# Bone Healing with or without Platelet-Rich Plasma around Four Different Dental Implant Surfaces in Beagle Dogs

Philipp Streckbein, MD, DDS;* Wilfried Kleis, MD, DMD;† Rainer S. R. Buch, MD, DMD;‡ Torsten Hansen, MD, PhD;§ Gernot Weibrich, MD, DMD, PhD†,¶

## ABSTRACT

*Purpose:* Surface development is one of the major aims in dental implant engineering. Additive application of substances could possibly improve the new bone formation around dental implants. The present study evaluated the bone reaction on four different implant surfaces with or without platelet-rich plasma (PRP).

*Materials and Methods:* Four self-tapping titanium screw implants (Brånemark MK III [Nobel Biocare, Göteborg, Sweden], Osseotite [3i, Miami, FL, USA], Xive [Densply Friadent, Mannheim, Germany], and Compress [IGfZ eG, Diez, Germany]) with different surfaces were inserted in each hemimandible of 12 female beagle dogs; the implant positions and the application of PRP were randomized. After intravital fluorochrome staining, sacrifices and biopsies harvesting were performed after 6 weeks (five dogs; one dog died before) and 12 weeks (six dogs) and the respective specimens were analyzed.

*Results:* The only significant difference in bone remodeling was found for the Compress implants with increased bone formation compared with the Brånemark implants at 12 weeks (sign test, $p = .03$). Comparing the histological and histomorphometric specimens of all other implant surfaces with respect to peri-implant bone remodeling and the resulting bone-implant contact rates (BICRs), no statistically significant differences were seen in the PRP or non-PRP groups (sign test, all $p$ values $\geq .063$).

*Conclusions:* This study found no significant differences in the BICR for roughened implant surfaces compared with machined surfaces. In this animal model, the addition of PRP did not demonstrate evidence of faster bone formation or the resulting BICR.

KEY WORDS: animal study, dental implant surfaces, histomorphometry, peri-implant bone, platelet-rich plasma

## INTRODUCTION

Most clinically available implants have modified surfaces (e.g., machined, or roughened and surface increased by sandblasting, etching, or oxidation), and each manufacturer claims that their modification optimizes osseointegration. To date, most comparative studies have compared machined titanium implant surfaces with the most recent surface modification developed by the same manufacturer. These studies have shown that higher bone-implant contact rates (BICRs) result from increased and accelerated bone healing using roughened implant surfaces.[1–3] The clinical use of an anodic oxidized surface (TiUnite) increased implant

*Senior consultant, Department of Cranio-Maxillo-Facial Surgery, Justus Liebig University, Giessen, Germany; †senior consultant, Department of Oral and Maxillofacial Surgery, Johannes Gutenberg University, Mainz, Germany; ‡senior consultant, Specialty Practice in Cranio-Maxillo-Facial and Plastic Surgery, Wiesbaden, Germany; §senior consultant, Department of Pathology, Johannes Gutenberg University, Mainz, Germany; ¶senior consultant, Department of Prosthetic Dentistry, Johannes Gutenberg University, Mainz, Germany

Reprint requests: Philipp Streckbein, Department of Cranio-Maxillo-Facial Surgery, University Hospital Giessen/Justus Liebig University, 35392 Giessen, Germany; e-mail: philipp.streckbein@uniklinikum-giessen.de



DOI 10.1111/cid.12026

survival with the immediate loading of dental implants from 80 to 97% compared with a machined implant design,[4,5] demonstrating the clinical relevance. Limited data are available comparing implant surfaces of different manufacturers.[6]

In 1998, Marx and colleagues[7,8] found that platelet-rich plasma (PRP) had a positive effect on bone remodeling because it was a source of autologous growth factors. Platelets contain a variety of growth factors.[9] The use of PRP to support the osseointegration of endosseous dental implants also resulted in significantly increased bone remodeling in animal experiments,[10] although some apparently contradictory results have been reported.[11–13]

The present study analyzed the bone healing pattern on four different implant surfaces with respect to their effects on peri-implant bone remodeling and the resulting BICR. In addition, the influence of the additional application of PRP was evaluated.

## MATERIALS AND METHODS

### Implants and Surfaces

The following implant types with different surface properties were used (Figure 1):

1 *Brånemark* (MK III): a self-tapping titanium cylindrical screw. External implant-abutment connection. Nobel Biocare (Göteborg, Sweden), 7.0 mm length, 3.75 mm diameter. The TiUnite surface is processed by anodic oxidation with a machined neck (0.5 mm), which has to be above the bone level.

