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REPORTE DE CASOS / *Case Report*

SINUS FLOOR ELEVATION USING A NEW BOVINE BONE GRAFTING MATERIAL. CASE REPORT AND BONE GRAFTING MATERIALS UPDATE

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Abstract

Bone grafting is important to preserve the alveolar bone ridge height and volume for dental implant placement. Even though implant-supported overdentures present highly successful outcomes, it seems that a great number of edentulous individuals have not pursued implant-based rehabilitation. The cost of the treatment is one of the reasons of discrepancy between highly successful therapy and its acceptance. Therefore, the development of biomaterials for bone grafting with comparable characteristics and biological effects than those renowned internationally, is necessary. In addition, domestic manufacture would reduce the high costs in public health arising from the application of these biomaterials in the dental feld. The purpose of this clinical case report is to provide preliminary clinical evidence of the efficacy of a new bovine bone graft in the bone healing process when used for sinus floor elevation.

Keywords: bovine bone graft, new bone formation, sinus augmentation, osteoconduction.

Resumen

El uso de injertos óseos es importante para preservar la altura y el volumen de la cresta alveolar para la colocación de implantes dentales. Si bien las sobredentaduras implanto-soportadas presentan resultados altamente exitosos, la mayoría de las personas desdentadas no han sido rehabilitadas mediante implantes dentales. Uno de los principales motivos por los cuales los pacientes no aceptan este tipo de tratamiento, altamente exitoso, es el elevado costo del mismo. Por ello, es necesario el desarrollo de biomateriales de injerto óseo con características y efectos biológicos comparables a los reconocidos internacionalmente. Asimismo, la fabricación nacional reduciría los altos costos en Salud Pública derivados de la aplicación de estos biomateriales en el campo dental. El objetivo de esta comunicación es presentar un caso clínico a fin de proporcionar evidencia preliminar acerca de la eficacia de un nuevo injerto de hueso bovino en el proceso de cicatrización ósea en el levantamiento del piso del seno maxilar.

Palabras clave: *hueso bovino, neoformación ósea, osteoconducción, elevamiento del piso del seno maxilar.*

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Introduction

Bone grafting implantation is the main treatment modality for bone defect repair and reconstruction.[1] In oral and maxillofacial areas, bone grafting aims to replace the volumetric bone loss that frequently occurs by systemic pathologies, periodontal defects, and tooth loss.[2]

The mechanisms underlying bone healing promoted by a bone graft are osteogenesis (osteo-differentiation and subsequent new bone formation by donor cells derived from the host or graft), osteoinduction (induction of undifferentiated and pluripotent cells to develop osteogenesis into the bone-forming cell lineage), and osteoconduction (the ability to support the attachment of osteoblast and osteo-progenitor cells, and the migration and ingrowth of these cells within the three dimensional architecture of the graft),[3,4] in combination or alone.[5]

Bone grafting materials are classifed as autografts (derived from the same individual), allografts (derived from a different individual from the same species), xenografts (derived from a different species), and alloplasts (derived from synthetic sources).[6] Autografts are the 'gold standard' in the reconstruction of bone defects due to their osteoconductive as well as osteoinductive properties.[7] Although they present excellent biological outcomes, they also have a number of drawbacks. In this regard, the use of autografts increases the operative time due to graft harvest, increases the donor site morbidity and, increases the graft resorption. In addition, they represent a big challenge for the operator since they need to be molded and have limited availability, especially in the pediatric population.[8] Allografts are typically obtained from human corpses and require to be processed before being used.[9,10] Allograft bone is available as cortical, cancellous, corticocancellous forms, or as demineralized bone matrix. It can be processed as mineralized or demineralized, fresh, fresh-frozen, or freeze-dried forms.[11,12] The benefts of allografts include their availability in different shapes and sizes. This is particularly advantageous since avoids donor site morbidity.[13] The major disadvantages of allografts are the potential for disease transmission and graft rejection. In order to decrease the risk of transmitting infectious diseases, allografts need to be treated. The techniques employed include treatment with hypotonic solutions, acetone, ethylene oxide or gamma irradiation that may eliminate cellular and viral particles.[14] However, these processes eliminate the bone cells and denature proteins present in the graft altering the osteoconductive and osteoinductive properties and eliminating the osteogenic properties.[15] In addition, allografts are capable to induce immunological reactions that interfere with the bone healing process leading to rejection of the graft.[13,16-18]

