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Guided tissue regeneration with bioabsorbable barriers III 10-year results in infrabony defects

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Abstract

Objective: Evaluation of the 10-year results after GTR-therapy of infrabony defects using two bioabsorbable barriers in a randomized-controlled clinical trial.

Material and Methods: In 15 patients with periodontitis, 15 pairs of infrabony defects were treated. For each patient, one defect received a polydioxanon (test: T) and the other received a polylactide acetyltributyl citrate (control: C) barrier by random assignment. At baseline, 12 and 120 ± 6 months after surgery, the clinical parameters and standardized radiographs were obtained.

Results: Nine patients were available for the 120-month re-examinations. Twelve and 120 ± 6 months after therapy statistically significant ($p \leqslant 0.004$) vertical probing attachment level (PAL-V) gain was found in both groups (T12: 3.9 ± 1.6 mm; T120: 2.4 ± 1.8 mm; C12: 4.0 ± 1.1 mm; C120: 2.4 ± 1.7 mm). From 12 to 120 months both groups experienced PAL-V loss (T: 1.4 ± 1.5 mm, $p = 0.021$; C: 1.6 ± 2.5 mm, $p = 0.09$). After 120 month, two teeth were lost in the control group (one periapical lesion, and one due to unknown reason). The study failed to show statistically significant differences between both groups regarding PAL-V gain 120 months after surgery.

Conclusions: PAL-V gain achieved after GTR therapy in infrabony defects using both bioabsorbable barriers was stable after 10 years in 15 of 22 defects (68%).

Key words: guided tissue regeneration; interproximal infrabony defects; long-term results; periodontitis; randomized-controlled clinical trial

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Open flap debridement (OFD) results predominantly in reparative healing, i.e. the formation of a long junctional epithelium (Zappa 1991b, Windisch et al. 2002). The potential of bioabsorbable barrier membranes to facilitate periodontal regeneration has been demonstrated in several histometric studies in animals (Magnusson et al. 1988, Kon et al. 1991, Caffesse et al. 1994) and some histological studies in humans (Zappa 1991b, Windisch et al. 2002). Clinical studies have observed more favourable results after GTR-therapy using bioabsorbable barriers than OFD in vertical bony defects (BD) (Murphy & Gunsolley 2003, Needleman et al. 2006). Clinical studies on regenerative therapy of infrabony lesions using non-resorbable and/or different bioabsorbable barriers reported results for observation periods of 5 years (Cortellini et al. 1996a, Kim et al. 2002, Eickholz et al. 2004, 2007, Sculean et al. 2004, Mengel et al. 2006, Slotte et al. 2007) and 6–7 years (Stavropoulos & Karring 2004). Results after longer observation periods are scarce (Cortellini & Tonetti 2004, Sculean et al. 2006). To date, there are only two clinical trials with observation periods of 10 years comparing the results after implantation of non-resorbable and bioabsorbable barriers in class II furcation defects (Eickholz et al. 2006) and in infrabony defects (Pretzl et al. 2008).

Thus, the objective of the present randomized-controlled clinical trial was (i) to assess and (ii) to compare clinical and radiographic results 10 years after GTR therapy using bioabsorbable barriers. The population had been evaluated after 6 (Dörfer et al. 2000), 12 (Eickholz et al. 2000) and 60 months (Eickholz et al. 2004) already.

Conflict of interest and source of funding statement

No conflict of interests.
This study was self-funded by the authors and their institutions.

Material and Methods

Patients

Fifteen patients (12 female), under periodontal treatment at the Section of

Periodontology, Department of Operative Dentistry and Periodontology, Dental School, University of Heidelberg, took part in the present study (Dörfer et al. 2000, Eickholz et al. 2000, 2004). They ranged in age from 22 to 64 years (42.1 ± 12.8) and suffered from moderate to severe, untreated periodontal disease. Nine patients were diagnosed as suffering from chronic periodontitis and six patients exhibited aggressive periodontitis. Each patient contributed one pair of similar contra lateral infrabony defects. Two defects were taken as a pair when they fulfilled the following criteria: both defects were of the same extent, located contra laterally in the same jaw (maxilla or mandible) and affecting the same type of tooth (molar, bicuspid and canine). After enrolment of the patients the study protocol, risks, benefits and procedures were explained and informed consent was obtained. The study was approved by the Institutional Review Board for Human Studies of the University of Heidelberg.

