Surgical Therapy of Peri-Implant Disease: A 3-Year Follow-Up Study of Cases Treated With 3 Different Techniques of Bone Regeneration

Fouad Khoury*† and Rainer Buchmann‡

Background: Advanced peri-implant intrabony defects require comprehensive surgical treatment regimens different from periodontal therapy strategies. The purpose of this longitudinal trial was to evaluate the peri-implant outcomes following guided bone regeneration with 3 treatment protocols.

Methods: In 25 patients, 41 peri-implant defects with supporting bone loss >50% of the implant length were treated with flap surgery plus autogenous bone grafts alone (FG) (controls, n = 12) plus non-resorbable (FGM) (test 1, n = 20) or bioabsorbable barriers (FGRM) (test 2, n = 9) and supportive antimicrobial therapy. Following submerged healing, the membranes were removed (FGM), and the peri-implant probing depths (PD), probing bone levels (BL), mobility scores (PT), and intrabony defect height (DH) were radiographically evaluated at baseline, 6 months, and 1 and 3 years post-therapy.

Results: Non-surgical/anti-infective therapy resulted in a limited improvement of PD scores after 6 months. At the 3-year visit, surgical treatment revealed significant changes from baseline for the controls and both of the test groups for PD: 5.1 ± 2.7 mm (FG), 5.4 ± 3.0 mm (FGM), and 2.6 ± 1.6 mm (FGRM), and for BL: 3.2 ± 2.4 mm (FG), 3.4 ± 2.4 mm (FGM), and 2.3 ± 1.6 mm (FGRM), Mann-Whitney test, $P \leq 0.05$. The changes for DH and PT were significant only for FG- and FGM-treated subjects. The overall improvement for FGRM-treated patients during the 3-year observation was less marked. However, the differences between the 3 surgical treatment protocols did not affect the treatment outcomes after 3 years.

Conclusions: Autogenous bone grafting is an appropriate treatment regimen to augment open crater-formed peri-implant defects. Although certain clinical situations require an additional fixation of barrier membranes, their routine application should be approached with caution. *J Periodontol 2001;72:1498-1508.*

KEY WORDS

Peri-implant diseases; grafts, bone; dental implants/adverse effects; membranes, barrier; membranes, bioabsorbable; guided bone regeneration; outcome assessment.

* Department of Oral and Maxillofacial Surgery, Westfalian Wilhelm-University, Münster, Germany.
† Private Clinic Schloss Schellenstein, Olsberg, Germany.
‡ Department of Periodontology and Oral Biology, Goldman School of Dental Medicine, Boston University, Boston, MA, and Department of Periodontology, Westfalian Wilhelm-University.

Implant dentistry is a relatively new and fast growing area of oral health services in many countries. For successful treatment results and patient satisfaction with dental implants, treatment approaches must include prevention and treatment of peri-implant infections.[1,2] Periodontal and peri-implant soft tissues are often discriminated by inflammatory diseases with oral pathogens emerging either at teeth, implants, or within intra-implant components.[3,4] Fairly compelling evidence indicates that a major goal of implant dentistry today should be the control of periodontal microbiota in the oral cavity. Once a peri-implant inflammatory process is ongoing, implant sites compromised by severe loss of peri-implant–supported bone often undergo explantation followed by renewed implant treatment with a concomitant implanto-prosthetic restorative therapy.[5] To enhance the level of patient expectations and compliance, it is of special interest to determine whether it is possible to maintain the affected implant by bone grafting techniques or guided bone regeneration (GBR) procedures and rebuild the previously lost peri-implant tissues. At present, there is insufficient information on the efficacy of various treatment protocols for peri-implantitis. The number of animal stud-

ies documenting the success of regenerative treatment protocols with bone grafts, substitutes, or growth factors is increasing.[6-8] However, in humans, only case reports are available,[9] and longitudinal studies evaluating different treatment approaches in peri-implant diseases remain outstanding.

Thus, the objective of the present longitudinal trial was to compare the clinical outcomes of 3 different treatment approaches aimed at reconstructing advanced, intraosseous, peri-implant intrabony defects. The hypothesis was that guided bone regeneration with autogenous bone grafts and additional application of barrier membranes would improve the treatment results over a 3-year maintenance period in patients with severe loss of peri-implant–supporting bone.

MATERIALS AND METHODS

Subjects

The data for this study were taken from 25 subjects of the Schellenstein Clinic in Olsberg, Germany, with an age range from 43 to 53 years and a total of 41 peri-implant defects at IMZ and F2[§] dental implants. Patients selected to enter into the study were screened for peri-implant disease by radiographic evidence of intrabony defects exceeding more than 50% of the implant length (Fig. 1) and an average loading time of 5.8 ± 2.6 years. The mean age of the patients (22 females and 3 males) was 48.2 ± 6.3 years at the last visit. All subjects had either removable or fixed partial dentures and were treated for periodontal disease if tooth replacement was due to periodontitis. Health questionnaires given to the patients elicited information regarding tobacco use, drug and alcohol consumption, implant and periodontal therapy or antibiotics in the previous 3 months, and any systemic condition that might have affected the inflammatory peri-implant disease process, and that might require premedication for therapy; for females, additional information regarding birth control medication, menstruation, and pregnancy was gathered. The baseline demographic and clinical characteristics of the 25 peri-implant patients enrolled in the study are represented in Table 1.

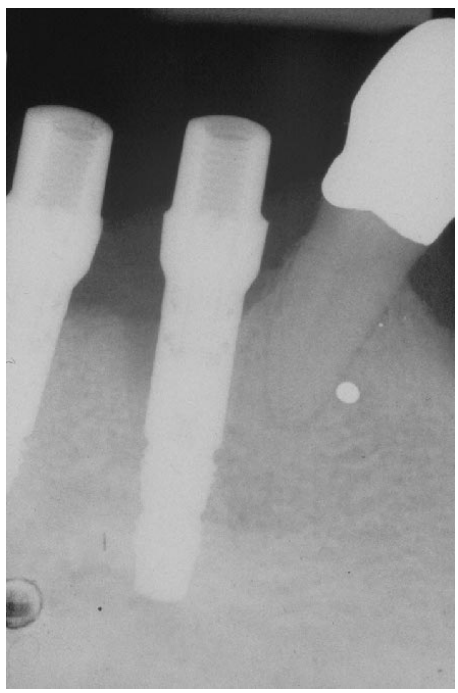

Figure 1.
Peri-implant intrabony defect at Frialit 2-implant regio 32 extending two-thirds of the vertical peri-implant defect height, with clinically visible signs of inflammation including suppuration.