Synthetic bone grafts are osteoconductive and have been shown to integrate to bone.[19] There are many available synthetic graft materials, including bioactive glasses, a- and b-tricalcium phosphate (TCP), and synthetic hydroxyapatite.[19] Ideally, a synthetic bone graft should be biocompatible and cause minimal fbrotic changes.[20] Bioactive glass or "bioglasses" have been widely used as bone substitutes because of their ability to join and integrate to the bone tissue, forming a layer of active apatite on the surface, with similar characteristics to bone.[21] These biomaterials are resorbable and dissolution of their products (soluble silicon and calcium) upregulates seven families of osteoblastic genes promoting osteogenesis.[21,22] Among synthetic materials, synthetic hydroxyapatite, a crystalline phase of calcium phosphate found naturally in the mineral of bone, exhibits initial mechanical rigidity and structure, and demonstrates osteoconductive as well as angiogenic properties *in vivo*.[20] The synthetic hydroxyapatite, is a biocompatible and osteoconductive material due to its physicochemical characteristics.[23] This material al-

lows keeping the space flled extremely well, providing a physical matrix for the deposition of new bone. For these reasons, synthetic hydroxyapatite has high success in the felds of biology, medicine and dentistry

Due to the great popularity of dental implant surgery, the demand for alveolar ridge reconstruction, including sinus augmentation and immediate implant procedure, increased. This new trend in dentistry for implants boosted the development of new grafting materials. Ideally, a bone graft should be biocompatible, biodegradable, osteoconductive, osteoinductive, structurally similar to bone, easy to use, and cost-effective.[5] Within these parameters, a growing number of bone graft alternatives are commercially available and frequently used in dentistry.

In this regard, xenografts, frequently derived from bovine, porcine and coral sources[5], are a suitable alternative. Bovine bone is one of the most popularly used xenografts. This source material is desirable because it is readily available an inexpensive. However, bovine bone grafts require proper preparation to avoid risks such as transmission of zoonoses.[24] Several studies have shown that organic or inorganic matrix derived from bovine bone is biocompatible and osteoconductive.[24, 25] These important biological properties allow the apposition of newly formed bone by osteoprogenitor cells and the partial remodeling by osteoclasts and osteoblasts of the host.[26] Moreover, the large interconnecting pore volume and its composition encourage the formation and ingrowth of new bone at the implantation sites.

Different types of bone grafts are available in the international market. However, it is essential to have a wide variety of them to improve the competitiveness of each product in terms of quality, commercial value and clinical use. Therefore, the development of biomaterials for bone grafting produced by domestic manufactures, with comparable characteristics and biological effects than those well-known internationally, is necessary in order to reduce the high costs in public health arising from the application of these biomaterials in the dental feld.

Synergy Bone Matrix (SBM) (Odontit Implant Systems, Argentine) is a bovine bone graft material manufactured in Argentina, approved by the ANMAT (National Administration of Drugs, Foods and Medical Devices, Argentina) and the FDA (Food and Drug Administration, United States). SBM consists of sterile biocompatible anorganic porous bone mineral matrix for use in periodontal, oral and maxillofacial surgery. It is produced by removal of organic components from bovine bone. Therefore, SBM provides a supportive structure for osteoconduction. The presence of pores in Synergy is of great importance for repairing bone defects.

Even though there is evidence about the osteoconductive properties of SBM in experimental models in rats,[27] to date, there is no clinical evidence in the literature about the use of SBM in sinus floor elevation. The purpose of the present clinical case report is to provide clinical evidence of the effcacy of this new bovine bone graft in the healing process of alveolar bone when used for sinus floor elevation.

Case report

A 54-year-old female patient was referred to the Department of Clinical Operative and Prosthesis II, Dental School, University of Buenos Aires, Buenos Aires, Argentina for rehabilitation of her edentulous maxilla. Radiographic and cone beam computed tomography (CBCT) exhibited severe atrophy in the posterior region of the maxilla (Figure 1). The medical history did not reveal any systemic disease and the patient did not report to be under any medication. The patient aimed to rehabilitate the upper arch with a fxed implant-supported prosthesis. The proposed treatment plan was divided in two stages. The frst stage included the confection of a

complete upper denture, as well as, a surgical and radiological stent, and the reconstruction of the posterior maxillary alveolar ridge. The second stage, after 6 months, consisted in the placement of 4 dental implants in the posterior maxilla. All clinical procedures were conducted under the patient's written informed consent.

