BioMed Research International

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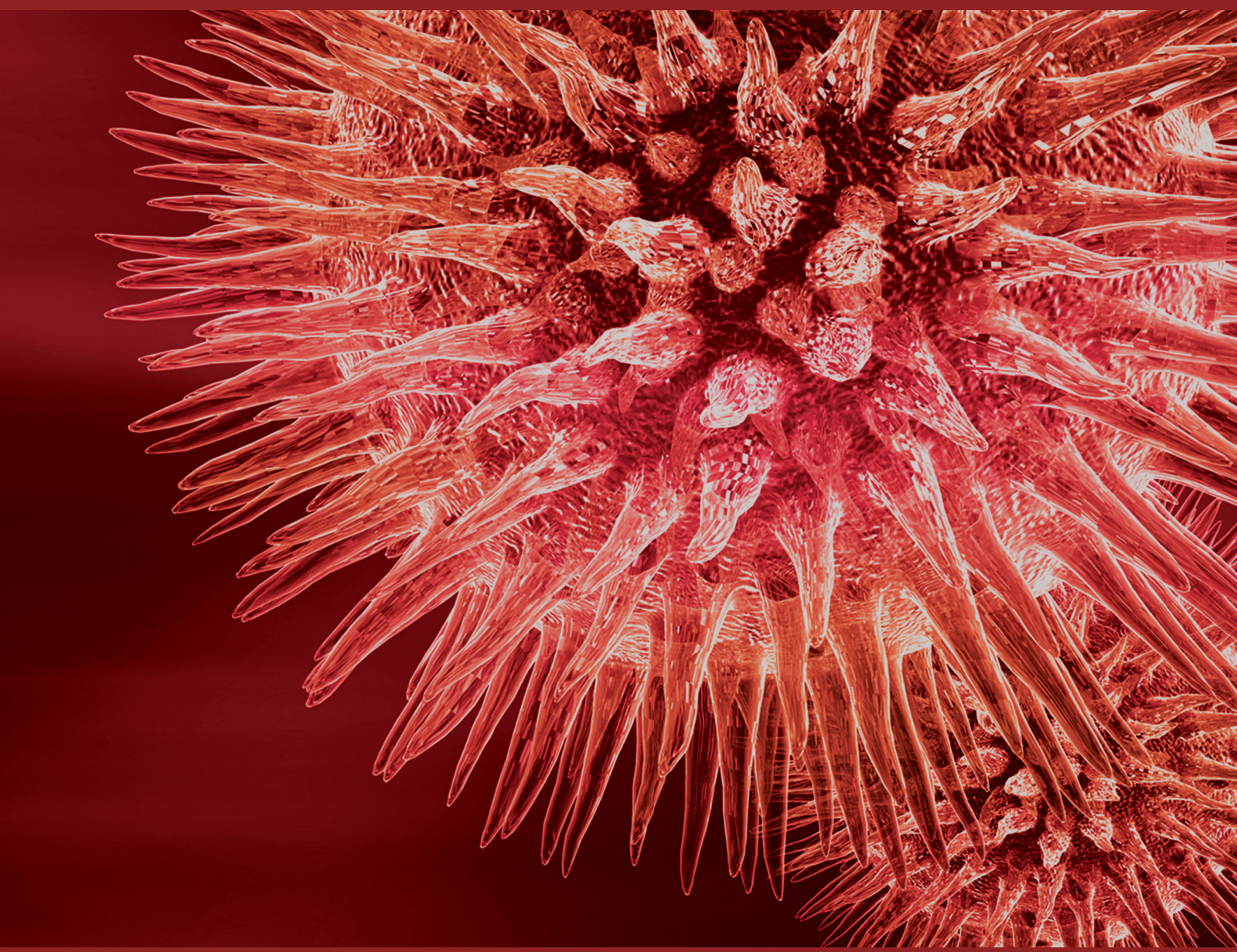
Guest Editors: Carmen Mortellaro, Sérgio Alexandre Gehrke, and Eitan Mijiritsky



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Editorial

Reconstructive and Regenerative Therapy of Atrophic Jaws with New Implant Techniques: Preclinical and Clinical Studies

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Nowadays, dental implants represent a reliable and successful procedure for the prosthetic restoration of partially and totally edentulous patients, with high survival and success rates in the short, medium, and long term.

However, a sufficient amount of bone—in terms of height and width of the residual bone crest—is needed to place dental implants in the proper position and inclination, to allow the placement of a biologically, functionally, and aesthetically integrated prosthetic restoration.

Therefore, in the last years, several bone regeneration techniques have been developed, to allow proper placement of dental implants and the successful prosthetic restorations of patients with different types of bone defects. Among these techniques, there are onlay/inlay block regeneration, guided bone regeneration (GBR) with membranes, split crest techniques, maxillary sinus augmentation, and many others.

The objective of the bone regeneration is to promote the formation of new bone, in order to reconstruct an atrophic alveolar ridge before or in conjunction with implant placement, through the use of different biomaterials (autografts, allografts, xenografts, and synthetic materials) alone or in conjunction with biostimulants (growth factors or stem cells).

At the moment, in the international scientific community, there is great interest in the surgical techniques used for bone regeneration, from the most conventional (x example, bone regeneration with autografts or allografts blocks, or GBR with membranes) to the most modern and revolutionary (such as regeneration with custom-made synthetic scaffolds obtained with the modern digital technologies).

Moreover, bone regeneration is related to technological development and the discovery of new materials. For example, the biological regeneration with platelet concentrates is today another important interdisciplinary field of research, in which engineering principles and basic sciences are used to develop biological substitutes that can repair and regenerate the function of bone tissue damaged by trauma, degenerative diseases.

Today, some progress has been made in specific surgical applications, such as GBR and maxillary sinus augmentation, that represent safe and predictable treatment procedures; the real "last challenge" of biomaterials research in dentistry appears to be the vertical bone regeneration through onlay blocks of different materials, supported by a valid blood perfusion that can guarantee that "biological push" that eases the regeneration process within the entire block.

In the present special issue you will find a collection of articles dealing with different strategies for the bone regeneration in dentistry and maxillofacial surgery.

Carmen Mortellaro
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Clinical Study

Maxillofacial Prosthesis in Dentofacial Traumas: A Retrospective Clinical Study and Introduction of New Classification Method

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Background. Maxillofacial trauma represents a field of common interest as regards both the maxillofacial surgery and prosthodontics, especially for the functional and aesthetic stomatognathic rehabilitation. This condition necessitates relationship between maxillofacial surgeon and prosthodontist, to achieve the ultimate treatment goal. *Purpose*. The purpose of this study is to make predictable patients outcomes classifying their clinical data, using certain parameters and introducing a new classification method. *Materials and Methods*. We have chosen 7 parameters to classify the entity of the damage of these patients and to make their treatment and their prognosis predictable: number of teeth lost (T1–T4), upper/lower maxilla (U/L), alveolar/basal bone (Alv/B), gingival tissues (G), soft tissues (S), adult/child (a/c), and reconstructed patient (R). *Results and Conclusions*. The multidisciplinary approach and the collaboration between multiple clinical figures are therefore critical for the success of the treatment of these patients. The presence and quantification of above parameters influence the treatment protocol; patients undergo different levels of treatment depending on the measured data. The recognition of certain clinical parameters is fundamental to frame diagnosis and successful treatment planning.

1. Introduction

Trauma is the leading cause of death in the first 40 years of life [1]. WHO Statistics indicate that 1 million people die and between 15 and 20 million are injured annually in road traffic accidents [1].

Craniomaxillofacial trauma is relatively common and the vast majority involve concomitant soft tissue injuries [2].

Management of these injuries includes treatment of facial bone fractures, dentoalveolar trauma, and soft tissue injuries, as well as associated injuries [3].

Maxillofacial trauma represents a field of common interest as regards both the maxillofacial surgery and prosthodontics, especially for the functional and aesthetic stomatognathic rehabilitation.

This condition necessitates relationship between maxillofacial surgeon and prosthodontist, to achieve the ultimate treatment goal.

Many variables must be considered during treating traumatized patients: age, sex, sites, etiology, concurrent loss of tissues, associated fractures, treatment modality, complications, and postoperative assessment and follow-up [4].

Epidemiologically most affected individuals are male (M : F 3 : 2) aged between 15 and 40 years [1, 5–8].

Premaxilla is the most affected area with regard to its particular anatomical conditions that predispose to increased exposure trauma.

For the same reason the incidence is doubled in subjects with a maxillary protrusion (2nd class first division).

Fractures of the jaws are frequently associated with dentoalveolar fractures: the association can take place indirectly through occlusion forced to concomitant low kinetic energy trauma (assaults, falls, and sports injuries) or directly as a result of traumatic events at high speed (traffic accidents, gunshot fire).

Table 1

Groups	Classification	Subgroups	Treatment
A (32)	T1-T2; Alv	—	Implants insertion +− contextual bone regeneration
B (13)	T3-T4; AlvB	B1 (10)	Bone graft from intraoral sites + implants insertion
		B2 (3)	Bone graft from other sites + implants insertion
C (5)	T3-T4; AlvB; S	—	Flap + implants insertion

The most common etiologic agents are represented by road accidents, assaults, falls, blows gunshot, sports injuries, or workplace injuries.

Other risk groups are epileptics, drug addicts, or patients receiving radiotherapy of the jaws.

Such injuries' outcomes represent a big challenge for maxillofacial and oral surgeons and in the end for the prosthodontist because the dentoalveolar defects can reduce the retention and stability of the prosthesis.

Prosthodontist has different treatment options to replace missing soft and hard tissues, including removable dental prostheses.

The options for a prosthetic rehabilitation are either the tooth-supported prosthesis or implant supported overdenture [9].

Concerning the rehabilitation choice between fixed and removable prosthesis, technical considerations are important, such as implant position, aesthetic result, or psychological considerations like acceptability of a removable prosthesis, and not less important, the economic possibilities [10]. However each rehabilitation proposal must be fitted on patient necessity and request.

Rehabilitation should be planned, when possible, before surgical treatment, in order to cooperate with the maxillofacial surgeon in choosing the most appropriate restorative treatment [11].

The purpose of this study is to make predictable patients outcomes classifying their clinical data, using certain parameters and introducing a new classification method.

2. Materials and Methods

This study is based on a retrospective review performed on 50 patients outcomes of trauma treated in Implantoprosthesis Unit of Head and Neck Department in "La Sapienza" University of Rome, Policlinico "Umberto I" (Table 1).

All the patients were rehabilitated in the period between 2008 and 2015 and received bone reconstruction, implant positioning, and fixed prosthesis. All the patients are in follow-up. All patients have inserted prosthesis at least six months before.

We have chosen 7 parameters to classify the entity of the damage of these patients and to make their treatment and their prognosis predictable: number of teeth lost (T1–T4), upper/lower maxilla (U/L), alveolar/basal bone (Alv/B), gingival tissues (G), soft tissues (S), adult/child (a/c), and reconstructed patient (R) (Table 2).

For prosthetic rehabilitation, we placed dental implants from three different manufacturers: "3i Biomet," "BioHorizons Laser-Lock tapered," and "Zimmer Trabecular Metal" implants.

Table 2

Parameters	Meaning	Classification
T	Number of teeth lost	T1 <2; T2 2-3; T3 4-5; T4 >5
U/L	Upper/lower maxilla	U; L; UL
Alv/B	Alveolar/basal bone	Alv; B; AlvB
G	Gingival tissue	G
S	Soft tissue	S
a/c	Adult/child	a; c
R	Reconstructed patient	R

All three kinds of implants have tapered body type and internal hex connection; the main differences are surface treatment that consists in three different technologies favoring osseointegration (NanoTite, Laser-Lock, and Trabecular Metal) and the tantalum composition of "Zimmer Trabecular Metal."

3i Biomet NanoTite implant's surface maximizes the potential biological benefits of Calcium Phosphate (CaP).

Laser-Lok is a series of precision-engineered cell-sized channels laser-machined onto the surface of dental implants and abutments that allows physical connective tissue attachment.

Zimmer Biomet's Trabecular Metal Material is a highly porous biomaterial made from elemental tantalum with structural, functional, and physiological properties similar to those of bone. This material features an open, engineered, and interconnected pore structure to support bony in-growth and vascularization.

We divided the 50 patients in 3 different groups (group A, group B, and group C) based on the amount of tissue loss suffered.

All implants received a prosthesis after 3 months from healing screws insertion.

32 patients (group A) were affected by dentoalveolar bone loss due to low kinetic energy traumas as falls and assaults. Each patient of this group lost no more than 3 teeth (T1-T2) in the same site and basal bone was not involved in fracture.

18 received immediate implant insertion; 14 necessitated bone regeneration using particulate bone and collagen membranes contextually to implant positioning.

In 16 cases we did not need bone regeneration so we placed the implants after 1 month from site reclamation. We used 21 "3i Biomet," 11 "BioHorizons Laser-Lock tapered," and 36 "Zimmer Trabecular Metal" implants for a total of 68

implants positioned. In 2 cases of this group we needed bone grafts contextual to implant positioning. Healing screws were inserted at 4 months from implant positioning. All implants received a prosthesis after 3 months from healing screws insertion.

14 patients necessitated primary guided bone regeneration (GBR) using particulate "Zimmer Copios bone" and "Zimmer Collagen membranes" rebuilt after 2 months on average from site reclamation.

In 11 cases we performed implant insertion after primary bone reconstruction simultaneously to a further bone graft during implant surgery; in 3 cases bone reconstruction was made in two steps.

After bone reconstruction we waited 6 months on average before implant positioning; in the 3 cases with a two-step reconstruction we waited 1 year.

We placed 27 "3i Biomet," 18 "BioHorizons Laser-Lock tapered," and 11 "Zimmer Trabecular Metal" implants for a total of 56 implants positioned.

Healing screws were inserted at 4 months from implant positioning.

All group A patients have 1-year follow-up with no complications.

13 patients (group B) were affected by basal bone loss and required reconstruction surgery primary to implant positioning. Each patient of this group lost more than 3 teeth (T3, T4). 10 patients (B1) received bone graft taken from intraoral sites as mandibular angle, symphysis, and retromolar. The remaining 3 patients (B2) needed major quantity of bone: it was taken from iliac crest, skullcap, and fibula.

So we placed 11 "3i Biomet," 9 "BioHorizons Laser-Lock tapered," and 29 "Zimmer Trabecular Metal" implants for a total of 49 implants positioned.

Healing screws were inserted at 4 months from implant positioning.

All implants received a prosthesis after 3 months from healing screws insertion.

All group B patients have 1-year follow-up with no complications.

5 patients (group C) have lost soft tissues, big portions of basal bone, and more than 5 teeth (T4). We performed a flap revascularized fibula. These patients had the more difficult prosthetic rehabilitation due to the big loss of tissues. So we designed a maxillofacial prosthesis comprising a primary structure supported by implants and a secondary structure with aesthetic and functional characteristics.

So we placed 8 "3i Biomet," 10 "BioHorizons Laser-Lock tapered," and 16 "Zimmer Trabecular Metal" implants for a total of 34 implants positioned.

Healing screws were inserted at 4 months from implant positioning.

All implants received a prosthesis after 3 months from healing screws insertion.

All group C patients have 1-year follow-up with no complications.

Evaluation included assessment of implant survival, mucositis, and peri-implantitis. Measurements of bone level changes were made clinically and radiologically by 3 different operators of the department, by evaluating bone level mesially and distally to each implant at implant placement, 4, 6, 12 months later. We measured the vertical distance from the neck of the implant to the crest of the surrounding bone tissue to evaluate peri-implant bone loss.

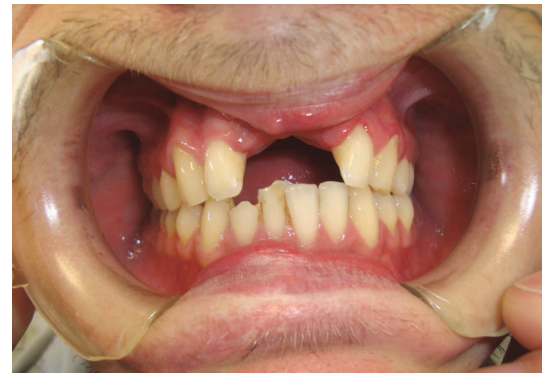


Figure 1

Each implant inserted underwent clinical examination in 5 different times:

(1) when entering with the execution of an intraoral X-ray and a torque control insertion;

(2) after 4 months during healing screws insertion with the execution of an intraoral X-ray;

(3) after 3 months from the inclusion of the healing screws with the execution of a rx intraoral and a peri-implant survey;

(4) after further 6 months by performing an intraoral X-ray and a peri-implant survey;

(5) last check 6 months later from the previous one with the aid of only peri-implant survey.

3. Results

3.1. Case 1: Group A. A 24-year-old male patient suffered a traumatic event using a circular saw.

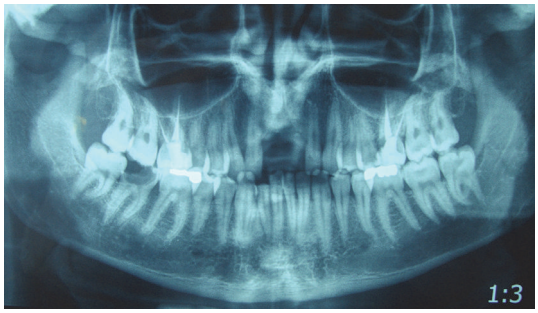
The injury caused the loss of teeth 1.1 and 2.1, and the loss of a portion of basal bone in premaxilla area, leaving an edentulous concave that extends 2 × 0,5 cm (Figure 1).

Rx orthopanoramic showed the extent and the type of bone loss, and so we required a CT cone-beam to study prosthetic rehabilitation (Figure 2).

The analysis of CT examination leads to the choice of the treatment plan, which includes the performance of a bone graft and 6 months later the insertion of two implants by "two-stage" technique.

Then a dental impression in alginate was taken to build a resin removable partial denture to rehabilitate the patient provisionally.

The regeneration is accomplished through the use of an allograft of bovine particulate bone ("Zimmer CopiOs bone") and a resorbable collagen membrane 20 × 30 mm ("Zimmer Collagen membrane"), while in second surgery 2 implants 4.1 mm × 11.5 mm were placed with trabecular morphology



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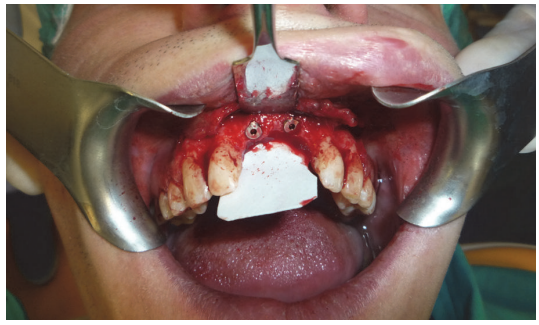

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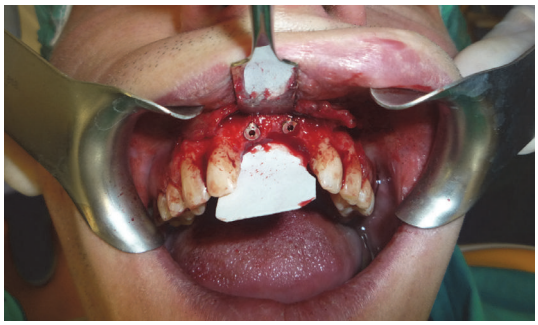


Figure 3

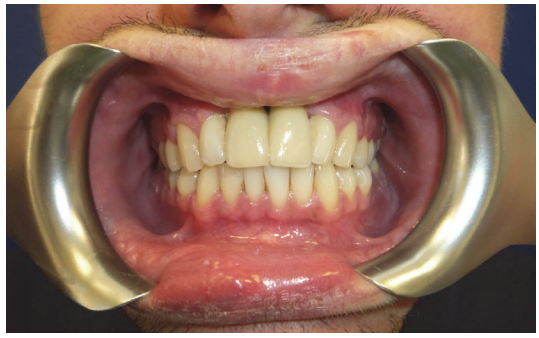


Figure 5

and tantalum coated ("Zimmer Trabecular Metal") (Figures 3 and 4).

Removable partial denture was modified to not load on inserted implants.

After 4 months healing screws were inserted, and 3 months later the patient was prosthesized by 2 zirconium crowns.

The entire dental treatment lasted 8 months; follow-up at one year was uneventful (Figure 5).

3.2. Case 2: Group B1. A 41-year-old female patient was wounded by a ballistic trauma that caused the loss of teeth 4.3, 4.2, 4.1, 3.1, and 3.2, the loss of a big portion of basal bone and gingiva in this area, and the loss of an eye (Figure 6).

At first, we took a dental impression in alginate to build a resin removable partial denture to rehabilitate the patient provisionally.

In collaboration with Maxillofacial Unit a treatment plan waiting 8 months from mandibular repositioning was scheduled which provided a surgical bone graft from intraoral sites and the subsequent implants placement (Figure 7).

At first surgery bone regeneration was performed taking the bone from the mandibular angle. After 9 months we placed 2 implants 3.7 mm × 11.5 mm "Zimmer Trabecular Metal" and 2 implants 4.1 mm × 13 mm "Zimmer Trabecular Metal" (Figure 8).

Removable partial denture was modified to not load on inserted implants.

In the same area a fornix depth was performed using a conformer to earn attached gingiva. After 4 months healing screws were inserted, and 3 months later the patient was prosthesized by 5 metal-ceramic crowns (Figure 9).

The entire dental treatment lasted 14 months; follow-up at one year was uneventful.

3.3. Case 3: Group B2. A 23-year-old female patient suffered multiple facial fractures due to a fall from a great height.

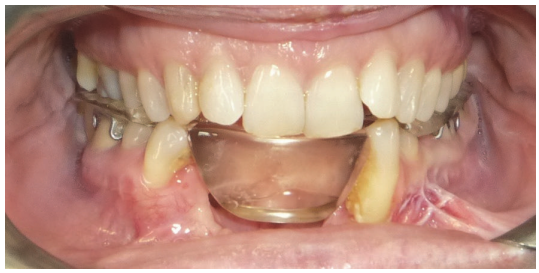
At first aid, CT showed both maxillary sinus' anterior and medial wall fractures with concomitant hemosinus, compound fracture of the right orbital floor, fracture of mandibular symphysis with involvement of alveolar processes, compound fracture of the right mandibular condyle with medial displacement of the proximal fragment, fracture of the left and front side of hard palate with involvement of the anterior alveolar process, and fractures of nasal septum and bones.

After establishing vital functions, the patient was operated on; surgery included reduction and contention of all fractures and concomitant extraction of 3.1, 3.2, 3.3, 3,4, 4.1, 4.2, 4.3, 4.4, and 4.5.

Nine months later the patient began prosthetic rehabilitation protocol; in fact she removed the restrains and surgery had success (Figure 10).

Then a dental impression was taken in alginate to build a resin removable partial denture to rehabilitate the patient provisionally (Figure 11).

A radiographic-surgery template was projected to give reference points to prosthodontist because the patient suffered a big loss of hard and soft tissue.



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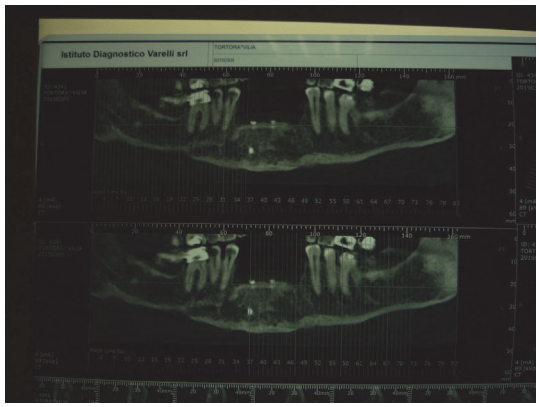

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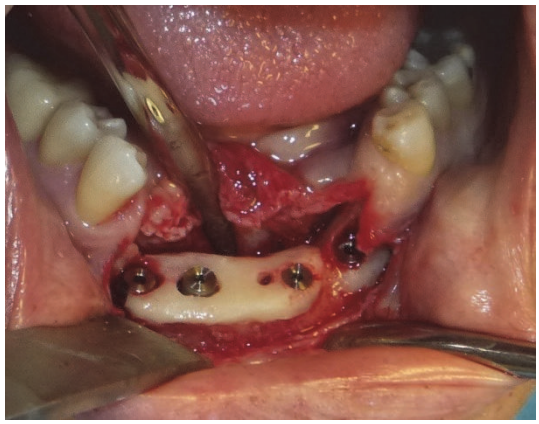

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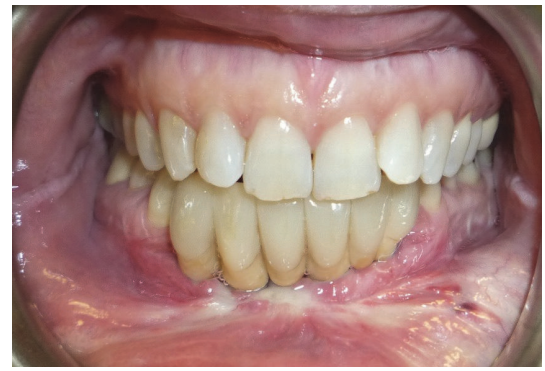

Figure 9

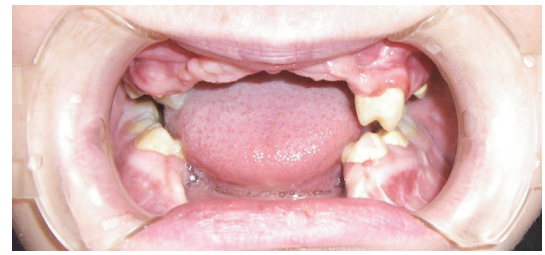

Figure 10

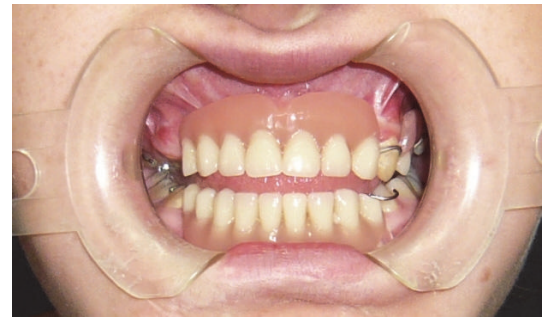

Figure 11

The CT cone-beam with template inserted showed us the quality and the quantity of bone directing choice of kind of implants and implants positioning.

