Pablo Galindo-Moreno
Gustavo Ávila
Juan Emilio Fernández-Barbero
Francisco Mesa
Francisco O'Valle-Ravassa
Hom-Lay Wang

Clinical and histologic comparison of two different composite grafts for sinus augmentation: a pilot clinical trial

Authors' affiliations:
Pablo Galindo-Moreno, Oral Surgery Department, School of Dentistry, University of Granada, Granada, Spain
Gustavo Ávila, Hom-Lay Wang, Department of Periodontics and Oral Medicine, School of Dentistry, University of Michigan, Ann Arbor, MI, USA
Juan Emilio Fernández-Barbero, Human Anatomy and Embryology Department, School of Medicine, University of Granada, Granada, Spain
Francisco Mesa, Periodontology Department, School of Dentistry, University of Granada, Granada, Spain
Francisco O'Valle-Ravassa, Pathology Department, School of Medicine, University of Granada, Granada, Spain

Correspondence to:
Dr Pablo Galindo-Moreno
C/Recogidas
39 5° Izq
18005 Granada
Spain
Tel.: +34 958 520658
Fax: +01 734 936 0374
e-mail: pgalindo@ugr.es

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Abstract

Background and objectives: Sinus augmentation is a procedure used for augmenting insufficient bone height that is often observed in the maxillary posterior areas. Many different techniques as well as bone graft regimens have been suggested for performing this procedure. It was the goal of this study to compare, clinically and histologically, two different composite grafting regimens used for sinus augmentation.

Material and methods: Five patients, needing a bilateral sinus augmentation to allow implant placement, were recruited for this study. Right sinuses were grafted with cortical bone (collected from overlying the sinus membrane) and bovine hydroxyapatite (HA), while the left side sinuses were grafted with overlying autologous bone plus a bioglass (BG) material. Bone core biopsies were taken at 6 months after sinus graft or at the time of implant insertion. A waiting period of 6 additional months was granted to allow healing, before prosthetic restoration and functional loading. The level of peri-implant bone was evaluated 12 months after loading. A comparative histomorphometric analysis was conducted and a statistical analysis was performed.

Results: All implants in both groups were functional after a 12-month loading period. No bone loss was observed radiographically or clinically in both groups. Histologic analysis revealed that both composite grafts had a high biocompatibility. In the bovine HA-containing group, minimal xenogenic graft absorption was noted. In contrast, BG group samples presented a high absorption rate with some remaining particles imbedded in new normal bone.

Conclusions: Sinus augmentation using a combination of autogenous bone plus either bovine HA or BG is a predictable technique.

Sinus augmentation is a surgical approach commonly used for the rehabilitation of the posterior edentulous maxilla with dental implants, when there is insufficient bone height. The application of this surgical approach allows clinicians to restore that area, using implant-supported prosthesis over implants of ideal dimensions. It has been reported that the more the remaining bone height, the higher the success rate (Peleg et al. 1999). Similar results were also reported by Jensen & Greer (1992). They showed a 100% success rate if the remaining bone from the floor of the sinus cavity to the alveolar crest was ≥ 7 mm, vs. 29% if the residual bone height was <3 mm. Nevertheless, the overall success rate for the sinus augmentation has been reported as more than 90% (Wallace & Froum 2003). Currently, two major

techniques are available to perform this procedure: the use of osteotomes (Summers 1994) and a lateral window approach (Tatum 1986). Many bone substitutes or combination of grafts have been suggested and tested with promising outcomes. Several studies have shown that the healing waiting periods after sinus augmentation are largely dependent upon the type of bone graft used (Froum et al. 2006), which may also have a considerable impact in the restorative timing.

