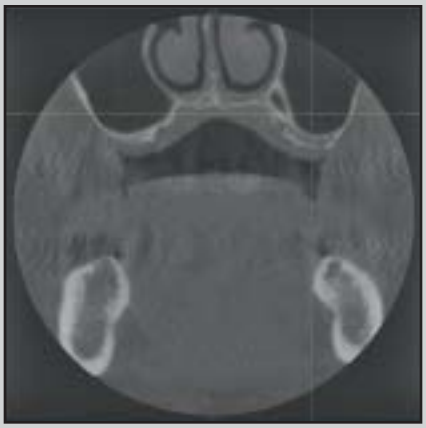
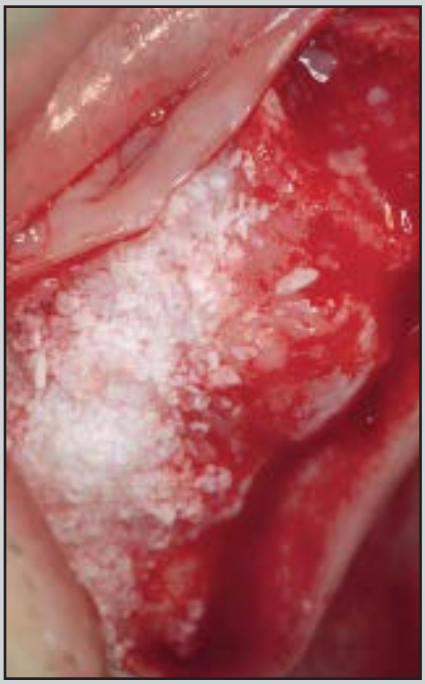
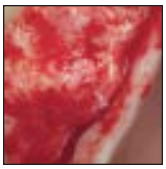




The Use of Recombinant Human Platelet-Derived Growth Factor for Maxillary Sinus Augmentation



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The maxillary sinus augmentation procedure has become a predictable treatment to regenerate bone for implant placement. The purpose of this study was to evaluate the effect of recombinant human platelet-derived growth factor BB (rhPDGF-BB) combined with a deproteinized cancellous bovine bone graft for sinus augmentation. The lateral window approach was used for maxillary sinuses with minimal residual bone. After a healing period of 4 months, dental implants were placed and then restored following a 2-month osseointegration period. The result demonstrated increased bone height and ISQ values and a 100% survival rate. This study indicates that the addition of rhPDGF-BB to deproteinized cancellous bovine bone accelerated the healing period in maxillary sinuses with minimal native bone. Int J Periodontics Restorative Dent 2017;37:219–225. doi: 10.11607/prd.2776

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Dental implants are an approach to oral rehabilitation that permit an extracted tooth to be replaced without affecting adjacent teeth. Their advantages have been definitively characterized and include no need for preparation of adjacent teeth and the ability to secure a removable prosthesis. However, their success depends on many factors, the most critical of which is sufficient quantity and quality of bone. In particular, the edentulous posterior maxilla often presents a challenge for implant treatment due to the location of the maxillary sinus and its pneumatization as a result of tooth loss and aging. Moreover, loss of posterior maxillary teeth is frequently accompanied by resorption of the remaining alveolar bone, resulting in diminished bone height and poor bone quality.

Various regenerative techniques have been proposed in the posterior maxilla, including vertical bone augmentation, distraction osteogenesis, and sinus augmentation. While these approaches differ significantly, their common aim has been to increase bone width and height, thus ensuring appropriate implant placement. Based on clinical evidence, sinus augmentation currently yields the most predictable outcome.[1] A systematic review indicates that the predictability of sinus augmentation depends on

the use of a particulate graft and covering the lateral window with a barrier membrane.[2] Various particulate grafting materials and occlusive membranes have been used with sinus augmentation. Autogenous bone has both osteoinductive and osteoconductive capacities. Allografts are commonly used to mimic these characteristics. Similarly, several studies have reported on xenografts with osteoconductive potential. Recent clinical research has investigated the use of biologics.[3–9] Biologics are essential for tissue formation, including stimulation or inhibition of cell adhesion and control of proliferation, migration, and differentiation. The rationale for their use relates to possible reduction in healing time, donor site morbidity, and surgical complications. Many studies consider biologics a valid alternative option for maxillary sinus augmentation.[3] Molecules of interest in the field of regenerative dentistry include bone morphogenetic protein (BMP) and platelet-derived growth factor (PDGF).[3–9]