The case study directed us to rehabilitate the patient by implant supported prosthesis consisting of 3 different components: a titanium base screwed on implants, a titanium structure (primary structure) assembled on the base, and a composite coated structure (secondary structure) that reproduced teeth and gum.

At first surgery we placed five implants "Zimmer Trabecular Metal" 4,7 × 11,5 mm in mandible and 8 implants "Zimmer Trabecular Metal" 4,1 × 10 mm in maxilla with simultaneous bone graft using "Zimmer CopiOs bone" and "Zimmer Collagen membrane" (Figures 12 and 13).

In mandible a fornix depth was performed using a conformer to earn attached gingiva.

After 4 months we inserted healing screws and after 6 months we started testing metal structure and teeth (Figure 14).

The entire dental treatment lasted 22 months; follow-up at one year was uneventful (Figure 15).

3.4. Case 4: Group C. A 29-year-old male patient was wounded by a ballistic trauma that caused the destruction of right premaxilla and of dental elements 1.1, 1.2, 1.3, 1.4, 1.5, and 2.1 and adjacent soft tissue.

The patient lost a big portion of labial soft tissue and showed a retracting and hypertrophic scar in this zone (Figures 16 and 17).

At first surgery the reconstruction of the area was performed by osteomyocutaneous fibula free flap. Four months

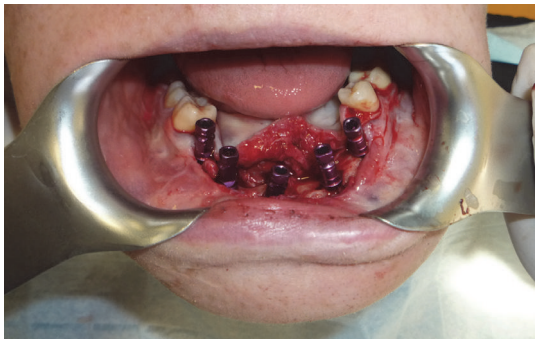

Figure 12

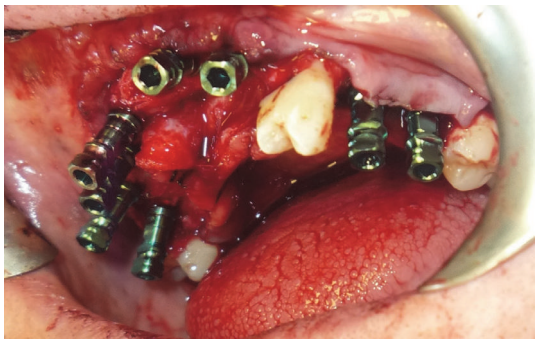

Figure 13

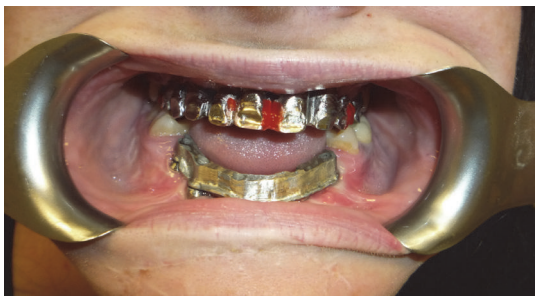

Figure 14

later the patient began prosthetic rehabilitation by implant supported prosthesis consisting of 3 different components: a titanium base screwed on implants, a titanium structure (primary structure) assembled on the base, and a composite coated structure (secondary structure) that reproduced teeth and gingiva.

Then a dental impression was taken in alginate to build a resin removable partial denture to rehabilitate the patient provisionally.

A radiographic-surgery template was projected to give reference points to prosthodontist because the patient suffered a big loss of hard and soft tissue due to the injury.

At second surgery we placed six implants "Zimmer Trabecular Metal" 4.1 × 10 mm in dental element loss position.

In a second step, the reconstruction of the upper lip using an Abbè mucocutaneous flap was performed (Figure 18).

After 4 months we inserted healing screws and after 6 months we started testing metal structure and teeth.

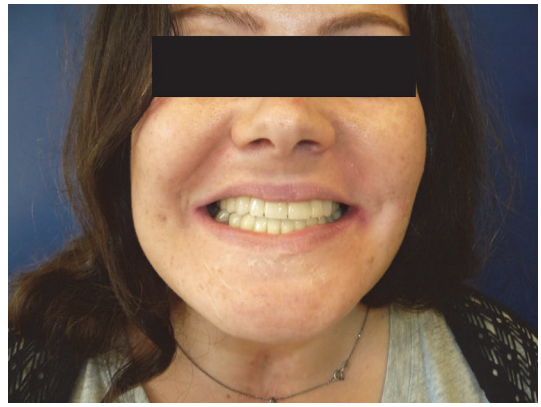

Figure 15

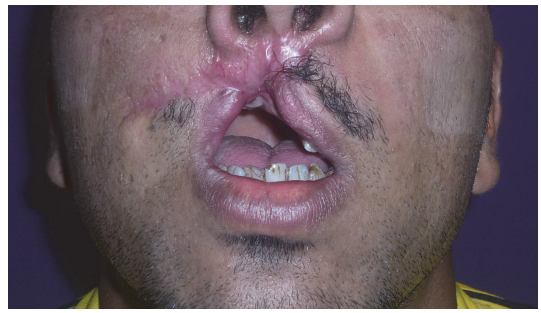

Figure 16

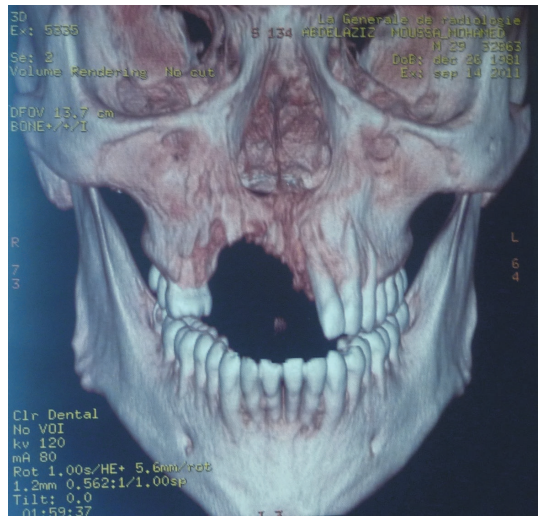

Figure 17

The entire dental treatment lasted 14 months; follow-up at one year was uneventful (Figure 19).

3.5. Clinical Evaluation. Cumulative implant survival rate in all groups (A, B1, B2, and C) is 97,1% (n = 201/207) to date and all implants had at least 12 months of clinical follow-up after functional loading.

6 implants (1 in group B1, 2 in group B2, and 3 in group C) were loss due to peri-implantitis.

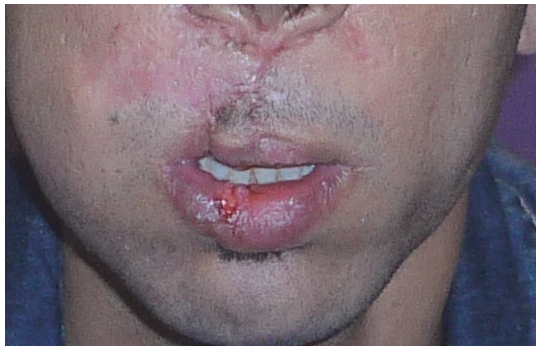

Figure 18

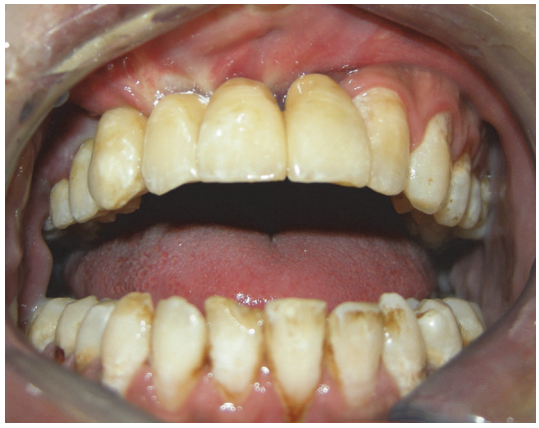

Figure 19

Mean crestal marginal bone loss was 0.17 ± 0.25 mm after 2 months of functional loading on periapical radiographs, 0.22 ± 0.4 mm at 4 months, 0.3 ± 0.46 at 6 months, and 0.58 ± 0.62 at 1 year.

Implant stability was evaluated by Periotest values at 6 months. The mean Periotest value and Standard Deviation for implant at 6 months were -2.15 ± 1.19 (group A), -2.21 ± 1.57 (group B1), -2.29 ± 1.70 (group B2), and -1.50 ± 1.62 (group C).

4. Discussion

During the treatment of the traumatized patients, prosthodontist finds a lot of variable pathologic situations that involve other medical specialties as maxillofacial surgery, plastic surgery, emergency surgery, otolaryngology, physiotherapy, speech therapy, orthopedics, and ophthalmology.

The multidisciplinary approach and the collaboration between multiple clinical figures are therefore critical for the success of the treatment of these patients.

The purpose of this study is to make predictable patients outcomes classifying their clinical data, using certain parameters and introducing a new classification method.

The decision to introduce a new classification comes from the complete separation in actual classifications between dental trauma and facial trauma, except Andreasen's classification [12].

Comparing and accumulating data from different studies is extremely difficult due to the differences in the definitions and classifications used [13].

Andreasen's classification represents the most complete classification containing 19 groups and includes injuries to the teeth, supporting structures, gingiva, and oral mucosa but does not include facial and rehabilitation features. It is a modification of World Heal Organization's (WHO) classification of dental trauma [14] that includes only injuries to the teeth and contains a group named "other injuries including laceration of oral soft tissues" that is misleading for investigating purposes.

Ellis' classification [15] and Garcia-Godoy's classification [16] are other modifications of WHO classification of dental trauma that also do not have groups about alveolar, maxilla, or mandibular trauma.

The most commonly used classification for describing facial fractures remains that classically described by LeFort [17], which alone yields insufficient information for fracture description and the complete planning of treatment [18].

Other classifications were described to supplement the LeFort description and were based on detailed descriptions of fractures of individual midfacial regions, such as orbitozygomatic fractures classified by Zingg et al. [19] and the nasoethmoid classification by Leipziger and Manson [20, 21].

Unfortunately all these classifications do not consider oral tissues and dental involvement.

In our classification proposal the presence and quantification of above parameters influence the treatment protocol; patients undergo different levels of treatment depending on the measured data.

The etiology of the trauma has a significant influence on clinical parameters; serious road accidents, falls from great heights, and ballistic trauma by firearms are the etiologic categories in which patients are more difficult to treat.

Our clinical experience allowed the formulation of this indexing to help physician to make predictable patients outcomes: common parameters of reference permit a better disease framing to treat patients strategically.

Treatment is influenced by the entity and by the presence of these clinical parameters: a greater number of lost teeth (T) require more time for prosthetic rehabilitation; basal bone damage (B) involves a lack of support for implants placement that need a bone graft or a reconstructive surgery; gingival tissue (G) could need a periodontal surgery intervention; soft tissue damage (S) could require a plastic surgery; and finally reconstructed patients (R) involve multidisciplinary approach and are more difficult to rehabilitate.

5. Conclusion

Facial traumas necessitate the collaboration between many clinical figures as maxillofacial surgeon, plastic surgeon, and prosthodontist. The multidisciplinary approach is helped by a painstaking clinical data collection. The recognition of certain clinical parameters is fundamental to frame diagnosis and successful treatment planning. Patients suffering soft tissues damage and reconstructed patients are the most difficult to rehabilitate. Predictability of patients outcomes

is the key to better plan traumatized patients. Soft tissues represent a subjective element of evaluation that can alter our parameters.

Ethical Approval

Ethical commission of University of Rome La Sapienza approved this work.

Consent

Written informed consent was obtained from our patient giving permission to publish this case report and accompanying images.

Competing Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

Acknowledgments

The authors thank the patients who allowed the publication of this case report.

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Clinical Study

Custom-Made Synthetic Scaffolds for Bone Reconstruction: A Retrospective, Multicenter Clinical Study on 15 Patients

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Purpose. To present a computer-assisted-design/computer-assisted-manufacturing (CAD/CAM) technique for the design, fabrication, and clinical application of custom-made synthetic scaffolds, for alveolar ridge augmentation. *Methods*. The CAD/CAM procedure consisted of (1) virtual planning/design of the custom-made scaffold; (2) milling of the scaffold into the exact size/shape from a preformed synthetic bone block; (3) reconstructive surgery. The main clinical/radiographic outcomes were vertical/horizontal bone gain, any biological complication, and implant survival. *Results*. Fifteen patients were selected who had been treated with a custom-made synthetic scaffold for ridge augmentation. The scaffolds closely matched the shape of the defects: this reduced the operation time and contributed to good healing. A few patients experienced biological complications, such as pain/swelling (2/15: 13.3%) and exposure of the scaffold (3/15: 20.0%); one of these had infection and complete graft loss. In all other patients, 8 months after reconstruction, a well-integrated newly formed bone was clinically available, and the radiographic evaluation revealed a mean vertical and horizontal bone gain of 2.1 ± 0.9 mm and 3.0 ± 1.0 mm, respectively. Fourteen implants were placed and restored with single crowns. The implant survival rate was 100%. *Conclusions*. Although positive outcomes have been found with custom-made synthetic scaffolds in alveolar ridge augmentation, further studies are needed to validate this technique.

1. Introduction

The rehabilitation of partial and total edentulism using dental implants is today considered a successful treatment procedure, with very high survival and success rates [1–3].

However, it is frequently the case that the available bone is not sufficient for a direct implant insertion. Maxillary/mandibular bone defects are rather frequent, as a result of different processes such as tooth loss, periodontal disease, trauma, and tumours [4, 5]. In all these cases, the placement of an implant in the correct three-dimensional (3D) position can be unachievable, and therefore the complete restoration of the function and aesthetics of the patient with an implant-supported restoration is impossible [4, 5].

Even if the literature has reported successful long-term results with the use of short [6, 7] and tilted implants [8] in regions with high bone resorption, the best option from a functional and aesthetic point of view remains to reconstruct the normal bone volume of the dentoalveolar process [5].

Many different techniques have been developed in order to reconstruct alveolar ridge defects and therefore allow the correct 3D insertion of dental implants [9–14]. Among the different procedures that can be used to regenerate bone defects are guided bone regeneration (GBR) with membranes [9], the application of onlay/inlay bone blocks [10, 11], maxillary sinus augmentation [12], and the use of bone distraction [13] or the split-crest technique [14].

Although all these surgical techniques can be successful in regenerating bone, the incidence of failures and problems that occur during these augmentation procedures is rather high [4, 5, 9–13]. In fact, these techniques are complex and require skill and experience from the operator; the operating time can be lengthy with major discomfort for the patient, and the risk of complications can be high [4–6, 9–13].

The most predictable material for regeneration of the dentoalveolar process is autogenous bone, due to its peculiar properties: it is in fact osteoinductive, osteoconductive, and inherently osteogenic [15]. However, this material requires harvesting from other anatomical sites (intra- or extra-orally); in order to reduce patients' discomfort and the complications related to the harvesting procedures, several bone substitutes have been introduced, such as allografts, xenografts, and, more recently, alloplasts [15, 16].

An ideal bone substitute should have excellent osteo-conductivity: in fact, it should be capable of guiding the growth and proliferation of osteoblasts onto its surface [16, 17]. Ideally, it should be osteoinductive too: it should stimulate the differentiation of mesenchymal stem cells into the osteoblastic lineage [17, 18].

Recently, the use of scaffolds made of synthetic alloplastic materials has gained attention [19]. Since the crystalline phase of natural bone is hydroxyapatite, synthetic ceramics are now frequently used as bone substitutes [19].

An ideal bone substitute should easily fit into the receiving site, with a perfect shape, obtained with simple procedures [20, 21]. With the conventional augmentation procedures, the blocks of different materials have to be manually adapted during the surgery [20–24]. This procedure is time-consuming and is highly dependent on the clinician's skill and experience. The complexity of these procedures can lead to the modification of the scaffold properties [20–24]; this can result in a gap between the scaffold and the natural bone that needs to be filled with particulate grafts.

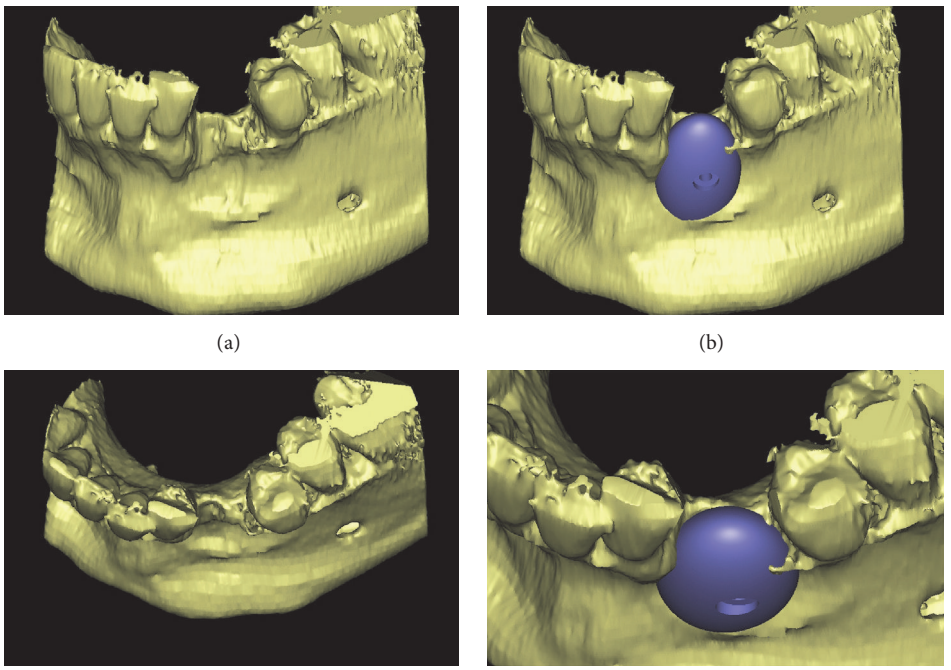
With the development of new digital technologies, it is now possible to analyse the bone defects in 3D and to customize bone grafts that fit perfectly into the receiving site [20–22]. In fact, the recent improvements in computer-guided technologies provide clinicians with the possibility of evaluating the size and shape of the bone defect in 3D, before the surgery, with the aid of a cone beam computed tomography (CBCT) examination [20–25]. CBCT files can be transferred to specific reconstruction software, where a 3D model of the maxilla/mandible of the patient can be easily obtained [25, 26]. Finally, a custom-made bone graft can be designed directly on this 3D model, using powerful computer-assisted-design (CAD) software [20, 21, 25, 26]. The custom-made bone graft is then milled with a computer-numeric-control (CNC) machine, in the selected material (allograft, xenograft, or alloplast), according to the file received from the 3D planning made by the surgeon [20, 21, 25, 26]. This custom-made bone graft will be easily adapted in the surgical site, with high accuracy: this approach can facilitate surgery, reducing the operative time and discomfort of the patient [20, 21, 25, 26].

The aim of the present retrospective clinical study is to report on the clinical and radiographic outcomes of bone reconstruction procedures performed with custom-made synthetic bone grafts, in three different clinical centres.

2. Materials and Methods

2.1. Inclusion and Exclusion Criteria. The data of the patients considered for inclusion in the present retrospective clinical study came from the dental records of two different private clinics (located, resp., in Gravedona, Como, and Rome, Italy) and from the database of the dental clinic of the Insubria University (Varese, Italy). Inclusion criteria for this retrospective study were patients with a single tooth gap in the anterior/posterior maxilla or mandible, with a residual bone width of 3-4 mm, associated with a 3-wall bone defect. All these patients needed bone augmentation, prior to allowing the proper placement of dental implants and the fabrication of a functional and aesthetically acceptable implant-supported restoration. Exclusion criteria were the presence of active periodontal disease or active infection at the surgical site; poor oral hygiene or hygienic compliance; heavy cigarette smoking (>15 cigarettes/day); treatment with bisphosphonates (intraoral and/or intravenous) and any medical/general condition that could contraindicate surgery (such as immunocompromised status, uncontrolled diabetes, chemotherapy/radiotherapy of the head/neck, hepatitis, and HIV). All patients received full information about the risks related to the treatment procedure and therefore signed an informed consent form. The local ethics committee approved the present study, which was conducted in accordance with the Declaration of Helsinki on experimental studies involving human subjects, as revised in 2008.

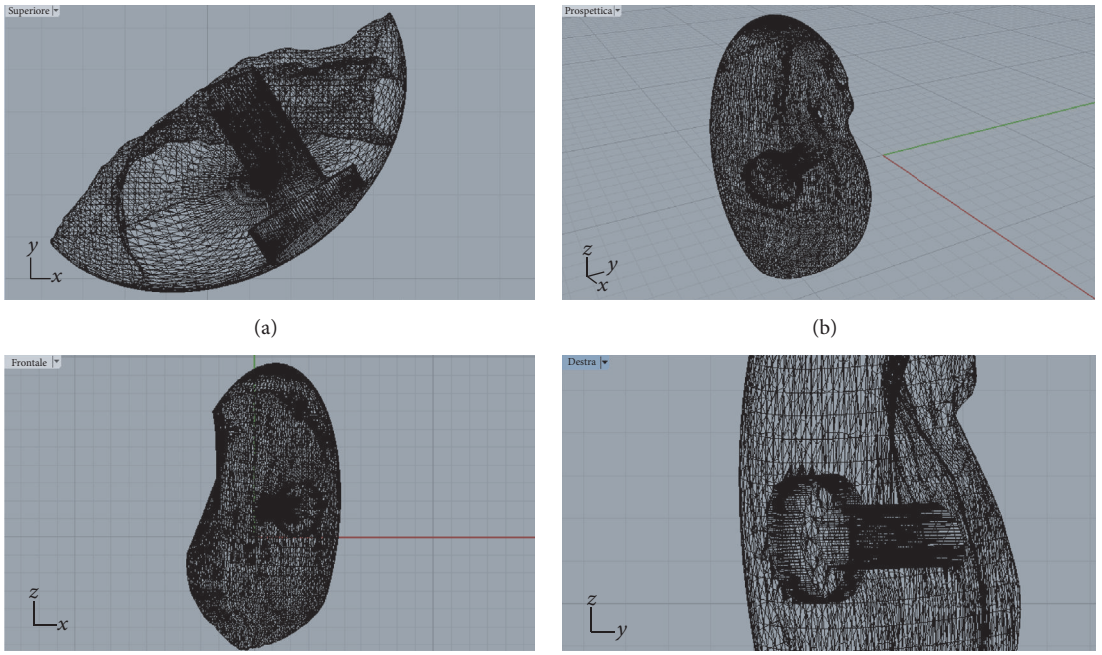
2.2. Data Acquisition and Elaboration. A careful assessment of the oral hard and soft tissues was performed on each patient. Panoramic and periapical radiographs were the primary investigation; after that, each patient underwent a CBCT examination, with a modern scanner (CS 9300, Carestream Health, Rochester, NY, USA). Different fields-of-view (FOV) were selected, according to the clinical indications. CBCT datasets of the partially edentulous ridges, acquired in the DICOM (Digital Imaging and Communications in Medicine) format, were then uploaded onto a proprietary 3D reconstruction software (Mimics, Materialise, Leuven, Belgium) where bone segmentation was carefully performed, using thresholding tools. A virtual model of the partially edentulous ridge was therefore obtained, where the bone defect was clearly visible, and a first drawing of the scaffold could be performed (Figures 1(a), 1(b), 1(c), and 1(d)); both these models were saved as a solid-to-layer (STL) files and then transferred to another proprietary CAD software (Rhino, Robert McNeel & Associates, Seattle, WA, USA). The aforementioned software allowed the completion of the 3D design of the anatomically-shaped, custom-made scaffold. This scaffold was designed with a hole in its centre (Figures 2(a), 2(b), 2(c), and 2(d)) to allow the placement of a fixation screw, saved again as an STL file and reimported into the Mimics software. Here, the correct size/shape of the scaffold was verified; in addition, the adaptation to the bone



(a) (b)

(c) (d)

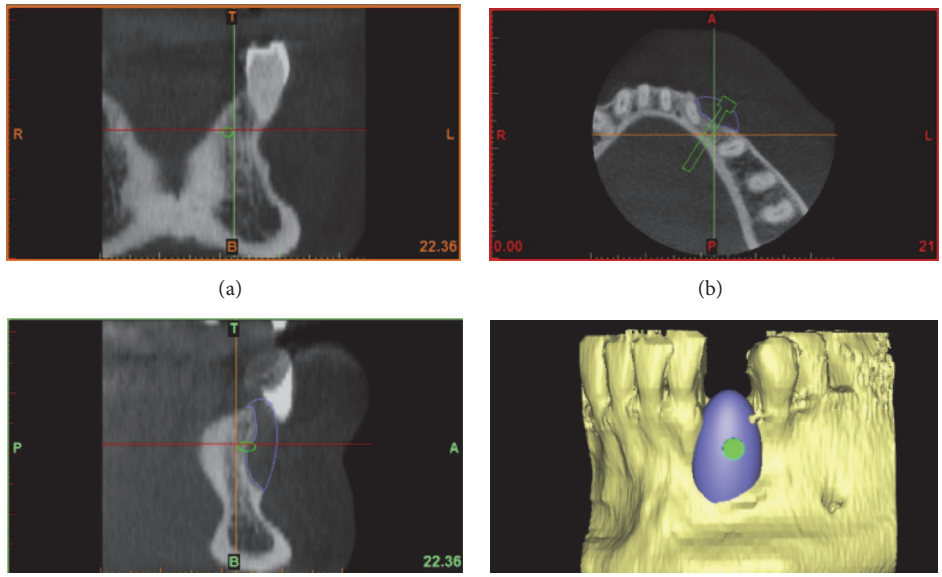
Figure 1: Virtual 3D model of the deficient ridge and first drawing of the customized scaffold (Mimics®, Materialise. Leuven, Belgium): (a) frontal view of the ridge without the customized scaffold; (b) frontal view of the ridge with the customized scaffold; (c) occlusal view of the ridge without the customized scaffold; (d) occlusal view of the ridge with the customized scaffold.



