Correlation of Platelet Growth Factor Release in Jawbone Defect Repair – A Study in the Dog Mandible

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ABSTRACT

Background: Platelet concentrate/platelet-rich plasma (PRP) has been studied extensively in various experimental models and there is some agreement among workers to its early effect in bone regeneration and healing. We have earlier showed in vitro that titanium in whole blood activates the thrombogenic response to a higher degree than PRP and that a fluoridated test surface augmented the effect compared with control.

Purpose: We designed this study to evaluate the effect of PRP and whole blood on bone regeneration in a dog implant defect model and, in addition, the effect of a test surface modified in hydrofluoric acid. A correlation attempt between platelet count, release of growth factors, and bone regeneration was made.

Materials and Methods: Six dogs were used and simultaneously with the experimental surgery and implant installation, autologous PRP was prepared. Defects were prepared (6 mm in diameter and 5 mm deep), and implants were installed (TiO_2 gritblasted and hydrofluoric acid treated [test] or TiO_2 gritblasted [control], 5 mm in diameter and 9 mm long) in defects filled with either PRP or whole blood. Randomization of sides between PRP and whole blood, and sites for test and control implants were made. Blood samples were collected from PRP and whole blood. The dogs were killed after 5 weeks of healing, and samples with implants and surrounding bone were collected and processed for analysis. Enzyme linked immunosorbent assays were used for detection of growth factors in PRP.

Results: The mean increase of platelet count was 424% in PRP. A correlation for platelet counts and transforming growth factor β was found in each dog ($r^2 = 0.857$). Approximately 50% of the region of interest (ROI) in the defects was filled with new bone after 5 weeks. No difference could be observed in ROI by using PRP or whole blood in the defects regarding new bone formation, bone in contact with implant, or distance to first bone contact. However, the fluoridated implants exhibited more new bone formation ($p = .03$) compared with control, regardless of comparing PRP or whole blood, and also displayed a shorter distance from first bone contact to the margin of the bone envelope ($p = .05$).

Conclusions: Platelet concentrate/PRP failed to show more new bone regeneration in a peri-implant defect model compared with whole blood. Implants treated with hydrofluoric acid displayed higher percentages of bone fill in the defect.

KEY WORDS: bone formation, dental implants, experimental study, growth factors, platelet-rich plasma

INTRODUCTION

Since Marx and colleagues in 1998 described the effects of platelet-rich plasma (PRP) in maxillofacial reconstruction, the interest and the amount of published literature have increased significantly.[1] Clinical and experimental investigations have been undertaken in many fields of dentistry and medicine, and the clinical use of platelet concentrate has been promising, but its

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DOI 10.1111/j.1708-8208.2011.00405.x

effect is hard to prove in different studies.[2,3] A broad spectrum of applications has been tested (e.g., soft tissue healing, tendon and bony repair), however, in the field of maxillofacial reconstructions, the effect on bone regeneration and integration of dental implants have been most contradictory.[4]

The present research group has performed studies[5–7] where, for instance, PRP has been evaluated for incorporation of particulate bone grafts in patients. The results of the studies indicated that new bone formation in particulate bone grafts is enhanced with PRP, as also reported by others.[6,8] On the other hand, an in vitro study demonstrated less pronounced thrombogenic activation by titanium in whole blood than in PRP, resulting in less release of growth factors (GFs) in the latter. Moreover, the thrombogenic activation was stronger for fluoridated than for nonfluoridated titanium.

Therefore, this study was designed to evaluate the integration of fluoridated titanium implants in bone defects in the presence of PRP or whole blood. The possible correlation between GF release in PRP and new bone formation was also investigated.

MATERIALS AND METHODS

Animals

Six female (age 2 years) Labrador Retriever dogs weighing between 25.5 and 30.0 kg were used in the study. The dogs were kept in the Laboratory for Experimental Biomedicine at the Sahlgrenska Academy, University of Göteborg.

The study protocol was approved by the Regional Ethical Committee for Animal Research at the Sahlgrenska Academy, University of Göteborg.

Anesthesia

As presurgical sedative, an intramuscular (i.m.) (0.05 mg/kg) of acepromazin (Plegicil® vet., Pharmaxim AB, Helsingborg, Sweden; 10 mg/mL diluted with 0.9% NaCl to 2 mg/mL) was given. General anesthesia induced with intravenous propofol (Rapinovet® vet., Schering-Plough, Stockholm, Sweden) 4 mg/kg, continued by endotracheal intubation, and maintained by isofluran (Isoba® vet., Schering-Plough, Stockholm, Sweden). Buprenorphin, i.m. 0.018 mg/kg (Temgesic®, Meda AB, Göteborg, Sweden) was used as analgesics.

