Reconstruction of the Severely Resorbed Maxilla with Autogenous Bone, Platelet-Rich Plasma, and Implants: 1-Year Results of a Controlled Prospective 5-Year Study

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ABSTRACT

Background: Prosthetic treatment of the edentulous maxilla may require bone augmentation to enable placement and integration of dental implants. This constitutes a complex healing situation, and resorption of the grafted bone and failure of the implants often occur. The application of autogenous platelet-rich plasma (PRP) has been suggested to improve incorporation and preservation of bone grafts.

Purpose: The aim of this controlled clinical study was to evaluate whether PRP in conjunction with grafting of particulated autogenous bone to the maxilla could improve the integration and clinical function of dental implants. An additional aim was to compare block bone grafts without PRP with PRP-treated particulated bone.

Material and Methods: Nineteen consecutive patients were included in the study and treated with iliac bone grafts and dental implants in the maxilla according to a split-mouth design. In the anterior maxilla, particulated bone mixed with PRP (test) was compared with onlay block grafts without additional PRP (control). In the posterior maxilla, particulated bone grafts with (test) or without (control) PRP were placed as sinus inlay grafts. After 6 months of healing, 152 implants (8 implants/patient) (TiOblast™, Astra Tech AB, Mölndal, Sweden) were placed. Test (PRP; 76 implants) and non-PRP (76 implants) sides were evaluated and compared by implant survival rate, marginal bone level, and implant stability using resonance frequency analysis (RFA) during 1 year in function.

Results: Two control implants in control sites in two patients were lost at abutment connection. After 1 year in function, no further implants were lost, giving an overall survival rate of 98.7%. The marginal bone level measurements showed no significant differences, although there was a tendency toward less resorption on PRP sides. RFA measurements showed statistically significantly higher implant stability quotient values for PRP sites at abutment connection in the anterior but not in the posterior regions.

Conclusions: The present clinical study showed that a high implant survival rate and stable marginal bone conditions can be achieved after 1 year of loading in the maxilla following autogenous bone grafting whether or not PRP is used. RFA measurements revealed differences at abutment connection, which could be explained by the type of graft rather than as an effect of PRP. Although no obvious positive effects of PRP on bone graft healing could be demonstrated, the handling of the particulated bone grafts was improved.

KEY WORDS: autogenous bone grafts, clinical study, dental implants, platelet-rich plasma

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Autogenous bone grafts are commonly used for reconstruction of the deficient maxillary alveolar ridge to enable placement and integration of implants

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to support dental prostheses. Different augmentation techniques have been described in the literature,[1–6] and varying clinical outcomes have been reported.[7–10] The use of bone grafts and implants constitutes a complex healing situation because both incorporation and maintenance of the bone graft and integration and survival of the implants are required for a successful clinical outcome. According to the literature, resorption of the grafted bone is commonly experienced and the survival rate of the implants is generally lower than in nongrafted patients.[11,12] The reasons for resorption and loss of implants are not fully understood but relate to factors such as donor site, handling and size of the graft, surgical technique, timing of implant placement, healing protocols, prosthetic factors, and patient-related factors.[13]

Onlay block grafts, harvested from the mandible, the calvarium, or the iliac crest, shaped for placement on the maxilla with titanium screws and/or plates, have commonly been used in several studies.[7,8] The cancellous part is usually placed onto the remaining maxilla with the cortical part facing laterally. An obvious risk is ingrowth of soft tissue between the grafted bone and the maxilla, which may result in areas of fibrous tissue incorporated into the graft. A particulated bone graft placed on the maxilla represents a more homogeneous mass, which may eliminate this potential problem. On the other hand, particulated bone is obviously less resistant to soft tissue pressure during healing.

The use of autogenous growth factors derived from the patients' own platelets (platelet-rich plasma [PRP]) to enhance the healing of bone grafts has been described by Marx and colleagues.[14] It has been speculated that local growth factors in the platelets (transforming growth factor [TGF]-β, platelet-derived growth factor [PDGF], and insulin-like growth factor) may facilitate the healing of the graft and counteract resorption. The gel formed by the platelets can be added to particulated bone, giving a moldable graft that is easily placed at the recipient site.[15]

The objective of the present prospective clinical study was to evaluate the survival rate and marginal bone levels of dental implants placed in the resorbed edentulous maxilla after bone grafting with or without adjunctive PRP. In addition, implant stability was evaluated by resonance frequency analysis (RFA) at implant installation, at abutment connection, and after the first year of loading.

