Histological Findings Following the Use of a Space-Making Device for Bone Reformation and Implant Integration in the Maxillary Sinus of Primates

Giovanni Cricchio, DDS;* Vinícius Canavarros Palma, DDS, PhD;† Paulo E.P. Faria, DDS;‡ José Américo de Oliveira, DDS, PhD;§ Stefan Lundgren, DDS, PhD;¶ Lars Sennerby, DDS, PhD;** Luiz A. Salata, DDS, PhD††

ABSTRACT

Background: Previous studies have shown that membrane elevation results in predictable bone formation in the maxillary sinus provided that implants can be placed as tent poles. In situations with an extremely thin residual crest which impairs implant placement, it is possible that a space-making device can be used under the sinus membrane to promote bone formation prior to placement of implants.

Purpose: The present study was conducted to test the hypothesis that the use of a space-making device for elevation of the sinus membrane will result in predictable bone formation at the maxillary sinus floor to allow placement of dental implants.

Materials and Methods: Eight *tufted capuchin* primates underwent bilateral sinus membrane elevation surgery, and a bioresorbable space-making device, about 6 mm wide and 6 mm in height, was placed below the elevated membrane on the sinus floor. An oxidized implant (Nobel Biocare AB, Gothenburg, Sweden) was installed in the residual bone protruding into the created space at one side while the other side was left without an implant. Four animals were sacrificed after 6 months of healing. The remaining four animals received a second implant in the side with a space-making device only and followed for another 3 months before sacrifice. Implant stability was assessed through resonance frequency analysis (RFA) using the Osstell™ (Osstell AB, Gothenburg, Sweden) at installation, 6 months and 9 months after the first surgery. The bone-implant contact (BIC) and bone area inside the threads (BA) were histometrically evaluated in ground sections.

Results: Histologically there were only minor or no signs of bone formation in the sites with a space-making device only. Sites with simultaneous implant placement showed bone formation along the implant surface. Sites with delayed implant placement showed minor or no bone formation and/or formation of a dense fibrous tissue along the apical part of the implant surface. In the latter group the apical part of the implant was not covered with the membrane but protruded into the sinus cavity.

Conclusions: The use of a space-making device, with the design used in the present study, does not result in bone formation at the sinus floor. However, membrane elevation and simultaneous placement of the device and an implant does result in bone formation at the implant surface while sites with implants placed 6 months after membrane elevation show only small amounts of bone formation. It is suggested that lack of stabilization of the device and/or a too extensive elevation of the membrane may explain the results.

KEY WORDS: bone formation, dental implants, maxillary sinus, membrane elevation, osseointegration

*PhD fellow, Department of Oral and Maxillofacial Surgery, Umeå University, Umeå, Sweden; †doctor, Universidade de Cuiaba, Oral and Maxillofacial Surgery and Integrated Clinic; ‡doctorate fellow, Department of Oral & Maxillofacial Surgery, Faculty of Dentistry of Araçatuba, University of São Paulo, São Paulo, Brazil; §professor, Department of Basic Sciences, University of the State of São Paulo, Faculty of Dentistry of Aracatuba, Brazil; ¶professor, Department of Oral and Maxillofacial Surgery, Umeå University, Umeå, Sweden; **professor, Department of Biomaterials, Sahlgrenska Academy, Gothenburg University, Göteborg, Sweden; ††associate professor, Department of Oral & Maxillofacial Surgery and Periodontics, Faculty of Dentistry of Ribeirão Preto, University of São Paulo, Ribeirão Preto, Brazil

Reprint requests: Prof. Luiz A. Salata, The University of São Paulo, Faculty of Dentistry of Ribeirão Preto, Department of Oral & Maxillofacial Surgery and Periodontics, Avenida do Cafe s/n, Campus USP 14040-904 Ribeirão Preto, São Paulo, Brazil; e-mail: lasalata@forp.usp.br

© 2009, Copyright the Authors
Journal Compilation © 2009, Wiley Periodicals, Inc.