All patients were asked about current and past cigarette consumption. Patients who reported to smoke or had quit smoking for <5 years were classified as smokers (Lang et al. 2003). All patients included in this study were then retrospectively tested for the interleukin-1β polymorphism using this test kit (GenoType PRT Parodontitis-Risiko-Test, Hain Life Science GmbH, Nehren, Germany). Therefore, a foam swab was moved over cheek mucosa for 20 s to sample cells and then sent for analysis to the laboratory.

Clinical examinations

Clinical examinations have been described in detail before (Dörfer et al. 2000, Eickholz et al. 2000, 2004). Thus, only brief descriptions are provided here. The gingival index (GI) and plaque index (PlI) (Löe 1967) were assessed at six sites per tooth. Probing pocket depths (PPDs) and vertical probing attachment levels (PAL-V) were measured to the nearest 0.5 mm using a pressure-controlled straight, rigid, periodontal probe [TPS probe (universal explorer), Ivoclar-Vivadent AG, Schaan, Liechtenstein] at baseline and at 12 month re-examinations. The TPS probe is for single use and was no longer available at the 120 ± 6 months re-examination. Thus, 120 months after therapy the clinical parameters were assessed (GI, PPD, PAL-V, PlI) using a simple manual rigid probe (PCPUNC15, Hu Friedy, Chicago, IL, USA) all by the same examiner (B. P.).

Radiographic examinations

After completion of initial treatment, bone status around teeth exhibiting symmetrical defects was assessed by obtaining standardized radiographs using modified film holders (VIP 2 Positioning, UpRad Corp., Fort Lauderdale, FL, USA). The design of these film holders has been described extensively before (Duckworth et al. 1983, Eickholz et al. 1996). Intra-oral dental films (Ultraspeed, Eastman Kodak Co., Rochester, NY, USA), size 2, were exposed to an X-ray source (Heliodent 70, 70 kV, 7 mA, Siemens, Bensheim, Germany) and developed under standardized conditions (baseline and 12-month radiographs: Periomat; 120 months radiographs: XR24 Nova, Dürr Dental GmbH, Bietigheim-Bissingen, Germany). Using the individualized film holders, radiographs were obtained 12 and 120 ± 6 months after surgery.

Periodontal surgery

Periodontal surgery was initiated on the defect located on the patient's left side. Treatment of the defect on the right side was performed at the same appointment or followed 1–3 weeks later. For each patient, treatment assignment was made according to a table of random digits (Werner 1984); one side would receive a bioabsorbable polylactide acetyltributyl citrate barrier (Guidor Matrix Barrier, Guidor AB, Huddinge, Sweden) (control) and the other a bioabsorbable polydioxanon barrier (Mempol, Ethicon GmbH & Co. KG, Norderstedt, Germany) (test). Following an intra-crevicular incision, all teeth designated for GTR-therapy had a mucoperiosteal flap reflected to a height of 5 mm exposing the bony margin of the defect (Zappa 1991a). The flap was designed according to the modified papilla preservation technique to obtain primary closure of the barriers (Cortellini et al. 1995a). After complete removal of inflammatory granulation tissue, the root surfaces were thoroughly scaled and root planed. The distances of cemento-enamel junction (CEJ) to the alveolar crest (AC) as well as CEJ to the most apical extension of the BD (vertical bone level: PBL-V) were measured using the above-mentioned simple manual periodontal probe. The depth of the infrabony component of the defects (INFRA) was calculated as the difference of the distances PBL-V minus the smaller score of the buccal and lingual CEJ to AC measurements. The bony lesion was covered by the barrier, overlapping the margin of the BD by 3 mm. The membrane was adapted to the root surface by a suture around the root trunk. The mucoperiosteal flap was repositioned to cover the membranes completely. The flaps were sutured with Polyglactin 910 suture material (Vicryl™, Ethicon GmbH & Co. KG). GTR surgery was performed by four authors (C. D., T. S. K., H. S. and P. E.).

