this specimen, only very small amounts of the harvested autogenous bone could be observed. Since there was no sign of resorption of the ABBM particles, it was assumed that the autogenous bone used for augmentation has been resorbed and replaced by newly formed bone. There was no histological evidence of the GBR membrane.

Even though there were a limited number of histological specimens that could be analysed, no difference in the amount of newly formed bone observed between the apical and coronal part of the biopsies could be observed.

4.3 Horizontal Augmentation Utilizing a Native, Bilayer Collagen Membrane (HA/2)

This case series reported on patients presenting to a clinical practice and requiring horizontal bone augmentation for the purpose of implant placement. The indication for horizontal ridge augmentation generally resulted from a lack of horizontal bone width in the posterior maxilla or mandible. All patients presented with a horizontal ridge of 4 mm or less and in need of horizontal ridge augmentation prior to dental implant placement (**Table 9**). For the maxillary cases, if an additional sinus proximity was present, a sinus floor augmentation was carried out simultaneously (16 out of 18 maxillary cases).

Table 9: Horizontal Augmentation Study (HA/2): Surgical Sites Treated with Horizontal Ridge Augmentation for Subsequent Implant Placement

Patient # (Surgical Site #)	Gender	Age (years)	Maxilla / Mandible	Healing Time (months)		Histology
				Graft	Implant	
1 (1)	Male	62	Maxilla	8.00	6.00	Yes
2 (1)	Male	58	Maxilla	8.00	7.75	Yes
2 (2)			Mandible	9.25	6.00	Yes
3 (1)	Female	72	Maxilla	13.00	6.00	
4 (1)	Female	37	Mandible	13.25	5.25	
5 (1)	Male	57	Maxilla	8.00	6.25	
5 (2)			Maxilla	8.00	6.25	
6 (1)	Female	49	Mandible	7.5	4.25	
7 (1)	Male	50	Maxilla	7.00	6.25	
8 (1)	Male	62	Mandible	8.00	5.75	
9 (1)	Female	61	Maxilla	8.25	5.75	Yes
9 (2)			Maxilla	10.25	5.75	
10 (1)	Male	34	Maxilla	7.00	20.25	Yes
11 (1)	Female	57	Mandible	6.50	3.50	
12 (1)	Female	53	Mandible	6.00	7.75	Yes
13 (1)	Female	62	Mandible	8.00	4.75	
14 (1)	Male	59	Maxilla	10.00	6.00	Yes
15 (1)	Female	30	Maxilla	7.75	5.50	
16 (1)	Female	47	Mandible	7.50	9.00	
16 (2)			Mandible	7.50	9.00	
17 (1)	Female	39	Maxilla	8.25	14.75	Yes
17 (2)			Mandible	13.00	14.00	
18 (1)	Female	71	Maxilla	10.00	6.00	
19 (1)	Female	55	Mandible	9.25	10.00	
20 (1)	Female	54	Maxilla	11.25	6.00	Yes
21 (1)	Female	61	Maxilla	8.50	6.00	
21 (2)			Maxilla	8.50	6.00	
22 (1)	Male	38	Maxilla	9.25	5.25	
23 (1)	Male	61	Mandible	8.00	6.00	
24 (1)	Male	51	Maxilla	7.00	4.50	
25 (1)	Female	37	Mandible	14.00	3.25	
N (Data Available)		**25**		**31**	**31**	
Mean (SD)		**52.7 (11.4)**		**8.90 (2.06)**	**7.06 (3.52)**	
Median		**55.0**		**8.00**	**6.00**	
Interquar-tile Range		**(47.0, 61.0)**		**(7.5, 10.0)**	**(5.5, 7.75)**	
Range		**(30, 72)**		**(6.0, 14.0)**	**(3.25, 20.25)**	

SD = Standard Deviation

Seventy-eight (78) implants were placed in 25 patients with 31 knife-edge ridges (15 females and 10 males with a mean age of 52.7 years (**Table 9**).

Intraoperative measurements indicated an average residual bone width of 2.20 mm (SD=0.65 mm; range 1–4 mm) (**Table 10**).