DOI 10.1111/j.1708-8208.2009.00158.x

INTRODUCTION

Various maxillary sinus floor augmentation procedures have been used for reconstruction of the posterior maxilla in conjunction with simultaneous or delayed placement of endosseous dental implants.[1–4] Clinical studies have demonstrated that the mere elevation of the sinus membrane and simultaneous placement of dental implants resulted in bone formation without the use of adjunctive grafting materials as studied radiographically.[5–8] A recent animal experiment from the present research group could histologically verify bone formation and implant integration, following sinus membrane elevation with no differences when comparing maxillary sinuses subjected to membrane elevation, only with sinuses grafted with autogenous bone.[9] A prerequisite with the membrane elevation technique is that dental implants can be placed to serve as tent poles for the sinus membrane. However, in many cases, the residual alveolar crest is too thin or of too low density to allow for firm primary stability of dental implants. It is well known from the literature that bone can be predictably formed in secluded spaces on bone surface by using various kinds of barrier membranes or devices.[10] Thus, it is possible that such a device can be used also for bone formation in the maxillary sinus. This hypothesis was tested in two patients (Cricchio and colleagues, unpublished data). A replaceable bone window was prepared at the lateral aspect of the maxillary sinus and careful dissection and elevation of the membrane was made. An about 8-mm-high space-making device made of a bioresorbable polymer was introduced into the maxillary sinus floor in order to keep the membrane elevated for new bone formation. Six months later it was evident that new bone, 3–4 mm in height, had been formed at the floor of both sinuses in both patients. However, the new bone did not allow for placement of 10-mm implants with full bone coverage. Nevertheless, the 3–4 mm of new bone made it possible to place implants with sufficient primary stability to perform a new sinus membrane elevation procedure as previously described.[6] The results from the treated patients demonstrated that bone can form in a secluded space in the maxillary sinus without the presence of a dental implant. However, the findings were disappointing with regard to the amount of formed bone. It is possible that the material used in some way disturbed healing which may explain the small amounts of bone. Therefore, it was decided to make an experimental study to obtain histology of the bioresorbable polymer device when used for augmentation of the maxillary sinus floor.

The present study was conducted to test the hypothesis that the use of a space-making device for elevation of the sinus membrane will result in predictable bone formation at the maxillary sinus floor to allow the placement of dental implants.

MATERIALS AND METHODS

This animal study was carried out in accordance with the rules by the Brazilian Institute for Protection of the Environment (IBAMA) and approved by the Animal Ethic Committee at the Faculty of Dentistry of the University of the State of São Paulo – UNESP, Aracatuba, Brazil.

A total of eight young adult male tufted capuchin monkeys (*Cebus apella*), 8–12 years old and weighing between 2.0 and 3.0 kg were included in this study. Before surgery, the animals were maintained in individual cages at the Primate Procreation Nucleus, Faculty of Dentistry, UNESP, Aracatuba, Brazil, with water and food *ad libitum*. For all procedures involved in the study, the primates were first sedated with ketamine hydrochloride (Ketamin™, Cristalia Produtos Químicos Farmacêuticos Ltd., Campinas, Brazil), 10 mg/kg body weight administered intramuscularly. Prior to surgery or any animal manipulation, general anesthesia was obtained with pentobarbital sodium (Abbott Laboratories North Chicago, Chicago, IL, USA), in the dosage of 30 mg/kg. The anesthesia was supplemented by local administration of 2% mepivacaine HCI with 1:100,000 epinephrine (DFL Ltd., Rio de Janeiro, Brazil). Prior to surgeries, the animals received dental prophylaxis and all the surgical sites were washed with 0.12% chlorhexidine gluconate solution (Periogard™, Colgate-Palmolive Ltd., São Paulo, Brazil). The surgeries were performed under sterile conditions.

Surgeries

The first, second, and third upper premolars and the first molar were extracted bilaterally 3–4 months prior to the start of the experiment. Extractions were performed under general anesthesia, according to the technique described above. All animals underwent bilateral maxillary sinus surgery. After a mid-crestal incision and vertical releasing incisions, mucoperiosteal flaps were raised and reflected at the edentulous posterior maxilla

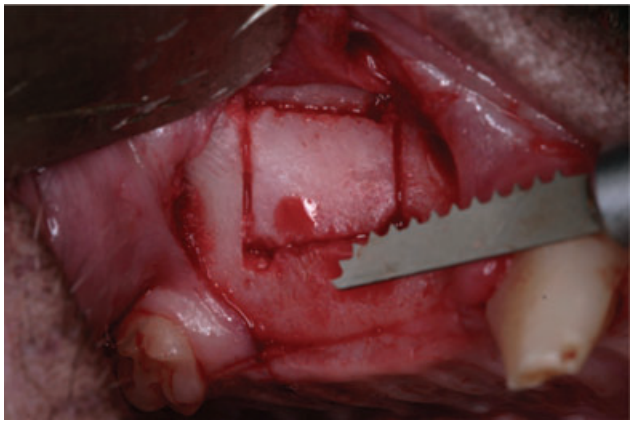

Figure 1 Showing the preparation of the replaceable bone window.