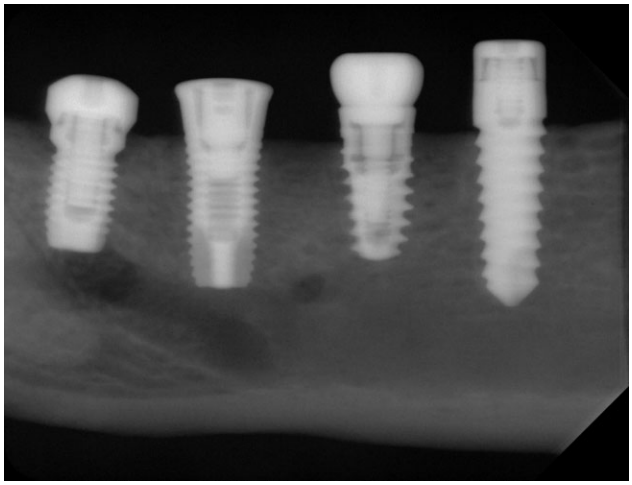

**Figure 1** X-ray of the four inserted implants in the mandible (from *left* to *right*: Brånemark, Osseotite, Xive, Compress).

2 *Osseotite*: a self-tapping titanium cylindrical screw. Internal implant-abutment connection. 3i (Miami, FL, USA), 8.5 mm length, 4.0 mm diameter. The Osseotite surface is doubly acid etched with a machined neck (3.0 mm), which can be in part above the bone level.

3 *Xive*: a self-tapping titanium conical screw. Internal implant-abutment connection. Densply Friadent (Mannheim, Germany), 8 mm length, 3.8 mm diameter. The Friadent Plus surface is grit blasted, acid etched, and neutralized with a machined neck (1.0 mm), which has to be above the bone level.

4 *Compress*: a bone displacing/condensing conical titanium screw. External implant-abutment connection. IGfZ eG (Diez, Germany), 12 mm length, 4.0 mm diameter. The surface is machined, and the apical third is sandblasted with a machined neck (2.5 mm), which can be in part above the bone level.

### Animal Model

After approval from the local animal care committee and the local ethics committee, 12 female beagle dogs weighing 12 to 16 kg and aged 12 to 15 months were used. All animals had undergone extraction of the premolars in the lower jaw on both sides 3 months before implant installation.

### PRP Production

PRP was produced using the Platelet Concentrate Collection System (BIOMET 3i, Palm Beach Gardens, FL, USA), which led to an average of sixfold increase in the resulting thrombocyte count. The mean (± SD) growth factor levels achieved were 259 ± 89 pg/mL PDGF-AB and 294,438 ± 72,339 pg/mL TGF-β1. The detailed production process and the constitution of the resulting blood product compared with other PRP production methods have been described.[14,15]

### Surgical Procedure and PRP Application

After inducing general anesthesia with an intramuscular injection of Dormitor (medetomide), 35 µg/kg body weight, and an intravenous injection of Disoprivan 2% (propofol), 2 mg/kg body weight, after raising a full flap four different implant types were placed on each side of the lower jaw, according to the respective manufacturer's recommendations. In combination with healing abutments (Brånemark and Xive) and cover screws (Osseotite and Compress), a transmucosal healing approach was used. On one side of the lower jaw, PRP was added

during implant insertion (0.5-mL PRP was injected into each prepared cavity and the surface of the implant was moistened with PRP). The hemimandible receiving PRP was determined by the flip of a coin, and the implant's positions were sorted at random. The wound was closed using absorbable polyglactin sutures (Vicryl 3.0, Ethicon GmbH, Norderstedt, Germany). After 2 weeks (postoperatively) of soft food, the dogs were fed with a standard diet ad libitum.

### Antibiotic Coverage and Fluorochrome Staining Sequence

For postoperative antibiotic coverage, the animals were treated with an intravenous injection of Tardomycel (benzylpenicillin–procaine) (0.1 mL/kg body weight) every 48 hours for 10 days. Sequential intravital staining of the regenerating bone was performed postoperatively with 3% alizarin (0.83 mL/kg body weight) during week 1 (postoperative days 0 and 7), 1% calcein green (5 mL/kg body weight) in weeks 2 and 3 (postoperative days 14 and 21), and 6% xylenol orange (1.5 mL/kg body weight) in weeks 4 and 5 (postoperative days 28 and 35).