MATERIALS AND METHODS

Patients

From June 1999 to March 2001, 19 consecutive patients were included in the study (2 men and 17 women; mean age 58 years, range 35–75 years) and surgically treated by the same surgeon (Table 1). The patients were consecutively recruited from patients referred to the clinic (Maxillofacial Unit, Stockholm Söder Hospital, Stockholm, Sweden) for implant treatment in the totally edentulous maxilla. The patients were presurgically evaluated by clinical and radiographic examinations. The available bone volume was assessed by computed tomographic scans considering both vertical and horizontal deficiencies in the anterior and posterior parts of the maxilla using the Cawood and Howell classification.[16] Patients were included if they satisfied the following criteria:

- Edentulous maxilla with a bone height of 2 to 5 mm under the maxillary sinuses and/or an alveolar crest width of less than 3 mm in the area planned for placement of dental implants
- Smoking less than 10 cigarettes/day
- Not abusing alcohol
- 20 to 75 years of age
- No medical contraindications for surgery and/or general anesthesia using the American Society of Anesthesiologists standards
- Signed informed consent to participate in the study

The general medical status of the patients is presented in Table 1. One patient had mild osteoporosis, and none of the patients were diabetic. Prior to treatment, 12 patients were smokers (< 10 cigarettes/day). One patient smoked during the period from bone grafting to abutment connection. At the 1-year follow-up, 4 of 19 patients were smoking.

Of the 19 patients included, 2 had residual intact molars. One patient had previously lost two of four implants placed 2 years earlier, whereas the remaining two were removed at the bone grafting procedure. All patients were free of local infections and were without mucosal dehiscences in the edentulous area of proposed grafting. The study was reviewed and approved by the regional ethical research committee.

Principal Study Protocol

All 19 patients were subjected to bilateral inlay and onlay bone grafting procedures as described in detail below.

TABLE 1 Medical Status of Patients

Patient No./ Sex/Age	Medical Record of Importance	Previous Smoking (Y/N)	Smoking during Treatment (Bone Graft Abutment) (Y/N)	Smoking at 1-Year Follow-Up (Y/N)
1/F/65	Healthy	Y	N	N
2/F/68	Hypertension	Y	N	N
3/F/64	Hypotension	Y	N	Y
4/F/55	Healthy	Y	N	Y
5/F/63	Healthy	N	N	N
6/F/67	Healthy	Y	N	Y
7/F/65	Previous metabolic disturbances	N	N	N
8/F/51	Healthy	N	N	N
9/F/50	3 yr post breast cancer	N	N	N
10/M/75	5 yr post gastric cancer	Y	N	N
11/F/71	Healthy	Y	N	N
12/F/53	Healthy	Y	Y	Y
13/F/57	Hypertension		N	N
14/F/58	Healthy	Y	N	N
15/F/62	Osteoporosis	Y	N	N
16/F/50	Healthy	N	N	N
17/F/35	Healthy	N	N	N
18/F/46	Metabolic disturbances, hypotension, depression	Y	N	
19/M/50	Healthy	Y	N	N

Both maxillary sinuses were grafted with particulated autogenous bone, the left side with adjunctive PRP (test) and the right side without (control). The left side of the anterior maxilla was grafted with particulated bone graft with PRP (test) and the right side with blocks of bone without PRP (control) (Figure 1). In addition, 10 of the patients received particulated bone grafts to the floor of the nose on the left side with (test) and the other side without adjunctive PRP (control). Dental implants were placed after 6 months of healing, and abutments were connected after another 6 months. The patients were finally examined after 1 year of loading.

Implants

Dental titanium threaded implants with a surface modified by titanium oxide blasting were used in the study (TiOblast™, Astra Tech AB, Mölndal, Sweden). Healing abutments were placed in all cases. Microimplants, 5 mm long and 2 mm in diameter, with a titanium oxide blasted surface were used for histologic evaluation. These implants were installed horizontally in the graft 3 months after the bone grafting procedure in a separate session in which bone biopsies were also collected. The histologic findings will be reported in a separate article.

Resonance Frequency Analysis

The stability of the dental implants was assessed by RFA (Osstell™, Integration Diagnostics AB, Göteborg, Sweden). A transducer was attached to the implants, and measurements were made in implant stability quotient (ISQ) units (where 1 ISQ corresponds to 50 Hz). The instrument gives a value between 1 and 100 ISQ, where 1 is the lowest and 100 the highest degree of stability (Figure 2).

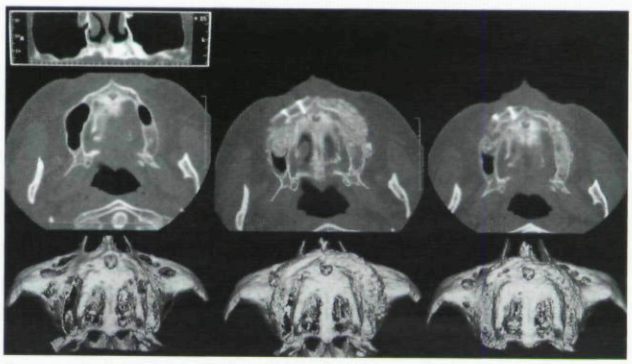

Figure 1 Computed tomographic scans of a study patient's maxilla preoperatively, postoperatively, and after 6 months of healing after the bone graft.

