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ORIGINAL ARTICLE

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GTR treatment of intrabony defects with PLA/PGA copolymer or collagen bioresorbable membranes in combination with deproteinized bovine bone (Bio-Oss)

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Abstract The objectives of this study were to evaluate the results of guided tissue regeneration (GTR) treatment of intrabony defects with two kinds of bioresorbable membranes, with deproteinized bovine bone (Bio-Oss) used as an adjunct. Twenty-eight patients with at least one intrabony defect with a probing pocket depth (PPD) $\geq$7 mm and radiographic evidence of an intrabony component (IC) $\geq$4 mm were randomly treated with either a polylactic/polyglycolic (PLA/PGA) acid copolymer or a collagen bioresorbable membrane combined with Bio-Oss implantation. Immediately prior to surgery (baseline) and after 1 year, the following parameters were recorded: (1) PPD, (2) gingival recession (REC), (3) probing attachment level (PAL), (4) presence/absence of plaque (PI), and (5) presence/absence of bleeding on probing (BOP). Occurrence of membrane exposure during healing and the smoking habits of the patients were also recorded. Statistical analysis was carried out using x^2-tests and t-tests. There were no significant differences between the two membrane groups regarding the clinical parameters at baseline. Statistically significant clinical improvements (PAL gains, reduced PPDs) were observed 1 year after treatment in both groups. There were no significant differences, however, between the PLA/PGA and the collagen membrane groups regarding any of the evaluated parameters (mean PAL gain: 2.9 mm vs 3.9 mm; mean residual PPD: 4.8 mm vs 4.1 mm, respectively). The membrane material per se does not seem to be a critical factor for the outcome of GTR treatment of intrabony defects with bioresorbable membranes.

Keywords Bioresorbable membranes · Collagen · Deproteinized bovine bone · Guided tissue regeneration · PLA/PGA

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Introduction

Guided tissue regeneration (GTR), a biological treatment concept, is aimed at ensuring that cells with the capacity to regenerate a particular type of lost or diseased tissue are allowed to populate the defect/wound during healing, for example, by means of a physical barrier such as a membrane. [10]. Several case series and controlled clinical trials have demonstrated that considerable clinical improvements—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 the GTR concept. In addition, several reports have provided histological evidence in humans that GTR treatment results in true regeneration of the attachment apparatus on roots previously affected by periodontitis (for review see [11]).

The first generation of devices (membranes) for GTR were mainly made from non-bioresorbable materials—e.g., from porous or non-porous polytetrafluorethylene (PTFE). In order to overcome the shortcomings associated with a second surgical intervention for barrier removal, a variety of natural or synthetic bioresorbable materials were introduced as membrane barriers for GTR. Controlled studies comparing the results of GTR using non-bioresorbable barriers with results of GTR using bioresorbable barriers (for instance, for the treatment of intrabony defects) demonstrated that both kinds of membranes yield similar clinical improvements [6]. The bioresorbable membranes most commonly used are products derived from poly (α-hydroxy) acids, including polylactic acid (PLA), polyglycolic acid (PGA) and their copolymers or collagen (for review see [20]). Membranes

deriving from PLA/PGA copolymers or collagen differ regarding their physical characteristics, and they are absorbed through different biologic processes, i.e., primarily through hydrolysis in the case of PLA/PGA copolymers and through enzymatic degradation in the case of collagen. To date, there are only a limited number of studies comparing the clinical results following the use of different kinds of bioresorbable membranes [5, 7, 9, 13].

The aim of the present study was to evaluate the outcome of GTR treatment of intrabony defects with either a PLA/PGA copolymer or porcine collagen types I and III bioresorbable membrane, in both cases with deproteinized bovine bone used as an adjunct.