### Specimen Preparation

One of the 12 animals died 5 days after the operation. The animals were euthanized at 6 ($n = 5$) and 12 ($n = 6$) weeks for histomorphometric evaluation of BICR and bone fluorescent markers. Specimens were cut along the implant axis and prepared using a technique that produces thinly ground layers of tissue (40–60 µm thick), as described by Donath and Breuner.[16]

### Histomorphometric Evaluation

Transmission light microscopy was used to compare the implant position in the mandible. After a histomorphometric analysis of fluorochrome staining, the specimens were stained with toluidine blue and examined histologically. The BICR was measured histomorphometrically.

To analyze peri-implant bone remodeling, the fluorochrome staining of the peri-implant bone was quantified at three locations for each implant: at implant threads no. 1 and 3 and the apical edge. Four photographs were taken of the same area (region of interest was an image section of 1,950 × 1,545 pixel, clinically the height of one implant thread) for each of the three positions (Leica DMRX, Leica Microsysteme, Wetzlar, Germany; CCD color video camera, Sony Europe, Berlin, Germany; ×100 magnification), one using transmission light microscopy with no specific filter and three using fluorescence microscopy images to analyze the fluorochromes alizarin, calcein green, and xylenol orange (Figure 2). The four images were stored digitally and then evaluated histomorphometrically using a picture-analysis system (Image Tool for Microsoft Windows, University of Texas Health Science Center, San Antonio, TX, USA). Using this system, the number of pixels labeled with fluorochrome was determined separately for alizarin, calcein green, and xylenol orange as a percentage of the total regenerated bone surface in the three pictures of the different implant areas. The mean alizarin staining in each of the implant areas was considered to be a measure of bone remodeling in the first postoperative week, the mean calcein green staining was the measure for the second to third postoperative week, and the mean xylenol orange was the measure for the fourth and fifth weeks.

After staining the specimens with toluidine blue, a digital image of the entire implant, together with the adjacent osseous tissue, was made at ×16 magnification. The BICR was determined as a percentage of the implant surface with direct bone contact to the total implant surface in the analyzed specimen using a picture-analysis system (Image Tools: Adobe Photoshop CS and Paint Shop Pro 7 for Microsoft Windows).

### Statistical Methods

All of the quantitative measurements were characterized using descriptive statistics ($n$, mean, standard deviation, median, minimum, maximum, and quartiles).

To determine whether the surface modification of the implant influenced bone remodeling and resulting BICR, the animals at 6 and 12 weeks were analyzed for each implant group under two different conditions: (1) with PRP application in local bone and (2) without PRP application. Sign tests for non-normally distributed, linked data were calculated, and the $p$ values are shown separately for the PRP test groups and the non-PRP control groups. A similar analysis for possible differences between the four different implant types was performed (sign test).

To determine whether the PRP influenced peri-implant bone remodeling and the resulting BICR, the PRP groups were analyzed versus the non-PRP groups separately for the 6- and 12-week postoperative specimens. Sign tests were performed separately for the four implant groups.

The total fluorochrome-labeled bone surface for each dye was calculated at the bottom, middle, and top

