KEY WORDS
Autogenous bone, Bone substitute, Dental implants, Guided bone regeneration

Case series

ONE-STAGE HORIZONTAL GUIDED BONE REGENERATION WITH LAYERED AUTOLOGOUS BONE, ANORGANIC BOVINE BONE AND COLLAGEN MEMBRANES: SIX-YEAR RESULTS OF A PROSPECTIVE CASE-SERIES STUDY

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PURPOSE. To present the results recorded six years after implant placement and simultaneous one-stage horizontal guided bone regeneration (GBR) using layers of autologous bone and anorganic bovine bone in association with resorbable collagen membranes.

MATERIALS AND METHODS. This study was designed as an uncontrolled prospective case series. Partially edentulous patients having less than 6.0 mm and more than 4.0 mm of residual horizontal bone width were selected and consecutively treated with implant placement and simultaneous horizontal bone regeneration using autologous bone and anorganic bovine bone placed in layers and covered with a resorbable collagen membrane. Outcome measures were: implant and prosthesis failures, any complications, peri-implant marginal bone level changes, probing pocket depth (PPD), and bleeding on probing (BoP).

RESULTS. In total, 45 consecutive patients (20 males and 25 females) of mean age 52.1 years each received at least one GBR procedure with contemporary placement of 63 implants. At follow-up examination 6 years after implant placement, six patients with seven implants dropped out. Of the remaining 39 patients (56 implants), no implant or prosthesis failed. In six patients (13.3%), the collagen membrane became slightly exposed one to two weeks after bone augmentation. Four of these patients were moderate smokers. Post-hoc analysis using Fisher's exact test found a significant association (P = 0.0139) between smoking and early membrane exposure. No late complications occurred. Mean marginal bone level at implant placement was 0.12±0.14 (95% CI 0.08-0.17). A statistically significant amount of bone loss occurred between implant placement and six-year follow-up (difference 0.8±0.29 mm; 95% CI 0.71-0.88; P = 0.0000). The mean BoP value measured at definitive restoration delivery was 1.23±0.93 (IQR 0.4; 1.1; 1.8), while six years after implant placement it was 1.21±0.58 (IQR 0.8; 1.1; 1.6), but the difference was not statistically significant from baseline (0.02 0.79; 95% CI -0.32–0.36; P = 0.906). The mean PPD value measured at definitive restoration delivery was 2.62±0.59 mm (95% CI 2.45-2.79), while six years after implant placement it was 2.77±0.67 mm (95% CI 2.56-2.98). The difference from baseline was not statistically significant (0.15 0.63; 95% CI -0.12-0.42; P = 0.272).

CONCLUSIONS. Within the limitations of the present study, one-stage horizontal guided bone regeneration with layered autologous bone, anorganic bovine bone and collagen membranes seems to be a viable option for the reconstructive treatment of horizontal bony defects at implant placement.

CONFLICT OF INTEREST STATEMENT
This study was not financially supported by any company, and there are no conflicts of interest.

INTRODUCTION

Implant-supported prostheses are a valid treatment option for restoring partially and completely edentulous ridges. However, biological and technical complications still occur, and the long-term success of implant therapy can be influenced by several factors. Among the most important factors for predictable long-term results is bone volume at implant insertion[1]. According to the international literature, a buccal bone wall thickness of 1.5 mm at implant placement is advisable[2], as is a minimum distance of at least 1.5-2 mm from adjacent teeth, in order to obtain lasting aesthetic and functional outcomes[3].

In recent years, there has been a growing trend towards minimally invasive surgery, and the research shows similar rates of prosthesis and implant failures for short and longer implants placed in augmented bone in the posterior mandible[4]. Nevertheless, biological and technical complication rates are reported to be higher at longer implants placed in vertically augmented posterior mandibles[4]. On the other hand, narrow implants should be used with caution when replacing posterior teeth due to the risk of fracture[5,6].