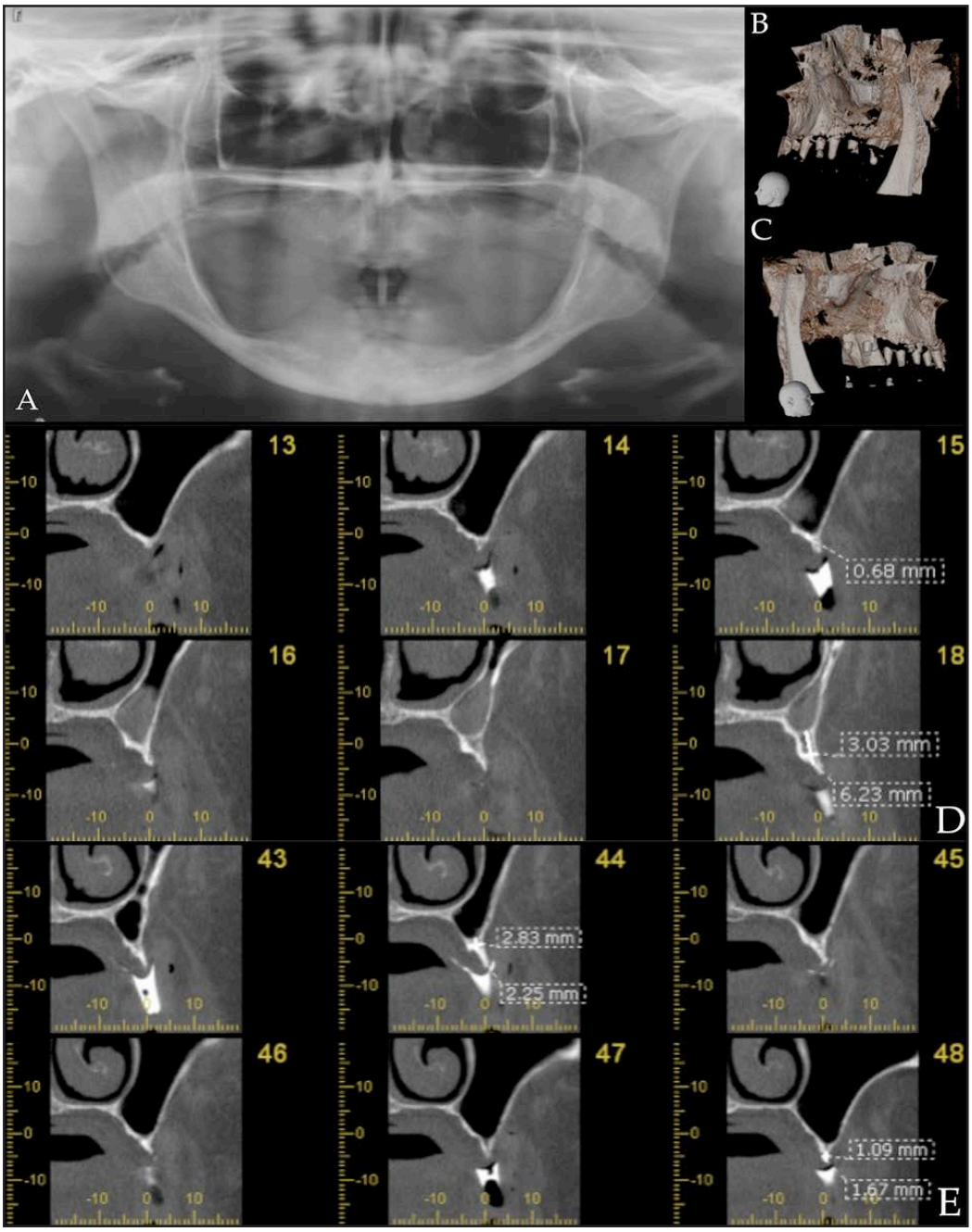

Figure 1. Pre-operative diagnostic images. All images show a dramatic loss of bone in the upper left and right maxilla. A: Panoramic X-ray showing edentulus maxilla and mandible. B, C. 3-D reconstruction of the left (B) and right (C) maxilla with the surgical stent. D, E: Coronal cut from a cone beam computed tomography scan from the left (D) and right (E) maxilla.