PDGF has been extensively characterized. Specifically, recombinant human PDGF-BB (rhPDGF-BB) has been investigated in preclinical and clinical dental models. The principal application of rhPDGF-BB is in periodontal and bone regeneration. These studies have used various carriers depending on the indication.[10] The studies conducted in this field have shown that it is effective for periodontal regeneration of well-contained defects.[11] However, clinical research on rhPDGF-BB for bone regeneration is limited.[8] The purpose of this case series study was to evaluate the effect of rhPDGF-BB combined with a deproteinized cancellous bovine bone graft for lateral window sinus augmentation.

Materials and Methods

An Institutional Review Board approved the study. Study inclusion criteria included need for implants in the posterior maxilla, absence of systemic conditions that represented a contraindication to surgical intervention, nonsmokers or mild smokers, insufficient bone height (≤ 1 mm), and bone width ≥ 5 mm. Exclusion criteria included inability to maintain proper oral hygiene, untreated dental disease, acute or chronic sinusitis, residual bone height > 1 mm, and bone width < 5 mm. Study subjects had a cone beam computed tomography (CBCT) scan examination prior to surgery to assess bone volume and health of the maxillary sinuses (Fig 1a).

The lateral window sinus lift approach was used to augment the bone in the maxillary sinus. A crestal incision was combined with vertical release(s), allowing for a full-thickness flap and exposing the lateral wall of the maxilla (Fig 1c). Piezoelectric and high-speed surgical burs were used for preparation of the window to access the sinus membrane. Once the window was established, the sinus membrane (Fig 1d) was carefully elevated with blunt instruments to minimize membrane tears. The graft material was prepared by soaking each 0.5-g deproteinized cancellous bovine bone (0.25–1.0 mm Bio-Oss, Geistlich) with 0.5 mL of 0.3 mg/mL rhPDGF-BB (GEM 21S, Osteohealth) for 15 minutes. The graft was placed in the space apical to the elevated sinus membrane (Fig 1e). The osteotomy window was covered with bioresorbable collagen membrane (Bio-Gide, Geistlich, or BioMend, Zimmer) and the flap was sutured without tension (Figs 1f and 1g). A second CBCT scan was exposed after 4 months of healing, prior to implant insertion, to measure the bone volume changes and plan for the dental implants (Fig 1b). Dental implants were inserted according to the manufacturer's recommendation using a submerged technique. Implant stability quotient (ISQ) was measured at the time of implant insertion. After a healing period of 2 months, a second-stage surgery was performed. At this uncovering surgery, ISQ was again measured. A definitive fixed restoration was fabricated and inserted.

Data collection included demographic parameters of sex, age, medical conditions, and medications. CBCT measurements included baseline and postaugmentation (4 months) bone height. Measurements were taken at the proposed implant positions. Dental implant position and implant dimensions were recorded. ISQ measurements were taken at implant insertion and at second stage. Dental implant survival was assessed at second stage and at 1, 3, 6, 12, and 24 months postloading. Statistical analysis included mean and standard deviations, life table analysis for implant survival, and *t* test for comparisons.