(a) (b)

(c) (d)

Figure 2: The customized synthetic scaffold was designed with a hole in its centre to allow the placement of a fixation screw (Rhino®, Robert McNeel & Associates, Seattle, WA, USA): (a-b-c-d) different views of the scaffold design.



(a) (b)

(c) (d)

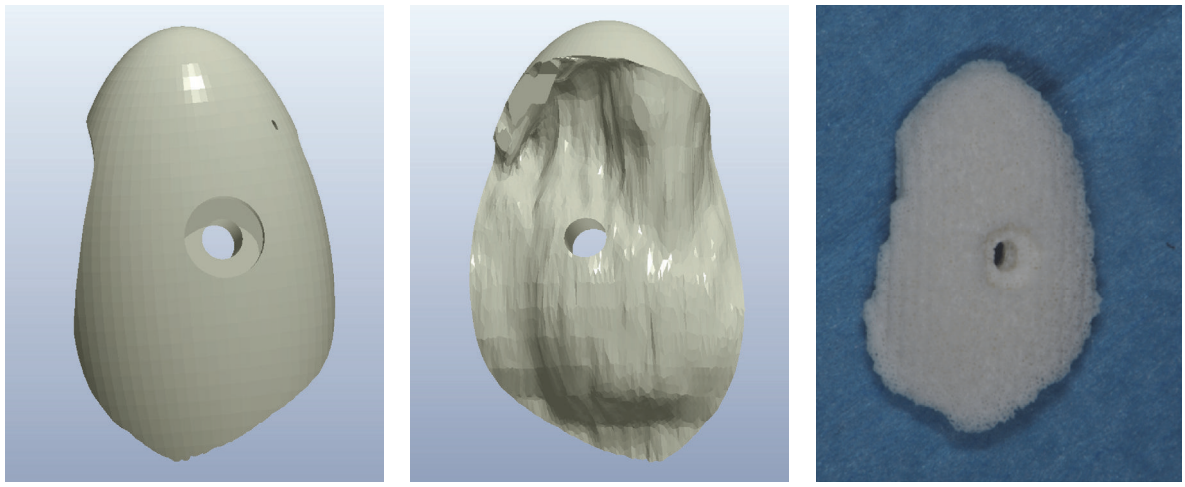
Figure 3: The proper size/shape of the customized scaffold was verified and the adaptation to the bone defect and the congruence with the bony walls was perfectioned (Mimics®, Materialise. Leuven, Belgium): (a) frontal view; (b) axial view; (c) lateral view; (d) 3D reconstruction.

defect and the congruence with the bony walls was perfected (Figures 3(a), 3(b), 3(c), and 3(d)).

2.3. Fabrication of the Customized Synthetic Scaffolds. The 3D virtual model of the custom-made scaffold was imported into a proprietary computer-assisted-manufacturing (CAM) software (Hyperdent, Open Mind Technologies AG, Wessling, Germany) and used to generate a set of tool-paths for fabrication by a proprietary CNC milling machine (DWX-51, Roland DG Mid Europe, Acquaviva Picena, AP, Italy). A synthetic micro-macroporous biphasic calcium-phosphate (BCP) block, consisting of 70% beta-tricalcium-phosphate and 30% hydroxyapatite (BTK, Dueville, Vicenza, Italy) was selected as the material of choice for the fabrication of the custom-made scaffolds. The block was therefore placed into the CNC milling machine, and milled into the size/shape of the 3D virtual model, so that a custom-made synthetic BCP scaffold was fabricated (Figures 4(a), 4(b), and 4(c)). The custom-made synthetic block was sterilised and it was therefore ready for clinical use.

2.4. Bone Reconstruction. After the injection of local anaesthesia, a full-thickness flap was elevated. The main incision (which was slightly palatal/lingual to the bone crest) was connected with two deep, lateral releasing incisions, in order to properly view the area of the defect. The bony architecture, and consequently the bone defect, was fully exposed. A series of small perforations, 1-2 mm deep, were made on the defect walls, in order to increase the amount of bleeding at the surgical site (Figure 5(a)). The custom-made, synthetic scaffold was then placed into position (Figure 5(b)) and fixed to the remaining wall by means of a titanium mini-screw, positioned through the predetermined hole (Figure 5(c)). Care was taken not to break the synthetic scaffold during fixation. An absorbable collagen membrane was used in order to protect the scaffold (Figure 5(d)). Before suturing, the mucoperiosteal flap was widely mobilised by means of a series of horizontal releasing incisions directly on the periosteum. The widely mobilised flap was thereby sutured in position, without any tension, by means of absorbable sutures. All patients were prescribed oral antibiotics, amoxicillin plus clavulanic acid, 1 gr every 12 hrs for an entire week. Postoperative pain was controlled with analgesics, 600 mg of Ibuprofen every 12 hours for the first 2/3 days. Finally, chlorexidine 0.12% mouth rinses were prescribed, 2/3 times a day for one week.

2.5. Implant Placement and Prosthetic Procedures. The sutures were removed 8–12 days after the surgery. An undisturbed 8-month healing protocol was strictly followed by all patients. During this healing period, the patients were not allowed to use any temporary removable partial denture, in order to avoid any possible compression on the regenerated area. Eight months after the regenerative surgery, the surgical site was exposed again, through the elevation of a full-thickness flap. The mini-screw used for fixation was removed, and the regenerated site showed an increased bone thickness with a considerable amount of new, well-integrated bone (Figures 6(a) and 6(b)). The surgical site was then prepared with a sequence of drills of ascending diameter and a screw-shaped dental implant was inserted (Figures 6(c) and 6(d)). The implant was located in the perfect 3D position, in a clinically well-integrated, regenerated bone (Figure 7(a)), as confirmed by the CBCT control examination (Figure 7(b)). Sutures were performed and the implants were left submerged for a period of 2-3 months. After this short healing period, the implant was uncovered: for the third time, a full-thickness surgical flap was raised (Figure 8(a)); the cover cap (Figure 8(b)) was



(a) (b) (c)

Figure 4: A block of synthetic micromacroporous biphasic calcium-phosphate (BCP), consisting of 70% beta-tricalcium-phosphate and 30% hydroxyapatite (BTK®, Dueville, Vicenza, Italy), was placed into the CNC milling machine (DWX-51®, Roland DG Mid Europe, Acquaviva Picena, AP, Italy) and milled into the size/shape of the 3D virtual model, so that a customised synthetic BCP scaffold was fabricated: (a) buccal aspect of the scaffold design; (b) lingual aspect of the scaffold design; (c) the milled customized scaffold ready for clinical use.

replaced by a transmucosal healing abutment (Figure 8(c)) and interrupted sutures were performed. Two weeks later, impressions were taken for the fabrication of a provisional resin restoration (Figure 8(d)). This temporary restoration remained in situ for a period of 2 months; then it was replaced by the definitive metal-ceramic or full-ceramic crown (Figures 9(a), 9(b), 9(c), and 9(d)). All temporary and definitive restorations were single crowns, cemented with a temporary zinc-eugenol cement (TempBond®, Kerr, Orange County, CA, USA). Occlusion was carefully checked intraorally, using articulating papers. All patients were placed on a 6-month maintenance program.

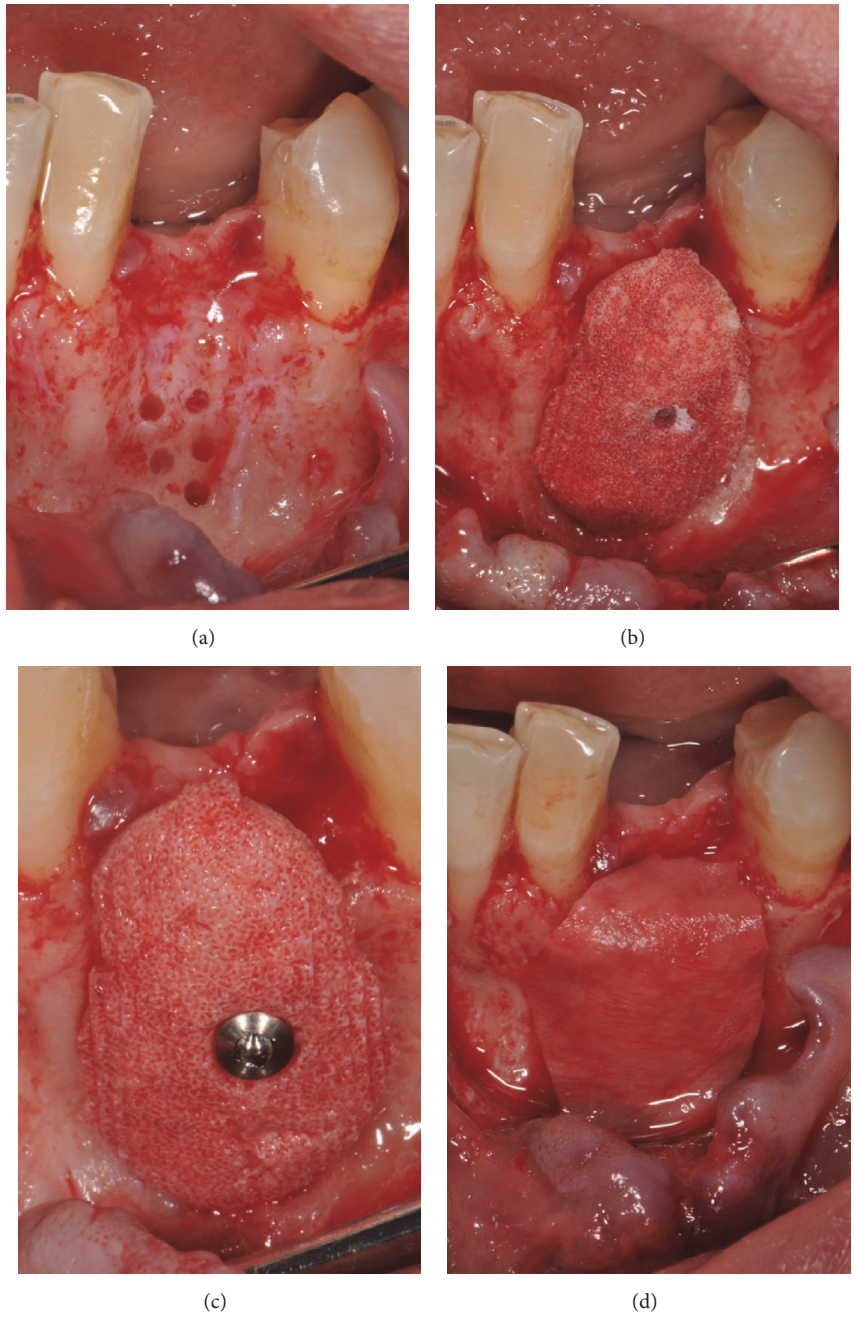
2.6. Clinical and Radiographic Outcomes. The main clinical and radiographic outcomes of the present study were vertical/horizontal bone gain, any biological complication occurring after bone reconstruction, and implant survival. All these outcomes were carefully checked, in all patients, 6 months after implant placement and at each subsequent follow-up appointment.

2.6.1. Vertical and Horizontal Bone Gain. The vertical and horizontal dimensions of the alveolar ridge were measured in the CBCT sections, before and 8 months after the reconstructive surgery, in mm. Before reconstructive surgery, one first linear measure was taken at the future implant location. Eight months later, immediately after the placement of the implants, the same measures were repeated at the same location. These second measures were registered; then the vertical and horizontal bone gain were calculated as the difference between the second and first measurements.

2.6.2. Implant Survival. At each follow-up control appointment, the single crowns were removed and the stability of the implants was tested. An implant was classified as a surviving implant if still in function, without any problem, at the last follow-up control. Conversely, absence of osseointegration with implant mobility, progressive marginal bone loss due to bacterial tissue invasion (peri-implantitis), and severe marginal bone loss in the absence of symptoms/signs of infection were the conditions in which an implant was considered failed and had to be removed.

2.6.3. Biological Complications. The biological complications were divided into early complications (i.e., complications that occurred *before* the implant placement, such as pain or discomfort after reconstructive surgery, edema, swelling, intra- or extra-oral contusion, early scaffold exposure and infection, with partial/complete loss of the graft) and late complications (i.e., complications that occurred *after* the placement of the implant, such as late graft dehiscence/exposure and infection, peri-implant mucositis, peri-implantitis, and any peri-implant bone loss without signs of infection). With regard to late biological complications, peri-implant mucositis was defined as an inflammation of the soft tissues around the implant, with pain/discomfort and swelling, but in absence of peri-implant bone loss [27]. Peri-implantitis was defined as a condition in which pain, suppuration, exudation, and fistula formation were present, with peri-implant marginal bone loss >2.5 mm and probing pocket depth ≥6 mm [27]. Peri-apical radiographs were taken, at different follow-up sessions, in order to evaluate the presence of any radiolucency around the fixtures.

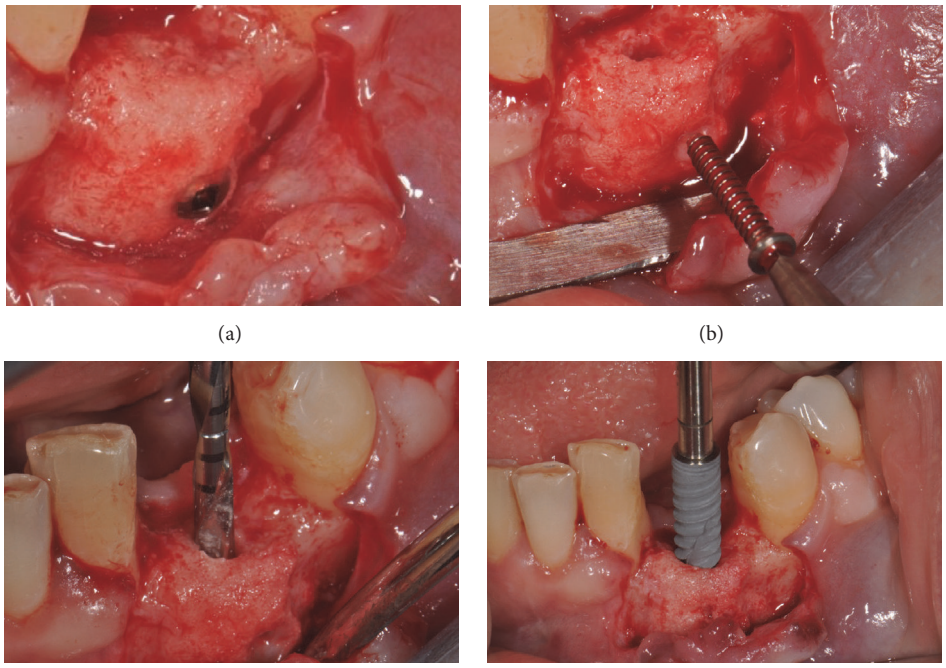
2.7. Statistical Evaluation. Patient demographics and distribution of implants were analysed using descriptive statistics. Means and standard deviations, ranges, and confidence intervals (95%) were calculated for quantitative variables, such as



(a) (b) (c) (d)

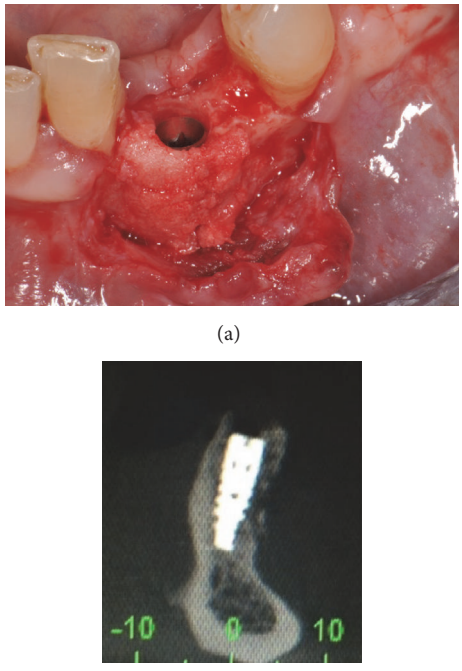
Figure 5: Bone reconstruction: (a) a full-thickness flap was elevated in order to fully expose the bone defect, and a series of little perforations, 1-2 mm deep, were made on the defect walls, in order to increase the amount of bleeding at the surgical site; (b) the customized synthetic scaffold was placed in position; (c) the scaffold was fixed to the remaining wall by means of a titanium mini-screw, positioned through the predetermined hole; (d) an absorbable collagen membrane was placed, in order to protect the scaffold.

patient age, and gain in vertical and horizontal dimensions of the alveolar ridge. Absolute and relative frequency distributions were calculated for qualitative variables, both patient-related (patient gender, smoking habit) and implant-related (implant site and position, type of prosthetic restoration). The incidence of early and late biological complications (pain/discomfort and edema/swelling after surgery, early/late scaffold exposures and/or infection, partial/complete graft loss, peri-implant mucositis, peri-implantitis, peri-implant bone loss in absence of clinical signs of infection) as well as the implant survival rate was calculated and expressed as percentages. All computations were carried out inside a dedicated datasheet (Excel 2003; Microsoft, Redmond, WA, USA).



(a) (b) (c) (d)

Figure 6: After 8 months from the regenerative surgery, the implant was placed: (a) after the elevation of a full-thickness flap, the regenerated site showed an increased bone thickness with a considerable amount of new, clinically well-integrated bone; (b) the mini-screw used for fixation was removed; (c) the preparation of the surgical site was performed with drills of increasing diameter; (d) a 3.5 diameter × 13 mm length implant (NobelActive®, Nobel Biocare, Kloten, Switzerland) was placed in the regenerated site.

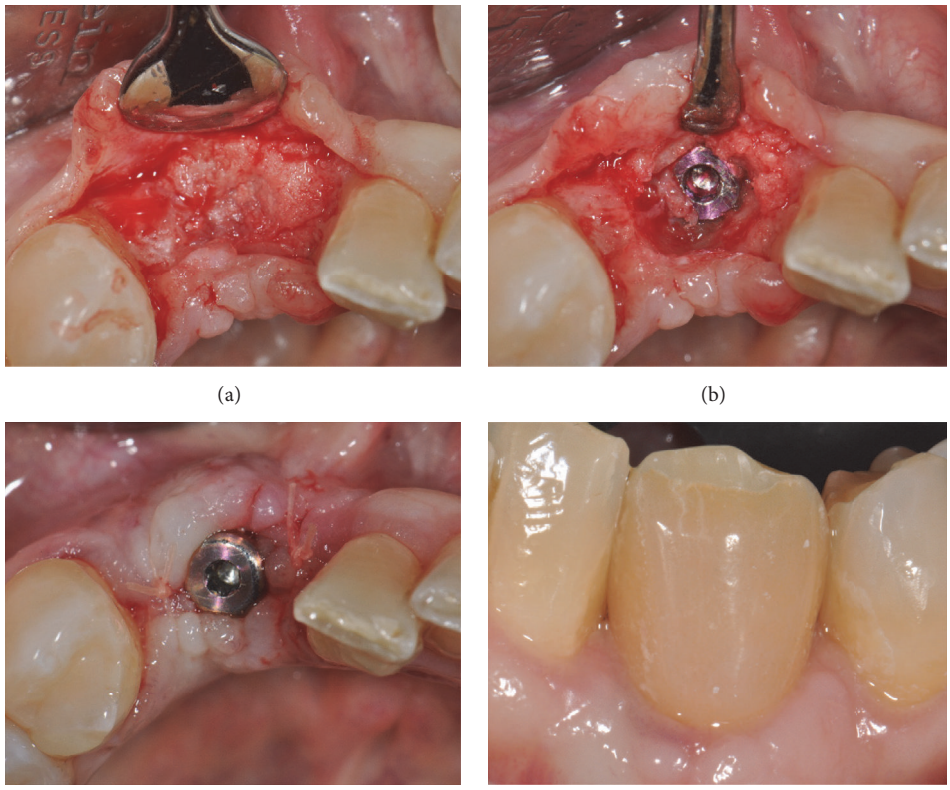


(a) (b)

Figure 7: The implant was located in the perfect 3D position: (a) it was placed in a clinically well-integrated, regenerated bone; (b) as confirmed by the CBCT control examination.

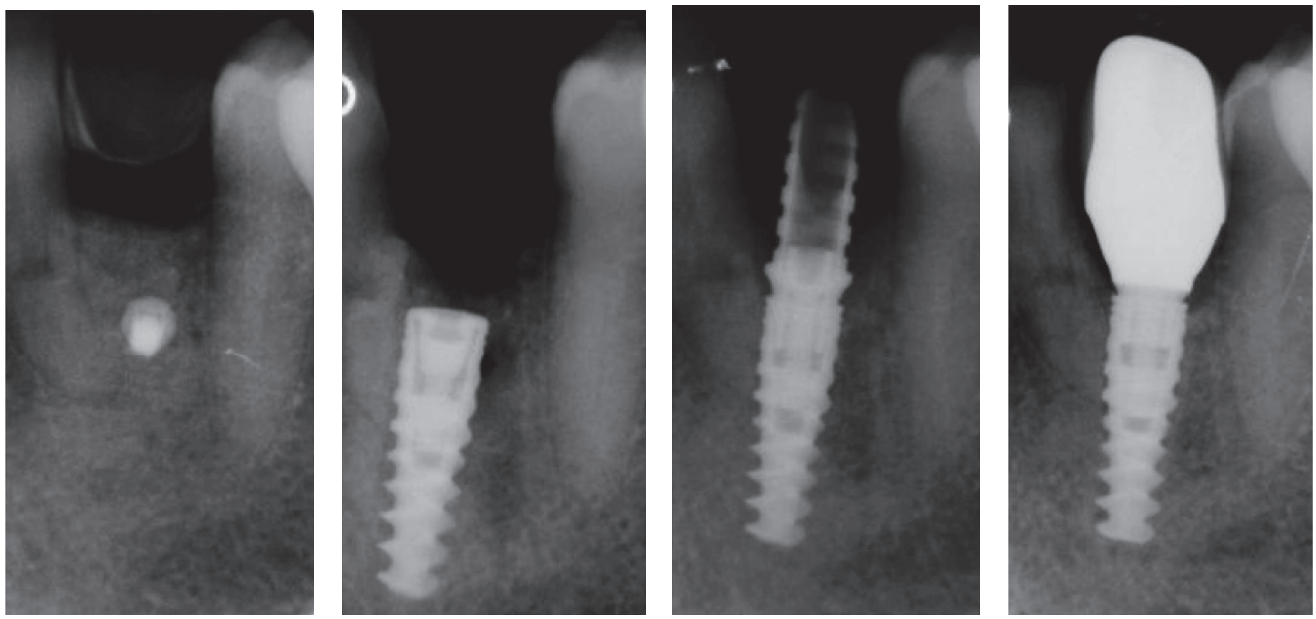
3. Results

Fifteen patients (6 males and 9 females; aged between 48 and 65 years, mean age 54.2 ± 5.5 years, median 55, confidence interval 95%: 51.5–56.9) were selected for the present clinical retrospective study. Among these, four were smokers (4/15: 26.6%). All patients had been treated with a custom-made synthetic scaffold over a 7-year period, between January 2007 and January 2014; therefore the follow-up varied from 2 to 8 years (with a mean follow-up time of 4.7 years). In all patients, the regenerative surgical procedure went well. In fact, the custom-made synthetic scaffolds perfectly fitted in the bone anatomy and were therefore easily adapted to the bone defects during surgery, secured by titanium mini-screws. This excellent matching of the size/shape helped the surgeon to reduce the operation time. The healing period was uneventful for 10 patients. Five patients, however, experienced early biological complications. In fact, two of these patients (2/15: 13.3%) had mild pain and slight edema/swelling in the first week after surgery. These light symptoms/signs disappeared within two weeks. However, in the other three patients (3/15: 20.0%), early exposure of the custom-made synthetic bone graft occurred, 1, 3, and 5 months after the reconstructive surgery, respectively. These early exposures forced the surgeon to open a new full-thickness flap and to remove part of the synthetic scaffold, with the aid of a piezo-electric device. The surface of the graft was carefully cleaned, and the flap was sutured over



(a) (b) (c) (d)

Figure 8: After being submerged for a period of 2-3 months, the implant was uncovered and a prosthetic restoration was placed: (a) a full-thickness surgical flap was raised; (b) the implant was uncovered; (c) the cover cap was replaced by a transmucosal healing abutment and interrupted sutures were performed; (d) two weeks later, the provisional crown was placed.



