Pablo Galindo-Moreno
Gustavo Ávila
Juan Emilio Fernández-Barbero
Mariano Aguilar
Elena Sánchez-Fernández
Antonio Cutando
Hom-Lay Wang

Evaluation of sinus floor elevation using a composite bone graft mixture

Authors' affiliations:
Pablo Galindo-Moreno, Oral Surgery Department, School of Dentistry, University of Granada, Granada, Spain
Gustavo Ávila, Department of Periodontics & 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
Mariano Aguilar, Pathology Department, School of Medicine, University of Granada, Canada, Spain
Elena Sánchez-Fernández, *Antonio Cutando*, Oral Surgery Department, School of Dentistry, University of Granada, Granada, Spain
Antonio Cutando Special Cares in Dentistry Department, School of Dentistry, University of Granada, Granada, Spain
Hom-Lay Wang, Department of Periodontics & Oral Medicine, School of Dentistry, University of Michigan, Ann Arbor, MI, USA

Correspondence to:
Dr Pablo Galindo-Moreno
C/ Recogidas, 39 5° Izq,
18005 Granada
Spain
Tel.: +34 95 852 0658
Fax: +01 734 936 0374
e-mail: pgalindo@ugr.es

Date:
Accepted 15 May 2006

To cite this article:
Galindo-Moreno P, Ávila G, Fernández-Barbero JE, Aguilar M, Sánchez-Fernández E, Cutando A, Wang H-L. Evaluation of sinus floor elevation using a composite bone graft mixture.
Clin. Oral. Impl. Res. **18**, 2007; 376–382
doi: 10.1111/j.1600-0501.2007.01337.x

Key words: autogenous bone, bone regeneration, bovine hydroxyapatite, implants, platelet-rich plasma, PRP, sinus lift

Abstract

Background: The performance of implant surgery in the posterior maxilla often poses a challenge due to insufficient available bone. Sinus floor elevation was developed to increase needed vertical height to overcome this problem. The present study described and reported a simple, safe and predictable bone graft mixture for the sinus lifting procedure.

Material and methods: Seventy patients were recruited for this study and underwent a sinus lift procedure. All sites were treated with a composite graft of cortical autogenous bone, bovine bone and platelet-rich plasma (PRP). A total of 263 implants (171 Astra Tech and 92 Microdent) were placed either simultaneously or delayed. All sites were clinically and radiographically evaluated 24 months after their prosthetic loading. Biopsy samples were taken from 16 delayed implant placement sites at the time of their implant placement.

Results: A 100% implant success rate was found after 24 months of functioning. Only two Microdent implants failed before loading, which translates to a 99% overall implant success rate. No statistically significant differences were found between simultaneous and delayed implant placement. Image processing revealed 34 $\pm$ 6.34% vital bone, 49.6 $\pm$ 6.04% connective tissue and 16.4 $\pm$ 3.23% remaining Bio-Oss® particles. However, the histomorphometric analysis showed that the bovine bone was incorporated into new bone formation.

Conclusion: The results showed that a composite graft comprised of cortical autogenous bone, bovine bone and PRP mixture can be successfully used for sinus augmentation.

Tooth loss in the posterior maxilla results in a rapid resorption of both horizontal and vertical alveolar bone due to lack of intraosseous stimulation by periodontal ligament fibers (Bays 1986). In addition, the absence of upper molars leads to increased osteoclast activity in Schneider's membrane, causing pneumatization of the sinus by resorbing bone within a few months.

It is widely acknowledged that the best therapeutic option for replacing absent teeth is the placement of osseointegrated implants (Van Steenberghe 2000). However, their placement in the posterior maxilla frequently poses a challenge because of the small height of residual bone and the supposedly 'poor quality' of bone in this area (Davies 2003). One cause of failure of most implants placed in these areas without sinus lifting is not so much the 'quality' of type IV bone but rather the use of implants that are too short to resist the strong occlusal forces exerted in this area (Zinner & Small 2004). If a surgical sinus lift technique is not applied before implant treatment, there is also a risk of perforation

of the sinus membrane that may result in sinusitis, possible implant migration to the maxillary sinus and other complications (Kamada et al. 2003; Raghoebar & Vissink 2003; Galindo et al. 2005).

In the 1980s, Boyne & James (1980) and Tatum (1986) described techniques for bone grafting of the maxillary sinus with the aim of obtaining more bone and increasing the likelihood of successful implant placement. Since then, various modifications of the technique and different filling materials have been proposed, aimed at reducing complications and increasing the success rate.

The rationale for using a composite bone graft that includes cortical autogenous bone, bovine bone and platelet-rich plasma (PRP) is explained as follows; Autologous bone grafts obtained from the patient are the most widely used bone graft (Daelemans et al. 1997). These can be procured either intraorally [from the mandible (Cordaro 2003), the tuberosity itself (Pacifici et al. 2003)], extraorally [from the iliac crest (Triplett & Schow 1996; Lorenzetti et al. 1998; Timmenga et al. 2003), calota (Iizuka et al. 2004) or even from the tibia (Herford et al. 2003)]. The autograft has been regarded as the gold standard for sinus floor elevation (Daelemans et al. 1997; Cordaro 2003) because it contains osteogenic, osteoinductive, osteoconductive properties, a high number of viable cells and is rich in growth factors (such as PDGF and TGF-β) (Mundy et al. 1995; Khan et al. 2000). The viable cells consist of osteoblasts, undifferentiated mesenchymal cells, monocytes and osteoclast precursor cells (Takahari et al. 2002), and participate in the remodeling and formation of *de novo* bone (Martin & Sims 2005). The enriched growth factors promote proper bone healing. Nevertheless, due to its limited availability and potential donor site morbidity, bone substitutes such as demineralized freeze-dried bone allograft (DFDBA) (Piattelli et al. 1996; Paul et al. 2001), bovine bone (Maiorana et al. 2000), resorbable and non-resorbable hydroxyapatite (HA) (Moy et al. 1993; Karabuda et al. 2001; Haas et al. 2003), tricalcium phosphate (Scher et al. 1999; Zerbo et al. 2005) and coralline derivatives composed of phosphate and calcium carbonate (Velich et al. 2004) have been developed and used.