Peri-Implant Parameters

Subjects fulfilling the inclusion criteria were invited to participate in the study and, if accepted, signed informed consent forms. All patients were monitored at baseline and 3 years after treatment. Probing depths (PD, the distance between the peri-implant gingival margin and the bottom of the peri-implant pocket) and probing bone levels (BL, under local anesthesia[‖]; the distance from the implant shoulder to the deepest depth at which the probe met strong resistance from contact with bone) were measured at 4 sites per implant (mid-buccal, disto-buccal, mid-lingual, disto-lingual) using a periodontal probe[¶] with a 3-3-2-3 mm calibration and a 0.4 mm diameter tip. The PD and BL measurements (reproducibility ±1 mm greater than 95%) were performed by the same calibrated examiner. The implant mobility status (PT) was assessed[#] and calculated as the mean of the oral and vestibular measurements. Prior to the examinations, the mobility equipment was standardized with the acrylic hollow cylinder as recommended by the manufacturer with a reproducibility of ±1 PT score. For radiographic evaluation of the vertical intrabony defect height (DH), parallel techniques with XCP (extension cone parallel technique) devices were used. The bite block of the XCP device was properly placed at the implant, and the x-ray cylinder adjusted so that the central ray was perpendicular to the implant axis. Following processing, the distance from the implant shoulder to the vertical bottom of the intrabony defect was measured as DH on the film[**] with a sliding gauge[††] to the nearest millimeter.

Microbial Examinations

Subgingival peri-implant plaque samples were taken at each of the 41 diseased peri-implant sites. After iso-

§ Friadent GmbH, Mannheim, Germany.
‖ Ultracain DS forte, Hoechst Marion Roussel, Frankfurt, Germany.
¶ PCP 11, Hu-Friedy, Chicago, IL.
# Periotest, Siemens, Bensheim, Germany.
** Ektaspeed plus EP-22P, Eastman Kodak Co., Rochester, NY.
†† Beerendonk, Seitz & Haag, Linden, Germany.

Table 1.

Baseline Demographic and Clinical Characteristics of Peri-Implantitis Subjects

	Test 1 (FGM)	Test 2 (FGRM)	Control (FG)	Total
N subjects	11	7	7	25
Gender (M/F)	0/11	2/5	1/6	3/22
Age (years)	55.5 ± 14.1*	48.6 ± 8.1	49.4 ± 5.2	48.2 ± 6.3
Functional loading (years)	5.5 ± 1.9	7.1 ± 3.0	4.1 ± 1.8	5.8 ± 2.6
N sites examined	20	9	12	41
% sites with BL <4 mm (n)	0	0	0	0
% sites with BL 4-6 mm (n)	15.0 (3)	22.2 (2)	25.0 (3)	19.5 (8)†
% sites with BL >6 mm (n)	85.0 (17)	77.8 (7)	75.0 (9)	80.5 (33)†

* Mean ± SD.
† Exact chi-square, $P \leq 0.880$.

lating the area with a cotton roll and gently air drying, supragingival deposits were carefully removed with a curet tip.‡‡ Peri-implant plaque samples were then collected by inserting a sterile endodontic paper point§§ to the bottom of the peri-implant defect for 10 seconds. They were immediately transferred into an Eppendorf vial with 500 µl of one-quarter concentrated, ice-cold, filter-sterilized Ringer's solution and suspended for 10 seconds in an ultrasonic unit.‖‖ *Actinobacillus actinomycetemcomitans* was isolated and quantitatively enumerated as previously described.[10] Briefly, the peri-implant plaque samples were spread on freshly prepared TSBV agar, incubated for 3 days, and quantitatively evaluated in colony-forming units (CFU/ml). The identification of peri-implant pathogens, as routinely performed in our laboratory, has been described in detail elsewhere.[11] In summary, for each of the 25 subjects, the 4 most prevalent types of microbial colonies were selected on incubated blood agar plates for identification. From each of these 100 selected colonies, 4 subcultures were prepared. One was also incubated and used for identification of the bacterial colonies.¶¶ The remaining 3 subcultures were used for further susceptibility testing.

Susceptibility Testing

Susceptibility testing was conducted for amoxicillin/clavulanate potassium,## metronidazole,*** tetracycline,††† clindamycin,‡‡‡ erythromycin,§§§ and ciprofloxacin‖‖‖ utilizing the E-test.¶¶¶ After 7 days of incubation, the concentration of the drug that inhibits 90% of bacterial growth in vitro was read from the strip as minimal inhibitory concentration (MIC) in µg/ml,[11] and the agent with the lowest MIC value was selected for prescription.

Treatment Protocol

For each of the 25 subjects, a 2-stage peri-implant treatment plan was established to resolve the inflammatory tissue response at the diseased peri-implant site and augment the peri-implant defect with autogenous bone grafts.

Non-surgical/anti-infective therapy. After removal of the prosthetic restoration, we repeatedly performed subgingival irrigation of the peri-implant defects with 0.2% chlorhexidine digluconate solution.### Under local anesthesia,‖ all patients received implant scaling†† plus systemic antimicrobial therapy as recommended following susceptibility testing. Furthermore, patients were enrolled in an individual oral hygiene program with weekly prophylaxis and repeated motivation and instruction in self-performed oral hygiene. The reevaluation of primary treatment results was carried out after 6 months as already documented.[12]

Surgical treatment. The peri-implant defects were selected for augmentation either with flap surgery and autogenous bone grafts alone (control) or, in addition, non-resorbable (test 1) or bioabsorbable barrier membranes (test 2) according to the experience of the investigator. A sulcular incision with a mesial and distal extension was made around the neck of the implant abutments, and full-thickness flaps were reflected on the facial and lingual surfaces to access the peri-implant defect (Fig. 2). Granulomatous tissue was carefully removed, and the surgical site repeatedly rinsed with 0.2% chlorhexidine digluconate solution. Citric acid (pH = 1) was applied for 1 minute to decontaminate the implant surface, which was then rinsed with H_2O_2 and 0.9% saline. Curettage of the intrabony defect was done to stimulate spongious bleeding. In addition, bone blocks and particulated bone were harvested as autogenous grafting material from the adjacent alveolar ridge, retromolar, or submental chin area,[13,14] shaped to defect size, and carefully inserted to augment the intrabony crater. The bone blocks were stabilized with osteosynthesis screws (Fig. 3). Non-

†† Implacare, Hawe Neos, Dioggio, Switzerland.
§§ Roeko, Langenau, Germany.
‖‖ Sonorex RK 82, Bandelin Electronic KG, Berlin, Germany.
¶¶ Rapid ID 32A, BioMerieux, Nuertingen, Germany.
Augmentin, SmithKline Beecham Pharma, Munich, Germany.
*** Clont, Bayer Vital GmbH, Leverkusen, Germany.
††† Doxycyclin 100, Heumann Pharma GmbH, Nuremburg, Germany.
‡‡‡ Sobelin, Pharmacia GmbH, Erlangen, Germany.
§§§ Erythrocin, Abbott, Wiesbaden, Germany.
‖‖‖ Ciprobay, Bayer Vital GmbH.
¶¶¶ AB Biodisk, Solna, Sweden.
Chlorhexamed fluid, Procter & Gamble, Schwalbach, Germany.