Among the many surgical techniques proposed to reconstruct the atrophic posterior mandible[7,8], horizontal guided bone regeneration with resorbable membranes with either simultaneous or staged implant placement has demonstrated high implant survival rates in several studies[9-11]. In a previous report with 30 months of follow-up, the use of a 2.0 mm layer of particulated autologous bone on the implant threads, and a 2.0 mm layer of anorganic bovine to cover the resorbed ridge, in combination with the resorbable collagen membrane, proved to be a viable treatment option for the reconstruction of horizontal bony defects[7]. However, most of the literature published to date is based on short-term follow-up studies or long-term retrospective research[12].

Hence, the aim of this prospective case series study was to evaluate the outcomes of implants placed with the so called one-stage approach, using autologous bone and anorganic bovine bone placed in layers and covered by resorbable collagen membranes for the augmentation of horizontal bony defects, at six-year follow-up. This report is written in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines (http://www.strobe-statement.org).

MATERIALS AND METHODS

This prospective case-series study analysed data collected from partially edentulous augmentation patients aged 18 years or older, rehabilitated in either the mandible or maxilla using implants with anodized surface (TiUnite, Nobel Biocare, Göteborg, Sweden), placed between January 2012 and December 2012 in the alveolar crest with residual horizontal ridge of between 4 to 6 mm.

Patients were not admitted to the study if any of the following exclusion criteria applied: American Society of Anesthesiologists (ASA) class III or IV; psychiatric contraindications; pregnancy or nursing; alcohol or drug abuse; heavy smoking (>10 cigarettes/day); radiotherapy to head or neck region within five years; high or moderate parafunctional activity; absence of teeth/denture in the opposite jaw; untreated periodontitis; implants placed immediately post-extraction; full-mouth bleeding and full-mouth plaque index of 25% or higher; or inability to understand and sign informed consent. Written consent was obtained from all patients after they were informed about the nature of the treatment. Data collection was designed to preserve patient anonymity.

One clinician (SMM) with expertise in dental implant placement and guided bone regeneration performed all the surgical procedures, and another (MP), experienced in implant-supported

prostheses, performed all prosthetic procedures in one private practice in Arzachena, Sardinia, Italy.

All patients were treated using computer-assisted template-based implant placement. Traditional dental photography (**FIG. 1**), study models and preoperative cone-beam computed tomography (CBCT) scans were obtained and matched. Implant insertion was planned with the aid of a diagnostic wax-up of the ideal prosthetic and aesthetic position. All patients received two grams of amoxicillin (Zimox, Pfizer, Rome, Italy) one hour before surgery, and one gram twice daily for one week afterwards. Patients allergic to penicillin received 600 mg of clindamycin one hour before surgery, then a 300-mg dose four times a day for one week. Patients rinsed with 0.2% chlorhexidine solution (Curasept, Curaden Healthcare, Saronno, Italy) for one minute before surgery to disinfect the surgical site and minimise potential contamination from extraoral sources. Patients were treated under local anaesthetic (Septanest with adrenaline, 1/100,000, Septodont, Saint-Maur-des-Fossés, France).

Then, a mid-crestal incision was made into the keratinized tissue using a surgical blade n° 15, and a full-thickness flap was raised beyond the mucogingival junction, to at least five mm beyond the bone defect. Two vertical incisions were made two teeth away from the area to be augmented. In the posterior mandible, a lingual flap was raised, taking care to preserve sensitive maxillary and mandibular anatomic (e.g., mental and infraorbital nerves). The recipient site was then cleared of all soft tissue remnants.

Autogenous bone was harvested using a minimally invasive cortical bone collector (Safe Scraper, Micross, Meta, Reggio Emilia, Italy). Multiple decortication holes were made at the recipient site using a 2.0 mm round bur under irrigation with cool saline. Implants (NobelReplace Conical Connection, PMC, Nobel Biocare) were inserted in prosthetically driven positions with the aid of a surgical template (**FIG. 2**).

