COPYRIGHT © 2001 BY QUINTESSENCE PUBLISHING CO, INC. PRINTING OF THIS DOCUMENT IS RESTRICTED TO PERSONAL USE ONLY. NO PART OF THIS ARTICLE MAY BE REPRODUCED OR TRANSMITTED IN ANY FORM WITHOUT WRITTEN PERMISSION FROM THE PUBLISHER.

Long-term Results of Implants Treated with Guided Bone Regeneration: A 5-year Prospective Study

Nicola Ursula Zitzmann, Dr Med Dent[1]/Peter Schärer, Prof Dr Med Dent, MS[2]/
Carlo Paolo Marinello, Prof Dr Med Dent, MS[3]

The aim of this prospective 5-year longitudinal study was to follow endosteal implants in which guided bone regeneration (GBR) was applied during implant placement. In 75 patients, defects around implants (Brånemark System) were treated with Bio-Oss and Bio-Gide (112 implants). In split-mouth patients in this group, Bio-Oss and Gore-Tex were used in the second defect site (41 implants). All 75 patients had at least 1 implant that was entirely surrounded by bone and served as the control (112 implants). After placement of the definitive prostheses (single-tooth, fixed, or removable implant prostheses), patients were recalled after 6 months and then every 12 months during a 5-year observation period. The following variables were investigated: implant survival, marginal bone level (MBL), presence of plaque, peri-implant mucosal conditions, height of keratinized mucosa (KM), and marginal soft tissue level (MSTL). The cumulative implant survival rate after 5 years varied between 93% and 97% for implants treated with or without GBR. The mean MBL after 60 months was 1.83 mm for sites treated with Bio-Oss and Bio-Gide, 2.21 mm for sites treated with Bio-Oss and Gore-Tex, and 1.73 mm for the control sites. The MBL values were found to increase significantly with time and differed significantly among the treatment groups. During the observation period, KM varied between 3.16 and 3.02 mm. A slight recession of 0.1 mm was observed, and plaque was found in 15% of all sites and was associated with inflammatory symptoms of the peri-implant mucosa. It was observed that such symptoms and recession correlated more strongly with the type of restoration than with the type of treatment. This study demonstrated that implants placed with or without GBR techniques had similar survival rates after 5 years, but that bone resorption was more pronounced in sites with GBR treatment. It was assumed that the use of GBR is indeed indicated when the initial defect size is larger than 2 mm in the vertical dimension. (INT J ORAL MAXILLOFAC IMPLANTS 2001;16:355–366)

Key words: *bone level, dental implants, guided bone regeneration, keratinized mucosa, marginal soft tissue level*

The techniques of guided bone regeneration (GBR) are used during implant placement when stabilization of the implant in an optimal position is feasible, but part of the titanium surface is exposed. In this simultaneous application, GBR treatment is intended to cover the exposed implant surfaces with bone substance for functional reasons. In addition, it is optimal with regard to biology and esthetics, because the soft tissues are sufficiently supported by the underlying bone substance. It has been shown that, for these indications, use of the resorbable collagen membrane Bio-Gide (Geistlich Biomaterials, Wolhusen, Switzerland, and Osteohealth, Shirley, NY) in combination with the xenogenic bone grafting material Bio-Oss (Geistlich Biomaterials and Osteohealth) is a useful alternative to the well-established expanded polytetrafluoroethylene (e-PTFE) membranes.[1] In a split-mouth design, Zitzmann and associates compared the 2 different membrane materials and found no significant differences in defect reduction, with 92% for Bio-Oss/Bio-Gide and 78% for Bio-Oss/Gore-Tex

[1]Senior Lecturer, Clinic of Fixed and Removable Prosthodontics and TMJ Disorders, Dental School, University of Basel, Basel, Switzerland.
[2]Professor and Chairman, Department of Fixed and Removable Prosthodontics and Dental Material Sciences, Dental School, University of Zürich, Zürich, Switzerland.
[3]Professor and Chairman, Clinic of Fixed and Removable Prosthodontics and TMJ Disorders, Dental School, University of Basel, Basel, Switzerland.

Reprint requests: Dr Nicola Zitzmann, Clinic of Fixed and Removable Prosthodontics and TMJ Disorders, Dental School, University of Basel, Hebelstr. 3, CH-4056 Basel, Switzerland. Fax: +41-61-267 26 60. E-mail: N.Zitzmann@unibas.ch

COPYRIGHT © 2001 BY QUINTESSENCE PUBLISHING CO, INC. PRINTING OF THIS DOCUMENT IS RESTRICTED TO PERSONAL USE ONLY. NO PART OF THIS ARTICLE MAY BE REPRODUCED OR TRANSMITTED IN ANY FORM WITHOUT WRITTEN PERMISSION FROM THE PUBLISHER.

(W.L. Gore/Implant Innovations, West Palm Beach, FL).[1] The smaller amount of bone fill with Gore-Tex was caused by sites with wound dehiscences, which occurred frequently when the e-PTFE barrier was applied in immediate implant placement. These membrane exposures required additional surgical intervention to remove the e-PTFE material because of clinical signs of inflammation. The bone fill was significantly reduced (65%) when compared to uneventful healing around Gore-Tex barriers (98% bone fill). Wound dehiscences around the collagen membrane Bio-Gide did not cause clinical inflammatory reactions, and the bone fill during re-entry (87%) was not significantly different when compared to sites with uneventful healing (94%).[1]

Zitzmann and coworkers investigated different factors influencing the outcome of GBR treatment with Bio-Gide and Bio-Oss.[2] The authors observed that GBR was more successful around maxillary implants, especially if a provisional restoration was used during healing. Immediate and short-term delayed implant placement showed better results compared to long-term delayed implant placement. It was suggested that this was the result of preservation of the alveolar ridge, more favorable defect morphologies, and a higher regenerative capacity with early placement. In these studies, the bone fill was assessed clinically during re-entry and described as hard tissue if there was a minimum thickness of 1 mm attached to the implant surface in the former defect site.[1,2] To investigate the histologic structure of this regenerated substance, Zitzmann and colleagues harvested biopsies 6 to 7 months after alveolar ridge augmentation with Bio-Oss and Bio-Gide in humans.[3] They demonstrated that the regenerated mineralized bone contained both woven bone and parallel-fibered bone, with intimate contact with the Bio-Oss particles along 37% of its surface. Signs of resorption of the Bio-Oss granules were observed, and it was suggested that the material participates in the remodeling process.[3]

To investigate healing and bone-to-implant contact in augmented sites, Hockers and coworkers used GBR treatment with Bio-Oss and Bio-Gide during implant placement in dogs.[4] The authors found that 78% of the initial defect height was filled with regenerated bone after 4 months of healing. However, bone-to-implant contact was limited to 20% of the vertical defect dimension, and no direct contact was observed between the grafting particles and the implant surface.[4] Lekholm and associates did not apply any GBR treatment in cases of exposed implant surfaces and compared these sites with control implants that were entirely surrounded by bone during placement.[5] The authors found that the initial defects did not necessarily lead to inflammatory symptoms or to progressive marginal bone resorption after a 5-year period. Given these observations, Lekholm and associates questioned the need for GBR treatment and appealed for stricter indication criteria for the use of this technique.[5]

The purpose of this prospective 5-year longitudinal study was to follow implants in which GBR techniques were applied during implant placement. Implant survival, the radiologic bone level, and clinical parameters were observed over a 5-year period and compared with those of control implants placed in the same group of patients.