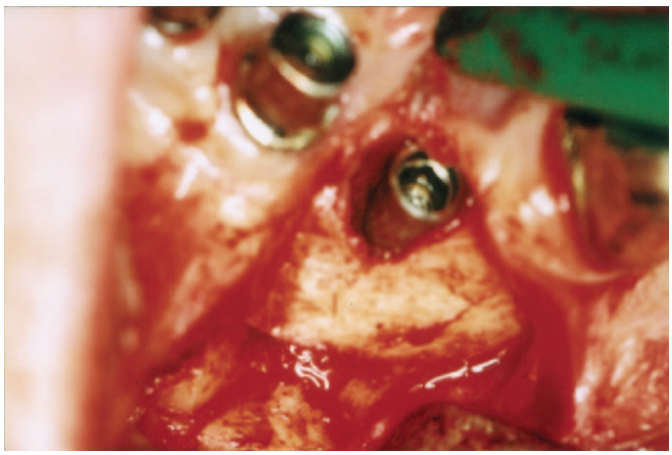

Figure 2.
Typical in situ *aspect of an open crater-formed peri-implant defect.*

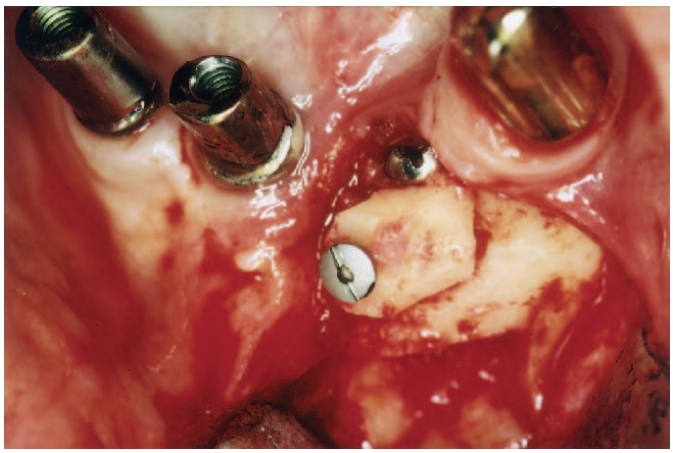

Figure 3.
The peri-implant defect is covered with a screw-fixed, autogenous bone graft harvested from the submental chin area after implantation of particulated bone into the intrabony defect area.

resorbable ePTFE membranes**** or bioabsorbable barriers†††† were placed over each fixture and adjusted to cover the bone crater. A 2-layer closure of the wound was completed using a rotated periosteal flap from the neighboring soft tissue to completely cover the periodontal defect and fixed with interdental sutures to allow submerged healing of the augmented implant sites. Antibiotics were administered to the patients 4 weeks prior to surgery (for 1 week), and later starting 1 day and finishing 7 days after surgery according to their individual antimicrobial susceptibility test results. The postsurgical follow-up included careful cleaning of the treated peri-implant sites 1 and 2 weeks post-therapy until the sutures were removed. Patients were directed to rinse with a 0.2% chlorhexidine digluconate solution twice daily for 2 minutes. The patients were enrolled in a supportive maintenance program and monitored on a 3- to 6-month recall schedule including repeated oral hygiene instructions and a full-mouth tooth cleaning according to their individual needs. Reentry to remove the ePTFE membrane was carried out 6 months after surgical treatment (Fig. 4).

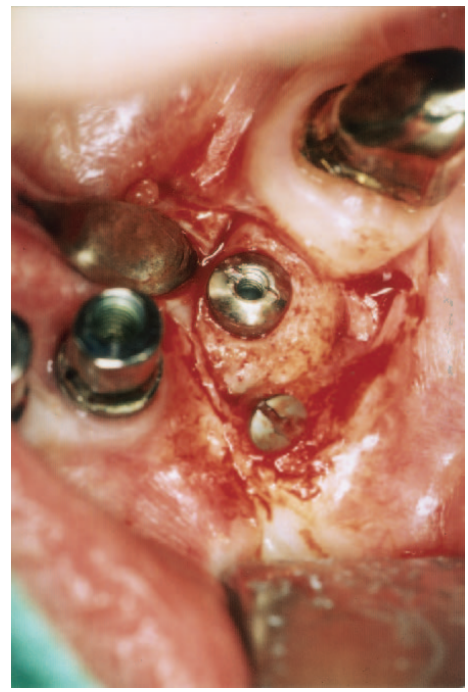

Figure 4.
Surgical reentry with removal of the ePTFE membrane after 6 months. Bone regeneration is visible.

Study Design

At the outset, peri-implant parameters were assessed as described above. The reexaminations were performed for all subjects at 6 months, 1, and 3 years following non-surgical/anti-infective and surgical therapy (Figs. 5 and 6). Eleven patients were selected for FGM therapy (test 1); 7 individuals were selected for FGRM treatment (test 2); and another 7 subjects served as controls (FG). All subjects fulfilled the treatment and time protocol. Post-therapy complications were recorded and enumerated according to the 3 treatment protocols.

Statistical Analysis

Data analysis and statistical tests were subjected to each treatment protocol on a patient-level basis using special software.‡‡‡‡ The chi-square test was performed to analyze the frequency distribution of sites within the 3 treatment groups according to the baseline probing bone level. For the peri-implant and radiographic parameters, medians, means, and standard

**** Gore Tex, W.L. Gore & Associates, Inc., Flagstaff, AZ.
†††† Bioguide, Geistlich, Switzerland.
‡‡‡‡ SPSS 10.0, SPSS Inc., Chicago, IL.

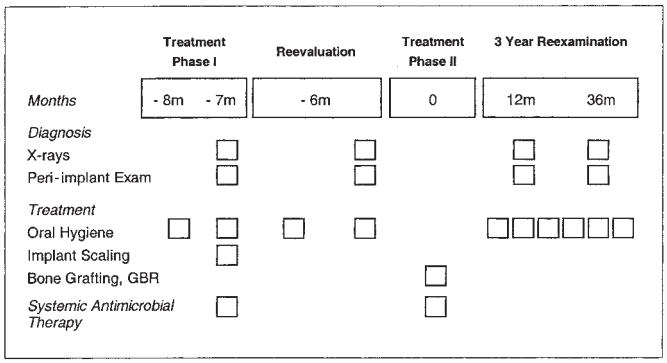

Figure 5.
Experimental protocol displaying the schedule for peri-implant examinations.

deviations were calculated. Due to the small sample size in each group, non-parametric tests were applied. Significant changes in the clinical parameters in each group over the 36-month observation period (intragroup comparison) were analyzed by the Mann-Whitney Wilcoxon signed rank test. Differences between the 3 treatment procedures (test 1, test 2, control) (intergroup comparison) were subjected to Kruskal-Wallis analysis. The location of differences between groups was analyzed by Mann-Whitney test using the Bonferroni adjustment to control for experiment-wise error rate. Statistical significance was determined at an alpha level of 0.05.