To prevent perisurgical infection 14 patients took 3 g amoxicillin 30–60 min. before surgery. One patient who had been identified as harbouring *Aggregatibacter* (*Actinobacillus*) *actinomycetemcomitans* subgingivally underwent all surgical procedures within 1 week. For that week the patient took 375 mg amoxicillin and 250 mg metronidazole three times daily. All patients rinsed with a 0.12% chlorhexidine gluconate solution (Chlorhexidin Mundspüllösung, Oral-B Laboratories GmbH, Frankfurt, Germany) for 2 min., two times daily, for 5–7 weeks after surgery. During this period, all patients had to refrain from individual mechanical plaque control and were thus seen at least every other week for control and gentle cleaning of the teeth under GTR therapy. If exposure of a barrier was noted the patient was advised to use a 1% chlorhexidine gluconate gel (Corsodyl Gel, Smith Kline Beecham, Bühl, Germany) once daily. Thereafter, patients were placed on a maintenance schedule including oral hygiene instruction and professional tooth cleaning once every 3 months for the first 2 years. Later on, most patients were seen for supportive periodontal treatment (SPT) every 4–6 months. Each supportive maintenance visit included the assessment of a full-mouth bleeding (gingival bleeding index; Ainamo & Bay 1975) and plaque score (plaque control record; O'Leary et al. 1972). A patient who complied with at least one SPT visit per year at the Section of Periodontology of the Department of Operative Dentistry and Periodontology of the University of Heidelberg was classified to have regular SPT (Kim et al. 2002, Eickholz et al. 2004, 2006, 2007).

Radiographic evaluation

All 54 radiographs were sorted in random order irrespective of the time point

at which they had been obtained (baseline, 12 or 120 months) and irrespective of the therapy mode by P. E. and numbered from 1 to 54. While sorting the radiographs P. E. determined the coronal landmark [CEJ or restoration margin (RM)]. Thereafter, they were digitalized and analysed beginning with number 1 in the order given by the numbers by one examiner (K. H.) who was blinded to the clinical results, the therapy mode and the time point at which the particular radiographs had been taken (baseline, 12 or 120 months) (Klein et al. 2001).

All radiographs were digitalized using a computer program (SIDEXIS nextGeneration 1.51, Sirona, Bensheim, Germany) and a flatbed scanner (Microtek ScanMaker i800, Microtek, Hsinchu, Taiwan) with a 600 dpi resolution and 8-bit grey values. The image files were stored as TIFF files and analysed by an examiner (K. H.) using the computer program SIDEXIS and a 19′ flat screen (Totoku CCL 192 plus, Totoku Electric, Ueda, Japan) in a particular room under exclusion of natural or artificial light. For evaluation the analysing tool of the program SIDEXIS was used. The image files were opened and magnified using the function ''zoom'' once. Then the distances CEJ/RM to AC, CEJ/RM to BD and the depth of the infrabony component (INFRA) were measured. Using the radiographs, new restorations or change of restorations at the defect site of the test teeth were recorded. Further, it was recorded whether new restorations had been placed that had destroyed the CEJ.

The definition of radiographic landmarks and measurement of the radiographic parameters CEJ/RM to AC, CEJ/RM to BD and INFRA have been described in detail before (Benn 1992, Eickholz et al. 1996, 2004, Klein et al. 2001).

Using 20 radiographs of infrabony defects unrelated to this study the examiner (K. H.) had been calibrated before evaluating the study radiographs. The principal investigator of the study (P. E.) instructed and trained the examiner in finding the anatomical landmarks and measuring the respective distances. Measurements of the principal investigator were defined as the gold standard. The radiographic examiner was calibrated until she was for 90% of her CEJ/RM-BD measurements within a 1 mm range to the gold standard.

Statistical analysis

The main outcome variable chosen for the comparison of the therapeutical effects of test and control was the stability of PAL-V gained 12 months after therapy, i.e. change of PAL-V from 12 to 120 ± 6 months after therapy. Change of the distance CEJ/RM to BD from 12 to 120 ± 6 months after therapy was considered a secondary endpoint. All other clinical and radiographic parameters were considered control variables.

The patient was defined as the statistical unit. Thus, for each patient and barrier material, the deepest site within a vertical defect at baseline was evaluated and examined after 12 and 120 ± 6 months. All parameters were tested for normal distribution using the Kolmogorov–Smirnov/Lilliefors test. The means at baseline and 12 as well as 120 ± 6 months after therapy were compared by the paired *t*-test or the Wilcoxon sign rank test (GI and PlI only) for test and control. Two teeth in the control group were missing 120 ± 6 months after therapy. Hence, from a total of 11 pairs of defects, only nine were available for paired analysis. For the comparison of test and control treatment, the changes from baseline to 12 as well as 120 ± 6 months later were calculated as differences, and the differences for the main outcome variable (PAL-V) between test and control were compared by the paired *t*-test. In addition, 95% confidence intervals of the mean difference between the therapeutical results after 12 and 120 ± 6 months were calculated. Statistical analysis was performed using a computer program (Systat™ for Windows version 10.0, Systat Inc., Evanston, IL, USA).