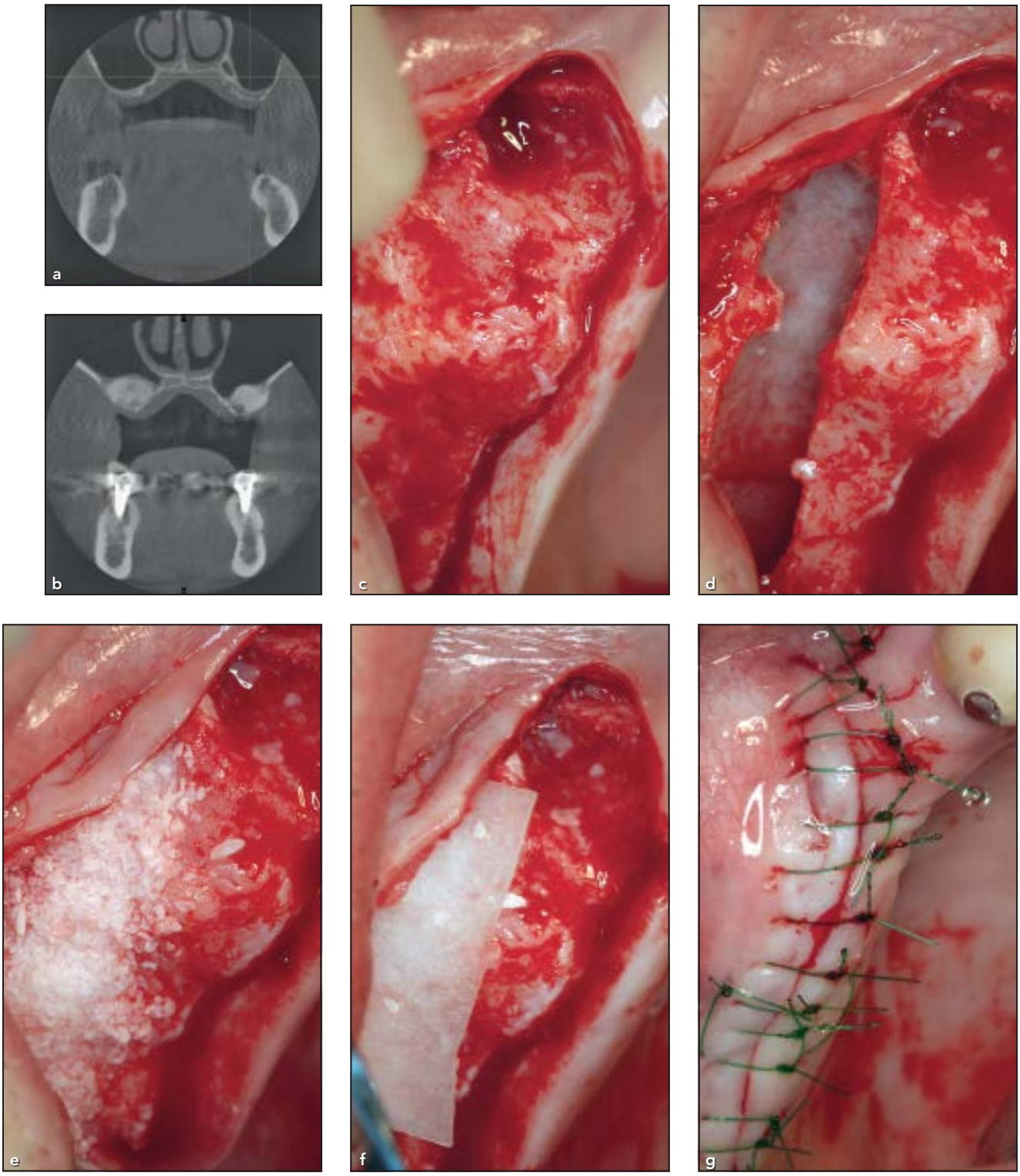

Fig 1 Case 1. (a) *Baseline CBCT scan.* (b) *CBCT scan at 4 months post-healing.* (c) *Full-thickness flap to expose the lateral wall of the maxilla.* (d) *An osteotomy was created to access the maxillary sinus.* (e) *The sinus was filled using a combination of rhPDGF-BB and Bio-Oss (Geistlich).* (f) *A resorbable membrane placed over the lateral wall.* (g) *Flap closure without tension.*

Table 1 Implant Position

Maxillary tooth position	Implants placed (% [n])
Second molar	13.3 (14)
First molar	38.0 (40)
Second premolar	29.5 (31)
First premolar	18.1 (19)
Canine	1.0 (1)

