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Smoking affects the outcome of guided tissue regeneration with bioresorbable membranes: a retrospective analysis of intrabony defects

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Abstract

Objectives: To disclose factors that may influence the results of guided tissue regeneration (GTR) treatment in intrabony defects with bioresorbable membranes.

Methods: Forty-seven intrabony defects in 32 patients were treated by means of polylactic acid/citric acid ester copolymer bioresorbable membranes. At baseline and after 1 year, the following parameters were recorded: (1) probing pocket depth (PPD), (2) gingival recession (REC), (3) probing attachment level (PAL) = PPD+REC, (4) presence/absence of plaque (PI), (5) presence/absence of bleeding on probing (BOP) and (6) intrabony component (IC) configuration (i.e. primarily presence of one, two, or three bone walls). Occurrence of membrane exposure and smoking habits were also recorded. Significance of differences between categorical variables was evaluated with McNemar's test, and between numerical variables with the *t*-test for paired observations. Generalized linear models were constructed to evaluate the influence of various factors on PAL gain and PPD after 1 year, including in the analysis only one defect per patient (i.e. 32 defects) chosen at random. Odds ratios were calculated using the Mantel–Haenszel method. Differences between smokers and non-smokers were evaluated by means of Pearson's χ^2 and Student's *t*-test for non-paired observations.

Results: At baseline, a mean PPD of 8.6 ± 1.1 mm and a mean PAL of 9.8 ± 1.6 mm was recorded. Statistically significant clinical improvements were observed 1 year after GTR treatment. An average residual PPD of 3.7 ± 1.1 mm and a mean PAL gain of 3.8 ± 1.5 mm were recorded. IC configuration and exposure of the membrane did not seem to influence the results, while a negative effect of smoking on the clinical parameters was observed. Smokers gained approximately 1 mm less in PAL than non-smokers (3.2 ± 1.4 versus 4.3 ± 1.3, respectively; $p = 0.03$) and had approximately seven times less chances to gain 4 mm in PAL as compared with patients who did not smoke (odds ratio: 0.15). PPD reduction was less pronounced in smokers than in non-smokers (4.5 ± 0.7 versus 5.5 ± 0.7, respectively; $p < 0.01$), resulting in somewhat deeper residual PPD in smokers than in non-smokers (3.6 ± 1.0 versus 3.4 ± 1.1; $p > 0.05$).

Conclusion: Smoking impairs the healing outcome of GTR treatment of intrabony defects with bioresorbable membranes.

Key words: bioresorbable membranes; clinical; guided tissue regeneration; intrabony; membrane exposure; retrospective; smoking

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Guided tissue regeneration (GTR) is an established treatment methodology, based on the biological principle that a desired wound-healing result can be achieved when it is ensured, for example by means of a physical barrier (e.g. membrane) that cells with the capacity to regenerate the particular type of lost/diseased tissue are allowed to populate the defect/wound during healing (Karring et al. 1993). A large number of studies have demonstrated that considerable clinical improvements (i.e. shallow probing pocket depths (PPDs), gains in probing attachment level (PAL), and bone fill) are obtained following treatment of a variety of periodontal defects according to this principle. In addition, several reports have provided histological evidence in humans that GTR treatment in fact results in true regeneration of the attachment apparatus on previously periodontitis-affected roots (for a review see Karring et al. 2003).

The membranes used for GTR may be either non-bioresorbable or bioresorbable, but the latter are usually preferred because they reduce the risk of site morbidity, patient discomfort, and costs. It has been demonstrated in several studies that clinical improvements of similar magnitude can be obtained after GTR treatment of intrabony periodontal defects with both kinds of materials (for a review see Stavropoulos 2002), and factors affecting the outcome of GTR therapy of such defects have been described in several reports (Tonetti et al. 1993, 1995, 1996, Falk et al. 1997, Trombelli et al. 1997, Mayfield et al. 1998, Ehmke et al. 2003). Among other factors, smoking for instance was found to have a detrimental effect on the treatment outcome with non-bioresorbable as well as bioresorbable membranes (Tonetti et al. 1995, Trombelli et al. 1997, Ehmke et al. 2003).