Table 10: Horizontal Augmentation Study (HA/2): Measurements of the Ridges Before and After Augmentation

Patient # (Surgical Site #)	Ridge Width (mm)			Implants Placed (#)	Follow-up (months)
	Baseline	Re-entry	Gain		
1 (1)	3.5	11.0	7.5	2	28.25
2 (1)	2.0	8.0	6.0	3	23.50
2 (2)	2.0	7.5	5.5	2	27.25
3 (1)	1.5	7.0	5.5	3	23.75
4 (1)	2.0	7.0	5.0	1	14.25
5 (1)	2.0	7.0	5.0	3	29.50
5 (2)	2.0	8.0	6.0	3	29.50
6 (1)	2.0	10.5	8.5	3	22.00
7 (1)	2.0	6.0	4.0	3	14.25
8 (1)	1.0	5.0	4.0	3	3.00
9 (1)	2.0	12.0	10.0	4	24.00
9 (2)	2.0	10.0	8.0	3	24.00
10 (1)	3.5	8.0	4.5	2	7.00
11 (1)	2.0	7.5	5.5	3	9.25
12 (1)	2.0	8.0	6.0	2	31.00
13 (1)	1.5	7.0	5.5	2	16.00
14 (1)	2.0	7.0	5.0	3	34.00
15 (1)	3.0	8.0	5.0	1	11.75
16 (1)	2.0	7.0	5.0	2	29.25
16 (2)	2.5	8.0	5.5	2	29.25
17 (1)	3.0	9.0	6.0	3	16.25
17 (2)	1.5	6.5	5.0	3	2.25
18 (1)	2.0	8.0	6.0	2	13.25
19 (1)	1.5	7.5	6.0	1	30.75
20 (1)	4.0	10.0	6.0	2	27.75
21(1)	2.5	8.0	5.5	4	12.75
21 (2)	2.5	8.0	5.5	4	12.75
22 (1)	2.0	8.0	6.0	1	16.50
23 (1)	2.5	7.5	5.0	2	23.75
24 (1)	2.0	8.0	6.0	4	39.50

Patient # (Surgical Site #)	Ridge Width (mm)			Implants Placed (#)	Follow-up (months)
	Baseline	Re-entry	Gain		
25 (1)	NR	NR	NR	2	21.75
N (Patient Data Available)	**30**	**30**	**30**	**31**	**31**
Mean (SD)	**2.20 (0.65)**	**8.00 (1.47)**	**5.80 (1.26)**	**2.52 (0.89)**	**20.90 (9.34)**
Median	**2.00**	**8.00**	**5.50**	**3.00**	**23.50**
Interquartile Range	**(2.00, 2.50)**	**(7.00, 8.00)**	**(5.00, 6.00)**	**(2.00, 3.00)**	**(13.25, 29.25)**
Range	**(1.0, 4.0)**	**(5.0, 12.0)**	**(4.0, 10.0)**	**(1.0, 4.0)**	**(2.25, 39.50)**

SD = Standard Deviation
NR = Not reported for patient with complication that resulted in minimal bone gain (2 mm)

All ridges were of insufficient width to place dental implants, as generally at least 6 mm are required (Esposito et al 2006a). A comparison between the baseline ridge width for the maxilla (58.1% of the surgical sites) and the mandible (41.9 % of the surgical sites) showed a mean residual ridge of 2.42 mm for the maxilla and 1.88 mm for the mandible.

After horizontal augmentation and a mean graft healing period of 8.9 months (SD=2.1 months; range 6.0 – 14.0 months) the mean ridge width was 8.00 mm (SD=1.47 mm), giving an increase of 5.80 mm (SD=1.26 mm) in ridge width. There were no discernible statistical differences in bone width gain between maxillary and mandibular sites (p=0.2405). After the graft healing period, a total of 78 implants with an anodized TiUnite® surface (Brånemark System®, Nobel Biocare, Göteberg, Sweden) were placed. See **Table 11**.

Implants were either 3.5 mm, 3.75 mm, 4.0 mm, or 4.3 mm in diameter, and implant lengths ranged from 7.0 mm to 13 mm, with the majority of implants being 13 mm in length (**Table 11**).

Table 11: Horizontal Augmentation Study (HA/2): Sizes of Implants Placed

Implant Length (mm)	Location of Implant Placement		Total
	Maxilla	Mandible	
3.5 mm Diameter			
13	1	--	**1**
3.75 mm Diameter			
8.5	--	2	**2**
10.0	--	8	**8**
11.5	2	11	**13**
13.0	25	--	**25**
4.0 mm Diameter			
7.0	--	1	**1**
8.5	--	1	**1**
11.5	3	4	**7**
13.0	19	--	**19**
4.3 mm Diameter			
10	--	1	**1**
Total	**50**	**28**	**78**

With one exception, the graft and implant healing periods were uneventful in all cases. One patient developed an abscess at the graft site (3.2%; 95% CI: 0.1%, 16.7%). The surgical site was opened and irrigated, and the patient was given antibiotics. The infection was treated effectively, but a major portion of the bone graft was lost and minimal bone gain of 2 mm was achieved. The patient was successfully retreated with grafting and subsequent implant placement. The placed implants have been loaded for almost two years.