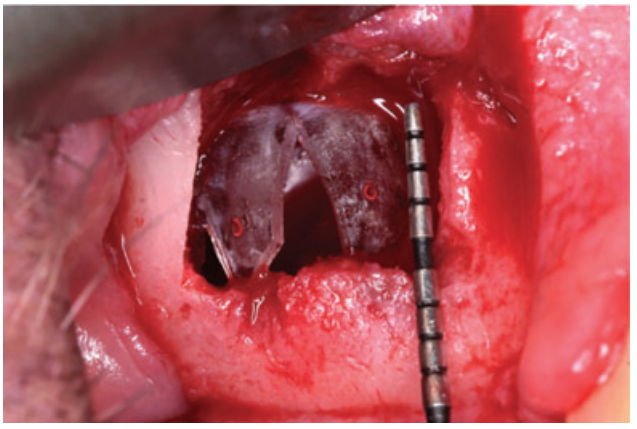

Figure 3 Showing the space-making device positioned into maxillary sinus after bone window removal and sinus membrane elevation.

on both sides in order to access the alveolar bone. The lateral aspect of the maxillary sinus was fully exposed using a reciprocating saw to create a 0.8 cm × 0.6 cm ± 0.2 cm window under continuous saline irrigation (Figure 1). The osseous window was freed by fracturing along the osteotomy lines, removed and kept in saline solution. The sinus membrane was then carefully elevated with specially designed elevators (Friatec™, Friedrichsfeld AG, Mannheim, Germany). All eight animals received a space-making device (polylactide 70/30, Radi Medical System AB, Uppsala, Sweden), approximately 6 mm wide and 6 mm high (Figure 2), which was introduced into the maxillary sinus cavity in order to maintain the sinus membrane elevated (Figure 3). One dental implant, 3.75 mm in diameter and 8.5 mm in length (MKIII TiUnite, Brånemark System™, Nobel Biocare AB, Gothenburg, Sweden) was placed into the obtained space at one side. The bone windows were then repositioned and stabilized with a tissue glue (Indermil™, Henkel Loctite Ltd., Whitestown, Republic of Ireland) (Figure 4). The mucoperiosteal flap was sutured with Vicryl 5-0 (Ethicon™, Johnson & Johnson, Sao Jose dos Campos, Brazil). The wound was finally rinsed with 0.12% chlorhexidine gluconate solution. After 6 months of healing, all animals were subjected to coronal computed tomography (CT) scanning (Toshiba Xvision™, Tokyo, Japan) of both

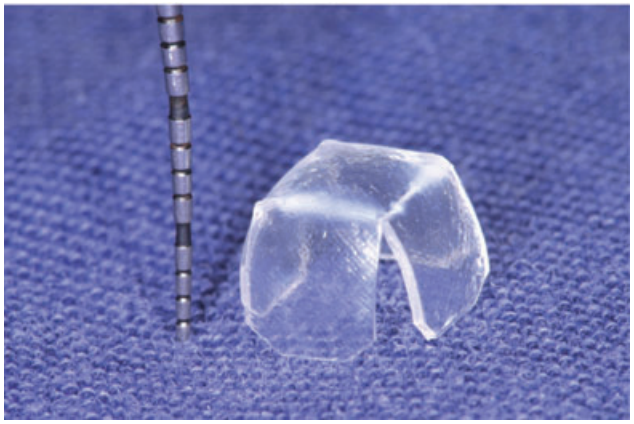

Figure 2 Showing the space-making device (polylactide 70/30) used in the present study.

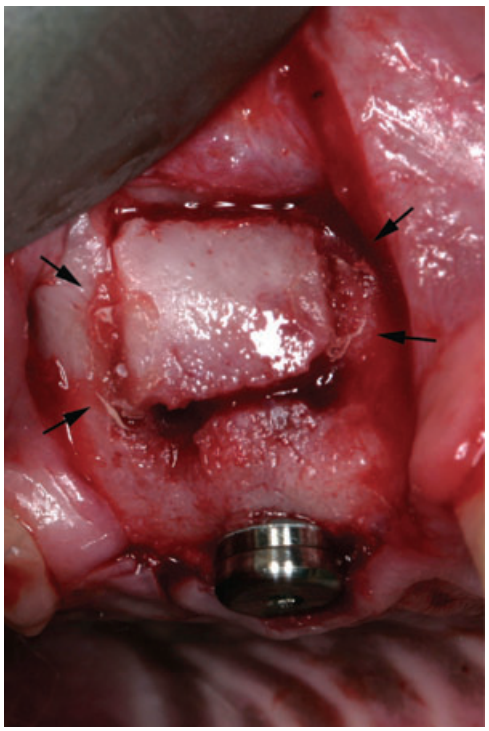

Figure 4 Showing the repositioned bone window which has been stabilized with cyanoacrylate glue (arrows).

sinus cavities and four animals received a second implant in the other sinus, which in the previous surgery had been implanted with the space-making device only (two-stages procedure). These implants were installed with no care about membrane elevation.