(a) (b) (c) (d)

Figure 9: Radiographic history of the case: (a) periapical rx taken immediately after the reconstructive procedure; (b) periapical rx taken immediately after implant placement; (c) the implant during the provisional phase, 4 months after placement of the fixture; (d) final rx control of the definitive crown, 3 years after implant placement.

it. All these patients were asked to apply 1% chlorhexidine gel, 2 times per day, over the site and were instructed to rinse with 0.12% chlorhexidine, 3 times per day, for a period of 1 week. After this treatment, two of the exposures were resolved with complete reepithelization of the areas and soft tissue closure, in a period of between 2-3 weeks: these early exposures did not prevent proper graft incorporation and consolidation into native bone. However, one of the exposures (1/15: 6.6%) could not be solved and determined the infection and complete loss of the graft, 5 months after surgery, in a 59-year old male smoking patient. In all the 14 remaining patients, after the 8-month healing period, a newly formed, well-incorporated bone was observed, completely filling the bony defects and therefore allowing the placement of an implant in the proper position. After 8 months, the CBCT evaluation revealed a mean vertical bone gain of 2.1 ± 0.9 mm (range 0–3.3 mm, median 2.4 mm, CI 95%: 1.7–2.5 mm) combined with a mean horizontal bone gain of 3.0 ± 1.0 mm (range 0–4.5 mm, median 3.2 mm, CI 95%: 2.5–3.5 mm). In total, 14 implants were successfully placed (6 in the anterior maxilla, 4 in the posterior maxilla, and 4 in the anterior mandible). All these implants (14/14: 100%) were restored with single crowns. No further (late) biological complications were reported, and an implant survival rate of 100% (14/14 surviving implants) was found.

4. Discussion

The use of implants for supporting dental prostheses is continuously expanding and it is estimated that the market will have the same trend in the future [1–3].

One of the main limitations of the implant treatment is the unavailability of adequate bone support, mainly caused by periodontal disease, but also as a result of tooth agenesis, traumatic injuries, or other lesions (cysts, tumors) [4, 5].

Many different surgical reconstructive techniques have been introduced in order to reestablish an adequate bone volume and allow proper implant placement [9–14]: among these, alveolar ridge augmentation by means of onlay/inlay bone blocks [10, 11], as well as GBR [9, 28], maxillary sinus elevation [12, 29], and split-crest [14] are the most popular.

Autogenous bone is still considered the material of choice in bone augmentation procedures [15]. However, the use of this material has disadvantages: the need for an additional surgical site, the more invasive procedure, the quantitative limit of bone that can be harvested from the donor site, and the morbidity for the patient [4, 16, 30]. For this reason, different materials have been proposed as possible alternatives, such as allografts [31] and xenografts [32]. Although both allografts and xenografts have been extensively used in bone reconstruction procedures [31, 32], the use of these materials will probably be restricted in future, because they may carry the risk of disease transmission: the processes for their preparation and sterilization might not totally exclude the presence of active viruses or prions [33, 34].

More recently, synthetic bone grafts (alloplasts) have been introduced, in order to overcome these limitations [19, 33–35]. The fundamental properties that a synthetic material should possess are biocompatibility, bioresorbability, and the presence of an architecture/structure similar to that of natural bone: the internal geometry of the biomaterial is, in fact, crucial for the biological behaviour and for promoting new bone formation [16–19, 35]. The modern synthetic porous scaffolds possess a controlled, high porosity and they have a honeycomb structure with several interconnections between different pores [16–19]. This peculiar architecture has proven to be able to stimulate differentiation of mesenchymal cells into functional osteoblasts and finally to promote new bone apposition [16–19]. In addition, the apatite porous spaces and concavities may represent a good microenvironment for angiogenesis, which is fundamental to bring cells and soluble signals like growth factors, and to sustain the regenerative process; angiogenesis is a prerequisite for osteogenesis [16–19].

Blocks of synthetic biomaterials are already available in the market. However, these blocks are prepared in preformed size/shapes and need to be adapted to the patient's bone defect during the surgery [20, 21, 23, 24]. The manual preparation of the required size/shape and the adaptation of these blocks to the bone defect are difficult for the surgeon and may lead to various risks such as the unsatisfactory stabilization/integration of the biomaterial block with the native bone, mobility, and failure of the entire procedure [20, 21, 23, 24]. Moreover, the manual adaptation of the graft greatly increases the time of surgery [23, 24].

Nowadays, modern digital technologies allow the surgeon to virtually design and then fabricate custom-made synthetic porous scaffolds, for use in bone reconstructive procedures [20, 23–26, 36]. In different medical fields, several studies have demonstrated that the combination of modern image acquisition techniques with 3D reconstruction software allows the clinician to obtain custom-made scaffolds for the regeneration of bone structures [20, 23–26, 36–40]. This powerful combination allows the surgeon to virtually plan the reconstruction of an atrophic bone area on his/her computer and to fabricate a custom-made biocompatible scaffold designing its size, thickness, and shape [20, 23–26, 36–40]. The fabrication of the scaffold can be obtained by milling blocks of synthetic bone substitutes that mimic the structure of natural bone and therefore promote the formation of new bone when implanted in the area of defect [36–40].

The CAD/CAM procedure for the fabrication and application of custom-made synthetic scaffolds can be divided into three different steps: the virtual planning and design of the scaffold, the milling of the scaffold into the exact size/shape from a preformed synthetic bone block, and, finally, the reconstructive surgery [20, 21, 24, 26]. The first step starts with a CBCT scan of the interested jaw and the upload of scan data into a 3D reconstruction software [20, 21]. This dedicated software allows the surgeon to analyse the defect area; with the aid of another reverse-engineering software, the virtual reconstruction is finalised [20, 21, 24, 26]. The second step is to transfer the files of the virtual scaffold into a milling machine, where the fabrication process starts, from a preformed standardized synthetic bone block [20, 21, 24, 26]. As soon as the custom-made scaffold is ready, it is sterilised

and finally delivered to the surgeon for the clinical application [24, 26].

Jacotti et al. [22] reported on the reconstruction of the atrophic right posterior mandible of a 48-year-old woman, using a dehydrated homologous bone block, shaped with a CAD/CAM technique. The CAD/CAM technique was aimed at avoiding the harvesting of autologous bone block and at assuring a perfect fitting of the block above the alveolar crest [22]. The CAD/CAM technique was successful, with an horizontal bone gain of 6.0, 7.3, and 8.0 mm (mean, 7.18 mm) at sites 6, 12, and 18 mm posterior to the right mental foramen, respectively, 7 months after the reconstructive surgery [22]. Similar results were reported by Figliuzzi et al. [21] for reconstruction of vertical bone defects of the posterior mandible. In this clinical research article, the accuracy of the CAD/CAM scaffolds helped to reduce the time for the operation and contributed to the good healing of the defects; in fact, 6 months after the surgery, a newly formed and well-integrated bone was observed, completely filling the mandibular posterior defects [21]. Accordingly, implants were placed with good primary stability [21]. After 1 year of function, the implant-supported restorations showed no complication, with an excellent biological and esthetic integration [21]. In a case report and review of the literature, Garagiola et al. [36] confirmed the time efficiency and reliability of these CAD/CAM procedures.

In our present study, we have reported on the clinical and radiographic outcomes obtained with this innovative, CAD/CAM procedure for alveolar ridge augmentation. From a surgical point of view, the custom-made synthetic scaffolds were of satisfactory size, shape, and appearance; they matched the defect area, suited the surgeon's requirements, and were easily implanted. This perfect match contributed to reducing the time for surgery and to the good healing of the bone defect. Only a limited number of patients experienced biological complications, such as pain/swelling (2/15: 13.3%) and exposure of the scaffold (3/15: 20.0%); one of these patients, however, experienced infection of the scaffold and complete graft loss. In all other patients, 8 months after reconstruction, a well-integrated newly formed bone was clinically available, and the CBCT evaluation revealed a mean vertical and horizontal bone gain of 2.1 ± 0.9 mm and 3.0 ± 1.0 mm, respectively. Fourteen implants were placed and restored with single crowns. The implant survival rate was 100%.

The present CAD/CAM technique for the fabrication of custom-made synthetic scaffolds for alveolar ridge reconstruction undoubtedly has varied benefits: in fact, the accurate reproduction of the patient's anatomy helps to reduce the time needed for the surgical procedure and therefore the morbidity and risk of infection for the patient [20, 21, 24, 26]. In addition, the increased stability of the bone block may contribute to faster and better bone healing and graft incorporation/consolidation [20, 21, 24, 26]. No gaps were evidenced between the custom-made synthetic scaffolds and the natural bone during the surgery.

However, this procedure has limitations. As reported by the current literature, for a successful alveolar ridge augmentation it is necessary to achieve a perfect fit of the bone block, a precise stabilization of the graft but also a well vascularized bone bed [20, 21]. The custom-made scaffolds can certainly help to obtain an excellent fit and stability of the graft; however, they must be limited in dimensions, to allow for proper cellular and vascular penetration [20, 21, 24]. If the graft is too big, in fact, the vascular penetration cannot be completed and there is the possibility of early or late graft exposure, with high risk of infection of the graft: in this sense, there is no difference between the present CAD/CAM technique and the more conventional techniques using onlay grafts for alveolar ridge augmentation. In the present study, the graft bed had been prepared using small perforations, 1-2 mm deep, on the bony walls, in order to increase the amount of bleeding. It is clear that the larger the graft is, the more difficult it is for cells and vessels to colonize it. In the present study, we did not treat defects wider than 12 mm in height and 10 mm in width; in addition, patients had 3-wall bone defects. Despite this, the present procedure presented a rather high percentage of biological complications, such as early graft exposure (20%). The exposure of the synthetic scaffold must be considered an adverse event and a difficult complication to manage: in fact, it can lead to partial or complete loss of the graft [20, 21]. In the last few years, several synthetic scaffolds with different macro- and microporosity and geometry have been introduced [16–19, 35]. These materials can certainly improve the healing processes; however, the perfect characteristics for a synthetic porous scaffold still need to be elucidated. When future innovations provide the possibility to seed customized scaffolds with components such as growth factors and stem cells, the indication of this procedure might be extended to bigger defects [26, 37, 39]. Another limitation of the present surgical technique for alveolar ridge augmentation is that it requires a high level of surgical skill, particularly with regard to the ability to properly treat soft tissues [20, 26]. Once again, in this sense, there is no difference compared to the more conventional techniques. In fact, a tension-free primary closure of the flap is essential, in order to avoid exposure of the synthetic scaffold. An early (or late) exposure may, in fact, jeopardize the success of the regenerative procedure [20, 26]. Lastly, the final limitation of the present CAD/CAM technique is related to the presence of metal crowns or amalgam restorations close to the area to be reconstructed [20, 26]. When the images from the CBCT are inserted in the software for the treatment planning, the metal artifacts might not allow the clinician to clearly identify the margins of the bone defect: this may potentially lead to an inappropriate design of the scaffold and consequently to a poor clinical adaptation.

Although the procedure for the design, fabrication, and clinical application of custom-made synthetic bone grafts described here presents the aforementioned limitations, our present positive clinical and radiographic outcomes seem to suggest it as a possible alternative to conventional surgical techniques, such as alveolar ridge augmentation with onlay/inlay autogenous bone blocks [20, 21, 26]. It is important, however, to point out the inherent limits of our present study. In fact, it is retrospective in design and the conclusions are based on a limited number of patients (15). Further studies with a larger patient sample and with a more appropriate design (prospective controlled studies or even

better, randomized controlled trials) are needed to confirm the positive outcomes emerging from our investigation.

5. Conclusions

In the present retrospective clinical study, we have presented an innovative CAD/CAM technique for the design, fabrication, and clinical application of custom-made synthetic bone grafts, for alveolar ridge augmentation. Although positive clinical and radiographic outcomes have been found in this study, with an excellent fit of the scaffolds during surgery and a well-integrated newly formed bone clinically available 8 months after bone reconstruction, a rather high incidence of biological complications, such as early graft exposure (20%), were reported. Further studies with a larger patient sample and an appropriate design (such as prospective studies or randomized controlled trials) are therefore needed to draw specific conclusions about the reliability of the present technique and to confirm our positive clinical and radiographic outcomes.

Competing Interests

No conflict of interests is reported for this study, since the authors have not received any kind of support (financial support or supply of materials from industrial companies) for the realisation of the present clinical investigation.

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Research Article

The Synergistic Effect of Leukocyte Platelet-Rich Fibrin and Micrometer/Nanometer Surface Texturing on Bone Healing around Immediately Placed Implants: An Experimental Study in Dogs

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Aims. This study evaluated the effects of L-PRF presence and implant surface texture on bone healing around immediately placed implants. *Methods*. The first mandibular molars of 8 beagle dogs were bilaterally extracted, and implants (Blossom™, Intra-Lock International, Boca Raton, FL) were placed in the mesial or distal extraction sockets in an interpolated fashion per animal. Two implant surfaces were distributed per sockets: (1) dual acid-etched (DAE, micrometer scale textured) and (2) micrometer/nanometer scale textured (Ossean™ surface). L-PRF (Intraspin system, Intra-Lock International) was placed in a split-mouth design to fill the macrogap between implant and socket walls on one side of the mandible. The contralateral side received implants without L-PRF. A mixed-model ANOVA (at $\alpha = 0.05$) evaluated the effect of implant surface, presence of L-PRF, and socket position (mesial or distal), individually or in combination on bone area fraction occupancy (BAFO). *Results*. BAFO values were significantly higher for the Ossean relative to the DAE surface on the larger mesial socket. The presence of L-PRF resulted in higher BAFO. The Ossean surface and L-PRF presence resulted in significantly higher BAFO. *Conclusion*. L-PRF and the micro-/nanometer scale textured surface resulted in increased bone formation around immediately placed implants.

1. Introduction

The phenomenon of osseointegration has allowed multiple specialties in dentistry and medicine to better rehabilitate form and function of a multitude of clinical scenarios that include tissue loss due to pathology or trauma. In dentistry, one of the most commonly encountered clinical situations is progressive alveolar bone loss that occurs after tooth extraction. It has been well characterized that this progressive loss may substantially reduce the ridge dimensions prior

to implant placement resulting in less favorable clinical conditions both functionally and aesthetically, before an implant is placed on the healed ridge [1–3].

In an attempt to improve the distribution and quantity of bone present around implants, along with decreasing treatment time for final prosthetic rehabilitation, minimally traumatic extraction techniques followed by immediate implant placement have been widely utilized and investigated [4–6]. Given the large number of preclinical and clinical investigations on this topic available in the literature, manuscripts have focused on currently utilized techniques and biomaterials associated, to systematically review survival outcomes and success of bone augmentation procedures, and most recently on esthetic outcomes [4–6].

Regardless of the surgical technique utilized, it is unequivocal that the extraction socket cervical dimensions are larger than the implant diameter and that a gap is going to be present between the implant and extraction socket walls [6]. Hence, a blood clot that forms between implant and socket walls and woven bone formation bridging the gap between implant allows for structural continuity between bone in intimate contact with surface and new bone formed due to socket healing [1–3, 7].

While this gap may be bridged with new bone forming within the extraction socket, several reports indicate that grafting procedures may be indicated to avoid soft tissue downgrowth between implant and the socket walls [8–11]. The graft material can be associated or not with a barrier membrane. This approach has been shown in both animal and clinical studies to increase the level of implant osseointegration, help maintain crestal bone levels, and improve esthetic outcomes, due to appropriate gap scaffolding that avoids soft tissue downgrowth at the gap region [12]. Despite improvements in clinical outcomes, graft material short- and long-term turnover rates, specially of xenografts and synthetic bioactive ceramics, are questionable due to the slow degradation characteristics of these materials, since slow graft material degradation and turnover may affect tissue quality and composition at the implant interface with the oral cavity [12]. Along with increased degrees of implant osseointegration reported in multiple manuscripts, a recent critical review by Wang and Lang [6] has pointed that concomitant guided bone regeneration (GBR) along with immediately placed implants may partially compensate alveolar bone resorption. Wang and Lang also pointed that GBR techniques utilizing various particulate materials were effective in ridge dimension preservation and that the application of GBR principles using bone substitutes along with a collagen membrane has shown clear effects on preserving alveolar ridge height and width [6].

Autologous tissue engineering approaches such as platelet-rich plasma (PRP), fibrin glues, and platelet-rich fibrin have been utilized in both orthopedic and oral and maxillofacial surgery in an attempt to hasten both bone and soft tissue healing [13, 14]. A recently published case report has presented promising results in socket and ridge maintenance after tooth extraction by utilizing a leucocyte and platelet-rich fibrin (L-PRF) along with an xenograft as a scaffolding biomaterial between immediate implant and fresh extraction socket wall [15]. Since L-PRF may be engineered to present easily shapeable resilient membrane forms that carry cells that may enhance both hard and soft tissue healing through the sustained release over time of growth factors from active platelets, leukocytes, and other circulating cells, such biomaterial may be presented as an alternative to classic GBR procedures for socket/ridge preservation with or without immediate implant placement [13]. Extensive reviews have elaborated on the potential use of L-PRF on periodontal [16] and reconstructive oral surgeries for dental implant treatment [17] with promising outcomes, reportedly due to its unique fibrin architecture and leukocyte content when compared to PRP [18]. In addition, depending on implant surface topographic characteristics in multiple length scales [19–21], higher degrees of interaction between surface and the high fibrin content of L-PRF may provide a seamless pathway for osteogenic cell migration between the healing socket walls and the implant surface, facilitating the device osseointegration [19–21]. The specific interaction between L-PRF and nanoscale topography within a larger-scale microtopography, fabricated by robotic microblasting of a resorbable blasting media powder, warrants investigation. Previous work has shown promising results for this nanoenabled surface with a substantial increase in osseointegration parameters compared to alumina-blasted acid-etched [22] and to dual acid-etched surfaces [23]. Thus, the aim of this investigation was to morphologically/metrically evaluate the effect of L-PRF and implant surface texture on bone healing around implants placed immediately after tooth extraction in a beagle dog model. The postulated hypothesis was that the combination of L-PRF with an implant surface presenting micrometer/nanometer scale texturing would result in higher degrees of osseointegration of immediately placed implants.

2. Materials and Methods

2.1. Study Design

2.1.1. Implants. This study utilized screw root-form Blossom implants (Intra-Lock International, Boca Raton, FL) of 3.75 mm in diameter and 13 mm in length. Two different implant surfaces were utilized, namely, a dual acid-etched (DAE) surface and the commercially available Ossean surface (Intra-Lock International, Boca Raton, FL). Both surfaces have previously been characterized, where the DAE surface presents textured micrometer scale and smooth nanometer scale whereas the Ossean surface presents textured nanometer scale within the textured micrometer scale [24]. A total of 16 implants of each surface were utilized in the present study.

2.1.2. Preclinical In Vivo Model. Following approval of the bioethics committee for animal experimentation at the Ecole Nationale Veterinaire D'Alfort, France, 8 beagle dogs (approximately 2-year-old dogs) were acquired for the study and allowed to acclimate for 2 weeks prior to surgery. All surgical procedures were performed under general anesthesia. The preanesthetic procedure comprised an intramuscular (IM) administration of acepromazine maleate (0.2 mg/kg), diazepam (0.5 mg/kg), and fentanil (4 mg/kg). Anesthetic

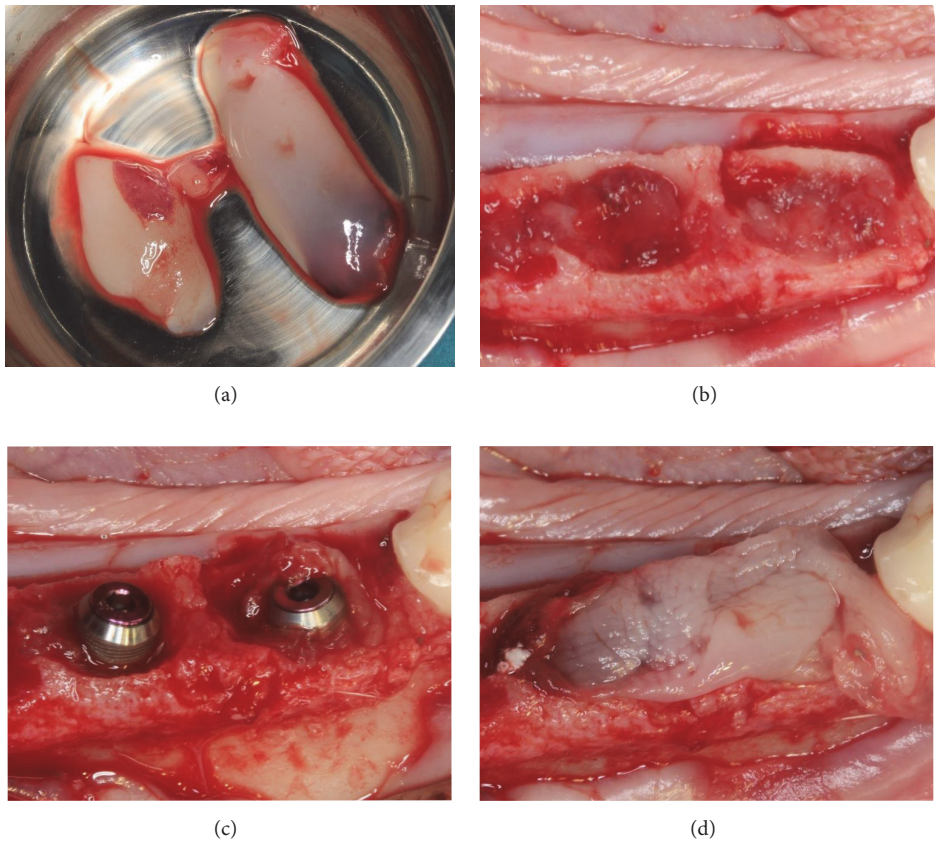

Figure 1: (a) L-PRF after processing and (b) its placement into the mesial and distal molar extraction sockets prior to (c) implant placement. (d) An extra L-PRF layer was placed over the implants prior to soft tissue closure.

induction was then achieved through ketamine (3 mg/kg), and general anesthesia was then obtained and maintained by 1 to 2% halothane.

Bilateral extractions of the mandibular first molars were performed. Mucoperiosteal flaps were elevated and teeth were sectioned in the buccolingual direction to allow non-traumatic individual root extraction by means of root elevators and forceps. One implant of each surface was placed in a split-mouth design at the mesial or distal extraction sockets in an interpolated fashion per animal so that the number of DAE and Ossean implant surfaces was equally distributed per mesial and distal sockets. On one side of the mandible, the implants were placed to the level of the buccal bone plate and soft tissue closure was achieved through standard suture procedures. On the contralateral side, L-PRF was prepared from each individual animal, by drawing venous blood using proprietary tubes and spinning them through a proprietary centrifuge at 2700 rpm for 12 minutes, or 400 RCF (CE/FDA cleared, IntraSpin, Intra-Lock, Boca Raton, FL) (Figure 1(a)). Both mesial and distal sockets were then filled with L-PRF (Figure 1(b)) and the implants placed within the socket to the buccal plate level. L-PRF in a membrane shape, obtained from the XPression fabrication kit, (Intra-Lock, Boca Raton, FL) was placed over the implants prior to standard soft tissue suture closure (Figure 1(d)). After placement, a minimum gap of 2 mm was left between the implant and the buccal plate (Figure 1(c)). Drilling direction aimed to avoid invasion of the lingual plate during osteotomy preparation or after implant placement (Figure 2). Remarkably similar implant placement patterns were observed due to the split-mouth design where one side did receive L-PRF whereas the other did not. Healing cover screws were adapted to the implant internal connection. Flaps were repositioned and sutured on both sides of the mandible with 4.0 PGA suturing material (Vicryl, Ethicon Johnson & Johnson, Miami, FL, USA). Postsurgical medication included IM administration of antibiotics (Cefazolin 30 mg/kg every 12 hours for 3 days) and anti-inflammatory (0.2 mg/kg per day for 3 days). Euthanasia was performed by anesthesia overdose, 6 weeks after implant placement.

