The goal of this retrospective study was to evaluate the survival rates of dental implants placed in sinuses grafted with a 50:50 composite ratio of autogenous bone and a natural fluorohydroxyapatite (FHA) combined with platelet-rich plasma (PRP) using an immediate-load protocol. The authors hypothesized that a 50:50 composite ratio of FHA and autogenous bone combined with PRP would permit immediate loading without compromising implant survival rates. Eleven patients with bilateral partial edentulism of the posterior maxilla were enrolled in this retrospective study. Autogenous bone used in the graft procedure was harvested from the tibia of the left lower extremity. Each patient was grafted with a 50:50 composite ratio of autogenous bone and FHA. Membranes were not used to cover the lateral wall osteotomy site. Platelet-rich plasma was added to the graft material to accelerate and enhance bone regeneration. Four to 6 months after the grafting procedure, 37 hydroxyapatite-coated dental implants were surgically placed and immediately loaded between 72 hours and 5 days later with custom titanium abutments and acrylic provisional restorations placed out of functional occlusion. Six months later, definitive ceramometal restorations were cemented on to the custom abutments. Patients were observed over a 52-week period. The overall implant survival rate was 97.3%. Histologic and histomorphometric analysis of core samples revealed formation of new vital bone in different graft specimens ranging from 23% to 34%. In each core bone sample, 100% of the bone sample was determined to be vital. In the grafted maxillary sinus, the natural FHA combined with autogenous bone in a 50:50 composite ratio with PRP is a suitable graft material permitting immediate load without compromising implant survival rates while decreasing the overall healing time.

Key Words: fluorohydroxyapatite (FHA), autogenous bone, platelet-rich plasma, immediate nonfunctional load, implant survival rates, vital bone formation

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INTRODUCTION

The maxillary sinus elevation procedure with bone graft augmentation was first reported by Boyne and James.1 The objective of this surgical procedure is to increase the amount of vital bone to allow surgical placement of implants, which will permit successful implant osseointegration and increase implant survival. In an evidence-based review by Wallace and Froum,2 the average implant survival rate was 91.8%. With the use of rough-surfaced implants and particulate bone, the average implant survival rate reported was 94.5%. With the addition of membranes placed over the lateral wall osteotomy site, the implant survival rate increased to 98.6%.

Despite previous studies reporting high implant survival rates in the maxillary sinus grafted with a variety of different graft materials and combinations, there is little information describing graft maturation and attempts to decrease graft healing time to permit immediate or early implant placement. There are even fewer reports in the literature describing immediate or delayed loading with and without functional occlusion. There are even fewer reports of implants placed in the nongrafted posterior maxilla.

Tarnow and colleagues3 reported their experience with intermediate loading in the edentulous maxilla. In 4 patients, 10 implants were placed in each patient. Thirty-three implants were immediately loaded with a provisional restoration. Six months after implant placement, the definitive restorations were fabricated and delivered to the patients. Follow-up ranged from 1 to 4 years with no implants lost, for a 100% survival rate. Horiuchi et al4 reported their experience with immediate loading of the edentulous maxilla in 5 patients. Each patient received a minimum of 8 implants that were immediately loaded. A healing period of 4 to 6 months, the definitive prostheses were delivered to the patients. Two of 44 implants failed, for an implant survival rate of 96.5%. Misch and Degidi5 presented a 2-center study consisting of 31 edentulous patients. In 2 patients, 18 implants were surgically placed and immediately loaded on the day of surgery with provisional acrylic resin restorations. Four to 7 months later, the definitive restorations were fabricated. Follow-up ranged from 1 to 5 years with no implants lost, for a 100% survival and success rate.

In the grafted maxillary sinus, there is only 1 article6 in the English dental implant literature describing immediate load of implants placed in the grafted maxillary sinus. Thirty-three sinuses were grafted with platelet-rich plasma (PRP)–sprayed autogenous bone and a xenograft substitute material. A total of 77 implants were immediately placed and provisional acrylic restorations delivered to the patients but placed out of functional occlusion. The author reported an overall 2-year implant survival rate of 98.7%. However, the author did not include information regarding initial vertical bone height using any recognized bone classification system, such as that described by Ca-wood and Howell.7 The study also did not include histologic data or histomorphometry.