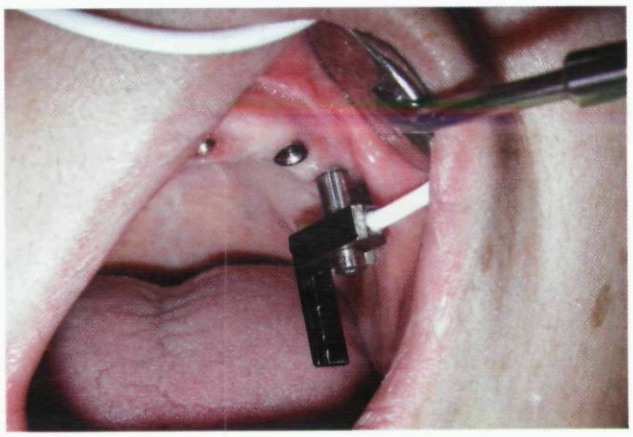

Figure 2 Transducer used with the resonance frequency analyzer equipment.

Preparation of PRP

All patients were subjected to perioperative withdrawal of 450 mL of whole blood from a peripheral vein of the arm or foot before a preparation of PRP was made using a Sequestra 1000® gradient density cell separator (Medtronic, Minneapolis, MN, USA) in the operating room. Citrate phosphate dextrose (63 mL) (Terumo Corp., Tokyo, Japan) was added to achieve anticoagulation, and the blood was then separated into PRP and red blood cells collected in platelet-poor plasma (PPP) as described by Marx and colleagues.[14] The cell separation was done in two steps, with the first at 5,600 rpm and the second at 2,400 rpm to finally extract the platelets in a concentrated form in plasma. The platelet count ($\times 10^9$/L) was preoperatively recorded in venous whole blood (on admission of the patient to the hospital) and after the preparation in the PRP. A sample of PRP from the patients was submitted for machine platelet count (Table 2).

The PPP with red blood cells was transfused back to the patients during surgery, and the PRP (approximately 60 mL) was temporarily saved in its blood bag.

Autologous thrombin was attained by adding 0.33 mL of CaCl (18 mg/mL) (Apoteksbolaget, Umeå, Sweden) to 10 mL of anticoagulated PRP in a small glass bowl. After approximately 6 minutes, a gel was formed. The gel was then gently squeezed, and the solution slowly extracted from it was used as autologous thrombin. By means of initiating a clot formation, 4 mL of PRP was mixed with 1 mL of the autologous thrombin in a 10 mL syringe and 1 mL of air for mixing the components. After approximately 2 minutes, the syringe contained a gel that could then be used with the bone.

Bone Graft Harvesting

Under general anesthesia, bone was harvested from the right ($n = 17$) or left ($n = 2$) anterior iliac crest starting 2 cm posterior to the anterior superior iliac spine and thus obtaining a corticocancellous bone graft. The graft technique aimed at leaving the lateral part of the crest intact, thus using the medial cortical part and obtaining the cancellous bone through that entry. Bovine collagen (Lyostypt®, B. Braun Surgical GmbH, Melsungen, Germany) was used as a coagulum stabilizer on the open bone surface, and an activated drain was used. The incision was closed in layers.

The bone graft taken from the ilium was particulated in a bone mill (Tessier Osseous Microtome, Stryker Leibinger, Freiburg, Germany) into particles of 3 × 3 mm and then mixed in a first session with PRP in the bone mill container.

TABLE 2 Whole Blood and PRP Platelet Counts (/μL) and Concentration Result

Patient	Preoperative	PRP	× Concentration
1	201	355	1.75
2	236	223	0.94
3	Unknown	Unknown	—
4	187	33	0.18
5	240	491	2.05
6	336	43	0.13
7	288	528	1.83
8	268	704	2.63
9	328	963	2.94
10	176	314	1.78
11	302	360	1.19
12	345	646	1.87
13	197	907	4.60
14	358	1,378	3.85
15	301	616	2.05
16	247	677	2.74
17	262	1,181	4.51
18	294	1,509	5.13
19	260	997	3.83
Overall mean	258	662	2.6 (SD 1.3)
Mean first 9 patients	252	406	1.3 (SD 1.1)
Mean last 9 patients	285	919	3.3 (SD 1.5)

PRP = platelet-rich plasma.