Postoperative swelling of the donor sites was most pronounced in most cases at 48 hours postoperatively. Swelling gradually subsided but was still visible at one week and disappeared completely after ten days. Postoperative discomfort was primarily associated with tension from the swelling, but pain was minimal.

No residual pieces of the membrane were observed at the second stage surgeries. There were no device-related adverse effects related to the use of the native collagen membrane in these augmentation procedures. Healing was similar for the mandibular

and maxilliary cases. Upon reopening of the surgical site at implant placement, the tissue beneath appeared healthy, with a healthy periosteal layer between the soft tissue and the bone, similar to results previously reported for non-resorbable and collagen membranes (Schenk et al 1994; Maiorana et al 2005).

After on average implant healing time of 7.1 months implant healing time (SD=3.5 months; range 3.25 – 20.25 months), the healing abutments were placed in the 31 surgical sites. In seven cases, primary implant stability was sufficient to place the healing abutments at implant placement. All implants appeared clinically stable upon reopening and were maintained for provisional and definitive prosthetic restoration.

All 78 implants have survived to date (100.0% at all time points; life table analysis) with an average follow-up of 20.9 months (SD=9.3 months). There does not appear to be any difference in implant survival between implants placed in the mandible or the maxilla.

Histological Findings:

Nine specimens were examined histologically. The histological samples were taken at a mean 8.4 months of graft healing, during the implant placement from the implant osteotomies utilizing a two millimeter trephine for implant site preparation. Histomorphometric analysis demonstrated that autogenous or regenerated bone represented a mean of 31.0% of the specimens, ABBM 25.8%, and marrow space 43.2%. See **Table 12**.

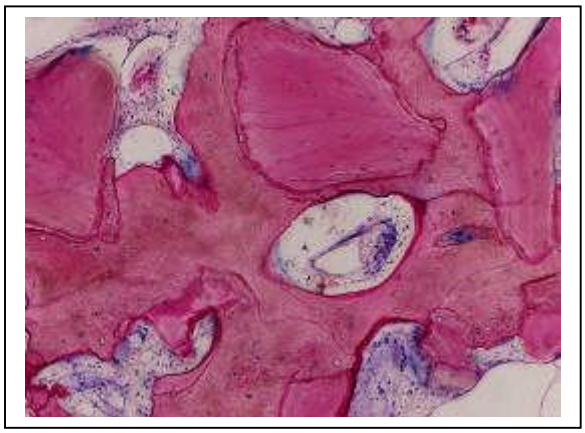
Table 12: Horizontal Augmentation Study (HA/2): Histology Results

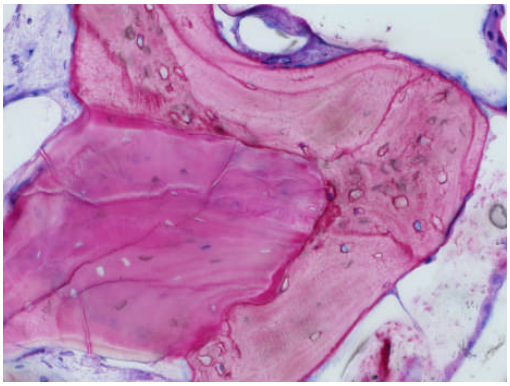
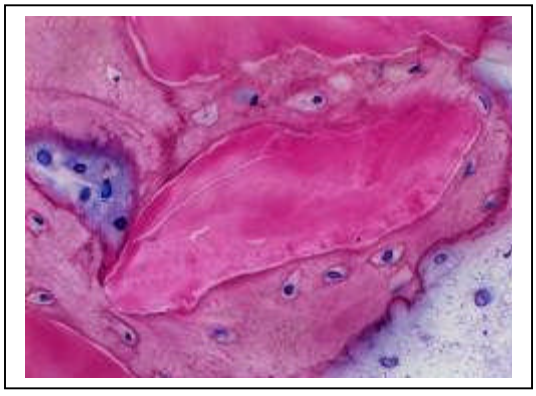
Statistic	**% of Specimens (N = 9)**		
	Autogenous Bone	**ABBM**	**Marrow Space**
Mean	31.00	25.80	43.20
Median	31.50	20.60	38.30
Std. Dev.	10.80	14.80	10.50
Range	18.49, 53.63	9.10, 51.16	30.40, 60.18