Bovine anorganic bone (Bio-Oss®, Geistlich Pharma AG, Wolhusen, Switzerland) was a popular bone graft for this procedure (Hürzeler et al. 1997; Piattelli et al. 1999; Valentini et al. 2000). It is a biologically safe material but also remains long enough to permit slow apposition of *de novo* bone formation. It has been widely used and associated with high clinical success rates (Carmagnola et al. 2000, 2002). The use of bovine bone in combination with autologous bone offers many additional advantages. First, it allows the volume of the graft to be doubled, avoiding the need to harvest large amounts of autologous bone. Second, the osteoconductive properties of bovine bone act as a scaffold that is essential for bone remodeling (Davies 1996). Third, bovine bone is a calcium-deficient carbonate apatite with a crystal size of approximately 10 nm (Paul et al. 1993). Thus, the surface area of each graft particle is considerably greater than that of porous bioceramics, making its resorption considerably slower. This could maintain the space longer, which is another pre-requisite for the bone augmentation (Wang & Boyapati 2006). Lastly, its modulus of elasticity is similar to that of natural bone (Rueger 1992) to ensure a proper uneventful healing. It is because of these properties that we chose this bone graft.

Recently, PRP was advocated for use in sinus floor elevation (Philippart et al. 2005) due to its high concentration of growth factors (platelet-derived growth factors, insulin-like growth factors as well as vascular endothelium growth factors and transforming growth factor-β). Marx et al. reported a 1.62–2.16-fold greater bone maturation of grafts mixed with PRP and a higher bone density (74 ± 11% vs. 55.1 ± 1%) at sites where PRP was added in comparison with grafts and sites, respectively, without PRP addition. Many authors have reported positive sinus lift outcomes after using PRP mixed with bone substitute, whether autogenous, allogenic or alloplastic (Kassolis et al. 2000; Rosenberg & Torosian 2000; Lozada et al. 2001; Fürst et al. 2003; Maiorana et al. 2003; Rodríguez et al. 2003). Besides the above-mentioned properties, PRP has an important adhesive capacity via its hemostatic capacity of fibrin (Rousou et al. 1984; Yoshida et al. 2000; Vaiman et al. 2005). This facilitates handling of the bone graft mixture (Vachiramon et al. 2002).

Hence, it was the purpose of this study to evaluate clinically, radiographically, as well as histomorphometrically the efficacy of this composite graft (autogenous bone, bovine HA and PRP) during the sinus floor elevation procedure.

Material and methods

The study population 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 a fixed implant-supported prosthesis. The exclusion criteria were the presence of uncontrolled systemic disease (e.g., diabetes or blood/immune disorders) and a previous history of chronic sinusitis or allergies with a respiratory component. Seventy patients were selected for the study, 48 males and 22 females, who all signed their informed consent according to the Helsinki protocols (World Medical Association Declaration of Helsinki 2000). The study protocol was approved by the Human Subject Review Committee at University of Granada.

Smokers were not excluded from the study but were informed that tobacco use is contraindicated in an intraoral surgery setting as it compromises the quality of the sinus lift and reduces the success rate of implants. Out of the 24 smokers enrolled in the study, 20 had stopped the habit by 2 year after the surgery.

Surgical procedure

Patients received 875 g of amoxicillin/clavulanic acid (1 capsule/8 h) 1 day before the surgery and 7 days post-surgically. Three patients who were allergic to penicillin received 300 mg clindamycin (1 capsule/8 h) for the same time period instead. All patients underwent surgery under local anesthesia with 1% (1 : 100,000) vasoconstrictor (adrenalin).

The decision to place simultaneous implants during the sinus floor elevation or at a later date depended on whether the crest had sufficient residual bone height to ensure primary stability of the implant. The minimum amount to indicate immediate implantation was 5 mm (Zinner & Small 2004). Based on this criterion, 82 sinuses were selected to receive implants, a total of 215 : 135 Astra Tech (Astra Tech, Möndal, Sweden) and 80 Microdent (Microdent Implant System, Barcelona, Spain) during

sinus lift surgery, whereas the implantation was deferred in 16 sinuses (total of 48 implants: 36 Astra Tech and 12 Microdent). Hence, a total of 263 implants were used: 171 Astra Tech implants with Tio-Blast surface and 92 Microdent implants with sandblast surface treatment.

An incision was made in the palatal aspect of the alveolar crest in the edentulous area. After elevation of a full-thickness mucoperiosteal flap, access was gained to the anterior bony wall of the sinus. The bone window was obtained using a curved cortical bone collector (Safescraper®, purchased from Meta, Reggio Emilia, Italy), removing all cortical bone up to the sinus membrane and keeping it for the subsequent graft preparation. The bone collector was used to procure cortical bone that was needed for the sinus lift.

Once the membrane was exposed, it was elevated with instruments. The sinus was never lifted more than 2 cm to avoid occluding the sinusal ostium (Ziccardi et al. 1995), and was never lifted less than 12 mm to allow placement of implants of sufficient size to guarantee adequate long-term stability of the implant-supported prosthesis.