Sinus elevation surgery and guided tissue regeneration

The bilateral sinus elevation procedure was performed using the technique previously described by Tatum.[28] Briefly, after anesthesia with infltrative local carticaine hydrochloride 4% with adrenaline 1:100.000 (Totalcaína Forte, Microsules Bernabó, Argentina), a mucoperiosteal flap was elevated with releasing vertical incisions. Once exposed the buccal wall of the remaining alveolar process and the anterolateral wall of the Highmore antrum, a surgical stent was used to locate the lateral window. An oval osteotomy was performed with high-speed handpiece and a round diamond bur under copious irrigation with saline, leaving a "bone island", in the lateral wall of the sinus, attached to the Schneider membrane (Figure 2). This fragment of bone was then turned medially and positioned towards the sinus floor. The sinus membrane was then elevated across the floor and up the medial wall. A bilateral guided bone regeneration procedure was performed using the bovine bone grafting material SBM. In order to adjust the consistency and handling characteristics of SBM, it was mixed with sterile saline (0.9% Sodium Chloride) (Figure 2C).

The size of the granules was 350- 840 #m. The graft was covered with a resorbable collagen membrane (BioCollagen, Bioteck, Italy). Finally, the flap was repositioned and sutured without tension. The patient was instructed to perform oral hygiene and to rinse twice a day during 7 days with chlorhexidine digluconate 0.12% for disinfection of the surgical wound. Amoxicillin-clavulanate 875 mg was prescribed twice a day for 7 days and 500 mg of naproxen was administered every 8-12 hours for 5 days to control postoperative pain. Soft diet was also recommended. The sutures were removed after 7 days. CBCT scans and panoramic x-rays were obtained pre-operative, 6 months after stage 1 and 4 months after stage 2. A biopsy of each treated area was taken with a trephine bur during the implant placement surgery.

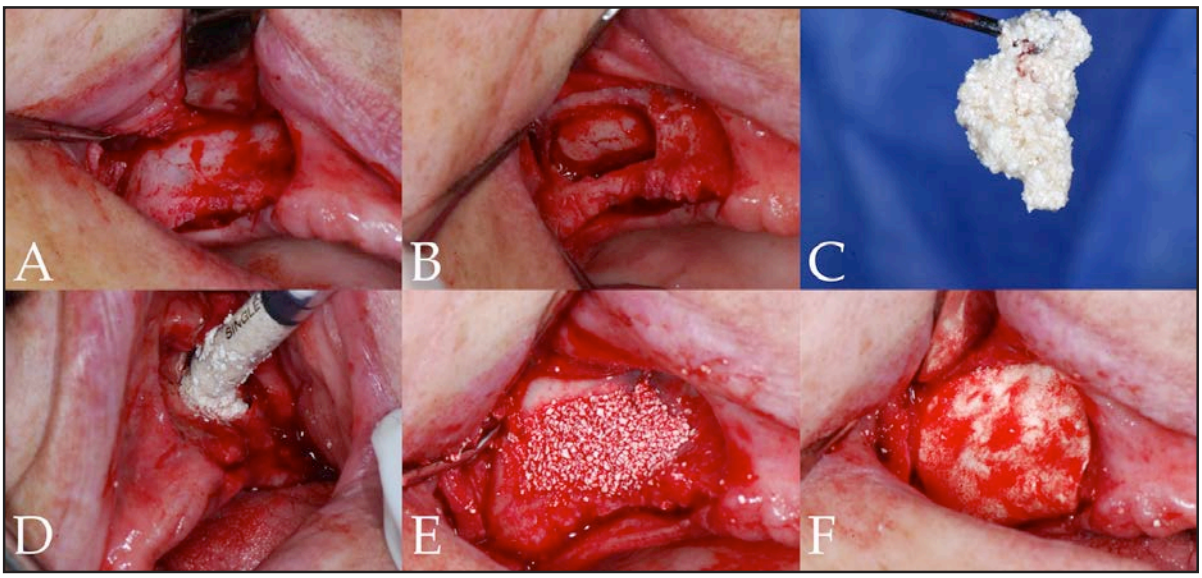

Figure 2. Sinus elevation surgery and guided tissue regeneration. A: elevation of mucoperiosteal flap. B: Oval osteotomy and "bone island" in the lateral wall of the sinus attached to the Schneider membrane. C: Synergy Bone Matrix (SBM). D, E: Placement of SBM for guided bone regeneration. F. The graft was covered with a resorbable collagen membrane.