The aim of the present study was to report on the results of GTR treatment in intrabony defects with bioresorbable membranes and to identify factors that may influence treatment outcome.

Material and Methods

Forty-seven interproximal intrabony defects in 32 adult patients (13 males and 19 females, mean age: 41 years) presenting for treatment at the Department of Periodontology and Oral Gerontology, Royal Dental College, University of Aarhus, Denmark, were treated by means of GTR. Twenty-one subjects had one defect, eight subjects had two defects, two subjects had three defects, and one subject had four defects. Approximately 3 months after initial periodontal treatment, which consisted of oral hygiene instruction and scaling and root planing, the defects presented the following characteristics: (a) probing pocket depth (PPD) $\geqslant$7 mm and radiographic evidence of an intrabony component (IC) of $\geqslant$4 mm, which did not include a furcation involvement; (b) the site had not been treated surgically within the last year before the study; (c) systemic antibiotics had not been used within the last 6 months prior to treatment.

The following surgical procedure was used. After local anesthesia, intrasulcular incisions were made on the buccal and oral aspects of the jaw at the defect site and extended to the adjacent teeth mesially and distally. Care was taken to preserve as much as possible of the interdental tissues at the defect site. Full-thickness mucoperiosteal flaps were then raised at both the buccal and oral aspects of the teeth. The defect was debrided and the roots were scaled and planed, and rinsed with sterile saline. It was then assessed whether the defect was mainly of a one-, two-, or three-wall type, and whether it was $\geqslant$4 mm deep. A polylactic acid/citric acid ester copolymer bioresorbable barrier membrane (Guidor®, Guidor AB, Huddinge, Sweden) was trimmed and adapted to fully cover the defect. The membrane was extending at least 3 mm beyond the margins of the defect, and was stabilized by means of a resorbable ligature, incorporated in the membrane, around the neck of the adjacent teeth. (Fig. 1a–d). The mucoperiosteal flaps were coronally displaced to cover the membrane. In order to avoid tension on the tissues, horizontal split-thickness and/or vertical releasing incisions were made as needed. The flaps at the defect site were secured in position by means of vertical mattress and single interdental 4.0 teflon sutures (Gore-Tex® suture material, W.L. Gore & Associates, Flagstaff, AZ, USA). The sutures were removed 2–3 weeks later.

The patients received a combination of amoxicillin 750 mg (Imacillin®, Astra Danmark A/S, Albertslund, Denmark) and metronidazol 250 mg (Elyzol®, Dumex, A/S Copenhagen, Denmark) systemically for a period of 5 days, starting 1 h before surgery. They were instructed to rinse with a 0.2% solution of chlorhexidine digluconate (CHX) twice a day and to avoid brushing the operated area for 6 weeks post-operatively. Hereafter careful mechanical oral hygiene measures including interproximal tooth cleaning were re-instituted. The patients were recalled for control and professional prophylaxis, consisting of supragingival polishing with a rubber cup once per week for the first 6 weeks. At these visits it was recorded whether the membrane had become exposed. In case of membrane exposure, the patients were asked to apply locally a 1% CHX gel twice a day until the membrane had disappeared and oral hygiene could be re-instituted. Once per month for the following 5 months, the patients were examined and calculus, if present, was removed and the teeth were polished. Deep subgingival instrumentation was avoided at the GTR-treated sites during the first year after surgery.