Local anesthesia was given at the experimental site of surgery (Citanest®, AstraZeneca AB, Södertälje, Sweden, 30 mg/mL; 1.8 mL per jaw).

Surgical Procedure and Experimental Protocol

Three months prior to the start of the experiment, four mandibular premolars were extracted bilaterally. At the time of experimental surgery, mucoperiosteal flaps were elevated and three defects were prepared with a 6.0 mm–diameter trephine drill. A total of 18 TiO_2-gritblasted and hydrofluoric acid-treated implants (TiOB-F, Osseospeed™, Astra Tech AB, Mölndal, Sweden) and 18 nonfluoridated implants (TiOB, Microthread™, Astra Tech AB), 3.5 mm in diameter and 9 mm in length, were used. The implants were placed centric in the defect so that approximately 4 mm were in bone and 5 mm exposed to the defect. The defect width, from implant surface to the bone wall, was about 1.25 mm (Figure 1). Each side received either two TiOB-F and one TiOB implant or two TiOB and one TiOB-F implant by randomization. PRP and whole blood were randomly administered to the right or the left side of the mandible.

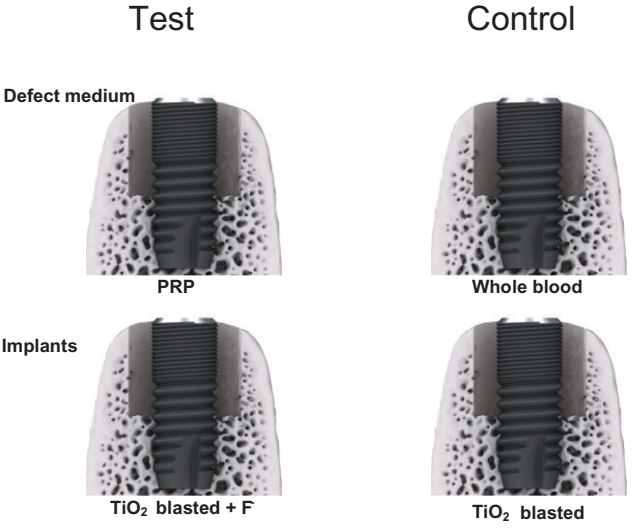

Figure 1 Four different variables were tested in the defect model. Sides of test and control (PRP and whole blood) were randomized to either the left or right side, and test and control implants (TiO_2 blasted + F^- and TiO_2 blasted) were randomized to positions within each jaw in both sides. Implants of 3.5 mm wide and 9 mm long were placed in defects with Ø 6 mm and depth of 5 mm. Supporting cancellous bone was therefore 4 mm after placement of implants; the distance from implant to defect wall was estimated to be 1.25 m. (PRP = platelet-rich plasma.)

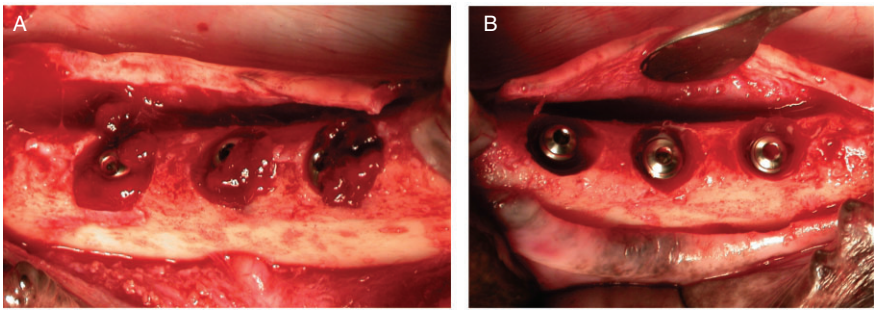

Figure 2 *A*, In all animals, sides were randomized between test (PRP) and control (whole blood). Implants with hydrofluoric acid modifications (test) or without (control) were randomly inserted in each jaw in either one or two positions in the three defects per jaw, respectively. This figure illustrates the platelet gel placed in the defects of the PRP side. Note the total size of defects of 6.0 mm and the defect space beside the implant of approximately 1.25 mm around implants. *B*, Defects on whole blood side were passively filled with blood as control medium randomly assigned to one of the sides of each dog mandible. (PRP = platelet-rich plasma.)