Bone Grafting Procedures

Inlay Grafting with Particulated Bone. The maxillary bone was exposed through a full-thickness crestal incision with posterior vertical releasing incisions. A full-thickness flap was elevated. A cortical window of approximately 1 × 2 cm was outlined with a round bur on the frontal anterior aspect of the maxillary sinus wall bilaterally. The schneiderian membrane was gently lifted and pushed medially together with the bony window, taking care not to lacerate the membrane if possible. Lacerations were recorded in the patient record and are presented in Table 3. The cortical window was therefore dislocated medial and superior to the placed graft. Particulated, compressed bone was then placed and packed in the anterior and lower parts of the maxillary sinus (see Figure 1 and Figure 3). Following the study protocol, the right prepared sinus cavity was filled with bone without PRP and the left side was accordingly filled with bone prepared and mixed with PRP prior to placement. The amount of bone compressed and placed was recorded in milliliters (Table 4) using a cut syringe as described by Whitman and Berry.[17]

TABLE 3 Lacerations of the Sinus Membrane (Yes/No)

Patient	Right	Left
1	Y	Y
2	Y	N
3	N	N
4	N	Y
5	N	N
6	N	N
7	N	N
8	Y	N
9	N	N
10	N	N
11	N	Y
12	N	N
13	Y	N
14	N	Y
15	N	N
16	N	Y
17	Y	N
18	Y	N
19	Y	N
Total 38	7	5

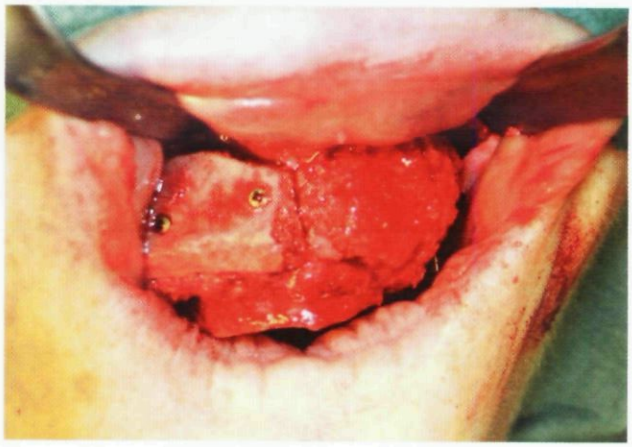

Figure 3 Clinical perioperative situation of grafted maxilla. Particulated bone with platelet-rich plasma on the left side and block bone on the right side.

Onlay Grafting with Bone Blocks, Maxillary Right Side. From the iliac crest, a corticocancellous block of bone was placed as a screw-retained graft on the right frontal subnasal area of the maxilla. The recipient site on the maxilla was freed from periosteum and prepared with a round bur until small spots of bleeding were noted. Care was taken to adjust the graft to fit the anatomy of the maxilla, and a minimum of two 1.7 mm titanium screws (6–13 mm length) were used for securing the graft without any possibility of micromovement. The volume of the bone grafted in this area was determined using the Archimedes principle by lowering the piece of bone into saline and measuring the volume by displacement as presented in Table 4.

Onlay Grafting with Particulated Bone, Maxillary Left Side. As in the left sinus area, the left frontal subnasal part of the maxilla was grafted with particulated bone mixed with PRP. The maxilla was also prepared on this side, in the same manner as the right side, with a round bur, and the moldable mixture of bone and PRP was placed onto the buccal part of the maxilla. The amount of bone was recorded in the same manner as with the sinus augmentation procedures.

Finally, the buccal flap of soft tissue was elongated through small incisions of the periosteum to gain full and tension-free coverage of the grafted areas. The incisions were thereafter closed with resorbable sutures (Vicryl®, Johnson & Johnson AB, Sollentuna, Sweden).

More bone was grafted to the test side than to the control side, as seen in Table 4. In 10 patients, bone was also placed to the floor of the nose. Preparation of

TABLE 4 Volume of Grafted Bone (mL) (n = 19)

	Sinus		Front		Nasal Inlay (n = 10)	
	Control	Test	Control	Test	Control	Test
Mean	2.09	2.21	1.82	3.09	0.28	0.30
Range	1.0–3,0 (SD 0.48)	0.5–3.25 (SD 0.77)	1.0–3.0 (SD 0.54)	1.0–5.5 (SD 0.95)	0.25–0.5 (SD 0.07)	0.25–0.5 (SD 0.10)

38 sinuses in total resulted in seven lacerations of the right sinus membrane and five lacerations of the left side (see Table 3).

Implant Procedures

Six months after the grafting procedure, dental implants were installed under local anesthesia. A crest incision with buccal posterior releasing incisions was made, and a flap was elevated. Eight implants were installed in each patient using the Astra Tech TiOblast 3.5 mm fixture (n = 152). Implant lengths and differences between the test and control sides are presented in Table 5. Six months later, healing abutments were connected in a standard fashion. Healing abutments were used in all cases and were replaced by Uniabutments (Astra Tech, Mölndal, Sweden) at the start of the prosthetic work.