RESULTS

Clinical Parameters

Non-surgical/anti-infective therapy. Implant scaling with antimicrobial therapy resulted in a resolution of inflammation around the implant as displayed by probing depth measurements that revealed a marked improvement between 1.3 ± 1.1 mm in the FGRM group and 1.5 ± 1.2 mm in the FG and FGM group. Probing bone levels and vertical intrabony defect height were not measurably affected by the initial treatment as outlined in Figure 7 and Tables 2 through 5. The PT scores displayed a maximum change in the FGM group of 0.7 ± 2.6, while differences in the FG- and FGRM-treated subjects were negligible. In conclusion, non-surgical treatment of peri-implant disease resulted in a temporary improvement of the outcome measures as decontamination of the implant surfaces could not be achieved sufficiently.

Surgical therapy. At the outset, peri-implant probing depths (PD) displayed values of 8.2 ± 1.0 mm for FGM, 7.7 ± 0.5 mm for FGRM, and 8.0 ± 0.5 mm in the FG group. Within each group (intragroup comparison), the 1- and 3-year changes from baseline were statistically significant. The changes in probing

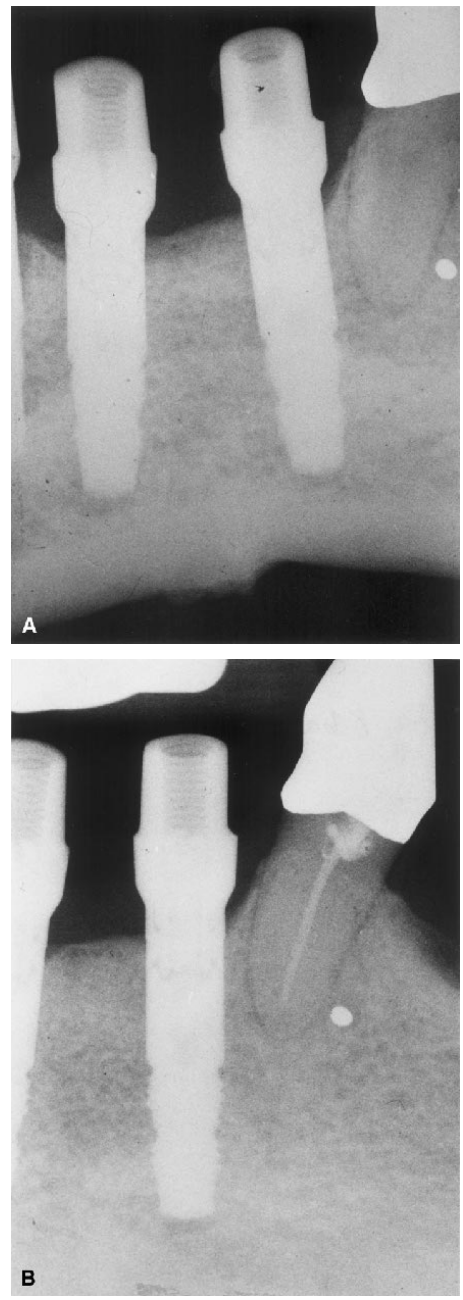

Figure 6.
*One- **(A)** and 3-year **(B)** radiographic evidence of complete intrabony regeneration, regio 32.*

depths at the 3-year reevaluation were 5.4 ± 3.0 mm (FGM), 2.6 ± 1.6 mm (FGRM), and 5.1 ± 2.7 mm (FG) (Mann-Whitney test, Fig. 7A, Table 2). There was a striking difference in PD change between the groups after the 1- and 3-year visit (Kruskal-Wallis test). The location of the differences was related to the FGRM-treated subjects compared to FG and FGM. Probing depth outcomes for FGRM patients after 3 years were less pronounced (2.6 ± 1.6 mm) and differed signifi-

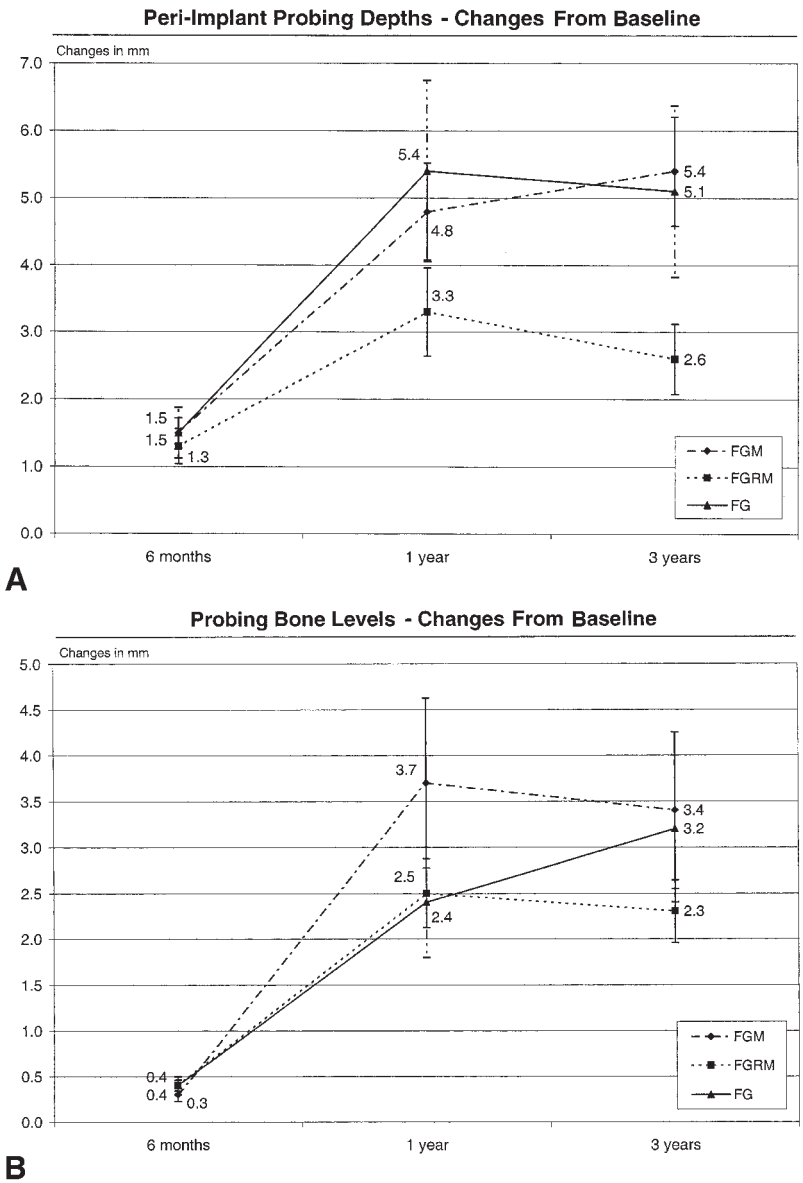

Figure 7.
Changes from baseline to 6 months, 1, and 3 years for peri-implant probing depths ***(A)*** *and probing bone levels* ***(B)***.

cantly from FG and FGM individuals (Mann-Whitney test, $P \leq 0.05$).