Postoperative Follow-Up

The animals were fed with a soft diet (Sustagen™, Nestle, São Paulo, Brazil) during the first 15 days and thereafter with fruits and cooked vegetables. Three times daily, the animals were given an oral dose of Cefalotina™ (20 mg/kg, Stiefel, Guarulhos, Brazil) mixed with fruits shakes for 7 days and Tylenol™ (30 mg/kg, Janssen-Cilag, Sao Jose dos Campos, Brazil) mixed with fruit shakes for 2 days and water *ad libitum*. The animals were inspected after the first, third, fifth, and seventh postoperative months for signs of wound and general health complications. During this period, a systematic periodontal care was carried out, as well as local application of 0.12% chlorhexidine gluconate solution.

Resonance Frequency Analysis (RFA)

The stability of the implants was measured with RFA (Osstell™, Integration Diagnostics AB, Göteborg, Sweden) in implant stability quotion (ISQ) units at implant insertion and after 6 and 9 months of healing.

Sacrifice and Specimens Post-Processing

Four animals were sacrificed 6 months after the first surgery, and other four animals with the additional implants were sacrificed 9 months after the initial surgery. Overall, four one-stage implants were evaluated at 6 months, four one-stage implants were evaluated at 9 months, and four two-stage implants were evaluated at 3 months. The animals were anesthetized with pentobarbital sodium associated with analgesics to undertake vascular perfusion with paraformaldehyde. The maxilla was retrieved *en bloc* and the surrounding soft tissues were detached. The specimens were trimmed and immersed in 4% paraformaldehyde in 0.1 M in sodium phosphate buffer (pH 7.4).

Histological Preparation and Assessments

The specimens were dehydrated in a series of ethanol embedded in hard-grade acrylic resin (LR White™, London Resin Company Ltd, Berkshire, England) and polymerized in dry heat oven at 60°C under vacuum environment. The plastic blocks were mounted on glass slides, and two buccal-palatine sections were taken from each implant (Microslice 2™, Ultratec Inc., Santa Ana, USA) and stained with toluidine blue/pyronin-Y method.

Histometric Analysis

All ground sections were examined under a Leica DMLB™ microscope (Leica Microsystems Wetzlar GmbH, Germany), equipped with a Leica Digital Camera DFC 300FX (Leica Microsystems Wetzlar GmbH, Germany). Histometric measurements were carried out using ×10 object lenses and a coupled Leica Qwin™ V3 software (Leica Microsystems Wetzlar GmbH, Germany). The analyses comprised measurements of the degrees of bone-implant contact and bone area both expressed in percentage.

Statistics

No statistic tests were applied because of the low number of animals. Descriptive data were presented in plot charts with group means.

RESULTS

Clinical, Anatomical, and CT Examination

In one animal, the sinus membrane elevation procedure caused extensive rupture of the membrane in both sides because of the presence of several septas. In eight cases, small membrane perforations (less than 1.0 mm) occurred without major clinical complications.

The postoperative period was uneventful and the animals were healthy throughout the follow-up time. One implant was found mobile and was removed after 6 months of healing. All other implants maintained their stability during the entire experimental period.

Examination of the retrieved specimens revealed that the space-making devices were, in the vast majority of the cases, bizarrely displaced from their original position in both sinuses (Figure 5). The CT examination confirmed these findings and also showed minimal deposition of mineralized bone especially where the device was used alone (Figure 6).

RFA Measurements

Implant stability measurements revealed firm primary stability for both simultaneous and delayed placement of the implants, 66.0 (standard deviation [SD] ± 4.7, $n = 8$) versus 67.0 (SD ± 1.2, $n = 4$). The follow-up

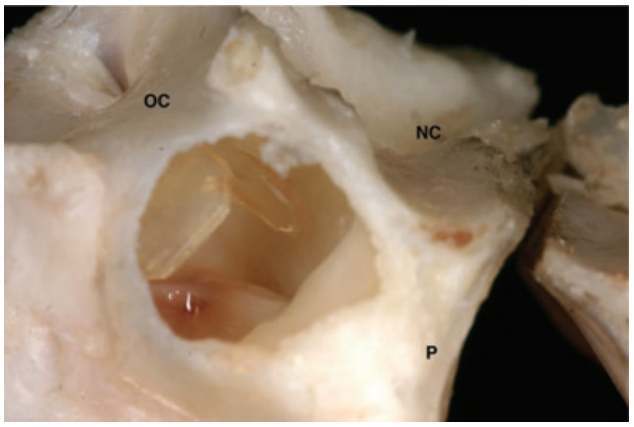

Figure 5 Showing a retrieved maxillary sinus cavity observed from a posterior aspect (access from the tuber). P, palatal; NC, nasal cavity; OC, orbital cavity.