2.1.3. Histological Preparation and Histomorphometry. At necropsy, the mandibles were retrieved by sharp dissection. The implants in bone were then separated from the mandible allowing blocks containing the implants in the mesial and distal sockets. The bone blocks were kept in 10% buffered formalin solution for 24 h and gradually dehydrated in a series of alcohol solutions ranging from 70 to 100% ethanol. Following dehydration, the samples were embedded in a methacrylate-based resin (Technovit 9100, Kulzer & Co, Wehrheim, Germany) according to the manufacturer's instructions. The sections, performed in a buccal-lingual

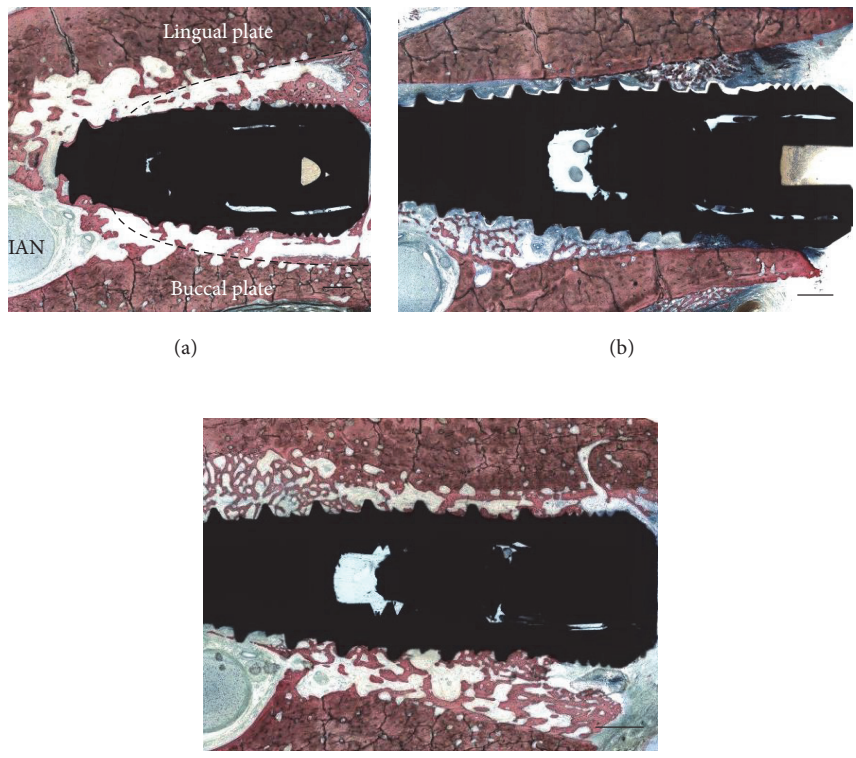

Figure 2: (a) Observation of histologic sections depicted the implant placed in the center of the socket (estimated by the dotted line) in proximity with the inferior alveolar nerve (IAN). The gap distance at the time of implant placement between the implant and buccal/lingual plates was also observed at six weeks and presented newly formed bone partially filling this gap. Bar = 2 mm. Representative histologic sections for implants placed in sockets (b) without L-PRF and (c) with L-PRF. The absence of PRF around the implant in (a) resulted in partial soft tissue apical migration in the gap comprised by the implant and extraction socket wall, while soft tissue apical migration in (b) was avoided by the presence of the L-PRF scaffold. No notable differences in socket healing pattern were observed between surfaces regardless of implant placement with or without L-PRF. Bar = 3 mm for (b and c).

direction, were then reduced to a final thickness of ~30 μm by means of a series of diamond blade sectioning and SiC abrasive papers (400, 600, 800, 1200, and 2400 Grit) in a grinding/polishing machine (Metaserv 3000, Buehler, Lake Bluff, IL, USA) under water irrigation [25]. The sections were then subjected to the Stevenel's Blue and Van Gieson staining technique. The percentage of bone area fraction occupancy (BAFO) was determined at a 50x magnification (Leica DM4000, Wetzlar, Germany) with the aid of computer software (Image J, NIH, MD, USA).

Statistical analysis was performed by mixed model ANOVA (at $\alpha = 0.05$). The statistical unit utilized for evaluation was the number of animals. The independent variables considered (individually or in combination) were implant surface, socket position (mesial or distal), and the presence of L-PRF. The dependent variable considered was BAFO.

3. Results

With the exception of one animal that developed a localized infection two weeks after surgery (excluded from statistical analysis), no complications were observed during animal surgical procedures or follow-up assessments, including post-operative infection or any other clinical concern.

General histologic analysis depicted the implant placed in the center of the socket at a distance from the buccal plate in proximity with the inferior alveolar nerve (Figure 2(a)). The gap distance present at the time of implant placement between the implant and buccal/lingual plates was easily depicted at six weeks and presented newly formed bone partially filling this gap. Representative histologic sections for implants placed in sockets with and without L-PRF are presented in Figures 2(b) and 2(c). The absence of L-PRF around implants most often resulted in partial soft tissue apical migration in the gap comprised by the implant and extraction socket walls, while soft tissue apical migration was avoided by the presence of the L-PRF scaffold between implant and socket walls. No notable differences in socket healing pattern, comprised by an intramembranous-like ossification pattern occurring between implant and socket walls, were observed between surfaces regardless of implant placement with or without L-PRF. Contact osteogenesis was observed for both groups through direct bone apposition onto both implant surfaces, and qualitatively higher amounts of bone were

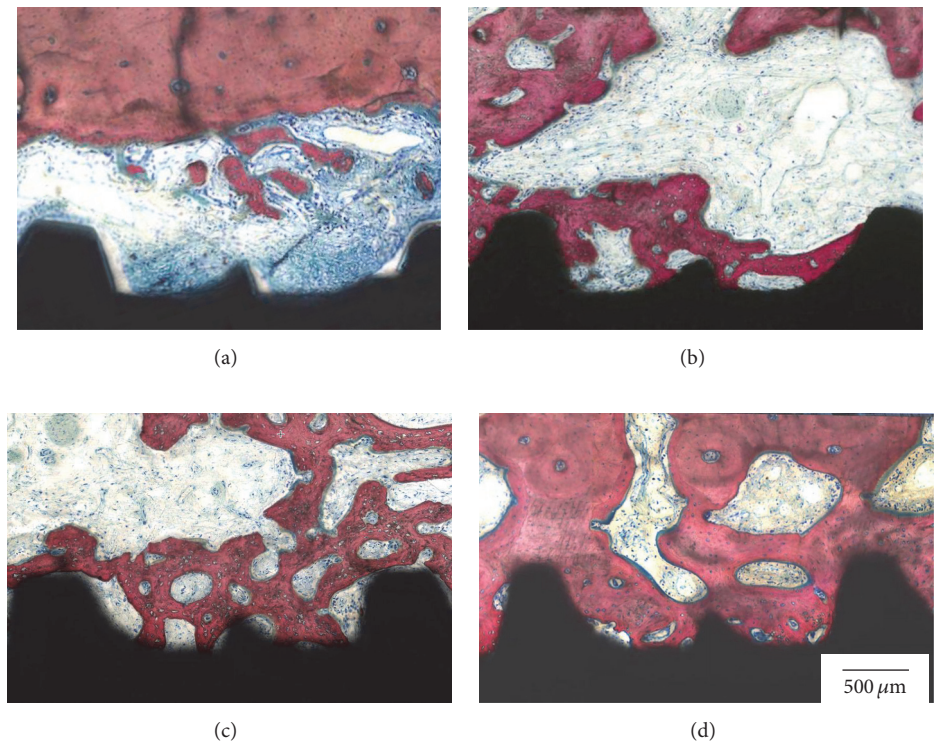

Figure 3: Representative histologic sections of the bone/implant interface for the (a) DAE without L-PRF, (b) Ossean without L-PRF, (c) DAE with L-PRF, and (d) Ossean with L-PRF.

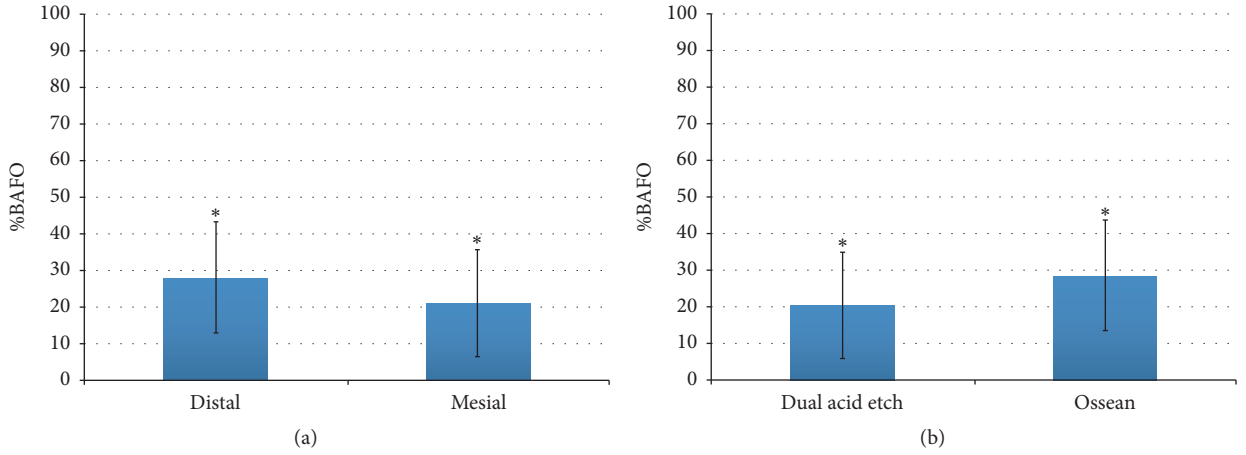

Figure 4: Statistical summary of (a) BAFO when surface and L-PRF presence were collapsed over socket position showed no statistical differences. Statistical summary of (b) BAFO when socket position and L-PRF presence were collapsed over implant surface showed higher mean values for the Ossean surface relative to the DAE surface. However, no statistical differences were detected. The same number of asterisks depicts statistically homogeneous groups.

observed in the proximity with both implant surfaces placed in sockets filled with L-PRF relative to implants placed into sockets filled with blood clot (Figure 3).

When BAFO values were collapsed over implant surface and the presence or not of L-PRF and evaluated as a function of socket position, no significant differences in BAFO ($p = 0.47$) were observed between groups despite lower mean values for dependent variables observed for the mesial socket relative to the distal socket (Figure 4(a)). When BAFO was evaluated as a function of implant surface (collapsed over socket position and the presence or not of L-PRF), no significant differences in BAFO ($p = 0.11$) were observed

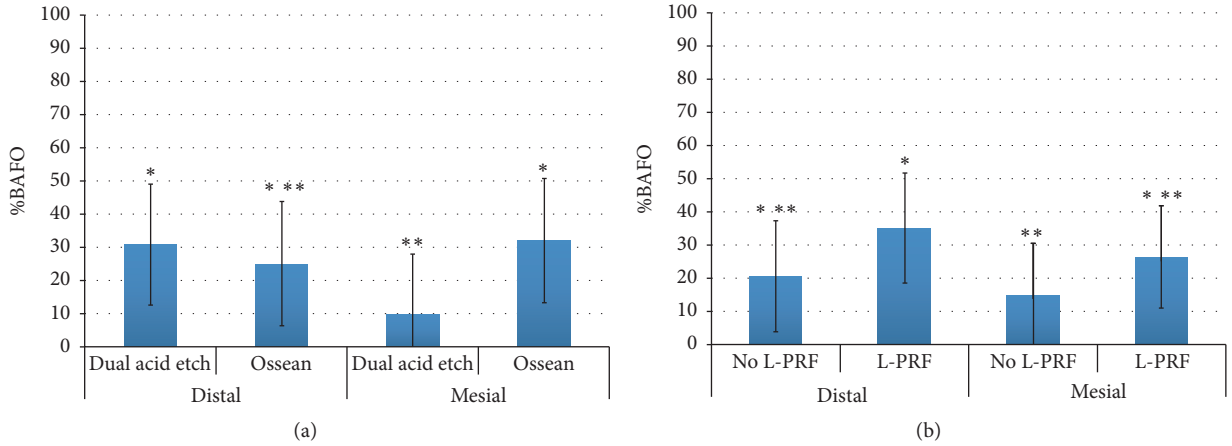

Figure 5: Statistical summary of (a) BAFO when L-PRF presence was collapsed over implant surface and PRF presence. While no effect of implant surface was detected for BAFO when the distal socket was considered, the Ossean surface presented significantly higher BAFO than the DAE surface in the medial socket. Statistical summary of (b) BAFO when implant surface was collapsed over implant surface and socket position. While no effect of L-PRF presence was detected for each individual socket, higher mean values of BAFO were observed for the sockets presenting L-PRF. A significant difference was observed between the medial socket without PRF and the distal socket with L-PRF. The same number of asterisks depicts statistically homogeneous groups.

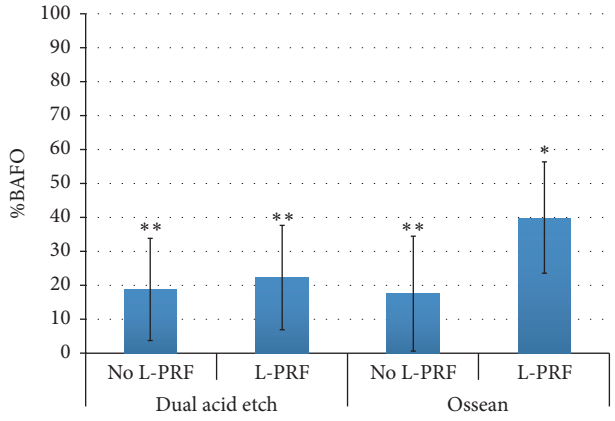

Figure 6: Statistical summary of BAFO when collapsed over socket position. A significant difference was observed when the Ossean surface was utilized with L-PRF relative to its counterpart without L-PRF. The same number of asterisks depicts statistically homogeneous groups.

despite higher mean values for both dependent variables observed for the Ossean surface relative to the DAE surface (Figure 4(b)).

While no effect of implant surface was detected for BAFO when the distal socket was considered, the Ossean surface presented significantly higher BAFO ($p = 0.015$) than the DAE surface in the mesial socket. A significant difference was observed between the mesial socket without L-PRF and the distal socket with L-PRF ($p = 0.02$). Finally, the combination of the Ossean surface and L-PRF presence resulted in significantly higher BAFO level relative to its no L-PRF counterparts and DAE surfaces with and without L-PRF ($p = 0.012$) (Figures 5 and 6).

4. Discussion

Dental implantology has been extensively researched in basic and clinical grounds and has for decades enjoyed the status of standard of care for the treatment of both partial and full edentulism. While reported high success rates [26, 27] have often been achieved through the classic protocol of delayed implant placement, when implants are placed at least twelve weeks following tooth extraction and following placement enough time is allowed for implant osseointegration and subsequent restoration, this classic approach may not necessarily lead to optimal treatment outcomes as other associated procedures may be required to further enhance clinical and esthetic outcomes [28]. Thus, modern clinical approaches that attempt to minimize tissue alteration after tooth extraction, while allowing for implant osseointegration in appropriate restorative positions for adequate function and esthetics, have been introduced and are currently under development [4–6].

A number of literature reviews on immediate implantation in fresh extraction sockets have evaluated the current state of the techniques [4, 6], biomaterials utilized [12], success, and esthetic outcomes [29] of these procedures. While it is general consensus that this treatment modality can be successful if well indicated, current materials utilized in an attempt to increase the degree of implant osseointegration by filling the gap between the implant and the socket walls include particulate grafting materials and barrier membranes. Despite improvements in clinical outcomes, slow graft material degradation and turnover may affect tissue quality and composition at the implant interface with the oral cavity [4, 6, 12].

The present investigation evaluated the effects of utilizing a validated tissue engineering approach through autogenous

processed L-PRF [13] in an attempt to maximize osseointegration of implants placed in fresh extraction sockets. The rationale for testing the effect of L-PRF in this clinical situation was based on the natural origin of autogenous processed L-PRF and its potential to promote osteogenesis within the socket due to its dense fibrin mesh and cellular content that could potentially provide a sustained release of growth factors, as well as its potential to act as a physical barrier to avoid soft tissue downgrowth [13, 15].

The rationale for investigating two distinct types of implant surface was based on the basic phenomenon of osseointegration in fresh extraction sockets where large gaps between implant and socket walls are often encountered and have to be bridged for optimal biomechanical competence of the device [7, 30]. From an ideal perspective, the blood clot filling the space between implant and socket wall would bridge them subsequently leading to a seamless osteogenic tissue link between the device and socket walls where osteogenic cells may migrate in an intramembranous-like healing pathway that has been reported to occur from the periphery of the socket towards its center [6]. This ideal scenario may be disrupted by a variety of reasons that include soft tissue migrating and disrupting the fibrin bridge as well as blood clot contracting usually away from the implant surface towards the socket and/or osteotomy wall leaving an interrupted pathway for cell migration towards the implant surface [6]. Through the utilization of a DAE surface that presents micrometer scale texture and the Ossean surface that presents micrometer and nanometer scales texture [31], the study design provided the opportunity to test the hypothesis that the implant surfaces could influence osseointegration in the natural healing scenario (blood clot filled extraction sockets) and when a mechanically robust tissue engineered scaffold interposed the implant and socket walls facilitating the establishment of a seamless pathway between implant surface and socket wall. The study design employing a split-mouth arrangement between the contralateral presence or absence of L-PRF for implant surfaces placed in the same contralateral socket (distal or mesial depending on animal sequence) allowed direct comparison between groups that were nested within the same animal subject.

Given the multiple variables evaluated in the present study, general statistical analyses showed various trends when two independent variables were collapsed over remaining independent variables. In general, higher mean BAFO values were observed for the Ossean surface relative to the DAE surface, higher mean BAFO values were observed when L-PRF was utilized, and lower mean BAFO values were observed for the mesial socket relative to the distal socket (possibly explained by the larger size of the mesial socket relative to the distal socket that would result in larger gaps between implant and socket walls).

In general, the histomorphologic results obtained from implants placed in fresh extraction sockets are in direct agreement with previous studies [6, 7, 30, 32], where bone growth from the socket walls partially filled the gap between implant and the socket walls. Also in line with previous reports [6, 7, 30, 32], intimate contact between bone and implant surface was observed regardless of implant surface group, and partial apical migration of soft tissue occurred mainly through the gap present between implant and the socket buccal plate. Where no L-PRF was present, histometric BAFO were slightly favored by the presence of the Ossean surface. However, higher contribution of the Ossean surface was observed for BAFO (significant) when the analysis was restricted to the larger mesial socket, suggesting a surface effect when more challenging clinical scenarios are concerned.

When the presence or absence of L-PRF was evaluated as a function of socket position, substantially higher degrees of BAFO were observed for sockets filled with L-PRF. The substantial increase in BAFO observed for both sockets due to the presence of L-PRF is likely accounted by improved cell migration through the stable L-PRF scaffold present between implant and socket walls.

Our histometric results for BAFO further highlight the biologic and scaffolding properties of L-PRF when placed in combination with the Ossean implant surface. This result unequivocally demonstrates the synergistic effect that exists between a micrometer and nanometer length scale and the L-PRF structure that allows significantly higher amounts (~90%) of bone formation between implant threads than the combination of the DAE surface and L-PRF. A potential physical explanation for the BAFO discrepancy observed between DAE and Ossean surfaces placed with L-PRF lies in their roughness pattern differences [31], where less developed surface area is available for the micrometer scale textured DAE relative to the micrometer and nanometer scale textured Ossean surface. Such large difference in developed surface area between surfaces may have resulted in less efficient interaction between the DAE surface and the L-PRF scaffold that potentially resulted in discontinuities between the socket wall and implant surface, thus restricting seamless cell migration. Another possible reason for the significant BAFO differences between DAE and Ossean surfaces placed with L-PRF is that identical levels of interaction occurred between both surfaces and L-PRF and a pathway between the healing socket walls and implant was present. In this case, osteogenic cells would equally populate regions in close proximity with the implant surface but the highly osteogenic characteristics of the Ossean surface relative to the DAE surface [22, 31, 33] accounted for phenotype alteration and higher degrees of bone formation as previously presented in a comprehensive histomorphologic, histomorphometric, nanobiomechanical, and gene expression assessment study [31].

General histomorphologic observations for the implants placed along with L-PRF in fresh extraction sockets differed from those where no L-PRF was utilized primarily due to the lack of soft tissue migration through the gap formed between implant and socket wall, suggesting L-PRF's efficiency as a barrier during healing. The osteogenic potential and adequacy of L-PRF substituting the blood clot during socket healing were confirmed since bone growth occurred from the socket walls towards the implant leading to substantial bone formation around implants irrespective of implant surface group.

It should be acknowledged that this study is an in vivo preclinical model on beagle dogs, suggesting that the synergistic effect of leukocyte platelet-rich fibrin (L-PRF) and

micrometer/nanometer surface texturing on bone healing around immediately placed implants should be evaluated in well-designed clinical trials in humans. Further studies are therefore needed to confirm the evidence emerging from the present research.

5. Conclusions

The postulated hypothesis that the combination of L-PRF with an implant surface presenting micrometer/nanometer scale texturing would result in higher degrees of osseointegration of immediately placed implants was accepted. Further studies are warranted to shed light on possible physical and molecular mechanisms that result in the substantial increase in the amount of bone in proximity with Ossean surface implant placed along with L-PRF.

Competing Interests

The authors report no conflict of interests for the present study.

Acknowledgments

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Clinical Study

Alveolar Ridge Reconstruction with Titanium Meshes and Simultaneous Implant Placement: A Retrospective, Multicenter Clinical Study

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Objective. To evaluate horizontal bone gain and implant survival and complication rates in patients treated with titanium meshes placed simultaneously with dental implants and fixed over them. *Methods.* Twenty-five patients treated with 40 implants and simultaneous guided bone regeneration with titanium meshes (i–Gen®, MegaGen, Gyeongbuk, Republic of Korea) were selected for inclusion in the present retrospective multicenter study. Primary outcomes were horizontal bone gain and implant survival; secondary outcomes were biological and prosthetic complications. *Results.* After the removal of titanium meshes, the CBCT evaluation revealed a mean horizontal bone gain of 3.67 mm (±0.89). The most frequent complications were mild postoperative edema (12/25 patients: 48%) and discomfort after surgery (10/25 patients: 40%); these complications were resolved within one week. Titanium mesh exposure occurred in 6 patients (6/25 : 24%): one of these suffered partial loss of the graft and another experienced complete graft loss and implant failure. An implant survival rate of 97.5% (implant-based) and a peri-implant marginal bone loss of 0.43 mm (±0.15) were recorded after 1 year. *Conclusions.* The horizontal ridge reconstruction with titanium meshes placed simultaneously with dental implants achieved predictable satisfactory results. Prospective randomized controlled trials on a larger sample of patients are required to validate these positive outcomes.

1. Introduction

Dental implants are a predictable treatment procedure for the prosthetic rehabilitation of partially and fully edentulous patients [1–3].

An adequate bone volume is required for insertion of dental implants [4, 5]; the absence of a sufficient amount of horizontal and vertical bone is a problem that can affect the survival and success rates of dental implants in the short, medium, and long term [4, 5].

Since frequently patients present with bone defects of variable entity [4, 5], different surgical techniques have been proposed to restore the ideal anatomical conditions required for implant insertion or to allow simultaneously positioned implants to succeed [6–14]. These techniques include onlay/inlay bone grafting [6, 7], distraction osteogenesis [8], maxillary sinus augmentation [9], inferior alveolar nerve transposition [10], alveolar ridge split [11], and guided bone regeneration (GBR) with resorbable [12] and nonresorbable membranes, such as those in polytetrafluoroethylene (PTFE) [13] or titanium [14].

GBR is considered one of the most predictable of these techniques in terms of clinical outcomes, as reported by several systematic reviews of the literature [12–15], particularly

where it is employed for the regeneration of defects of small and medium entities [16], or around dental implants [17]. The operating principle of GBR involves the placement of a mechanical barrier for the protection of the clot and the isolation of the bone defect from the surrounding connective tissues, in order to facilitate the selective recruitment of the mesenchymal cells responsible for new bone formation [12–15, 17]: this can allow the regeneration of the bone defect.

Bone regeneration with GBR has been demonstrated to be predictable, whether or not biomaterials are positioned below the membrane and are contained by it [12, 14, 16].

An ideal membrane should possess the following characteristics: biocompatibility, space maintenance capabilities, and ease of use [13, 14, 17, 18]. In the last few years, several types of membranes with different designs have been introduced, to facilitate the containment of the regenerative material that is often positioned below it and to prevent its dispersion, but also to simplify the work of the surgeon and the application of the membrane itself [13–18].

In particular, the titanium meshes represent a valid solution, because they meet most of the ideal requirements that a membrane should possess [14, 15]. Several clinical studies have demonstrated that titanium meshes can promote the formation of new bone, when positioned before [19–24] or simultaneously with dental implants [25–27].

The proper placement and stabilization of the titanium mesh into the defect site is of fundamental importance for the success of the regenerative therapy [13, 16–18]; one of the difficulties with these membranes can be related to this, particularly in case of simultaneous placement of the implant, for regeneration of small and medium size defects [17, 18, 25–27].

Recently, titanium meshes that can be fixed directly on the implant have been introduced, but there is still a lack of clinical studies evaluating the efficiency and predictability of these membranes [18, 26].

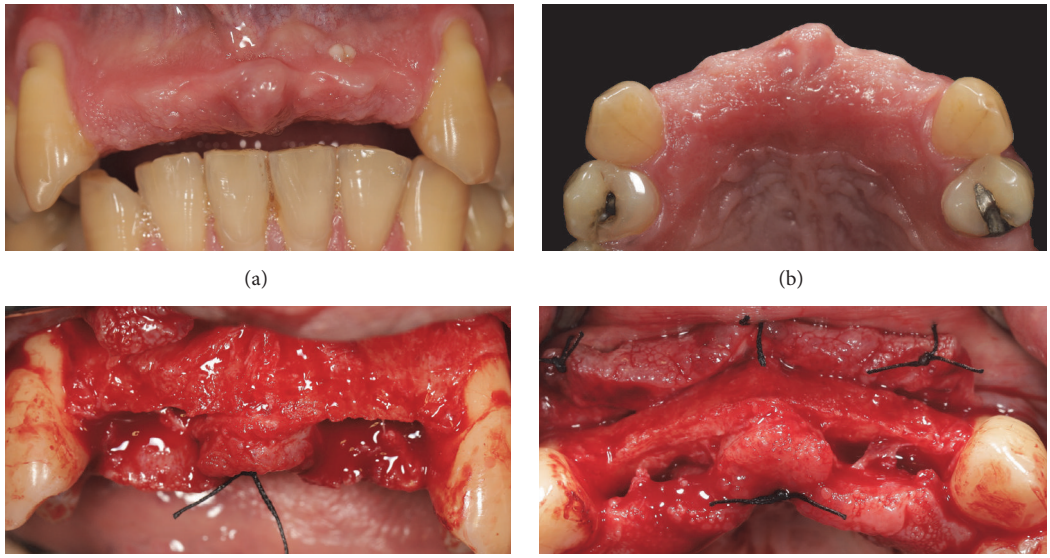
Therefore, the purpose of the present retrospective, multicenter clinical study is to evaluate the horizontal bone gain, the percentage of implant survival, and the degree of complications in patients treated with titanium meshes positioned simultaneously with dental implants and fixed over them.