Pre- and Postsurgical Care after Bone Grafts and Implant Installation

Antibiotics were administered perioperatively at the initiation of bone graft surgery with benzylpenicillin (3 g × 3) or clindamycin (600 mg × 3) and for the first 24 hours following. Prophylactic antibiotic cover continued for the 10 days following surgery, with either phenoxymethylpenicillin (1 g × 3) and metronidazole (400 mg × 3) or clindamycin (300 mg × 3).

At the time of the installation of dental implants, the patients routinely received 2 g of phenoxymethylpenicillin preoperatively and postoperatively 1 g three times daily for 5 days (one patient received clindamycin 300 mg × 3 owing to previous allergic symptoms from phenoxymethylpenicillin).

Analgesia was provided with acetaminophen and codeine or with a nonsteroidal anti-inflammatory drug for 1 to 2 weeks postoperatively following surgery. Dentures were not worn during the first month following the grafting procedure and for 10 days after implant placement. Before use, they were adjusted and relined with Viscogel® (Dentsply, York, PA, USA).

TABLE 5 Length of Inserted Implants (n = 152)

Length (mm)	n	Test	Control
9	9	6	3
11	23	11	12
13	51	27	24
15	63	30	33
17	6	2	4

Prosthetics

Seven different prosthodontists carried out the prosthetic rehabilitation. All patients received fixed prosthetic restorations with a gold or a titanium framework veneered with acrylic or porcelain teeth.

Follow-Up

Clinical Examinations. Throughout the surgical phase, the patients were closely monitored every week for the first month after surgery and were seen again at the third month postsurgery after bone grafting and implant installation. Any complications or problems were recorded. The patients were instructed in oral hygiene by their prosthodontists and checked regularly.

Radiographic Examinations. Parallel intraoral techniques were used for radiographic examinations and carried out at the Department of Dental Radiology, Eastman Institute, Stockholm, Sweden. Care was taken to obtain a clear image of the threads on both sides of the implants.

Marginal bone level was measured at baseline (after completion of prosthetic treatment) and after 1 year in function. The radiographs were displayed on a light box and captured by a charge-coupled device camera connected to a desktop computer using a picture analysis system (*NIH Image*, National Institutes of Health, Bethesda, MD, USA). Contrast and light were automatically optimized. The reference point was the end of the vertical section at the cervix of the implant. The

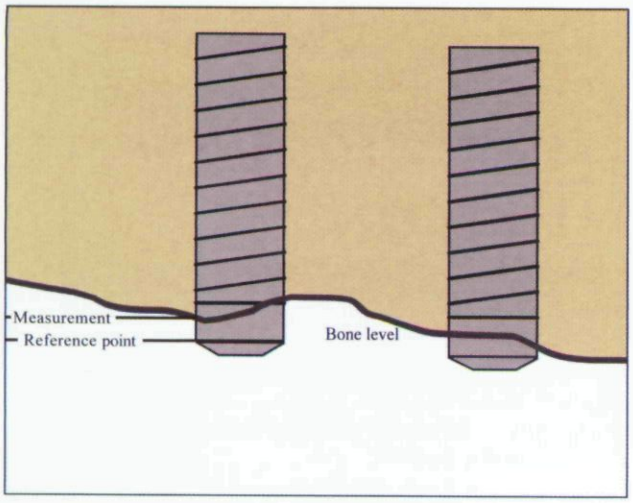

Figure 4 Marginal bone level. The reference point was the uppermost point of the cervical coronal part of the implant.

marginal bone level relative to the reference point was measured on the mesial and distal aspects of each implant. The reference point was the uppermost point of the vertical section at the cervix of the implant (Figure 4). A mean value was calculated for each implant.

Resonance Frequency Analysis. RFA was performed at implant installation, at abutment connection, and after 1 year of loading, meaning that the suprastructures were removed to allow the measurements. Different transducers (Osstell), according to and correcting for the different abutment or fixture level solutions, were used.

Statistics

The Wilcoxon signed rank test was used for pairwise comparison between test and control implants. The Spearman correlation test was used for correlations.

RESULTS

Observations after Surgery

Infections following bone grafting were rarely seen. However, two patients experienced localized (posterior sites) infections that resolved with local drainage and oral clindamycin.

A marked resorption of the bone graft was generally seen at the time of fixture installation at both test and control sides.

At abutment operation, four patients displayed a total of eight cover screws penetrating the mucosa. These patients also showed some marginal bone loss around the implants.

Clinical Follow-Up

All 19 patients were followed throughout the study period. At abutment operation, two fixtures from the control side (right side, third implant, position R3) in two patients were found to be mobile and were removed. No further failures were seen during the follow-up or at the first annual check-up, when all bridges were removed for implant stability measurements, giving a survival rate of 100% for test and 97.4% for control implants. The overall survival rate for all implants was 98.7% (Table 6). One bridge was found to be mobile owing to screw loosening.