During the 3-year observation period, probing bone levels (BL) revealed no statistically significant differences between the different treatment modalities (Kruskal-Wallis test). Within groups, the average probing bone level readings decreased from baseline levels of 7.7 ± 1.2 mm to 4.3 ± 2.1 mm (FGM), 7.4 ± 0.9 mm to 5.1 ± 1.5 mm (FGRM), and 7.3 ± 1.3 mm to 4.1 ± 2.1 mm (FG) at the 3-year reexamination (Mann-Whitney test, Fig. 7B, Table 3). Although the FGRM group benefited less from the treatment approach (3-year change: 2.3 ± 1.6 mm), the amount of change was not statistically different between the 3 treatment regimens (Kruskal-Wallis analysis, $P \leq 0.05$). Considering that the estimated measurement error of rigid periodontal probes is ±1 mm (95% confidence), these results suggest that the additional application of barrier membranes had no significant impact on the changes of clinically detectable bone levels 3 years post-therapy.

The intragroup comparison of the radiographically calculated intrabony defect height (DH) revealed an apparent decrease in DH scores following therapy for FG and FGM patients. Although DH levels decreased in the FGRM group, the change did not reach statistical significance (Mann-Whitney test, Table 4). The differences compared to baseline were most apparent in the FGM group, where non-resorbable barriers were additionally placed to cover the defect (Fig. 7C) (3-year change: 2.8 ± 3.1 mm). The smallest amount of change was observed in the FGRM group at 1.9 ± 3.2 mm. Nonetheless, between the 3 treatment protocols, the overall changes did not differ among the groups (Kruskal-Wallis analysis, $P \leq 0.05$, Table 4). The additional barrier placement did not improve the 3-year outcomes of intrabony defect height levels compared to autogenous bone grafting alone.

The baseline, 1-, and 3-year PT scores are summarized in Table 5. The PT levels started at 1.2 ± 2.7 (FGM), –0.6 ± 1.4 (FGRM), and –0.1 ± 2.2 (FG) and dropped to –0.8 ± 1.0 (FGM), –1.1 ± 1.2 (FGRM), and –1.8 ± 0.6 (FG) at the 3-year reexamination. Within the FGM group, the 3-year change of PT from baseline amounted to 2.0 ± 2.2 and was statistically significant (Mann-Whitney test, Fig. 7D). No significant differences occurred between the 3 treatment protocols (Kruskal-Wallis analysis). However, the PT values tended to differ between the FGM and FGRM group (Mann-Whitney test, $P \leq 0.05$). The PT levels reflected the functional stabilization of the implants during GBR therapy. They revealed no marked response in FGRM-treated subjects.

Healing Complications

The frequency distribution of complications during healing is represented in Table 6. It is noteworthy that complications were strongly associated with the barrier-membrane treatment protocols. Utilizing non-resorbable barriers, 60.0% of the implant sites (n = 12)

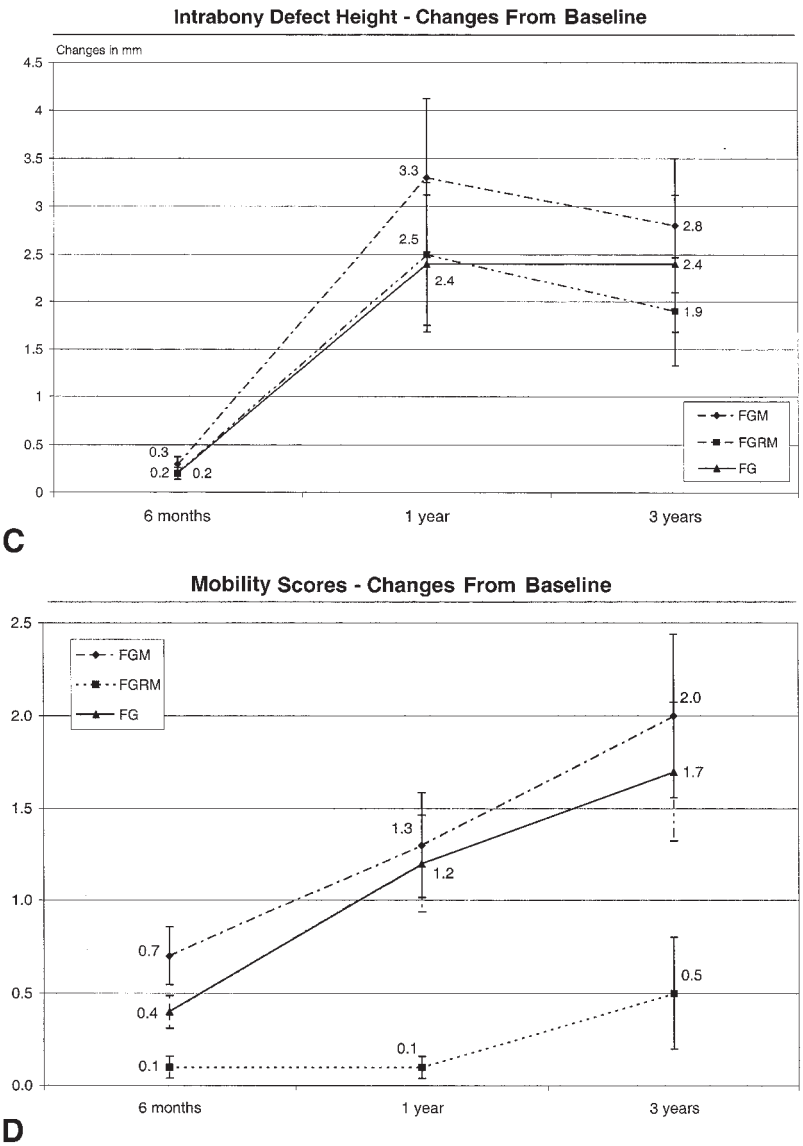

Figure 7. (continued)
Changes from baseline to 6 months, 1, and 3 years for vertical intrabony defect heights ***(C)*** *and PT scores* ***(D)***.

were affected by dehiscence (n = 4), exposure (n = 5), fistula (n = 2), or sequester formation (n = 1). Bioabsorbable membranes were less frequently applied to the defects. However, the percentage of early failures was 55.6%. In summary, 17 out of 29 barrier-treated implant sites (58.6%) were compromised by early post-therapy complications.