During the frst surgical stage, a post-operative follow-up 7 days after the procedure revealed that the edges of the flap wounds faced each other and there were no signs of dehiscence or inflammation. The patient did not report any discomfort, pain or inflammation of the treated areas. The post-operative CBCT, taken 6 months after this surgery, exhibited an increase of 10.7 mm and 10.8 mm in the height of the alveolar crest, and an increase in the alveolar crest width of 3.5 mm and 2.8 mm in the right and left side, respectively (Figure 3). Six months after the sinus lift surgery dental implants were placed in the areas that received the bone graft (stage 2). Dental implants in the areas grafted achieved primary stability, indicating that there was an accurate bone quality after the placement of the bone graft. Consistent with the digital imaging fndings, histological evaluation of the bone samples retrieved during the implant surgery revealed that SBM particles were osteoconductive. All particles were surrounded by new bone formation (Figure 4). There were fbro-angiogenic and fbrous areas associated to SBM, as well as gradual regression of associated fbrosis. The bone formation pattern was lamellar and trabecular, and the presence of osteoblast at the surface of the trabeculae, as well as osteocytes, was also observed. There were no signs of inflammation or bone sequestrae.

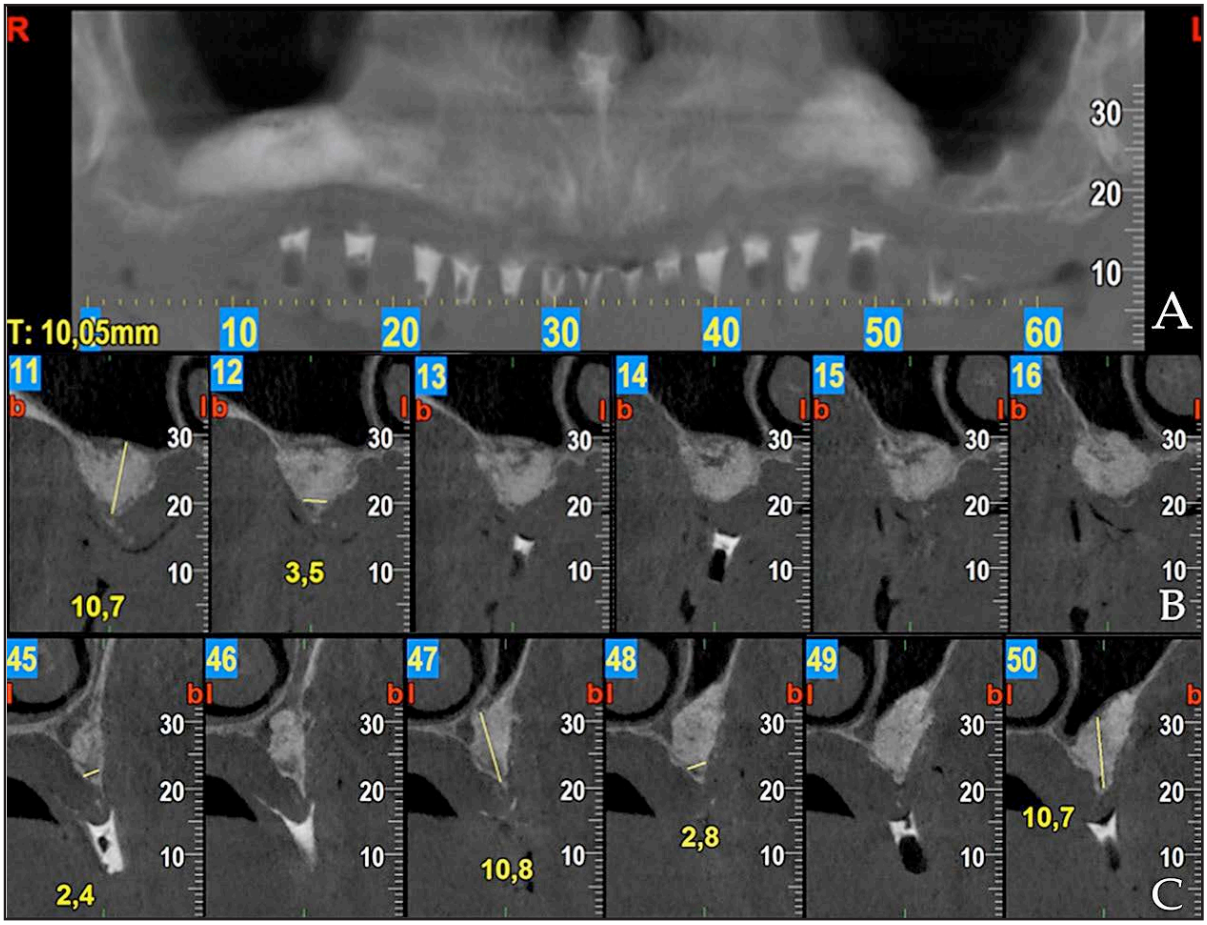

Figure 3. Post-operative CBCT (6 months after the sinus elevation surgery). A, B, C: There was an increase of 10.7 mm and 10.8 mm in the height of the alveolar crest, and an increase in the alveolar crest width of 3.5 mm and 2.8 mm in the right and left side, respectively.