Representative histology is presented in **Figure 9**. In all biopsy specimens evaluated, ABBM was connected with a dense network of newly formed bone of various degree of maturation. In two histologic specimens, the original cortical plate of the knife-edge ridge was observed and the augmentation area was connected with a dense network

of newly formed bone connected with the original bone. There was no histologic evidence of the GBR membrane.

Figure 9: **HA/2 Study**: (a) Overview of a histological section taken at 8 months of graft healing (Patient 1, **Table 9**). The original maxillary bone can be seen. The augmentation area is connected with newly formed bone to the original maxillary bone (original magnification x 50). (b) Formation of dense trabecular structures composed of newly formed bone with integrated ABBM granules (original magnification x 100). (c, d) Mixed deposition of lamellar and woven bone on ABBM by active osteoblasts (original magnification x 200, x 400). Connective tissue shows no signs of inflammatory reactions

(a)  (b) 

(c)  (d) 

5. DISCUSSION

5.1. Vertical Augmentation

Bone augmentation utilizing GBR techniques is well documented and characterized by high predictability and survival of implants (Buser et al 2002; Nevins et al 1998; Zitzmann et al 2001a). However, few publications have reported long-term results on vertical ridge augmentation following GBR (Simion et al 2001, 2004). These studies found that vertical bone regeneration of more than 4 mm could only be achieved with the use of autogenous bone chips. This is consistent with the present study, since up to 12 mm vertical bone gain was achieved. None of the sites showed less bone regeneration than the space created by the membrane; however, the 1 site in which early membrane removal was necessary showed minimal (2 mm) vertical bone gain. This indicates that a dimensionally stable barrier, such as the titanium-reinforced e-PTFE membrane, may be necessary for vertical augmentation.

After abutment connection, clinical follow-up demonstrated healthy peri-implant mucosa and a mean probing depth of 3.03 mm. These values are consistent with those reported previously in long-term studies on implants placed into native (Buser et al 1990; Lekholm et al 1994) and regenerated bone (Buser et al 2002; Simion et al 2001).

Crestal bone remodeling was measured from the implant-abutment junction. This showed an overall mean change of 1.01 mm in the first year and remained stable throughout the follow-up period. Similarly, 1.32 mm of remodeling was shown previously in a study reporting on 32 sites that were vertically augmented with autogenous bone chips and a titanium-reinforced e-PTFE membrane (Simion et al 2001). In the current study, there was a slight difference in the first year between the 3 groups examined in this report. However, the differences were not statistically significant and in fact could be expected by the span size and location of the defects.

The overall implant success rates within this study are consistent with published long- term results of implants placed in horizontally and vertically regenerated bone (Buser et al 2002; Simion et al 2001) and with results reported for implants placed in native bone (Adell et al 1981, 1990; Jemt & Lekholm 1993; Lekholm et al 1994, 1999). The overall cumulative implant survival rate of 100% and cumulative success rate of

94.7% in this study compare favorably with the aforementioned studies on implants placed in regenerated bone as well as native bone.

However, there was a marked difference in results reported in previous studies on vertical GBR and the current study. Implant survival and implant success rates were 92% and 76%, respectively, in a study that combined sinus augmentation and posterior maxillary vertical ridge augmentation (Simion et al 2004), whereas 100% implant success was achieved in a similar population in the current study (group C). However, in the previous report, only machined-surface implants were used, whereas enhanced-surface implants were used in the current study. The use of enhanced implant surfaces may have helped, especially in the posterior maxilla where the bone quality is typically poor. Also, in the previous report 7 patients (50%) were treated with a simultaneous technique, whereas in the current study the same type of patients were treated with a staged technique, which allowed more time for regenerated bone to mature prior to loading.