A synthetic, resorbable, osteoconductive, alloplastic bioglass (BG), composed by two different bioactive calcium phosphosilicate-like crystals (BG) has been developed as a bone grafting material. The major component of this material is a melt-derived calcium phosphorus sodium silicate, designed specifically for its absorbability and osteoconductive nature. The second component of this material is a calcium–phosphorus silicate bioactive glass, chemically similar to the major component, but derived via a solution–gelation (sol–gel) process. The sol–gel component allows more quickly absorbed than the standard melt-derived component (Wheeler et al. 2000), thus opening additional space between graft particles for tissue infiltration and thereby replaced by host bone (Vogel et al. 2001). This material is indicated in filling bony voids or gaps, without affecting the intrinsic stability of the osseous structure (Shapoff et al. 1997). However, so far only limited research has been conducted to test this material in sinus augmentation procedures. Therefore, the purpose of this study was to compare, clinically and histologically, this newly developed synthetic (BG) graft material to the commonly used bovine hydroxyapatite (HA) in sinus augmentation procedures.

Material and methods

Studied population

Five male patients, with a mean age of 62 (ranking from 45 to 78) were recruited for the study after informed consent and according to the principles of WHO Declaration of Helsinki (Schuklenk & Ashcroft 2000). All patients were partially edentulous and in need of bilateral sinus grafting for a future implant-supported restoration. Subjects for the study were selected according to the following inclusion criteria: patients were systemically healthy and did not take any drugs at least 2 weeks before the surgery, and had <5 mm remaining alveolar bone height. Smokers and patients suffering from any disease known to alter bone metabolism were excluded.

Surgical and restorative procedure

All the individuals were covered with 875/125 mg of amoxicillin/clavulanic acid, one tab every 8 h 1 day before the surgery. This medication was maintained for 7 days. Patients received bilateral sinus grafting during the same surgical procedure. All surgical procedures were performed under local anesthesia (Articain, Ultracain; Aventis Inc., Frankfurt, Germany). A modification of the conventional lateral wall approach (Kaufman 2003) was used to perform the sinus grafting in all patients. A bone scraper was used to collect autologous cortical bone and to expose the Schneiderian membrane, following the technique proposed by Galindo-Moreno et al. (2007).

To avoid any selection bias, all right sinus cavities were grafted with scraped autogenous cortical bone (ACB) in combination with 250–1000 μm particle size of bovine HA (Bio-Oss®; Geistlich Pharma AG, Wolhusen, Switzerland) in a 1 : 1 ratio. Left sinus cavities received another composite graft that contained a mixture of ACB and BG (Novabone®; Novabone Products, Jacksonville, FL, USA) in a 1 : 1 ratio. After bone grafting, an absorbable collagen membrane (Bio-Gide®; Geistlich Pharma AG) was placed over the lateral aspect of the bony window to prevent soft tissue invasion. Area was then carefully closed with surgical silk 4/0 (Laboratorio Aragó, Barcelona, Spain). In all cases primary wound closure was achieved.

After a 6-month healing period, a 3 mm trephine was used to collect bone core biopsies for future histologic analysis. The samples were collected by means of an osteotomy, in areas of planned implant location, of 12 mm in depth from the alveolar crest. All samples presented similar dimensions. A total of 28 implants (TioBlast®, Astra Tech, Mölndal, Sweden) were placed according to prosthetic treatment plan. Implants were covered for a two-stage surgical approach. After 6 months, they were surgically exposed for prosthesis fabrication. Delivery of implant-supported partial prosthesis took place 2 weeks after. The definitive restorations were cemented and occlusal adjustment performed. After implant loading, all patients were included in a maintenance program with 3 months recalls during the first year then every 6 months during the second year. Periapical radiographs of each implant were taken at the day of implant insertion, prosthesis delivery and 24 months after functional loading.

Radiographic peri-implant bone loss assessment

Each periapical radiograph was digitalized using a digital scanner. The mesial and distal, peri-implant marginal bone loss were obtained by subtracting baseline and 24 months after loading measurements using the Digident Dent-A-View V 1.0 image analysis program as described by Galindo-Moreno et al. (2005).