At present, there is no known correlation between implant survival and the amount of vital bone formation needed to support the implant under occlusal loads.8 The goal of this retrospective study was to evaluate the survival rates of dental implants placed in sinuses grafted with a 50:50 composite ratio of autogenous bone and a natural fluorohydroxyapatite (FHA), Algisorb (Osseous Technologies of America, Newport Beach, Calif) combined with PRP using an immediate-load protocol. We hypothesized that a 50:50 composite ratio of FHA and autogenous bone combined with PRP would permit immediate loading without compromising implant survival rates because of the amount of new and vital bone formation.

Random core bone biopsy specimens were harvested 3 to 4 months after sinus grafting to evaluate the amount of new vital bone formation. Histological and histomorphometric data will be analyzed and compared with the contemporary literature regarding bone formation and implant survival. The outcome of implants placed in the nonaugmented posterior maxilla or sinuses grafted with only autogenous bone as a control group is not part of this study.

Terminology

Until recently, there was no clear consensus as to the precise definition of immediate load and early load. As a result, considerable confusion existed as to when these terms should be applied. In 2004, the Immediate Function Consensus Conference9 was conducted to resolve this issue, and terminology regarding immediate load and its guidelines were developed. Using the terminology adopted from this conference, all 11 cases included in this study were defined as a nonfunctional immediate restoration. In each case, the implant prosthesis in a patient who is partially
edentulous was delivered within 2 weeks of implant insertion with no direct occlusal load.

**Review of the literature**

No quantitative correlation exists between formation of vital bone and implant success. In any grafting procedure related to successful implant osseointegration, the objective is the formation of 100% vital bone.10 The ideal graft material has yet to be discovered, and the current debate is which is the best bone graft material to use with the sinus lift elevation procedure that offers the best chance for implant survival.11–15

The normal posterior maxilla usually consists of 20%–25% type III or IV bone.16 Glauser et al17 reported a higher implant failure rate in the posterior maxilla, especially in type III and IV bone. They reported a 34% failure rate for implants placed in the posterior maxilla, compared with a 9% failure in other parts of the maxilla and mandible.

Gelbert et al16 reported an overall 3-year implant success rate of 90% when implants were placed in the grafted maxillary sinus for all graft materials combined. A meta-analysis by Tong and colleagues18 compared success rates of implants placed in sinuses grafted with different grafting materials, including autogenous bone. They concluded that autogenous bone should still be considered the gold standard for grafting the maxillary sinus.

For implants to survive under functional occlusal loads in the grafted maxillary sinus, the minimum percentage of vital bone has yet to be determined.9 In the sinus grafted with 100% autogenous bone, histomorphometric analysis revealed an average of 26% to 69% vital, mineralized bone formation.19–21 When graft substitute materials were used, the range of vital mineralized bone formed was between 5% and 45%.11,19,22,23 In a single case report by Froum et al,24 using a mineralized allograft combined with 10% autogenous bone, histomorphometric analysis of a bone core after 9 months of graft healing revealed bone formation of 25.2% with 16.8% residual graft material. In the nongrafted posterior maxilla, the average percentage of mineralized bone has been reported to be between 17.1% and 26.7%.25

In bone-grafting procedures, autogenous bone is still considered the gold standard because it can form new bone at the implant interface, recruit mesenchymal stem cells that will differentiate into osteoblasts and serve as a scaffold for the formation of new bone, and stimulate neoangiogenesis. In addition, autogenous bone contains large quantities of fibrin and platelets that are involved in wound healing.26–28

However, autogenous bone as the sole graft material has several disadvantages. Donor site morbidity and increased cost has led many clinicians to use other substitute graft materials with or without autogenous bone. Another disadvantage reported is early and severe graft resorption.12,14,29

Del Fabbro et al14 reported an 87.7% survival rate of implants placed in the grafted sinus using 100% autogenous bone. In their systematic review, they reported that of 3398 implants placed, 418 implants failed because of graft resorption. Nystrom and colleagues29 reported an implant survival rate of 77% after bone grafting using 100% autogenous bone harvested from the iliac crest. The low survival rate was attributed to resorption of graft volume.