A resorbable collagen membrane (Bio-Gide, Geistlich Biomaterials Italia, Thiene, Italy) was fixed on the lingual/palatal side with two titanium pins (Supertack, MCbio, Lomazzo, Italy). Exposed implant surface was covered with a layer of autologous bone alone, while a second layer of anorganic bovine bone material (Bio-Oss, Geistlich Biomaterials Italia) was positioned on top. Finally, the collagen membrane was trimmed to cover the entire volume of the graft, and additional titanium pins (two to three pins) were used to secure it on the vestibular side (**FIG. 3**). A periosteal incision was made between the two vertical incisions to allow tension-free flap closure and release. The flaps were sutured in two layers to prevent membrane exposure; horizontal mattress sutures (4-0 Vycril, Ethicon, Johnson & Johnson, Pomezia, Italy)

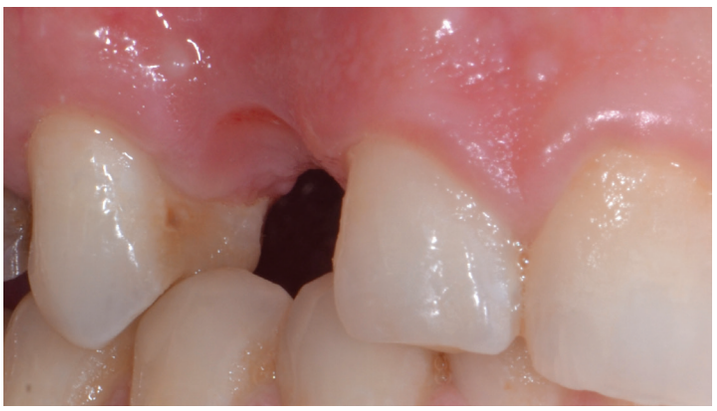

Fig. 1: *Initial clinical picture of a example case.*

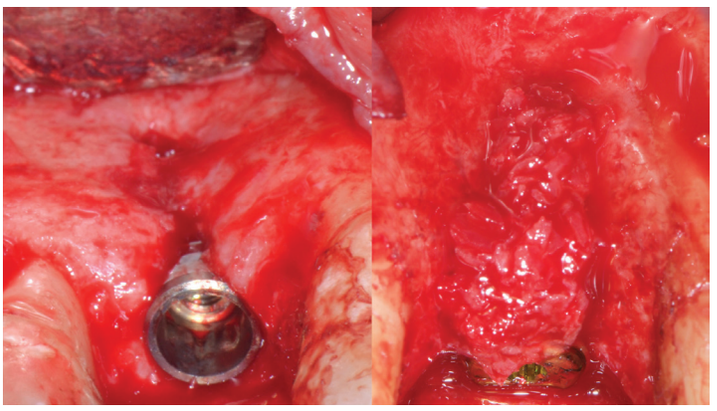

Fig. 2: *Guided bone regeneration. Defect after implant placement (left), and autogenous bone in the implant threads (right).*