At the day of surgery (baseline) and after 1 year, the following clinical parameters were recorded at each treatment site (both from the buccal and the palatal/lingual aspect) to the closest millimeter by means of a manual periodontal probe with a round tip of 0.5 and 1 mm marked increments (Hu-Friedy LL 20: Hu-Friedy Mfg. Co. Inc., Chicago, IL, USA): (a) PPD: the distance from the gingival margin to the level of probe-tip penetration; (b) gingival recession (REC): the distance from the cemento–enamel junction (CEJ) to the gingival margin – in case that the CEJ was difficult to distinguish or absent, the margin of a restoration or crown was used as the coronal reference point; (c) PAL: PPD+REC. In addition, presence or absence of plaque (PI) and presence or absence of bleeding on probing (BOP) were assessed. Information on the patients's smoking habits was collected at baseline and at the 1-year control. Patients declaring that they smoked regularly (at least five cigarettes on a daily basis) at both baseline and the 1-year control were classified as smokers. Furthermore, non-standardized radiographs were also taken at the 1-year control. Dentists undergoing specialty training in Periodontology performed the surgeries and the recordings at baseline and after 1 year.

Significance of differences for PI and BOP between baseline and 1-year data was evaluated with McNemar's test. Significance of differences between baseline and 1-year clinical data was

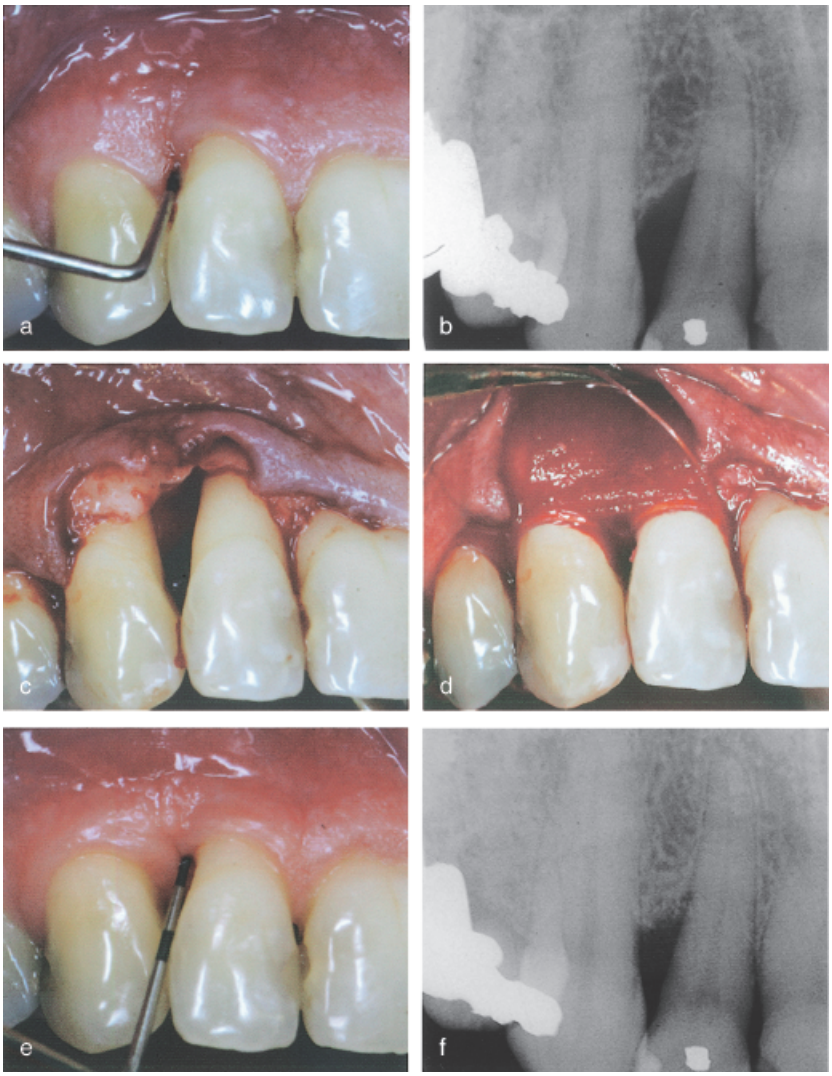

Fig. 1. Clinical photograph (a) and radiograph (b) at baseline, of a two-wall defect. After debridement (c), the defect is covered with a bioresorbable membrane (d). Clinical photograph (e) and radiograph (f) of the treated site after 1 year.