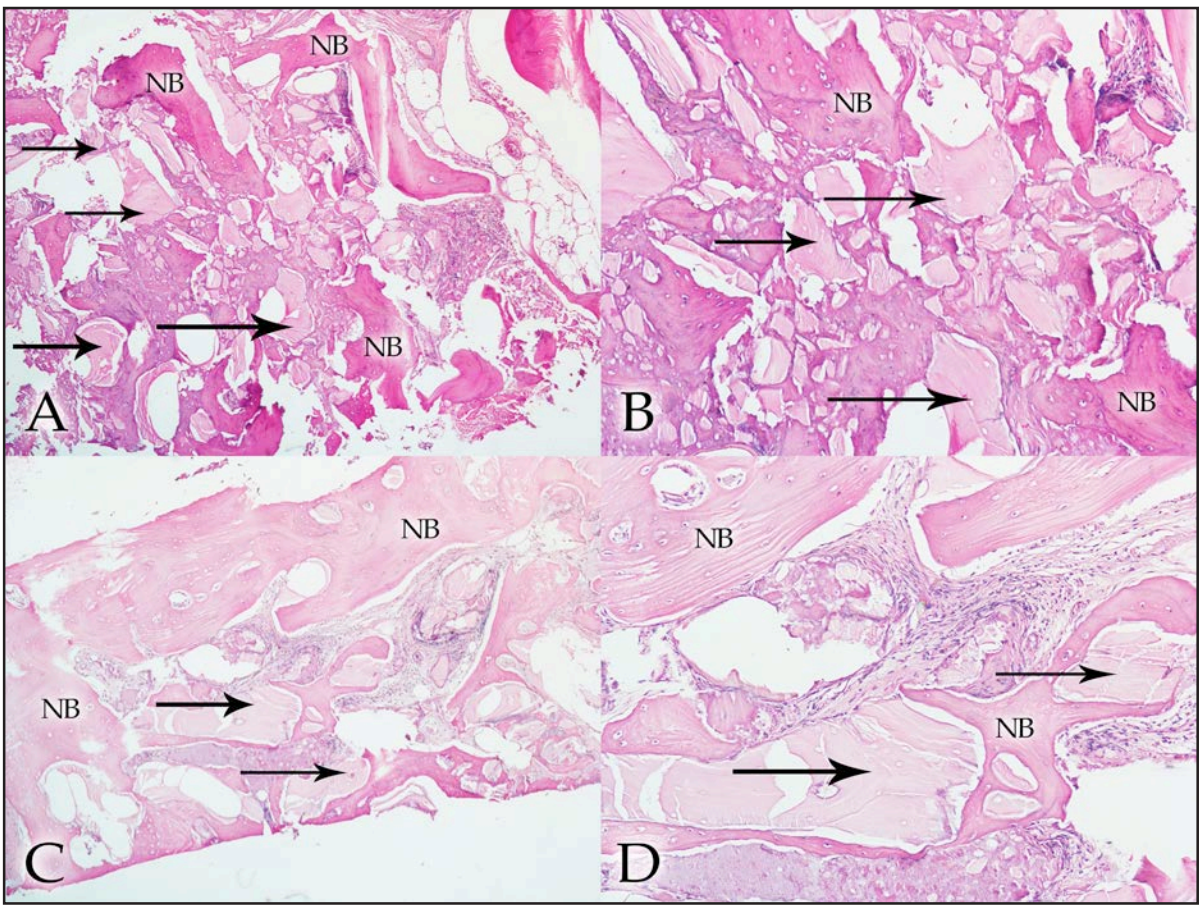

Figure 4. Histological evaluation of the areas grafted with Synergy Bone Matrix (SBM) at 4x, 10x or 20x magnification and stained with Hematoxylin-Eosin. New bone formation surrounding each particle was observed in right (A, B) and left (C, D) grafted sinus. Black arrows indicate SBM particles. NB: new bone formation.

Post-operative 4 month control digital images showed implant osseointegration (Figure 5). No peri-implant radiolucencies were observed. The regenerated bone gain by the graft placement in both sides was preserved (Figure 5). Clinical assessment of the dental implants did not exhibit mobility of the implants and a solid-deaf sound when performing percussion tests showed proper bone healing. The patient did not report pain; there was no leakage of purulent material or signs of inflammation. In addition, the grafted bone presented the similar density than the perisinusal bone at both sides.