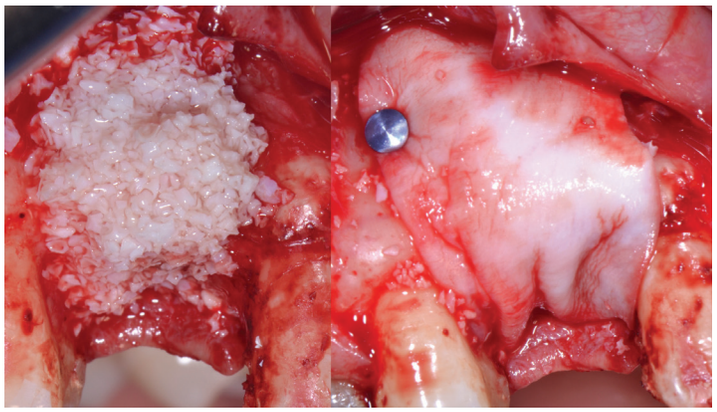

Fig. 3: *Anorganic bovine bone (left) and collagen membrane (right).*

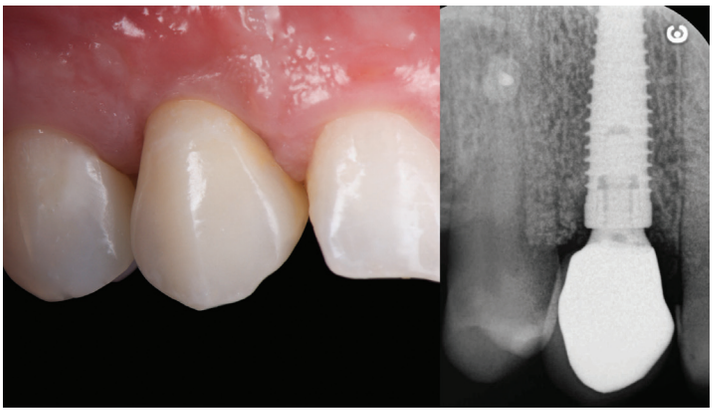

Fig. 4: *Clinical (left) and radiographic (right) view at definitive prosthesis fitting.*

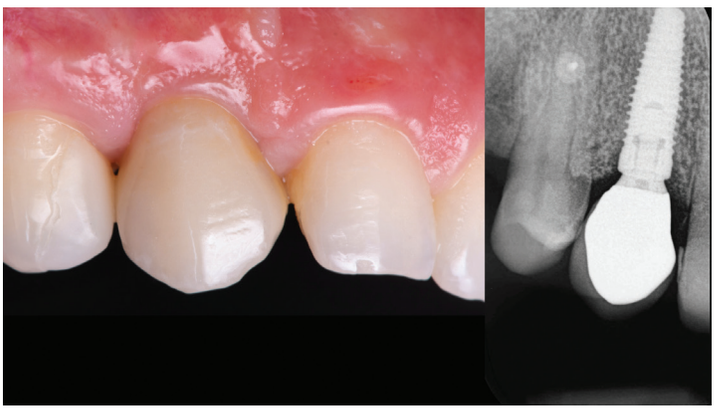

Fig. 5: *Clinical (left) and radiographic (right) view at 6-year post-loading follow-up.*

were placed four mm from the incision line, followed by single interrupted sutures placed near the edges of the flaps. Vertical incisions were sutured with single, interrupted sutures.
Postoperatively, a 4-mg/day dose of dexamethasone (Desoren, Rekah Pharmaceutical Products, Holon, Israel) was administered for two days, and 80 mg of ketoprofen (Oki, Dompé, Milan, Italy) was prescribed as needed. Patients were instructed to use chlorhexidine spray three times a day for two weeks, and to adhere to a soft-food diet for ten days. Sutures were removed after 10 to 14 days, while mattress sutures were removed two to three weeks after surgery.
Six months after implant placement, implants were exposed, and temporary crowns were fitted on titanium stock abutments. Six months later, definitive computer-aided design/computer-assisted manufacture (CAD/CAM), screw-retained, zirconia ceramic crowns were delivered (**FIG. 4**). Patients were followed up for six years after implant placement (**FIG. 5**).
Primary outcome measures were implant and/or prosthesis failure, as well as any complications. Implant failure was recorded upon the removal of implants dictated by implant mobility, progressive marginal bone loss, infection, or implant fracture. The stability of individual implants was measured by the prosthodontist at the time of temporary and definitive crown fitting (six and 12 months after implant placement, respectively) by applying 35 Ncm of removal torque. At each subsequent follow-up, implant stability was manually tested by the same prosthodontist using two dental mirror handles.
A prosthesis was considered a failure in any event that it need to be remade. Complications recorded were any abutment mobility, membrane exposure, subsequent infection, and/or

morbidity associated with the harvest site, as well as any prosthesis complications, such as fracture or chipping of the provisional or definitive ceramic crown, and any biological complications, including wound or implant infection, mucositis, abscesses or peri-implantitis.

