A Lateral Approach for Sinus Elevation Using PRGF Technology

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ABSTRACT

Purpose: A lateral approach for sinus elevation using plasma rich in growth factors (PRGF) technology is described. The long-term survival of dental implants installed following a two-stage procedure after sinus elevation using this procedure is reported, using implant loss as the outcome variable.

Materials and Methods: A retrospective cohort study design was used. Eighteen patients received 43 implants (BTI implants, Biotechnology Institute, Vitoria, Spain) with sinus floor elevation. All patients presented a residual bone height of class D (1–3 mm). Implants were installed using a low-speed drilling procedure (50 rpm) without irrigation. Finally, the histological and histomorphometric evaluation of eight samples from PRGF grafted sinus involved in the study was carried out 5–6 months posttreatment.

Results: The overall survival rate of dental implants was 100%. The mean follow-up period for all implants was 33 ± 7 months ranging from 24 to 44 months. In addition, the histomorphometrical evaluation of the samples evidenced a 25.24 ± 4.62% of vital newly formed bone, 50.31 ± 15.56% of soft connective tissue, and the remaining 24.46 ± 12.79% of bovine anorganic bone.

Conclusions: Based on these results, this new approach for sinus elevation and implant installation using PRGF technology can be considered safe, simple, effective, and predictable.

KEY WORDS: lateral approach, PRGF, sinus lift

INTRODUCTION

Implant insertion in the posterior region of the maxilla is a challenging procedure. Progressive resorption of both horizontal and vertical bone increases the cavity while reducing the thickness of the maxillary sinus floor.[1,2] The absence of upper molars may even increase bone resorption, leading to sinus pneumatization due to the increased osteoclast activity in the schneiderian membrane. These limitations may hamper implant installation and negatively affect successful osseointegration and stability of dental implants. In fact, several studies have reported that a higher rate of implant failures is observed in the upper jaw than other oral regions.[3–5]

The most frequently applied procedure to reestablish an adequate bone volume and ridge height in the posterior maxilla is the augmentation of maxillary sinus floor. The latter involves the modification of the sinus cavity with the aim of generating enough bone volume inside a space previously being a portion of the sinus cavity. The Caldwell-Luc procedure, consisting of a lateral approach via a trapdoor access to the maxillary sinus was first reported as a sinus lift approach.[6–9] Some years later, a less invasive osteotome technique which eliminated the need for a trapdoor access was described.[10–12] In this new approach, elevation of sinus floor was performed by inward collapse of the residual crestal floor, using specially designed osteotomes. One critical issue to succeed is the correct selection of the appropriate approach for each clinical situation. Some potential factors that may help the decision-making

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include the alveolar bone height and width, and the extent of the desired augmentation among others.

According to the consensus held on sinus lifting,[13] when residual bone height is between 1 and 3 mm, a lateral approach involving bone grafting material and a two-step implant placement is recommended. In the present article, we describe a lateral approach based on the application of the different formulations obtained from plasma rich in growth factors (PRGF) technology in sinus lift surgery. PRGF is an autologous plasma product rich in platelets which enables after activation with calcium the local release of multiple growth factors and bioactive proteins that modulate the processes of wound healing and tissue engineering.[14,15] Some distinguishing steps of this new lateral approach include the use of a mixture of bovine anorganic bone and PRGF-scaffold as sinus graft material, the use of liquid PRGF as culture medium to maintain the bone window until its reinsertion in its native anatomic location, and the use of autologous fibrin as sealing membrane. Additionally, an ultrasonic generator is used to open the bone window which enables an increased tactile control and avoids soft tissue damage.[16] Interestingly, once the osseous window is separated, it is placed in a solution of liquid PRGF to maintain its functionality until placing it again in its native anatomic location. Therefore, the original bone window is conserved and replaced in this new sinus lift approach. Last but not least, in the case of schneiderian membrane perforation, the biocompatible fibrin may be used as autologous sealant biomaterial.

Apart from describing this new approach, the long-term survival of dental implants installed following a two-stage procedure after sinus elevation using this procedure is reported, using implant loss as outcome variable.