After elevation of the sinus and protecting the membrane with a flat blunt-edged metal instrument, the alveolar crest was perforated with a very fine bur until the antral cavity was entered. The residual bone was then measured using a periodontal probe to determine whether the implantation could be performed immediately. If the residual bone throughout the alveolar process was 5 mm or more (Peleg et al. 1999), the sequence of drills required for the placement of implants was implemented, avoiding use of the final drill so the implant could be placed by exerting compression on the maxillary bone, favoring primary stability.

Subsequently, half of the graft was placed on the palatal wall of the sinus before placement of the implant, and the remainder was used to fill the sinus cavity once the implants were placed.

An absorbable collagen membrane (Bio-Gide®, Geistlich Pharma AG, Wolhusen, Switzerland) was then placed on the vestibular wall of the sinus to avoid migration of the graft and its invasion by soft tissues. This membrane was fixed with metal pins (Imtec Corp, Ardmore, OK, USA) to avoid its movement and, after release of the flap to facilitate a tension-free suture, it was sutured with 3-0 silk suture.

When the implant placement was deferred, the antral cavity was filled with the graft and an absorbable collagen membrane was placed following the method described above. After a period of 6–8 months, the implants were placed by the traditional method.

Preparation of mixture grafts

The grafts used in all of these patients comprised the following three components:

1. Autogenous cortical bone. This was harvested using the bone collector (Safescraper®), from the bony wall of the treated sinus and the periphery of the same surgical bed.
2. Bovine bone (Bio-Oss®). Small-particle (0.25–1 mm) bone was used.
3. Platelet-rich plasma. PRP was obtained following the recommended protocol of Anitua (1999). Between 10 and 20 cc of PRP was obtained and mixed with the autologous bone/bovine bone in aliquoted amounts.

Histological preparation

A 3 mm-diameter trephine was used to gather samples from patients indicated for deferred implantation (16 patients). At the time of taking the biopsies, after a minimum of 6 months of healing, bone density was similar to natural-type D_1–D_2 bone, according to Misch's classification (Misch 1988). Samples were immediately immersed in buffered 4%, pH 7.7 paraformaldehyde fixative for 5 days. They were dehydrated in alcohol baths of increasing concentrations and embedded in paraffin. Sections 5 μm wide were applied onto slides. The histological analysis was performed using the standard protocols of H–E and Masson trichromic stains, which allowed the observation of individual cells and differentiation of uncalcified osteoid (Wheater et al. 1987). Finally, the sections were covered with slip covers and examined using light microscopy (Microphot-FXA; Nikon, Tokyo, Japan).

Image processing

In order to assess the total percentages of vital bone, remaining Bio-Oss® particle and surrounding connective tissue, an image analysis process, using the software Image J^R, was performed on the sections obtained previously.

Implant success rate

Implant success was assessed using the criteria set up by Albrektsson et al (1986).

Results

Surgical technique and survival of implants

No dental injuries or tears of Schneider's membrane were noted during the procedures. No adverse events were recorded during the healing period in any of the patients, with no signs of infection. Only two Microdent implants failed before loading due to lack of osseointegration: one from the group of delayed and the other from the group of simultaneous placement. This translates to a 99.06% overall implant success rate after 24 months of functioning. No statistically significant differences were found between simultaneous and delayed implant placement.

Histology

Biopsy samples, taken with a 3 mm trephine, were obtained from 16 sinuses that were grafted and delayed for implant placement. Similar results could be expected in the simultaneous placement group, with regard to radiographic parameters. However, we did not take any biopsies from this group because of the ethical problems it would pose.

Histomorphometric analysis revealed that bovine bone was incorporated into new bone formation that showed an osteoid matrix (Fig. 1). Furthermore, most of the bovine bone particles remained vir-

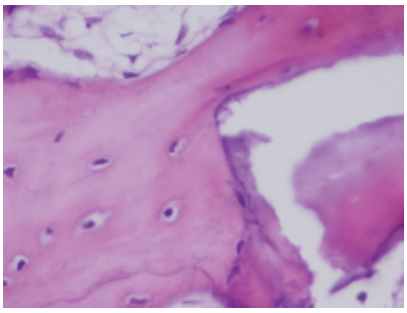

Fig. 1. Normal bone with active osteoblasts producing osteoid matrix * in presence of a fibrous type marrow (upper side of the picture) (Hematoxylin Eosin, × 60).

tually unaltered, except for some areas on the surface that were partially resorbed (Fig. 2). The majority of samples showed bovine bone crystals interposed with connective tissue. In these samples, the marrow was essentially fibrous with variable vascularity (Figs 1 and 3).

Image processing revealed 34 ± 6.34% vital bone, 49.6 ± 6.04% connective tissue and 16.4 ± 3.23% remaining Bio-Oss® particles (Table 1). Overall, bovine bone presented high biocompatibility, but demonstrated little new bone growth or graft resorption.

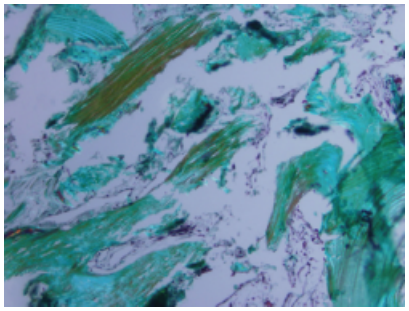

Fig. 2. Bovine bone (Bio-Oss®) included in fibrous tissue in presence of vital bone. The resorption of bovine bone takes place later than in autologous bone (Masson's trichromic observed without polarized light × 40).