Table 2 Bone Height Measurements

Baseline bone height (mm)	0.77 ± 0.28
Augmented bone height (mm)	13.03 ± 1.22

Table 3 Implant ISQ Measurement

	Baseline (implant placement)	After implant healing (8 wk)
Overall	53.76 ± 4.06	70.35 ± 6.33
Molar positions	54.02 ± 4.15	70.55 ± 7.14
Premolar positions	53.49 ± 3.93	70.21 ± 5.31

Results

The study sample included 46 patients, of whom 21 were men and 25 were women, aged 38 to 77 years (average 62.2 years). A total of 105 implants were placed. The implant locations included 40 first molars, 14 second molars, 19 first premolars, 31 second premolars, and 1 canine (Table 1). At baseline, the residual bone height was 0.77 ± 0.28 mm. After the 4-month healing period, there was a statistically significant increase in the augmented site height to 13.03 ± 1.22 mm (Table 2).

All surgical procedures were tolerated with only minor complications (Fig 2). Dental implants were present at all time periods, resulting in 100% survival. The ISQ was measured at implant placement and at 8 weeks following the implant healing period (Table 3). There was a statistically significant difference in the mean overall ISQ measurement when comparing the time of implant placement (53.76 ± 4.06) with second stage (70.35 ± 6.33). The initial ISQ for implants in the molar area was 54.02 ± 4.15, compared with 70.55 ± 7.14 after the healing period. Implants in the premolar area demonstrated a similar increase. ISQ at implant placement was 53.49 ± 3.93, compared with 70.21 ± 5.31 after the healing period.

Discussion

The sinus augmentation procedure has been a predictable solution for multiple restorative strategies in the posterior maxilla. The results of this study indicate that the addition of rhPDGF-BB enhanced the performance of the commonly used deproteinized cancellous bovine bone graft. The combination of rhPDGF-BB with the deproteinized cancellous bovine bone graft reduced the healing period to 4 months in a maxillary sinus with minimal residual bone.

A variety of materials, either singly or in combination, have been used to achieve predictibility in sinus augmentation.[2] Autografts and allografts have been considered for grafting materials due to their osteoconductive, osteoinductive, and/or osteogenesis properties. Despite the presence of these characteristics, each material has limitations such as high morbidity of the donor site, potential for disease transmission, immune rejection, variable clinical results, and inconsistent graft incorporation.[12,13]

Xenografts are another widely used graft material. As with allografts, patient morbidity is reduced. Xenografts have been shown to be better than autograft or allograft at maintaining load-bearing bone volume and a high percentage of vitality.[14] A commonly used xenograft material, Bio-Oss deproteinized cancellous bovine bone graft, has been shown to have osteoconductive properties and no inflammatory or adverse responses. In a case report, Traini et al[15] performed a