MATERIALS AND METHODS

The protocol was approved following the national and international (International Conference of Harmonization rules) policies on clinical studies. This study was carried out in Vitoria (Spain) and was comprised of patients with a loss of height in the posterior maxilla that required application of a sinus lift technique to allow rehabilitation with dental implants. The exclusion criterion was the absence of any local or systemic diseases that might contraindicate the treatment. All patients involved in the study presented a significant alveolar atrophy and a residual bone height of class D (1–3 mm).[13] A total of 18 consecutive patients were selected for the study, 12 females and 6 males, who received at least one dental implant in the maxilla for a total number of 43 implants (BTI implants, Biotechnology Institute, Vitoria, Spain) with sinus floor elevation. Smokers were not excluded from the study, but were informed that tobacco use is contraindicated in an intra-oral surgery setting as it may compromise the efficacy of the sinus lift procedure and reduce the long-term survival of implants.

Liquid PRGF and Fibrin Elaboration

Peripheral blood (20–30 mL) from each patient was taken by venipuncture before surgery and placed directly into 5-mL tubes (blood collecting tubes®, BTI) which contain 3.8% (wt/vol) sodium citrate as anticoagulant. Liquid PRGF was prepared by centrifugation (PRGF system®, Vitoria, Spain) at 460 g for 8 minutes at room temperature. The 0.5 mL plasma fraction located just above the red cell fraction, but not including the buffy coat, was collected and deposited in a glass dish. In order to initiate clotting and the formation of a three-dimensional fibrin matrix for the continuous release of growth factors and proteins, PRGF activator® was added to the liquid PRGF preparation (50 μL PRGF activator® per milliliter of preparation). In order to prepare the autologous fibrin membrane, the milliliter of plasma fraction located at the top of the tubes was transferred to a glass bowl. After adding PRGF activator®, it was incubated at 37°C for 40–45 minutes, allowing the formation of a biocompatible fibrin with excellent elastic and homeostatic properties.

Surgical Protocol

Antibiotics (2 g of amoxicillin clavulanic acid) were prescribed to each patient, starting 30 minutes before surgery and during 6 days postsurgically. Midazolam (7.5 mg, 1 tablet) were also administered 30 minutes preoperatively. Dexamethasone (4 mg) was administered orally before the surgery and for the next 3 days with a decreasing dose (3, 2, and 1 mg, respectively). Analgesics were used pre- and postoperatively during 2–3 days. Patients were instructed on how to maintain proper oral hygiene around implants.

The operative area was reached by means of a full-thickness flap. As it is illustrated in Figure 1, access to the cavity was obtained using a periodontal ultrasonic

