Aim. To evaluate clinical outcome 24 months after guided tissue regeneration (GTR) therapy of deep periodontal pockets in patients poorly responding to conventional flap surgery, to compare its efficacy with conventional flap surgery, and to analyze the factors associated with the healing outcome.

Methods. Twenty defects underwent GTR with ePTFE membranes. Clinical measurements were recorded at the baseline and at 6, 12 and 24 months after the surgery. The 24-months outcomes were compared to those in the same 20 patients previously treated with conventional flap surgery (intrasubject control), and in matched control patients who underwent conventional treatment alone.

Results. After 24 months, GTR treatment significantly reduced the probing pocket depth (dPPD=2.7±1.2 mm, p<0.001) and increased probing attachment level (dPAL=2.3±1.5 mm, p<0.001) in comparison to the previous conventional treatment. No significant difference was observed before the 24-month measurement compared to matched controls who responded well to the conventional treatment. However, 24 months after the surgery, dPAL obtained in the GTR group significantly exceeded that after conventional treatment. There was a significant association between 24-month dPAL and dPPD with the configuration and the intrabony depth of the defect, level of oral hygiene, and smoking status of the patient.

Conclusion. The efficacy of GTR is at least equal to that of conventional flap surgery. It is desirable in patients poorly responding to flap surgery alone. The gain and maintenance of clinical attachment is associated with the level of oral hygiene, smoking status, and morphology and intrabony depth of the defect.

Key words: dental implants; dental plaque; gingival pocket; guided tissue regeneration; oral hygiene; parodontosis; periodontal pocket; regeneration, guided tissue; smoking; surgical flaps

Ideally, periodontal regeneration is attempted after resolving the periodontitis that produced the loss of periodontal support. Guided tissue regeneration favors regeneration of new connective tissue attachment to denuded root surfaces by allowing selective coronal regrowth of periodontal ligament cells (1-3). The exclusion of gingival fibroblasts and epithelial cells by barrier membranes allows cellular elements derived from the periodontal ligament and alveolar bone to reach the root surface first after wounding, where they can regenerate new cementum and connective tissue attachment (4,5).

Due to their localized nature and dentoalveolar anatomy, periodontal infections frequently result in a pattern of breakdown characterized by the presence of intrabony lesions. In adult patients, the prevalence of intrabony defects is between 8% and 32% (6-9). Therefore, the treatment of intrabony defects is of utmost importance to clinical periodontal practice.

Guided tissue regeneration treatment is a highly effective and reproducible treatment modality in deep intrasosseous vertical defects and grade II furcations (2,10-16). The gain of new attachment following membrane placement has been documented by several short-term and some long-term studies using clinical measurements, radiographs, and reentry operations (2,10,11,17-25). Gottlow et al (17) examined long-term stability of the attachment gain obtained as a result of guided tissue regeneration. The results from 39 patients (52 teeth) indicated that the attachment can be preserved for periods up to five years in a well-maintained patient population. Cortellini et al (22) reported good long-term results of 40 intrabony defects in 23 patients with regular recall and low plaque scores. A net gain of new clinical attachment amounting to 1.37 mm after 4 years was reported by Weigel et al (25).

Guided tissue regeneration is a treatment of choice in patients with difficult periodontal conditions, when conventional measures fail. However, only a limited number of controlled clinical trials on the efficacy of guided tissue regeneration compared to conventional flap surgery have been published in recent years (26-31).

Since guided tissue regeneration is a relatively new technique, the determinants of treatment outcome
are still largely unpredictable (32). To improve the extent and predictability of clinical outcome, it is of paramount importance to identify critical factors associated with the healing response. Identification of these factors represents the first step towards their possible control. Recent evidence underlines the importance of patient-associated variables (e.g., cigarette smoking, oral hygiene) and defect characteristics (e.g., morphology) in determining the healing outcomes of guided tissue regeneration procedures (2, 10, 13, 14, 16, 22, 29, 33).