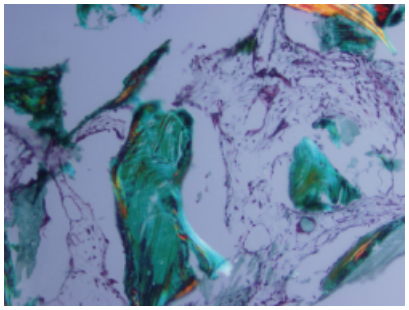

Fig. 3. It was observed vital bone surrounded by newly formed connective tissue *. This tissue is expected to transform into bone (Masson's trichromic with polarized light × 40).

Discussion

Sinus lift procedures have allowed implants to be placed in an atrophic maxilla with high success rates. As the first description of this approach by Boyne & James (1980), numerous modifications have been published and different graft materials have been used, all aimed at technique improvements and more predictable outcomes. The composite graft (cortical autogenous bone, bovine bone and PRP mixture) used in this study showed a 99% overall implant success rate and a 100% implant success rate after 24 months of loading. This is in agreement with Moy et al. (1993), Wallace & Froum 2003 and Velich et al. (2004). Moy et al. (1993) reported that a combination of bovine bone and autogenous bone yielded better outcomes when compared with other bone graft regimes. Froum et al. (1998) found similar implant success rates when bovine bone was used with or without autogenous bone. Velich et al. (2004) compared autogenous bone, heterografts, exogenous bone and synthetic materials used alone or in combination with growth factors or morphogenetic proteins for sinus lifting. They found no differences in outcomes among these materials, with the exception of gel-state calcium carbonate, due to the high absorption of this substance. Furthermore, there was no difference between simultaneous and delayed implant placement. This is in line with recent workshop conclusions (Wallace & Froum 2003).

Our histologic data revealed 34% vital bone, 49.6% connective tissue and 16.4% remaining Bio-Oss® particles. This is in agreement with several studies that showed similar or higher percentages of vital bone as ours (Wallace et al. 1996; Froum et al. 1998; Valentini et al. 2000). According to Valentini et al. (2000), the residual bovine bone particles reside in the connective tissue compartment and, when combined with newly formed vital bone, can create a graft of exceptionally high density. Furthermore, the histology of explants from the maxillary sinus does not show residual bovine HA particles in contact with the implant surface, suggesting implant–vital bone contact even though bovine HA was used for sinus floor elevation (Rosenlicht & Tarnow 1999)

The rationale to use a combination of autologous bone, PRP and bovine bone was based on a detailed study of the literature. Some authors considered autologous bone from extraoral sites such as the iliac crest or tibia to be the ideal material for sinus grafting (Chanavaz 1990; Block et al. 1998). However, there are major concerns with their use, including the need for hospitalization and general anesthesia, increased surgical time and costs, higher morbidity from the second surgical site and an increased risk of intra- and postoperative complications such as fracture (harvesting from tibia) or walking difficulty (harvesting from iliac crest) (Weikel & Habal 1977; Marx & Morales 1988). Moreover, there have been reports of ample resorption of grafts harvested from these sites (Ermis & Poole 1992; Kingsmill et al. 1999), possibly due to the embryological origin of the bone. Finally, the large amount of bone harvested at these sites was considered unnecessary to achieve a reliable sinus lift. The type of bone harvested from intraoral sites appears to be more appropriate. On the other hand, taking bone from the mandibular symphysis and ramus, while yielding adequate cortical bone (subsequently particulated for use), is frequently associated with devitalization of anterior mandibular teeth by involvement of tooth apices, changes in the facial es-

***Table 1*. Percentages per patient and mean average of vital bone, connective tissue and remaining Bio-Oss particles**

Subject	Remaining Bio-Oss	Vital bone	Connective tissue
B. A.	14.3	17	68.7
A. J.	9.9	46.6	43.5
J. M.	19.8	34.5	45.7
P. L.	14.5	35	50.5
P. U.	17.6	33.6	48.8
J. G.	14.9	36.1	49
J-M. J.	12.3	39.5	48.2
F. A.	17.3	34.4	48.4
L. L-G.	23.6	27.6	48.8
C. M.	15.7	33.7	50.6
A. M.	18.9	35.2	45.9
M. V.	14.2	29.8	56
J. C.	19.4	31.3	49.3
M. S.	17.4	41.2	41.4
I. G.	15.8	33.7	50.5
P. G.	16.7	34.1	49.2
Mean ± SD	16.4 ± 3.23	34 ± 6.34	49.6 ± 6.04

thetics of the patient, possible damage to the mental or lower dental nerves and increased risk of mandibular ramus fracture. Harvesting from the tuberosity, although simple and close to the surgical field, yields an inadequate amount of highly medullar and spongy bone.

Anorganic bovine bone provides a scaffold for *de novo* bone formation and the slow resorption of crystals, as demonstrated in our study, helps to maintain cells carried by the autologous bone, promoting the formation of new bone within the matrix (Carmagnola et al. 2003). Moreover, because it is deproteinized, biological risks are avoided. This bovine bone was also found to be more effective than HA as a bone substitute (Piattelli et al. 1999), and it appeared to favor a more physiological remodeling toward native bone (Berglundh & Lindhe 1997). In addition, this anorganic bovine bone has demonstrated good biocompatibility that elicits no foreign body reactions (Denissen et al. 1980; Hislop et al. 1993; McAllister et al. 1998). Hence, it has been widely used and associated with high clinical success rates (Carmagnola et al. 2000, 2002).