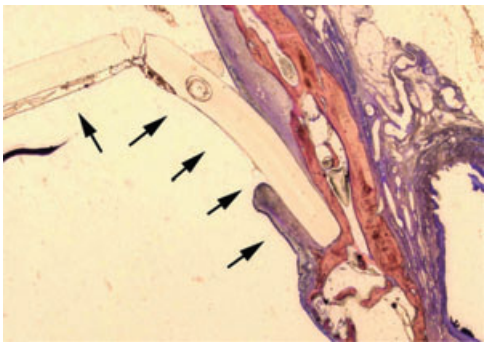

Figure 7 Light micrograph of a specimen retrieved 6 months after positioning of the space-making device (arrows). One leg of the device is partially integrated in the sinus buccal bone wall. There are no signs of bone formation in the space between the floor of the sinus and the device. Toluidine blue, ×10 magnification.

measurements of the simultaneously placed implants showed a slight decrease of stability to 65.4 ISQ (SD ± 4.9, $n = 7$) after 6 months and 64.7 ISQ (SD ± 3.1, $n = 3$) after 9 months. The delayed implants showed a more marked drop to 60.3 ISQ (SD ± 5.6, $n = 4$), Table 1.

Histological Examination

Space-making Device Only. No or only minor bone formation could be observed. An empty space in the center of the sinus and isolated segments of the space-making device was the main histological feature of these sites. The device's legs' tip were found partially bone-integrated in the sinus walls at six postoperative months (Figure 7). The device seemed well tolerated by the surrounding tissues, as no signs of inflammatory reaction could be detected in any of the cases. No signs of material resorption could be noticed during the whole experiment.

Space-Making Device and Simultaneous Implant Placement (One-Stage Procedure). As a consequence of devices' displacement, the sinus membrane was always captured outlining the implant surface and a process of new-bone formation could be seen bridging both structures (Figure 8). In some places, the bone was also found in direct contact with the device's outer surface as a consequence of a close proximity with an intact sinus membrane (Figure 9). The environment enclosed with the implant surface and the sinus membrane seemed to create the required conditions for new-bone deposition (Figure 10) after 6 and 9 postoperative months.

Space-Making Device and Delayed Implant Placement (Two-Stage Procedure). When an implant was installed 6 months after the space-making device, the former became osseointegrated solely at the residual bone. Part of the implants was immersed in fibrous tissue (Figure 11) after 3 months of healing.

Repositionable Bone Flap. The repostioned bone flaps were found in position and well-healed in all specimens. There were no signs of remaining glue or adverse tissue reactions such as infiltrate of inflammatory cells at these sites.

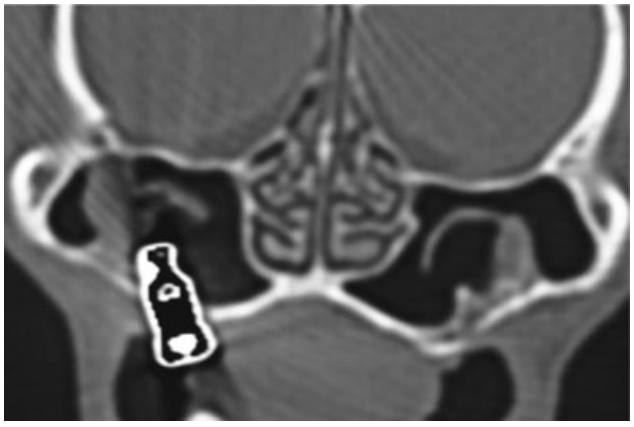

Figure 6 CT examination of one animal 6 months after the first surgery (implant plus space-making device on right side, space-making device only on left side).

Histometric Measurements

The quantitative analyses of the implants showed less degree of bone contacts and bone area filling the threads

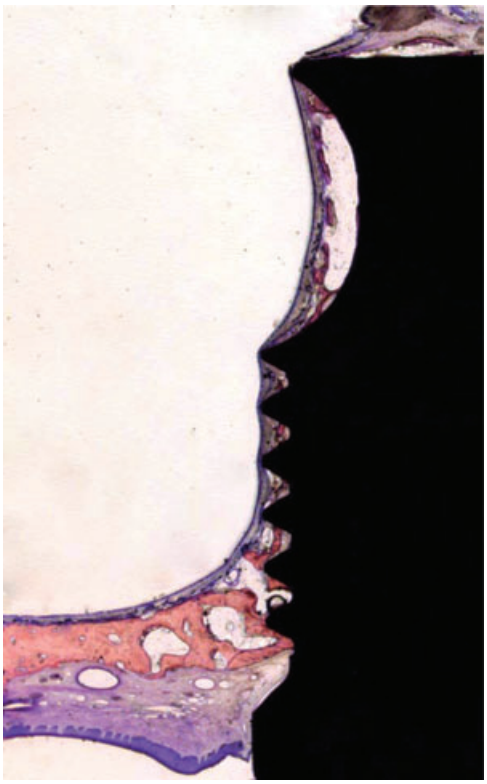

Figure 8 Light micrograph of a specimen retrieved 6 months after placement of the space-making device and the implant (one-stage procedure). The device was found to be completely displaced. The sinus membrane is lining the implant surface and bone formation is observed between the membrane and the implant surface. Toluidine blue, ×10 magnification.