Results

Eleven patients exhibiting 20 infrabony defects were available for the 120 ± 6-month re-examination (Table 1). One patient had died after the 24-month re-examination due to medical reasons not related to this study. One patient had moved to Thailand and was not available for the 120-month re-examination. Two further patients did not respond to several invitations to the re-examination. In two patients the respective teeth of the control group were missing at the 120-month re-examination. All anterior teeth entered into analysis were mandibular canines (Table 1). The characteristics of the remaining patients (age, number of SPT visits, mean full-mouth bleeding score and mean full-mouth plaque score of all SPT visits, interleukin-1β polymorphism) and location of the infrabony defects are given in Table 2. Three patients were classified as active and one as a former smoker (Table 2). Two patients failed to comply with regular SPT visits (Table 2). In these 20 remaining teeth from baseline to the 120 ± 6-month re-examination in two teeth (patient 2) restorations were renewed. However, the new restorations did not destroy the CEJ. No other test tooth received any new restoration during the entire observation period. Thus, restorative therapy is unlikely to have influenced clinical or radiographic evaluation.

Table 1. Number and distribution of defects according to jaw and tooth type

Type of tooth	Maxillary	Mandibular	Total	Patients
Anterior	–	4	4	2
Premolar	2	4	6	4
Molar	4	6	10	5
Total	6	14	20	

Clinical parameters

The healing phase passed uneventfully for all defects except for one infrabony defect that developed an infection 1 week after implantation of a polydioxanon barrier. After prescription of 250 mg amoxicillin two times daily for 2 weeks the infections disappeared (#6). The frequency of exposure of the barriers is given in Table 2. The mean and standard deviation of PlI, GI, PPD and PAL-V at baseline, 12 as well as 120 ± 6 months after surgery, changes 12 and 120 ± 6 months after surgery and differences between test and control for the remaining nine pairs of defects are given in Tables 3 and 4. Twelve and 120 months after surgery both groups failed to show statistically significant PlI changes. An insignificant improvement of the mean PlI in both groups was observed from 12 to 120 months (Table 3). Both groups showed statistically significant GI reduction from baseline to 12 months. From 12 to 120 months after surgery, a statistically insignificant increase in GI was observed in both groups (Table 3). Twelve and 120 months after surgery, statistically significant PPD reductions ($p \leqslant 0.004$;

Table 2. Patient and healing characteristics

Patient #	Age	Teeth		Membrane exposure (days after GTR)		Defect site	Regular recalls	Number of recalls	Mean ± SD GBI	Mean ± SD PCR	Smoking	Interleukin-1β polymorphism	Other
		test	control	test	control								
1	59	47	36	14	7	Mesial/distal	+	22	1.9 ± 2.1	17.0 ± 6.3	Never	–	–
2	49	26	16	–	7	Mesial/distal	+	21	2.1 ± 2.4	30.7 ± 14.4	Never	–	–
3	45	25	15	14	14	Distal/mesial	–	10	5.7 ± 4.3	13.2 ± 5.1	Never	–	–
4	54	36	46	14	–	Mesial	+	27	2.9 ± 4.3	29.5 ± 12.8	Never	–	–
5	35	34	43	7	–	Distal	+	15	5.1 ± 4.7	21.7 ± 18.6	Active	–	–
8	50	43	33	14	14	Mesial	–	8	7.4 ± 5.1	15.1 ± 11.2	Never	–	–
9	32	45	35	7	14	Mesial/distal	+	17	4.5 ± 3.5	13.9 ± 6.3	Never	–	–
10	20	36	46	28	–	Distal	+	21	5.2 ± 4.3	21.0 ± 12.3	Never	–	–
11	37	26	16	14	14	Distal	+	18	4.2 ± 3.1	32.5 ± 10.3	Former	–	–
12	64	25	15	7	7	Distal	+	19	9.0 ± 8.4	22.4 ± 7.1	Active	–	–
13	42	33	43	28	7	Mesial	+	17	8.0 ± 6.2	23.1 ± 10.2	Active	+	–

+, factor (e.g. regular recalls) present; –, factor absent; GBI mean ± SD, full-mouth bleeding scores of all recall visits; PCR mean ± SD, full-mouth plaque scores of all recall visits.