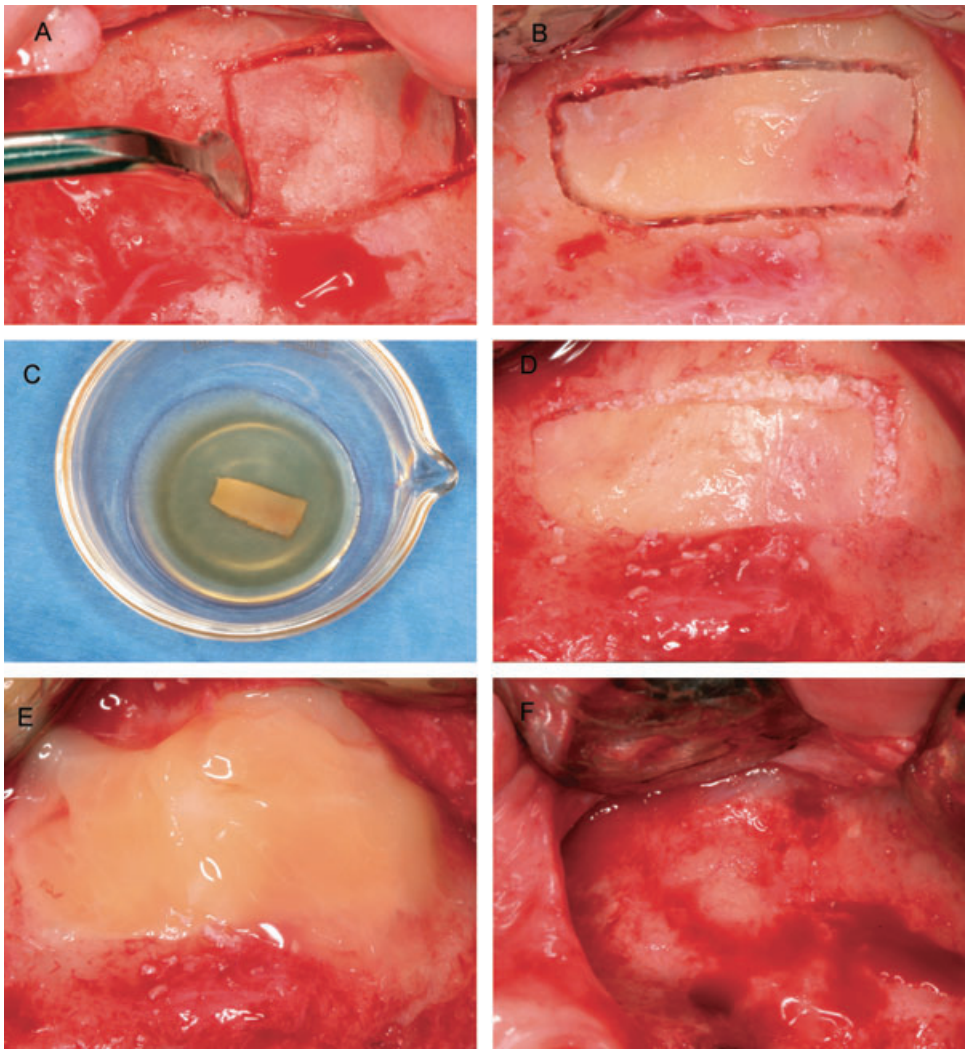

Figure 1 Schematic description of the new lateral approach for sinus elevation. (A) The surgical ultrasonic generator is used to create a vestibular osteotomy. (B) The bone window can be easily separated. (C) The bone window is maintained in liquid PRGF. (D) The window is easily replaced in its original anatomic location. (E) The bone window is covered with the autologous fibrin. (F) Reopening 5 months later.

generator (Ultrasonic®, BTI) combined with an independent irrigation system with BTI sterile pyrogen-free water. The osteotomy line is made by cutting and dispersing the osseous table in a controlled and progressive way. The ultrasonic tip of the device enables an increased tactile control and avoids soft tissue damage. A complete osteotomy along the perimeter of the osseous window is initiated and deepened until tactile sensation of the schneiderian membrane. Once the osseous window is separated, it is placed in a solution of liquid PRGF until placing it again in its native anatomic location. Therefore, the original bone window is conserved and replaced in this new sinus lift approach. Once the fenestration is completed, the schneiderian membrane in the sinus floor is carefully separated using the BTI membrane rasps to avoid any perforation of the schneiderian membrane. Interestingly, in the case of schneiderian membrane perforation, the biocompatible fibrin may be used as an autologous sealant biomaterial. The autologous fibrin is an alternative biomaterial to the collagen membrane. In addition, sinus walls will be scraped with the help of the ultrasonic device in order to promote the vascularization of the area and thus stimulate the later bone regeneration.

The graft material used in the present protocol to fill the cavity was a mixture of 1.5–2.5 g. of bovine anorganic bone (Bio-Oss®, Geistlich Biomaterials, Wolhusen, Switzerland) and activated liquid PRGF. The combination of bovine anorganic bone with PRGF allowed the formation of a clot in which the bovine bone

was incorporated. The latter facilitated the manipulation and administration of the bovine bone, increasing the biosafety of the approach. In fact, in the case of perforation, the use of PRGF avoids the risks of anorganic bone particle loss within the sinus cavity.

One interesting aspect of this approach is that the original bone window of the sinus is preserved, thus avoiding the use of artificial membranes. The bone window was placed in its original position after turning it 30°, obtaining an adequate primary stability.

The window was covered with autologous fibrin and sutured with 5-0 monofilament suture. A detailed description of the sinus elevation protocol is illustrated in Figure 1.