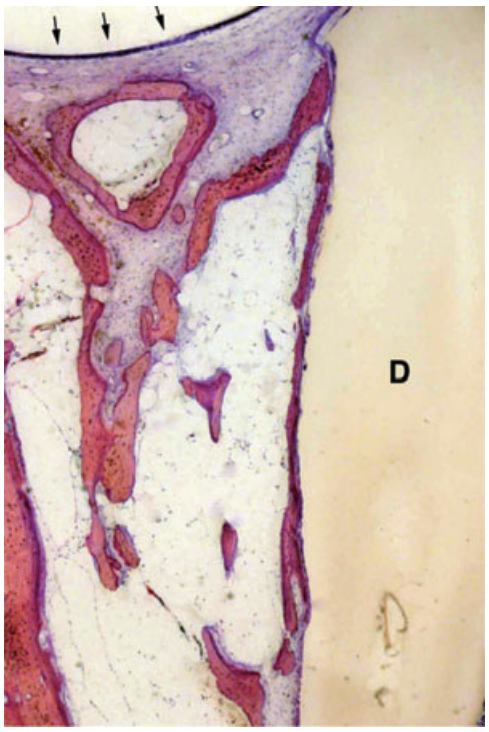

Figure 9 Light micrograph showing direct bone formation at the surface of the device (D) which is in close relation to the sinus membrane (*arrows*). Toluidine blue, ×4 magnification.

for the two-stage implants than for the one-stage implants (Table 1).

DISCUSSION

The present experimental study was designed to evaluate the use of a space-making device to maintain the sinus membrane elevated in order to allow for bone formation in the created space. The histology in the present study showed an inflammatory-free and favorable tissue response and even some direct bone formation on the polymer material after 6 months of healing. However, it was obvious that the device used in the present study did not fulfill its purpose, as the membrane was found beneath the device in most of the histological sections. The reason for this finding may lie in a postoperative displacement of the device during the early stages following implantation. It could also be due to the use of a too high device resulting in an extensive lifting of the membrane in this model study. This may have resulted in a rupture of the original membrane. Nevertheless, in

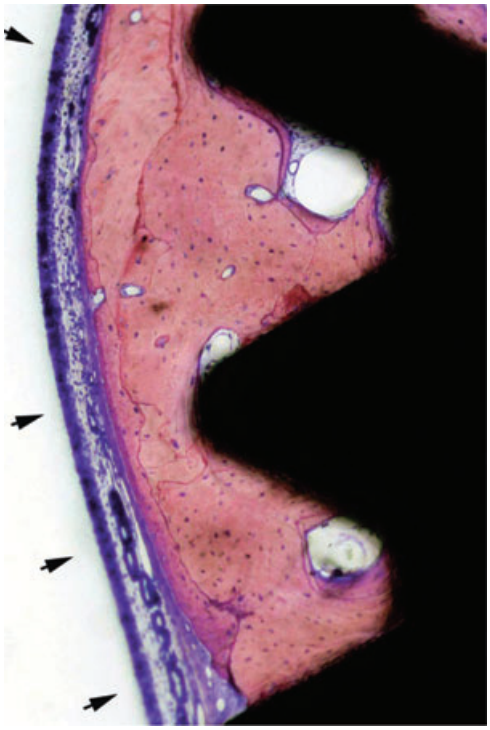

Figure 10 Light micrograph of a specimen retrieved 9 months after placement of space-making device and implant (one-stage procedure). The specimen shows new bone deposition filling the implant threads and covered by the sinus membrane (*arrows*). Toluidine blue, ×100 magnification.