In the present report, the complication rate was 2.78%. This is significantly lower than the complication rates reported in earlier clinical studies on vertical augmentation with GBR (ranging from 12.5% to 17%), and these earlier reports also included membrane exposures and/or subsequent infections (Tinti & Parma-Benfenati 1998; Simion et al 1994, 1998, 2004). The technique employed in this vertical augmentation study is essentially the same technique reported previously (Tinti & Parma-Benfenati 1998). However, this retrospective study represents the time period when vertical ridge augmentation was considered routine clinical practice and does not represent the initial learning curve. The results of this study indicate that (1) there can be reduced complication rates with vertical bone regeneration, (2) implants can be placed successfully in vertically regenerated bone, and (3) implants can survive over time with high clinical success rates.

Some similarities and differences have been identified between the present study and the previously reported studies. These studies should be analyzed in a meta-analytic fashion to coalesce the data into a more meaningful finding relative to the current state of the science on vertical augmentation. Also, since most of the vertical augmentation studies reported in the literature have been retrospective in nature, future research should focus on long-term, prospective studies.

5.2 Horizontal Augmentation Utilizing a New Synthetic Membrane (HA/1).

The case series presented herein demonstrates that the combination of particulated augmentation material (either autogenous bone alone or a combination of autogenous bone and ABBM) and a resorbable membrane can be safely and effectively used for horizontal augmentation of knife-edge ridges in the posterior maxilla or mandible. Even though the healing time between grafting and implant placement can be regarded as a compromise between the time to form sufficient amount of new bone and the need of a timely prosthetic solution for a patient, the benefit of this two-staged procedure is that it provides the amount of horizontal ridge width necessary to successfully place an implant.

Healing of the bone graft was uneventful for all cases in this prospective case series. The use of the synthetic membrane reported herein has shown good soft tissue compatibility, and no membrane exposures or infections occurred at any of the surgical sites. Similar results of soft tissue healing have been reported for both non-resorbable e-PTFE and resorbable synthetic and collagen membranes (Urban et al 2009a,b; Hämmerle et al 2008; Simion et al 1997). Recently, a new synthetic membrane composed of different resorbable materials has been used in preclinical animal models and clinical studies with similar results and comparable soft tissue healing (Herten et al 2009; Jung et al 2009a, b; Thoma et al 2009). Other authors, however, have reported more spontaneous exposures of collagen and e-PTFE membranes (Lindhe et al 2003; Moses et al 2005). Non-resorbable e-PTFE membranes are still regarded as the gold standard in GBR, however frequently reported soft tissue problems, as well as the need to remove the membrane, have supported the development and use of resorbable membranes (Lindhe et al 2003; Moses et al 2005). The lack of a titanium reinforced resorbable membrane can be overcome by secure fixation of the membrane on both the lingual/palatal and the vestibular side. This technique immobilizes the graft material, allowing for the formation of the desired amount of bone.

In this case series, there was a mean horizontal bone increase of 5.52 mm (± 1.40 mm), with some sites gaining up to 9 mm. Overall, only two cases resulted in a horizontal ridge width of less than 6 mm; however, in both cases, implant placement was achieved and have survived over 32 months months. Similarly, 4.6mm horizontal bone gain was

reported in a study utilizing autogenous bone blocks covered with ABBM particles and resorbable collagen membranes (von Arx & Buser 2006), whereas a somewhat less favorable result of 3.6mm horizontal bone gain was achieved when using ABBM particles alone as grafting material with collagen membranes (Hämmerle et al 2008). The differences may be attributed to the use of autogenous particles mixed with ABBM, which may have resulted in a more osteogenic graft. Also, the membrane used in this report has a longer resorption time, which may have allowed more time for the graft to mature.

Within the cases in this series, no differences could be detected between the sites augmented only with autogenous bone and those augmented with a mixture of autogenous bone and ABBM. However, the number of cases treated with autogenous bone alone is limited. In the cases treated with the mixture of autogenous bone and ABBM, the ABBM particles showed good incorporation with the newly formed ridge. This is supported by the available histology of the augmentation area showing that the ABBM was connected by a dense network of newly formed bone. In another published report in which autogenous bone blocks were covered with ABBM particles and collagen membranes, at re-entry the ABBM particles showed fibrous incapsulation only and no evidence of osseous integration (von Arx & Buser 2006). This may further support the use of particulated autogenous bone mixed with ABBM rather than ABBM layered on autogenous bone blocks.

Since all implants have survived to date, this case series demonstrates the feasibility of using a new resorbable membrane in GBR for horizontal ridge augmentation. However, the high rate of implant survival reported in this case series has to be viewed cautiously since implant success according to established methods has not yet been investigated.