MATERIALS AND METHODS

Seventy-five patients, 56 women and 19 men with an average age of 56.1 years (range 19 to 76), were included in the study during the period September 1994 to December 1995. The inclusion criterion was that a minimum of 2 implants (Brånemark System, Nobel Biocare, Göteborg, Sweden) should be placed and that 1 of them should present with bony defects as exposed implant surfaces during implant placement and require GBR techniques. The other implant site, which was entirely surrounded by bone, served as the control. The defects were filled with the xenogenic grafting material Bio-Oss and covered with the collagen membrane Bio-Gide. In 25 patients who presented with 2 defect sites at a minimal distance of 14 mm apart, Bio-Oss/Bio-Gide was used in one site and Bio-Oss/Gore-Tex was applied in the other site, according to a random selection. These patients were part of a prospective split-mouth group in which the 2 membranes were compared; in addition, they were provided with 1 or more control implants.

The defect dimensions, ie, length (from the top of the implant cylinder shoulder to the base of the defect), width, depth, and circumference, were measured using a periodontal probe (CP-12, Hu-Friedy, Chicago, IL). To calculate the area of the exposed implant portion, the surface was treated as made up of curved areas extrapolated onto a plane. Dehisced defects were calculated either as half-ellipses or as parts of a sine curve, while the surfaces of fenestrations were estimated as circles or ellipses. Details concerning the intraoperative measurements, augmentative procedures, and calculation of the defect surfaces have been described previously.[1]

A total of 112 implants were treated with Bio-Oss and Bio-Gide membranes. In another 41 sites, Gore-Tex (type GT4, 6, or 9, depending on the

COPYRIGHT © 2001 BY QUINTESSENCE PUBLISHING CO, INC. PRINTING OF THIS DOCUMENT IS RESTRICTED TO PERSONAL USE ONLY. NO PART OF THIS ARTICLE MAY BE REPRODUCED OR TRANSMITTED IN ANY FORM WITHOUT WRITTEN PERMISSION FROM THE PUBLISHER.

defect size) was used in combination with Bio-Oss, and 112 control implants were entirely surrounded by bone and did not require any GBR techniques. Patients were informed preoperatively about the treatment modalities in case of bone dehiscences and gave their informed consent. Re-entry was performed after 4 months of healing in the mandible and 6 months in the maxilla. Mucoperiosteal flaps were reflected, the regenerated hard tissue was assessed by probing, and any residual defects were measured in the same manner as at the time of implant placement. For the assessment during re-entry, a minimal thickness of 1 mm in regenerated bone was required (Figs 1a and 1b).

Patients were then provided with fixed or removable implant-supported prostheses and checked after 10 to 14 days. The majority of patients were restored with fixed prostheses; 24 single-tooth restorations were placed in 17 patients, and 29 implants in 6 patients were restored with removable prostheses. Oral hygiene instructions were given, with different oral hygiene measures chosen according to patients' individual needs and manual abilities. Patients were recalled after 6 months and once a year thereafter. The observation was scheduled over a period of 5 years from implant placement.

The following parameters were studied during the clinical examination after placement of the prosthesis and at every recall appointment: *(1)* implant survival; *(2)* marginal bone level (MBL), calculated from standardized radiographs; *(3)* presence of plaque; *(4)* peri-implant mucosal conditions; *(5)* height of the keratinized mucosa on the buccal aspect (KM); and *(6)* marginal soft tissue level related to the top of the abutment, ie, the crown margin (MSTL). The latter was expressed in millimeters to the nearest 0.5 mm and presented as a positive value when the abutment margin was located supramucosally or as a negative value with a submucosal position for this reference. Hence, a recession of the mucosal margin was expressed by increasing MSTL values. Keratinized mucosa was identified by its pink color and the lack of mobility. The distance between the soft tissue margin and the mucogingival junction was defined as the height of the keratinized mucosa (KM); it was measured to the nearest 0.5 mm on the buccal aspect of the abutments with a graded periodontal probe.

All implants were monitored according to the criteria defined by Albrektsson and coworkers,[6] who proposed that the success criteria for individual implant sites include implant stability; the absence of peri-implant radiolucency; and the absence of clinical symptoms such as pain, infection, neuropathies, and paresthesia. The restriction to less than 0.2 mm of annual vertical bone loss after the first year of loading was not applied as a success criterion, so that the term "implant survival," rather than "implant success," is used in the present study.[7] Since a widely accepted implant system (Brånemark System) was utilized, prostheses were generally not removed for individual mobility testing during recall visits unless something unexpected had occurred. The peri-implant mucosal conditions were assessed visually and by palpation. Mucosal problems were defined as presence of redness, hyperplasia, suppuration, swelling, and/or pain on palpation. These mucosal problems were assumed to be increasingly severe symptoms. The presence or absence of visible plaque at the soft tissue margin was assessed for each abutment site using an explorer. When the clinical examination was completed, patients were reinstructed in their individual oral hygiene programs and motivated to carry them out. In addition, a professional cleaning was performed.

Periapical radiographs of all sites were made in occlusal contact with the patient biting on the appropriate Rinn holder (Rinn XCP, Dentsply Rinn, Elgin, IL). The long-cone parallel technique (Oralix 65 S, Gendex Dental System, Hamburg, Germany) was applied so that implant threads were clearly visible (Figs 1c and 1d). When deviation from a proper parallel implant projection was observed, the radiograph was redone during the same visit. For investigation of the MBL, radiographs taken during the placement of the superstructure and after 1 to 5 years of observation were used. The measured distance between the tips of the implant threads, which is always 0.6 mm in reality, was used as the basis for assessing and calibrating the radiograph. The MBL was estimated to the nearest 0.3 mm (half interthread distance), with the abutment-implant junction (AIJ) as the baseline reference because implants had been placed initially with the upper implant shoulder margin (equal to AIJ) located at the height of the bone crest. Analogously, defect fill in cases of exposed surfaces was aimed at covering the surface up to the upper shoulder margin (equal to AIJ). Of the 2 values measured on the mesial and distal aspect, the greater distance was used. The clinical examinations and the measurements from the radiographs were performed by one of the authors, who was trained before the start of the study to assess the different clinical variables systematically and reliably. Radiologic assessments were redone after 1 week in 20 randomly selected patients to check intraobserver reliability. In 83% of the sites, the 2 measurements were identical. The difference between the first and second measurements was on average 0.005 mm (Wilcoxon paired test, $P = .74$), with a maximum of 0.3 mm.

COPYRIGHT © 2001 BY QUINTESSENCE PUBLISHING CO, INC. PRINTING OF THIS DOCUMENT IS RESTRICTED TO PERSONAL USE ONLY. NO PART OF THIS ARTICLE MAY BE REPRODUCED OR TRANSMITTED IN ANY FORM WITHOUT WRITTEN PERMISSION FROM THE PUBLISHER.