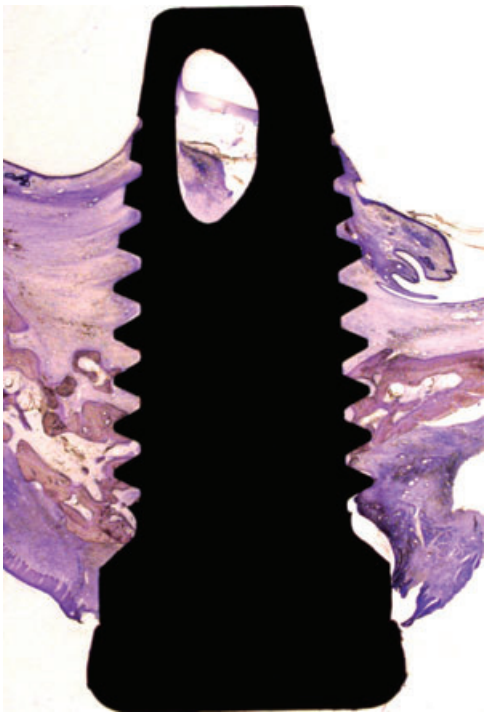

Figure 11 Light micrograph of a specimen retrieved 3 months after implant placement in a maxillary sinus previously subjected to membrane elevation and device positioning. The implant shows bone contacts with the residual crest but a fibrous tissue interface or no tissue in the sinus. Toluidine blue, ×10 magnification.

one-stage cases, with or without sinus membrane perforation at the end of the elevation surgery (no perforation, small perforation, and extensive perforation), the membrane could be histologically observed below the device.

The process of bone formation in the sinus cavity seemed to differ dramatically among the experimental sites. The use of the space-making device alone resulted in no or only minor signs of bone formation after 6 months of healing, even in cases where the sinus membrane was intact. When the device and the implant were placed at the same stage, the process of bone formation seemed to extend from the membrane toward the implant surface, resembling the outcomes previously reported by our group.[9] Differently, the two-stage procedure resulted in very few bone-to-implant contacts and no bone formation on the surface of the membrane. Altogether, these data may suggest that the fresh coagulum delivered during sinus elevation surgery in the presence of rough titanium surface forms an important combination to enhance bone proliferation.[8] The so-called bone contact osteogenesis theory that has been widely described and confirmed in a number of studies supports this speculation.[9,11,12] On the other hand, when the implant was installed using the two-stage approach, the implant was found in contact with fibrous tissue. This finding may be related to the trauma produced by the implant installation, as the histological outcomes of the group treated with the device only and assessed at 6 months postoperatively revealed an empty sinus cavity at this stage.

The RFA measurements revealed high primary implant stability in both simultaneous and delayed approaches. The delayed implants showed a marked drop of almost 7 ISQ units during 3 months, which probably reflected the unfavorable healing as observed with histology. The simultaneously placed implants showed bone formation and a high stability was maintained throughout the study.

TABLE 1 Results from Histometric Measurements of Bone-Implant Contact and Bone Area in the Implant Threads

	One-stage			Two-stage	
Animal	Baseline	6 months	9 months	Baseline	3 months
1	70	68	62	68	62
2	65	62	68	68	52
3	69	70	64	66	64
4	74	56	–	–	–
5	61	67	–	–	–
6	66	66	–	–	–
7	61	lost	lost	66	63
8	62	69	–	–	–
Mean (SD)	60.0 (4.7)	65.4 (4.9)	64.7 (3.1)	67.0 (1.2)	60.3 (5.6)

The findings from the present experimental study accord with the experiences from using a space-making device in a pilot study on two patients as described previously (Cricchio and colleagues, unpublished data). The outcomes of our study indicate that the lack of stabilization of the device underneath Schneiderian membrane was a crucial factor for the unfavorable results. One possible explanation could be the extensive elevation of the membrane that have widened the initial perforations observed during devices placement, which in turn led the latter to both protrude into sinus cavity and become unstable. As a consequence, the absence of a secluded empty space between the residual bone and a proliferated membrane on the sinus floor, like those required in guided bone regeneration (GBR)/guided tissue regeneration (GTR) techniques, might explain the very poor bone formation process within the sinus. The fact that the space-making device did not meet the expected biological functions demands separate analysis. The consistency of the material was rather rigid what made the device resistant to fine re-shaping. The device's surface was smooth and the legs large in width which increased the contact area with the sinus membrane. Considering the strong scientific evidences that the sinus membrane exhibits osteoinductive properties,[9,13] the device – to a certain extent – hindered this effect. In the developmental process of a space-making device to accomplish our purpose, the outcomes of the present study suggest: 1) the material should be liable to be shaped accordingly to sinus floor anatomical variations; and 2) the legs of the device should be permeable to cells and fluids exchange between the inner compartment of the sinus and the membrane. These modifications are now underway by our group.

A cyanoacrylate glue was used in the present study to enable stability of the replaceable bone window at the lateral aspect of the maxillary sinus. Previous experimental studies have shown acceptable soft tissue responses to cyanoacrylate.[14,15] The clinical experience with this kind of glue seems to be from soft tissue surgery and good outcomes have been reported.[16] An intact lateral sinus wall was found in the retrieved specimens of the present study, which indicates that the cyanoacrylate glue did not interfere with the healing process. However, further experimental studies are needed to evaluate the bone tissue responses to cyanoacrylate glue in detail.