DISCUSSION

Research and education are needed to steer implant practice to the benefit of patients.[2] However, we lack documentation to implement the best possible strategies for achieving appropriate solutions to treat human peri-implant diseases. Maintaining the compromised abutment site and the implant-supported prostheses provides the best possible treatment for patient benefits and satisfaction. In animal studies, it has been demonstrated that the combination of guided bone regeneration with either freeze-dried demineralized or hydroxyapatite grafting materials resulted in a variable, but greater amount of appreciable peri-implant bone fill than all other treatments.[6,15,16] Histologically, reosseointegration averaged 40% from the base of the defect.[17] In humans, new bone formation with a reduction in median marginal bone loss from 6.2 to 2.3 mm (62.9%) was observed in a prospective study 3 years after autogenous bone grafting alone.[18] These data obtained from non-submerged ITI screw implants utilizing corticocancellous bone grafts and air-polishing devices concur with the amount of bone gain we observed in our control group (3-year change in intrabony defect height, 64.3%). This might indicate that the source of autogenous bone grafts, the implant surface, and the decontamination procedure represent variables not necessarily associated with the success of bone regeneration. The initial depth and width of the peri-implant defect rather than single treatment steps are determinants of the amount of regenerated bone. It remains doubtful that real reosseointegration occurs. Several histological reports claimed that, following resolution of experimentally induced peri-implantitis at Brånemark fixtures with guided tissue regeneration and ePTFE barriers, a thin connective tissue capsule was found that separated the implant surface from the newly formed bone.[7,19,20] The bone-implant interface consisted of a 0.5 µ-wide unmineralized layer acting as a perimucosal seal, with a junctional epithelium-implant union coronally, and supported by a perpendicularly oriented connective-tissue implant junction apically. Previously, unexposed apical portions of the implant sites were anchored in compact bone.[20] Even if the clinical parameters in our study suggest that new bone gain might occur in peri-implant treated sites, a direct regrowth of bone cannot be expected. The application of systemic antimicrobials in peri-implant therapy, i.e. amoxicillin and metronidazole, accelerates the resolution of the plaque-associated infiltrate,[21] and decreases microbial and peri-implant parameters over a 1-year period.[22] A long-term effect on tissue formation in the implant-bone interface due to antimicrobial treatment has not been demonstrated.

In a 12-month case-control study in which a titanium foil-guided bone regeneration technique was assessed, loss of barriers occurred by denudation and infection

Table 2.

Peri-Implant Probing Depths (PD, mm) and Changes From Baseline to 3 Years

Therapy	Time	Median	Mean ± SD	Change (outset – 3 years)	Range	*P* Value* (after 3 years)
FGM (Test 1)	Baseline	8.3	8.2 ± 1.0		7.0 – 9.5	
	6 m	7.0	6.7 ± 1.1		6.0 – 8.5	
	1 y	3.0	3.4 ± 1.2		2.0 – 6.0	
	3 y	3.0	2.8 ± 1.3	5.4 ± 3.0	2.0 – 5.0	0.0001
FGRM (Test 2)	Baseline	7.5	7.7 ± 0.5		7.0 – 8.5	
	6 m	6.5	6.4 ± 0.9		6.0 – 8.0	
	1 y	4.0	4.4 ± 0.8		3.5 – 6.0	
	3 y	5.0	5.1 ± 1.2	2.6 ± 1.6	3.5 – 7.0	0.0200
FG (Control)	Baseline	8.0	8.0 ± 0.5		7.5 – 9.0	
	6 m	6.5	6.5 ± 0.8		6.0 – 8.0	
	1 y	3.0	2.6 ± 0.5		2.0 – 3.0	
	3 y	3.0	2.9 ± 0.6	5.1 ± 2.7	2.0 – 3.5	0.0010
				Change after 1 y†		0.011
				Change after 3 y		0.004
				Change from 1 y to 3 y		0.062
				FG vs. FGM* (after 3 y)		0.791
				FG vs. FGRM		0.002
				FGM vs. FGRM		0.001

* Mann-Whitney test, exact *P* value, $P \leq 0.05$.
† Kruskal-Wallis test, $P \leq 0.05$.

Table 3.

Peri-Implant Probing Bone Levels (BL, mm) and Changes From Baseline to 3 Years

Therapy	Time	Median	Mean ± SD	Change (outset – 3 years)	Range	*P* Value* (after 3 years)
FGM (Test 1)	Baseline	8.0	7.7 ± 1.2		5.0 – 9.0	
	6 m	7.5	7.4 ± 1.6		5.0 – 8.5	
	1 y	4.0	4.0 ± 1.9		2.0 – 7.0	
	3 y	4.0	4.3 ± 2.1	3.4 ± 2.4	2.0 – 7.0	0.001
FGRM (Test 2)	Baseline	7.5	7.4 ± 0.9		5.5 – 8.0	
	6 m	7.0	7.0 ± 1.3		5.5 – 8.0	
	1 y	5.0	4.9 ± 1.4		3.0 – 7.0	
	3 y	6.0	5.1 ± 1.5	2.3 ± 1.6	3.0 – 7.0	0.010
FG (Control)	Baseline	7.5	7.3 ± 1.3		5.5 – 9.0	
	6 m	7.0	6.9 ± 1.1		5.0 – 8.0	
	1 y	5.5	4.9 ± 1.7		3.0 – 7.0	
	3 y	4.0	4.1 ± 2.1	3.2 ± 2.4	2.0 – 6.0	0.012
				Change after 1 y†		0.304
				Change after 3 y		0.454
				Change from 1 y to 3 y		0.582
				FG vs. FGM* (after 3 y)		0.791
				FG vs. FGRM		0.710
				FGM vs. FGRM		0.151

* Mann-Whitney test, exact *P* value, $P \leq 0.05$.
† Kruskal-Wallis test, $P \leq 0.05$.

6 weeks after therapy.[23] These observations are supported by our results that complications increase whenever barrier membranes in GBR therapy are applied, regardless of the barrier type. We anticipate that complications are due to insufficient soft tissue coverage or the presence of pathogens at the implant fixture rather than to the barrier itself. Incomplete decontamination, biofilm-based antimicrobial resistances,[24] altered cell responses together with enhanced protease activities,[25] and foreign body reactions represent the biological background for the clinically reported complications. Data of non-infected dental implants reveal a lower incidence of complications.[26] Mechanical, laser-irradiated, chemical, and apparative techniques[27-30] for removal of microbial deposits and biofilm-associated bacteria on implant surfaces are available, with a trend towards air-powder abrasive devices in implant decontamination. Citric acid treatment is equally effective on either machined or hydroxyapatite surfaces in establishing the biocompatibility of an implant surface.[30]

In implant maintenance, it is meaningful to use clinical parameters to evaluate peri-implant health and disease.[31] However, the requirements are not exactly the same. The underestimation of bone loss by linear radiographic measurements is a questionable factor in peri-implant imaging and evaluation.[32] In our study, the intrabony defect height scores reached 88.23% (FGM) and 80.95% (FGRM) of the probing bone level values with some limitations in the FG group. However, the reliability of the bite block method for clinical trials was documented by Dubrez et al.,[33] who found 91% of the angular variations to be below the 1.4° threshold. The mobility (PT) readings are frequently used to interpret

Table 4.