Histologic preparation

Bone core samples were immersed in buffered 4%, pH 7.7 paraformaldehyde fixative for 5 days. After decalcified, during 8 days, in Decalcifier I compound by formaldehyde, formic acid and methanol (Surgipath Europe Ltd, Peterborough, UK), they were dehydrated in alcohol baths of increasing concentrations, and embedded in paraffin in an automatic tissue processor (Shandon Pathcenter, Thermo-Shandon, Pittsburgh, PA, USA). Subsequently, sections of 5 μm wide were obtained and placed on glass slides. The histologic analysis was made on dewaxed sections using the standard protocols for hematoxylin–eosin (H–E) and Masson's trichrome stainings. All samples were examined under light microscopy (Microphoto FXA, Nikon, Tokyo, Japan), and with polarized light.

Histomorphometric evaluation

For the analysis, the central portion of each core was selected to avoid any potential bias both the coronal (native host's remaining bone) and the apical portion (using a safe margin of 1.5–2 mm) were excluded from analysis. Histomorphometric measurement of the samples was conducted using Image J software, developed by the National Institute of Health (NIH) of

Table 1. **Histomorphometric values for sinuses grafted with bovine hydroxyapatite (HA) and autogenous bone collect from outside of lateral window by scrapper**

Bovine HA	Remaining particle (%)	Vital bone (%)	Connective tissue
J.C.	19.74	26.03	54.23
B.A.	16.62	19.98	63.39
J.A.	17.47	41.26	41.27
M.J.	15.87	33.75	50.38
A.C.	16.71	34.12	49.17
MEAN ± SD	17.28 ± 1.32	31.02 ± 7.33	51.68 ± 7.21

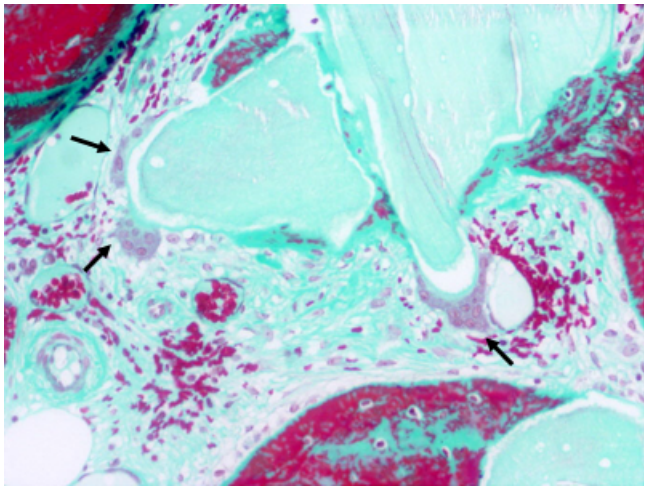

Fig. 1. Active osteoclasts arranged over a bovine hydroxyapatite particle surface (Masson's trichrome × 400).

Table 2. **Histomorphometric values for sinuses grafted with synthetic alloplast and autogenous bone collect from outside of lateral window by scrapper**

Bioglass	Remaining particle (%)	Vital bone (%)	Connective tissue (%)
J.C.	26.78	21.51	51.7
B.A.	14.21	37.28	51.49
J.A.	6.53	45.98	47.49
M.J.	10.9	29.36	59.74
A.C.	12.35	31.32	56.33
Media ± SD	14.15 ± 6.8	33.08 ± 8.18	53.35 ± 4.24

the United States of America. Values for the total percentage of vital bone (VB), remaining graft particle (RGP), and non-mineralized connective tissue (CT) were then calculated.

Statistical analysis

Data obtained from the histomorphometric analysis were statistically analyzed using a Wilcoxson' signed-rank test. To show the differences between groups, a *P*-value of <0.05 was considered statistically significant.