Table 3) and vertical attachment gains ($p \leqslant 0.004$; Table 4) were assessed for both test and control. In both groups a statistically insignificant mean increase of PPD was observed from 12 to 120 months (Table 3). In the test group a significant deterioration of PAL-V was observed from 12 to 120 months ($p = 0.021$). PAL-V loss in the control group was similar, but not statistically significant (Table 4). No statistically significant differences in PAL-V between test and control could be observed at baseline, 12 or 120 months post-surgically. Table 5 gives the PAL-V at baseline, 12 and 120 months after surgery for each individual patient and defect. A total of five defects showed attachment loss of more than 2 mm from 12 to 120 months: three in the test and two in the control group (Table 5). However, two additional test teeth were missing at the 120-months re-examination in the control group (Table 5): one tooth had been extracted 8 years after surgery due to a periapical lesion (#12). The other tooth was extracted approximately 7 years after baseline. However, at re-examination the patient (#3) could not tell the reason. Whereas patient #12 complied with regular SPT, #3 did not.

Bone parameters

For patient #1 120-month radiographs were not available. Thus, only a total of 16 sets of radiographs were analysed according to the split-mouth design. A minor statistically insignificant decrease of the distance CEJ to AC was observed for control 12 and 120 months after surgery. No change of the distance CEJ to AC after 12 months and a respective insignificant increase after 120 months were observed for the test group (Table 6). A statistically significant reduction of INFRA and bony fill assessed as a decrease of the distance CEJ to BD ($p < 0.05$) could be observed in both groups 12 months after surgery. Reduction of INFRA and bony fill was also found from baseline to 120 months in both groups. However, this change was statistically significant in the control group only. From 12 to 120 months the study failed to show statistically significant bone loss (Table 7). The analysis failed to reveal statistically significant differences between both groups (Table 7).

Table 3. Plaque and gingival index, probing pocket depths

	Plaque index		Gingival index		Probing pocket depth	
	polydioxanon ($n = 9$)	polylactide ($n = 9$)	polydioxanon ($n = 9$)	polylactide ($n = 9$)	polydioxanon ($n = 9$)	polylactide ($n = 9$)
Baseline	0.11 ± 0.33	0.33 ± 0.71	1.56 ± 0.88	1.33 ± 1.00	7.44 ± 1.40	7.72 ± 2.21
12 months	0.56 ± 0.88	0.89 ± 0.93	0.33 ± 0.71	0.22 ± 0.67	3.06 ± 1.38	2.56 ± 0.98
Change	0.45 ± 0.73	0.56 ± 1.13	− 1.23 ± 0.97	− 1.11 ± 1.05	− 4.38 ± 1.69	− 5.16 ± 2.32
p	0.104	0.131	0.005	0.008	< 0.001	<0.001
120 months	0.00 ± 0.52	0.33 ± 0.50	0.78 ± 0.97	0.79 ± 0.83	4.28 ± 1.86	4.56 ± 2.49
Change	− 0.11 ± 0.33	0.00 ± 1.00	− 0.78 ± 1.20	− 0.54 ± 0.73	− 3.16 ± 2.33	− 3.16 ± 1.32
p	0.347	1.000	0.088	0.059	0.004	< 0.001
Change 12–120 months	− 0.56 ± 0.89	− 0.56 ± 1.13	0.45 ± 1.01	0.57 ± 1.01	1.22 ± 2.08	2.00 ± 2.61
p	0.095	0.179	0.225	0.129	0.116	0.051

Table 4. Vertical probing attachment level

	Polydioxanon ($n = 9$)	Polylactide ($n = 9$)	*p*
Baseline	8.39 ± 1.52	8.50 ± 1.70	0.803
12 months	4.50 ± 1.71	4.44 ± 1.81	0.902
Change	3.89 ± 1.62	4.06 ± 1.10	0.799
p	< 0.001	<0.001	
120 months	5.94 ± 2.19	6.06 ± 2.58	0.879
Change	2.44 ± 1.83	2.44 ± 1.69	1.000
p	0.004	0.002	
Change 12–120 months	− 1.44 ± 1.51	− 1.62 ± 2.51	0.865
95% confidence interval	− 2.61 to − 0.28	− 3.54 to 0.32	
p	0.021	0.090	