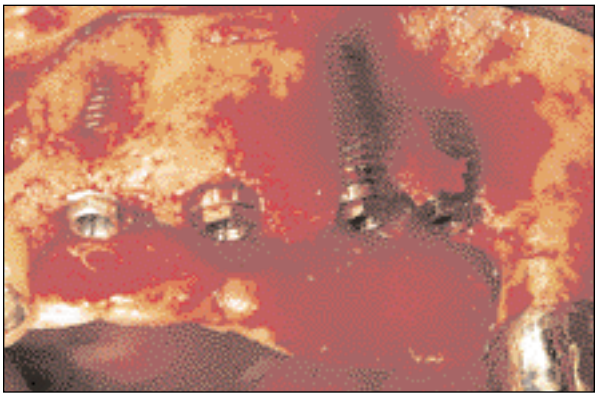

Fig 1a Clinical situation during implant placement in the maxilla with exposed implant surfaces (dehiscence defects in area of the left first and second premolars, fenestration area at the left lateral incisor, no defect area at the left canine) to be treated with GBR. The patient was part of a split-mouth study and treated with Bio-Oss/Bio-Gide in the right maxilla and with Bio-Oss/Gore-Tex in the left maxilla.

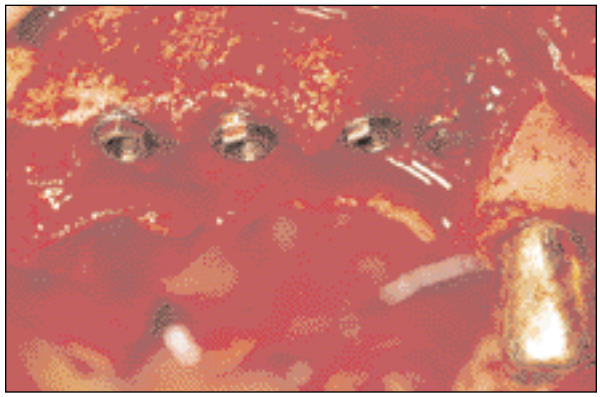

Fig 1b Re-entry of the same site, with elevated flap for assessment of the former defects.

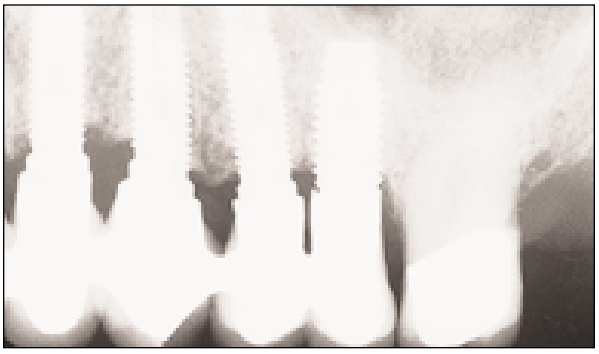

Fig 1c Radiographs at 12 months observation.

Fig 1d Same patient at 60 months observation.

To determine whether the type of restoration had an influence on the investigated variables, distribution of the 3 treatment groups (Bio-Gide, Gore-Tex, and control) was determined with respect to *(1)* fixed single-tooth restorations (type 1), *(2)* fixed partial dentures (type 2), and *(3)* removable overdenture prostheses (type 3). Additionally, clinical parameters were evaluated to see whether they differed according to the type of superstructure.

Statistical Evaluation

Analyses were carried out with STATA version 6.0 (Stata, College Station, Texas) statistical software. Prior to analysis of the data, the values for MBL, plaque, mucosal problems, KM, and MSTL were transformed to normality using the normal score transformation. The first objective was to assess whether there were significant changes with time after implant placement to the parameters implant survival, MBL, presence of plaque, existence of mucosal problems, KM, and MSTL. The second was to find out whether these parameters differed significantly with treatment group and with the type of restoration. The third objective was to investigate whether MBL, as the decisive measure of the treatment outcome, was also affected by one of the parameters plaque, mucosal problems, KM, and/or MSTL. A further question was whether mucosal problems and recession (increasing MSTL values) were influenced by increasing MBL values. The fourth objective was to assess the degree of correlation among the clinical parameters (plaque, mucosal problems, KM, and MSTL).

Cumulative implant survival rates were estimated at 6-month intervals during the first year (starting from the implant placement), and further evaluation was made at 12-month intervals. The estimation of the overall implant survival rate, as well as the survival rate by treatment group and type of restoration, was based on Kaplan-Meier. Cox proportional hazard models were applied to assess whether the rate for implant survival was significantly related to

COPYRIGHT © 2001 BY QUINTESSENCE PUBLISHING CO, INC. PRINTING OF THIS DOCUMENT IS RESTRICTED TO PERSONAL USE ONLY. NO PART OF THIS ARTICLE MAY BE REPRODUCED OR TRANSMITTED IN ANY FORM WITHOUT WRITTEN PERMISSION FROM THE PUBLISHER.

Table 1 Distribution of the Different Types of Restorations in the Treatment Groups (n and %)

	Group			
Restoration type	Bio-Gide/ Bio-Oss (n = 112)	Gore-Tex/ Bio-Oss (n = 41)	Control (no defect) (n = 112)	Total (n = 265)
Fixed single-tooth	17 (15.2)	3 (7.5)	4 (3.6)	24 (9.2)
Fixed > 1 unit (connected)	86 (76.8)	30 (72.6)	96 (85.5)	212 (79.8)
Removable overdenture	9 (8.0)	8 (20.0)	12 (10.9)	29 (11.1)

Fixed single-tooth restorations were significantly more frequent (compared to fixed partial dentures) in the Bio-Gide group versus the control group (P = .001).

Table 2 Mean Results for the Different Treatment Groups

	Group				
Variable	Bio-Gide/Bio-Oss	Gore-Tex/Bio-Oss	Control (no defect)	Log-rank test	*P* value
Survival (%)	95.4 (0.02)	92.6 (0.04)	97.3 (0.02)	63.9	.476
Marginal bone level (mm)	1.34 (0.79)	1.51 (0.96)	1.24 (0.80)	18.76	.0001
Plaque (%)	11.31 (0.01)	17.48 (0.02)	18.17 (0.01)	13.81	.001
Mucosal problems (%)	3.72 (0.01)	7.32 (0.02)	3.15 (0.01)	7.18	.03
Keratinized mucosa (mm)	3.52 (2.03)	2.99 (1.73)	2.70 (1.86)	55.53	<.0001
Marginal soft tissue level (mm)	–0.05 (0.93)	0.27 (1.39)	–0.15 (0.94)	17.41	.0002

Values in brackets represent standard errors for the parameters survival, plaque, and mucosal problems. Those for the parameters marginal bone level, keratinized mucosa, and marginal soft tissue level denote standard deviations.

the treatment group (Bio-Gide versus Gore-Tex versus control) or to the type of restoration. These models were used with frailties to account for the individual heterogeneity.

Linear regression models were applied to the normal scores for the MBL, KM, and MSTL parameters. In addition, logistic regression models were fitted to the binary variables "presence of plaque" and "mucosal problems." Random effects were introduced into the above-mentioned models to adjust for the extra-individual variation, since each patient had more than one implant.[8] The explanatory variables in both regression models were time, treatment group, and type of restoration. The significance of the explanatory variables was assessed using the likelihood ratio test (LRT).

For the third objective, linear regression was used on the parameter MBL with "plaque," "mucosal problems," "KM," and "MSTL" as explanatory variables. The linear regression was also applied to investigate the effect of MBL on the MSTL parameter. The logistic model was used to evaluate the influence of MBL on the occurrence of "mucosal problems." For the fourth objective, the effects of clinical parameters (plaque, KM, and MSTL) on "plaque," "mucosal problems," and "MSTL" were assessed with the logistic and linear models.