Results

Clinical and radiographic observations

No abnormal events were observed during the total 12-month healing period. All implants in both groups were functioning 24 months after loading. None of the implants presented signs or symptoms of inflammation or infection throughout the study period. Radiographic assessment revealed an average of 15.6 mm alveolar height gain. Furthermore, no evidence of bone loss around implants 2 years after loading.

Histomorphometric analysis

At the time of bone core biopsies collection, a D2 bone density according to Misch's classification (Misch 1990) was noted in the bovine HA + ACB group, while a D3–D4 bone quality was detected in the sites treated with BG + ACB.

Histologic examination revealed that bovine HA + ACB had a greater degree of maturation compared with BG + ACB. However, bovine HA particles appeared to be unaltered in their vast majority, with no signs of remodeling. A great amount of interposed non-mineralized CT and neoangiogenesis phenomena were observed. After healing and bone maturation (bone turnover), autogenous bone particles present in the collected samples are indistinguishable in their majority from newly formed or native bone, and cannot be easily separated, both components having the same origin. For this reason, it was decided to quantify its totality as VB. Mean values of 31.02 ± 7.33% for VB, 17.28 ± 1.32% for remaining bovine HA particles and 51.68 ± 7.21% for non-mineralized CT (Table 1). Cellular morphology and distribution around VB and bovine bone particles indicates that bone-remodeling events are in line with an ideal bone turnover (Fig. 1). No presence of inflammatory infiltrate could be observed in any of the samples, with irregular remaining bovine HA distribution.

Table 2 showed mean values for remaining alloplastic BG particle, VB and non-mineralized CT were 14.15 ± 6.8%, 33.08 ± 8.18% and 53.35 ± 4.24%, respectively. Despite BG particles are much smaller, their distribution within the composite graft was less homogeneous than those found in the HA group (Fig. 2). No inflammatory infiltrate was observed.

No statistical significant differences between the two groups were found (Table 3).

Discussion

Several studies have reported that sinus grafting techniques represent a predictable and successful bone augmentation for implant site development in the atrophic posterior maxilla (Valentini et al. 1998). Many techniques and biomaterials have been tested, showing good results (Esposito et al. 2006). Currently, autogenous bone is thought to be the gold-standard material for bone grafting techniques, including sinus augmentation (Block et al. 1998), because it possesses osteoconductive, osteoinductive, and osteogenic properties. These beneficial properties emanate from its structure and cellular/protein content

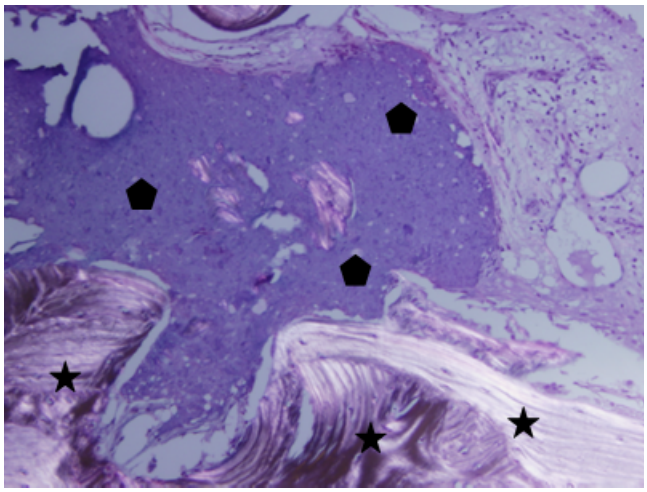

Fig. 2. Histologic sample of ACB + BG group (× 40 under polarized light). It can be observed newly formed bone, containing collagen (stars). That is the reason why refringent parallel layers are present in the vital bone, that contains ostecytes as well, vs. the bone substitute material remaining particles (BG), which do not present protein content (pentagons). Also, note the remaining BG particles in relation with non-mineralized CT and vital bone in absence of inflammatory infiltrate, which reflects its high biocompatibility.