Six months after sinus elevation, high-resolution scans of the mandibles were acquired with a computed tomography scanner and bone densitometry measured using the BTI scan® program. After evaluating the situation of the sinus and the schneiderian membrane, approximately two to three BTI dental implants were installed in each sinus using a two-stage procedure. All implant reception sites were prepared using a low-speed drilling procedure (50 rpm) without irrigation, as it has been described elsewhere.[17] Before installation, all implants were carefully humidified in liquid PRGF with the aim of bioactivating the implant surface.[18] The surgery guides were elaborated and provisional, and final prostheses adapted to each patient were prepared. Four months later, the second surgery was carried out and provisional prosthesis was installed during 8 weeks. Final restoration was carried out with cemented prosthesis using titanium abutments. Between November 2003 and July 2007, patients were called in for oral hygiene and clinical and radiographic examinations at least twice a year.

Histological Preparation

The bone samples used for histological evaluation were obtained after a healing period of 5–6 months as a by-product of implant placement using a trephine hollow drill, measured 8 mm in length and 2 mm in diameter. Processing and staining of the bone samples were carried out using a standardized protocol. Briefly, the samples were fixed in B5-fixative, decalcified with ethylenediaminetetraacetic acid, dehydrated in a graded series of alcohols, and embedded in paraffin. Then, 5-μm-thick serial sections were obtained and stained with hematoxylin-eosin. Additional sections were stained with alcian blue and Masson-Goldner trichrome to further differentiate and confirm the soft tissue layer, the grafted bovine hydroxyapatite, and the newly formed bone. For histomorphometric analysis, histological samples were examined by conventional optical microscopy using a Leica DMLB microscopy (Leica Microsystems, Wetzlar, Germany) and photographed with a digital camera, Canon EOS D30 (Canon Inc., Tokyo, Japan). The digitalized images were analyzed using the Image software (version 1.39, National Institutes of Health, Bethesda, MD, USA). For determination of the vital bone content, a 25× magnification was used, evaluating the complete section for each case (approximately 7.5 mm^2). The new bone, bovine hydroxyapatite particles and soft tissue areas were measured semiautomatically and expressed as percentage of the total area.

Statistical Analyses

Data collection and analysis was performed by two independent examiners (other than restorative dentists). Descriptive statistics were performed, and absolute and relative frequent distributions for qualitative variables and mean values and standard deviations for quantitative variables were calculated. Initially, a database was created using Microsoft Access®. The principal variable under study was implant loss. By implant loss was considered any implant lost due to biological (failure to achieve osseointegration or loss of acquired osseointegration) or biomechanical causes. The rest of variables for data analysis of this report included:

- Gender (female and male).
- Smoking habits (smoking ≥1 cigarette per day was classified as smoker).
- Implant diameter (ranging from 3.3 to 5.0 mm). Implant diameter was divided into three categories: 3.3 mm, 3.75–4 mm and 4.5–5 mm.
- Implant length (ranging from 7 to 15 mm). Implant length was divided into two categories: ≤10 mm and >10 mm.
- Prosthetic factors: divided into cemented bridge, cemented unitary, hybrid overdenture.

Data analysis was performed with SPSS 13 for Windows statistical software package (SPSS Inc., Chicago, IL, USA).

TABLE 1 Characteristics of the Inserted 43 BTI Dental Implants

		Length						
		7.0	8.5	10.0	11.5	13.0	15.0	Total
Diameter	3.30	0	1	0	0	0	1	2
	3.75	2	3	1	0	1	4	11
	4.00	0	0	0	1	2	7	10
	4.50	0	0	1	0	0	5	6
	5.00	0	0	1	2	5	6	14
		2	4	3	3	8	23	43

RESULTS

Descriptive Analysis

In the present retrospective study, the mean (±standard deviation) age of the 18 patients was 52 (±11) years (range 29–73) at the beginning of the study. Twelve patients were female (66.7%) and five patients were classified as smokers (27.8%). Table 1 shows the length and diameter of the inserted implants. In fact, the length of the inserted 43 implants ranged from 7 to 15 mm, whereas the diameter ranged from 3.3 to 5.0 mm. A detailed anatomic distribution of the implants is summarized in Figure 2. Regarding the prostheses employed, most of the implants supported cemented bridges (51.2%), 15 implants supported hybrid overdentures (34.9%), and only 6 implants had unitary cemented prostheses (14%).