CONCLUSIONS

It is concluded that the presently evaluated design of a space-making device did not result in predictable bone formation beneath the maxillary sinus membrane after a 6-month healing period. The lack of stabilization and the design of the space-making device may have played an important role for the outcomes. The results also confirm that a combination of a fresh coagulum and an oxidized implant surface results in predictable bone formation in the maxillary sinus elevation.

ACKNOWLEDGMENTS

This study was partially funded by Fapesp (The State of São Paulo Research Foundation, Brazil), Grant # 06/01322-8, and Nobel Biocare AB, Sweden.

CONFLICTS OF INTEREST STATEMENT

The authors have declared no conflicts of interest. [Correction added after online publication 23 October 2009: Conflicts of Interest Statement added.]

REFERENCES

1. Boyne PJ, James RA. Grafting of the maxillary sinus floor with autogenous marrow and bone. J Oral Surg 1980; 38:613–616.
2. Wood RM, Moore DL. Grafting of the maxillary sinus with intraorally harvested autogenous bone prior to implant placement. Int J Oral Maxillofac Implants 1988; 3:209–214.
3. Lundgren S, Moy P, Johansson C, Nilsson H. Augmentation of the maxillary sinus floor with particulated mandible: a histologic and histomorphometric study. Int J Oral Maxillofac Implants 1996; 11:760–766.
4. Hallman M, Sennerby L, Zetterqvist L, Lundgren S. A 3-year prospective follow-up study of implant-supported fixed prostheses in patients subjected to maxillary sinus floor augmentation with a 80 : 20 mixture of deproteinized bovine bone and autogenous bone. Clinical, radiographic and resonance frequency analysis. Int J Oral Maxillofac Surg 2005; 34:273–280.
5. Lundgren S, Andersson S, Sennerby L. Spontaneous bone formation in the maxillary sinus after removal of a cyst: coincidence or consequence? Clin Implant Dent Relat Res 2003; 5:78–81.
6. Lundgren S, Andersson S, Gualini F, Sennerby L. Bone reformation with sinus membrane elevation: a new surgical technique for maxillary sinus floor augmentation. Clin Implant Dent Relat Res 2004; 6:165–173.
7. Hatano N, Sennerby L, Lundgren S. Maxillary sinus augmentation using sinus membrane elevation and peripheral venous blood for implant-supported rehabilitation of the atrophic posterior maxilla: case series. Clin Implant Dent Relat Res 2007; 9:150–155.

8. Thor A, Sennerby L, Hirsch JM, Rasmusson L. Bone formation at maxillary sinus floor following simultaneous elevation of the mucosal lining and implant installation without graft material: an evaluation of 20 patients treated with 44 Astra Teach implants. J Oral Maxillofac Surg 2007; 65(Suppl. 1):64–72.
9. Palma VC, Magro-Filho O, de Oliveria JA, Lundgren S, Salata LA, Sennerby L. Bone reformation and implant integration following maxillary sinus membrane elevation: an experimental study in primates. Clin Implant Dent Relat Res 2006; 8:11–24.
10. Nyman S. Bone regeneration using the principle of guided tissue regeneration. J Clin Periodontol 1991; 18:494–498.
11. Davies JE. Understanding peri-implant endosseous healing. J Dent Educ 2003; 67:932–949.
12. Salata LA, Burgos PM, Rasmusson L, et al. Osseointegration of oxidized and turned implants in circumferential bone defects with and without adjunctive therapies: an experimental study on BMP-2 and autogenous bone graft in the dog mandible. Int J Oral Maxillofac Surg 2007; 36:62–71.
13. Gruber R, Kandler B, Fuerst G, Fischer MB, Watzek G. Porcine sinus mucosa holds cells that respond to bone morphogenetic protein (BMP)-6 and BMP-7 with increased osteogenic differentiation in vitro. Clin Oral Impl Res 2000; 15:575–580.
14. Inal S, Yilmaz N, Nisbet C, Güvenç T. Biochemical and histopathological findings of N-butyl-2-cyanoacrylate in oral surgery: an experimental study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006; 102:e14–e17.
15. Choi B, Kim B, Huh J, et al. Cyanoacrylate adhesive for closing sinus membrane perforations during sinus lifts. J Craniomaxillofac Surg 2006; 34:505–509.
16. Samuel PR, Roberts AC, Nigam A. The use of Indermil (n-butyl cyanoacrylate) in otorhinolaryngology and head and neck surgery. A preliminary report on the first 33 patients. J Laryngol Otol 1997; 111:536–540.

Copyright of Clinical Implant Dentistry & Related Research is the property of Blackwell Publishing Limited and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.