Preparation and Delivery of PRP and Blood Counts

Fifty cubic centimeter of venous whole blood was drawn from the radial vein of each dog during surgery. The blood was separated in a centrifuge (Platelet Concentrate Collection System, 3i, Palm Beach, FL, USA) using the manufacturer's instructions. Citrate phosphate dextrose at a ratio of 1 to 10 mL blood was added subsequently to achieve anticoagulation. After separation, a platelet concentrate was collected and the coagulation was initiated with 10% calcium chloride. Samples of activated PRP were collected and stored at −70°C for pending analysis. At the time of surgery, of the respective dog, a blood sample was collected and the peripheral platelet count in whole blood was recorded as well as platelet count in the PRP. Values for leukocytes and erythrocytes were recorded as well. Cell counts were made mechanically (ADVIA 120 Hematology Analyzer, Bayer Inc., Göteborg, Sweden at Cani-LabEqui-Lab, Halmstad, Sweden).

PRP was administered to the experimental sites with a syringe immediately after implant placement. On the whole blood side (control), passive filling of blood was ensured before suturing (Figure 2, A and B). The flaps were then repositioned and closed with resorbable sutures (Vicryl®, Johnson & Johnson AB, Sollentuna, Sweden).

Antibiotics (10 mg/kg amoxicillin/clavulanic acid, Synolux vet®, Orion Pharma AB, Animal Health, Sollentuna, Sweden) were administered twice daily during 8 days. The dogs were kept on a soft diet during the entire study period.

After 5 weeks of healing, the animals were euthanized by an overdose of pentobarbital (Mebumal®, ACO läkemedel, Solna, Sweden).

Tissue Processing

Implants and surrounding bone from the mandibles were retrieved *en bloc* and fixed by immersion in 4% buffered formaldehyde (Figure 3). Dehydration of the specimens was performed by an increasing and graded series of ethanol and subsequently infiltrated and polymerized in light-curing resin (Technovit® 7200 VCL, Heraeus Kulzer GmbH & Co., Wehrheim, Germany). Ground sections, approximately 20 µm thick, were taken through the central part of the block and along the longitudinal axis of the implants (buccal to lingual of the mandible) and prepared by sawing and grinding[9]

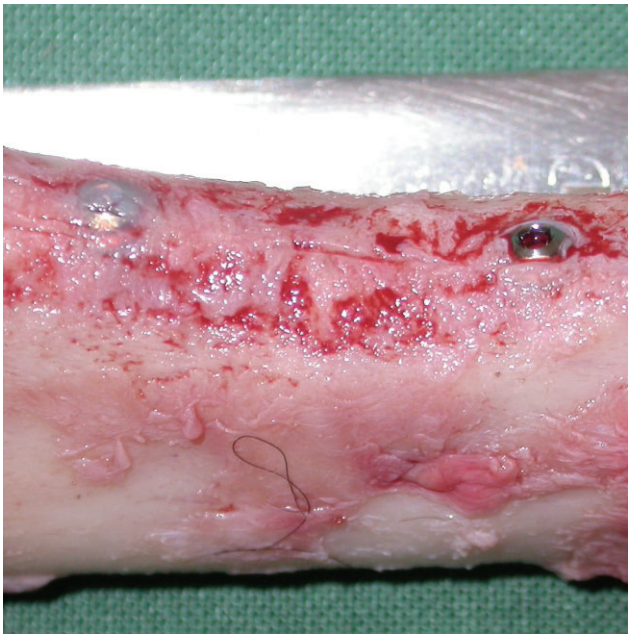

Figure 3 Samples were retrieved en bloc before sectioning and tissue processing. This example is from a test side with PRP. Bone levels at margins varied within sides as seen here. (PRP = platelet-rich plasma.)

(EXAKT Apparatebau GmbH & Co., Norderstedt, Germany). The sections were stained with toluidine blue, 1%.

Histological Examination

Examinations of each section were performed in a Nikon Eclipse 80i microscope (Teknooptik AB, Huddinge, Sweden) equipped with an Easy Image 2000 system (Teknooptik AB) using ×1.8 to ×100 magnifications for histological evaluation.

All measurements were made on both sides of the implants, resulting in a total of 72 sides in 36 specimens.

Morphometric calculations were made in a region of interest (ROI) as defined by the two defect walls (bottom and side), a line from the most superior point of the bone envelope at the defect wall (perpendicular to the implant) to the implant and the implant surface (Figure 4). The morphometry comprised the following measurements: (1) the percentage bone area in the ROI; (2) the percentage of bone-to-implant contact (BIC) in the ROI; and (3) the distance in millimeter from the superior border of the ROI perpendicular to the implant to the first point of new bone on the surface.