In the present study we (a) evaluated the gain of new clinical attachment 24 months following guided tissue regeneration therapy of deep periodontal pockets in patients poorly responding to conventional flap surgery, (b) compared the observed changes to those achieved through a conventional flap surgery approach, both in the same patients (before guided tissue regeneration) and in matched control subjects, and (c) analyzed significant factors associated with the healing outcomes.

Patients and Methods

Patients
Twenty healthy patients (mean age: 48.1±6.8 years, range: 33.1 to 58.4 years) from private practice were enrolled in the experimental group, with one tooth per patient selected for the study. Six subjects were classified as smokers (33). The experimental group was partly composed of a previous study population (34). Entry criteria were good general health and presence of deep intrabony defects with insufficient response to earlier conventional periodontal treatment (34). Teeth lost from the previous study sample due to traumatic occlusion after guided tissue regeneration treatment were excluded from the present investigation.

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The tooth population included 6 incisors, 5 canines, 2 bicusps, and 7 molars with vertical intrabony defects characterized by probing pocket depth of at least 7 mm and radiographic evidence of an intrabony component. Thirteen teeth were located in the maxilla and seven in the mandible. The initial therapy and measurements of clinical parameters probing attachment level (PAL), probing pocket depth (PPD), and the Plaque Index (PI) (35) were performed in a predetermined manner (34) and included 6 assessments per tooth. The recordings represented, at a given site, the greatest distance between the gingival margin or the cemento-enamel junction and the base of the probeable pocket.

The selection of sites was based on the judgement that the reduced, remaining periodontal support in combination with the particular defect morphology would hamper the long-term result of conventional therapy and cause tooth extraction.

Surgical and Postsurgical Procedures

Following anesthesia, mucoperiosteal flaps were elevated to access the defect using a modified Widman flap technique in a manner identical to that described in the previous study (34). Commercially available expanded polytetrafluoro ethylene (ePTFE) membranes (Gore periodontal material; Gore-tex W.L. Gore & Ass. Inc., Flagstaff, Ariz, USA) were used to cover the defects. The postsurgery protocol emphasizing wound stability and infection control was employed. Chlorhexidine mouthwash (Chlorhexamed-Fluid, Procter & Gamble GmbH, Schwalbach, Germany) was used postoperatively until 2 weeks after the removal of the membrane. Antibiotics were administered until 10 days after the surgery (doxycycline 100 mg per day). Four to 6 weeks following placement of the membrane, a second surgical procedure was performed to remove the barrier. On that occasion, membrane exposure was measured as the distance from the coronal margin of the membrane to the gingival margin.

The patients were scheduled for regular check-ups.

Control Groups

The study design is illustrated in Figure 1. The relative efficacy of guided tissue regeneration treatment (A2, Fig. 1) was determined (a) compared to the 24-month outcome achieved after the preceding conventional treatment of the same teeth in the experimental group (intra-subject controls, A1), and (b) compared to the 24-month outcome achieved through conventional treatment in a control group matched for the age, gender, smoking status, initial plaque index, clinical attachment loss, location and configuration of defect (inter-subject controls, B).

The study design aimed at assessing the relative efficacy of guided tissue regeneration treatment compared to conventional treatment. Intra-subject control group comprised "difficult" cases, i.e., patients showing complete or partial relapse within 24 months after flap surgery alone. The selection criterion for guided tissue regeneration treatment was the recurrence of the preoperative probing pocket depth or attachment level. Hence, surgery performed on these subjects was at the same sites as with conventional treatment. Inter-subject control group comprised "normal" cases subjected to the flap surgery alone.

Conventional treatment comprised all procedures described above apart from the insertion and removal of a barrier membrane, and included the routine prescription of prophylactic antibiotics (as described). The initial periodontal status was equal in all groups; however, borderline significance
was observed for the baseline probing attachment level difference between the guided tissue regeneration group (10.4 mm) and the B control group (9.4 mm).