The effect of PRP in the composite graft remains to be determined. However, it is our experience that PRP enhanced the graft-handling capacity via its fibrin capacity, thus making it easier for placement of the bone graft into the sinus chamber. Other effects of PRP reported in the literature were not easily confirmed in our study as our intent was not study the effect of PRP but rather to evaluate the overall effect of the composite graft. Nonetheless, Marx et al. reported a 1.62–2.16-fold greater bone maturation of grafts mixed with PRP and a higher bone density (74.0 ± 11% vs. 55.1 ± 1%) at sites where PRP was added in comparison with grafts and sites, respectively, without PRP addition. Others have also reported positive outcomes when PRP was mixed with bone substitute, whether autogenous, allogenic or alloplastic, for sinus floor elevation (Kassolis et al. 2000; Rosenberg & Torosian 2000; Lozada et al. 2001; Fürst et al. 2003; Maiorana et al. 2003; Rodríguez et al. 2003). On the other hand, other authors did not find PRP to be a potent bone-regenerating agent (Danesh-Meyer et al. 2001; Jakse et al. 2003; Wiltfang et al. 2003; Butterfield et al. 2005). Froum et al. (2002) drew the clear conclusion that, in sinus lift techniques, there were no significant differences in the production of vital bone or in the amount of implant–bone contact interface between sinuses filled with PRP and those filled only with bovine bone (Bio-Oss®). Future studies in this area are certainly needed.

In all cases, an absorbable collagen membrane was placed on the vestibular sinus wall to prevent invasion of the graft by soft tissues, which would reduce the amount and quality of the de novo formed mineralized tissue, as reported by various authors (Tawil & Mawla 2001; Carmagnola et al. 2003). An absorbable membrane was selected to obviate the need for a second surgery in patients who received their implants during the sinus lift surgery, as it has been demonstrated that regeneration is equally effective whether absorbable or non-resorbable barriers are used (Avera et al. 1997).

Within the limits of this study, a composite graft that utilizes cortical autogenous bone, bovine bone and PRP mixture is indicated for use as a successful bone graft regime for sinus augmentation.

Acknowledgements: *Disclaimers*: The authors do not have any financial interests, either directly or indirectly, in the products listed in the study.

要旨

問題の背景：上顎臼歯部のインプラント手術は骨量が不十分だと困難となる。上顎洞底挙上術はこの問題を克服するために骨の垂直的高径を増多するために考案された。本研究はサイナス・リフト術のための、単純で、安全かつ予知性の高い混合骨移植材料について報告する。

材料と方法：患者７０名を本試験に組み入れ、サイナス・リフト術を行った。全ての部位は自家皮質骨、牛骨と多血小板血漿（ＰＲＰ）の混合移植材料を用いた。合計２６３本のインプラント（Astra Tech 171本、Microdent 92本）を１回法または２回法によって埋入した。全ての部位は補綴物の荷重後２４ヶ月後に臨床検査と放射線像によって評価した。インプラント埋入時に、２回法で埋入した１６箇所から生検標本を採取した。

結果：機能開始後２４ヶ月後にインプラント成功率は100%であった。Microdent インプラント２本のみが荷重前に失われたので、インプラント総成功率は９９％となった。１回法と２回法の間に統計学的な有意差は認められなかった。画像処理は、生着骨 34 ±6.34%、結合組織 49.6± 6.04%および残存する Bio-Oss 粒子 16.4 ±3.23%を示した。しかし組織形態計測学的分析では牛骨は新生骨に取り込まれていた。

結論：これらの所見は自家皮質骨、牛骨とＰＲＰの混合移植材料は上顎洞増多術に成功裏に使用しうることを示した。

References

Albrektsson, T., Zarb, G.A., Worthington, P. & Eriksson, A.R. (1986) The long-term efficacy of currently used dental implants: a review and proposed criteria for success. *International Journal of Oral and Maxillofacial Implants* **1**: 11–25.

Anitua, E. (1999) The use of plasma-rich growth factors (PRGF) in oral surgery. *Practical Procedures and Aesthetic Dentistry: PPAD* **13**: 487–493.

Avera, S.P., Stampley, W.A. & McAllister, B.S. (1997) Histologic and clinical observations of resorbable and nonresorbable barrier membranes used in maxillary sinus graft containment. *International Journal of Oral and Maxillofacial Implants* **12**: 88–94.

Bays, R. (1986) The pathophysiology and anatomy of edentulous bone loss. *Reconstructive Preprosthetic Oral and Maxillofacial Surgery* **1**: 1–17.

Berglundh, T. & Lindhe, J. (1997) Healing around implants placed in bone defects treated with Bio-Oss: an experimental study in the dog. *Clinical Oral Implants Research* **8**: 117–124.

Block, M.S., Kent, J.N., Kallukaran, F.U., Thunthy, K. & Weinberg, R. (1998) Bone maintenance 5 to 10 years after sinus grafting. *Journal of Oral and Maxillofacial Surgery* **56**: 706–715.

Boyne, P.J. & James, R.A. (1980) Grafting of the maxillary sinus floor with autogenous marrow bone. *Journal of Oral Surgery* **38**: 613–616.

Butterfield, K.J., Bennett, J., Gronowicz, G. & Adams, D. (2005) Effect of platelet-rich plasma with autogenous bone graft for maxillary sinus augmentation in a rabbit model. *Journal of Oral and Maxillofacial Surgery* **63**: 370–376.

Carmagnola, D., Adriaens, P. & Berglundh, T. (2003) Healing of human extraction sockets filled with Bio-Oss®. *Clinical Oral Implants Research* **14**: 137–143.

Carmagnola, D., Berglundh, T., Araujo, M., Albrektsson, T. & Lindhe, J. (2000) Bone healing around implants placed in jaw defect augmented with Bio-Oss. An experimental study in dogs. *Journal of Clinical Periodontology* **27**: 799–805.