Secondary outcome measures were peri-implant marginal bone loss, bleeding on probing (BoP), and probing pocket depth (PPD). To measure the former, the distance from the most coronal margin of the implant collar and the most coronal point of bone-to-implant contact were evaluated on digital intraoral radiographs taken with the paralleling technique (Rinn XCP, Dentsply, Elgin, IL, USA). Radiographs taken at implant placement, initial loading, definitive restoration delivery, and three and six years after implant placement were accepted or rejected for evaluation based on the clarity of the implant threads. All readable radiographs were displayed on a 24-inch LCD screen (iMac, Apple, Cupertino, CA, USA) via image analysis software (DFW2.8 for Windows, Soredex), which was calibrated for each image using the known distance between two adjacent threads. Measurements of the mesial and distal bone crest level adjacent to each implant were made by to the nearest 0.01 mm and averaged at patient level. Probing pocket depth (PPD) and bleeding on probing (BoP) were measured using a periodontal probe (PCP-UNC 15, Hu-Friedy Manufacturing, Chicago, IL, USA) at definitive restoration delivery and at three and six years after implant placement by an operator who had not previously been involved in the study. Three vestibular and three lingual measurements were made for each implant, and then averaged at patient level.

Statistical analyses

Data analysis was carried out according to a pre-established analysis plan. Patient data was compiled in an Excel spreadsheet (Microsoft) that reflected the parameters in the records of the eligible patients. A clinician (MT) with expertise in statistics analysed the data using SPSS for Windows release 18.0 (SPSS, Chicago, IL, USA). Descriptive analysis was performed using means±standard deviations (95% confidence interval, CI) for numerical parameters, and number and % for dichotomous variables.

Comparisons were made between mean values at each time point and the baseline measurements (implant placement) using paired tests, to detect any changes in MBL, BoP and PPD. Fisher's exact test was also applied to detect any possible association between smoking and the risk of membrane exposure.

Data were averaged at patient level, and the patient was used as the statistical unit of the analyses. Median and interquartile range (IQR) values were also calculated for BoP and PPD in order to obtain a better description of the data set. All statistical comparisons were conducted at the significance level 0.05.

RESULTS

Fifty patients were initially screened for eligibility, but five patients were not enrolled because of their refusal to sign informed consent to the research. The remaining 45 consecutive patients (20 males and 25 females; mean age 52.1 years, range 24 to 78 years), with 63 implant sites classified as Cawood-Howell Class III, received at least one GBR procedure. Thirteen out of the 45 participants (28.8%) were moderate smokers.

At the 3-year follow-up examination, no participant had dropped out and no deviation from the original protocol had occurred, while six patients dropped out for reasons unrelated to the procedure (three patients moved to other cities and the other three declined to attend any follow-up appointment, declaring that they felt good) by the 6-year follow-up, at which no implant had failed and no prosthesis-related complication had been observed. However, in six patients (13.3%) the collagen membrane became slightly exposed one to two weeks after

surgery. Four of these patients were moderate smokers, and Fisher's exact test revealed a significant association (P = 0.0139) between smoking and early membrane exposure.

The exposed area of membrane exposure was treated via local application of 0.5% chlorhexidine gel (Curasept ADS 0.5% gel, Curaden Healthcare) twice a day for three weeks, and complete soft tissue healing was observed in all cases at between two to four weeks. Mean marginal bone level at implant placement was 0.12±0.14 mm (95% CI 0.11-0.19), while three years after implant placement it was 0.77±0.22 mm (95% CI 0.70-0.82), i.e., 0.65±0.18 mm from baseline (95% CI 0.60-0.69; P < 0.0000; **TABLE 1**). Six years after implant placement, the mean marginal bone level was 0.92±0.23 mm (95% CI 0.84–0.99), and the mean marginal bone loss experienced during the entire follow-up was therefore 0.80±0.19 mm (95% CI 0.72-0.88; P < 0.000; **TABLE 1**).

The mean BoP at the definitive restoration delivery was 1.23±0.93 (IQR 0.4; 1.1; 1.8), while six years after implant placement it was 1.21±0.58 (IQR 0.8; 1.1; 1.6) (**TABLE 2**). The difference in the latter from baseline was not statistically significant (0.02±0.79; 95% CI -0.32-0.36; P = 0.906).