Guided tissue regeneration surgery in the test group (A2) and conventional treatment of the inter-subject controls (B) was carried out by I.B., operator I, whereas the preceding conventional treatment in the test group (A1) was provided by J.B., operator II. The initial clinical assessments in the group A2 patients were made by J.B., while an independent trained evaluator assessed the treatment-related changes at 6, 12 and 24 months in the groups A1 and B. The evaluators were calibrated to equal assessment criteria.

Follow-up Measurements

Six, 12, and 24 months after surgery, each site exposed to treatment was reexamined. This included the assessment of probing pocket depth, probing attachment level, and PI at the surgically treated sites and was performed in a manner identical to that described for the baseline examination.

Data Analysis

Since not all the aspects evaluated per tooth were exposed to the guided tissue regeneration procedure, but may have been included in the flap procedure to get access for membrane placement to cover the defect, the site was chosen as the statistical unit (N). The sites with the deepest baseline probing pocket depth or probing attachment level associated with the defect treated by guided tissue regeneration were chosen for analysis. Data were expressed as means ±SD.

Probing attachment gain (dPAL0-24) and probing depth reduction (dPPD0-24) represented the difference between the baseline and 24-month measurements, and served as the 24-month outcome variables. They were compared in terms of the following patient variables and defect/surgery characteristics: Plaque Index (PI) <1 or ≥1, membrane exposure £1 or >1 mm, depth of defect £2 or >2 mm, type of defect: 2 or 3 osseous walls of defect no (1)/yes (2), smoking status no (1)/yes (2).

The significance of differences between numerical outcome variables was tested using non-parametric Wilcoxon matched-pairs test.

In view of a restricted sample size, the α error was set at 0.05. Taking into account the multiple comparisons made in this study, notations of significance were restricted to the comparisons made on the whole observation period (24 months). The significance level was adjusted to a reasonable extent according to the rule of thumb after Bonferroni, i.e., α’=α/number of multiple tests. The relevant number of multiple tests was determined depending on the kind of comparison made (see captions to the tables and figures). The adjustment was restricted to a significance level of α’=α/6=0.008 in face of the sample size (see Table 1).

Statistical power in this study was sufficient to evaluate differences within the limits of periodontal probing sensitivity, defined as ±1 mm (36,37).

Table 1: Clinical outcome (mean±SD) of guided tissue regeneration (GTR) treatment and conventional flap surgery (presurgery, 6, 12 and 24 months postsurgery; 20 patients).

Results

Baseline Characteristics

Thirteen sites showed 1/2-wall defects, and 7 sites 2/3-wall or 3-wall defects. The depth of the intrabony component of the defect was less or equal to 2 mm in 7 sites, while it exceeded 2 mm in 13 sites (2.96±1.63 mm).

The clinical parameters are shown in Table 1. The baseline probing attachment loss and probing pocket depth were slightly more marked in the test group (A1) compared to the controls (B).

At the time of the re-entry procedure, 8 patients in the study group had a minimal amount of membrane exposure (0 to 1 mm), whereas 12 patients showed 1 to 3 mm of the material coronally to the gingival margin.

The adherence to the reexamination regimen was suboptimal with a median of 3 visits per year. Mean baseline plaque index was 1.2±0.5 (range: 0.25 to 2.0) in the guided tissue regeneration treatment subjects (A2 group).

24-Month Treatment Outcomes

The absolute levels of clinical attachment and probing pocket depth observed at follow-up measurements (Table 1) were not significantly different between guided tissue regeneration treatment subjects (A2) and the inter-group controls (B), while they were markedly more favorable compared to the intra-subject control group (A1 group).

A significant gain of clinical attachment was obtained between the baseline and the 24-month observations, both in the guided tissue regeneration group A2 (dPAL0-24=2.3±1.5 mm) and B control group (dPAL0-24=1.3±1.2 mm). The net gain of clinical attachment after conventional treatment of
the study subjects A1 (dPAL0-24=0.3±1.3 mm) was not significantly different from zero. Significant reductions of probing pocket depth at 24 months were observed in all patient groups. While the improvement was not significantly different between guided tissue regeneration treatment subjects A2 (dPPD0-24=2.8±1.2 mm) and the inter-group controls B (dPPD0-24=2.0±1.5 mm), the decrease of pocket depth was markedly smaller under the intra-subject control condition A1 (dPPD0-24=0.6±1.1 mm, p£0.001).