RESULTS

The observation period ranged from 55 to 70 months (mean 59.1 months, standard error 0.57). During this period, 9 patients dropped out for different reasons: 4 patients died after 10, 12, 25, and 31 months' observation; 3 patients moved away after 15, 18, and 49 months' observation; and 2 elderly patients declined to continue with the recall appointments after the 4-year check-up.

The proportions of the type of restoration, ie, fixed single-tooth, fixed partial denture, and removable overdenture prosthesis, were different in each of the 3 treatment groups (Bio-Gide, Gore-Tex, and control; Table 1). There were a larger number of single-tooth restorations in the Bio-Gide group than in the control group. More Gore-Tex sites were restored with removable restorations than were control sites.

The cumulative implant survival rate was 95.8% for all 75 patients after the 5-year observation period. For implants treated with Bio-Gide, the survival rate was 95.4%. For the Gore-Tex group, it was 92.6%, and for the control implants, the survival rate was 97.3%. The differences were not statistically significant (LRT = 63.9, degrees of freedom = 63.87, P = .476; Table 2). One of the split-mouth patients (#10), who presented with porous bone quality in the edentulous maxilla, was responsible for

COPYRIGHT © 2001 BY QUINTESSENCE PUBLISHING CO, INC. PRINTING OF THIS DOCUMENT IS RESTRICTED TO PERSONAL USE ONLY. NO PART OF THIS ARTICLE MAY BE REPRODUCED OR TRANSMITTED IN ANY FORM WITHOUT WRITTEN PERMISSION FROM THE PUBLISHER.

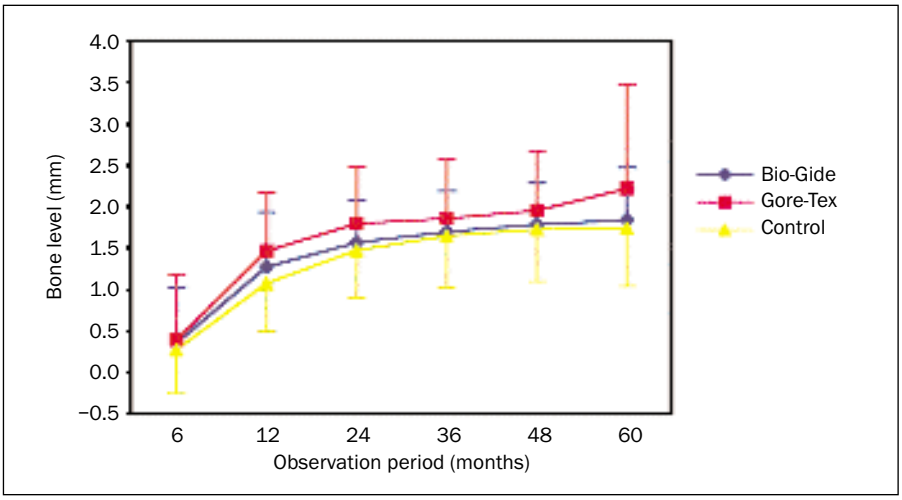

Fig 2 Mean marginal bone levels during 5 years of observation.

Table 3 Results of the Longitudinal Observations

	Time of examination							
Variable	**6 months**	**12 months**	**24 months**	**36 months**	**48 months**	**60 months**	**Log-rank test**	***P* value**
Survival (%)	99.2 (0.01)	97.7 (0.01)	96.9 (0.01)	95.8 (0.01)	95.8 (0.01)	95.8 (0.01)	0.69	.29
Marginal bone level (mm)	0.32 (0.64)	1.21 (0.65)	1.56 (0.59)	1.69 (0.59)	1.78 (0.60)	1.84 (0.78)	573.57	< .0001
Plaque (%)	7.95 (0.02)	20.45 (0.02)	14.39 (0.02)	13.64 (0.02)	18.94 (0.02)	15.53 (0.02)	21.21	.0007
Mucosal problems (%)	3.41 (0.01)	4.55 (0.13)	3.79 (0.01)	4.17 (0.01)	4.17 (0.01)	4.17 (0.01)	0.53	.99
Keratinized mucosa (mm)	3.16 (1.96)	3.13 (1.95)	3.13 (1.95)	3.06 (1.97)	3.0 (1.95)	3.02 (1.96)	1.68	.20
Marginal soft tissue level (mm)	–0.11 (0.97)	–0.06 (1.04)	–0.04 (1.03)	–0.04 (1.03)	–0.02 (1.05)	–0.01 (1.07)	1.44	.23

Value in brackets represent standard errors for the parameters survival, plaque, and mucosal problems. Those for the parameters marginal bone level, keratinized mucosa, and marginal soft tissue level denote standard deviations.

the majority of failures. The patient lost all 6 maxillary implants. One implant was lost 3 months after placement of the removable overdenture prosthesis, 2 implants were lost after 12 months, and 3 implants were lost after 30 months. In another patient provided with 2 implants (Bio-Gide and control), 1 implant was found to not be osseointegrated 3 months after re-entry, and the control implant provided with a single-tooth restoration was found to be mobile 3 months later. In another patient, an immediate implant initially covered with a Gore-Tex membrane was found to be mobile during re-entry. The membrane had been removed 8 weeks after implant placement because of continuing inflammation of the mucosa near to the membrane exposure. The effect of the restoration on the survival rate was found to be statistically significant (LRT = 57.4, degrees of freedom = 27.85, $P < .001$), because of the large number of failures in patient #10, who was restored with an overdenture prosthesis.

The longitudinal values of the MBL calculated for the Bio-Gide, the Gore-Tex, and the control implants are presented in Fig 2 and Table 3. The mean MBL was 0.35 mm (SD = 0.68) for Bio-Gide sites, 0.39 mm (SD = 0.79) for Gore-Tex sites, and 0.27 mm (SD = 0.52) for control sites at the 6-month examination. After the first 6 months of prosthetic loading, the MBL increased to 1.27 mm (SD = 0.66) for Bio-Gide sites, to 1.46 mm (SD = 0.70) for Gore-Tex sites, and to 1.07 mm (SD = 0.59) for control sites. The mean MBL at the 60-month exam was 1.83 mm (SD = 0.63) for Bio-Gide sites, 2.21 mm (SD = 1.26) for Gore-Tex sites, and 1.73 mm (SD = 0.70) for the control sites. The increase in the mean MBL values was found to be statistically significant with time (LRT = 573.57, $P < .0001$; Table 3). Since time was significantly related to MBL, an adjustment for time was made when comparing the MBL values in the treatment groups. The results showed that the average MBL values

COPYRIGHT © 2001 BY QUINTESSENCE PUBLISHING CO, INC. PRINTING OF THIS DOCUMENT IS RESTRICTED TO PERSONAL USE ONLY. NO PART OF THIS ARTICLE MAY BE REPRODUCED OR TRANSMITTED IN ANY FORM WITHOUT WRITTEN PERMISSION FROM THE PUBLISHER.