Radiographic Findings

The marginal bone level measurements showed a tendency to less resorption on the test (PRP) side, but the difference was not significant. The mean marginal bone level and standard deviation for all implant sites were 1.5 $\pm$ 1.7 mm on the control side (range 0–3.6 mm) and 1.3 $\pm$ 1.9 mm on the test side (range 0–3.6 mm) at baseline and 2.0 $\pm$ 0.9 mm (range 0–4.2 mm) on the control side and 1.8 $\pm$ 1.1 mm (range 0–3.8 mm) on the test side after 1 year in function (not significant). The mean marginal bone level in the posterior region (R/L 3 and 4) was 2.7 $\pm$ 1.0 mm on the control side and 2.7 $\pm$ 0.9 mm on the test side at baseline. After 1 year in function, the mean levels were 3.9 $\pm$ 0.8 mm on the control side and 3.7 $\pm$ 0.9 on the test side (not significant).

RFA Findings

RFA measurements revealed significantly better stability for implants at the test (PRP) sides at the time of

TABLE 6 Implant Study Life Table and Survival Rates

	No. of Implants	Failed Implants	Survival Rate in Interval (%)	Cumulative Survival Rate (%)
Abutment operation	152	2	98.7	98.7
1 yr of loading	150	—	100	98.7

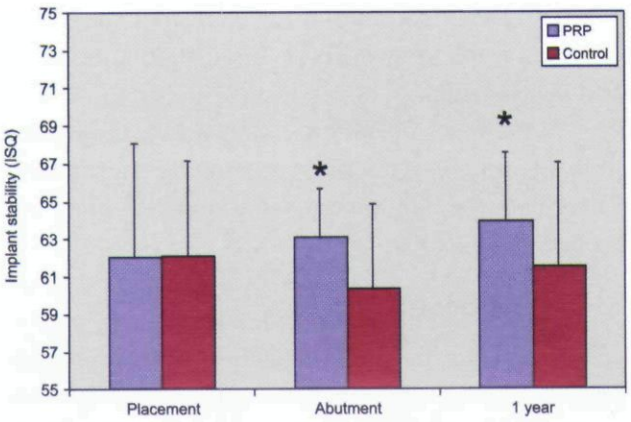

Figure 5 Results from resonance frequency analysis measurements comparing platelet-rich plasma (PRP) and control implants. ISQ = implant stability quotient. $^*p < .05$

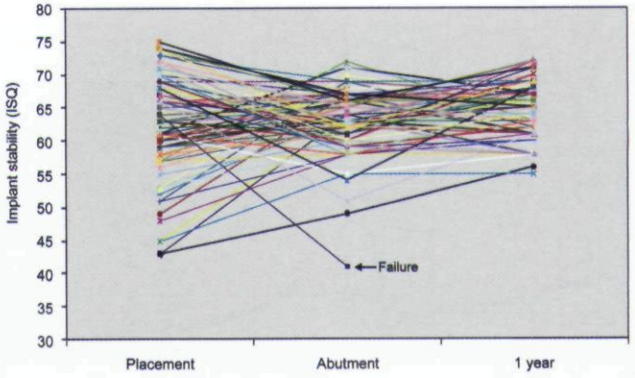

Figure 7 Plot of resonance frequency analysis values for all implants. Note decreasing values for failing implant. ISQ = implant stability quotient.

abutment connection ($p < .05$) and after 1 year of loading (Figure 5).

Comparison between implants placed in the anterior maxilla showed significantly better stability at the test side at abutment connection ($p < .05$) (Figure 6). No differences were seen for implants placed in the posterior regions, representing implants in grafted maxillary sinuses.

The one implant that was recorded of the two that failed showed a dramatic drop in stability from placement (ISQ 64) to abutment connection (ISQ 40) (Figure 7).

DISCUSSION

The present clinical study showed a successful clinical outcome after 1 year with implant-supported bridges following grafting of either blocks of bone or particulated bone to the severely resorbed edentulous maxilla, irrespective of whether PRP was used. Only 2 of 152 implants were lost during the study, which resulted in a survival rate of 98.7% after 1 year. The marginal bone conditions were stable, with no statistically significant differences between test and control sites. RFA showed significantly better implant stability for test sites at abutment connection and after 1 year of loading. Since, in the anterior region, implants in bone blocks were compared with particulated bone, it would seem logical that the type of graft would affect implant integration more strongly than the presence of PRP. This is supported by the fact that there was no difference when comparing the posterior implants placed in particulated bone with and without PRP. Moreover, it would be more likely to find PRP-mediated differences in the early phase of healing. Recently, Johansson and colleagues demonstrated lower insertion torque when placing implants in block bone grafts than in particulated bone grafts after 6 months.[18] Their results indicate a lower density for block grafts, which can explain the lower RFA values found in the present study.