Other Treatment-Related Changes

No significant differences in plaque accumulation were observed between the intra-subject control condition A1 and the inter-group controls B at baseline and 6-month measurements. However, the 12- and 24-month recordings showed significantly lower plaque scores in the guided tissue regeneration treatment group (Table 1).

Factors Affecting Guided Tissue Regeneration Treatment Outcome

There was a tendency for smokers to gain less attachment (dPAL0-24=1.0±1.0) compared to non-smokers (dPAL0-24=2.6±1.4) but this difference was not significant (p=0.07). The probing pocket depth was significantly reduced in non-smokers (dPPD0-24=3.2±0.8) compared to smokers (dPPD0-24=1.0±1.0, p=0.01) (Fig. 2).

The amount of probing attachment gained at 24 months after surgery was slightly yet not significantly, greater with better oral hygiene (PI<1) compared to modest or poor oral hygiene (dPAL0-24=3.0±1.3 vs 1.7±1.4). The difference of pocket depth reduction was also not statistically significant between the two groups (dPPD0-24=3.5±0.6 vs 2.5±1.2, p=0.13) (Fig. 3).

Attachment gain significantly varied between the groups, depending on the type of defect involved (p=0.011). 2- and 3-wall defects showed a higher amount of gained attachment (dPAL0-24=3.5±1.1) in comparison to 1-2-wall defects (dPAL0-24=1.6±1.2) (Fig. 4).

The intrabony depth of the defect significantly correlated with clinical attachment gain (p=0.01). Defects exceeding 2 mm in depth presented a greater amount of attachment gain after 24 months (dPAL0-24=2.9±1.3 vs 1.0±0.7) (Fig. 5).

Membrane exposure at the time of retrieval was not a statistically significant factor in determining the 24-month treatment outcome (p>0.05).

The additional efficacy of guided tissue regeneration (GTR) treatment (A2) compared to conventional flap surgery alone in the same patients (A1) and in matched controls (B). The difference between treatment outcomes obtained through GTR treatment compared to those achieved by the preceding conventional approach (A2 versus A1) is represented by continuous lines. The additional efficacy of GTR treatment increases during the first 12 months after the surgery, with a slight decrease toward 24-month measurement. Comparing the outcome of GTR treatment to conventional flap surgery in matched normal responders (A2 versus B, see broken lines), the additional efficacy of GTR treatment is markedly smaller until 24 months postsurgery, when the relative treatment effect in terms of clinical attachment gain reaches statistical significance (data point above dotted line).
Discussion
Despite the recent development of resorbable membranes, ePTFE membranes are not outdated. Their successful application has been proven in many scientific trials as well as in daily practice. The goal of the present study was to evaluate the efficacy of ePTFE membranes in the treatment of deep periodontal pockets compared to conventional treatment and to investigate possible determinants of clinical outcomes following guided tissue regeneration treatment. The possibility of a selection bias can be excluded since various tooth types and positions were included in the study and entry criteria were restricted by the extent and configuration of the defect. In agreement with previous observations (10,17,18,21), the present study demonstrated that periodontal treatment, based on the principle of guided tissue regeneration, resulted in varying amounts of clinical attachment gain, and that the gain of supporting tissues can be maintained over an extended period of time (17,25,29,38). Our clinical results are within the range of those reported for intrabony defects, even in patients showing a lower oral hygiene standard and various morphotype defects (11,26,34,39).