Carmagnola, D., Berglundh, T. & Lindhe, J. (2002) The effect of a fibrin glue on the integration of Bio-Oss with bone tissue. An experimental study in labrador dogs. *Journal of Clinical Periodontology* **29**: 377–383.

Chanavaz, M. (1990) Maxillary sinus: anatomy, physiology, surgery and bone grafting related to implantology. Eleven years of surgical experience (1979–1990). *Journal of Oral Implantology* **16**: 2–12.

Cordaro, L. (2003) Bilateral simultaneous augmentation of the maxillary sinus floor with particulated mandible. Report of a technique and preliminary results. *Clinical Oral Implants Research* **14**: 201–206.

Daelemans, P., Hermans, M., Godet, F. & Malevez, C. (1997) Autologous bone graft to augment the maxillary sinus in conjunction with immediate endosseous implants: a Retrospective Study Up to 5 years. *International Journal of Periodontics and Restorative Dentistry* **17**: 27–39.

Danesh-Meyer, M.J., Filstein, M.R. & Shanaman, R. (2001) Histological evaluation of sinus augmentation using platelet rich plasma (PRP): a case series. *Journal of the International Academy of Periodontology* **3**: 48–56.

Davies, J.E. (1996) In vitro modeling of the bone/implant interface. *Anatomical Record* **245**: 426–445.

Davies, J.E. (2003) Understanding peri-implant endosseous healing. *Journal of Dental Education* **67**: 932–949.

Denissen, H.W., De Groot, K., Makkes, P.C., Van den Hoof, A. & Klopper, P.J. (1980) Tissue response to dense apatite implants in rats. *Journal of Biomedical Materials Research* **14**: 712–721.

Ermis, I. & Poole, M. (1992) The effects of soft tissue coverage on bone graft resorption in the craniofacial region. *British Journal of Plastic Surgery* **45**: 26–29.

Froum, S.J., Tarnow, D.P., Wallace, S.S., Rohrer, M.D. & Cho, S-C. (1998) Sinus floor elevation using anorganic bovine bone matrix (osteoGraf/N) with or without autogenous bone: a clinical, histologic, radiographic, and histomorphometric analysis – Part2 of an ongoing prospective study. *International Journal of Periodontics and Restorative Dentistry* **18**: 529–543.

Froum, S.J., Wallace, S.S., Tarnow, D.P. & Cho, S-C. (2002) Effect of platelet-rich plasma on bone growth and osseointegration in human maxillary sinus grafts: three bilateral case reports. *International Journal of Periodontics and Restorative Dentistry* **22**: 45–53.

Fürst, G., Gruber, R., Tangl, S., Zechner, W., Haas, R., Mailath, G., Sanroman, F. & Watzek, G. (2003) Sinus grafting with autogenous platelet-rich plasma and bovine hydroxyapatite: a histomorphometric study in minipigs. *Clinical Oral Implants Research* **14**: 500–508.

Galindo, P., Sánchez-Fernández, E., Avila, G., Cutando, A. & Fernández, J.E. (2005) Migration of implants into the maxillary sinus: two clinical cases. *International Journal of Oral and Maxillofacial Implants* **20**: 291–295.

Haas, R., Baron, M., Zechner, W. & Mailath-Pokorny, G. (2003) Porous hydroxyapatite for grafting the maxillary sinus in sheep: comparative pullout study of dental implants. *International Journal of Oral and Maxillofacial Implants* **18**: 691–696.

Herford, A.S., King, B.J., Audia, F. & Becktor, J. (2003) Medial approach for tibial bone graft: anatomic study and clinical technique. *Journal of Oral and Maxillofacial Surgery* **61**: 358–363.

Hislop, W.S., Finlay, P.M. & Moos, K.F. (1993) A preliminary study into the uses of anorganic bone in oral and maxillofacial surgery. *British Journal of Oral and Maxillofacial Surgery* **31**: 149–153.

Hürzeler, M.B., Quiñones, C.R., Kirsch, A., Gloker, C., Schüpbach, P., Strub, J.R. & Caffesse, R.G. (1997) Maxillary sinus augmentation using different grafting materials and dental implants in monkeys. Part I. Evaluation of anorganic bovine-derived bone matrix. *Clinical oral implants research* **8**: 476–486.

Iizuka, T., Smolka, W., Hallermann, W. & Mericske-Stern, R. (2004) Extensive augmentation of the alveolar ridge using autogenous calvarial split bone grafts for dental rehabilitation. *Clinical Oral Implants Research* **15**: 607–615.

Jakse, N., Tangl, S., Gilli, R., Berghold, A., Lorenzoni, M., Eskici, A., Haas, R. & Pertl, C. (2003) Influence of PRP on autogenous sinus grafts: an experimental study on sheep. *Clinical Oral Implants Research* **14**: 578–583.

Kamada, M., Shimazu, K., Aoki, H., Shiroyama, A., Mouri, D. & Mouri, M. (2003) Maxillary sinusitis caused by oral implants. *Practica Oto-Rhino-Laryngologica* **96**: 231–236.

Karabuda, C., Ozdemir, O., Tosun, T., Anil, A. & Olgaç, V. (2001) Histological and clinical evaluation of 3 different grafting materials for sinus lifting procedure based on 8 cases. *Journal of Periodontology* **72**: 1436–1442.

Kassolis, J.D., Rosen, P.S. & Reynolds, M.A. (2000) Alveolar ridge and sinus augmentation utilizing platelet-rich plasma in combination with freeze-dried bone allograft: case series. *Journal of Periodontology* **71**: 1654–1661.