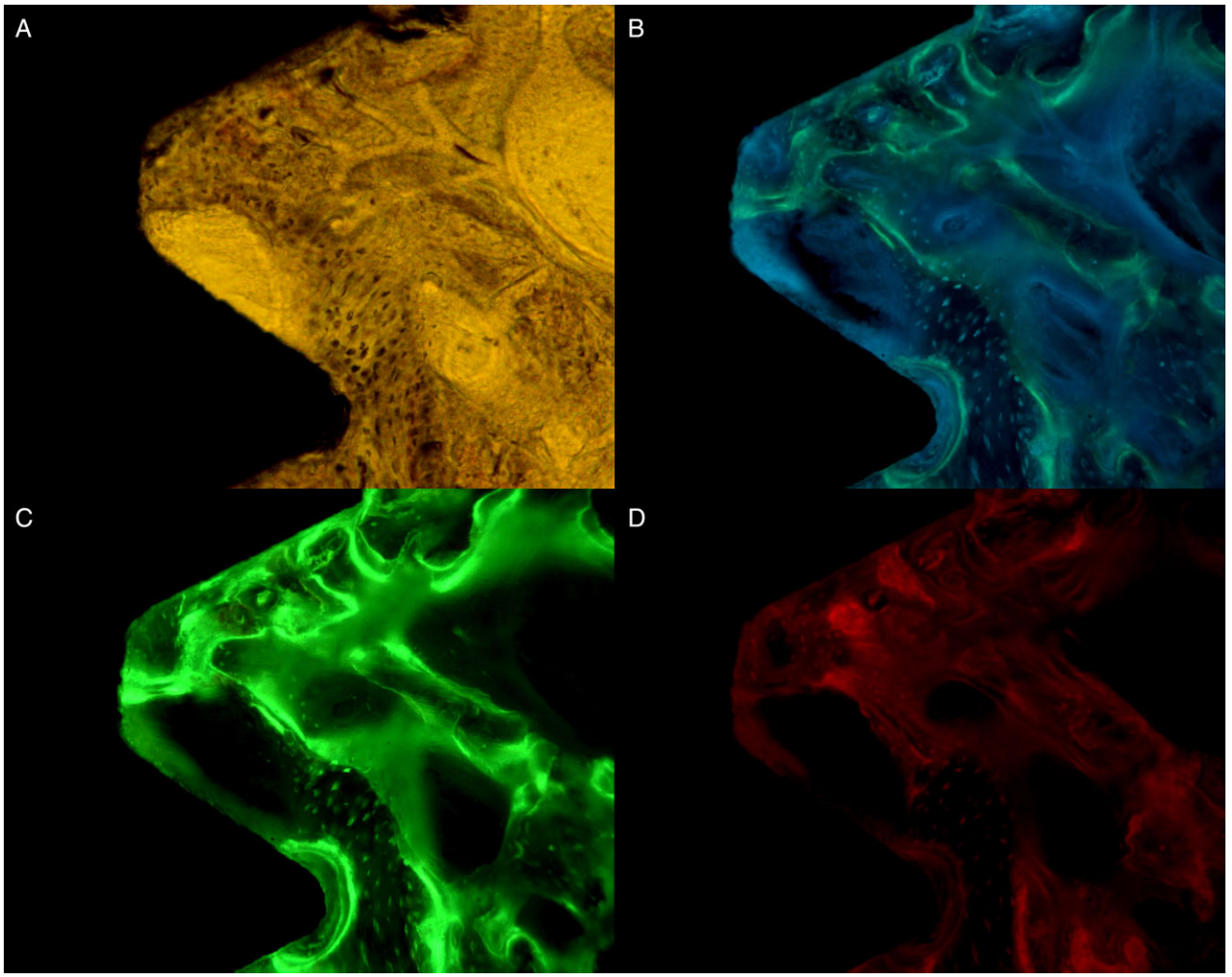


**Figure 2** Intravital fluorochrome-stained bone area of the 6-week nonplatelet-rich plasma (*A*, transmission light microscopy; *B*, alizarin; *C*, calcein green; and *D*, xylenol orange).

of each implant. The mean of the three totals per implant was used as a combined parameter for bone remodeling in the peri-implant region. The four paired median values for bone remodeling were displayed graphically for each of the four implant types using box plots. The alizarin data represented bone formation during the first week, the calcein green data bone growth during weeks 2 and 3, and the xylenol orange bone growth during weeks 4 and 5. To compare the total bone activity during the osseointegration process, the total fluorochrome labeling of each implant was calculated and displayed in a box plot for the four implant surfaces.

Box plots of bone remodeling and the BICR were drawn for the time-dependent implant groups ($n = 4$–$6$ implants/group), although the median, which has only limited statistical validity, was used for those groups.

## RESULTS

### Implant Loss

No implant loss occurred in the 6-week group. In the 12-week group, one Xive implant was lost 7 weeks postoperatively in the non-PRP group, whereas in one dog in the PRP group, one Xive implant was lost 2 weeks postoperative and one Osseotite implant was lost 3 weeks postoperative.

### Intravital Fluorochrome Staining

In the 6-week ($n = 5$) and 12-week ($n = 6$) specimens, the box plots showed only slight differences in fluorochrome-stained bone among the four implant types for alizarin, calcein green, and xylenol orange (Figure 3, A and B).