Recent reports in the literature indicate that the standard treatment of knife-edge ridges has changed in recent years (Hämmerle et al 2008). The use of bone grafting materials and resorbable membranes to treat knife-edge defects with horizontal augmentation may lead to less morbidity in the treatment of patients with these defects. In addition, the use of ABBM in these procedures may lessen the need of harvested autogenous bone and may generally lead to decreased morbidity and therefore increased

patient comfort and satisfaction associated with these regenerative procedures. The absence of major complications in any of the harvest sites in this case series supports the potential benefit of ABBM for use in these types of procedures. However, the positive results obtained in this case series need to be proven by larger randomized and controlled clinical trials.

5.3 Horizontal Augmentation Utilizing a Native, Bilayer Collagen Membrane (HA/2)

The case series presented herein demonstrates that the combination of particulated autogenous bone mixed with ABBM and a short-term resorbable, collagen membrane can be safely and effectively used for horizontal augmentation of knife-edge ridges in the posterior maxilla or mandible. Even though the healing time between grafting and implant placement can be regarded as a compromise between the time to form sufficient amount of new bone and the need of a timely prosthetic solution for a patient, the benefit of this two-staged procedure is that it provides the amount of horizontal ridge width necessary to successfully place an implant.

With one exception, healing of the bone graft was uneventful in this prospective case series, and there was an infection of the bone graft in this case (3.2%). This is similar to most recently reported complication rates on horizontal and vertical augmentation (Buser et al 2002; Urban et al 2009a, b).

The use of the collagen membrane reported herein has shown good soft tissue compatibility, and no membrane exposures occurred at any of the surgical sites. Similar results of soft tissue healing have been reported for both non-resorbable e-PTFE and resorbable synthetic and collagen membranes (Hämmerle et al 2008; Simion et al 1997; Urban et al 2009a, b, 2011a, b). Other authors, however, have reported more spontaneous exposures of collagen and e-PTFE membranes (Moses et al 2005; Lindhe et al 2003). Non-resorbable e-PTFE membranes are still regarded as the gold standard in GBR, however frequently reported soft tissue problems, as well as the need to remove the membrane, have supported the development and use of resorbable membranes (Moses et al 2005; Lindhe et al 2003). The lack of a titanium reinforced resorbable membrane can be overcome by secure fixation of the membrane on both the lingual/palatal and the

vestibular side. This technique immobilizes the graft material, allowing for the formation of the desired amount of bone.

In this case series, there was a mean horizontal bone increase of 5.80 mm (SD=1.26 mm), with some sites gaining up to 10.0 mm. All cases resulted in a horizontal ridge width of at least 5 mm, and implant placement was achieved. All implants have survived to date and are in function (2 to 40 months). Similarly, 4.6 mm horizontal bone gain was reported in a study utilizing autogenous bone blocks covered with ABBM particles and resorbable collagen membranes (von Arx & Buser 2006), whereas a somewhat less favorable result of 3.6 mm horizontal bone gain was achieved when using ABBM particles alone as grafting material with short-term resorbable, collagen membranes (Hämmerle et al 2008). The differences may be attributed to the use of autogenous particles mixed with ABBM, which may have resulted in a more osteogenic graft.

In this case series treated with the mixture of autogenous bone and ABBM, the ABBM particles showed good incorporation with the newly formed ridge. This is supported by the available histology of the augmentation area showing that the ABBM was connected by a dense network of newly formed bone. In another published report in which autogenous bone blocks were covered with ABBM particles and collagen membranes, at re-entry the ABBM particles showed fibrous incapsulation only and no evidence of osseous integration (von Arx & Buser 2006). This may further support the use of particulated autogenous bone mixed with ABBM rather than ABBM layered on autogenous bone blocks.

Since all implants have survived to date, this case series demonstrates the feasibility of using a more rapidly resorbing membrane in GBR for horizontal ridge augmentation. However, the high rate of implant survival reported in this case series has to be viewed cautiously since implant success according to established methods has not yet been investigated and the implants have been followed only for short term.

Recent reports in the literature indicate that the standard treatment of knife-edge ridges has changed in recent years (Hämmerle et al 2008; Urban et al 2011a, b). The use of bone grafting materials and resorbable membranes to treat knife-edge defects with horizontal augmentation may lead to less morbidity in the treatment of patients with these

defects. In addition, the use of ABBM in these procedures may lessen the need of harvested autogenous bone and may generally lead to decreased morbidity and therefore increased patient comfort and satisfaction associated with these regenerative procedures. The absence of major complications in any of the harvest sites in this case series supports the potential benefit of ABBM for use in these types of procedures. However, the positive results obtained in this case series need to be proven by larger randomized and controlled clinical trials.