Materials and methods

Twenty-eight interproximal intrabony defects in 28 adult patients presenting for treatment at the Department of Periodontology and Oral Gerontology, Royal Dental College, University of Aarhus, Denmark, or the Department of Conservative Dentistry and Periodontology, Johannes Gutenberg University, Mainz, Germany, were included in the study. Approximately 2 months after initial periodontal treatment, which consisted of oral hygiene instruction and scaling and root planing, the defects presented the following characteristics:

1. Probing pocket depth (PPD) $\geq$7 mm and radiographic evidence of an intrabony component (IC) $\geq$4 mm (Figs. 1a and 2a), which did not include a furcation involvement
2. The site had not been treated surgically within the last year before initiation of the study
3. Systemic antibiotics had not been used within the last 6 months prior to treatment

The defects were treated as follows. 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 $\geq$4 mm deep (Figs. 1b and 2b). A bioresorbable barrier membrane, made of either a PLA/PGA copolymer (Resolut XT, W.L. Gore & Associates, Flagstaff, AZ, USA), in Aarhus, or por-

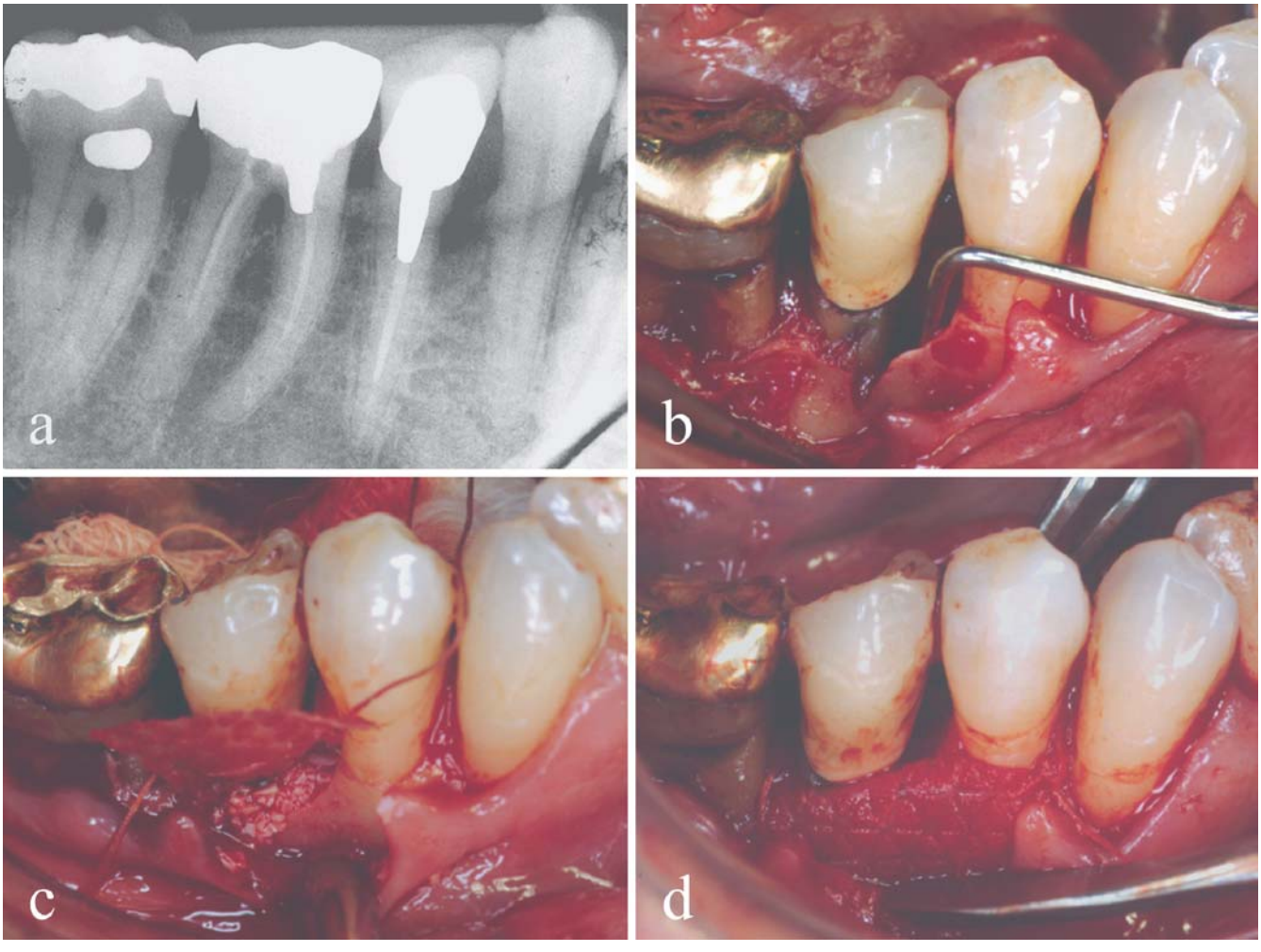

Fig. 1 Case treated with Resolut XT and Bio-Oss. At baseline, there was radiographic evidence of an intrabony component (IC) $\geq$4 mm **a.** This was confirmed during surgery after debridement of the defect **b**. The defect was filled with Bio-Oss **c** and covered with a Resolut XT membrane **d**