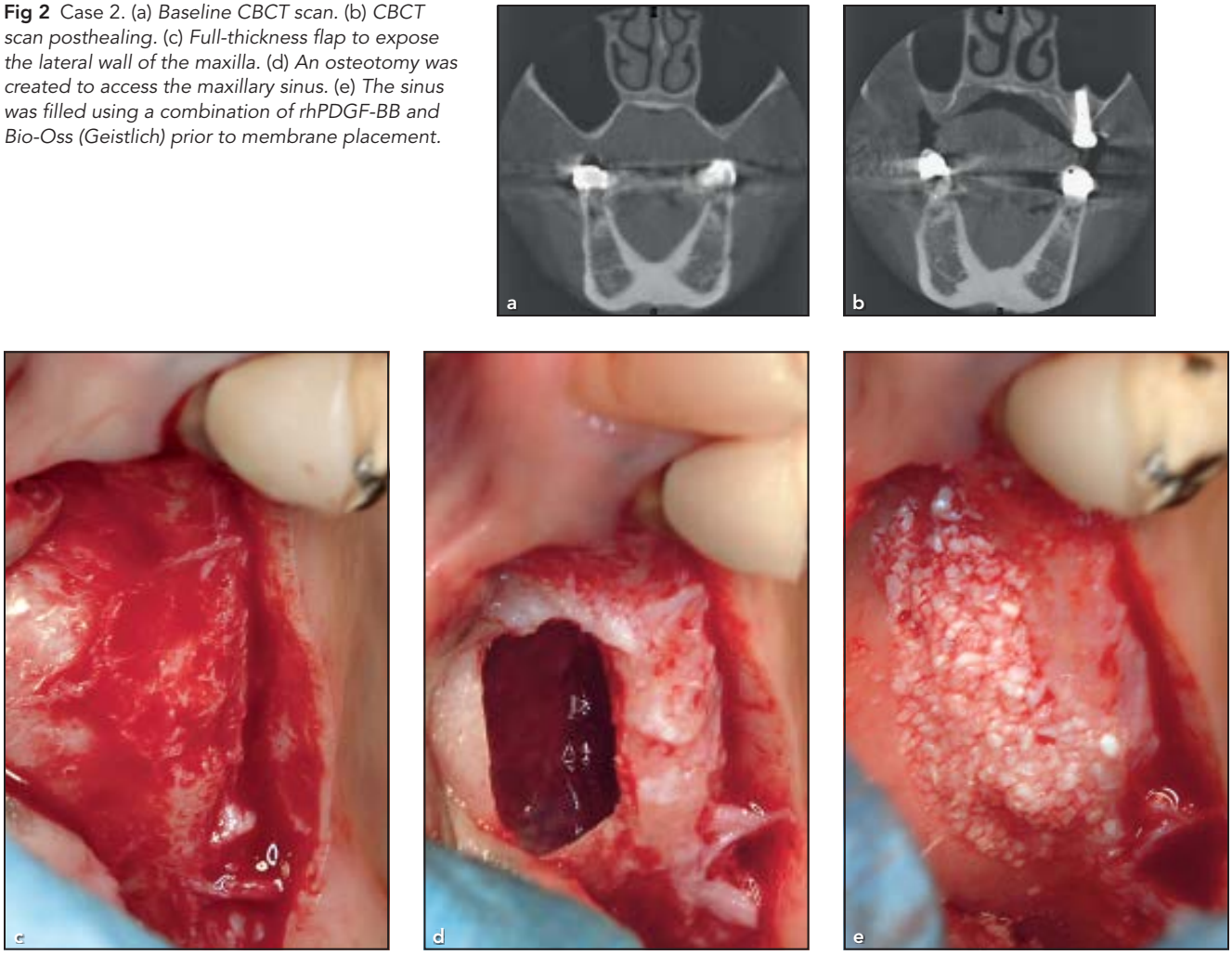

Fig 2 Case 2. (a) *Baseline CBCT scan.* (b) *CBCT scan posthealing.* (c) *Full-thickness flap to expose the lateral wall of the maxilla.* (d) *An osteotomy was created to access the maxillary sinus.* (e) *The sinus was filled using a combination of rhPDGF-BB and Bio-Oss (Geistlich) prior to membrane placement.*

histomorphometric analysis of maxillary sinus augmentation using Bio-Oss as a graft over a 9-year period. Data indicated a high level of osteoconductivity and biomimetic behavior.[15] A similar long-term study examined the amount of Bio-Oss ossification in a case of maxillary sinus augmentation. At 8 months, 2 years, and 10 years, histologic evaluations demonstrated a highly significant increasing trend in bone formation associated with Bio-Oss resorption.[16]

Conventional bone graft materials produce sufficient solutions to bone deficiency in the posterior maxilla. The improvement of the procedure over the current standard involves a reduction in the healing time, particularly in the severely resorbed maxilla. Biologics have long been believed to have the potential to accelerate the healing process. While bone substitutes have been effective as a graft material, they have also served as scaffolds to deliver bioactive molecules. Different scaffold materials are available that are biocompatible with biologics, including collagens, particulate grafts, and resorbable polymers.[10]