evaluated by means of Student's *t*-test for paired observations. Generalized linear models (GLMs) were constructed to evaluate the influence of baseline PPD and PAL, IC configuration (primarily one, two, or three wall), membrane exposure (exposed/non-exposed), oral hygiene (presence/absence of PI at the treated site at the 1-year control), and smoking habits (smoking/no smoking) on the primary outcome variables (i.e. PAL gain and PPD) after 1 year, including in the analysis only one defect per patient (i.e. 32 defects) chosen at random. Odds ratios for the factors with significant influence on PAL gain and residual PPD were calculated using the Mantel–Haenszel method, where it was found appropriate. Differences between smokers and non-smokers were evaluated by means of Pearson's χ^2 and Student's *t*-test for non-paired observations, including in the analysis the same 32 defects as above (i.e. only one defect per patient). Association between smoking and membrane exposure were evaluated by means of Pearson's χ^2 test. The level of significance was set at $p<0.05$. The calculations were performed with the SPSS for Windows, version 10.0.5, software package (SPSS Inc., Chicago, IL, USA).

Results

All surgically treated sites healed without significant problems (Fig. 1e and f). The site (buccal or palatal/lingual) of the interproximal defect with the deepest PPD value at baseline was chosen as the site of analysis. In case baseline PPD values did not differ, the site (buccal or palatal/lingual) with the deepest PPD after 1 year was chosen as the site of analysis.

Table 1 shows the clinical parameters at baseline and 1 year after treatment. A statistically significant decrease in the number of sites with BOP was observed from baseline to 1 year (McNemars's, $p<0.001$), although oral hygiene did not change significantly (McNemars's, $p=0.36$). One year after GTR treatment, a statistically significant PPD reduction and PAL gain was observed as compared with the baseline values (paired *t*-test, $p<0.001$) and 53.2% of the sites showed a PAL gain of 4 mm (Table 1). REC had also increased statistically significantly 1 year after treatment (paired *t*-test, $p<0.001$). In most of the cases, the radiographs showed almost total resolution of the bone defect with bone regeneration but also evidence of crestal resorption. In some instances a residual IC could be observed.

PPD at baseline did not seem to influence the amount of PAL gain (GLM, $p=0.10$) but seemed to influence the amount of PPD after 1 year, and the deeper the PPD at baseline the deeper the residual PPD (Table 2). Baseline PAL, on the other hand, seemed to influence the amount of PAL gain (Table 2) but not that of residual PPD (GLM, $p=0.90$). IC configuration did not influence significantly the amount of the primary outcome variables 1 year after treatment (GLM, $p=0.80$ and 0.82 for PAL gain and PPD, respectively). Membrane exposure occurred in 46.8% of the treated sites. In most of these cases the exposure presented as an ''opening'' (separation) of the interdental papillae. In only two cases had the gingival tissues receded on the palatal aspect, exposing a large area (approximately 4×4 mm) of the membrane. Both cases were in the same patient who suffered from diabetes. Most of the exposures (82%) occurred 2 and 3 weeks after surgery and were not associated with signs of excessive inflammation. In three cases (two of them in the same patient), membrane exposure occurred during the first post-operative week and in one case as late as 4 weeks after GTR. Usually, the exposed portion of the membranes had disappeared after approximately 2–3 weeks, disclosing new immature tissue formed underneath the barrier. None of the exposed membranes were removed, but occasionally the loose coronal portion of the membranes was carefully dissected free.

Table 1. Clinical parameters at baseline and 1 year after treatment, and PAL gain classes at the 1-year control, for all treated defects

	Baseline	1 year	*p*
N	47	47	
PI	45%	55%	0.36*
BOP	94%	32%	<0.001*
	mean ± SD	mean ± SD	
PPD	8.6 ± 1.1	3.7 ± 1.1	<0.001†
PPD reduction		4.9 ± 1.0	
REC	1.3 ± 1.4	2.4 ± 1.4	<0.001†
REC increase		1.1 ± 1.2	
PAL	9.8 ± 1.6	6.0 ± 1.7	<0.001†
PAL gain		3.8 ± 1.5	

PAL loss	0⩽PAL gain<2	2⩽PAL gain<4	4⩽PAL gain<6	6⩽PAL gain
0	3 (6.4%)	19 (40.4%)	17 (36.2%)	8 (17%)

*Analyzed with McNemar's test.