As it has been reported, 18 patients received 43 dental implants with sinus floor elevation according to the protocol described above. The mean follow-up period for all implants was 33 ± 7 months ranging from 24 to 44 months. The follow-up period for 25 out from 43 implants (58.1%) ranged between 12 and 24 months, whereas the other 18 implants range between 24 and 36 months. In the present retrospective study, the overall survival rate of dental implants installed after sinus floor elevation was 100% as no implants were lost during the observational period.

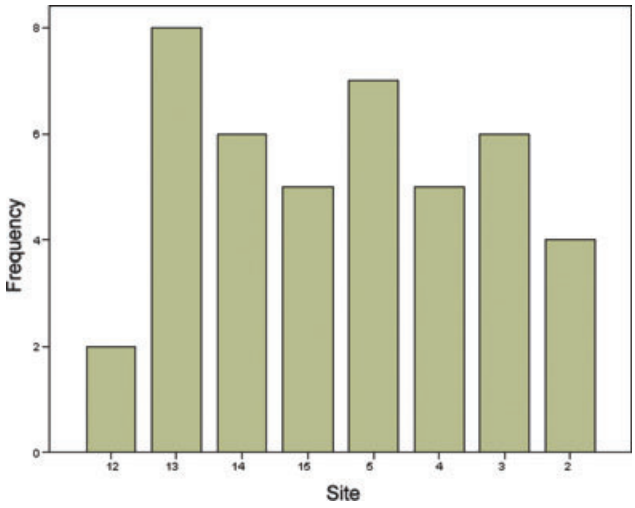

Figure 2 Anatomic distribution of the inserted dental implants.

TABLE 2 Histomorphometric Characterization of the Percentages of Newly Formed Bone, Connective Tissue, and Bovine Hydroxyapatite for Each Patient

Time (Months)	New Bone (%)	Bovine Hydroxyapatite (%)	Connective Tissue (%)
6	28.41	43.6	27.99
5	18.52	18.01	63.47
5	21.41	12.5	66.09
5	25.76	13.52	60.72
5	30.56	20.79	48.66
5	20.97	14.57	64.46
6	25.33	42.74	31.93
5	30.94	29.92	39.15

Regarding the histological and histomorphometrical findings, the evaluation of trephine core samples evidenced a 25.24 ± 4.62% of vital newly formed bone (while 50.31 ± 15.56% represented soft connective tissue and the remaining 24.46 ± 12.79% bovine hydroxyapatite) in eight sinus grafted with a combination of bovine hydroxyapatite and PRGF after a healing period of 5–6 months. A detailed characterization of the newly formed bone, connective tissue, and bovine hydroxyapatite for each patient is summarized in Table 2. In addition, Figure 3 shows the histological analysis of a representative bone biopsy in which new vital bone with abundant osteocytes can be clearly distinguished. The more in-depth analysis of the sample reveals several blood vessels scattered over the connective tissue, the new bone surrounding the grafted hydroxyapatatite, and multinucleated osteoclasts lying on the mineralized bone surface.

Finally, Figure 4 illustrates the clinical situation of a patient involved in the study who received dental implants following a two-stage procedure after sinus elevation using the new approach reported in this study.

DISCUSSION

The technique of sinus floor elevation has expanded prosthetic options by allowing the placement of dental