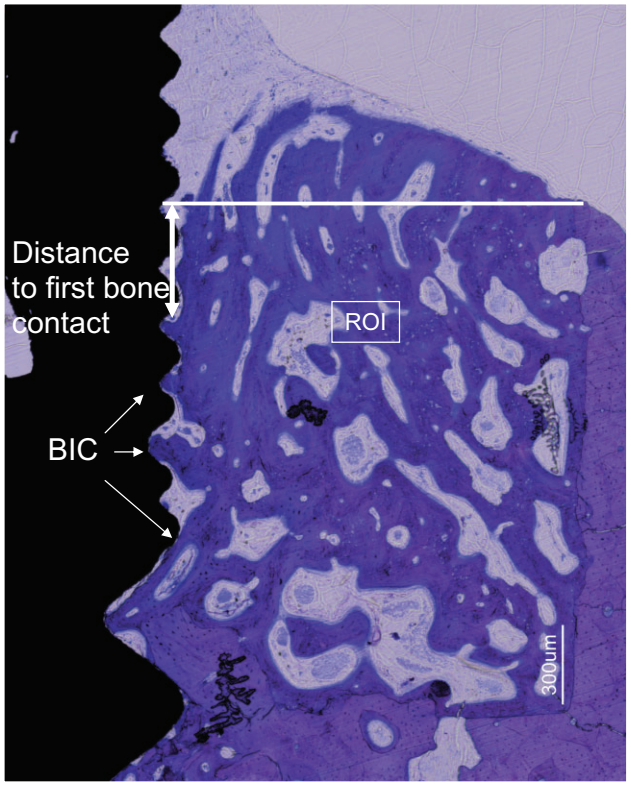

Figure 4 Illustration of ROI underline with implant wall and the two defect walls as borders. Distance to first bone contact measured from line at top of ROI to most coronal point of bone contact of implant. Areas of BIC pointed out.
(BIC = bone-to-implant contact; ROI = region of interest.)

Detection of GF Release in PRP

Enzyme immunoassays were used for detection of β-thromboglobulin (β-TG), platelet-derived GF (PDGF), vascular endothelial GF (VEGF), and transforming GF β (TGF-β). β-TG in plasma was analyzed using Asserachrom™ (Diagnostica Stago, Asnières-sur-seine, France). An immunoassay was used to detect the levels of PDGF in PRP after activation in the experiment (Quantikine™, R&D Systems, Inc., Minneapolis, MN, USA). For detection of VEGF, an enzyme linked immunosorbent assay (ELISA) for human VEGF was used (ELISA Development Kit 900-K10, PeproTech EC, London, UK). TGF-β was analyzed with a combined ELISA kit for mouse/rat/porcine/canine TGF-β 1 (Quantikine™, R&D Systems, Inc.).

Statistics

Mean values and standard deviations (SDs) for observations in each dog were calculated. Wilcoxon signed rank test was used and a p value $< .05$ was considered statistically significant. Paired Student's t-test was additionally used for the histomorphometric measurements.

RESULTS

Animals and Surgery

The surgery and postoperative healing were uneventful in all animals.

Blood Samples

The blood samples collected from the dogs preoperatively showed healthy conditions in blood counts (Table 1). Samples from the PRP revealed that white blood cell count after sequestration was lowered in four out of six dogs, whereas in two dogs the levels were slightly increased. Red blood cell (RBC) count showed reduction of erythrocytes in plasma (5.8×10^{12}/L to 0.3×10^{12}/L) to a mean level of 5.3% of the initial value. Reduction of hemoglobin levels in PRP corresponded well with RBC; 3.8% was found in PRP (see Table 1).

PRP Preparation

A mean volume of 7.8 mL (range 7.0–8.5 mL) of PRP was collected in the six animals. Mean preoperative platelet count was 255 (range 217–290) and after

TABLE 1 Blood Counts in Whole Blood and PRP

Dog No.	WBC* Preop	WBC-PRP	RBC† Preop	RBC-PRP	Hb Preop	Hb-PRP
1	10.7	1.0	5.6	0.04	128	0
2	6.2	4.4	5.5	0.4	140	8
3	8.1	3.2	5.7	0.09	140	0
4	6.4	7.8	5.8	0.3	140	4
5	8.9	9.1	6.9	0.82	154	17
6	9.3	8.9	5.3	0.17	121	2
Mean	8.3	5.7	5.8	0.3	137	5.2
SD	1.74	3.35	0.56	0.28	11.4	6.52

*Ref. value for dogs: $(6–17) \times 10^9$/L.
†Ref. value for dogs: $(5.5–8.5) \times 10^{12}$/L.
PRP = platelet-rich plasma; RBC = red blood cell; SD = standard deviation; WBC = white blood cell.

concentration 1055 (range 343–1343). In one of the six animals, the sequestration of platelets was lower, with only 18% increase from the basal platelet count (PRP platelet count, range 118%–564%, mean 424%). At the time of surgery, a note was made that the PRP had a weak and light appearance, which is later confirmed in the cell counts.

Detection of Growth Factors

The immunoassays used for β-TG and PDGF did not show any detectable levels in the samples implying that no cross reactions were seen for the antibodies used in these ELISAs and thus did not match the blood of the Labrador dog species.