Table 5. Vertical probing attachment levels for each patient individually in millimetres

Patient #	Polydioxanon			Polylactide		
	PAL-V baseline	12 months	120 months	PAL-V baseline	12 months	120 months
1	10.0	4.5	5.0	10.0	4.0	10.5*
2	9.0	4.0	6.5*	9.0	5.0	5.0
3	8.0	6.0	6.5	8.5	5.0	lost
4	9.0	4.0	6.5*	9.0	7.0	5.0
5	9.5	6.0	10.0*	10.0	5.0	9.0*
8	9.0	3.0	5.0	6.0	2.5	4.5
9	8.5	6.0	5.0	9.5	5.5	5.0
10	5.0	2.0	3.5	6.0	2.0	3.5
11	7.0	3.0	3.5	7.0	2.5	3.5
12	9.0	5.5	7.5	10.0	6.0	lost
13	8.5	7.5	8.5	10.0	6.5	8.5

*Loss of attachment > 2 mm from 12 to 120 ± 6 months after surgery.

Discussion

Many studies have revealed more favourable clinical results after GTR-therapy of infrabony defects with non-resorbable or bioabsorbable membranes than after OFD (Murphy & Gunsolley 2003, Needleman et al. 2006). Most clinical studies comparing PAL-V after therapy of infrabony defects using different regenerative methods (non-resorbable and bioabsorbable barriers or enamel matrix protein) failed to observe statistically significant or clinically relevant differences for observation periods up to 7 years (Kim et al. 2002, Eickholz et al. 2004, 2007, Mengel et al. 2006) (Table 8). Hence, this study was undertaken to examine the 10-year results of a longitudinal randomized-controlled clinical trial comparing the results of GTR therapy using two different bioabsorbable barriers in infrabony defects (Dörfer et al. 2000, Eickholz et al. 2000, 2004).

This clinical trial revealed similar or slightly better PAL-V gain in infrabony defects 12 months after surgery as compared with the results reported by other authors 12 months after GTR therapy in infrabony defects with similar or more favourable baseline characteristics: 3.04 mm (baseline PAL-V: 10.3 mm; baseline INFRA: 5.9 mm) (Tonetti et al. 1998); ePTFE: 4.1 mm (baseline PAL-V: 10.3 mm; INFRA: 5.8 mm) (Cortellini et al. 1995b); 3.1 mm (baseline PAL-V: 7.8 mm; INFRA: 4.2–4.4 mm) (Pontoriero et al. 1999); and 3.0 mm (baseline PAL-V: 8.3 mm; INFRA: 4.0 mm) (Cortellini et al. 1998). However, Cortellini and colleagues observed more favourable PAL-V gains in defects with more pronounced baseline vertical attachment loss and infrabony defect depth: titanium-reinforced ePTFE: 5.3 mm (baseline PAL-V: 9.9 mm; INFRA: 5.5 mm) (Cortellini et al. 1995b); ePTFE: 5.2 mm (baseline PAL-V: 10.8 mm; INFRA: 7.0 mm) (Cortellini et al. 1996b); and bioabsorbable barriers: 4.6 mm (baseline PAL-V: 11.1 mm; INFRA: 7.2 mm) (Cortellini et al. 1996b). The characteristics of infrabony defects have been shown to influence periodontal healing before (Cortellini et al. 1998, Klein et al. 2001). Hence, these differences are in accordance with the observation that baseline PAL-V and height of the infrabony component correlated positively with vertical attachment gain after GTR therapy. The few studies that report on stability 5–7 years after GTR therapy observed a change of PAL-V' ± 1 mm (Kim et al. 2002, Sculean

et al. 2004, Stavropoulos & Karring 2004, Mengel et al. 2006, Slotte et al. 2007) or a moderate PAL-V loss of $\geqslant 1.0$ mm (Cortellini et al. 1996a, Kim et al. 2002, Eickholz et al. 2004) (Table 8). This is in accordance with the PAL-V loss observed in this study 120 ± 6 months after therapy.