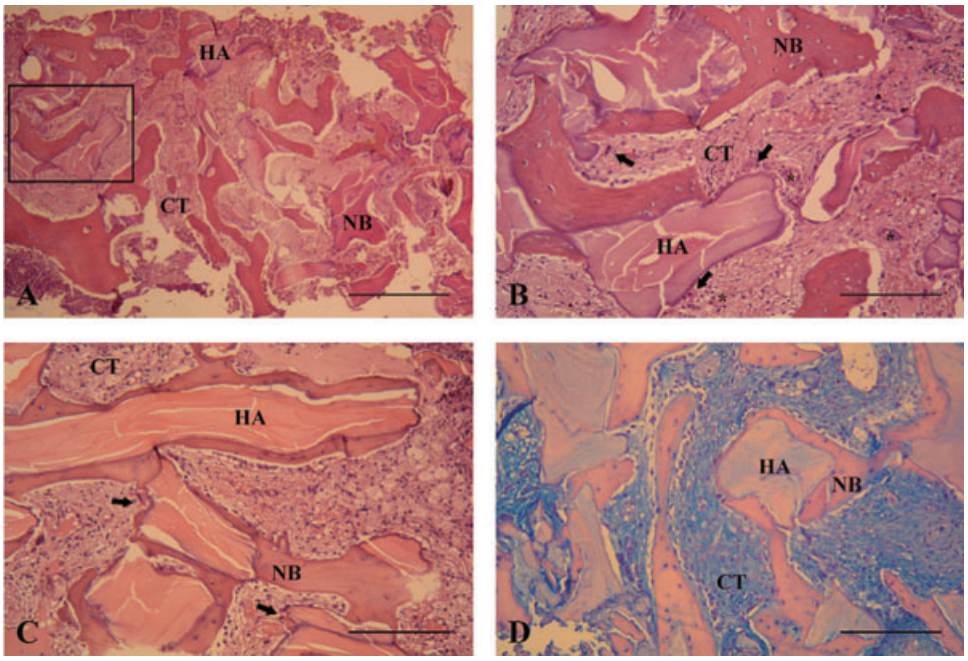

Figure 3 Histological analysis of representative bone biopsy: (A) Haematoxylin-eosin section from tissue made up of 25.76% new bone (NB), 13.52% bovine hydroxyapatite (HA), and 60.72% connective tissue (CT). (B) Higher magnification of the area marked in panel A showing new vital bone with abundant osteocytes. Note the presence of osteoclasts (arrows). Several blood vessels can be observed scattered over the connective tissue (asterisks). (C) Haematoxylin-eosin and (D) alcian blue phomicrographs showing new bone surrounding the grafted hydroxiapatatite; multinucleated osteoclasts can be observed lying on the mineralized bone surface (arrows). Collagenized connective tissue in blue is especially evident in the alcian blue staining (stainings: A, B C, Haematoxylin-eosin; D, alcian blue) (Scale bars: A, 700 mm; B, C, D, 200 mm).

implants in maxillary segments with atrophic ridges and pneumatized sinuses. In the present study, we describe and evaluate the biosafety and efficacy of a lateral approach for sinus lift specifically recommended for severely resorbed maxillae. In these situations, the selection of a lateral approach for the sinus elevations and a two-stage technique for implant installation is highly recommended. Additionally, bone graft insertion is frequently used with the aim of increasing the bony support for oral implants.[19,20] In fact, it is important to remember that the clinician always aims to preserve an adequate and viable bony mass to meet the future implant-prosthetic requirements.

The new lateral approach described in this study has some distinguishing and specific characteristics which may offer potential advantages compared with conventional sinus elevation surgery. These include, for example, the use of a surgical ultrasonic generator to create a vestibular osteotomy, a low-speed drilling procedure for implant installation, and the application of PRGF technology in several steps of the lateral approach.[15,21] As a consequence, there is a significant improvement in terms of manipulation of the graft, viability of the bone window, biosafety, and even bone regeneration.

An ultrasonic generator is used to create the osteotomy. The ultrasounds generated at the active tip of the device facilitate the opening of the bone window. The osteotomy line can be easily made by cutting the osseous table in a progressive, precise, and controlled way.[16] Another interesting property of the ultrasonic device is that it provides greater tactile control and minimizes the damage on surrounding soft tissues, reducing clearly the risks of perforating the schneiderian membrane. In addition, the visualization of the surgical area is improved because of the cleaning effect of the irrigation liquid under the action of the ultrasounds. In fact, the latter transforms the liquid jet into a low-pressure aerosol that facilitates the cleaning of the area, reducing the risks of subcutaneous emphysema. The thin cutting provided by the ultrasonic device facilitated the removal and the posterior reinsertion of the bone window after a slight adjustment.