Khan, S.N, Bostrom, M.P.G. & Lane, J.M. (2000) Bone growth factors. *Tissue Engineering in Orthopedic Surgery* **31**: 375–387.

Kingsmill, V.J., Boyde, A. & Jones, S.J. (1999) The resorption of vital and devitalized bone *in vitro*: significance for bone grafts. *Calcified Tissue International* **64**: 252–256.

Lorenzetti, M., Mozzati, M., Campanino, P.P. & Valante, G. (1998) Bone augmentation of the inferior floor of the maxillary sinus with autogenous bone or composite bone grafts: a histologic-histomorphometric preliminary report. *International Journal of Oral and Maxillofacial Implants* **13***: 69–76.*

Lozada, J.L., Caplanis, N., Proussaefs, P., Willardsen, J. & Kammeyer, G. (2001) Platelet-rich plasma application in sinus graft surgery: part I – Background and processing techniques. *The Journal of Oral Implantology* **27**: 38–42.

Maiorana, C., Redemagni, M., Rabagliati, M. & Salina, S. (2000) Treatment of maxillary ridge resorption by sinus augmentation with iliac cancellous bone, anorganic bovine bone, and endosseous implants: a clinical and histologic report. *International Journal of Oral and Maxillofacial Implants* **15**: 873–878.

Maiorana, C., Sommariva, L., Brivio, P., Sigurtà, D. & Santoro, F. (2003) Maxillary sinus augmentation with anorganic bovine bone (bio-oss) and autologous platelet-rich plasma: preliminary clinical and histologic evaluations. *International Journal of Periodontics and Restorative Dentistry* **23**: 227–235.

Martin, T.J. & Sims, N.A. (2005) Osteoclast-derived activity in the coupling of bone formation to resorption. *Trends in Molecular Medicine* **11**: 76–81.

Marx, R.E. & Morales, M.J. (1988) Morbidity from bone harvest in major jaw reconstruction: a randomized trial comparing the lateral anterior and posterior approaches to the ilium. *Journal of Oral and Maxillofacial Surgery* **46**: 196–203.

McAllister, B.S., Margolin, M.D., Cogan, A.G., Taylor, M. & Wollins, J. (1998) Residual lateral wall defects following sinus grafting with recombinant human osteogenic Protein-1 or Bio-Oss in the chimpanzee. *International Journal of Periodontics and Restorative Dentistry* **18**: 227–239.

Misch, C.E. (1988) Bone character: second vital implant criterion. *Dentistry Today* **7**: 39–40.

Moy, P.K., Lundgren, S. & Holmes, R.E. (1993) Maxillary sinus augmentation: histomorphometric analysis of graft materials for maxillary sinus floor augmentation. *Journal of Oral and Maxillofacial Surgery* **51**: 857–862.

Mundy, G.R., Boyce, B., Hughes, D., Wright, K., Bonewald, L., Dallas, S., Harris, S., Ghosh-Choudhury, N., Chen, D., Dunstan, C., Izbicka, E. & Yoneda, T. (1995) The effects of cytokines and growth factors on osteoblastic cells. *Bone* **17**: 71S–75S.

Pacifici, L., Casella, F. & Ripari, M. (2003) Lifting of the maxillary sinus: complementary use of platelet rich plasma, autologous bone deproteinised bovine bone. Case report. *Minerva Stomatologica* **52**: 471–478.

Paul, B.F., Horning, G.M., Hellstein, J.W. & Schafer, D.R. (2001) The osteoinductive potential of demineralized freeze-dried bone allograft in human non-orthotopic sites: a pilot study. *Journal of Periodontology* **72**: 1064–1068.

Paul, C., Schelickewei, W., Kuner, E.H. & Schenk, R.K. (1993) Bovines apatit- wertigkeit beim knochenersatz. In: Pesch, H.J., Stöss, H. & Kummer, B., eds. *Osteologie Aktuell. S*, 288–291. Berlin: Springer.

Peleg, M., Mazor, Z. & Garg, A.K. (1999) Augmentation grafting of the maxillary sinus and simultaneous implant placement in patients with 3 to 5 mm of residual alveolar bone height. *International Journal of Oral and Maxillofacial Implants* **14**: 549–556.

Philippart, P., Daubie, V. & Pochet, R. (2005) Sinus grafting using recombinant human tissue factor, platelet-rich plasma gel, autologous bone, and anorganic bovine bone mineral xenograft: histologic analysis and case report. *International Journal of Oral and Maxillofacial Implants* **20**: 274–281.

Piattelli, A., Scarano, A., Corigliano, M. & Piattelli, M. (1996) Comparison of bone regeneration with the use of mineralized and demineralized freeze-dried bone allografts: a histological and histochemical study in man. *Biomaterials* **17**: 1127–1131.

Piattelli, M., Favero, G.A., Scarano, A., Orsini, G. & Piattelli, A. (1999) Bone reactions to anorganic bovine bone (Bio-Oss) used in sinus augmentation procedures: a histologic long-term report of 20 cases in humans. *International Journal of Oral and Maxillofacial Implants* **14**: 835–840.

Raghoebar, G.M. & Vissink, A. (2003) Treatment for an endosseous implant migrated into the maxillary sinus not causing maxillary sinusitis: case report. *International Journal of Oral and Maxillofacial Implants* **18**: 745–749.

Rodríguez, A., Anastassov, G.E., Lee, H., Buchbinder, D. & Wettan, H. (2003) Maxillary sinus augmentation with deproteinated bovine bone and platelet rich plasma with simultaneous insertion of endosseous implants. *Journal of Oral and Maxillofacial Surgery* **61**: 157–163.