†Analyzed with the *t*-test for paired observations.

PI, plaque; BOP, bleeding on probing; PPD, probing pocket depth; REC, gingival recession; PAL, probing attachment level; SD, standard deviation.

Table 2. Results of generalized linear models on factors that may influence PAL gain and residual PPD, 1 year after GTR surgery (estimates of only significant factors are presented)

Source	DF	Sum of squares	Mean square	*F*-value	*p*
PAL gain					
model	7	29.92	4.27	3.06	0.02
error	24	33.55	1.40		
total	31	63.47			
$R^2 = 0.47$					
			95% CI		
	estimate	*t* for H_0	lower	upper	*p*
smoking	−1.33	−2.74	−2.33	0.33	0.01
baseline PAL	0.49	2.57	0.009	0.89	0.02
PPD					
model	7	19.15	2.74	5.11	0.001
error	24	12.85	0.53		
total	31	32.00			
$R^2 = 0.60$					
			95% CI		
	estimate	*t* for H_0	lower	upper	*p*
smoking	0.82	−2.74	0.20	1.44	0.01
baseline PPD	0.69	3.92	0.33	1.05	0.001

PAL, probing attachment level; PPD, probing pocket depth; GTR, guided tissue regeneration; CI, confidence interval.

Occurrence of membrane exposure did not seem to influence the amounts of PAL gain or PPD after 1 year from treatment (GLM, $p = 0.93$ and 0.74, respectively). Similarly, presence of PI at the treated site at the 1-year control did not seem to influence the primary outcome variables (GLM, $p = 0.10$ and 0.92 for PAL gain and PPD, respectively).

None of the patients classified as smokers at baseline altered smoking habits during the study, and no patient started smoking regularly during the follow-up period. Smoking seemed to have a statistically significant negative effect on the amounts of PAL gain and residual PPD after 1 year from treatment (Table 2). Patients who were smokers gained approximately 1 mm less attachment than patients who did not smoke (Table 3) and had approximately seven times less chance to gain more than 4 mm attachment compared with non-smokers (Table 4). PPD reduction in smokers was significantly smaller than in non-smokers (Table 3), and smokers had a slightly greater risk to present with a residual PPD of 5 mm or deeper compared with patients who did not smoke (Table 4), although this association did not reach statistical significance. Statistical analysis failed to reveal any differences between smokers and non-smokers regarding the clinical parameters at baseline, except for baseline PPD (Table 3), and regarding the incidence of membrane exposure (Pearson's χ^2, $p = 0.46$), although it was higher in smokers (60%) than in non-smokers (47%).

Discussion

The results of the present study showed that smoking exerted a detrimental effect on the outcome of GTR treatment of intrabony defects with bioresorbable membranes. Patients who were smokers gained on average 1.1 mm less in PAL than non-smokers and had approximately seven times greater risk to gain <4 mm attachment than those who did not smoke. These findings are in agreement with those of previous reports on GTR treatment in intrabony defects with non-bioresorbable membranes (Tonetti et al. 1995, Trombelli et al. 1997) and corroborate the results of a recently published study on bioresorbable membranes (Ehmke et al. 2003). In these studies, smokers treated with non-bioresorbable membranes gained on average 2.0–3.1 mm less in PAL than non-smokers 6 months to 1 year after GTR surgery (Tonetti et al. 1995, Trombelli et al. 1997). Apparently this was because of the fact that smokers tended to loose a major portion of the newly formed tissues under the membranes during the maturation phase (i.e. after membrane removal) more frequently than patients who did not smoke (relative risk: 4.3) (Tonetti et al. 1995). Similarly, Trombelli et al. (1997) reported that bone gain was less pronounced (approximately 3.0 mm less) in patients who smoke as compared with those who did not. In a recently published report on GTR treatment in intrabony defects with the same kind of bioresorbable membranes as the ones used in the present study, patients who smoked gained on average 2.0 mm less bone than those who did not smoke, and smokers had approximately 4.5 times less chances than non-smokers to gain >2 mm of bone, 1 year