A study by Uchida et al30 using computerized diagnostic software calculated that 5.47 mL of graft material would be required to graft the sinus to surgically place 3 or more implants. To graft both sinuses, more than 11 mL of autogenous bone would be required, and the mandible is unable to provide this amount of bone. For this reason, bone graft substitutes have been developed to be used alone or in combination with autogenous bone.

Graft substitutes such as xenografts, allografts, and alloplasts have all been tried in the maxillary sinus.11,13,23 Formation of bone is dependent on osteoprogenitor cells that can transform into osteocompetent osteoblasts.31 The population of osteoblasts is significantly reduced because of a deficiency in the amount of available mineral matrix and marrow in the atrophic posterior maxilla. To withstand occlusal loads under function, the graft material must resorb and be replaced with new vital bone.31 It has been shown that bone substitute materials are nonvital foreign bodies that provide only a scaffold for the formation of new bone.32 These biomaterials stimulate the proliferation, differentiation, and migration of osteogenic cells. They do not provide the cellular elements required for osteogenesis, as they possess only osteoconductive properties.20,31 Therefore, the need to add autogenous bone as an osteogenic and osteoinductive factor may still be necessary in composite grafts.

A nonanimal, graft substitute biomaterial used in this study is a commercially available marine carbonated red algae, *Corallina officinalis*, which is chemically converted into hydroxyapatite (HA).32 The chemical composition is 100% inorganic calcium phosphate. It is characterized by interconnecting pores and a large specific surface area composted of HA similar to spongy cancellous bone and dental enamel.32–33

Biomaterial processing involves pyrolytical segmentation of the algae and hydrothermal transformation of the calcium carbonate into FHA. During
processing, the organic components are completely removed. The particle size averages 0.5–1.0 mm, and the 3-dimensional morphologic structure contains a pore system with a mean diameter of 10 μm that is periodically septated every 50 to 100 μm in length. Every pore is limited by 1 layer of small FHA crystallites with a size of 25–35 nm. Advantages of this natural FHA’s graft material are that it is available in unlimited quantities, is inexpensive, does not illicit an immune response, and is replaced by bone due to the surface porosity and osteoclastic resorption. 32–34

This macroporous ceramic material is composed of 100% HA and possesses specific mechanical and physiochemical properties similar to spongy cancellous bone. It promotes the migration, proliferation, and differentiation of osteocytes. 32–35 Studies have shown that bony defects implanted with FHA become vascularized and covered with natural bone while the material is slowly resorbed. 33,34,36

A number of animal and human histomorphometric studies have shown that the marine algae derived hydroxyapatite FHA is osteoconductive, porous, and demonstrates a high resorption and remodeling rate. 32,33 All of these properties result in early revascularization of the FHA particles and new bone formation. This entire process of early graft turnover is stimulated by the osteoconductive properties of the material. 32–38

Platelet-rich plasma

Platelet-rich plasma applied to autogenous bone grafts was first reported by Whitman and colleagues. 39 Bone formation is accelerated by the liberation of specific growth factors contained in the alpha granules of the platelets. 40 In their clinical studies with mandibular reconstruction, Marx et al 40 demonstrated that the addition of PRP resulted in early graft consolidation and mineralization in half the time of grafts without the addition PRP. Bone healing was accelerated approximately 2 times that of autogenous bone grafts without PRP. Bone grafts in general produce a trabecular dense bone area that is equal to or greater than that of the nongrafted posterior mandible. But with the use of PRP, it was observed that trabecular bone density improved by 15% to 30%. Histomorphometric analysis showed a greater amount of mineralized bone density (75% ± 11%) compared with bone grafts without PRP (55% ± 8%). Their results showed that the addition of PRP accelerated the rate of bone formation during the first 6 months after grafting. Subsequent studies 41,42 demonstrated that using PRP during implant surgery promotes implant osseointegration and bone regeneration.