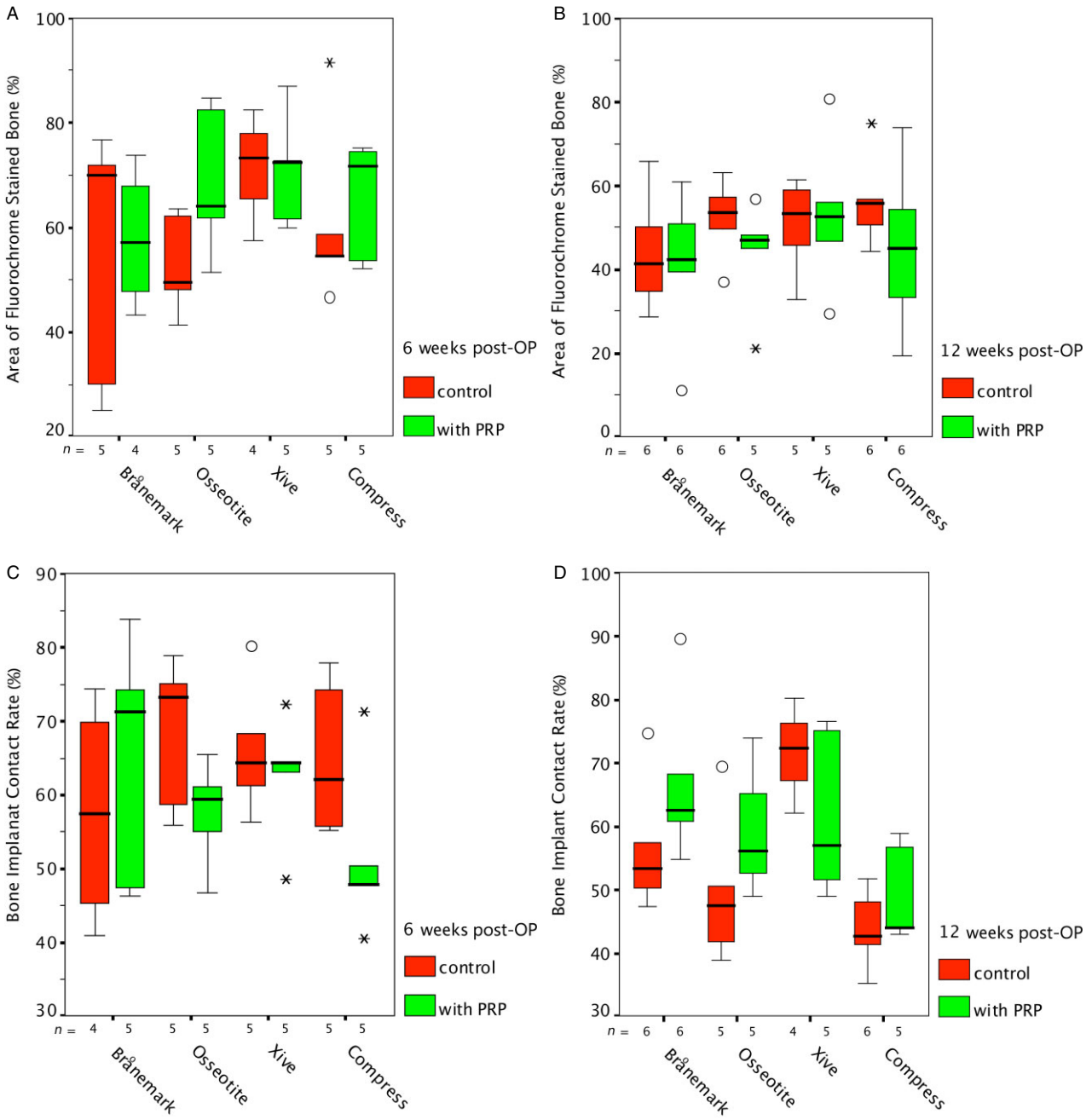


**Figure 3** *A*, Total fluorochrome-stained bone area (6 weeks/alizarin + calcein green + xylenol orange) for the four implant surfaces. *B*, Total fluorochrome-stained bone area (12 weeks/alizarin + calcein green + xylenol orange) for the four implant surfaces. *C*, Bone-implant contact rate (6 weeks) for the four implant surfaces. *D*, Bone-implant contact rate (12 weeks) for the four implant surfaces (post-OP = postoperative; PRP = platelet-rich plasma).

## Analysis of the Implant Surfaces for the Non-PRP Group

An analysis of the three individual fluorochromes revealed no statistically significant difference among the implant surfaces (sign test, 6 weeks: all $p \geq .125$; 12 weeks: all $p \geq .063$).

As a marker of total bone remodeling, the median total fluorochrome-stained area (sum of the alizarin + calcein + xylenol staining) differed, although not significantly, among the four implant types in the 6-week specimens (see Figure 3A), whereas the median total fluorochrome staining was more similar among the four implants in the 12-week specimens (see Figure 3B). Based on the sign test, the only significant difference in bone remodeling was found for the Compress implants with increased bone formation compared with the

Brånemark implants at 12 weeks ($p = .031$; 12 weeks, all other $p \geq .063$; 6 weeks, all $p \geq .125$).

There was no significant morphological or histomorphometric difference in the BICR in either the 6- or 12-week specimens (see Figure 3, C and D; sign test, 6 weeks: all $p \geq .063$; 12 weeks: all $p \geq .125$). At 12 weeks, the median BICR was higher with the Xive implant (non-PRP group: 69.5 ± 8.2%) than with the other three implants (non-PRP group: Brånemark 56 ± 9.7%, Osseotite 49.6 ± 11.9%, and Compress 43.6 ± 5.7%).