Discussion

This is the frst study that provides clinical and histological evidence of the effcacy of SBM, a new bovine bone graft manufactured in Argentina, in the healing process of alveolar bone when used for sinus floor elevation. Similarly to what our group observed in experimental studies in rats[27], the results of the present report provide evidence for the biocompatibility and osteoconductive properties of SBM. Bone graft implantation is the main treatment modality for bone defect repair and reconstruction.[1] In this sense, demineralized bovine bone, offers excellent biocompatibil-

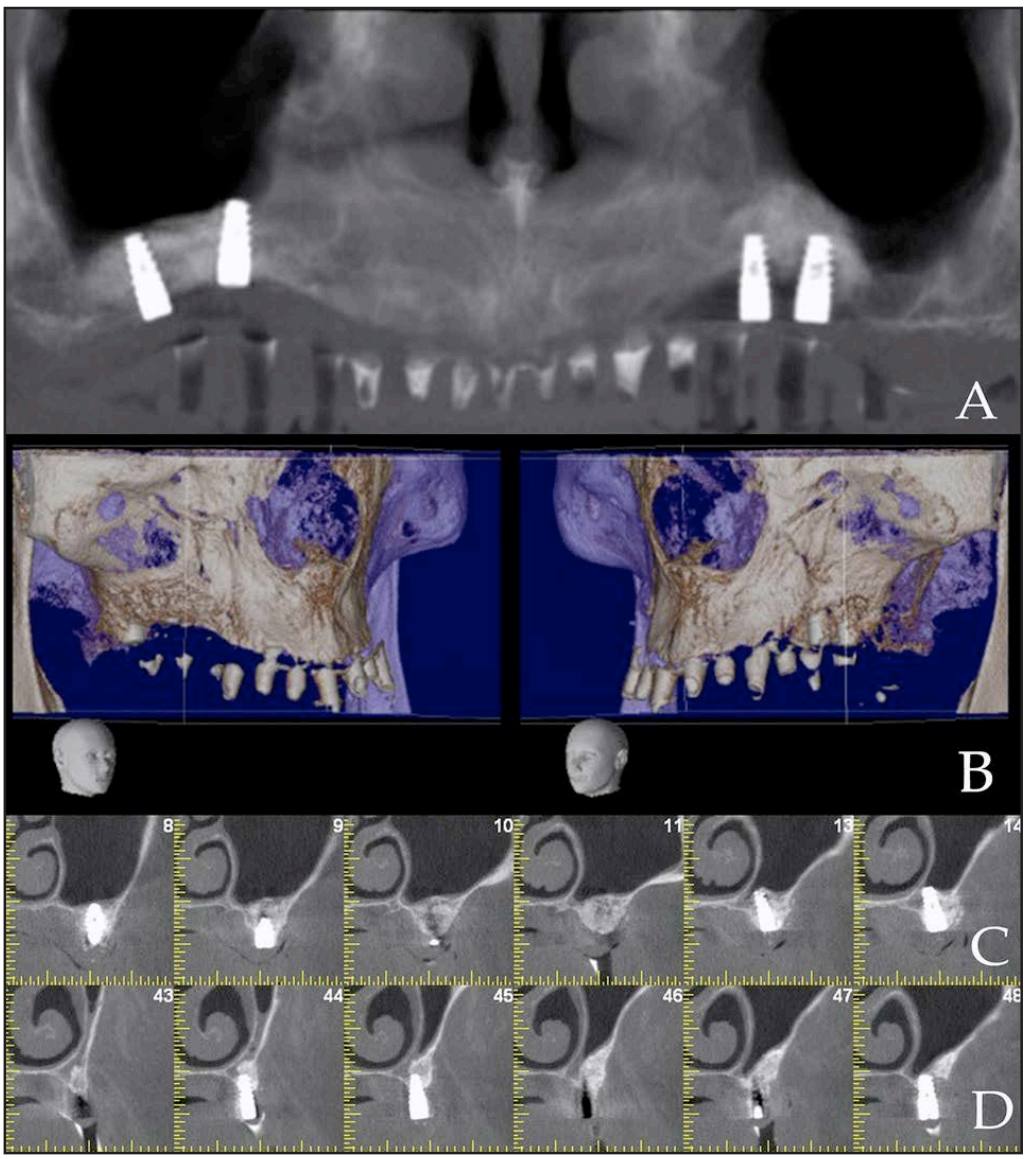

Figure5. Post-dental implant placement diagnostic images. All images show bone gain in both sides of the maxilla that persisted after the placement of dental implants. A: Panoramic X-ray from a CBCT showing the increase in alveolar bone height and dental implants on the right and left side. B: reconstruction of the left and right maxilla with the surgical stent. C, D: coronal cut from a CBCT scan from the left (C) and right (D) maxilla.