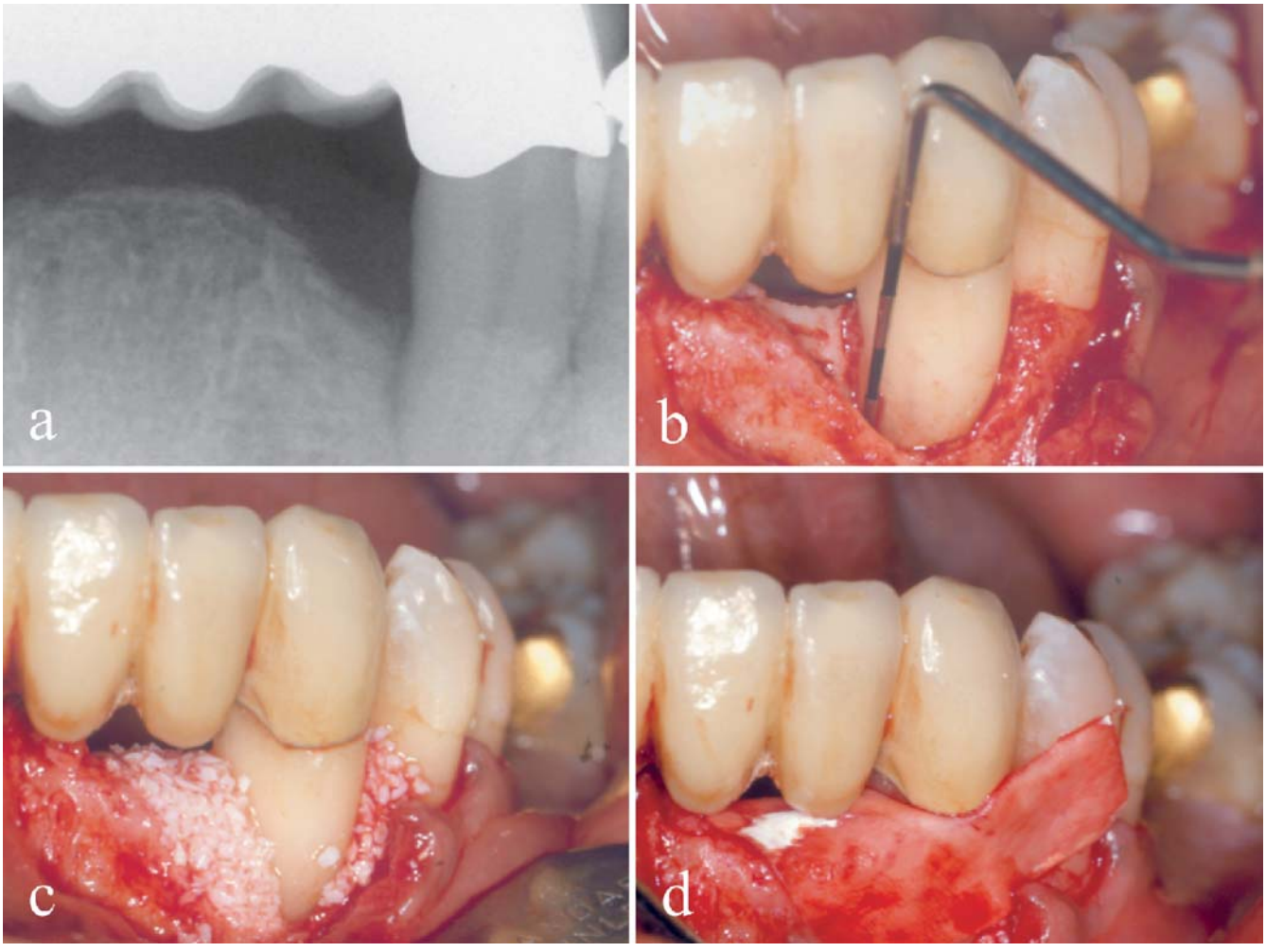

Fig. 2 Case treated with Biogide Perio and Bio-Oss. At baseline, there was a radiographic evidence of an intrabony component (IC) ≥4 mm **a**. This was confirmed during surgery after debridement of the defect **b**. The defect was filled with Bio-Oss **c** and was covered with a Biogide Perio membrane **d**

cine collagen type I and III (Biogide Perio, Geistlich, Wolhusen, Switzerland), in Mainz, was trimmed and adapted so that it totally covered the defect and extended at least 3 mm beyond its margins. The membrane was either fixed by means of a resorbable ligature around the necks of the adjacent teeth (Resolut XT) or simply adapted in place (Biogide Perio), according to the manufacturer's surgical protocol. Prior to the final placement of the membrane, Bio-Oss (Geistlich, Wolhusen, Switzerland) impregnated with sterile saline was loosely packed into the defect without overfilling it (Fig. 1c and d, and Fig. 2c and d). Then, the mucoperiosteal flaps were coronally displaced in order to fully 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 sutured 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.

Systemic antibiotics (500 mg amoxicillin, 3 times a day) were administered for 1 week postoperatively and chemical plaque control (0.2% chlorhexidine digluconate rinsing twice a day) was instituted for a period of 4 weeks, after which mechanical oral hygiene measures, including interproximal tooth cleaning, were reinstituted. Additionally, the patients were recalled for control and professional prophylaxis with supragingival polishing with a rubber cup, once every second week during the first 2 months after treatment. At these visits it was recorded whether the membrane had become exposed. The patients were then examined once per month for the rest of the study period, upon which calculus, if present, was removed and the teeth were polished. Deep subgingival instrumentation and probing were avoided at the experimental sites during the entire 12-month study period.