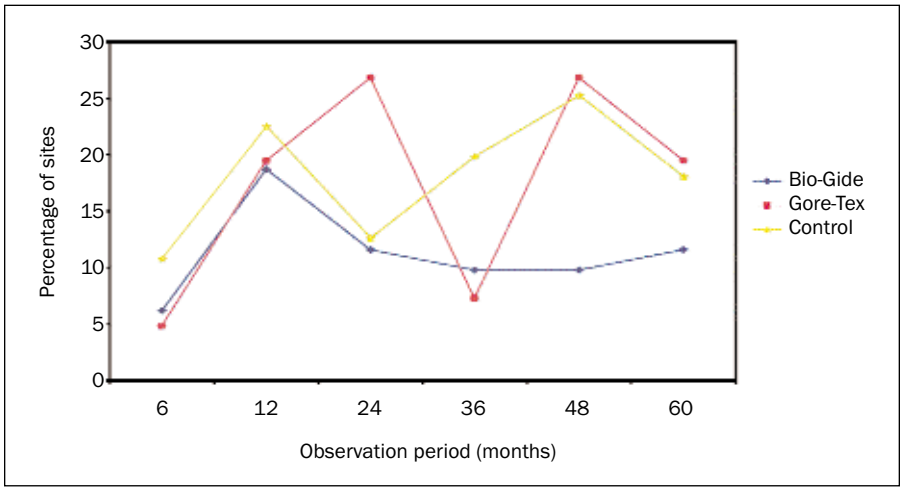

Fig 3 Frequency of plaque during 5 years of observation.

were significantly higher for the Bio-Gide and the Gore-Tex sites when compared to the control (LRT = 7.94, P = .005, and LRT = 26.98, P < .0001, respectively). A comparison of the 2 GBR materials revealed that Gore-Tex sites had significantly higher MBL values than Bio-Gide sites (LRT = 9.10, P = .0026). The MBL was not influenced by the type of restoration (LRT = 1.27, P = .259).

Regarding oral hygiene conditions at the GBR-treated implants and control sites, it was observed that the majority of patients maintained acceptable standards of oral hygiene over the years. Overall, plaque was present in 15% of all sites. After placement of the prosthetic restoration, the prevalence of plaque was 7.95%. It had increased to 20.45% at the 12-month observation and then decreased to 14.39% after 24 months (Table 3). During the observation period, the prevalence of plaque was not linear (Fig 3). However, in comparison to the baseline examination after placement of the final prosthesis, the differences were statistically significant (LRT = 21.21, P = .0007). The occurrence of plaque was significantly associated with the type of treatment (LRT = 13.81, P = .001) and also with the type of restoration (LRT = 11.42, P = .003). The highest frequencies of plaque were found in removable overdenture prostheses (23.6%), compared to 10.4% for fixed single-tooth restorations and 14.7% for fixed partial dentures.

In 16 patients, inflammatory symptoms of the peri-implant mucosa (mucosal problems) occurred and affected 12 Bio-Gide sites, 6 Gore-Tex sites, and 10 control implants. The symptoms were observed repeatedly in the same subjects. Mucosal problems were not associated with the time of observation (Table 3). In 3 patients who were restored with overdenture prostheses, hyperplasia was occasionally found and associated with visible plaque accumulation around the prefabricated bar. In 1 patient who presented with a slight swelling around 1 implant, a loose abutment screw was found when the screw-retained implant prosthesis was removed. Suppuration was detected at 11 sites and was not necessarily associated with other symptoms. Pain on palpation was found 6 times and affected 2 sites (Gore-Tex and control). In both sites, the symptom was associated with redness, suppuration, and swelling. Table 4 presents the frequency of the different symptoms, with the most severe one counted for each implant site. Of the control sites, 3.15% were affected with mucosal problems; 3.72% of the Bio-Gide sites and 7.32% of the Gore-Tex sites were affected (Table 2). A comparison of the frequencies of this variable in the 3 groups revealed that implants initially treated with Gore-Tex were 2.42 times more likely to develop mucosal problems than control sites (LRT = 7.18, P = .03, odds ratio = 2.42; Fig 4). The difference between Bio-Gide and Gore-Tex was also statistically significant (LRT = 4.78, P = .03, odds ratio = 2.04). The association between the type of restoration and the occurrence of mucosal problems was highly significant (LRT = 41.30, P < .0001), with a higher prevalence in removable restorations (14.4%) compared to fixed single-tooth (6.3%) or fixed partial (2.4%) restorations.

The KM decreased from 3.16 mm (SD = 1.96) at 6 months to 3.02 mm (SD = 1.96) at 60 months (LRT = 1.69, P = .20; Table 3, Fig 5). The overall KM was 2.70 mm (SD = 1.86) in the control group,

COPYRIGHT © 2001 BY QUINTESSENCE PUBLISHING CO, INC. PRINTING OF THIS DOCUMENT IS RESTRICTED TO PERSONAL USE ONLY. NO PART OF THIS ARTICLE MAY BE REPRODUCED OR TRANSMITTED IN ANY FORM WITHOUT WRITTEN PERMISSION FROM THE PUBLISHER.

Table 4 Frequency of Mucosal Problems

Symptom	6 months	12 months	24 months	36 months	48 months	60 months	Frequency
Redness	7	8	2	4	5	4	30
Hyperplasia	2	2	5	3	1	1	14
Suppuration	0	1	1	2	3	4	11
Swelling	0	0	2	0	1	0	3
Pain on palpation	0	1	0	2	1	2	6
Total	9	12	10	11	11	11	64

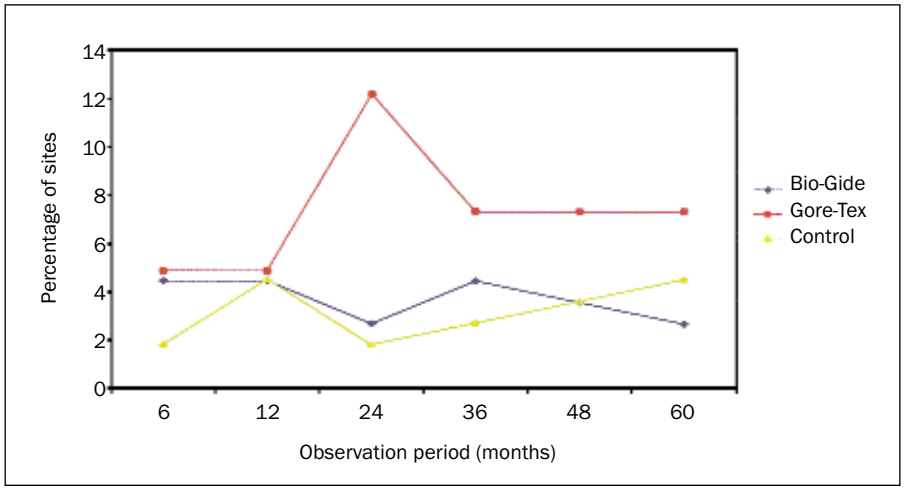

Fig 4 Frequency of mucosal problems during 5 years of observation.

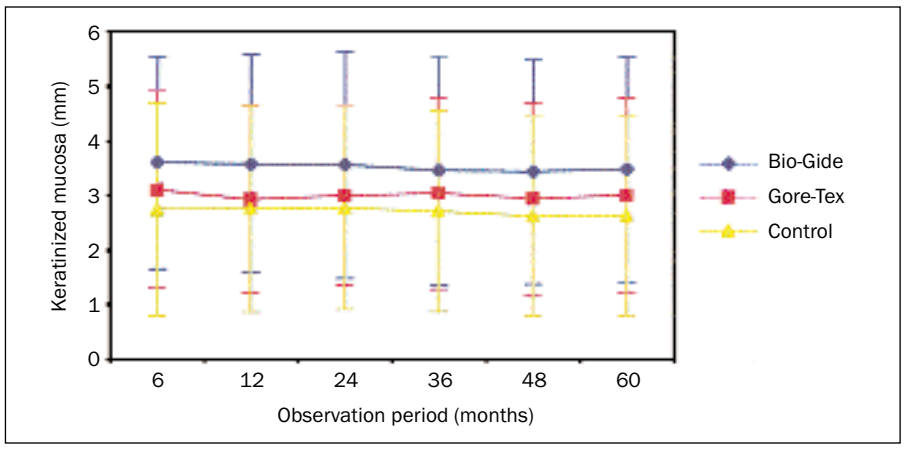

Fig 5 Keratinized mucosa during 5 years of observation.