### Analysis of the Implant Surfaces for the PRP Group

Identical analyses were performed for the PRP test group (see Figure 3, A–D). No statistically significant differences among implant surfaces were seen (sign test, 6 weeks: all $p \geq .125$; 12 weeks: all $p \geq .375$ and BICR: sign test, 6 weeks: all $p \geq .063$; 12 weeks: all $p \geq .063$).

### Analysis of the Possible PRP Influence for the Four Implant Surfaces

The box plots for comparison of the PRP groups versus the non-PRP groups with respect to the fluorochrome staining (see Figure 3, A and B) and the resulting BICR (see Figure 3, C and D) of the 6- and 12-week specimens showed no significant difference (sign test, 6 weeks: all $p \geq .063$; 12 weeks: all $p \geq .062$).

## DISCUSSION

The fluorochrome staining procedure used here is an established method.[17] The bone surface area determined morphometrically can be used as a measure of bone remodeling.[18–21] For most of the fluorochrome-stained specimens, the median in the 12-week groups was slightly less than the respective median in the 6-week group. This suggests that the major part of osseointegration of the implants had essentially occurred at some time point between 6 and 12 weeks and that some of the fluorochrome vanished during the final healing process. Nevertheless, the amount of fluorochrome staining was a strong indicator of the healing processes in progress.

The PRP production process has been validated,[22] the increase in the resulting thrombocyte count was sufficient (sixfold), and the respective growth factor levels were evaluated.

During implant insertion, the PRP was partly pushed out from the prepared socket. Nevertheless, the method for local PRP instillation into the implant cavity used in this study is a in the literature-documented technique, which has proven to be sufficient to achieve increased bone healing.[23]

During the first postoperative week (alizarin staining), the resorption of damaged peri-implant bone cells predominates.[24] Bone reconstruction begins in the second postoperative week, resulting in staining with the fluorochrome marker.

At 6 weeks, the slightly higher total fluorochrome staining with the Brånemark and Xive implant surfaces seemed to reflect higher bone remodeling than with the Osseotite and Compress implants. After the next 6 weeks, when fluorochrome staining was not longer applied to the animals, the amount of fluorochrome staining had decreased by more than one-third only in the Brånemark and Xive specimens, suggesting ongoing bone remodeling, whereas the staining with the Osseotite and Compress implant surfaces remained stable, suggesting only minor bone remodeling during weeks 7 to 12.

At 12 weeks, the median total fluorochrome-stained area was different among the four implant surfaces in the non-PRP group only for a single pair of implants: the Compress implant gave the highest value, which differed significantly from the value for the Brånemark implant in the non-PRP group.

With the additional application of PRP, there was no statistically significant difference in peri-implant bone remodeling among the four implant surfaces at 6 or 12 weeks.

At 6 weeks, the BICR, which might be expected to be higher for the conical Osseotite, Xive, and Compress implants compared with the cylindrical Brånemark implant (due to the condensing of lateral bone caused by the conical implant designs) in fact showed no statistically significant difference among the four different implant surfaces. The application of PRP did not result in a statistically significant change in the BICR.

At 12 weeks, the box plot displayed the highest BICR for the Xive implant followed by the Brånemark, Osseotite, and Compress. The BICR boxes for the PRP groups seemed to be slightly higher than the controls, but a statistical evaluation suggested that the differences were not significant.

BICR values of 40 to 50% seem reasonable compared with rates reported in other studies of implant surfaces. Trisi and colleagues obtained a BICR of 47% for the Osseotite implant in human maxillae,[25] Kim and

colleagues reported a BICR of 47.7 ± 13.4% for 36 implants with TiUnite surfaces in 12 dogs,[26] Shibli and colleagues found a BICR of 32.19 ± 15.68% for seven implants with TiUnite surfaces in seven humans,[27] and Grassi and colleagues obtained a BICR of 42.83 ± 9.80% for 14 implants with sandblasted acid-etched surfaces in 14 humans.[28] In addition, Sul and colleagues showed that the TiUnite surface resulted in increased removal torque compared with the Osseotite surface.[29] Lang and colleagues reported a BICR of 61% for SLActive and SLA surfaces in human specimens after 42 days for newly formed bone. At 7 and 14 days, they reported of a composition of old bone, new bone, and bone debris in direct contact to the implant surface. At the beginning, all device surfaces were partially coated with bone debris. A significant fraction of this bone matrix coating became increasingly covered with newly formed bone.[30] Consistent to the study of Lang and colleagues, the study presented here did not reveal much bone debris at the 6- and 12-week specimens.