However, looking only at means does not account for the two teeth missing at the 120 ± 6-month re-examination. According to information provided by the dentist of patient 12, the tooth was lost due to a periapical lesion and thus may not count as a periodontal complication. The reason for extraction of the other tooth (patient 3) could not be determined. This loss might be due to a periodontal complication. The mean PAL-V loss observed in the polylactide group does not fully describe periodontal stability. We defined a defect experiencing PAL-V loss from 12 to 120 ± 6 months of more than 2 mm as an instable site. Failure from 12 to 120 ± 6 months is not distributed equally over all patients. Cortellini and colleagues had revealed patient characteristics like irregular attendance of SPT, smoking and a general tendency of attachment loss during SPT (loser patients) to account for most attachment losses (Cortellini et al. 1996a). Other authors had attempted to explain this tendency of attachment loss by the presence of the interleukin-1 gene polymorphisms (De Sanctis & Zucchelli 2000). Taking the instable defects and lost teeth together, failure of GTR therapy was observed in three defects treated with polydioxanon (#2, 4, 5) and in four defects treated with polylactide (#1, 3, 5, 12). Patient 3 failed to attend SPT regularly; patients 5 and 12 were active smokers. For patients 1, 2 and 4 risk factors for periodontal breakdown cannot be identified at the patient level. Further, patient 5 was the only indivi-

Table 6. Distances of the cemento-enamel junction to the alveolar crest and the infrabony component

	Cemento-enamel junction to alveolar crest		Infrabony component	
	polydioxanon ($n = 8$)	polylactide ($n = 8$)	polydioxanon ($n = 8$)	polylactide ($n = 8$)
Baseline	4.95 ± 2.05	5.60 ± 2.46	5.43 ± 1.90	5.65 ± 2.43
12 months	4.87 ± 1.92	5.08 ± 2.11	3.70 ± 1.64	3.54 ± 2.01
Change	0.08 ± 0.62	0.52 ± 0.93	1.73 ± 1.45	2.11 ± 1.55
p	0.717	0.157	0.012	0.006
120 months	5.17 ± 2.24	4.99 ± 2.24	3.72 ± 3.00	3.49 ± 1.62
Change	-0.22 ± 1.36	0.61 ± 1.35	1.71 ± 2.83	2.16 ± 1.96
p	0.662	0.243	0.132	0.017
Change 12–120 months	-0.30 ± 1.16	0.09 ± 0.81	-0.02 ± 2.52	0.05 ± 1.84
p	0.486	0.763	0.981	0.489

Table 7. Distance of the cemento-enamel junction to the bony defect

	Polydioxanon ($n = 8$)	Polylactide ($n = 8$)	*p*
Baseline	8.77 ± 2.53	9.61 ± 3.13	0.084
12 months	7.14 ± 2.71	8.13 ± 3.07	0.229
Change	1.63 ± 1.47	1.48 ± 1.57	0.841
p	0.016	0.033	
120 months	7.62 ± 4.28	7.91 ± 2.95	0.732
Change	1.15 ± 2.53	1.70 ± 1.45	0.591
p	0.239	0.013	
Change 12–120 months	-0.48 ± 2.64	0.22 ± 1.57	0.566
95% confidence interval	-2.68 to 1.72	-1.08 to 1.52	
p	0.619	0.701	

Table 8. Stability of attachment gain 5–7 years after regenerative therapy

Authors	Number of defects	Therapy	INFRA (mm)	PAL-V gain (mm)	PAL-V gain (mm)	PAL-V stability
Cortellini et al. (1996a)				12 months	5 years	
	44	ePTFE	ND	4.0 ± 2.1	2.8	-1.2 ± 1.4
Kim et al. (2002)				6 months		
	8	ePTFE	3.7 ± 1.3	2.6 ± 1.4	1.6 ± 1.5	-1.0 ± 2.1
	8	PLA/PGA	4.2 ± 1.1	3.0 ± 1.7	3.0 ± 0.7	0.0 ± 1.2
Sculean et al. (2004)				12 months	1.3 ± 1.2	-0.3
	10	OFD	3.8 ± 1.2	1.6 ± 1.0		
	11	EMD	3.9 ± 1.5	3.4 ± 1.1	2.9 ± 1.6	-0.5
	10	PLA/PGA	3.8 ± 1.7	3.2 ± 0.8	2.7 ± 0.9	-0.5
	11	EMD&PLA/PGA	3.7 ± 1.5	3.0 ± 1.0	2.6 ± 0.7	-0.4
Eickholz et al. (2004)				12 months		
	13	PLA	5.0 ± 2.0	4.0 ± 0.9	2.4 ± 1.0	-1.6 ± 1.1
	13	Polydioxanon	4.9 ± 1.3	3.5 ± 1.5	2.2 ± 1.8	-1.2 ± 1.9
Mengel et al. (2006)				12 months		
	22	PLA/PGA	6.1 ± 2.5	3.4 ± 2.3	3.0 ± 2.0	-0.4
	20	Bioactive glass	5.4 ± 0.9	2.8 ± 1.9	3.3 ± 2.1	0.5
Slotte et al. (2007)				12 months	4.3 ± 2.0	0.1
	24	PLA or collagen and bovine bone mineral	7.9 ± 2.0	4.2 ± 2.1		
Stavropoulos & Karring (2004)				12 months	6–7 years	
	25	PLA	ND	3.8 ± 1.4	3.6 ± 1.4	-0.2