For VEGF, only a weak cross reactivity was seen. The levels are presented in Figure 5.

TGF-β was detected and data are presented in Figure 6. These values were found to correlate to the platelet count found in PRP for each dog ($r^2 = 0.857$), as seen in Figure 7. As a second step, attempts to correlate levels of TGF-β detected with new bone formation, BIC, and distance to first bone contact in the samples with PRP (in both surfaces) were made. A correlation was, however, not found when comparing all six dogs as one unit. In contrast, if the dog with the deviant platelet count was excluded in the regression, a tendency of correlation was observed in the regression for TGF-β and distance to first bone contact (Figure 8) but not for new bone formation and BIC.

Histology and Histomorphometry

Bone was found to regenerate from both the bottom and the lateral wall (corner) of the defect in an angle toward the top of the implant. Resorption of the marginal bone was seen in the majority of specimens (Figure 9).

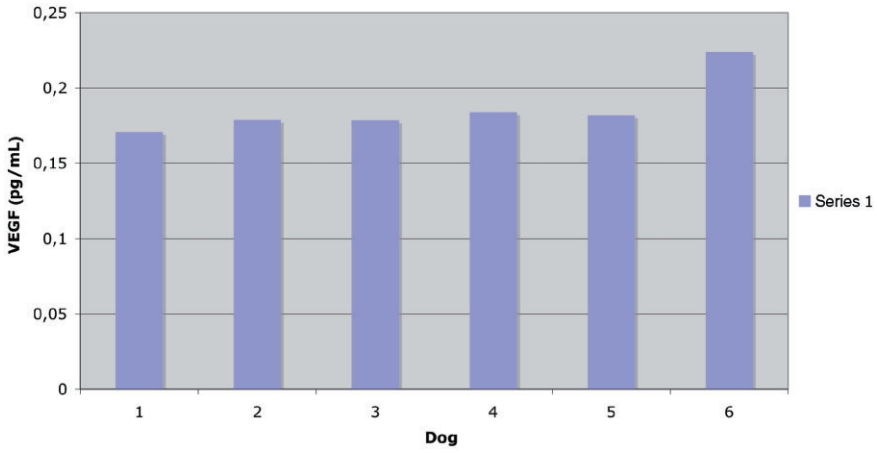

Figure 5 Only traces of VEGF were detected indicating a low level of cross reactivity with the specific ELISA used in the experiment. (ELISA = enzyme linked immunosorbent assay; VEGF = vascular endothelial growth factor.)

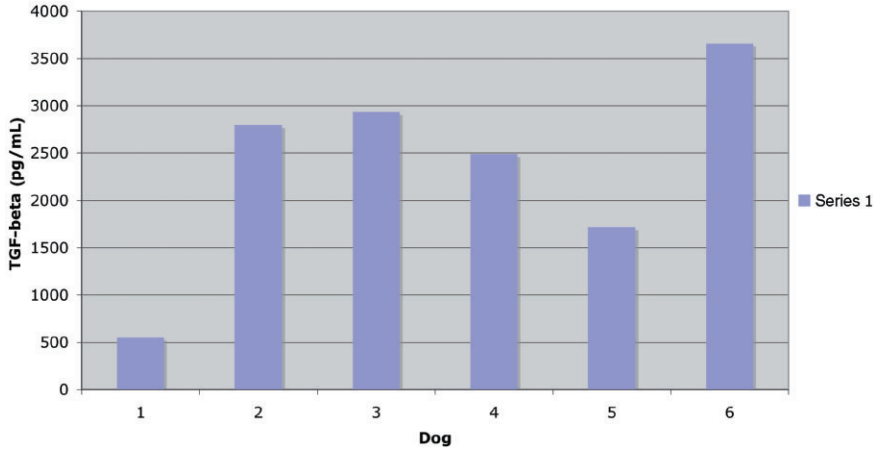

Figure 6 Levels of TGF-β in PRP. Note the comparably low level for dog no. 1, which correlates well with the low amount of platelets in PRP for this dog compared with platelet count in whole blood (18% increase) (see Table 1). (PRP = platelet-rich plasma; TGF-β = transforming growth factor β.)

TiOB-F versus TiOB Implants

Fifty-six percent (SD ± 6) of the ROI in the defect was filled with new bone for TiOB-F implants and 51% (SD ± 6) for TiOB implants after 5 weeks of healing. There was a statistically significant difference ($p = .03$) in favor for the TiOB-F implants (Table 2).

No difference in BIC was found between test and control implants in blood or PRP (Table 3).