Table 3. Clinical characteristics in smokers and non-smokers at baseline and 1 year after GTR

	Non-smokers	Smokers	*p*
Baseline			
N	17	15	
PI	47%	60%	0.46
BOP	100%	87%	0.12
IC (one, two, three walls)	18%, 53%, 29%	20%, 67%, 13%	0.54
	mean ± SD	mean ± SD	
PPD	8.9 ± 1.2	8.1 ± 1.0	0.03
REC	1.4 ± 1.3	1.3 ± 1.4	0.87
PAL	10.3 ± 1.2	9.4 ± 1.7	0.07
1 year			
N	17	15	
PI	59%	60%	0.95
BOP	29%	27%	0.86
exposure	47%	60%	0.46
	mean ± SD	mean ± SD	
PPD	3.4 ± 1.1	3.6 ± 1.0	0.61
PPD reduction	5.5 ± 0.7	4.5 ± 0.7	<0.01
REC	2.6 ± 1.4	2.6 ± 1.2	0.92
REC increase	1.2 ± 1.2	1.3 ± 1.7	0.95
PAL	6.0 ± 1.6	6.2 ± 1.7	0.81
PAL gain	4.3 ± 1.3	3.2 ± 1.4	0.03

Categorical variables were analyzed with Pearson's χ^2 test.
Numerical variables were analyzed with the *t*-test for non-paired observations.
GTR, guided tissue regeneration; PI, plaque; BOP, bleeding on probing; IC, intrabony component; PPD, probing pocket depth; REC, gingival recession; PAL, probing attachment level; SD, standard deviation.

Table 4. Risk assessment and distribution of sites with PAL gain of 4 mm or residual PPD of 5 mm in regard to smoking status

	Smoking		Odds ratio (95% CI)	χ^2 significance
	no	yes		
PAL gain <4 mm	4 (12%)	10 (31%)		
PAL gain $\geqslant 4$ mm	13 (41%)	5 (16%)	0.15 (0.03–0.73)	0.02
residual PPD <5 mm	14 (44%)	11 (34%)		
residual PPD $\geqslant 5$ mm	3 (9%)	4 (13%)	1.69 (0.31–9.21)	0.54

PAL, probing attachment level; PPD, probing pocket depth; CI, confidence interval.

post-treatment (Ehmke et al. 2003). Impaired outcome after GTR treatment of various types of periodontal defects in smokers has also been reported in other studies (Luepke et al. 1997, Trombelli & Scabbia 1997, Mayfield et al. 1998).

The precise mechanism by which smoking interferes with the outcome of GTR treatment is not yet understood, but it has been shown in in vitro studies that nicotine and smoking by-products adversely affect the proliferation, attachment, and chemotaxis of periodontal ligament cells (Giannopoulou et al. 1999, Cattaneo et al. 2000) and enhance the effect of periodontal pathogen toxins (Sayers et al. 1999). In addition, reduced peripheral blood supply because of vasoconstriction induced by nicotine and reduced oxygen transport and metabolism caused by carbon monoxide have been observed in smokers (Silverstein 1992). Thus, it seems that smoking may interfere within several stages of the reparatory/regenerative process in the periodontal wound and thereby compromise healing in general. This in turn may explain the impaired flap survival, characterized by the increased frequency of membrane exposure observed in smokers as compared with non-smokers in the present and other studies (Trombelli & Scabbia 1997, Trombelli et al. 1997). However, exposure and the subsequent microbial colonization of the membranes seems not to be as crucial for the treatment outcome of GTR procedures with bioresorbable barriers as previously acknowledged for non-bioresorbable membranes (Trombelli et al. 1995, 1997). As in the present study, Mayfield et al. (1998) and Ehmke et al. (2003) did not find any association between the occurrence of membrane exposure and the healing outcome. Falk et al. (1997), on the other hand, using the same kind of bioresorbable membranes as the ones used in the present study observed that early (<2 weeks) exposure had a statistically significant negative effect on PAL gain, and Machtei (2001) in a recent meta-analysis of studies reporting on the outcome of GTR treatment in intrabony defects with various types of bioresorbable membranes, also found exposure to negatively affect PAL gain. However, in both these latter studies, defects with exposed membranes showed an average PAL gain of 4.2 mm, and it is a matter of discussion whether the observed differences between sites with exposed and non-exposed membranes (range: 0.5–0.8 mm) are in fact clinically relevant. In the present study, the patients received systemic antibiotics in association with GTR surgery, rinsed with CHX twice per day for 6 weeks post-operatively, and in case of membrane exposure a 1% CHX gel was applied locally twice a day. Thus, it seems that membrane infection can be controlled and good regenerative results obtained if a proper pre- and post-operative anti-infective care is provided.