Vertical Intrabony Defect Height (DH, mm) and Changes From Baseline to 3 Years

Therapy	Time	Median	Mean ± SD	Change (outset – 3 years)	Range	*P* Value* (after 3 years)
FGM (Test 1)	Baseline	5.0	5.1 ± 3.1		3.0 – 9.0	
	6 m	5.0	4.8 ± 2.2		2.5 – 8.5	
	1 y	2.0	1.8 ± 2.4		1.5 – 6.9	
	3 y	2.0	2.3 ± 2.5	2.8 ± 3.1	1.5 – 7.1	0.037
FGRM (Test 2)	Baseline	7.0	6.4 ± 3.2		2.5 – 9.0	
	6 m	6.5	6.2 ± 3.0		2.2 – 8.0	
	1 y	5.0	3.9 ± 2.8		1.5 – 7.0	
	3 y	6.0	4.5 ± 3.3	1.9 ± 3.2	1.5 – 8.0	0.102
FG (Control)	Baseline	4.0	3.5 ± 3.4		2.5 – 8.0	
	6 m	3.5	3.3 ± 2.9		2.2 – 8.0	
	1 y	1.0	1.1 ± 1.2		2.0 – 3.0	
	3 y	1.0	1.1 ± 1.3	2.4 ± 2.7	2.0 – 3.5	0.040
					Change after 1 y*	0.544
					Change after 3 y	0.746
					Change from 1 y to 3 y	0.066
					FG vs. FGM* (after 3 y)	0.596
					FG vs. FGRM	0.805
					FGM vs. FGRM	0.536

* Mann-Whitney test, exact *P* value, $P \leq 0.05$.
† Kruskal-Wallis test, $P \leq 0.05$.

Table 5.

PT Scores and Changes From Baseline to 3 Years

Therapy	Time	Median	Mean ± SD	Change (outset – 3 years)	Range	*P* Value* (after 3 years)
FGM (Test 1)	Baseline	0.5	1.2 ± 2.7		–1.7 – 7.0	
	6 m	–0.1	0.5 ± 2.1		–1.9 – 5.5	
	1 y	–0.5	–0.1 ± 1.4		–2.0 – 2.0	
	3 y	–1.0	–0.8 ± 1.0	2.0 ± 2.2	–2.3 – 1.0	0.034
FGRM (Test 2)	Baseline	–1.0	–0.6 ± 1.4		–2.5 – 1.0	
	6 m	–1.0	–0.7 ± 1.5		–2.5 – 1.0	
	1 y	–1.0	–0.7 ± 1.1		–2.0 – 1.0	
	3 y	–1.0	–1.1 ± 1.2	0.5 ± 0.3	–3.0 – 1.0	0.599
FG (Control)	Baseline	0.0	–0.1 ± 2.2		–2.5 – 4.0	
	6 m	–0.5	–0.5 ± 2.4		–2.5 – 3.0	
	1 y	–1.5	–1.3 ± 1.1		–2.5 – 1.0	
	3 y	–2.0	–1.8 ± 0.6	1.7 ± 1.8	–2.5 – 1.0	0.088
					Change after 1 y*	0.068
					Change after 3 y	0.088
					Change from 1 y to 3 y	0.447
					FG vs. FGM* (after 3 y)	0.964
					FG vs. FGRM	0.097
					FGM vs. FGRM	0.044

* Mann-Whitney test, exact *P* value, $P \leq 0.05$.
† Kruskal-Wallis test, $P \leq 0.05$.

low degrees of implant mobility and displacement. The observations in our study agreed with previous data observed following maxillary sinus augmentation[34] and ranged from PT +1 to PT –1, thus representing the functional stabilization of the implant abutments during GBR therapy. In the FGRM barrier group, the 3-year PT change (0.5 ± 0.3 PT) was not significant and corresponded to minor changes of the PD, BL, and DH scores compared to the FGM and FG subjects. The inflammatory tissue response that is always associated with the bioresorptive process of bioabsorbable barriers[35] might be responsible for the trend of minor treatment-induced changes in the FGRM patients.

In conclusion, the hypothesis that subjects with severe peri-implant disease benefit from the additional application of barrier membranes in GBR treatment could not be supported by the present study. Furthermore, the following conclusions may be drawn: 1) the submerged healing of autogenous bone grafts in advanced peri-implant disease represents an appropriate treatment regimen to augment the open crater-formed defects, and is significantly associated with a long-term stability of peri-implant health; 2) the additional application of barriers does not improve the overall treatment outcomes 3 years following guided bone regeneration; and 3) certain clinical situations such as an enlarged extent of the osseous peri-implant defect, the availability of particulated bone grafts, and the necessity to stabilize bone grafts might require the additional fixation of barrier membranes. However, their routine application should be approached with caution.

ACKNOWLEDGMENTS

A large part of this work was performed in collaboration with R.F. Mueller, Department of Periodontology, University of Münster. The authors are indebted to M.E. Nunn for her comprehensive statistical analysis. We

Table 6.

Frequency Distribution of Early Healing Complications Following 3 Different Treatment Regimens for Peri-Implant Disease

	Test 1 (FGM)	Test 2 (FGRM)	Control (FG)	Total
Dehiscence (n)	4	2	0	6
Barrier exposure (n)	5	1	0	6
Fistula (n)	2	0	0	2
Sequester (n)	1	2	0	3
None (n)	8	4	12	24
% of sites with complications (n)	60.0 (12)	55.6 (5)	0.0 (0)	41.5 (17)
N implant sites	20	9	12	41

gratefully acknowledge Prof. T.E. Van Dyke for his editorial contributions.