The TiOB-F implants exhibited a closer distance (millimeter) to first bone contact measured from a perpendicular point on the implant to the most superior point of the bone envelope compared with the control, irrespective of defect-fill PRP or whole blood ($p = .0511$). In those samples, the bone had contact higher up on the surface of the TiOB-F implants closer to the marginal reference point compared with the control TiOB implants in defects filled with whole blood ($p = .019$) (Table 4).

PRP versus Whole Blood

The morphometric measurements revealed no differences between PRP and whole blood defects for any of the parameters (see Table 3).

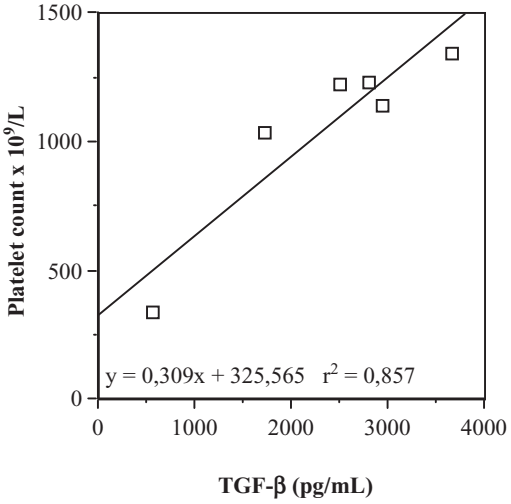

Figure 7 Regression analysis of correlation between platelet count and release of TGF-β. Note the value of dog 1 in the left lower corner of the plot. (TGF-β = transforming growth factor β.)

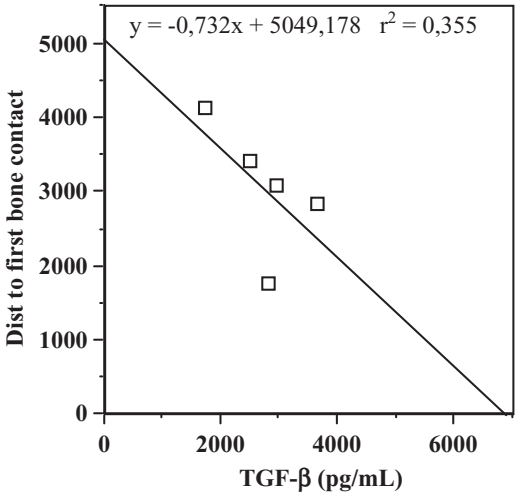

Figure 8 Regression analysis of correlation between distance of bone contact on the implants in the defects and release of TGF-β when the one deviating sample of platelet count (dog 1) is left out. (TGF-β = transforming growth factor β.)

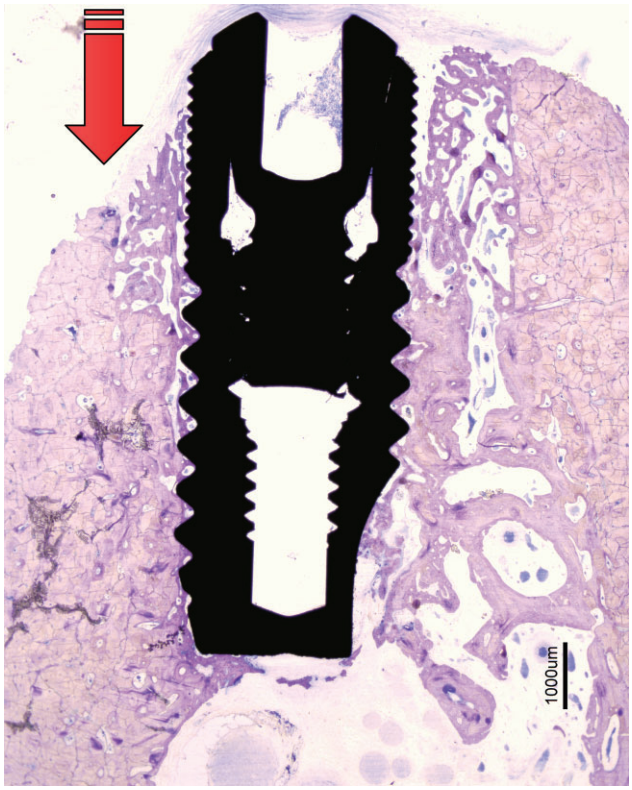

Figure 9 At the harvesting of the samples, a resorption of the bone envelope had simultaneously taken part as well as new bone formation in the defect illustrated by the implant top positioned above the bony envelope.

DISCUSSION

The present study confirmed previously reported findings that PRP does not enhance regeneration of bone defects and the integration of dental implants.[3] Administration of PRP in the defects around the implants in the present animal model did not result in increased new bone formation or bone-implant contacts. Interestingly, the fluoridated implants exhibited significantly more new bone in the defects filled with blood compared with the control implants. Moreover, the distance to the first bone contact was significantly shorter for the TiOB-F than for TiOB implants in the defects filled with blood. It may be speculated that a stronger activation of the coagulation cascade by the fluoridated implant may explain the differences.