Rousou, J.A., Engelman, R.M. & Breyer, R.H. (1984) Fibrin glue: an effective hemostatic agent for nonsuturable intraoperative bleeding. *Annals of Thoracic Surgery* **38**: 409–410.

Rosenberg, E.S. & Torosian, J. (2000) Sinus grafting using platelet-rich plasma – Initial case presentation. *Practical Periodontics and Aesthetic Dentistry* **12**: 843–850.

Rosenlicht, J. & Tarnow, D.P. (1999) Human histology evidence of functionally loaded hydroxyapatite-coated implants placed simultaneously with sinus augmentation: a case report 2 1/2 years post-placement. *International Journal of Oral and Maxillofacial Implants* **25**: 7–10.

Rueger, J.M. (1992) Knochenersatzmittel. In: Rehn, J., Schweiberer, L. & Tschernee, H., eds. *Hgr. Hefte zur Unfallheilkunde*. Berlin: Springer.

Scher, E.L.C., Day, R.B. & Speight, P.M. (1999) New bone formation after a sinus lift procedure using demineralized freeze-dried bone and tricalcium phosphate. *Implant Dentistry* **8**: 49–53.

Takahari, N., Udagawa, N., Takami, M. & Suda, T. (2002) Cells of bone: osteoclast generation. In: Bilezikian, J.P., Raisz, L.G. & Rodan, G.A., eds. *Principles of Bone Biology*, Vol. 1, 1st edition, 111. San Diego: Academic Press.

Tawil, G. & Mawla, M. (2001) Sinus floor elevation using a bovine bone mineral (Bio-Oss) with or without the concomitant use of a bilayered collagen barrier (Bio-Gide): a clinical report of immediate and delayed implant placement. *International Journal of Oral and Maxillofacial Implants* **16**: 713–721.

Tatum Jr, H. (1986) Maxillary and sinus implant reconstructions. *Dental Clinics of North America* **30**: 207–229.

Timmenga, N.M., Raghoebar, G.M., van Weissenbruch, R. & Vissink, A. (2003) Maxillary sinus floor elevation surgery. A clinical, radiographic and endoscopic evaluation. *Clinical Oral Implants Research* **14**: 322–328.

Triplett, R.G. & Schow, S.R. (1996) Autologous bone grafts and endosseous implants: complementary techniques. *Journal of Oral and Maxillofacial Surgery* **54**: 486–494.

Vachiramon, A., Wang, W.C. & Vachiramon, T. (2002) Delayed immediate single-step maxillary sinus lift using autologous fibrin adhesive in less than 4-millimeter residual alveolar bone: a case report. *Journal of Oral Implantology* **28**: 189–193.

Vaiman, M., Shlamkovich, N., Eviatar, E. & Segal, S. (2005) Use of fibrin glue as a hemostatic in endoscopic sinus surgery. *Annals of Otology, Rhinology and Laryngology* **114**: 237–241.

Valentini, P., Abensur, D., Wenz, B., Peetz, M. & Schenk, R. (2000) Sinus grafting with porous bone mineral (Bio-Oss) for implant placement: a 5-year study on 15 patients. *International Journal of Periodontics and Restorative Dentistry* **20**: 245–253.

Van Steenberghe, D. (2000) From osseointegration to osseoperception. *Journal of Dental Research* **79**: 1833–1837.

Velich, N., Németh, Z., Tóth, C. & Szabó, G. (2004) Long-term results with different bone substitutes used for sinus floor elevation. *Journal of Craniofacial Surgery* **15**: 38–41.

Wallace, S.S. & Froum, S.J. (2003) Effect of maxillary sinus augmentation on the survival of endosseous implants. A systematic review. *Annals of Periodontology* **81**: 328–343.

Wallace, S.S., Froum, S.J. & Tarnow, D.P. (1996) Histologic evaluation of sinus elevation procedure. A clinical report. *International Journal of Periodontics and Restorative Dentistry* **16**: 47–51.

Wang, H-L. & Boyapati, L. (2006) ''PASS'' principles for predictable bone regeneration. *Implant Dentistry* **15**: 10–17.

Weikel, A.M & Habal, M.B. (1977) Meralgia paresthetica: a complication of iliac bone procurement. *Plastic Reconstructive Surgery* **60**: 572–574.

Wheater, P.R., Burkitt, H.G. & Daniels, V.G. (1987) *Funtional Histology*. New York: Churchill Livingston.

Wiltfang, J., Schlegel, K.A., Schultze-Mosgau, S., Nkenke, E., Zimmermann, R. & Kessler, P. (2003) Sinus floor augmentation with β-tricalciumphosphate (β-TCP): does platelet-rich plasma promote its osseous integration and degradation? *Clinical Oral Implants Research* **14**: 213–218.

World Medical Association Declaration of Helsinki, (2000) www.wma.net

Yoshida, H., Hirozane, K. & Kamiya, A. (2000) Adhesive strength of autologous fibrin glue. *Biological and Pharmaceutical Bulletin* **23**: 313–317.

Zerbo, I.R., Bronckers, A.L.J.J., Lange, G.D. & Burger, E.H. (2005) Localisation of osteogenic and osteoclastic cells in porous β-tricalcium phosphate particles used for human maxillary sinus floor elevation. *Biomaterials* **26**: 1445–1451.

Ziccardi, V.A., Smith, J.A. & Braun, T.W. (1995) Osteoma of the maxillary antrum. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics* **80**: 378–379.

Zinner, I.D. & Small, S.A. (2004) Maxillary sinus grafts and prosthetic management. In: Zinner, I.D. & Panno, V., eds. *Implant Dentistry: From Failure to Success*. 1st Edition, 99–100. Hong Kong: Quintessence Books.