REFERENCES

1. Mombelli A. Prevention and therapy of peri-implant infections. In: Lang NP, Karring T, Lindhe J, eds. *Proceedings of the 3rd European Workshop on Periodontology: Implant Dentistry*. Berlin: Quintessence Publishing; 1999:281-303.
2. Schou L. Responsiveness to patients in implant dentistry: Expectations, satisfaction and behaviour. In: Lang NP, Karring T, Lindhe J, eds. *Proceedings of the 3rd European Workshop on Periodontology: Implant Dentistry*. Berlin: Quintessence Publishing; 1999:333-346.
3. Persson LG, Lekholm U, Leonhardt A, Dahlén G, Lindhe J. Bacterial colonization on internal surfaces of Branemark system implant components. *Clin Oral Implants Res* 1996;7:90-95.
4. Buchmann R, Khoury F, Pingel D, Müller RF, Lange DE. Intraimplant microbiota of oral implants. *J Dent Res* 2000;79(Spec. Issue):168(Abstr. 193).
5. Mombelli A. Etiology, diagnosis and treatment considerations in peri-implantitis. *Curr Opin Periodontol* 1997;4:127-136.
6. Hürzeler MB, Quinones CR, Morrison EC, Caffesse RG. Treatment of peri-implantitis using guided bone regeneration and bone grafts, alone or in combination, in beagle dogs. Part 1: Clinical findings and histologic observations. *Int J Oral Maxillofac Implants* 1995;10:474-484.
7. Persson LG, Ericsson I, Berglundh T, Lindhe J. Guided bone regeneration in the treatment of peri-implantitis. *Clin Oral Implants Res* 1996;7:366-372.
8. Hanisch O, Tatakis DN, Boskovic MM, Rohrer MD, Wikesjö UM. Bone formation and reosseointegration in peri-implantitis defects following surgical implantation of rhBMP 2. *Int J Oral Maxillofac Implants* 1997;12:604-610.
9. Hämmerle CHF, Fourmousis I, Winkler JR, Weigel C, Brägger U, Lang NP. Successful bone fill in late peri-implant defects using guided tissue regeneration. A short communication. *J Periodontol* 1995;66:303-308.
10. Buchmann R, Müller RF, Heinecke A, Lange DE. *Actinobacillus actinomycetemcomitans* in destructive periodontal disease. Three-year follow-up results. *J Periodontol* 2000;71:444-453.
11. Kleinfelder JW, Müller RF, Lange DE. Antibiotic susceptibility of putative periodontal pathogens in advanced periodontitis patients. *J Clin Periodontol* 1999;26:347-351.
12. Buchmann R, Khoury F, Hesse T, Müller RF, Lange DE. Antimicrobial therapy of peri-implant disease (in German). *Z Zahnärztl Implantol* 1996;12:152-157.
13. Khoury F. The modified alveolar-extension-plastic (in German). *Z Zahnärztl Implantol* 1987;3:174-179.
14. Khoury F. Surgical aspects and results for improvement of alveolar bone prior to implant therapy (in German). *Z Zahnärztl Implantol* 1994;3:237-245.
15. Hürzeler MB, Quinones CR, Schupbach P, Morrison EC, Caffesse RG. Treatment of peri-implantitis using guided bone regeneration and bone grafts, alone or in combination, in beagle dogs. Part 2: Histological findings. *Int J Oral Maxillofac Implants* 1997;12:168-175.
16. Machado MA, Stefani CM, Sallum EA, Sallum AW, Tramontina VA, Nociti FH Jr. Treatment of ligature-induced peri-implant defects by regenerative procedures: A clinical study in dogs. *J Oral Sci* 1999;41:181-185.
17. Singh G, O'Neal RB, Brennan WA, Strong SL, Horner JA, Van Dyke TE. Surgical treatment of induced peri-implantitis in the micro pig: Clinical and histological analysis. *J Periodontol* 1993;64:984-989.
18. Behneke A, Behneke N, d'Hoedt B. Treatment of peri-implantitis defects with autogenous bone grafts: 6-months to 3-year results of a prospective study in 17 patients. *Int J Oral Maxillofac Implants* 2000;15:125-138.
19. Persson LG, Araujo MG, Berglundh T, Grondahl K, Lindhe J. Resolution of peri-implantitis following treatment. An experimental study in the dog. *Clin Oral Implants Res* 1999;10:195-203.
20. Schupbach P, Huerzeler M, Grunder U. Implant-tissue interfaces following treatment of peri-implantitis using guided tissue regeneration: A light and electron microscopic study. *Clin Oral Implants Res* 1994;5:55-65.
21. Ericsson I, Persson LG, Berglundh T, Edlund T, Lindhe J. The effect of antimicrobial therapy on peri-implantitis lesions. An experimental study in the dog. *Clin Oral Implants Res* 1996;7:320-328.
22. Mombelli A, Lang NP. Antimicrobial treatment of peri-implant infections. *Clin Oral Implants Res* 1992;3:162-168.
23. Gaggl A, Schultes G. Titanium foil-guided tissue regeneration in the treatment of peri-implant bone defects. *Implant Dent* 1999;8:368-375.
24. Slots J, MacDonald ES, Nowzari H. Infectious aspects of periodontal regeneration. *Periodontol 2000* 1999;19:164-172.
25. Wakabayashi RC, Wong F, Richards DW, Johnson PW. Protease repertoires of cells adherent to membranes recovered after guided tissue regeneration. *J Perio Res* 1996;31:171-180.
26. Mayfield L, Nobreus N, Attstroem R, Linde A. Guided bone regeneration in dental implants using a bioabsorbable membrane. *Clin Oral Implants Res* 1997;8:10-17.
27. Matarasso S, Quaremba G, Coraggio F, Vaia E, Cafiero C, Lang NP. Maintenance of implants: An in vitro study

of titanium implant surface modifications subsequent to the application of different prophylaxis procedures. *Clin Oral Implants Res* 1996;7:64-72.
28. Haas R, Dortbudak O, Mensdorff-Pouilly N, Mailath G. Elimination of bacteria on different implant surfaces through photosensitization and soft laser. An in vitro study. *Clin Oral Implants Res* 1997;8:249-254.
29. Zablotsky M, Meffert R, Mills O, Burgess A, Lancaster D. The macroscopic, microscopic and spectrometric effects of various chemotherapeutic agents on the plasma-sprayed hydroxyapatite-coated implant surface. *Clin Oral Implants Res* 1992;3:189-198.
30. Dennison DK, Huerzeler MB, Quinones C, Caffesse RG. Contaminated implant surfaces: An in vitro comparison of implant surface coating and treatment modalities for decontamination. *J Periodontol* 1994;65:942-948.
31. Salvi GE, Bardet P, Lang NP. Clinical parameters in longitudinal implant studies. In Lang NP, Karring T, Lindhe J, eds. *Proceedings of the 3rd European Workshop on Periodontology: Implant Dentistry*. Berlin: Quintessence Publishing; 1999:217-227.
32. Brägger U, Häfeli U, Huber B, Hämmerle CHF, Lang NP. Evaluation of postsurgical crestal bone level adjacent to nonsubmerged dental implants. *Clin Oral Implants Res* 1998;9:218-224.
33. Dubrez B, Jacot-Descombes S, Cimasoni G. Reliability of a paralleling instrument for dental radiographs. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1995;80: 358-364.
34. Buchmann R, Khoury F, Faust C, Lange DE. Peri-implant conditions in periodontally compromised patients following maxillary sinus augmentation. A long-term post-therapy trial. *Clin Oral Implants Res* 1999;10:103-110.
35. Buchmann R, Hasilik A, Heinecke A, Lange DE. PMN responses following use of 2 biodegradable GTR membranes. *J Clin Periodontol* 2001;28:1050-1057.

Send reprint requests to: Dr. Fouad Khoury, Private Clinic Schloss Schellenstein, Am Schellenstein 1, 59939 Olsberg, Germany. Fax: 49 2962 971922; e-mail: prof.khoury@t-online.de.

Accepted for publication May 11, 2001.