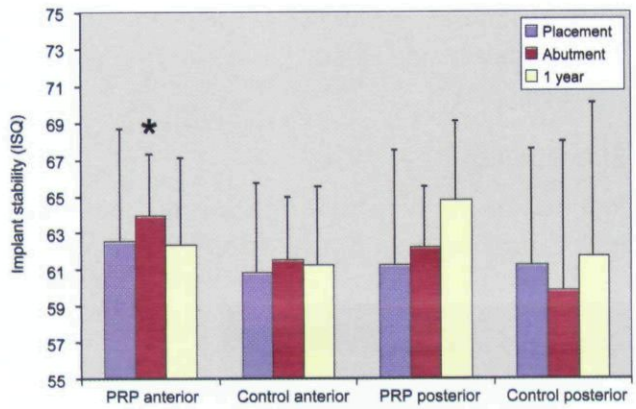

Figure 6 Results from resonance frequency analysis measurements comparing platelet-rich plasma (PRP) and control implants placed in the anterior and posterior maxilla. ISQ = implant stability quotient. $^*p < .05$

Numerous previous publications have reported autogenous bone grafting techniques to the severely resorbed maxilla.[7,9,10,12] Blocks of bone seem to be the preferable choice for onlay grafting, whereas particulated bone is mainly used for maxillary sinus floor augmentation. Extensive resorption of block bone has been reported; which, in part, may be the result of the revascularization process.[12] In 1985, Boyne and colleagues described a technique in which cancellous bone and marrow were held together by a titanium mesh implant

to reconstruct the resorbed maxillary alveolar crest.[19] Resorption of the graft was less in the maxilla (10–20%) than in the mandible over a maximum observation period of 10 years in a report of 15 patients.

The present clinical investigation was designed to evaluate the use of particulated bone mixed with PRP as an alternative to onlay bone blocks. One reason was that particulated bone with PRP is easier to mold to the new contour of the residual bone crest. Further, it was hypothesized that particulated bone with PRP would be incorporated more quickly because angiogenic and osteogenic cells may have an immediate access to the spaces between the particles of the graft and PRP may have a stimulating effect on cell migration and differentiation. The present study design had an impact on the RFA measurements at abutment connection and after 1 year in function because implants placed in particulated bone showed a higher stability than implants in block bone. It was therefore not possible to prove that this was an effect of PRP and not of the type of graft, as discussed above. Nevertheless, although no positive effects of PRP on the bone graft could be demonstrated, it facilitated handling of the particulated bone graft. The clinical, radiographic, and RFA outcomes showed that particulated bone can be used as onlay grafts.

The literature on the combination of particulated autogenous bone, platelet gel, and dental implants is sparse, as also concluded in recent review articles.[20–23] Most studies combining bone grafts and PRP have not investigated healing of implants. Matras pointed out the potential of fibrin glue in oral and maxillofacial surgery.[24] Marx and colleagues evaluated 88 patients with mandibular continuity defects who were randomized for treatment with autogenous bone grafts with or without the addition of PRP.[14] At baseline, a monoclonal antibody study indicated that the sequestered platelets and the particulated iliac donor bone matched each other, showing levels of TGF-β and PDGF present in the PRP preparation and receptors positive for TGF-β and PDGF in the bone graft. After the final consolidation time of 6 months, dental implants were placed with at least one implant per grafted area. This enabled them to obtain cores of bone for histomorphometric analysis. Monoclonal antibody staining confirmed the presence of TGF-β-positive but not PDGF-positive cells. The histomorphometric analysis revealed more trabecular bone area in the PRP group (74.0 ± 11%) than in the bone graft group without PRP (55.1 ± 8%) and the native mandible (38.9 ± 6%). Furthermore, on panoramic radiographs after 2, 4, and 6 months, the PRP-treated defects matured twice as rapidly as the control group.

Similar clinical findings had earlier been reported by Tayapongsak and colleagues, who used autologous fibrin as an adhesive for particulated bone grafts in mandibular reconstruction.[25] Of 33 cases reviewed, 32 were reported to be successful and to fulfill the criteria of Marx and Stevens for successful mandibular reconstruction.[26] Three advantages of the method were pointed out by Carlson in the discussion following the article: (1) autologous fibrin adhesive (AFA) helped prevent displacement of the grafted bone particles after placement into the recipient site, (2) AFA seemed to facilitate remodeling, and (3) the use of AFA seemed to reduce the rate of wound dehiscences and complications following the bone grafting.[27] In the present study, molding of the graft was improved by adding platelet gel. Moreover, neither wound dehiscence nor infections were seen in the test or control sides in our 19 patients throughout the study. Histologic analysis of biopsies retrieved after 3 and 6 months from the study patients is presently being performed, which may cast light on the possible effects of PRP on bone formation and remodeling.