The following clinical parameters were recorded at each treatment site (both from the buccal and the palatal/lingual aspect) to the closest millimeter at the day of surgery (baseline) and after 1 year, by means of a manual periodontal probe with a round tip of 0.5 mm and 1 mm marked increments (Hu-Friedy LL 20):

1. PPD: the distance from the gingival margin to the level of probe-tip penetration
2. Gingival recession (REC): the distance from the cemento-enamel junction (CEJ) to the gingival margin. If the CEJ was difficult to distinguish or absent, the margin of a restoration or crown was used as the coronal reference point
3. Probing attachment level (PAL): PPD + REC

In addition, presence or absence of plaque (PI) and presence or absence of bleeding on probing (BOP), were assessed. Pre-surgical (at baseline) and postoperative (at the 1-year control) radiographs were taken with the long-cone-paralleling technique. The smoking habits of the patients were also recorded, both at baseline and at the

1-year control. Patients who declared that they smoked regularly (at least five cigarettes daily) at both baseline and the 1-year control were classified as smokers. Since the present investigation was not a randomized, controlled clinical trial, it was not attempted to balance the two groups regarding the smoking habits of the patients. In each center, the same investigator made the recordings at baseline and after 1 year. The two investigators were previously prepared regarding the reproducibility of measuring, in a specially arranged session (data not presented).