Only few controlled clinical trials on the efficacy of guided tissue regeneration compared to conventional flap surgery in intrabony defects have been published so far, mostly relying on small sample sizes and short observation periods. Nygaard-Ostby and coworkers (30) compared clinical healing following guided tissue regeneration in deep intrabony pockets to healing following gingival flap surgery alone. Six months after the surgery, significant differences between guided tissue regeneration and control treatments were observed in probing depth reduction (1.7±1.5 mm). Pritlove-Carson et al (28) compared guided tissue regeneration utilizing Gore-Tex membranes with conventional surgery in 20 matched periodontal defects in 9 subjects. At 12 months, probing depth reductions were significantly greater at the Gore-Tex treated sites, but no difference in probing attachment level gains were found in comparison to conventional flap surgery.

Two recent studies reviewed the current periodontal literature with respect to guided tissue regeneration in intrabony defects and furcations using meta-analysis (40,41). Laurell et al (41) reviewed studies presented during the last 20 years on the surgical treatment of intrabony defects. In total, guided tissue regeneration resulted in significant pocket reduction and clinical attachment level gain of 4.2 mm, which correlated significantly to the defect depth. The intrabony defect has to be at least 4 mm deep in order to benefit from guided tissue regeneration procedures.

In the present study, we determined the amount of clinical improvement by means of a triple study design comprising conventional and guided tissue regeneration treatment conditions of the study group and conventionally treated matched control subjects (Fig. 6). As expected, the treatment outcomes of the guided tissue regeneration treatment were clearly superior to those achieved by the preceding conventional approach (A2 versus A1) throughout the whole observation period. On the other hand, additional efficacy of guided tissue regeneration treatment was markedly smaller when compared to conventional flap surgery in matched normal responders (A2 versus B). The results suggest that guided tissue regeneration procedures have clinical potentials similar to conventional flap surgery in intrabony defects under the given protocol. There is a clear indication for guided tissue regeneration treatment in patients responding poorly to flap surgery alone.

Current clinical indications for the use of guided periodontal tissue regeneration include degree II furcation defects and 2- or 3-walled vertical interproximal and circumferential intrabony defects, with a tendency of complex, combined defects to display the best results (42). Other types of periodontal defects can also be treated with this technique, but the predictability of success is decreased. Our statistical analysis indicated that 24-month clinical attachment gain was, indeed, greater in 2+3-wall and 3-wall defects than in 1+2-wall defects. Our findings correspond to those of Becker and coworkers (10,38) who observed the best responses to guided tissue regeneration in 3-wall intrabony defects. However, in several studies the intrabony depth of the defect appears to be a significant confounding factor in the assessment of the impact of the type of defect and, thus, to yield conflicting results. Since the mean defect depth was not significantly different between 2-/3-walled and 1-/2-walled defects, our results suggest that both variables are significant predictors of the treatment outcome.

Membrane coverage by a flap is thought to minimize postsurgical gingival shrinkage due to the irritating effect of the membrane (43). It has been demonstrated that the exposure of ePTFE membrane may result in a gross contamination by oral bacteria (44). In our study, however, membrane exposure appeared not to be a statistically significant factor in determining the 24-month
treatment outcome. This observation is in line with the results of a controlled clinical trial on class II furcation defects reported by Machtet al (45).

Apart from the defect morphology and surgical parameters, smokers present a less favorable response following both non-surgical and periodontal therapeutic (16,17,22,29,31,33,46). In the present study, absence of smoking was associated with greater probing depth reduction 24 months after the surgery. These results are in agreement with recent findings indicating a significant negative impact of smoking status on the clinical outcome after the guided tissue regeneration procedure due to impaired wound healing (29,33,47).

The level of oral hygiene is an important determinant of the healing response following both conventional and periodontal surgery (22,48). The marked improvements obtained with guided tissue regeneration treatment in the present study may partly be accounted for by a higher level of oral hygiene during the maintenance phase compared to the control conditions. Within the guided tissue regeneration group, however, the clinical response was not significantly associated with the level of oral hygiene during the maintenance phase. Our results indicate that guided tissue regeneration is a highly efficacious treatment even with suboptimal oral hygiene and various morphotype defects. However, subjects who maintain good oral hygiene and have minimal gingival inflammation can be expected to develop a better regenerative response (45).

References

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