***Table 3.* Wilcoxson signed ranks test ($P<0.05$ was considered statistically significant)**

	Remaining particle	Vital bone	Connective tissue
	Bovine HA/ synthetic graft	Bovine HA/ synthetic graft	Bovine HA/ synthetic graft
Statistical contrast *Z*	− 0.94	− 0.4	− 0.4
Statistical significance (*P*)	0.34	0.68	0.69

HA, hydroxyapatite.

(Khan et al. 2000). Nevertheless, the need for bone harvesting from another donor sites may imply additional complications to the patients as well as to the clinicians (e.g., time, cost, skill and morbidity), in addition to its limited quantity. Hence, many alternative bone substitutes emerged as an alternative to overcome these deficiencies.

Results obtained from this study indicated that the use of both, bovine HA and synthetic BG, in combination of autogenous particles is compatible with excellent clinical outcomes, showing similar percentages of VB, CT as well as residual graft particles. This is in agreement with systematic reviews that have concluded that bone-substitute materials are as effective as autogenous bone when used alone or in combination with autogenous bone, in terms of survival and success rate for implants placed after sinus grafting (Wallace & Froum 2003; Del Fabbro et al. 2004). Similar findings were also reported by Froum and collaborators. They showed similar long-term outcomes when sinus augmentation was performed with either autologous bone alone or in combination with bovine HA (Froum et al. 1998). Hallman and colleagues found that slightly higher implant survival rates were associated with the use of a purely bovine HA graft (96%) vs. a composite graft consisting of autologous bone and bovine HA (94.4%) or autologous bone alone (82.4%), 12-months after loading (Hallman et al. 2002; Merkx et al. 2003). Merkx and colleagues reported that addition of autogenous bone provide a higher VB proportion than that obtained when xenogenic substitutes are used exclusively (Ulm et al. 1999; Galindo-Moreno et al. 2007).

Our group has advocated for a surgical approach in which cortical bone is obtained from the lateral wall of the sinus cavity via scraped, then combined with an xenogenic bone substitute (Olson et al. 2000). This approach not only allows the clinician to collect autologous bone to be used as part of the grafting material, but also eliminates the need for a second surgical site to harvest autogenous bone.

Percentage of VB is an important parameter to be assessed in these type of studies. An average of 31–33% was found in our sample. This is in accordance with the results provided by Ulm and colleagues in which a mean of 23% of trabecular bone was identified (Thomas et al. 2005). This could also explain the higher success rates of implants inserted in grafted sinuses compared with those placed in pristine bone of the posterior maxilla (Vrouwenvelder et al. 1993; Gatti et al. 2006; Scarano et al. 2006).

The synthetic alloplastic BG material used in this study primarily consists of a mixture of two different types of calcium phosphosilicate-like crystals. This material is osteoconductive and has a high absorption rate. It has a Young's modulus of 30–35 GPa, which is close to that of cortical bone (Schlegel & Donath 1998). This material has been shown to accelerate osteogenic activity and early alkaline phosphatase expression *in vitro*. In addition, because it is naturally resorbed, a subsequent release of calcium and phosphate ions occurs, which could stimulate osteoblast differentiation (Gatti et al. 2006).

Although the data from our study failed to show any statistical significant difference between ACB + HA and ACB + BG for the parameters evaluated, it is important to note that the clinical bone density at the time of implant placement was higher in the HA group. This is further confirmed with the histologic observation, where BG disorganization was evident. This is unlike to happen in the bovine HA specimen where the remaining particles arrangement was more homogeneous. Interestingly, in some locations, remaining HA particles started to be degraded, with the presence of active osteoclasts on the surface (Fig. 1). However, it is known that absorption rate of bovine HA is very low (Schlegel & Donath 1998), which could explain that differential behavior between samples.

Nevertheless, it can be finally concluded that both composite grafts are a valid choice for sinus augmentation procedures.

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