Several recombinant human molecules, including BMP-2 and PDGF-BB, have been used for bone regeneration for alveolar and sinus augmentation. Triplett et al[5] reported that rhBMP-2/absorbable collagen sponge (ACS) safely induced adequate bone regeneration for the placement and functional loading of

dental implants in patients requiring staged maxillary sinus floor augmentation.[5] In a case series study, Jensen et al[4] reported on 10 patients with 19 zygomatic implants to treat severe maxillary atrophy using rhBMP-2/ACS to graft the sinus for immediate functional loading in an All-On-Four design. After 1 year, all sinus grafts had formed bone and an implant failure rate of 5.2% was reported.[4] However, Kao et al[17] indicated that using rhBMP-2/ACS in combination with a bone graft material yielded a negative outcome. Histomorphometric measurement of bone formation in a lateral window sinus augmentation was compared using rhBMP-2/ACS combined with Bio-Oss or Bio-Oss graft alone. Histology demonstrated that new bone formation was significantly less in patients where BioOss was combined with rhBMP-2/ACS.[17]

The addition of rhPDGF-BB to anorganic bovine bone collagen matrix has been shown to stimulate proliferation and attachment of osteoblastic cells. Wallace and Froum[2] suggest that it may be feasible to adsorb PDGF on a bone collagen matrix for clinical applications.[2] Several preclinical studies have been conducted in which rhPDGF-BB-infused anorganic bone mineral blocks significantly enhanced bone formation and gingival healing in large, critical-size alveolar bone defects in dogs.[18] In a clinical case report of simultaneous vertical guided bone regeneration in the posterior maxilla using rhPDGF-BB, autogenous bone, anorganic bone mineral, and barrier membranes demonstrated successful combined sinus augmentation and vertical alveolar ridge augmentation.[7,19]

Clinical studies using a combination of rhPDGF-BB and BioOss for sinus augmentation have documented the benefit of the molecule. In a case series, Nevins et al[6] reported that histologic sections showed efficient replacement of the typically slowly resorbing anorganic bovine bone mineral matrix particles with newly formed bone. Froum et al[8] reported that vital bone formation was significantly greater in the 4- to 5-month histologic sections of rhPDGF-BB/BioOss when compared with BioOss alone. However, this difference could not be observed in the 7- to 9-month specimens. As the present data indicates, more rapid formation of bone was seen with the addition of rhPDGF-BB.

The present study used the Osstell ISQ meter, as it provided a noninvasive method to determine implant stability. Implant stability can provide indirect evidence of graft maturation. In addition, changes in implant stability have been shown to aid in decision making regarding timing of implant restoration and follow-up.[20] The high ISQ readings at placement in this study indicated that the addition of rhPDGF-BB to deproteinized cancellous bovine bone graft resulted in sufficient new bone during the shortened 4-month healing period. Typically, the period required for the bone to be formed in sinus augmentation ranges from 7 to 9 months.

ISQ values have also been shown to be an indicator of implant survival. In the present study, implants demonstrated a mean ISQ > 70 at second stage with no failures. Ostman et al[21] indicated that resonance frequency analysis (RFA) may serve as a valuable tool for documenting the clinical outcome of implant treatments. Implants with high ISQ values at placement and restoration demonstrated superior outcomes. Conversely, low ISQ readings could indicate implant failure. Sacarano et al[22] indicated a statistically significant correlation between an ISQ < 40 and irretrievably failed implants. Rodrigo et al[23] reported a statistically significant correlation between RFA values and implant outcome. No implant with ISQ > 60 failed, while 19 % of implants with ISQ < 60 failed.[23]

Conclusions

The maxillary sinus augmentation procedure has become a predictable treatment to regenerate bone for implant placement. Biologic materials may provide clinicians with an effective treatment option that can overcome some of the issues associated with conventional bone graft materials, including prolonged healing time and severe bone loss. The results of this study indicate that the addition of rhPDGF-BB to deproteinized cancellous bovine bone was able to accelerate the healing period in maxillary sinuses with minimal native bone.

Acknowledgments

The authors reported no conflicts of interest related to this study.

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