3.52 mm (SD = 2.03) for Bio-Gide, and 2.99 mm (SD = 1.73) for Gore-Tex. These differences were statistically significant (LRT = 55.53, $P < .0001$; Table 2). The frequency of KM = 0 (no keratinized mucosa) was 3.8% (Bio-Gide), 6.2% (Gore-Tex), and 9.2% (control). These frequencies were significantly associated with the type of treatment (LRT = 16.99, $P = .001$).

The mean MSTL related to the top of the abutment was found to be in a submucosal position, indicated by negative mean values during the entire observation period. The values increased continuously, although this was not statistically significant, from –0.11 mm after placement of the prostheses to –0.01 mm at 60 months (LRT = 1.44, $P = .23$; Table 3, Fig 6). In the control group, the mean MSTL

COPYRIGHT © 2001 BY QUINTESSENCE PUBLISHING CO, INC. PRINTING OF THIS DOCUMENT IS RESTRICTED TO PERSONAL USE ONLY. NO PART OF THIS ARTICLE MAY BE REPRODUCED OR TRANSMITTED IN ANY FORM WITHOUT WRITTEN PERMISSION FROM THE PUBLISHER.

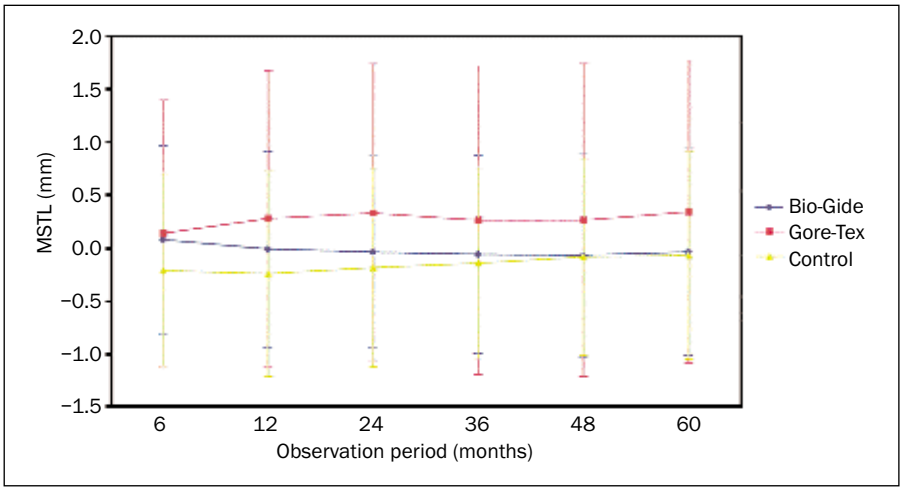

Fig 6 Marginal soft tissue level (MSTL) during 5 years of observation.

was –0.15 mm (SD = 0.94); for the Bio-Gide sites it was –0.05 (SD = 0.93), and for the Gore-Tex sites the mean MSTL was 0.27 mm (SD = 1.39). These differences were statistically significant (LRT = 17.41, $P = .0002$; Table 2). The influence of the type of restoration on MSTL was greater (LRT = 81.0, $P < .0001$) than the influence of the different treatment groups. Recession (with positive MSTL values) was most frequently observed in removable restorations (72.4%), while in fixed restorations the MSTL was most frequently found in an epimucosal or submucosal position (84.7% for single-tooth and 73.4% for fixed partials).

Relationships Between Clinical Parameters and Treatment Outcome (MBL)

The investigation of the association between the clinical parameters and MBL revealed that there was a positive association between mucosal problems and MBL (LRT = 17.23, $P < .0001$). A statistically significant relationship was also observed for recession and MBL (LRT = 40.38, $P < .0001$). The presence of plaque and the height of the KM had no significant influence on the MBL. A positive relationship was also found for the influence of MBL values on mucosal problems and on recession (LRT = 41.85, $P < .0001$): for each increase of MBL by 1 mm, the risk of developing mucosal problems increased 1.71 times (LRT = 12.43, $P = .0004$, odds ratio = 1.71).

Correlations Between Clinical Parameters

There is a strong association between the presence of plaque and the occurrence of mucosal problems. It was found that sites presenting with plaque were 7.74 times more likely to have mucosal problems than those without plaque (LRT = 56.85, $P < .0001$, odds ratio = 7.74). A positive correlation between the presence of plaque and MSTL values (LRT = 19.59, $P < .0001$) was also found.

When sites with and without keratinized mucosa were compared (KM = 0 versus KM > 0), no statistically significant correlations were found between plaque and the presence of keratinized mucosa (LRT = 1.61, $P = .20$). However, when the KM value was taken as a continuous variable, it was estimated that the likelihood of having plaque decreased with larger KM values (LRT = 12.23, $P = .0005$, odds ratio = 0.88). When estimating the influence of KM on mucosal problems, it was found that the absence of keratinized mucosa (KM = 0) was not significantly associated with mucosal problems. However, if keratinized mucosa was present on the buccal aspect (KM > 0), it was less likely, though not statistically significant, that mucosal problems would develop when compared to sites with KM = 0 (LRT = 1.90, $P = .17$, odds ratio = 0.54). The absence of KM indicated increasing MSTL values (LRT = 26.16, $P < .0001$). No association was found between recession (positive MSTL values) and the occurrence of mucosal problems (LRT = 0.59, $P = .44$).

DISCUSSION

The present study has shown that: *(1)* implants placed with or without GBR techniques had similar survival rates after 5 years of observation; *(2)* the MBL increased significantly over time, and the increase for the sites with GBR treatment was greater than that in the control sites; and *(3)* the presence of plaque was associated with mucosal problems, and the likelihood

COPYRIGHT © 2001 BY QUINTESSENCE PUBLISHING CO, INC. PRINTING OF THIS DOCUMENT IS RESTRICTED TO PERSONAL USE ONLY. NO PART OF THIS ARTICLE MAY BE REPRODUCED OR TRANSMITTED IN ANY FORM WITHOUT WRITTEN PERMISSION FROM THE PUBLISHER.

of having plaque decreased with larger KM values. The clinical parameters revealed differences between the 3 groups regarding the frequency of plaque, mucosal problems, the height of KM, and the MSTL. However, the type of restoration had a stronger influence than did the type of treatment on mucosal problems and recession (MSTL).

In the present study, implant survival did not differ significantly in the 3 groups; the cumulative 5-year survival rate varied between 92% and 97% for implants placed with or without GBR treatment. These results compare well with the 97.5% survival rate reported by Nevins and coworkers[9] after 6 to 74 months of loading in a multicenter study. The authors used autogenous bone or allogenic bone (demineralized freeze-dried bone [DFDB] or freeze-dried bone) in combination with e-PTFE membranes for the simultaneous or the staged approach. Fugazzotto[10] used DFDB alone or as a composite with tricalcium phosphate to fill defects around implants and for alveolar ridge augmentations in a staged approach. For both indications, he applied a Gore-Tex membrane and followed 626 implants in 331 patients. Fugazzotto reported about 98.6% survival after a loading period of 6 to 51 months; the majority of failures occurred in single-tooth replacements and were associated with short implant length.