The analysis of the BICR revealed no significant difference among the four different implant surfaces, possibly due to methodical difficulties with the statistical analyses founded in the limited number of specimens for some surface/time of healing creates ($n = 4$–6 per group). Other authors described significant improvement of the BICR for roughened surfaces in animal studies.[1,2] In a clinical approach, the survival rate of immediately loaded implants could be relevantly improved by the application of roughened TiUnite surface structure compared with machined surface.[4,5] Therefore, most manufacturers modified their actual clinically available implant surface structures accordingly.

The additional application of PRP did not result in a significant improvement of bone regeneration or BICR. These data suggest that the macrodesign (cylindrical vs conical) and the technique for roughening the implant surface do not lead to significant effects for peri-implant bone remodeling or the resulting BICR under the conditions analyzed in this study. These results are valid for implants positioned in local bone; however, it is unclear whether similar results would be obtained in augmented bone.

## CONCLUSION

The evaluations of the present study did not indicate superiority of any of the tested implant surfaces. The use of PRP did not improve the results either clinically relevant or statistically significant. The topical use of PRP to support bone regeneration cannot be recommended as a standard method for dental implant treatment.

## ACKNOWLEDGMENTS

We thank Professor Hafner for the evaluation of the growth factor levels and Dr. Hitzler for the standardized evaluation of platelet concentrates (Institute of Clinical Chemistry and Laboratory Medicine at Johannes Gutenberg University, Mainz, Germany).

## SOURCE OF FUNDING AND CONFLICT OF INTEREST

This study was supported by Nobel Biocare Deutschland GmbH, Köln, Germany, 3i, Miami, FL, USA, Densply Friadent GmbH, Mannheim, Germany, and IGfZ eG, Diez, Germany, who provided the implants and the platelet concentrate collection system without charge. Despite this funding, the authors declare no conflict of interest.

## REFERENCES

1. Zechner W, Tangl S, Furst G, et al. Osseous healing characteristics of three different implant types. Clin Oral Implants Res 2003; 14:150–157.
2. Weng D, Hoffmeyer M, Hurzeler MB, Richter EJ. Osseotite vs. machined surface in poor bone quality. A study in dogs. Clin Oral Implants Res 2003; 14:703–708.
3. Oyonarte R, Pilliar RM, Deporter D, Woodside DG. Peri-implant bone response to orthodontic loading: part 2. Implant surface geometry and its effect on regional bone remodeling. Am J Orthod Dentofacial Orthop 2005; 128: 182–189.
4. Glauser R, Lundgren AK, Gottlow J, et al. Immediate occlusal loading of Branemark TiUnite implants placed predominantly in soft bone: 1-year results of a prospective clinical study. Clin Implant Dent Relat Res 2003; 5(Suppl 1):47–56.
5. Glauser R, Ree A, Lundgren A, Gottlow J, Hammerle CH, Scharer P. Immediate occlusal loading of Branemark implants applied in various jawbone regions: a prospective, 1-year clinical study. Clin Implant Dent Relat Res 2001; 3:204–213.
6. Weibrich G, Kleis W, Buch RSR, Hansen T, Streckbein P. Knochenumbaurate vier verschiedener Implantatoberflächen in regionalem Knochen mittels Polyfluorochrom Markierung in Beagle Hunden [Bone remodeling analysis of four dental implant surfaces in local bone using polyfluorochrome sequential labeling in beagles]. Z Zahnärztl Implantol 2009; 3:238–249.