This is in accordance with a previous in vitro study where a more pronounced thrombogenic activation was observed for fluoride-treated implant surface than a control surface.[7] A higher local release of GFs and generation of thrombin in the defect adjacent to the implant may explain the observed higher rate of bone regeneration.

The concentration of PRP in this study is in accordance with previous studies[1,8,10] and the release of TGF-β correlated well to the level of concentrated platelets. Unfortunately, albeit not possible to detect any PDGF in the samples, it illustrates more the low sensitivity of the commercially available ELISA test that was used in this and other studies. However, Vieweg and colleagues[11] found a cross reaction between human and beagle dog PDGF-AB and could detect PDGF in plasma with human ELISA kits used on dog serum. The drawbacks with the ELISA test used here in this study were further illustrated in the failure to detect β-TG and only traces of VEGF.

TGF-β, PDGF, and other chemoattractants[2] trigger leukocytes to migrate from adjacent vessels into the blood clot of bone defect.[12] An elevated level of thrombin has a similar effect and may contribute to a faster

TABLE 2 New Bone Formation in Defects. Mean Values within Each Dog Have Been Calculated In Order to Get One Value per Dog for Each of the Treatments. There Was a Statistically Significant Difference between TiOB and TiOB-F But None between PRP and Blood

	PRP	Blood	TiOB	TiOB-F	PRP Blood	TiOB-TiOB-F
N	6	6	6	6	6	6
Min	0.4461	0.4838	0.4297	0.5002	–0.1349	–0.0736
Median	0.5146	0.5208	0.5246	0.5383	–0.0228	–0.0604
Max	0.6531	0.6534	0.5872	0.6411	0.0779	–0.0035
Mean	0.5266	0.5453	0.5124	0.5595	–0.0187	–0.0471
SD	0.0744	0.0606	0.0587	0.0587	0.0746	0.0306
p Value	NA	NA	NA	NA	0.6875	0.03125

NA = not applicable; PRP = platelet-rich plasma; SD = standard deviation.

TABLE 3 BIC in Defect. Mean Values within Dog Have Been Calculated In Order to Get One Value per Dog for Each of the Treatments. The Difference neither between TiOB and TiOB-F nor between PRP and Blood Was Statistically Significant

	PRP	Blood	TiOB	TiOB	PRP Blood	TiOB-TiOB-F
N	6	6	6	6	6	6
Min	0.1018	0.0968	0.1310	0.0915	−0.1313	−0.1838
Median	0.2129	0.2203	0.2283	0.2029	0.0129	0.0185
Max	0.3875	0.2738	0.2870	0.3238	0.1828	0.1235
Mean	0.2230	0.2128	0.2194	0.2164	0.0103	0.0030
SD	0.0971	0.0633	0.0642	0.0929	0.1176	0.1115
p Value	NA	NA	NA	NA	1.0000	0.8438

BIC = bone-to-implant contact; NA = not applicable; PRP = platelet-rich plasma; SD = standard deviation.

organization of the blood clot into a granulation tissue, which subsequently can promote bone formation in a defect.[13–15] The presence of erythrocytes in whole blood (reduced in PRP) may also facilitate bone healing as their presence causes the blood clot to be less dense. The fibrinolytic activity by fibroblasts was reported to be enhanced by hemoglobin in a study by Yoshida and colleagues.[16] Erythrocytes and hemoglobin were obviously present in the defects with whole blood to a higher degree. Therefore, the erythrocytes may give the clot a less dense structure, which in turn may have enhanced the migration of osteogenic cells to the area and support healing with bone.[17] As discussed by Davies, the ability of the implant surface to retain the fibrin and restrain the contraction of the maturing clot on the implant surface is of great importance in a model like this, where the bone formation has to start from a distance of the implant surface.[15]

The defect model in the dog mandible that was chosen has been used and reported on extensively in the literature.[18–22] Akimoto and colleagues[20] investigated the effect of the defect width on bone regeneration. They found that, after 12 weeks of healing, a wider gap between the bony defect wall and the implant (0.5, 1.0, and 1.4 mm) resulted in significantly less BIC and more apical positioned height of BIC on the implant surface.