2. Materials and Methods

2.1. Patient Selection. Patients enrolled in the present retrospective multicenter study were identified through the customized records of five different private dental clinics. Only records of patients with partial edentulism of the maxilla and/or mandible (with a period of edentulism of at least 4 months) or in need for replacement of nonrestorable failing teeth at the time of recruitment, who had been treated with titanium mesh and simultaneous implant placement in a period between January 2013 and December 2014, were reviewed. Further inclusion criteria for the present study were insufficient width of a portion of the alveolar process, with the need for horizontal augmentation of at least 3-4 mm, age > 18 years, good systemic and oral health, dentition in the opposing jaw, detailed information about the treatment, and a minimum follow-up of 1 year. In fact, the customized records of patients had to include all patient-related (gender, age at surgery, smoking habit, and history of periodontal disease) and implant-related (site, position, type of mesh used, type of prosthetic restoration, and date of provisional and definitive prosthesis delivery) information; in addition, they had to contain information about the occurrence of implant failures and/or biological and prosthetic complications during the entire follow-up period, since any complication that was manifested clinically was routinely referred back to the specialist practice for control. Exclusion criteria were any systemic disease that could contraindicate surgery (such as uncontrolled diabetes mellitus, immunocompromised status, coagulation disorders, radiotherapy, chemotherapy, alcohol or drug abuse, and use of oral and/or intravenous aminobisphosphonates), poor oral hygiene, and active periodontal infections. All patients had been informed about the planned treatment and had signed an informed consent form. All data were inserted into spreadsheet software and used for statistical evaluation. The study was performed in accordance with the principles outlined in the Helsinki Declaration on Human Experimentation, as revised in 2008.

2.2. Preoperative Work-Up. A preliminary clinical and radiographic examination had been performed prior to commencing the surgical procedures. All patients received a session of professional oral hygiene, with scaling and root planning, two weeks before surgery. In addition, patients were instructed about common oral hygiene procedures and were prescribed with chlorhexidine 0.2% mouthrinses, twice a day for 2 weeks, so that, before entering the surgical procedures, they all had an adequate plaque control. At the same time, a thorough radiographic examination was performed, in order to precisely assess the width of the (residual) alveolar process. Cone beam computed tomography (CBCT) scans were taken; then, raw CBCT data were imported into reconstruction software, where a careful three-dimensional (3D) evaluation of the alveolar process was performed. Linear and volumetric measurements were obtained, in order to fully disclose the anatomy of the bone site and therefore to choose the most appropriate implant and titanium mesh for reconstruction.

2.3. Dental Implants and Titanium Meshes. All patients were installed with tapered implants (AnyRidge®, MegaGen, Gyeongbuk, South Korea) characterised by strong self-cutting threads. These implants featured a 5 mm deep conical connection (10°) combined with an internal hexagon [28–30]. The aforementioned implants had a nanostructured calcium-incorporated surface [31]. The titanium membranes (i–Gen membranes, MegaGen, Gyeongbuk, South Korea) were available in 9 different configurations (type A for incisors/cuspids, type B for premolars, and type C for molars) with different size and shape (small, regular, or wide) in order to allow the clinician to graft all different sites (anterior and posterior sites) where a stable implant has been placed, but surrounding bone was insufficient. All these titanium meshes incorporated up to a 100° bend to provide adequate

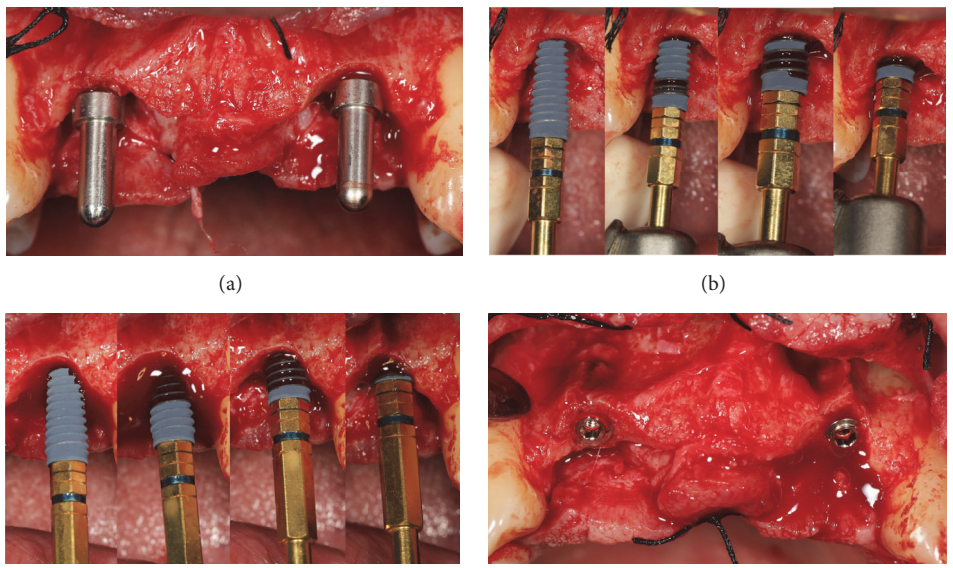


(a) (b) (c) (d)

Figure 1: Presurgical clinical situation and elevation of full-thickness flap exposing the deficient alveolar ridge. (a) Preoperative clinical picture, frontal view; (b) preoperative clinical picture, occlusal view; (c) elevation of the mucoperiosteal flap, frontal view; (d) elevation of the mucoperiosteal flap, occlusal view.

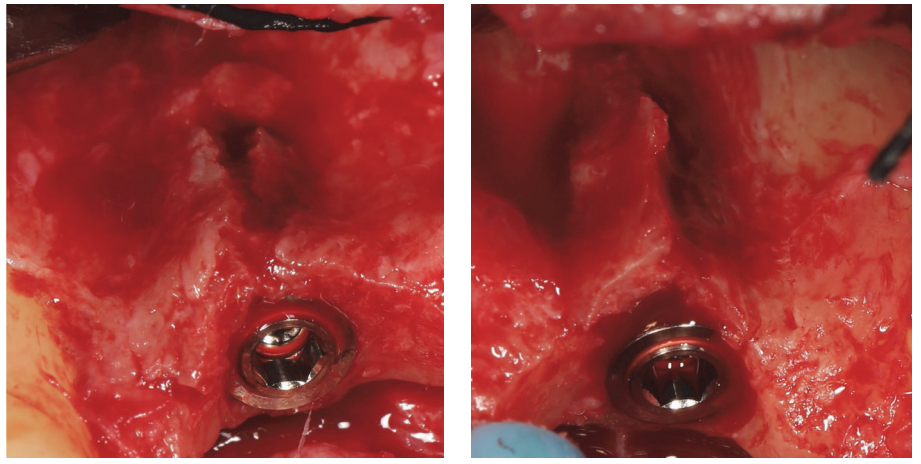
space for GBR. The titanium meshes had to be fixed on specially designed flat abutments (i–Gen screws, MegaGen, Gyeongbuk, South Korea) of variable height (1–3 mm), by means of a cover screw. The i–Gen kit included 12 titanium membranes, 6 i–Gen screws (flat abutments) for providing adequate space for regeneration, 6 cover screws for fixing the membrane to the flat abutments, and a hand hexagonal driver.

2.4. Surgical and Prosthetic Procedures. All the surgical and prosthetic procedures were performed under the same protocols, in the five different private clinical centers. After local anaesthesia, a paramarginal incision was made, connected with two wide releasing incisions. A full-thickness flap was raised to expose the residual bone and elevated on the buccal and palatal (lingual) aspect of the ridge (Figure 1); sutures were used for retraction. Several horizontal incisions were made in the periosteum, in order to widely mobilize the flap as far as possible, in the coronal direction. In the case of healed ridges, the surgeon proceeded with the osteotomy, starting with a 2.0 mm diameter pilot drill, to the desired depth. The preparation of the surgical site was based on the bone quality, using the set of helicoidal drills. After the preparation of the surgical sites, the implants were placed, slightly below the crestal level, using a hand ratchet (Figures 2 and 3). In patients with severely compromised dental elements, which called for extraction and immediate implant treatment, the teeth were gently extracted taking care not to further damage the remaining buccal bone wall. The alveolus was carefully cleaned in order to remove any granulation tissue. After irrigation with sterile saline, the integrity of the socket walls was checked. Once this was verified, the procedure continued with the preparation of the implant site. Once again, drill selection was based on the receiving site's bone quality; the implants were in a slightly subcrestal position, using a hand ratchet. For both healed and postextraction sites, there was not a specific threshold for insertion torque; the surgeon was free to decide the type of preparation and consequently the insertion torque. The stability of the implants was determined clinically as the absence of movement by the removal of the implant driver without use of the stabilizing wrench. After implant placement, the flat abutment of variable height (1–3 mm) was connected to the fixture, according to the clinical indications: a standard 1 mm cuff height was used in case of sufficient vertical space, but 2 or 3 mm cuff height could be chosen according to the situation. Then, the proper titanium membrane was selected, according to the size and shape of the bone defect. Each titanium membrane was adjusted to the individual anatomy and modelled in order to prepare the space for the regenerative material: these spaces were then filled with particulate bone grafts (Bio–Oss®, Geistlich Pharma AG, Wolhusen, Switzerland). The amount of material was sufficient to fill the space between the titanium meshes and the deficient buccal bone close to the fixtures (Figure 4). The titanium meshes were capable of maintaining the particulate bone *in situ*; then, they were fixed with a cover screw. An absorbable collagen membrane (Biomend® 15 × 20 mm, Zimmer Biomet, Warsaw, Ind, USA) could be adapted over the titanium meshes, according to the clinicians' preferences. The soft tissues were adapted over the membranes and care was taken in order to avoid tension during sutures. A tension-free closure was obtained through horizontal mattress sutures; single-loop sutures were made to further seal the incision line. Ice-packs were provided postoperatively, with the recommendation to keep them onto the treated area for at least 2 hours. Patients were prescribed oral antibiotics, amoxicillin plus clavulanic



(a) (b) (c) (d)

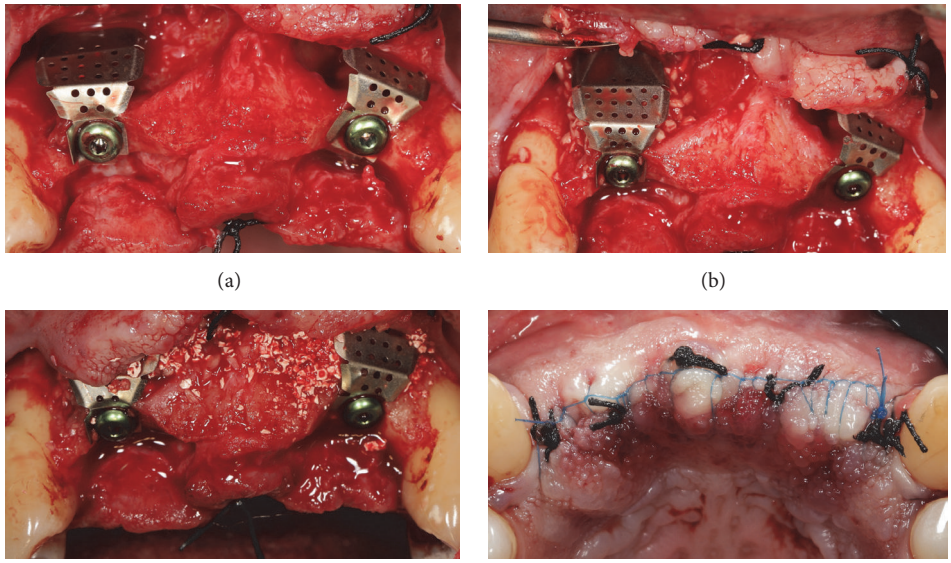
Figure 2: Preparation of the surgical sites and placement of the implants (AnyRidge, MegaGen, Gyeongbuk, Republic of Korea). (a) The implant sites have been prepared; (b) placement of the first implant in the position of the right lateral incisor; (c) placement of the second implant in the position of the left lateral incisor; (d) the implants *in situ*.



(a) (b)

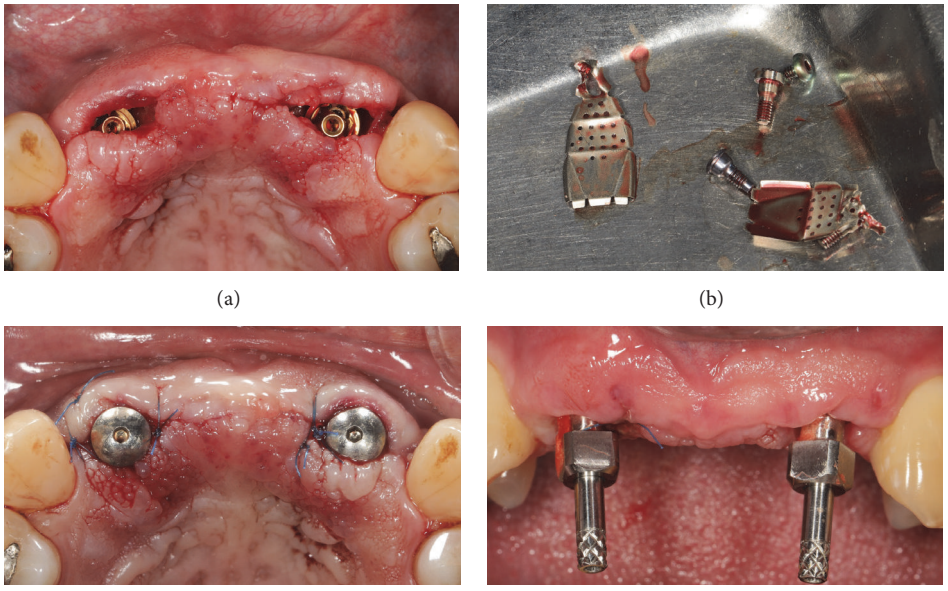
Figure 3: Details of the implant sites. (a) Details of the right implant site: fenestration of the thin buccal bone wall; (b) details of the left implant site: the buccal bone wall is thin and requires to be reinforced and protected.

acid 1 gr every 12 hours, for 6 days. Postoperative pain was controlled by administering 600 mg ibuprofen every 12 h for 2 days. Patients were instructed to rinse with chlorhexidine digluconate 0.2%, 2-3 times per day, for an overall period of 2-3 weeks, with the recommendation to discontinue tooth brushing in the surgical area. A soft diet was recommended in this period, in order to avoid any trauma in the site of surgery; coherently, patients were asked not to wear removable dentures, where present, for a period of 1 month after surgery. Patients were recalled and checked at 2, 5, and 10 days after operation, to monitor their healing; 14 days after surgery, sutures were removed. After 3-4 months, a second-stage surgery was performed at the recipient sites. The fixtures were uncovered, and the titanium screws and meshes were removed (Figures 5 and 6); transmucosal healing abutments were positioned and sutures were performed around them. Two weeks later, impressions were taken, and temporary resin restorations (single crowns, SCs, and fixed partial prostheses, FPPs, either screw-retained or cemented) were provided. The temporary acrylic resin restorations were left for a period of 3 months, after which the definitive ceramometallic restorations were provided. All definitive restorations were



(a) (b) (c) (d)

Figure 4: Placement of the titanium meshes (i–Gen, MegaGen, Gyeongbuk, Republic of Korea) and sutures. (a) The titanium meshes are connected to the implants and screwed on with the aid of a connecting screw; (b) particulate bone grafts are placed below the titanium mesh screwed on the right lateral incisor; (c) particulate bone grafts are placed below the titanium mesh screwed on the left lateral incisor; (d) sutures are performed.



(a) (b) (c) (d)

Figure 5: Second-stage surgery, removal of the titanium meshes and impressions. (a) and (b) Four months after placement, the titanium meshes were removed; (c) healing abutments were placed in position; (d) two weeks after placement of the healing abutments, impressions were taken.

ceramometallic, screwed, or cemented with temporary zinc oxide-eugenol cement (Figure 7). Before the delivery of the final restorations, occlusion was carefully checked. Maintenance care was provided every 6 months. All patients were controlled 1 year after the placement of the fixtures.

2.5. Primary Outcomes

2.5.1. Horizontal Bone Gain. The horizontal dimensions of the alveolar ridge were measured in the CBCT sections, before and 4 months after the surgery, in mm. Basically,

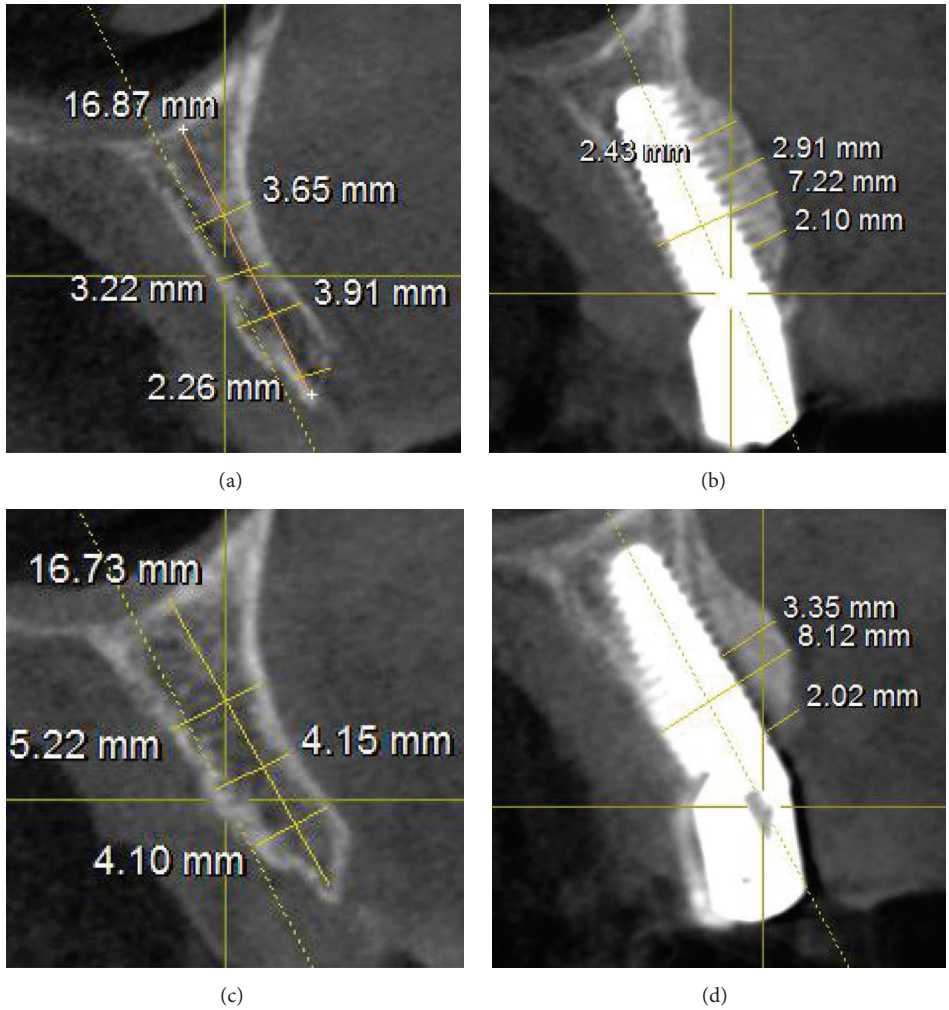


Figure 6: Cone beam computed tomography (CBCT) scans of the sites before surgery and after removal of the titanium meshes, three months later. (a) Right side: preoperative situation with a very thin residual alveolar ridge; (b) right side: the radiographic situation three months after surgery; (c) left side: preoperative situation with a thin residual alveolar ridge; (d) left side: the radiography three months after surgery.

before implant placement, one first linear measure was taken at the future implant location; this measure was taken where CBCT evaluation revealed the maximum bone deficiency. After the second-stage surgery for the removal of the titanium mesh, the same measure was repeated at the same location. This second measure was registered; then the horizontal bone gain was determined by the difference between the second and the first measurement.

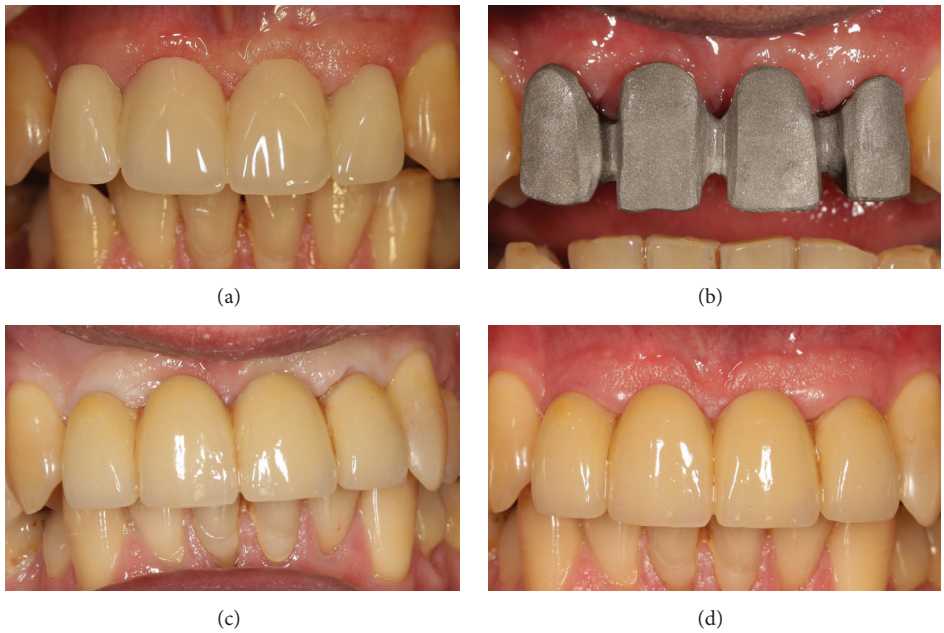
2.5.2. Implant Survival. One year after implant placement, the prosthetic restorations were removed and the stability of all fixtures was verified. An implant was classified as "surviving" if still in function, without any problem, at the 1-year follow-up control. Conversely, failure to osseointegrate with implant mobility, progressive marginal bone loss due to bacterial tissue invasion (peri-implantitis), severe marginal bone loss in the absence of symptoms/signs of infection, and implant body fracture were the conditions in which implant removal was required.

2.6. Secondary Outcomes

2.6.1. Early Biological Complications. Early complications were those that occurred immediately after surgery, or in the immediate aftermath (1-2 weeks), such as pain/discomfort, swelling/edema, and extraoral contusion.

2.6.2. Late Biological Complications. All complications occurring from the third week after surgery, until the end of the study, were classified as late biological complications. These complications included titanium mesh exposure, partial or complete loss of the graft, and any disturbance in the function of the implant characterized by a biological process affecting the supporting tissues (peri-implant mucositis and peri-implantitis) and any peri-implant bone loss exceeding 1.5 mm, but in the absence of clinical signs of infection.

Peri-implant mucositis is the condition in which soft tissue inflammation, pain, and swelling are present, but



(a) (b)

(c) (d)

Figure 7: Prosthetic rehabilitations. (a) The provisional restoration *in situ*, two weeks after the first impressions; (b) three months later, the precision of final structure is tested clinically; (c) the application of the definitive metal-ceramic FPP; (d) the final FPP at the final control.

in the absence of peri-implant bone loss; conversely, peri-implantitis is the condition in which pain, suppuration, exudation, and fistula formation are present, with concomitant probing pocket depth ≥6 mm and peri-implant marginal bone loss >2.5 mm.

The peri-implant marginal bone loss was calculated as previously reported [28–30]. In brief, intraoral periapical radiographs were taken at different times (at implant placement and 4 months and 1 year later, resp.) for each implant, using a rigid film-object X-ray source being coupled to a beam-aiming device (Rinn®; Dentsply, Elgin, IL, USA), in order to achieve reproducible exposure geometry. Customized polyvinyl-siloxane film holders were used to maintain the same angulation. Mesial and distal marginal bone levels of all implants were measured at different times with the aid of an ocular grid (4.5x magnification). The coronal margin of the implant neck and the most coronal bone-to-implant contact point were used as references for the linear measurements. To account for variability, the implant length was measured radiographically and compared with the actual dimensions; ratios were calculated to adjust for distortion. Peri-implant marginal bone loss was then calculated, as modification in the peri-implant marginal bone level at different time periods, on the mesial and distal implant side: the average from the mesial and distal calculations was used as the final value.

2.6.3. Prosthetic Complications. All prosthetic complications that had affected the implant-supported restorations, from the placement of the provisional restorations and until the end of the study, were carefully registered. Mechanical complications included all complications occurring at prefabricated components (such as abutment screw loosening and abutment fracture) whereas technical complications included all complications of the laboratory-fabricated suprastructure or its materials (loss of retention, ceramic chipping, or fracture).