7. Marx RE. Platelet-rich plasma (PRP): what is PRP and what is not PRP? Implant Dent 2001; 10:225–228.
8. Marx RE, Carlson ER, Eichstaedt RM, Schimmele SR, Strauss JE, Georgeff KR. Platelet-rich plasma: growth factor enhancement for bone grafts. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998; 85:638–646.
9. Kiuru J, Viinikka L, Myllyla G, Pesonen K, Perheentupa J. Cytoskeleton-dependent release of human platelet epidermal growth factor. Life Sci 1991; 49:1997–2003.
10. Kim SG, Chung CH, Kim YK, Park JC, Lim SC. Use of particulate dentin-plaster of Paris combination with/without platelet-rich plasma in the treatment of bone defects around implants. Int J Oral Maxillofac Implants 2002; 17:86–94.
11. Terheyden H, Roldan-Ossa JC, Miller J, Jepsen S, Acil Y. Platelet-rich plasma in bone regeneration – preliminary results of two experimental studies. Implantologie 2002; 10:195–205.
12. Schaaf H, Streckbein P, Lendeckel S, et al. Topical use of platelet-rich plasma to influence bone volume in maxillary augmentation: a prospective randomized trial. Vox Sang 2008; 94:64–69.
13. Broggini N, Hofstetter W, Hunziker E, et al. The influence of PRP on early bone formation in membrane protected defects. A histological and histomorphometric study in the rabbit calvaria. Clin Implant Dent Relat Res 2011; 13:1–12.
14. Weibrich G, Kleis WK, Hafner G. Growth factor levels in the platelet-rich plasma produced by 2 different methods: curasan-type PRP kit versus PCCS PRP system. Int J Oral Maxillofac Implants 2002; 17:184–190.
15. Weibrich G, Kleis WK, Hitzler WE, Hafner G. Comparison of the platelet concentrate collection system with the plasma-rich-in-growth-factors kit to produce platelet-rich plasma: a technical report. Int J Oral Maxillofac Implants 2005; 20:118–123.
16. Donath K, Breuner G. A method for the study of undecalcified bones and teeth with attached soft tissues. The Säge-Schliff (sawing and grinding) technique. J Oral Pathol 1982; 11:318–326.
17. Rahn BA, Perren SM. Xylenol orange, a fluorochrome useful in polychrome sequential labeling of calcifying tissues. Stain Technol 1971; 46:125–129.
18. Knöfler W, Graf H, Gröschel T, Löwicke G. Zur Knochenreaktion auf Biomaterialien. II. Ergebnisse der fluoreszenzmikroskopischen Untersuchung zur Beobachtung der initialen Knochenbildung. Z Zahnärztl Implantol 1990; VI:145–152.
19. Schlegel KA, Kloss FR, Schultze-Mosgau S, Neukam FW, Wiltfang J. Healing patterns at the bone-implant-interface using different topical measurements. Dtsch Zahnärztl Z 2002; 57:194–199.
20. Terheyden H, Jepsen S, Möller B, Tucker M, Rueger D. Sinus floor augmentation with simultaneous placement of dental implants using a combination of deproteinized bone xenografts and recombinant human osteogenic protein-1. Clin Oral Implants Res 1999; 10:510–521.
21. Wetzel A, Stich H, Caffesse R. Bone apposition onto oral implants in the sinus area filled with different grafting materials. Clin Oral Implants Res 1995; 6:155–163.
22. Weibrich G, Kleis WK, Streckbein P, Moergel M, Hitzler WE, Hafner G. Comparison of point-of-care methods for preparation of platelet concentrate (platelet-rich plasma). Int J Oral Maxillofac Implants 2012; 27:762–769.
23. Zechner W, Tangl S, Tepper G, et al. Influence of platelet-rich plasma on osseous healing of dental implants: a histologic and histomorphometric study in minipigs. Int J Oral Maxillofac Implants 2003; 18:15–22.
24. Weibrich G, Hansen T, Kleis W, Buch R, Hitzler WE. Effect of platelet concentration in platelet-rich plasma on peri-implant bone regeneration. Bone 2004; 34:665–671.
25. Trisi P, Lazzara R, Rebaudi A, Rao W, Testori T, Porter SS. Bone-implant contact on machined and dual acid-etched surfaces after 2 months of healing in the human maxilla. J Periodontol 2003; 74:945–956.
26. Kim SK, Lee HN, Choi YC, Heo SJ, Lee CW, Choie MK. Effects of anodized oxidation or turned implants on bone healing after using conventional drilling or trabecular compaction technique: histomorphometric analysis and RFA. Clin Oral Implants Res 2006; 17:644–650.
27. Shibli JA, Grassi S, de Figueiredo LC, Feres M, Iezzi G, Piattelli A. Human peri-implant bone response to turned and oxidized titanium implants inserted and retrieved after 2 months. Implant Dent 2007; 16:252–259.
28. Grassi S, Piattelli A, de Figueiredo LC, et al. Histologic evaluation of early human bone response to different implant surfaces. J Periodontol 2006; 77:1736–1743.
29. Sul YT, Johansson C, Albrektsson T. Which surface properties enhance bone response to implants? Comparison of oxidized magnesium, TiUnite, and Osseotite implant surfaces. Int J Prosthodont 2006; 19:319–328.
30. Lang NP, Salvi GE, Huynh-Ba G, Ivanovski S, Donos N, Bosshardt DD. Early osseointegration to hydrophilic and hydrophobic implant surfaces in humans. Clin Oral Implants Res 2011; 22:349–356.