Cancellous marrow grafts 43 contain mesenchymal stem cells that contain the receptors for platelet-derived growth factor (PDGF) and transforming growth factor-β (TGF-β). Combined with tissue growth factors, mesenchymal stem cells have the ability to differentiate into osteogenic cells, which will stimulate bone formation. In a dog model, Gerard et al 44 showed that PRP enhanced early healing by increasing the amount of nonviable grafted bone that was resorbed and increasing the amount of new vital bone that was formed during the first 2 months after grafting. This benefit was no longer observed between 3 and 6 months after grafting. Using immunohistochemical analysis in a rabbit calvarial model, Aghaloo et al 45 demonstrated an increase in expression of PDGF, TGF-β, and basic fibroblast growth factor at 1 to 2 months when PRP was added to an autogenous bone graft. All 3 growth factors have been shown to increase new bone formation. 45

Platelet-rich plasma has also been shown to be potentially useful with various xenogenic, allogenic, and alloplastic graft materials. 42,46,47 It has been observed that PRP has enhanced the osteoconductive and possibly the osteoinductive properties of these graft materials. 42,47 Kim and colleagues 48 speculated that the addition of PRP to osteoconductive graft materials may potentiate osteoinduction. Endothelial cells, adipocytes, fibroblasts, and macrophages constitute the marrow stromal cell population and may be transformed into osteoblasts via critical biochemical signals from cytokines in the PRP.

Although PRP has been shown to enhance wound healing, other studies have questioned the healing benefits of PRP. 49–51 In a canine model, Choi et al 49 suggested that PRP did not appear to enhance bone formation in autologous grafts of the mandible. They observed no accelerated bone formation but suggested that the addition of PRP could actually interfere with bone healing. A study by Butterfield and associates 52 failed to provide a statistically significant direct stimulatory effect on healing of autogenous bone grafts in maxillary sinus augmentation procedures in the rabbit model. In a similar study using a sheep model, Jakse et al 53 found no statistically significant advantage of using PRP with autogenous bone grafts in the grafted maxillary sinus.

**Materials and Methods**

Setting and participants

To complete this clinical study, a retrospective cohort study design was implemented. All participants were referred from the patient’s family dentist to replace
any missing teeth in the posterior maxilla with implant-supported ceramics-metal restorations. Eleven participants were enrolled in this study and consisted of 7 Asians, 3 Caucasians, and 1 Polynesian. Of the 11 patients, 8 were female and 3 were male. Women ranged in age from 28 to 73 years. The mean age of this group was 49.9 years. Of the 3 males participating in the study, their ages ranged from 42 years to 57 years. The mean age for this group was 49.3 years. The mean age for both groups was 49.9 years.

Twenty-two maxillary sinuses were bone grafted in a total of 11 (8 women and 3 men) patients from February 2003 to January 2006. Their general health was classified according to standards set by the American Society of Anesthesiologists (ASA) on a 5-grade scale.54 The patients in this study were classified as ASA health status grade 1 (no systemic disease) or grade 2 (mild systemic disease). Smokers were not excluded from the study. Of the 11 participants, 2 patients were smokers. Both patients reported smoking more than 10 cigarettes per day. Preoperative prophylactic antibiotics were not prescribed to any of the patients. However, oral penicillin 500 mg 4 times per day for 5 days was prescribed postoperatively. If the patient was allergic to penicillin, oral clindamycin 150 mg was the alternative antibiotic prescribed.

Treatment options were discussed with every patient, and all of the participants selected the treatment plan requiring maxillary sinus elevation. Patients included in the study were selected after a careful review of their medical history and an examination that included panoramic radiographs or in-office cone beam computerized tomography (CBCT) scans (Imaging Sciences International, Hatfield, Pa). Patients were selected according to specific inclusion criteria: Cawood and Howell classification V and VI,7 in which the posterior vertical bone height is 5.0 mm or less; all participants required the sinus lift elevation procedure with bone graft augmentation for the placement of dental implants in the posterior maxilla. To participate in the study, each patient had to agree to the following: multiple office visits for observation, radiographs, CBCT scans, photographs, and core biopsies of the grafted maxilla for histologic analysis. Patients with relative contraindications such as controlled diabetes mellitus, hypertension, or use of anticoagulants and patients with a history of osteoporosis taking oral bisphosphonate (BP) medications were included in the study. Of the 11 patients, 5 patients were taking BP medications. Of special interest, 4 women were taking Fosamax (Merck & Co, Whitehouse Station, NJ) and 1 was taking Actonel (Procter & Gamble Pharmaceuticals, Cincinnati, Ohio). All 5 patients were prescribed these 2 BP medications for greater than 3 years. Patients with the following were excluded from the study: ASA class III and IV, immunosuppressive disorders, current alcohol or substance abuse, excessive parafunctional habits, untreated periodontal disease, pregnant or nursing women, patients exposed to radiation of the jaws due to malignancies, untreated insulin-dependent diabetes mellitus, coagulopathies, and chronic steroid use. The study was approved by the Institutional Review Board of Touro University international, Department of Health Sciences.