2.7. Statistical Analysis. Patient demographics and distribution of implants were analyzed using descriptive statistics.

Means and standard deviations as well as ranges and confidence intervals (95%) were calculated for quantitative variables, such as patient age, gain in horizontal dimensions of the alveolar ridge, and peri-implant marginal bone loss. Absolute and relative frequency distributions were calculated for qualitative variables, both patient-related (patient gender, age classes, smoking habit, and history of periodontal disease) and implant-related (implant site and position, surgical protocol, implant length and diameter, and type of prosthesis). The Chi-square test was used to evaluate the differences among the groups. The level of significance was set at 0.05. The incidence of biological complications (pain/discomfort and swelling/edema/extraoral contusion after surgery, membrane exposures and/or infection, graft loss, peri-implant mucositis, and peri-implantitis) and prosthetic complications (abutment screw loosening, abutment fracture, loss of retention, and ceramic chipping or fracture) as well as the implant survival rate were calculated, 1 year after implant placement. The implant survival rate was calculated both at the patient and at the implant level. All computations were carried out with dedicated statistical analysis software.

3. Results

In total, 25 patients (15 males, 10 females; aged between 43 and 69 years, mean age 54.3 ± 7.5) who had been treated with

Table 1: Patient-related information.

	N° patients (%)	p–value*
Overall	25 (100%)	
Gender		
Males	15 (60%)	0.3173
Females	10 (40%)	
Age at surgery		
43–51	11 (44%)	
52–60	8 (32%)	0.4677
61–69	6 (24%)	
Smoking habit		
Yes	8 (32%)	0.0719
No	17 (68%)	
History of periodontal disease		
Yes	7 (28%)	0.0278
No	18 (72%)	

*Chi-square test.

Table 2: Implant-related information.

	N° implants (%)	p–value*
Overall	40 (100%)	
Site		
Maxilla	32 (80%)	0.0001
Mandible	8 (20%)	
Position		
Incisor/cuspids	12 (30%)	
Premolars	22 (55%)	0.0074
Molars	6 (15%)	
Protocol		
Healed ridges	31 (77.5%)	0.0005
Postextraction sockets	9 (22.5%)	
Length		
8.0 mm	7 (17.5%)	
10.0 mm	18 (45%)	0.0203
11.5 mm	10 (25%)	
13.0 mm	5 (12.5%)	
Diameter		
3.5 mm	19 (47.5%)	
4.0 mm	14 (35%)	0.0655
4.5 mm	7 (17.5%)	
*Type of prosthesis***		
SCs	17 (43.6%)	
FPPs (2 units)	12 (30.8%)	0.0225
FPPs (3 units)	6 (15.4%)	
FPPs (4 units)	4 (10.2%)	

*Chi-square test test.
**Calculated on the 39 surviving implants.

implant placement with simultaneous GBR with titanium meshes, were selected for the present retrospective, multicenter clinical study. The distribution of the patients is illustrated in Table 1. This distribution was uniform among the different groups, as no differences were found in the distribution by gender ($p = 0.3173$), age ($p = 0.4677$), or smoking habit ($p = 0.0719$); however, most of the patients had no history of periodontal disease ($p = 0.0278$). Forty implants were placed (32 in the maxilla and 8 in the mandible; 12 in anterior regions and 28 in posterior regions). Thirty-one implants were placed in healed sites, while 9 implants were installed in fresh extraction sockets. The distribution of the implants is shown in Table 2. There were significant differences in the distribution of the implants among the different groups. In fact, most of the implants were placed in the maxilla ($p = 0.0001$), were premolars ($p = 0.0074$), and were placed in healed ridges ($p = 0.0005$); the most frequently used implants were 10.0–11.5 mm in length ($p = 0.0203$) and the most frequent prosthetic restorations were SCs and short-span 2-unit FPPs ($p = 0.0225$). No differences were found in the distribution of the implants by diameter (0.0655). Forty titanium meshes were placed: 12 type A membranes (2 small, 7 regular, and 3 wide), 22 type B membranes (5 small, 13 regular, and 4 wide), and 6 type C membranes (2 small, 2 regular, and 2 wide). An absorbable collagen membrane was employed to protect the titanium meshes in 12 cases (12/25: 48%).

At the second-stage surgery and after the removal of the titanium meshes, the CBCT evaluation revealed a mean horizontal bone gain or augmentation of 3.67 mm (±0.89; median 3.6; CI 95%: 3.40–3.94). With regard to early biological complications, 10 patients (10/25: 40%) reported mild pain for the 3-4 days following surgery; however this discomfort was well tolerated with analgesics; conversely, 15 patients (15/25: 60%) had no discomfort or pain at all. Twelve patients (12/25: 48%) experienced mild postoperative edema; in 2 patients (2/25: 8%) this edema coexisted with extraoral contusion in the region. Eleven patients (11/25: 44%) had no edema at all. The mean time between implant placement and second-stage surgery (removal of the titanium meshes and placement of healing abutments) was 3.8 months. In most of the patients (19/25: 76%), healing proceeded without any delayed complication, and grafts appeared well incorporated into native bone. However, titanium mesh exposure occurred in 6 patients (6/25: 24%). In all these cases, weekly examinations were carried out, and mesh exposure was treated with a gentle cleaning of the area with an extra soft toothbrush soaked in chlorhexidine 1% gel. In addition, patients were asked to apply 1% chlorhexidine gel, 2 times per day, and were instructed to rinse with 0.12% chlorhexidine, 2-3 times per day. After this treatment, in 4 of these exposures, spontaneous coverage of the titanium membrane was found, with complete reepithelization of the areas and soft tissue closure, in a period between 3 and 4 weeks. These exposures did not prevent proper graft incorporation into native bone. In the remaining 2 cases, however, the titanium mesh had to be removed, because of nontreatable soft tissue defects followed by infection and loss of the graft. In one patient, the loss of the graft was partial, and it did not affect the survival of the implant; in the other one, however, the infection caused the complete loss of the graft and the implant. This implant failure was classified as "early failure," because it

Table 3: Peri-implant marginal bone loss between groups of implants at different time periods, in mm (implant level).

	Baseline, 4 months	Baseline, 1 year
	N^*; mean (SD); median; CI 95%	N^*; mean (SD); median; CI 95%
Overall	39; 0.40 (±0.20); 0.35; 0.34–0.46	39; 0.43 (±0.15); 0.44; 0.39–0.47
Healed sites	30; 0.42 (±0.21); 0.36; 0.35–0.49	30; 0.43 (±0.15); 0.44; 0.38–0.48
Extraction sockets	9; 0.35 (±0.17); 0.34; 0.24–0.46	9; 0.41 (±0.17); 0.44; 0.30–0.52

N^* = number of the surviving implants.

occurred 2 months after surgery (before the connection of the prosthetic abutment) in a 45-year-old smoking female patient, without history of chronic periodontal disease. No other implant failures were reported. Among the restorations, 17 were SCs (17 implants), 6 were 2-unit FPPs (12 implants), 3 were 3-unit FPPs (6 implants), and 2 were 4-unit FPPs (4 implants), representing a total of 27 fixed partial prosthetic units available for analysis. No prosthetic complications were registered. All the 39 surviving implants were followed up for 1 year, for an overall survival rate of 97.5% (implant-based) and 96.0% (patient-based). The peri-implant marginal bone levels at the 1-year examination are reported in Table 3.

4. Discussion

Several clinical studies [19–25] and systematic reviews [14, 15, 18] have documented the predictability of titanium meshes in supporting horizontal and vertical guided bone regeneration.

However, only a few of these studies [25–27] reported on alveolar ridge reconstruction with titanium meshes and simultaneous implant placement.

Von Arx and Kurt [25] have reported on guided bone regeneration with autogenous bone grafts harvested intraorally from the mandible covered with titanium mesh, which was rigidly affixed with microscrews to the residual jaw bone. In total, 20 implants were placed in 15 patients. Height of implant exposure (mean 6.5 mm), dehiscences (80%) or fenestrations (20%), and graft height (mean 6.2 mm) were measured [25]. After 6 months, the titanium mesh and microscrews were removed and bone regeneration was assessed [25]. The mean height of the integrated bone graft was 5.8 mm, corresponding to a mean bone fill of 93.5% [25]. The postoperative healing was overall excellent with only one site developing a soft tissue dehiscence with subsequent mesh exposure (complication rate 5%) [25]. The authors demonstrated that a titanium mesh in combination with autogenous bone grafts can represent an effective regenerative procedure for peri-implant bone defects [25].

In another study of Jung and colleagues [26], ten patients with dehiscences or fenestrations at the time of implant placement were treated with a mixture of autogenous bone particulate and allograft covered and protected by a preformed titanium mesh, which was fixed directly on the implant neck. No complications were reported in the postoperative period nor in the following months [26]. Four months after placement, small biopsies were taken from the regenerated areas: these specimens demonstrated successful and satisfactory bone regeneration, with 80% vital bone, 5% fibrous marrow tissue, and 15% remaining allograft [26]. All implants were successfully in function after a period of 1 year [26]. The authors concluded that the use of preformed titanium meshes can represent a reliable treatment procedure around peri-implant alveolar bone defects: in addition, they are extremely easy to apply, by fixing them on the implant shoulder, and simple to remove [26].

In the study of Konstantinidis and colleagues [27], peri-implant dehiscences of 26 patients who were installed with 36 implants were treated with GBR, using an alloplastic calcium-phosphosilicate putty protected by either collagen membranes (27/36 implants) or titanium meshes (9/36 implants). All implants were followed for a period of 1 year and all complications were registered [27]. During the second-stage surgery for the removal of the titanium membranes, the mean bone gain accounted to 3.23 (±2.04 mm). Almost 75% of the peri-implant defects achieved complete regeneration [27]. No complications were reported. A negative correlation was found between patient age and complete coverage of the peri-implant defect [27]. The overall implant survival rate was 97.2% at 1 year; therefore the authors concluded that the use of an alloplast in combination with either a collagen membrane or a titanium mesh can be considered a successful treatment option in case of peri-implant dehiscences of small or medium entity [27].

In our present study, the alveolar ridge reconstruction with titanium meshes and simultaneous implant placement has proved to be a reliable and effective treatment, with an average horizontal bone gain of 3.67 mm (±0.89).

This is in accordance with the contemporary scientific literature [15, 17, 18, 25–27], which reported that GBR with titanium membranes represent a predictable technique for horizontal bone regeneration and the treatment of small- and medium-sized defects around dental implants.

As reported in different systematic reviews [12, 14, 15, 18], the ideal membrane should possess the following characteristics: biocompatibility, ability to prevent the penetration of unwanted cell lines and to maintain its space, and ease of clinical handling.

The titanium meshes used in the present study meet almost all these requirements: in fact, they are biocompatible, they are efficiently integrated with the tissue, and they can effectively prevent the colonization of the site by connective tissue. In addition, they have excellent space maintenance capabilities and they are easy to use. A membrane, in fact, should be sufficiently stiff to be able to counteract the pressure exerted by external forces (such as tensions within the surgical flap and muscular tensions), but at the same

time quite malleable/easy to be adapted to the defect site [12, 14, 15, 18]. The titanium meshes used here ensure excellent mechanical properties: in fact, they are able to preserve the space effectively and to contain the regenerative material (be it bone or particulate biomaterial) with great efficiency, preventing the collapse of the overlying soft tissue, or the compression generated by the same, that could determine the dispersion of the particulate during healing. Not least, they are easy to handle and can be easily adapted to the site and fixed directly to the implant, allowing the surgeon to sculpt the contours of the alveolar tissue to be regenerated. The ease of use is a key factor, since the easier is the application and adaptation of the membrane, the greater are the chances of success of regenerative therapy [15, 18, 26]. In this context, the possibility to have membranes of different sizes and shapes can be extremely helpful for the surgeon. The titanium meshes used in the present study are available in 9 different configurations, characterized by different size and shape: this helps the clinician to graft different sites (anterior and posterior sites), as alveolar bone has different widths according to locations. In fact, for incisors and cuspids, "narrow" membranes can be used, which have 4.5 mm buccal horizontal extension from the center of fixture; for premolars, "regular" membranes, which have 5.5 mm buccal extension, can be selected. For molars, a wider membrane (6.5 mm buccal horizontal extension) can be used, particularly with immediate placement cases with wall defects; these wider membranes have also a palatal/lingual extension to cover palatal/lingual wall defects.

From the analysis of the current literature, the biological complications emerge as the main problem occurring with titanium membranes, both in the immediate postoperative and in the following months [12, 14, 15, 18–27]. Our present work appears to confirm, at least in part, the evidence emerging from the literature [12, 14, 15, 18].

In this retrospective work on 25 patients, the most frequent complication, which occurred in 12 patients (12/25: 48%), was represented by the postoperative edema; the second complication was represented by postoperative pain or discomfort, which occurred in 10 patients (10/25: 40%). Both of these complications were classified as early complications; however, they were minor in nature as they could be easily managed with anti-inflammatory drugs, resolving already during the first week. The third complication per incidence (6/25: 24%) was instead represented by the exposure of the titanium mesh. The exposure of the titanium mesh is certainly one of the most insidious complications to handle, as reported in the literature [12, 14, 15, 18]; in fact, it can cause the failure of the regenerative technique. In our work, in 4 patients, this complication was managed with success and did not give consequences; in 2 patients it instead determined the infection of the graft, with the necessity of early removal of the titanium membrane. One of these two patients lost part of the graft, while the other lost the entire graft and the fixture. The implant survival at 1 year from the placement of the final restoration was high, with only one lost implant placed out of 40 (implant-based survival 97.5%). No prosthetic complications were registered, either mechanical or technical. The implants used in this study, in fact, present a conical connection (10°) combined with an internal hexagon, characterized by high mechanical stability [28–30]. The conical implant-abutment connections can guarantee high stability, as demonstrated by several recent works [32–34]. In addition, these implants possess an integrated platform switching [29, 30]; this is useful to maintain and preserve the tissue volumes, as previously reported [35–37]; accordingly, a minimal bone resorption was found around the implants, with a mean overall peri-implant marginal bone loss of 0.40 mm (±0.20) 4 months after the implant placement; this bone loss increased to 0.43 mm (±0.15) at the 1-year follow-up control.

Our present study has limits. First, although it is based on data collected from different centers (where surgeons have worked under the same surgical and prosthetic protocols), it is retrospective: retrospective studies are not the best solution to investigate clinical issues and certainly have a lower value than prospective studies. For this reason, further prospective clinical studies or even better, randomized controlled trials will be needed to confirm our present positive outcomes. Second, our present work is based on a limited number of patients (and implants), and the implants here were followed up for a short time (1 year). Therefore, further long-term studies on a larger sample of patients will be needed to evaluate the efficacy of the present treatment and the reliability of these new titanium meshes for bone regeneration of small- and medium-sized peri-implant bone defects.

5. Conclusions

In the present retrospective multicenter study, the authors have reported on guided bone regeneration with titanium meshes and simultaneous implant placement. In particular, a new type of titanium mesh that can be fixed directly on the fixture has been used for bone regeneration of small- and medium-sized peri-implant bone defects. Overall, the horizontal ridge reconstruction with titanium meshes positioned simultaneously with dental implants achieved predictable satisfactory results. In fact, after the removal of the titanium meshes, the CBCT evaluation revealed a mean horizontal bone augmentation of 3.67 mm (±0.89). Mild postoperative edema (48%) and pain/discomfort (40%) after surgery were the most frequent biological complications encountered, but these early complications were completely resolved within one week after surgery. Titanium mesh exposure occurred in 6 patients (24%): one of these patients suffered partial loss of the graft and another complete graft loss and implant failure. After 1 year from implant placement, an overall satisfactory implant survival rate of 97.5% (implant-based) and a limited mean peri-implant marginal bone loss of 0.43 mm (±0.15) were found. The present positive outcomes can be considered encouraging but must be confirmed by further long-term controlled studies on a larger sample of patients.

Competing Interests

The authors declare that they have no competing interests in relation to the present study.

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Clinical Study

Comparison of Bone Resorption Rates after Intraoral Block Bone and Guided Bone Regeneration Augmentation for the Reconstruction of Horizontally Deficient Maxillary Alveolar Ridges

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Purpose. Bone atrophy after tooth loss may leave insufficient bone for implant placement. We compared volumetric changes after autogenous ramus block bone grafting (RBG) or guided bone regeneration (GBR) in horizontally deficient maxilla before implant placement. *Materials and Methods*. In this retrospective study, volumetric changes at RBG or GBR graft sites were evaluated using cone-beam computed tomography. The primary outcome variable was the volumetric resorption rate. Secondary outcomes were bone gain, graft success, and implant insertion torque. *Results*. Twenty-four patients (28 grafted sites) were included (GBR, 15; RBG, 13). One patient (RBG) suffered mucosal dehiscence at the recipient site 6 weeks after surgery, which healed spontaneously. Mean volume reduction in the GBR and RBG groups was 12.48 ± 2.67% and 7.20 ± 1.40%, respectively. GBR resulted in significantly more bone resorption than RBG ($P < 0.001$). Mean horizontal bone gain and width after healing were significantly greater in the GBR than in the RBG group ($P = 0.002$ and 0.005, resp.). Implant torque was similar between groups ($P > 0.05$). *Conclusions*. Both RBG and GBR hard-tissue augmentation techniques provide adequate bone graft volume and stability for implant insertion. However, GBR causes greater resorption at maxillary augmented sites than RBG, which clinicians should consider during treatment planning.

1. Introduction

Adequate hard tissue around a dental implant is crucial for the long term success of the implant placement. However, unfavorable conditions, due to oral infections, bone atrophy after dental extractions, and long term edentulism, may result in insufficient available bone, making implant placement impossible. A variety of surgical techniques, such as onlay grafts, ridge splitting, distraction osteogenesis, and guided bone regeneration (GBR), have been recommended for the rehabilitation of resorbed alveolar ridges to ensure that implants are placed under optimum conditions [1]. Onlay bone graft applications and GBR have become some of the most common treatment modalities for overcoming hard-tissue defects in preprosthetic surgery [1].

Autogenous bone blocks are still considered the gold standard for the reconstruction of deficient alveolar ridges, because of their osteogenic potential [2]. The use of intraoral autogenous bone blocks has been reported as a reliable and predictable technique for increasing moderately to severely deficient alveolar ridges [3].

Guided bone regeneration is another method for augmenting bone volume and uses barrier membranes containing autogenous bone and/or bone substitutes [1]. The application of resorbable membranes has many advantages, such as easy manipulation, an undemanding flap design, and a

reduced risk of membrane exposure, in comparison to nonresorbable membranes [1, 4]. Therefore, in recent years, the use of resorbable collagen membranes for GBR has increased markedly, particularly for horizontal augmentation [1].

Augmented bone stability is considered to be an important factor for the success of the procedure, especially in two-stage regeneration procedures. Bone remodeling has a major influence on long-term clinical outcomes, and graft stability is desirable for integrating dental implants so as to ensure a good outcome [1]. Deproteinized bovine bone (DBB) is an osteoconductive bone substitute that can withstand resorption during healing and can provide a good scaffold for natural bone growth [4]. DBB can be used with autogenous bone and its slow resorption properties could be an advantage in that it helps to maintain the volumetric stability of augmented bone [4].

Little is known about the volumetric extent of resorption of intraoral block bone grafts and GBR augmentation prior to implant placement. Treatment planning could be facilitated if the resorption rate of the grafted bone volume is known, as clinicians can then choose the optimum treatment modality for patients and may not need to perform repeat surgeries to increase bone volume, which has a marked impact on patient morbidity.

The primary aim of the present study was to evaluate the volumetric changes in patients who underwent autogenous ramus block bone grafting (RBG) or GBR in horizontally atrophic maxillae, based on three-dimensional (3D) analysis of cone-beam computed tomography (CBCT) images. More specifically, this study aimed to compare the resorption rates of horizontally augmented alveolar bone between RBG and GBR techniques and to estimate the bone gain achieved before implant placement. The null hypothesis was that there would be no difference between the two interventions in terms of the rate of volume reduction of the grafted bone.

2. Materials and Methods

2.1. Study Design and Sample Selection. This retrospective study included patients with deficient alveolar ridges who underwent intraoral onlay block bone grafting, using the ramus of the mandible, or GBR, between January 2013 and January 2014, at the Department of Oral Implantology Istanbul University Faculty of Dentistry or the Department of Oral and Maxillofacial Surgery, Aydın University Faculty of Dentistry, Istanbul, Turkey. Subjects were derived from a population of patients with moderate to severe bone resorption and required implant placement in the maxillary alveolar ridge. Sample selection was performed by retrospective chart review.

Inclusion criteria for this study were as follows: the presence of a deficient maxillary ridge requiring two-stage horizontal bone augmentation for dental implant placement; the presence of a residual alveolar ridge with residual bone width < 5 mm and adequate bone height; bone volume at the ramus donor site that allowed harvesting of a block graft; availability of CBCT data acquired before, 3 weeks after surgery, and at last follow-up (healing periods for RBG and GBR were 4 months and 6-7 months, resp.). The exclusion criteria were as follows: lack of CBCT data; previous surgery at the recipient site; systemic diseases that might unfavorably influence soft and/or hard-tissue healing; chronic periodontitis in the remaining teeth; bone defects due to tumor resection; pathologic lesions prior to operation; a history of radiotherapy in the head and neck region; and smoking.

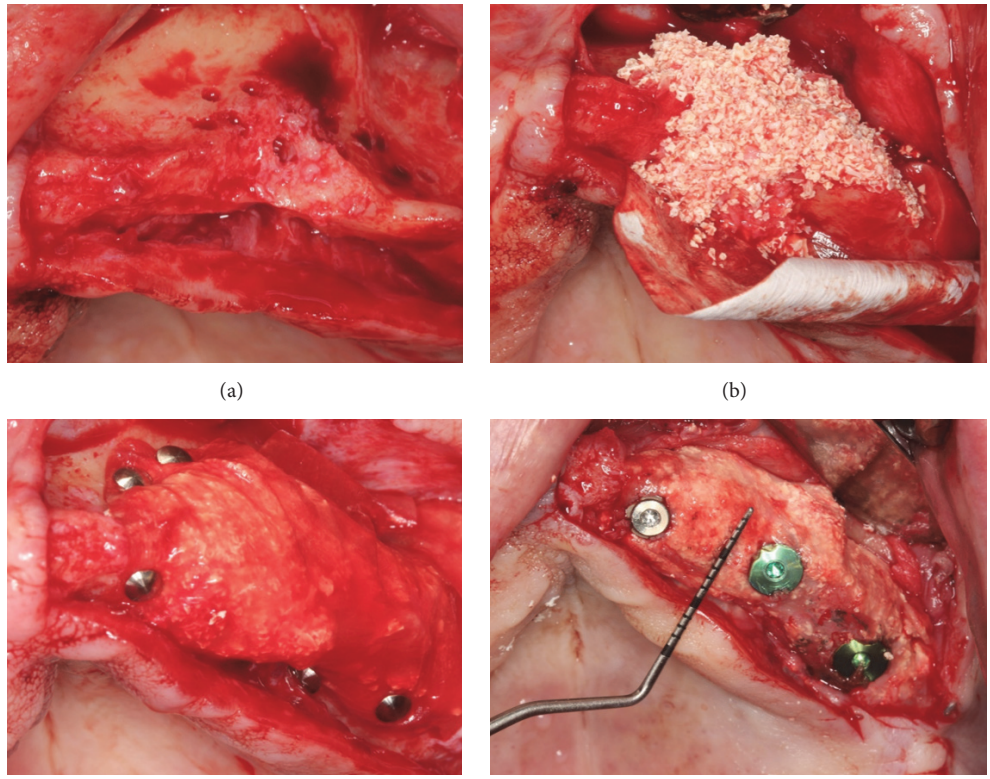
The decision to use GBR or RBG as treatment choice was based on patient-specific anatomical handicaps; for instance, if during treatment planning based on CBCT sufficient autogenous bone particles could be acquired from near the recipient site, GBR treatment was chosen; however, if not, RBG treatment was chosen.

The study protocol followed the Declaration of Helsinki and was approved by the ethical committee of the Aydın University, Turkey (approval protocol number: 480.2/116). Written informed consent was obtained from all patients.

2.2. Surgical Methods. All patients were treated with a two-stage approach by either of two surgeons (GBR group: B. Alper Gultekin; RBG group: Elcin Bedeloglu). All surgical procedures were performed under local anesthesia. Prior to surgery, all patients were instructed to rinse their mouths with 0.2% chlorhexidine mouthwash (Chlorhex, Drogsan Pharma, Istanbul, Turkey) for 1 min.

For the GBR group, crestal and vertical incisions were made along the residual alveolar ridge. A mucoperiosteal flap was gently elevated to allow complete visualization of the horizontal defect and the surrounding bone. The native bone was perforated by drilling under saline irrigation, to ensure vascularization between the graft and the recipient site. The recipient bone was curetted to remove any soft tissue that may impede bone healing. Autogenous bone particles were harvested from near the recipient site using a bone scraper (Safe scraper, META, Reggio Emilia, Italy) and mixed with DBB (particle size, 0.25–1.0 mm; Bio-Oss, Geistlich Pharma AG, Wolhusen, Switzerland) in a ratio of approximately 1 : 1 to form the composite graft. Resorbable collagen membrane (Bio-Gide, Geistlich Pharma AG, Wolhusen, Switzerland, or Mem-Lok, Collagen Matrix, Franklin Lanes, NJ, USA) was trimmed according to the contours of the grafting site and then applied for horizontal augmentation. After grafting, the resorbable membrane was immobilized with tacks (Pinfix, Sedenta, Istanbul, Turkey) into the palatinal and buccal sites. Flaps were repositioned with interrupted nonresorbable mattress sutures, with periosteal-releasing incisions (Figure 1).