The MBL observed for the control group in the current investigation was 1.7 mm after 5 years; this mean value is in accordance with the results reported by other authors. Ahlqvist and associates[11] calculated a bone loss of 1.6 mm after the first year and an additional amount of 0.1 mm during the second year of loading with screw-retained implant prostheses. Naert and colleagues[12] found a mean marginal bone loss of about 2 mm after a 1-year loading period when a bar-retained removable prosthesis was placed on 4 implants. When these mean values are compared, care must be taken to utilize the same reference point for measuring the MBL around implants from radiographs. Similar to the present study, Ahlqvist and associates[11] and Naert and associates[12] used the abutment-implant junction as the reference point. In previous reports from Adell and coworkers,[13] the apical implant shoulder margin was used as a reference, and a mean bone loss of 1.5 mm after the first year of loading with a screw-retained implant prosthesis was observed. To be able to compare these values, 0.8 mm should be added to the results of the latter study to compensate for the implant shoulder height.

There are few reports concerning the MBL of implants in which GBR was used. Jovanovic and colleagues[14] treated dehiscence defects with e-PTFE membranes and investigated the MBL from radiographs around 12 implants. They found a mean level of 1.73 mm 6 to 12 months after prosthesis placement. Buser and associates[15] investigated the long-term stability of implants placed in augmented alveolar ridges. After 5 years, all 12 implants had maintained osseointegration, with a mean bone loss of 0.3 mm measured from the radiographs. Lekholm and coworkers[5] investigated a group of patients retrospectively who had been provided with fixed or removable prostheses, including edentulous and partially edentulous situations. The authors found the bone level of control implants, which were entirely surrounded by bone during placement, at 1.7 threads on average after 5 years. This value corresponds to approximately 2.2 mm, provided that the upper shoulder margin serves as the reference and an interthread distance of 0.6 mm is assumed. If implant surfaces were found to be exposed during placement, Lekholm and coworkers did not apply any GBR techniques; they found the MBL at 1.1 threads (corresponding to about 1.8 mm) in cases of dehiscence defects around the implant shoulder. If fenestration defects had occurred along the implant axis, the mean bone loss reached 1.9 threads (corresponding to about 2.4 mm) after 5 years. These values are hard to interpret, since the initial defect size ("some threads were exposed") is not related to the final bone level measurements. However, Lekholm and coworkers questioned the necessity of GBR treatment in cases of exposed implant surfaces since, in their study, exposed threads did not necessarily lead to a progression in marginal bone loss or to mucosal problems. The authors concluded that stricter indication criteria should be considered for GBR treatment.[5]

The results of the current study have shown that, after a period of 5 years, the MBL varied between 1.8 and 2.2 mm when GBR (with Bio-Oss and resorbable or non-resorbable membranes) was applied, compared to the control group, with a mean MBL of 1.7 mm. The increase in resorption was generally more pronounced during the first 2 years after implant placement. Since a marginal bone level between 1.7 and 2.2 mm can be expected with or without GBR treatment after a 5-year period, it can be concluded that GBR is indeed indicated when the initial defect size is larger than approximately 2 mm in the vertical dimension. In other words, it seems unlikely that GBR offers any advantages in treating small defects, since resorption around 1.7 to 2.2 mm on average is anticipated in implants that are either entirely surrounded by host bone or placed in regenerated sites.

In the current study group, KM on the buccal aspect was present in the majority of the sites (91% to 96%). This incidence is higher than the reports in the literature. Lekholm and coworkers[16] found no KM in

COPYRIGHT © 2001 BY QUINTESSENCE PUBLISHING CO, INC. PRINTING OF THIS DOCUMENT IS RESTRICTED TO PERSONAL USE ONLY. NO PART OF THIS ARTICLE MAY BE REPRODUCED OR TRANSMITTED IN ANY FORM WITHOUT WRITTEN PERMISSION FROM THE PUBLISHER.

57% of the buccal sites in the maxilla and 68% in the mandible. Aspe and associates[17] observed no KM in 74% of the buccal sites and described the absence of KM as "the rule rather than the exception." In a more recent study by Wennström and colleagues, only 24% of the implants were found to be bordered by lining mucosa without KM.[18] The increased number of sites with KM, which was also observed in the current study, may be, according to Wennström and colleagues, explained by differences in the surgical handling of the soft tissue.[18] In the material presented here, great care was taken to place the incision in a paracrestal position on the lingual aspect and to move keratinized mucosa to the buccal during re-entry. The KM and MSTL values were found to be stable over time in all 3 groups. Differences among the groups and also between Bio-Gide and Gore-Tex were statistically significant, with the largest KM values for Bio-Gide. The greater amount of keratinized mucosa measured for GBR-treated sites (Bio-Gide or Gore-Tex) might be the result of the development of more scar tissue than in control sites.

In the present study, the incidence of plaque was 8% after placement of the definitive prosthesis and increased to 20% at 12 months. Plaque and mucosal problems were more frequently observed in sites restored with overdenture prostheses. For a few elderly patients, appropriate oral hygiene was not feasible because of their lack of manual dexterity, which worsened during the long period of observation. In this context, professional cleaning by the dental hygienist is essential, and was, in general, performed following recall visits.

Gore-Tex sites showed the highest incidence of inflammatory symptoms of the peri-implant mucosa (mucosal problems). The highest values (12.2% at 24 months) were associated with a high prevalence of plaque (27%). The larger MSTL values in Gore-Tex sites may be explained in part by the initial problems that occurred with Gore-Tex exposures and premature membrane removal. Additionally, it should be taken into account that both mucosal problems and recession (positive MSTL values) were found more frequently with the removable overdenture prostheses, and this influence was greater than the type of GBR treatment. The greatest changes in the marginal levels of the bone and the soft tissues (MBL and MSTL) were observed during the 6- and 12-month examinations, while changes were found to be less pronounced after 1 and 5 years. This indicates that maturation of the soft and hard tissues takes place during the initial phase, which is in accordance with the observation of Bengazi and associates, who described establishment of the marginal soft tissue level as an "early healing event."[19]

In the current investigation, it was clinically observed that suppuration occurred only in sites with subgingival crown margins, mostly in combination with a large amount of KM. Since it has been demonstrated that bacteria penetrate through the microgap at the abutment-prosthesis interface,[20] the reason for suppuration might be, in addition to the bacterial challenge, the sealing effect of a large, cuff-like keratinized and collagen-rich masticatory mucosa. It has been shown in the present study that the presence of plaque enhances the risk of developing mucosal problems and also slightly increases the risk of mucosal recession. It was also demonstrated that mucosal problems can be associated with bone resorption, as seen in the radiographs. Although in the current study the presence or absence of KM was not statistically significantly related to the oral hygiene status, it was found that sites with higher KM values had a lower occurrence of plaque accumulation. Additionally, the presence of KM was associated with fewer mucosal problems, versus sites bordered by lining mucosa only (KM = 0).