The inconclusive results from experimental studies of bone grafts and PRP further underline the complexity of the issue.[28,29] Fennis and colleagues used a goat model to evaluate the effect of PRP in an angular resection and immediate reconstruction setting.[30,31] Radiographic and histological examinations showed enhanced bone healing after 6 and 12 weeks but not after 3 weeks. Jakse and colleagues failed to demonstrate any positive effects of PRP used in a sinus lift study on sheep.[32] Similar results were reported by Butterfield and colleagues using a sinus lift model in rabbits.[33] Autogenous iliac crest grafts with or without PRP were evaluated after 2, 4, and 8 weeks. Histomorphometric analyses of the grafted sites showed no differences.

At the start of the present study, only one technique for preparing PRP preoperatively was available, which was the same as used by Marx and colleagues.[14] However, we used autologous thrombin for clotting, whereas Marx and colleagues used bovine thrombin. The reason was the current concern about the risk of transmitting and inducing diseases, such as Creutzfeldt-Jakob, and the possibility of cross-reactions with human factor Va, causing episodes of bleeding.[34]

More efficient methods ensuring high concentrations of platelets have been developed since the initiation of the study. The learning curve for the perioperative PRP preparation was evident in our results. The range of the concentrated platelet count varied, which consequently divided the patients into two groups: one with a lower concentration of platelets in PRP and one with higher platelet counts in PRP. This may have affected the results. Marx and colleagues measured a 338% increase in the mean PRP platelet count compared with baseline.[14] This observation is important because the biologic effectiveness of PRP is probably dose dependent. In our study, patients in the latter group had a mean platelet concentrate increase of 330%, which is in accordance with the results of Marx and colleagues.[14]

Weibrich and colleagues evaluated the influence of donor age, gender, and platelet count on growth factor levels in PRP.[35,36] Different methods of extracting PRP affected the total amount of growth factor reported.[37–39] The optimal platelet concentration needed for a significant clinical effect on osseous regeneration is presently not known. Peri-implant bone regeneration with PRP around dental implants was tested in a rabbit model by Weibrich and colleagues.[40] Femora were exposed, PRP was injected into the implant cavity, and the implant was also moistened with PRP before insertion. On the control side, the implant was inserted without PRP. Sequential intravital staining was performed, and histomorphometric evaluation followed after 4 weeks. The preparation of PRP, as in our study, produced different platelet concentrations. Intermediate platelet concentrations (×2–6 concentration, 503,000–1,729,000 platelets/μL PRP) produced a positive effect on the regenerated bone with the histologic labeling techniques tetracycline, xylenol orange, and calcein injected on days 7, 14, and 21, respectively. To the surprise of the authors, the higher concentrations of PRP seemed to inhibit bone regeneration. Levels below 1,000,000 platelets/μL PRP had a suboptimal effect on bone regeneration. No difference in bone-to-implant contact was found in any of the platelet concentration groups. The authors concluded that PRP did not accelerate the osseointegration rate of the endosseous implants used in the study. Further studies on the contents of PRP and its interactions with growth factors are necessary to optimize its use and its potential clinical effect in humans.

With regard to the timing of implant placement, today most clinicians favor a staged procedure before simultaneous placement of implants. A staged procedure allows for primary healing and revascularization of the bone graft prior to implant placement, improving implant integration. In a series of studies by Rasmusson and colleagues, it was shown that a staged procedure resulted in more bone in contact with the implant surface and greater implant stability as measured with RFA.[41–43] This was confirmed in a clinical histologic study by Lundgren and colleagues using microimplants retrieved from grafted patients and evaluated with histology.[44] Microimplants placed after 6 months of healing showed more bone contact than microimplants simultaneously placed with the dental implants.

A staged procedure also facilitates correct positioning of implants, which Blomqvist and colleagues showed is necessary for the maintenance of implant stability during functional loading.[45] However, their implants were placed after 6 months of healing, which may explain the low failure rate.

Most studies on bone grafting of the totally edentulous maxilla reporting high failure rates have used implants with a turned and relatively smooth surface. Ivanoff and colleagues demonstrated histologically more bone contact with TiOblast microimplants than with machined controls after 2.5 to 8 months of healing in a group of 27 patients.[46] It is therefore possible that the use of TiOblast implants influenced the outcome of the present study positively.

The RFA measurements revealed that the levels of implant stability in the grafted maxillae corresponded well with those of other clinical studies. Implants with low RFA values increased in stability over time, whereas high initial stability decreased to around ISQ 60.[47–49] Failing implants showed a dramatic loss of stability from placement to abutment connection. At the 1-year control, no implant showed a critically low ISQ value (< 50), indicating successful integration of all remaining implants.

CONCLUSIONS

The present clinical study showed that a high implant survival rate and stable marginal bone conditions can be achieved after 1 year of loading in the maxilla with autogenous bone grafting whether or not PRP is used. RFA measurements revealed differences at abutment connection, which could be explained by the type of graft rather than as an effect of PRP. Although no obvious positive effects of PRP on bone graft healing were

demonstrated, the handling of the particulated bone grafts was improved.

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