For the RBG group, crestal and vertical incisions were made along the residual alveolar ridge at the recipient site. The mucoperiosteal flap was gently elevated to allow complete visualization of the horizontal defect and the surrounding bone. The native bone was perforated by drilling under saline irrigation, to ensure vascularization between the graft and recipient site. To harvest the bone block, infiltration anesthesia was also administered to the left or right donor site. In the ramus zone, midcrestal incision was performed. After reflection of the full-thickness flap and exposure of the donor site, a mandibular block bone was harvested by splitting the outer cortical plate according to the required size to produce a bone block from the retromolar area. In all patients, piezoelectric surgery (Piezon Master, EMS,



(a) (b)

(c) (d)

Figure 1: Resorbable collagen membrane and composite graft (autogenous particle bone and deproteinized bovine bone) were applied for horizontal augmentation (a–c); implants were placed after healing (d).

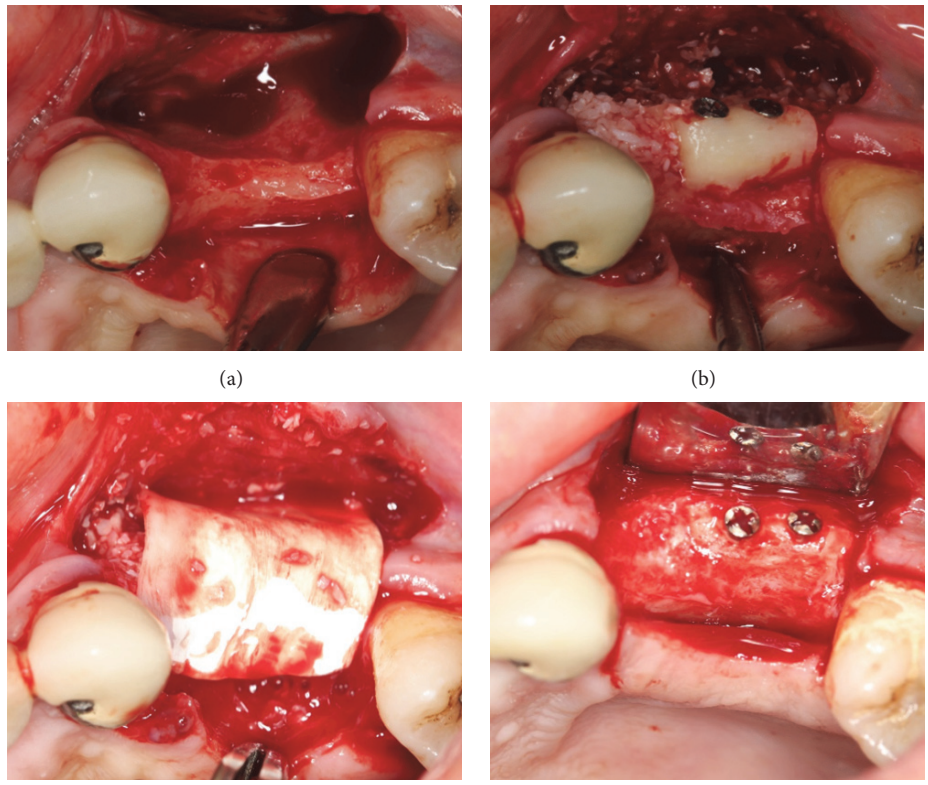
Basel, Switzerland) or rotary instruments were used, under copious irrigation, to harvest the bone block. A surgical chisel and hammer were used to mobilize the block graft. The block bone graft was recontoured, using a diamond bur, to ensure that it was optimally adapted to the recipient site as an onlay. It was then fixed to the residual ridge, using one or two screws, to inhibit micromovement during healing. Graft corners between the graft and native bone were smoothed to avoid undesirable exposure because of pressure during healing. A particulate deproteinized bovine bone graft (Bio-Oss) was used to fill the voids around the block bone and recipient site. A resorbable collagen membrane (Bio-Gide) was used for covering the graft particles and block bone without tacks (Figure 2). A periosteal-releasing incision was made to allow passive primary closure of the flap. Wound adaptation was achieved with horizontal mattress and interrupted 4–0 nonabsorbable monofilament sutures (Seralon, Serag-Wiesner, Naila, Germany).

All patients were prescribed postsurgical medications, including antibiotics (1000 mg amoxicillin and clavulanic acid, twice daily for a week, starting from the day of surgery), analgesics (600 mg ibuprofen, to be taken per requirement, every 6 h), and 0.2% chlorhexidine mouthwash (twice daily for 2 weeks, starting from the day after surgery). Dexamethasone (4 mg per day) was administered for 3 days to minimize edema. An extraoral cold pressure dressing was applied to minimize postoperative swelling. Oral sutures were removed 3 weeks after surgery. Patients in the RBG and GBR groups were allowed healing periods of 4 and 6-7 months, respectively, before placement of rough-surface dental implants. Patients were prohibited the use of temporary prostheses during the healing period. Patients then received fixed cement-retained porcelain-fused-to-metal crowns and bridges or removable-bar overdenture prosthetic restorations.

2.3. Study Variables. The primary predictor and outcome variables were the augmentation technique (RBG or GBR) and the rate of resorption at the augmented site, before implant placement, respectively. Secondary study variables included the success of bone grafting, bone gain, and implant stability.

2.4. Clinical Assessment. Patients in both treatment groups were evaluated clinically. Any complications, such as graft or block exposure, infection, immobilization of the block graft, loss of bone particles, and adequate bone volume during implant placement, were evaluated. The clinical success of implant placement at the graft site was evaluated on the basis of implant stability at the second stage surgery. Final insertion torques ($<$ or $\geq$35 Ncm) of implants during placement at graft sites were recorded using a physiodispenser (W&H ImplantMed, Burmoos, Austria).

2.5. Radiographic Assessment. Pre- and postsurgical repetitive radiological assessments were performed using CBCT to evaluate volumetric changes at the augmented sites. Images



(a) (b) (c) (d)

Figure 2: The block bone graft was fixed to the residual ridge with screws and a particulate deproteinized bovine bone graft was used to fill the voids around the block bone and the recipient site (a, b); a resorbable collagen membrane was used to cover the grafted site (c); grafted site after 4 months of healing (d).

were acquired before surgery, within 3 weeks (V1), and after 4 or 6-7 months after bone grafting (V2), depending on the treatment method. Image analysis was performed using the i-CAT 3D imaging system (Imaging Sciences International Inc., Hatfield, PA, USA), with a field of view of 13 × 8 cm and a voxel size of 0.25. The methodology for digital volumetric calculation has been described earlier [5]. The augmented area was traced as a region of interest. Imaging data of the augmented sites were transferred to a new workstation, where the volumetric changes in bone grafts were analyzed using MIMICS 14.0 software (Materialise Europe, World Headquarters, Leuven, Belgium). Augmented sites were reconstructed in 3D to assess postsurgical volumetric changes at two reference time points (V1 and V2). In order to ensure the reproducibility of volumetric measurements during different time periods, graft sites were selected using anatomical landmarks, fixation tacks, and screws as points of reference (Figure 3). During digital reconstruction of the augmented sites, resorbable membranes, tacks, and native bone, screened at regions of interest in augmented sites, were included in volumetric measurement. Presurgical residual bone width (W0) and augmented bone width (W1) after healing were measured linearly, 2 mm apical to the top of the crest, at a point near the planned implant insertion site, using the i-CAT software. In addition, bone gain was calculated for horizontally augmented sites. A single value of bone gain was anticipated for each graft site. In cases where more than one implant was to be placed at the graft site, the greatest horizontal bone gain was considered for further analysis. All radiographic volumetric and linear measurements were acquired and recorded by the same calibrated independent examiner (T. Emre Kose) under identical conditions, in order to prevent bias and ensure excellent reliability ($R = 0.964$).

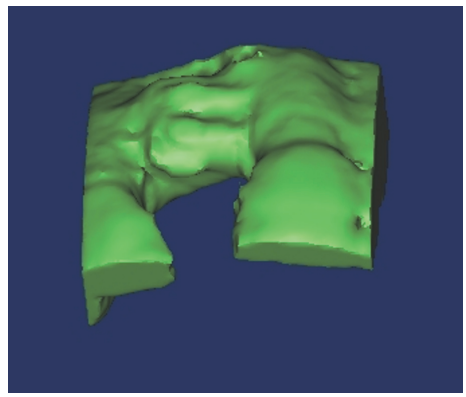


Figure 3: Digital reconstruction was performed by selecting the grafted site, and volumetric changes were analyzed.

2.6. Statistical Analysis. Statistical analyses were performed using the Number Cruncher Statistical System 2007 (Kaysville, Utah, USA). Descriptive statistical values were

Table 1: Descriptive summary of the study sample.

Study variable	Descriptive statistics
Sample size	
Patients, *n*	24
Sites, *n*	28
Demographic variables	
Gender	
M/F, *n* (%)	11 (39.3)/17 (60.7)
Age (years), mean ± sd (min–max)	48.82 ± 10.17 (28–67)
Health status variables	
ASA classification	
I	24 (100%)
Groups: numbers and sites, *n* (%)	
GBR horizontal	15 (53.6)
RBG horizontal	13 (46.4)
Implant torque, *n* (%)	
Up	15 (53.6)
Down	13 (46.4)
Edentulism, *n* (%)	
Total	8 (28.5)
Partial	20 (71.5)
Prosthesis design, *n* (%)	
Fixed	20 (71.4)
Removable	8 (28.6)

ASA, American Society of Anesthesiology; GBR, guided bone regeneration; RBG, ramus block bone graft.

expressed as mean, standard deviation, minimum, maximum, frequency, and percentages. Independent samples *t*-tests were used to test differences in quantitative variables between two independent groups. Yates' continuity correction was used to test differences in qualitative variables between the two independent groups. Pearson's correlation coefficient was used to analyze the correlation among quantitative variables. Linear regression analysis was conducted to analyze the possible risk factors for change in volume (V1-V2). P values less than 0.05 were considered statistically significant.

3. Results

Of the 26 patients initially enrolled in the study, two were excluded because of the poor quality of imaging data. Eventually, 24 patients with 28 grafted sites (GBR, 15; RBG, 13) were determined to be eligible for inclusion in this study (Table 1). Bilateral augmentation was performed in two patients in each group. In a single patient in the RBG group, mucosal dehiscence was observed at the recipient site at 6 weeks after operation, as a complication. The minor exposed site was removed by using a diamond bur under copious irrigation, and the exposed region disappeared spontaneously in subsequent weeks, without infection. After healing, implants were placed at the graft site, without any complications. Following graft integration, a total of 41 rough-surface dental implants (GBR, 23; RBG, 18) were successfully placed, without encountering any primary stability problems at the reentry stage. Only in one case in the GBR group was contour augmentation (DBB and collagen membrane were used) applied during implant placement, to thicken the buccal bone.

There were no significant differences in patient's age, sex distribution, implant torque values, and presurgical bone width (W0) between the two groups ($P > 0.05$; Table 2). Bone width (W1) and bone gain (W1-W0) after healing in the GBR group were significantly higher than those in the RBG group ($P = 0.005$ and $P = 0.002$, resp.; Table 2).

The mean values of percent volume reduction after healing in the GBR group (12.48 ± 2.67%) were significantly higher than those of the RBG group (7.20 ± 1.40%, $P < 0.001$; Table 3). Although the postaugmentation graft volumes (V1 and V2) of the GBR group were higher than those of the RBG group, no statistically significant differences were found ($P > 0.05$; Table 3).

No significant correlation was found between variables (age, gender, pre- and postsurgical bone width, bone gain, and implant torque) and rate of graft resorption (V1-V2) in the groups ($P > 0.05$, Table 4). No significant correlation was found between the initial postaugmentation bone volume (V1) and the rate of resorption (V1-V2) in GBR and RBG groups separately ($P > 0.05$, Table 4). However, the initial postaugmentation graft volume (V1) and rate of graft resorption (V1-V2) were found to be significantly and positively correlated ($r = 0.459$, $P = 0.014$).

Linear regression analysis was used to identify factors involved in V1-V2 change. The model was found to be statistically significant and variables in the model explained 72.8% of the V1-V2 model variance (F: 25.050, $P < 0.001$, R^2_{adj}: 0.728, Table 5). When the effect of other variables was held constant, application of RBG rather than GBR resulted in a 6.030 decrease in V1-V2 change (β [95% confidence interval, 95% CI]: −6.030% [−7.742%, −4.317%], $P < 0.001$, Table 5). When the effect of other variables was held constant, a unit increase in V1 caused an increase of 0.0086% in the V1-V2 value (β [95% CI]: 0.0086% [0.0002%, 0.0015%], $P = 0.012$, Table 5).

4. Discussion

A prosthetically driven treatment approach recommends that a deficient edentulous ridge that precludes optimum implant placement requires bone reconstruction [6]. The maxilla is prone to resorption in a centripetal direction; therefore, a deficiency in bone width after tooth loss is very common in the upper jaw. The present study aimed to compare GBR and RBG groups for horizontal deficiency in the maxillary alveolar ridge in terms of the resorption of bone at graft sites and of augmentation treatment success.

Although we observed a significant volumetric reduction in the bone graft in both groups, the extent of resorption during follow-up in the GBR group was greater than that in the RBG group. According to the literature, sites augmented with mandibular block bone have resorption rates between 5% and 28% [2, 6–14]. Cordaro et al. reported resorption of

Table 2: Study variables versus predictor variable (augmentation technique).

	GBR ($n = 15$) Mean ± SD	RBG ($n = 13$) Mean ± SD	P
Patient number	13	11	
Graft sites	15	13	
Age, years	48.73 ± 10.96	48.92 ± 9.61	[a]0.962
Gender, F/M, n			
Male	5 (33.3)	6 (46.2)	[b]0.761
Female	10 (66.7)	7 (53.8)	
Implant torque, sites			
Up	6 (40.0)	9 (69.2)	[b]0.243
Down	9 (60.0)	4 (30.8)	
W0, mm	3.51 ± 0.70	3.42 ± 0.60	[a]0.720
W1, mm	8.93 ± 0.93	7.96 ± 0.71	[a]0.005**
W1-W0, mm	5.42 ± 0.76	4.54 ± 0.59	[a]0.002**

[a]Independent samples t-test; [b]Yates' continuity correction; **$P < 0.01$.
GBR, guided bone regeneration; RBG, ramus block bone graft; W0, presurgical bone width; W1, bone width after healing; W1-W0, bone gain after healing.

Table 3: Association between predictor (augmentation technique) and primary outcome (resorption) variable.

	GBR ($n = 15$) Mean ± SD	RBG ($n = 13$) Mean ± SD	P
V1, mm^3	5557.50 ± 1060.73	4959.11 ± 1152.21	[a]0.164
V2, mm^3	4853.61 ± 885.61	4594.13 ± 1035.67	[a]0.481
V1-V2 (%)	12.48 ± 2.67	7.20 ± 1.40	[a]<0.001**

[a]Independent samples t-test; **$P < 0.01$.
GBR, guided bone regeneration; RBG, ramus block bone graft; V1 and V2, initial postaugmentation and posthealing graft volumes, respectively; V1-V2 (%), resorption rate.

Table 4: Study variables versus primary outcome (resorption) variable.

	V1-V2 (%)	
	Mean ± SD	P
Gender, F/M, n		
Male	10.11 ± 3.25	[a]0.924
Female	9.98 ± 3.64	
Implant torque, sites		
Up	9.28 ± 3.19	[a]0.219
Down	10.87 ± 3.61	
	r	P
Age, years	0.105	0.597
W0, mm	0.110	0.576
W1, mm	0.252	0.196
W1-W0, mm	0.210	0.283
V1		
GBR	0.387	0.154
RBG	0.541	0.056
Total	0.459	0.014*

[a]Independent samples t-test; r: Pearson's correlation coefficient; *$P < 0.05$.
V1-V2 (%), resorption rate; W0, presurgical bone width; W1, bone width after healing; W1-W0, bone gain after healing; V1, initial postaugmentation graft volume.

mandibular autogenous block graft sites (22%) in all of their patients at 4 months after maxillary augmentation [11]. In some of their cases, they used DBB and collagen membrane to reduce the resorption rate. Linear measurements were performed using a millimeter-graduated caliper. In another study, Hernández-Alfaro et al. found a 5% resorption rate after total reconstruction of the atrophic maxilla by using intraoral bone blocks and biomaterials [12]. In their study, 3D analysis was performed to measure the changes at the grafted site by means of CBCT scans. Pistilli et al. have reported a 25% bone resorption rate from the initial volume of autogenous onlay blocks [13]. In another study, Lumetti et al. found a 28% resorption rate after ramus or symphysis autologous block bone grafting for augmenting horizontal ridges [14]. In the present study, we generally found less bone resorption in the RBG group than in previous related intraoral block grafting studies [11, 13, 14]. Several factors may influence resorption rates after block bone grafts, such as the type of reconstruction, technique, the cortical bone amount and density at the donor site, biomaterial usage, healing time, and most importantly the measurement method [1, 2, 8–10]. In most previous studies, measurements were made linearly, which induces a high risk of bias.

Mandibular bone blocks are more resistant to resorption due to the vast amount of cortical bone (intramembranous bone graft); however, this advantage may hold a risk in terms of integration of the block and natural bone, due to the limited

Table 5: Linear regression analysis to identify predictors of V1-V2 change.

	β	P	95% CI for β	
			Lower bound	Upper bound
Constant	21.499	<0.001**	13.606	29.392
Augmentation technique (RBG)	−6.030	<0.001**	−7.742	−4.317
V1	0.0086	0.012*	0.0002	0.0015

*$P < 0.05$; **$P < 0.01$.
RBG, ramus block bone graft; V1, postaugmentation graft volume; CI, confidence interval.

revascularization and poor regeneration potential of the block [1, 6]. Lozano et al. observed that the revascularization process of a block graft increases with time [15]. In the present study, we waited 4 months to enhance vascularization and integration of graft, and we did not observe any complications related to block disintegration during implant placement. All blocks were used in deficient maxillae; blood supply to the maxilla may be better than that to the mandible, which may be another reason for the good integration during healing [13]. Block bone coverage of the recipient site with bone substitutes with low turnover rates, such as DBB and resorbable collagen membranes, may reduce the rate of bone resorption after block bone grafting [4]. Maiorana et al. found that DBB coverage of onlay block grafts reduced resorption by almost 50% in comparison to that in the absence of coverage [16, 17]. Bone substitutes may also contribute to the creation of a smooth connection between bone block and natural bone and can provide a scaffold for the regeneration of bone at these gaps [4, 16]. Another advantage of using resorbable rather than nonresorbable membranes is the elimination of second stage surgery. Although the barrier function cannot be controlled by the clinician and space maintenance is limited, it is likely that the use of resorbable membrane with tacks in the GBR group and without tacks in RBG group would be suitable for the reconstruction of deficient sites.

Bone gain and survival rates of implants in sites grafted using the GBR treatment approach are well documented; however, the stability of regenerated bone has been assessed in very few studies [18, 19]. In the present study, we found more resorption in the GBR group than in the RBG group, but the resorption rate was lower than in other GBR-related bone resorption studies [18, 19]. Mordenfeld et al. found 37% to 46% resorption rates after lateral augmentation with a GBR approach, using two different compositions of graft materials [18]. In their study, composite grafts (DBB and autogenous bone) were covered with collagen membranes, without any fixation. Although they used CBCT scans for measurement, they calculated the changes in graft volume as the product of slice thicknesses of the region of interest and the sum of volumes, rather than obtaining measurements as a single unit [18]. In another study, Sterio et al. observed the resorption or displacement of 50% of horizontal graft material after 6 months of healing [19]. The authors used cancellous allografts and collagen membranes without tacks in order to increase bone width and evaluated the changes in bone dimension by CBCT and 2D measurements using calipers. Proussaefs and Lozada observed a 15.11% resorption rate at 6 months after bone grafting using a composite (DBB and autogenous bone particles) and nonresorbable membrane [20], based on linear measurements made on laboratory casts derived from intraoral impressions.

In the present study, a 12.5% rate of resorption was found for the GBR group after healing. One of the reasons for the reduced resorption observed in the GBR group may be that tacks were used to squeeze the particulate composite graft under the membrane to mimic a block graft to ensure space maintenance and resist the pressure that may be induced by the flap, cheek, or other forces during healing [21]. In the RBG group, space maintenance is achieved by the block itself, and therefore resorbable membrane can be used without tacks and prevent cells, such as epithelial cells, and connective tissue from impeding bone regeneration. Another reason for the reduced resorption of GBR is that it involves a composite of a low turnover graft material and autogenous particulate bone. Autogenous bone particles may accelerate integration with graft particles and decrease the volume reduction of the grafted bone. During healing, vascularization may initiate from perforated residual bone. During drilling and implant placement, the bone appeared to be in a good state, and composite graft particles had become well integrated. It seems that 6-7 months of healing may be sufficient for the formation of a rigid grafted bone that can facilitate implant stability in horizontally deficient ridges. However, one of the major drawbacks of GBR compared to RBG is the necessity for a longer healing period. RBG may be a better option requiring a substantially shorter treatment time than GBR, when time is critical for clinicians and patients.

Dasmah et al. compared graft resorption rates after using autogenous iliac particulates and a block bone treatment approach in the reconstruction of atrophic maxilla [22]. Although they found no statistical difference between the two groups, a marked resorption rate (80%) was observed in both groups. In the present study, we found lower resorption rates than those reported by Dasmah et al. [22]. Usage of intraoral sources, such as the ramus or symphysis for block grafting, and biomaterials, such as autogenous particulate grafts in the GBR approach, seems to eliminate unpredictable resorption. Another possible reason for the lower rate of resorption in both groups in the present study than in previous studies involving GBR and RBG is that we did not use removable provisional restorations during the healing stage. It is well known that any soft tissue support prosthesis may increase the resorption of both the residual and grafted bone [23]. In light of the promising results in terms of the GBR resorption rates observed in the present study, we speculate that a collagen membrane, composite graft, and

tacks can offer an alternative to nonresorbable membranes. The latter membranes have many disadvantages, such as a high risk of wound infection, requirement for second stage surgery, and a long learning curve in terms of reconstruction of horizontal defects, before implants can be placed.

Both groups in the present study exhibited adequate horizontal bone gain for implant placement after the healing period. There is a great discrepancy in the literature about the extent of horizontal bone gain after bone augmentation with RBG and GBR. Previous studies involving two-stage approaches have reported a mean horizontal bone gain ranging from 4 to 6 mm after RBG [3, 4, 7, 10, 24, 25], while the mean horizontal bone gain in GBR approaches has been reported to range from 1.37 to 6 mm [18, 19, 21, 26, 27]. Our results for both groups are in agreement with those of previous studies. In the present study, the GBR group demonstrated significantly greater bone gain for horizontal augmentation than did the RBG group after healing. In the RBG group, the maximum cutting depth of the bone block is limited by the anatomical restrictions of the lower jaw; therefore, horizontal bone gain is of necessity directly proportional to the thickness of the harvested bone block. In the GBR group, horizontal bone gain can be increased with the amount of composite graft used. However, clinicians should consider the differences in the extent of graft resorption when choosing between these two different treatment approaches.

The present study reported predictable and reliable results for horizontal reconstruction of the maxilla and achieved 100% implant stability at these augmented sites. This result is in accordance with many studies [1, 6, 11]. In the present study, graft sites reconstructed by both treatment approaches had exhibited deficiency in the horizontal dimension. Augmentation of the bone resulted in some part of the implant body being in contact with matured bone, which would increase the primary stability during placement and consequently reduce the risk of implant stability failures. Another reason for enhancing the primary stability of the implants is the placement of implants in a well-revascularized and healed, rigid, grafted area using a two-stage approach. Healed grafted sites may thus have enhanced potential for implant stability [1, 11, 15, 16].

We did not observe any complications, such as infection, temporary or permanent sensory disturbance, or membrane exposure in our patients. Only in the RBG group was the minor dehiscence of the mucosa at the recipient site observed in one case, but this was managed after removing the exposed area. Complications following block bone harvesting at the ramus, as compared to other intraoral donor sites, such as the symphysis, are less common [28]. In the present study preoperative treatment planning was meticulously performed based on 3D images obtained by CBCT in both groups, and all anatomical restrictions, such as the mandibular alveolar nerve, and the thickness of the buccal cortical bone in retromolar areas were evaluated before harvesting the block bone in RBG group. It may not be possible to make such an extensive evaluation using two-dimensional (2D) radiographs. It can be speculated that both treatment approaches are safe and reliable when using 3D radiographic preoperative evaluation.

In the present study, treatment outcomes were evaluated in 3D using CBCT, rather than making linear measurements by caliper, periodontal probe, or 2D radiographs, such as panoramic radiography. 2D techniques do not provide adequate and reliable measurements for the evaluation of volumetric changes in alveolar crest grafts over time. Additionally, these techniques do not have the ability to measure 3D changes precisely [6, 21]. It can be speculated that CBCT is a reliable and predictable 3D radiographic technique for acquiring high-quality volumetric measurements after ridge augmentation.

One of the limitations of the study is that graft resorption was evaluated during the healing stage only. Nevertheless, bone resorption is expected to be greater before implant placement and loading and to slow significantly thereafter [6, 23]. Therefore, evaluation of resorption is more important before implant placement. Another limitation is the lack of histological analysis in both groups after healing. Nevertheless, the present study provides valuable insights into the volumetric resorption after two intraoral surgical techniques before implant placement.

5. Conclusion

It may be concluded that the use of both RBG and GBR for hard-tissue augmentation provides an adequate volume of bone and stability for implant insertion. However, GBR results in greater resorption at maxillary augmented sites than RBG. Therefore, clinicians should consider the differences in the extent of graft resorption when planning treatment.

Competing Interests

None of the authors has any relevant financial relationship(s) with a commercial interest.

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