Significance of differences of baseline categorical variables between the groups was evaluated by the Fisher's exact test. Significance of differences of baseline numerical variables between the groups was evaluated by the Students *t*-test for non-paired observations. Significance of differences between baseline and 1-year categorical variables was evaluated by the McNemar's test. Significance of differences between baseline and 1-year numerical variables was evaluated by the Students *t*-test for paired observations. Significance of differences of the primary outcome variables (i.e., PPD and PAL gain) 1 year after treatment between the groups was evaluated by the Students *t*-test for non-paired observations. Significance of differences regarding the frequency of exposure and distribution of smokers between the groups were analyzed with Fisher's exact test. The level of significance was set at $P \leq 0.05$.

Results

There were no differences between the two groups regarding their baseline clinical characteristics (Table 1). Treatment resulted in considerable clinical improvements in both the Resolut XT + Bio-Oss and the Biogide Perio + Bio-Oss treated teeth, and a statistically significant PPD reduction of 4.0 mm and 5.14 mm and a PAL gain of 2.9 mm and 3.9 mm, respectively, were observed at the 1-year examination. The differences, however, between the two treatment groups were not statistically significant (Table 2 and Fig. 3). Based on the present material and with the alpha error set to 0.05, the power of the study was 0.27. Comparison of the pre-surgical radiographs with the ones taken at the 1-year control showed that, in most of the cases, treatment resulted in an almost total resolution of the bone defect (with bone fill but also evidence of crestal resorption) in both groups (Fig. 4a and b). The radiographical examination did not reveal any apparent differences between the two membrane groups.

Membrane exposure was a rather frequent event in both treatment groups (57% in the Resolut XT + Bio-Oss and 21% in the Biogide Perio + Bio-Oss). In most of the cases, membrane exposure presented as a separation of the interdental papillae, which occurred 2 to 3 weeks after surgery without signs of excessive inflammation. 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. There was no statistically significant difference between the two groups regarding the frequency of membrane exposure (Fisher's exact test, P=0.12).

Nine patients in the Resolut XT + Bio-Oss group (64%) and two (14%) in the Biogide Perio + Bio-Oss group were regular smokers at the beginning of the study, and none of them had quit smoking during the observation period. The difference between the two groups regarding the distribution of smokers and nonsmokers was statistically significant (Fisher's exact test, P=0.02). In the PLA/PGA copolymer membrane group, four out of the five nonsmokers gained $\geq$4 mm attachment, while five out of the nine smokers gained only $\leq$2 mm attachment. In the porcine collagen type-1 membrane group, the two patients who were smokers showed a PAL gain of 3 mm, i.e., the lowest amount of PAL gain observed in this group.

Table 1 Baseline data of the two treatment groups (*PI* presence/absence of plaque, *BOP* bleeding on probing, *PPD* probing pocket depth, *REC* gingival recession, *PAL* probing attachment level)

	Resolut XT + Bio-Oss	Biogide Perio + Bio-Oss	$P^{\dagger}$
PI	7%	6%	
BOP	71%	54%	
PPD baseline	8.8±1.3	9.2±1.3	0.39†
REC baseline	1.1±0.9	0.9±1.3	0.51†
PAL baseline	9.9±1.9	10.1±1.5	0.83†

† Resolut XT + Bio-Oss vs Biogide Perio + Bio-Oss, analyzed with the Student's *t*-test for independent observations

Discussion

The present study showed that significant clinical improvements in terms of PPD reduction and PAL gain were

Table 2 Clinical data in mm (mean±SD) at baseline and 1 year after GTR surgery (*PPD* probing pocket depth, *REC* gingival recession, *PAL* probing attachment level)

	Resolut XT + Bio-Oss	$P^{\S}$	Biogide Perio + Bio-Oss	$P^{\S}$	$P^{\dagger}$
PPD baseline	8.8±1.3		9.2±1.3		0.39†
PPD 1 year	4.8±1.2		4.1±0.8		0.09†
PPD reduction	4.0±1.2	<0.001§	5.1±1.7	<0.001§	0.05†
REC baseline	1.1±0.9		0.9±1.3		0.51†
REC 1 year	2.2±1.8		2.1±1.1		0.71†
REC increase	1.1±1.6	0.02§	1.2±0.8	<0.001§	0.88†
PAL baseline	9.9±1.9		10.1±1.5		0.83†
PAL 1 year	7.0±2.4		6.2±0.5		0.18†
PAL gain	2.9±2.3	<0.001§	3.9±1.3	<0.001§	0.14†