ity and physicochemical properties due to its mineral similarity with the host tissues.[29]

SBM is an anorganic bovine bone xenograft indicated for bone defects flling due to their osteoconductive properties. In experimental models, the bone defect above a critical size requires a scaffold to guide bone repair. Deproteinized bovine bone mineral is osteoconductive and provides excellent biocompatibility because it has similar physicochemical characteristics to that of the mineral component of the original bone.[30] These two important biological properties allow apposition of new bone formed by osteoprogenitor

cells located in the host tissue. It is noteworthy that bovine bone inorganic-phase not only promotes the deposition of calcium and phosphate ions, but also it is partially remodeled by osteoclasts and osteoblasts of the host.[25] In addition, the large interconnecting pore volume and its composition encourage the formation and ingrowth of new bone at the implantation sites.

Bone is a dynamic tissue that undergoes remodeling. Bone remodeling is a coupled process that starts with osteoclastic bone resorption followed by osteoblastic bone formation.[31] The osteoclastic resorption of the graft is affected by the particle size as well as the composition and porosity of the material.

Initially, once the graft material is placed, it suffers osteoclastic bone resorption followed by bone formation by osteoblastic action. The porosity of the particles enhances new bone formation by allowing the migration and proliferation of osteoblast and mesenchymal cells.[32] In addition, the microporosity of the particles is believed to enhance ionic exchange with body fluids.[32] This characteristic allows each particle of SBM to serve as a 3-D scaffold in which osteoblast and osteoprogenitor cells migrate and form bone. Consistent with this, we reported active osteogenesis in experimental models using SBM, as evidenced by the presence of bone surfaces covered by osteoblasts around the implanted bone grafts and the formation of mature Haversian systems.[33] Moreover, after 4 weeks, the collagen fbers were replaced by mature bone.[33]

The loss of teeth in the posterior area of the maxilla leads to adverse consequences on masticatory function and occlusal balance. These outcomes negatively results in psychophysical conditions associated with temporomandibular joint and muscle diseases. A frequent problem in oral rehabilitation with implant-supported prostheses in the posterior maxilla is the lack of bone volume associated with alveolar ridge resorption or maxillary sinus pneumatization.[34] The reabsorption of the alveolar bone, adjacent to the floor of the maxillary sinus, may be aggravated by the increase in osteoclastic activity that originates in the periosteum of Schneider's membrane after tooth loss, due to the absence of osteogenesis normally stimulated by the functional load on the bone. In this sense, the bone volume is limited due to the pneumatization of the maxillary sinus on one hand, and the loss of height and width of the alveolar process, on the other. The maxillary sinus floor elevation technique is used to increase the bone volume in that area. This technique consists in elevating the membrane of the floor of the maxillary sinus, and flling the intermediate space with bone substitutes[28] to promote bone formation.[35] The results of this procedure can be affected by the surgical techniques used: simultaneous placement versus delayed implantation of the implant, use of barrier membranes on the lateral window, graft material selection and surface characteristics and length and width of the implants. Depending on the type of graft, the particles are partially reabsorbed and replaced by the patient's own bone during the healing time.[36]

In agreement with Shirmohammadi et al. and Wallace et al. on sinus augmentation utilizing Bio-Oss (BO) as bone graft,[37,38] the case report presented here evidences the effcacy of SBM in the bone healing process, showing osteoconductive properties when used as a grafting material for sinus lift elevation. In this respect, biopsies of the grafted areas showed that SBM particles were surrounded by vital new bone, without evidence of inflammation and bone sequestrae after 6 months of implantation. We neither observed inflammation nor thickening of the repaired Schneiderian membrane.

The use of bone grafts is important to preserve the alveolar bone ridge height and volume indispensable for dental implant placement. Despite the highly successful outcomes for the implant-supported overdentures, it seems that a majority of edentulous individu-

als have not pursued implant-based rehabilitation. Among the reasons cited for this discrepancy between highly successful therapy and its acceptance is the cost of the treatment.[38]

Even though additional comparative studies with greater number of patients and histomorphometric analysis are needed to assess the survival of implants placed in sinuses grafted with SBM, the present case report indicates that SBM is effcient to increase the bone volume of the alveolar crest.

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