Wennström and coworkers[18] investigated the soft tissue conditions around Brånemark System implants that had been in function for a minimum of 5 years. The authors observed 18% plaque-carrying sites facially and 39% plaque in the approximal areas. They reported that the lack of KM did not impede proper oral hygiene and had no significant effect on oral health conditions, expressed in Gingival Index, probing depth, and bleeding on probing.[18] Strub and associates[21] reported from an experimental study with dogs that the application of free gingival grafts increased the amount of KM but did not improve the condition of the peri-implant mucosa. On the other hand, Warrer and coworkers[22] reported from an experimental study with monkeys that implant sites without KM demonstrated significantly more recession after 9 months of plaque accumulation, while sites with KM showed only minimal soft tissue recession.

Bengazi and colleagues[19] investigated 41 patients, who were provided with Brånemark System implants, over a period of 2 years. The authors distinguished between sites with lining mucosa (lacking KM) and sites with masticatory mucosa. They found that an "apical displacement of the gingival margin" (recession) was more common in the sites without KM and that the majority of this recession was limited to ≤ 1 mm. After 6 and 24 months, no further recession was observed at sites without KM, while a slight increase of 0.2 mm was found in sites bordered by masticatory mucosa. The authors concluded that the lack of KM did not significantly affect the amount of soft tissue recession.[19]

COPYRIGHT © 2001 BY QUINTESSENCE PUBLISHING CO, INC. PRINTING OF THIS DOCUMENT IS RESTRICTED TO PERSONAL USE ONLY. NO PART OF THIS ARTICLE MAY BE REPRODUCED OR TRANSMITTED IN ANY FORM WITHOUT WRITTEN PERMISSION FROM THE PUBLISHER.

In the present study, changes in the marginal soft tissue level revealed a minor recession of 0.1 mm during the entire observation period. Correspondingly, a slight shrinkage of approximately 0.14 mm was estimated for the height of KM. The changes in both variables (MSTL and KM) were not statistically significant and were in a range that did not imply any clinical consequences. According to the reported results, possible advice is that care should be taken during re-entry to shift part of the KM to the buccal aspect. However, additional surgical intervention to enhance the zone of masticatory mucosa is normally not required. This is because deterioration in the health conditions of the soft tissue around dental implants may not be expected, provided that appropriate oral hygiene conditions can be maintained.

SUMMARY

The application of GBR techniques with Bio-Gide or Gore-Tex membranes in combination with Bio-Oss grafting material during implant placement did not increase the susceptibility to implant failure during a longitudinal observation of 5 years. However, the marginal bone level was significantly increased at GBR sites compared to control sites, while the differences in mucosal problems and recession were more strongly associated with the type of implant restoration than with the application of GBR treatment.

ACKNOWLEDGMENT

The authors would like to gratefully acknowledge the statistical assistance of Dr Penelope Vounatsou, Department of Public Health and Epidemiology, Swiss Tropical Institute.

REFERENCES

1. Zitzmann NU, Naef R, Schärer P. Resorbable versus nonresorbable membranes in combination with Bio-Oss for guided bone regeneration. Int J Oral Maxillofac Implants 1997;12:100–109.
2. Zitzmann NU, Schärer P, Marinello CP. Factors influencing the success of GBR: Smoking, timing of implant placement, implant location, bone quality and provisional restoration. J Clin Periodontol 1999;26:673–682.
3. Zitzmann NU, Schärer P, Marinello CP, Schüpbach P, Berglundh T. Alveolar ridge augmentation with Bio-Oss. A histological study in humans. Int J Periodontics Restorative Dent 2001;21(3):289–295.
4. Hockers T, Abensur D, Valentini P, Legrand R, Hämmerle CHF. The combined use of bioresorbable membranes and xenografts or autografts in the treatment of bone defects around implants. Clin Oral Implants Res 1999;10:487–498.
5. Lekholm U, Sennerby L, Roos J, Becker W. Soft tissue and marginal bone conditions at osseointegrated implants that have exposed threads: A 5-year retrospective study. Int J Oral Maxillofac Implants 1996;11:599–604.
6. Albrektsson T, Zarb G, Worthington P, Eriksson AR. The long-term efficacy of currently used dental implants: A review and proposed criteria of success. Int J Oral Maxillofac Implants 1986;1:11–25.
7. Chan MFW-Y, Närhi TO, de Baat C, Kalk W. Treatment of the atrophic edentulous maxilla with implant-supported overdentures: A review of the literature. Int J Prosthodont 1998;11:7–15.
8. Diggle PJ, Liang K-Y, Zeger SL. Analysis of Longitudinal Data. New York: Oxford University Press, 1994:169–189.
9. Nevins M, Mellonig JT, Clem DS III, Reiser GM, Buser DA. Implants in regenerated bone: Long-term survival. Int J Periodontics Restorative Dent 1998;18:35–45.
10. Fugazzotto PA. Success and failure rates of osseointegrated implants in function in regenerated bone for 6 to 51 months: A preliminary report. Int J Oral Maxillofac Implants 1997; 12:17–24.
11. Ahlqvist J, Borg K, Gunne J, Nilsson H, Olsson M, Åstrand P. Osseointegrated implants in edentulous jaws. A 2-year longitudinal study. Int J Oral Maxillofac Implants 1990;5: 155–163.
12. Naert I, Gizani S, van Steenberghe D. Rigidly splinted implants in the resorbed maxilla to retain a hinging overdenture: A series of clinical reports for up to 4 years. J Prosthet Dent 1998;79:156–164.
13. Adell R, Lekholm U, Rockler B, Brånemark P-I. A 15-year study of osseointegrated implants in the treatment of the edentulous jaw. Int J Oral Surg 1981;10:387–416.
14. Jovanovic SA, Spiekermann H, Richter EJ. Bone regeneration around titanium dental implants in dehisced defect sites. A clinical study. Int J Oral Maxillofac Implants 1992;7:233–245.
15. Buser D, Dula K, Lang NP, Nyman S. Long-term stability of osseointegrated implants in bone regenerated with the membrane technique. Clin Oral Implants Res 1996;7:175–183.
16. Lekholm U, Adell R, Lindhe J, et al. Marginal tissue reactions at osseointegrated titanium fixtures. (II). A cross-sectional retrospective study. Int J Oral Maxillofac Surg 1986; 15:53–61.
17. Aspe P, Zarb GA, Schmitt A, Lewis DW. The longitudinal effectiveness of osseointegrated dental implants. The Toronto study: Peri-implant mucosal response. Int J Periodontics Restorative Dent 1991;11:95–111.
18. Wennström JL, Bengazi F, Lekholm U. The influence of the masticatory mucosa on the peri-implant soft tissue condition. Clin Oral Implants Res 1994;5:1–8.
19. Bengazi F, Wennström JL, Lekholm U. Recession of the soft tissue margin at oral implants. Clin Oral Implants Res 1996; 7:303–310.
20. Quirynen M, Bollen CML, Eyssen H, van Steenberghe D. Microbial penetration along the implant components of the Brånemark system. Clin Oral Implants Res 1994;5:239–244.
21. Strub JR, Gaberthüel TW, Grunder U. The role of attached gingiva in the health of peri-implant tissue in dogs. Part I. Clinical findings. Int J Periodontics Restorative Dent 1991; 11:317–333.
22. Warrer K, Buser D, Lang NP, Karring T. Plaque-induced peri-implantitis in the presence or absence of keratinized mucosa. Clin Oral Implants Res 1995;6:131–138.