§ Baseline vs 1 year, analyzed with the Student's *t*-test for paired observations
† Resolut XT + Bio-Oss vs Biogide Perio + Bio-Oss, analyzed with the Student's *t*-test for independent observations

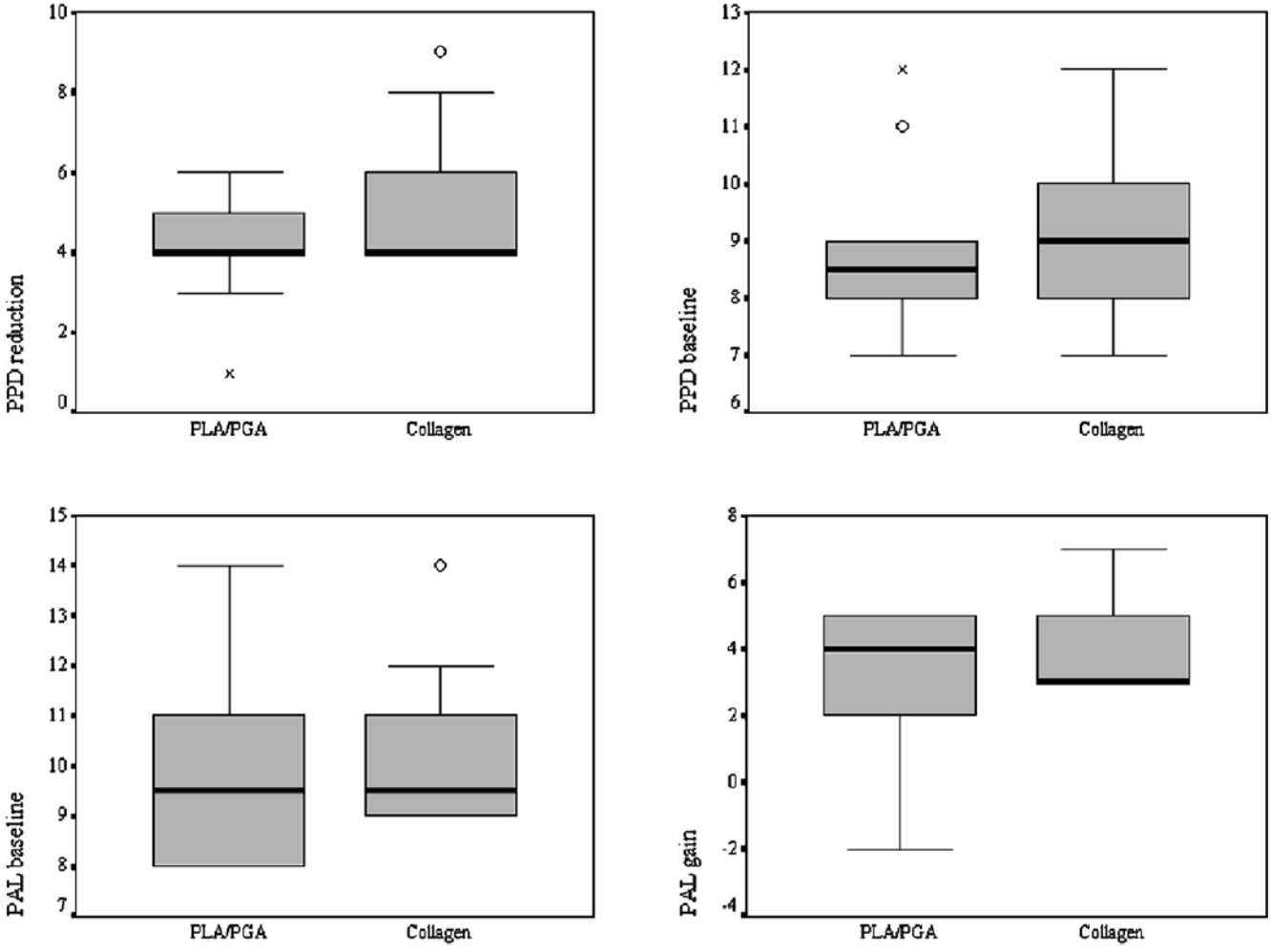

Fig. 3 Box plots based on the median, quartiles, and extreme values for baseline PPD **a**, PPD reduction **b**, baseline PAL **c**, and PAL gain **d**. The *box* represents the interquartile range, which contains 50% of values. The *lines* extending from the *box* indicate the highest and lowest values, excluding outliers. A *line* across the *box* indicates the median. (*o* outlier, *x* extreme)

achieved after GTR treatment of intrabony periodontal defects with bioresorbable barrier membranes made of either PLA/PGA copolymer or porcine collagen types I and III, with deproteinized bovine bone used as an adjunct.

Membranes made from different bioresorbable materials present differences in their physical characteristics (for review see [20]) that potentially could influence the results of GTR treatment. For instance, the PLA/PGA copolymer membranes used in the present study are more rigid than the collagen ones and are generally stabilized with sutures around the adjacent teeth. The collagen membranes are rather soft and are, normally, simply adapted over the defect. Theoretically, there is a risk that soft membranes may collapse onto the root surface and/or into the defect, resulting in a reduction/elimination of the space available for tissue ingrowth. Additionally, lack of stabilization of the membranes may result in loss of a tight adaptation of the devices around the teeth, which in turn may lead to soft (gingival) tissue invasion inside the membrane-protected space, thus impairing regeneration. On the other hand, the PLA/PGA copolymer membranes used in the present study are absorbed after a shorter period than are the porcine collagen ones. The time necessary for barriers to function, as well as the need for the membranes to be absolutely occlusive, in order to obtain successful/maximum regeneration are issues that are not yet completely clarified. However, the lack of significant differences between the two treatment groups in the present study in terms of clinical improvements supports the view that the membrane material per se is not a critical factor for the outcome of GTR treatment. This view is supported by the findings of the rather few previously published reports [5, 7, 9, 13], in which average PAL gains of similar magnitude (range: 2.6–3.9 mm) were observed 6–12 months after GTR treatment of intrabony defects with various kinds of bioresorbable membranes. However, the possibility cannot be excluded that, in the present study, the grafting of deproteinized bovine bone into the defects has stabilized some of the membranes and/or prevented their collapse, thus masking