In our study, after 5 weeks of healing, we found the defects to be well filled with tissue around implants. Histologically, approximately 50% of the defect was filled with newly formed bone. Boticelli[23] studied the events of healing in marginal defects around implants. In a series of papers, it was noted that there was a substantial alteration (horizontal resorption of the buccal bone [56%] and palatal/lingual [30%]) of the adjacent bone in extraction sites after 4 months of healing; the gaps resolved through bone formation from the inside and bone resorption from the outside.[24] In another paper, the formation of woven bone, in a defect similar to the ones in our study (5 × 1.25 mm), was 32.1% (SD

TABLE 4 Distance (mm) to First Bone Contact Measured from a Perpendicular Point on the Implant to the Most Superior Point of the Bone Envelope. Mean Values and Standard Deviations (SDs) Are Shown. Comparisons between Defect Fill (PRP or Blood) and between Test and Control Surfaces Are Given

	PRP	Blood	PRP/TiOB-F	PRP/TiOB	Blood/TiOB-F	Blood/TiOB
Mean	2.83	3.08	2.61	3.11	2.64	3.52
SD	1.29	0.81	1.19	1.44	0.63	0.77
	Comparisons between defect fill and test and control implants					
	PRP vs blood	PRP + blood/TiOB-F vs PRP + blood/TiOB		PRP/TiOB-F vs PRP/TiOB	Blood/TiOB-F vs blood/TiOB	
p Value	0.4937	0.0511		0.4329	0.0191	

PRP = platelet-rich plasma; SD = standard deviation.

3.9). The values from our study are presented in Table 2 (e.g., for PRP, all implants are 52.7, SD 7.4).

Exploring the effects of local administration of GFs in implant defects, Cochran and colleagues concluded, in a fox-hound dog study in mandibular defects around implants, that rhBMP-2 enhanced bone formation in defects.[25] Furthermore, two previous canine model studies reported on the effect of bone regeneration of a PDGF/insulin-like GF-1 (IGF-1) combination around implants and found a positive effect on bone formation with addition of this GF combination.[26,27] Lynch and colleagues[26] used press-fit titanium implants and observed a significant difference with GF addition for BIC and bone fill in peri-implant space after 7 and 21 days. Stefani and colleagues[27] used fresh extraction sockets in the mandible of dogs and administered 4% methylcellulose gel with or without the PDGF/IGF-1 combination. These authors concluded that the tested combination of GFs had effect in the early phase of bone regeneration as they found a higher degree of BIC after 3 than in 12 weeks.

The use of PRP to enhance osseointegration of implants with or without an adjacent defect has been discussed earlier, but the effects on the human situation are not well understood.

In a study on 12 adult minipigs, Zechner and colleagues[28] investigated the effects of topical application of PRP on the integration of machined, hydroxyapatite-coated, and anodized implants. The influence of PRP was found to be significant with regard to BIC after 6 weeks but not after 12 weeks. It was observed that the effect of PRP was less with increasing distance from the site of application. In our study, the only variable that had effect on bone regeneration was the implant surface and not the "medium" (whole blood vs PRP). Furthermore, Casati and colleagues[10] used machined-surface implants in a peri-implant defect-PRP model in mongrel dogs. Buccal dehiscence-type defects (4 mm × 5 mm) were created in the mandible, implants were installed, and PRP was randomly administered. No differences in BIC or bone density were found after 3 months of healing. The authors concluded that no effect of PRP was seen.

The use of autogenous bone grafts is considered to be a method of choice in reconstructive surgery, but the volume of bone remaining after healing is difficult to predict.[29] As it is considered that bone GFs work via the receptors of target cells, it is logical that Sanchez and colleagues found that PRP failed to prove any positive results on bone formation to xenogeneic bone grafts in a peri-implant defect model.[30–32]

Gerard and colleagues[8] evaluated the effect of PRP in combination with bone grafts in a critical size defect model in the mandible of dogs. Mandibular inferior border defects were created bilaterally and grafted with autogenous particulate bone with or without PRP. After healing intervals of 1, 2, 3, and 6 months in the test group and 6 months of healing in the control, radiography and epifluorescence analysis were performed. The authors reported that the bone apposition rate was equal in test and control sites. Bone density was higher in the non-PRP grafts after 1 and 2 months and no differences were observed after 3 and 6 months. Interestingly and in accordance with data from a human study from our group,[6] more new bone formation and grafted bone resorption were observed after 1 and 2 months. The bone forming in the PRP-treated grafts displayed a significantly more active surface, which was also observed in human biopsies in a previous study from our group.[6]

In conclusion, PRP is commonly used in different clinical situations in an attempt to improve soft and bone tissue healing. In spite of this, experimental and clinical studies fail to demonstrate any advantages with the use of PRP. The results from the present study showed that PRP does not improve bone regeneration in peri-implant defects compared with whole blood. However, the results indicate that fluoridated titanium implants display a higher degree of bone fill than non-treated control implants.

This study was sponsored by Astra Tech AB and by grants from the Swedish Dental Association and Uppsala County Council, Uppsala, Sweden.

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