The most important innovation of this sinus lift approach relies on the application of PRGF technology into several key steps of the protocol. The preparation

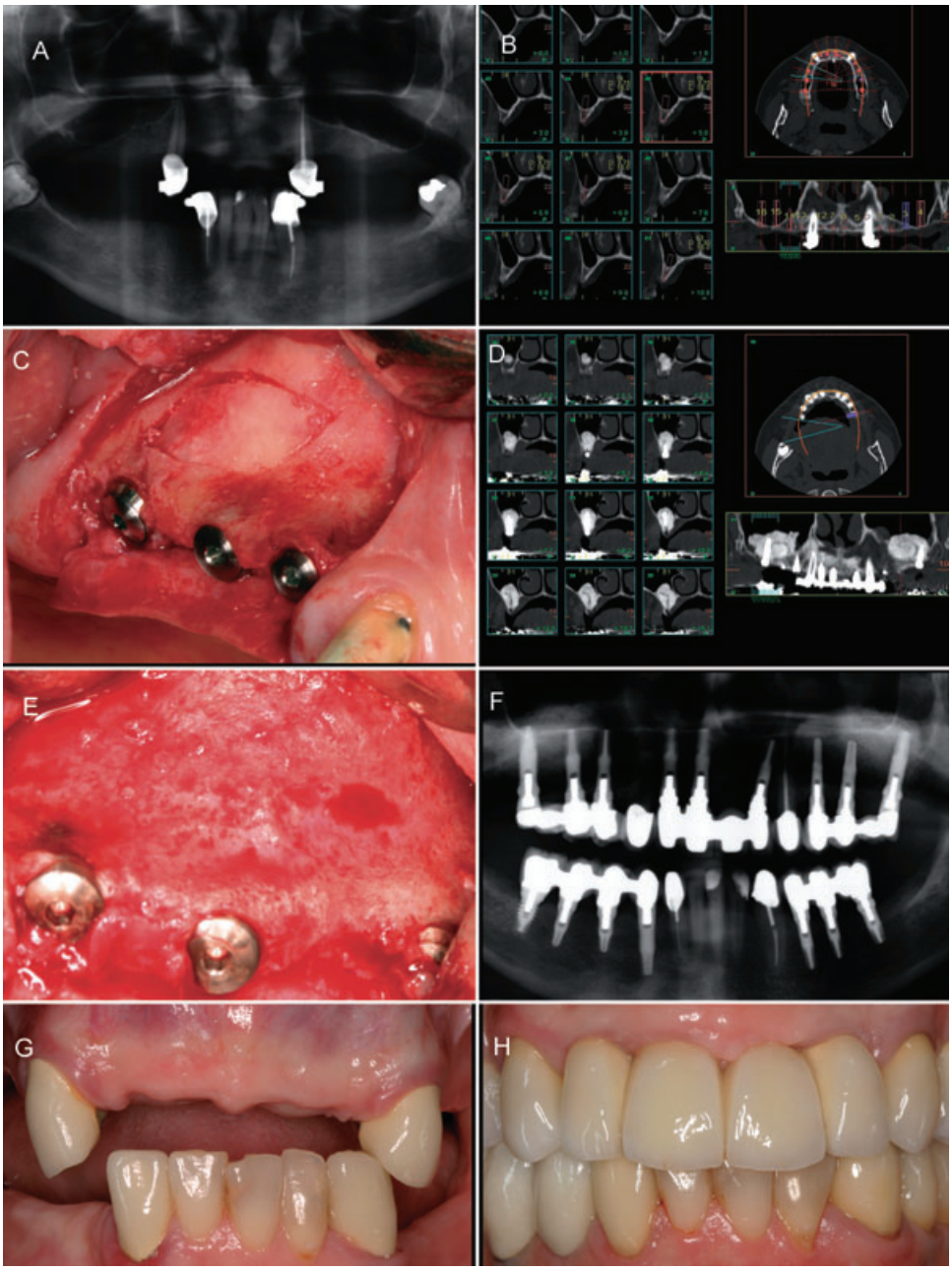

Figure 4 Forty-eight-year-old woman with partial edentoulism. (A) The treatment plan for the upper maxilla required 2 sinus elevations. (B) Pretreatment radiograph. (C) The bone-window is reinserted in its native location. (D) Radiograph of the patient 5 months posttreatment. (E) Reopening 5 months posttreatment. (F) Radiograph 2 years posttreatment. (G) Image of the patient before the treatment. (H) Image 1 year after the treatment.