Procedure

Patients fulfilling selection criteria were invited to participate in this study. Patient privacy and confidentiality, including informed written consent, were always obtained. To identify each participant and keep the identity confidential for this study, each participant was assigned a number to which only the surgeon has access. Data were collected from the time of sinus grafting and implant placement until the last office evaluation based on the 52-week observation protocol. Clinical information recorded in the patient database included patient age, sex, and medical history. Research information included graft material, number of implants placed in the maxilla, height of existing alveolar crest in the posterior maxilla prior to and after surgery, postoperative complications, and failure of any implants to osseointegrate.

Patients were examined clinically for signs of postoperative complications including inflammation, infection, wound breakdown, and resorption at the surgical site. Panoramic radiographs and CBCT scans were obtained to evaluate graft and implant healing postoperatively at 1 month, 3 months, 6 months, 9 months, and 1 year. The last office appointment marked the formal termination of the study for each individual participant. However, patient follow-up continues beyond the formal endpoint of 52 weeks for purposes of long-term evaluation of the graft material and implant survival for future research studies.

Graft materials

In each patient, autogenous particulate bone was harvested from the tibia of the left lower extremity according to Lee.55 All sinuses were grafted with a 50:50 composite ratio of autogenous and FHA.

Dental implants

Multithreaded, internal hexed straight and tapered screw-type implants with HA surfaces (Zimmer Dental, Carlsbad, Calif) were surgically placed into the grafted
maxillary sinuses. Data from panoramic radiographs and CBCT scans were used to select implant location, implant length and diameter, and amount of bone graft material.

**Sinus graft surgical technique**

The sinus lift elevation technique used in the present study is similar to what is described by Tatum. All of the cases were performed in the office under local anesthesia or intravenous sedation. In every instance, the oral cavity was rinsed for 60 seconds with 0.12% chlorhexidine gluconate mouthwash (Peridex, Proctor & Gamble, Cincinnati, Ohio) preoperatively, and the patient was draped in sterile fashion to ensure strict asepsis.

In some cases, a perforation of the Schneiderian membrane was observed while attempting to elevate it off of the walls of the sinus cavity. In each instance, membrane perforations were repaired by placing a resorbable collagen membrane saturated with PRP (Biomend Extend, Zimmer Dental, Encino, Calif) over the perforation. Once the membrane was elevated out of the surgical field, the graft material was mixed with PRP and then carefully packed into the sinus floor. After the graft material was packed into the maxillary sinus, the soft-tissue flap was reapproximated and passively sutured using 4–0 silk sutures without tension. Sutures were removed 2 weeks after surgery. The graft material was allowed to mature, allowing the formation of new, vital bone around the graft particles for a period of 3 to 4 months before implant placement. At the time of implant surgery, the immediate nonfunctional load protocol was initiated.

**Platelet-rich plasma preparation technique**

Approximately 55 mL of whole blood from every patient was obtained from the antecubital fossa of the arm via venipuncture using a 23-gauge needle. The blood is collected and anticoagulated with an anticoagulant citrate dextrose-A solution. The venous blood is then injected into a disposable dual chamber, which is placed into a cell separator. Over a 13-minute period, the blood is processed using a microprocessor-controlled, automated cell separator (Harvest Technologies, Plymouth, Mass). At a speed of 5600 rpm, the cell separator divides the venous blood into 3 components: PRP, platelet-poor plasma, and red blood cells.

Centrifugation of 55 mL of whole blood results in 10 mL of PRP. Five thousand units of bovine thrombin (King, St Louis, Mo) are mixed with 10% calcium chloride (American Regent, Shirley, NY). The mixture is applied to the bone graft material, and activation of PRP results in degranulation of the platelets and immediate release of its growth factors.