6. CONCLUSIONS

6.1 Vertical Augmentation

The results of this retrospective study suggest that the following conclusions can be made: (1) vertical augmentation with e-PTFE membranes and particulated autografts is safe and predictable, with minimal complications; (2) clinical success and survival of implants placed in vertically augmented bone with the GBR technique appear similar to success and survival of implants placed in native bone under loading conditions, regardless of the harvest site, surgical area, or defect size; and (3) the success and survival rates of implants placed simultaneously with sinus and vertical augmentation techniques compare favorably to those in sites requiring vertical augmentation of single- or multiple-tooth ridge defects.

6.2 Horizontal Augmentation Utilizing a New Synthetic Membrane (HA/1).

In this case series, the treatment of horizontally deficient alveolar ridges with the GBR technique using autogenous bone with or without the addition of ABBM and a resorbable barrier membrane can be regarded as successful and may lead to implant survival. The regenerated bone can lead to good osseointegration of the dental implant. Histological evaluation of the regenerated bone has shown that the autogenous bone is mostly resorbed and replaced by vital bone and the bone substitute particles are connected by new vital bone.

6.3 Horizontal Augmentation Utilizing a Native, Bilayer Collagen Membrane (HA/2)

In this case series, the treatment of horizontally deficient alveolar ridges with the GBR technique using autogenous bone mixed with ABBM and a native collagen resorbable barrier membrane can be regarded as successful and may lead to implant survival. Within the timeframe of the study the regenerated bone leads to good osseointegration of the dental implant. Histologic evaluation showed that ABBM was connected with a dense network of newly formed bone of various degree of maturation.

7. FUTURE PERSPECTIVES IN RIDGE AUGMENTATION.

In order to reduce morbidity of harvesting autogenous bone, some recombinant growth factors have recently been investigated.

It has been demonstrated in a canine preclinical study that rhBMP-2 induced bone allows installation, osseointegration, and long-term functional loading of machined, threaded, titanium dental implants (Jovanovic et al 2003). Publications have reported on the clinical use of rhBMP-2 on an absorbable collagen sponge in a phase II study (three treatment groups: two doses of rhBMP-2 and autograft) and a pivotal study (two treatment groups: one dose of rhBMP-2 and autograft) for sinus floor augmentation (Boyne et al 2005; Triplett et al 2009). Both studies found that the regenerated bone was sufficient to place and functionally load implants. In addition, Triplett et al noted that in the pivotal study there was “a 17% rate of long-term parasthesia, pain, or gait disturbance related to the bone graft harvest” in the autograft treatment group (2009).

The use of platelet-derived growth factor (PDGF) in combination with deproteinized bovine bone block has also been studied in a dog model (Simion et al. 2006). The results of this preclinical canine study demonstrated that purified recombinant PDGF-BB, used in combination with a deproteinized bovine block, and without placement of a barrier membrane, has the potential to regenerate significant amounts of new bone in severe mandibular ridge defects.

Several case studies utilizing different versions of the above mentioned combinations of autogenous bone, ABBM and rhPDGF-BB were recently published (Simion et al. 2007, 2008, Urban et al. 2009, 2011c) and demonstrated successful histological and clinical results.

This modality has the potential to completely eliminate the need of bone harvesting and any bone filler materials, and preliminary results are encouraging. However, the clinician must recognize that there is limited clinical information available on these new modalities, and no information on resorption of the regenerated bone, implant survival and crestal remodeling around implants. Further documentation from long-term, randomized, controlled clinical studies are necessary to recommend these new treatment modalities in everyday clinical practice.

8. OVERALL CONCLUSIONS

Vertical and horizontal augmentation with GBR represents the current state of the science in implant dentistry. Given adequate care in selecting cases for these procedures and complying with surgical and postsurgical treatment protocols, the results are beneficial to the patient with a relatively low risk of complications. Tissue engineering may hold the promise of a new vertical and horizontal augmentation procedure, but the potential of this treatment modality in everyday clinical practice will require the results of long-term, randomized, controlled clinical studies to confirm the risk/benefit as compared to vertical and horizontal augmentation with GBR.

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