rich in growth factors (PRGF) is an optimized platelet-rich product.[14,15,21] First, it is a 100% autologous product that it is easily and rapidly obtained from patient's blood, and because the donor and receptor is the same, the immunological concerns are circumvented. PRGF is obtained from a simple spin method and using small and variable blood volume depending on the type of surgery. In the PRGF preparation, sodium citrate and calcium chloride are used as anticoagulant and clot activator, respectively. The former protects the platelets from fragmentation avoiding the loss of growth factor content, while the latter enables a safer and a more sustained and physiological release of the stored growth factors.[22] This is particularly interesting as the potential risks associated with the bovine thrombin are avoided. From a safety point of view, PRGF does not contain neutrophils which express matrix-degrading enzymes that could destroy surrounding injured or healthy cells.

Last but not least, by controlling the elaboration protocol and coagulation degree of the samples, it is possible to obtain almost four different formulations with therapeutic potential,[15] including the PRGF supernatant, the liquid PRGF that can be used to bioactivate dental implants in order to improve their osseointegration,[18,23] the scaffold-like PRGF with potential to promote bone and soft tissue regeneration, and the biocompatible and elastic fibrin which can be used as an autologous sealant biomaterial in the case of schneiderian membrane perforation. Moreover, the same fibrin membrane is used to seal the implant defects with the aim of preventing the invasion of soft tissues which may reduce the amount and quality of newly formed bone.

The rationale for using PRGF is that provides a natural source of proteins such as fibrinogen, fibronectin and vitronectin, and growth factors including platelet-derived growth factor, transforming growth factor-β, vascular endothelial growth factor, insulin-like growth factor, hepatocyte growth factor, angiopoietins, platelet factor-4, and thrombospondin among others to the local milieu, which may drive tissue regeneration mechanisms.[23] In addition, the combination of these formulations with biomaterials may increase the versatility of the technology. Assuming this knowledge, a mixture of bovine anorganic bone and PRGF was employed as graft material. The use of this biological graft in sinus lift not only provides a pool of growth factors to the local environment but also facilitates the handling, manipulation, and administration of the anorganic bone particles, and increases the overall volume of the graft. This is especially interesting and definitive in the case of membrane perforation. Although much work lies ahead in order to properly evaluate and characterize the role of PRGF in this biological graft, some studies have reported beneficial outcomes when a platelet rich product was combined with different bone substitutes (autogenous, allogenic, or alloplastic) for sinus floor elevation.[24–28]

The liquid PRGF can be used as culture medium to maintain the viability and functional properties of autologous bone.[29] Assuming this, another key application of PRGF in this protocol is to provide a biological active medium that will conserve the functional properties of the osseous window. Therefore, in this approach, the original bone window of the sinus is preserved and reinstalled in its original position, thus avoiding the use of artificial membranes. Last but not least, after sinus elevation, all implants were installed following a low-speed drilling procedure without irrigation and humidified with PRGF before insertion.[17,30]

The findings from this present retrospective study indicate that the new lateral protocol described for sinus elevation and posterior implant installation provides a safe, successful, and predictable treatment procedure. In fact, 18 patients received 43 dental implants after sinus elevation and the survival of the latter was followed-up during 33 ± 7 months. Results show that survival rate of the implants was 100%. No remarkable side effects such as pain, infection, or major inflammation were observed during the study time period. An excellent epithelization of soft tissues was detected.

The histological analysis of a representative bone biopsy revealed new vital bone with abundant osteocytes and several blood vessels scattered over the connective tissue. The histomorphometric analysis of the samples showed an average of newly formed bone higher than 25%. Future studies are under preparation to evaluate the potential of PRGF-derived growth factors in promoting and accelerating bone regeneration.

In summary, this study describes a new lateral approach for sinus elevation and two-stage implant placement using a surgical ultrasonic generator, a low-speed drilling procedure for implant installation, and especially PRGF technology. The survival rate of implants installed following this procedure was 100%. It is also important to remark that the present technology is cheap for the patient and easy for the clinicians Preliminary results of this retrospective study suggest that this new protocol can be considered safe and predictable. Waiting for future prospective studies, the results herein reported may be helpful for clinicians to improve their decision making and thus enhance implant success.

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CONFLICTS OF INTEREST STATEMENT

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[Correction added after online publication 23 October 2009: Conflicts of Interest Statement added.]

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