**Implant surgery and bone core biopsies**

After a healing period of 3 to 4 months, implants were surgically placed into the grafted maxilla. Custom surgical templates were prefabricated prior to surgery, which allows the implant team to determine the correct number of implants, their position, size, and custom abutments before surgery. The surgical guide was based on the preoperative treatment plan formulated by the restoring general dentist and surgeon.

Under local anesthesia, 8 random core biopsies from the grafted posterior maxilla were taken using a trephine bur with an inner diameter of 2 mm and an outer diameter of 3 mm from the alveolar crest of the implant site. Immediately after the biopsy specimen was removed from the posterior maxilla, the implant was surgically placed into the osteotomy site according to the implant manufacturer’s protocol.

**Prosthetic protocol**

After each implant was surgically placed in the maxilla, the implant position was indexed by the surgeon with the closed tray technique using the impression coping provided by the implant manufacturer and a polyvinylsiloxane impression material to facilitate the fabrication of the provisional acrylic resin restoration. The Screwvent dental implant (Zimmer Dental) is supplied with a premounted titanium abutment that serves as the fixture mount, temporary abutment, and impression coping for indexing to transfer the position of the surgically placed implant to the master cast. The decision to place the provisional restoration 72 hours to 5 days later was determined by the limited time available for this procedure following surgery between the surgeon, patient, and dental laboratory. The custom abutment and provisional restoration was fabricated by the dental laboratory and returned to the surgeon. When the custom abutment was placed on the implant, it was only hand tightened. The provisional restoration was then adjusted chairside and cemented with temporary cement out of occlusion. Six months later, final impressions were obtained by the restorative dentist, and the definitive ceramometal restorations were fabricated and delivered to the patient. During placement of the final ceramometal restorations, all custom abutments were tightened to 30 Ncm.

**Specimen processing**

All core bone biopsies were sent to the Hard Tissue Research Laboratory of the University of Minnesota.
School of Dentistry, Department of Oral and Maxillofacial Pathology, for histologic and histomorphometric analyses. Each core bone biopsy contained both the grafted area and the native, alveolar crest (Figure 1) of the maxillary sinus floor. Biopsy samples were fixed in 10% buffered formalin and submitted for histologic examination. All specimens were dehydrated with a graded series of ethanol for 9 days. After dehydration, each sample was infiltrated for 20 days with a light-curing embedding resin (Technovit 7200 VLC, Kulzer, Wehrheim, Germany). The specimens were then embedded in Technovit 7200 VLC and polymerized by 450 nm light, with the temperature of the specimens not exceeding 40°C. Each specimen was then prepared by the cutting and grinding method of Rohrer and Schubert. Each specimen was cut to a thickness of 150 μm on an EXAKT cutting and grinding system (EXAKT Technologies, Oklahoma City, Okla). Each specimen slide was polished to a thickness of 55 μm with a series of polishing sandpaper discs ranging from 800 to 2400 grit (EXAKT microgrinding system) followed by a final polish with 0.3-μm alumina polishing paste. Following final polishing, the specimen slides were stained using Stevenel’s blue and van Gieson’s picro fuchsin and subjected to histological evaluation by light microscopy. Specimens were evaluated using 2 slides to prevent sampling bias.

Microphotographs were obtained, scanned, digitized, and analyzed using a Zeiss Axiolab photomicroscope (Carl Zeiss, Jena, Germany) and Nikon Coolpix 4500 digital camera (Nikon Corp, Tokyo, Japan). All core specimens were photographed at a fixed focal point and ×25 magnification for histomorphometric evaluation. Histomorphometric measurements were completed with a Macintosh G4 computer (Apple, Cupertino, Calif.) and a public domain image program (NIH Images, US National Institutes of Health) along with Adobe Photoshop (Adobe, San Jose, Calif.). The data were exported to Microsoft Excel (Microsoft Co, Redmond, Wash) for histomorphometric calculations. Histomorphometric analysis was performed, and the following parameters were measured in terms of the percentage of the total core area: new bone formation, residual graft material, and marrow space.