TABLE 1 MEAN MARGINAL BONE LEVELS AND LOSS

	Implant placement & GBR	3 years after implant placement & GBR	6 years after implant placement & GBR
Marginal bone level	N = 45 0.12±0.14 (0.11-0.19)	N = 45 0.77±0.22 (0.70-0.82)	N = 39 0.92±0.23 (0.84-0.99)
Difference from baseline		N = 45 0.65±0.18 (0.60-0.69)	N = 39 0.8±0.19 (0.72-0.88)
P value		0.0000	0.0000

In parenthesis 95% confidence intervals

TABLE 2 MEAN BOP AND PPD

	Implant placement & GBR	6 years after implant placement & GBR
BoP	N = 45 1.23±0.93 IQR 0.4; 1.1; 1.8	N = 39 1.21±0.58 IQR 0.8; 1.1; 1.6
Difference from baseline		N = 39 0.02±0.79
P value		0.906
PPD	N = 45 2.62±0.59 IQR 2.3; 2.5; 2.9	N = 39 2.77±0.67 IQR 2.0; 3.0; 3.0
Difference from baseline		N = 39 0.15±0.63
P value		0.272

In parenthesis 95% confidence intervals

The mean PPD measured at the definitive restoration delivery was 2.62±0.59 mm (IQR 2.3; 2.5; 2.9), while six years after implant placement it was 2.77±0.67 mm (IQR 2.0; 3.0; 3.0). The difference from baseline was not statistically significant (0.15 0.63; 95% CI -0.12–0.42; P = 0.272) (**TABLE 2**).

DISCUSSION

The aim of this case series was to investigate the 6-year clinical and radiographic data of one-stage horizontal guided bone regeneration with layered autologous bone, anorganic bovine bone and collagen membranes. The results confirmed the 3-year findings[7] supporting one-stage GBR as a viable technique for augmenting bone thickness at implant placement.

Autogenous bone blocks are among several techniques reported to improve bone thickness for implant purposes[13,14], and, compared with other regenerative techniques, were considered the gold standard approach for most reconstructive procedures[12-14]. However, the technique is plagued by several limitations, including additional operative time for graft harvest, donor site morbidity, graft resorption, and limited availability[14].

To overcome these limitations, two layers of 2.0 mm each of different graft materials were used and covered by a collagen membrane. The first layer was composed of autogenous bone alone, placed on the implant threads, while the second layer was composed of 100% of bovine-derived xenograft, placed on top.

Recently, a similar procedure, mixing particulated autogenous bone graft in different proportions, has been proposed with the aim of improving the osteogenetic proprieties of the graft. A ratio of 1:1 has been proposed[15], but a systematic review by Jensen and co-authors was unable to confirm or refute the presumed improve benefits of mixing particulated autogenous bone with bovine-derived xenograft[16]. Nevertheless, the clinical and radiographic results of this study confirm other reports on the use of bovine-derived grafting materials and resorbable collagen membrane to treat horizontal defects, namely that long-term success may be possible when atrophic ridge augmentation is needed[15-18].

Narrow diameter implants (2.75 to 3.25 mm) have been proposed as a minimally invasive alternative to horizontal ridge augmentation in the posterior mandible[6,19]. Encouraging long-term results have been reported for narrow diameter implants splinted under a single prosthesis[20]. This type of procedure usually requires fewer surgical phases and tends to be more affordable than horizontal GBR. However, conclusions as to its efficacy have tended to be hampered by small sample sizes and short follow-up periods.

All implants were placed using guided bone regeneration in combination with computer-guided surgery. Combination of guided implant placement and guided surgery has been demonstrated to be a valid method[21,22]. A major benefit of computer-guided surgery is its prosthetically driven approach, which may contribute to less marginal bone loss in the medium-term follow-up period[23]. Although the implant survival rate was high throughout the long follow-up in this study, no comparison of bone levels can be made due to the lack of a control group. Randomized controlled trials with at least five years of follow-up are needed to compare one-stage horizontal GBR and implant placement with other minimally invasive techniques.

CONCLUSIONS

Despite the limitations of the present study, horizontal guided bone regeneration in combination with a resorbable membrane appears to be a valid and less invasive means of horizontally augmenting bone widths of between 4 mm and 6 mm at implant placement, with high long-term implant survival rates.

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