dual who had instability of regenerated attachment at both test teeth. Looking at possible site-specific risks early (at 7 days after surgery) membrane exposure is recorded for the ''loser'' sites of patients 1, 5 and 12 (De Sanctis & Zucchelli 2000). Other studies investigating the interleukin-1 polymorphism as a putative risk factor for attachment loss after periodontal regeneration failed to find a correlation (Cortellini & Tonetti 2004, Eickholz et al. 2007). However, other sites with early membrane exposure remained stable over 10 years. Only 15 (68%) of all re-examined defects (22) could be kept stable over 10 years. However, total failure (tooth loss) was observed in only two of 22 defects (9%).

Both barrier membranes used in this clinical trial are not commercially available. The experimental polydioxanon membrane never made it to the market and the polylactide membrane disappeared from the market. Thus, the results of this study cannot be used to decide what particular membrane material should be used. However, the study adds information to the small data pool of 10 years results after regenerative periodontal therapy.

Generally, radiographic vertical bone gain as assessed by radiographs was less pronounced than PAL-V gain. This corroborates with earlier studies that have demonstrated that bone tissue healing (reduction of the distance CEJ/RM to BD on radiographs) in most cases is less pronounced than soft tissue healing (PAL-V gain) (Falk et al. 1997, Eickholz & Hausmann 2002). However, PAL-V gain and bone gain as assessed by transgingival bone sounding (Eickholz et al. 2004) or digital subtraction analysis of radiographs (Eickholz & Hausmann 2002) is often correlated. The results of re-entry studies are controversial: some corroborate our findings [Bender et al. 2005 (paste group), Matos et al. 2007 (particular group)], some show the same amount of PAL-V gain and bony fill [Bender et al. 2005 (decalcified freeze dried bone), Matos et al. 2007 (hydrogel group)] and some show even more bony fill than PAL-V gain [Bender et al. 2005 (putty group)]. The latter observation certainly is due to measurement error. In all studies that show the same amount of PAL-V gain and bony fill a grafting material was used.

The sample size (nine patients) of this study was too small to show the equivalence of both barrier materials with sufficient test power after 120 ± 6 months. For a clinically relevant difference ($\delta \geq 1$ mm), with a type I error $\alpha < 0.05$ and a standard deviation of the difference between test and control for change of PAL-V from 12 to 120 ± 6 months of $s = 2.84$ mm, a test power of 15.4% was calculated. However, a difference in PAL-V between test and control from 12 to 120 ± 6 months of 0.2 mm can certainly be considered as clinically irrelevant.

Within the limitations of the present study, we may draw the following conclusions:

- The vertical attachment gains and bony fill achieved after GTR therapy using bioabsorbable barriers can be maintained stable up to 10 years after surgery in 15 of 22 (68%) infrabony defects.
- Irregular attendance of SPT and smoking jeopardize long-term stability after GTR therapy.

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Clinical Relevance

Scientific rationale for study: Short-term clinical studies have shown the superiority of GTR over OFD in infrabony defects. However, GTR therapy takes considerable effort and is expensive. Thus, information on the long-term stability of results after GTR therapy is required to determine the cost–benefit ratio of this technique.

Principal findings: The study failed to show statistically significant differences between test and control 120 months after therapy.

Practical implication: Treatment results assessed 12 months after GTR therapy with bioabsorbable barriers may be maintained stable in 68% of all treated defects over 10 years.