Criteria for implant success

All implants with the provisional and definitive restoration were determined to be successful if the following criteria were observed up to 1 year after implant placement: (1) no implant mobility, (2) no complaint of pain around the implant, (3) no evidence of infection associated with the implant, and (4) no neurosensory deficits reported by the patient.

Results

No intraoperative or postoperative complications were observed in any patient. A total of 39 dental implants were placed in the grafted sinuses. In 2 patients, implants placed in the second molar regions were determined to be mobile at the time of implant placement and were not immediately loaded. Both of these implants followed the conventional Branemark protocol and were loaded 6 months after implant placement with definitive ceramometal restorations. Therefore, these 2 implants were not included in this study. However, a third implant did fail to osseointegrate in the second molar region. The patient reported pain with mastication after 2 months in function. The implant was removed and replaced 1 month later and restored following the conventional Branemark protocol. This implant failed 30 weeks after placement of the definitive restoration and was removed. The patient elected to defer further attempts to restore the second molar area with another implant.

Histological and histomorphometric results

A total of 22 sinuses were grafted with a 50:50 composite ratio of autogenous bone and FHA. Platelet-rich plasma was applied to every graft mixture before it was lightly packed into the sinus cavity. Thirty-seven implants were placed in the grafted sinuses 3 to 4 months after grafting each sinus. Eight of the sites were examined for histological and histomorphometric evaluation by taking trephine core samples prior to placing the implants at times ranging from 3 to 4.3 months following grafting. The amount of new bone formation in the core samples ranged from 23% to 34% (Table). Residual FHA particles
ranged from 0% to 28% of the core samples. Of special significance is that 100% of each bone core sample was determined to be vital. New bone formation totally encompassing residual graft particles is occasionally seen (Figure 2). New bone formation appeared to take place in 1 of 2 methods. Osteoblasts have formed an osteoid on the surface of particles of FHA. The osteoid undergoes calcification, trapping osteoblasts, which become osteocytes of the new vital bone. This new vital bone is noted as forming in contact with particles of FHA in Figure 3. The other method, which is of particular interest, is the manner of forming new bone within cells of the FHA, which is seen so well in Figures 4a and 4b. In this type of intraporous bone formation, there appears to be an induction of bone formation within the substance of the FHA itself. One assumes in the first method the FHA particles on whose surface the new bone formed were resorbed by osteoclastic-type cells. In the second method, once the FHA particle has become calcified, it most likely undergoes normal bone remodeling.

**DISCUSSION**

This retrospective study was designed to evaluate the survival rate of dental implants placed in sinuses grafted with a 50:50 composite ratio of autogenous bone and FHA with PRP over a 52-week period. We hypothesized that this specific composite graft ratio could provide an advantage over other graft materials and combinations, permitting implementation of the nonfunctional immediate load protocol of the grafted sinus that would result in a shorter healing time compared with the conventional Branemark protocol.

A major limitation of this retrospective study is that no graft control group was used as a comparison.

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*FHA indicates fluorohydroxyapatite.

![Figure 2](image2.jpg)

**Figure 2.** New, vital autogenous bone formed around fluorohydroxyapatite graft material (arrows; original magnification ×100). Stevenel's blue and van Gieson's picro fuchsin.

![Figure 3](image3.jpg)

**Figure 3.** High-power view shows new, vital autogenous bone (NB) forming on the surface of fluorohydroxyapatite (FHA) graft particles. Osteoid (OS) in contact with the FHA graft material. Osteoblasts (OB; original magnification ×200). Stevenel's blue and van Gieson's picro fuchsin.
However, biased and inaccurate reporting could occur when comparing different groups to observe a specific outcome. To offset this limitation, data were collected retrospectively, and although the number of participants is considered low, patients were treated during different time periods.

The literature has shown a wide range of the percentage of vital new bone formation using various bone graft substitutes, ranging from 14% to 44%. In their study, Hallman and associates showed that the combination of a bovine xenograft and autogenous bone and platelet fibrin glue in an 80:20 ratio grafted in the maxillary sinus yielded a 90% implant success rate at 1 year after loading. Histomorphometric analysis at 6 months demonstrated 21.2% vital lamellar bone formation. At 3 years postgrafting, further analysis showed 50.7% vital lamellar bone formation.