Presence of plaque on the site at the day of GTR surgery (Falk et al. 1997) and high full-mouth plaque scores 1 year after surgery (Tonetti et al. 1996) were previously found to negatively affect PAL gain. In the present study, poor oral hygiene, expressed as presence of plaque at the site at the 1-year control, was not found to influence the treatment outcome. However, presence of plaque at the site at one single time point (e.g. at the 1-year control), although may be indicative of neglectful oral hygiene practices, does not necessarily reflect the daily oral hygiene level/situation at the site during the entire experimental period. Apparently, in the present study, plaque did not stay long enough at the membrane-treated sites for a clinically detectable periodontal destruction to occur.

Earlier reports have suggested that larger amounts of PAL gain are obtained in deep three-wall intrabony defects as compared with two- and one-wall defects, after GTR treatment (Cortellini et al. 1993, Selvig et al. 1993). However, a careful analysis of results from GTR treatment of intrabony lesions has revealed that there is no significant association between the

number of residual osseous walls of the defect and the treatment outcome (Tonetti et al. 1993, 1996, Trombelli et al. 1997, Mayfield et al. 1998). The results of the present study corroborate the findings of these latter reports. On the other hand, PAL gain after 1 year was significantly correlated with PAL at baseline. The greater the baseline PAL value was, the larger the PAL gain was. Similar findings have been reported earlier by Falk et al. (1997) and Mayfield et al. (1998). However, although such correlations between linear measurements of PAL at baseline and PAL gain after treatment may be observed, it has been previously shown that the potential of PAL gain (expressed as percentage of the baseline PAL) is, indeed, similar in deep and shallow defects (Cortellini et al. 1998).

The improvements in clinical parameters (PAL gain = 3.8 mm, residual PPD = 3.7 mm) 1 year after GTR treatment in the present study are similar to the calculated weighted means presented recently (Stavropoulos 2002) in a review of 39 studies (published between 1990 and 2000) reporting about the results of treatment of 1019 intrabony defects by means of various types of bioresorbable membranes (PAL gain = 3.6 mm, residual PPD = 3.6 mm). PPD measurements are not useful for assessing the efficacy of regenerative techniques because reductions in PPD may occur not only as a result of regeneration, but also because of increased periodontal health or REC. It has been suggested, therefore, that only PAL (and bone) changes should be evaluated (Reddy & Jeffcoat 1999). However, PPD evaluation after regenerative treatment is just as critical as PAL gain, since deep residual PPD is a risk indicator for the progression of periodontitis (Armitage 1996). In the present study, smoking was found to negatively influence the amount of residual PPD and smokers had a somewhat higher risk to present with a residual PPD of 5 mm. Additionally, PPD reduction in smokers was statistically significantly smaller than in non-smokers. However, a definite conclusion on the effect of smoking on the amount of residual PPD cannot be drawn based on the present material (since statistical significance was not always observed).

In conclusion, the results of the present study support the view that smoking impairs the healing outcome of GTR treatment of intrabony defects with bioresorbable membranes significantly, and patients scheduled for such treatment should be informed on the potential consequences of not quitting smoking.

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