Like PRP, autogenous bone contains large quantities of growth factors such as PDGF, TGF, and bone morphogenetic proteins, all of which are involved in osteogenesis. Because of its cellular nature and osteoinductive properties, the addition of 50% autogenous bone to the graft mixture will accelerate the formation of new vital bone. All of these growth factors lead to improved angiogenesis and revascularization of the graft, which results in enhanced wound healing, allowing for an overall shorter healing time. Release of these growth factors allows for the stimulation of stem cells and osteoblast progenitor cells to initiate early osteogenesis and angiogenesis.

A number of studies have shown that FHA particles become well vascularized after several weeks and gradually resorb and are replaced with new bone through the process of remodeling. This process is most likely due to the porous structure and the osteoconductive properties of the graft material. In a study by Shopper et al., histomorphometric analyses demonstrated 23% new bone formation after 7 months of maxillary sinus grafting. In addition to the observation of new bone apposition along the surface of the FHA particles, new bone was also observed growing into the pores of this graft material, as well. With increased graft healing time, histomorphometric analysis showed $40.8\% \pm 15.3\%$ formation of new trabecular bone after 15 months. In the study by Simunek et al., the percentage of residual graft material also decreased linearly from $34.5\% \pm 8.65\%$ to $13\% \pm 9.6\%$ over a 6- to 15-month observational period.

Intraporous bone growing into the 10-μm-diameter pores of the FHA graft particles has not been reported with other graft materials with pore size diameters smaller than 40 μm. This important finding was first reported by Schopper et al. and they hypothesized that the interconnecting 10-μm pores might be capable of permitting bone growth in vivo. This impressive finding was observed in one of our core samples. Vital bone was observed growing into
the FHA graft material from the central portion rather than from the periphery (Figure 4a and 4b).

In the study by Ewers, a 95.5% implant survival rate over a 156-month observational period was reported following the conventional Branemark protocol (6 months of graft healing, followed by another 6 months of implant healing). The high implant survival rate is most likely due to the graft material features of porosity, absorption, and resorption that permits accelerated formation of new bone.

Using the immediate load protocol, provisional restorations were placed on to the implants 2 to 4 months after grafting. During the 52-week observational period, only 1 implant was lost, for a 97.3% survival rate. Like the high implant survival rate observed by Ewers, we believe that our immediate load results are due not only to the osteoconductive properties and structural architecture of the FHA graft material but also to the osteopromotive effects of PRP and osteogenic and osteoinductive properties of autogenous bone. Attempts were made to correlate implant survival rates with histologic and histomorphometric data over a 3- to 4-month healing period.

Both participants who reported smoking cigarettes did not experience any complications, including failure of the implant to successfully osseointegrate in the grafted maxillary sinus. Studies have documented significantly higher rates of implant failure in the smoking patient compared with the nonsmoking patient, especially when implants were placed in the grafted sinus. It has been suggested that poor bone quality leads to higher implant failure rates in all patients, and improving the bone quality in patients who smoke cigarettes may decrease the implant failure rate.

Despite the reports of the adverse effects of smoking on wound healing of the oral cavity and implant survival, especially in the graft maxillary sinus, other studies do not support these findings. At present, no clinical study has examined the survival rate of a large sample of implants placed in the grafted maxillary sinus in the smoking population. In a study by Peleg and colleagues, no statistically significant difference in implant failure rate was observed between smokers and nonsmokers.

Recently, there have appeared a significant and growing number of articles in the worldwide dental and medical literature describing the complication of an osteonecrosis of the jaws associated with the use of the intravenous and, most recently, the oral form of BP drugs that have been refractory to any definitive form of treatment. Although the endpoint of this retrospective study is beyond the 52-week observation period, patient monitoring continues. In the 5 patients taking the oral form of the BP drugs to treat osteoporosis, no complications of bisphosphonate-associated osteonecrosis of the maxilla have been observed.

Conclusion

The preliminary results of this retrospective study suggest that a nonfunctional, immediate load protocol for the grafted maxillary sinus with high implant survival rates can be achieved in a shorter period of healing time compared with the conventional Branemark protocol when using a 50:50 composite ratio of FHA and autogenous bone with PRP. Further long-term studies with sufficient power are needed to confirm the encouraging results of this study.

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