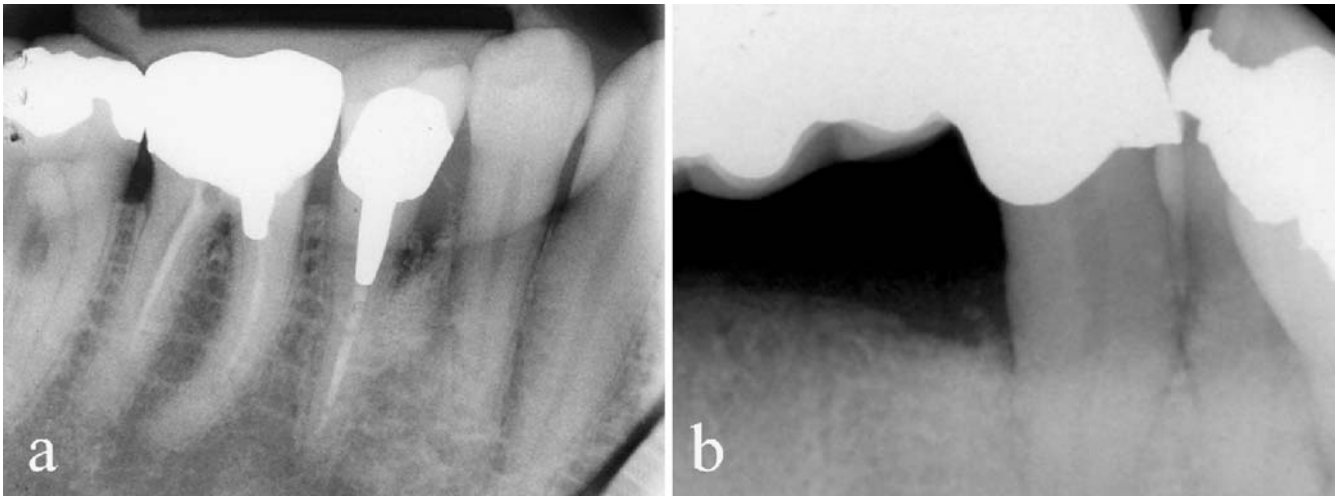

Fig. 4 Radiographs at 1-year-control for cases presented in Figs. 1 and 2. It can be observed that treatment resulted in an almost total resolution of the bone defect (with bone fill but also evidence of crestal resorption), irrespective of the use of a Resolut XT **a** or a Biogide Perio **b** membrane

or eliminating potential differences in their clinical performance.

Although the differences in terms of clinical response between the two groups in the present study were not statistically significant, patients treated with the PLA/PGA copolymer membranes gained on average approximately 1 mm less attachment than those treated with the collagen types I and III membranes. The less favorable response of the PLA/PGA group could be due to the fact that there were more smokers in this group than in the collagen types I and III membrane group. This view is supported by the results of several studies showing that smoking exerts a negative effect on the outcome of GTR treatment of various types of periodontal defects [8, 19, 22, 23, 24]. In a retrospective analysis of factors influencing the outcome of GTR treatment in intrabony defects by means of PLA/citric acid ester copolymer bioresorbable membranes, Stavropoulos et al. [19] found that smokers gained approximately 1 mm less in PAL than did nonsmokers (3.2 mm vs 4.3 mm, respectively), and smokers were approximately seven times less likely to gain $\geq$4 mm in PAL as compared with patients who did not smoke (odds ratio: 0.15). In fact, in the PLA/PGA group in the present study the majority of smokers gained $\leq$2 mm attachment, while all (except one) nonsmoking patients gained $\geq$4 mm attachment. Similarly, in the group receiving porcine collagen types I and III membranes, the two patients who smoked showed a PAL gain of 3 mm, i.e., the lowest amount of PAL gain observed in that group. On the other hand, it is unlikely that the less favorable response of the PLA/PGA group is due to the larger number of sites with BOP at baseline in that group compared with the collagen group, since only full-mouth bleeding scores (FMBS) after treatment (i.e., at the evaluation time-point) and not baseline BOP scores, have been associated with reduced PAL gains after GTR [21].

Bone grafting in combination with GTR is applied with the intention of supporting and stabilizing the membrane (thus preventing membrane collapse) and/or promoting bone healing although recent controlled experimental studies have questioned the potential of the deproteinized bovine bone product used in the present study to truly enhance bone regeneration when used as an adjunct to GTR [3, 4, 17, 18], human histologic case reports suggest that Bio-Oss grafting in intrabony defects treated with resorbable membranes produces some amounts of true periodontal regeneration (i.e., formation of new cementum with functionally oriented inserting collagen fibers on a previously denuded root surface, and bone regeneration) [2, 14, 16]. In the present study, comparison of the pre-surgical radiographs with the ones taken at the 1-year control showed that, in most of the cases, treatment resulted in an almost total resolution of the bone defect (with bone fill but also evidence of some crestal resorption). However, radiographic data assessing bone fill after GTR in combination with a mineralized bone graft, such as the deproteinized bovine bone product used in the present study, should be interpreted with caution since these grafts are barely distinguishable from the host bone. Previous reports (case series and controlled studies) on GTR treatment of intrabony defects in combination — with Bio-Oss reported PAL gains ranging from 2.2 mm-to 5.3 mm after treatment [1, 12, 15]. For instance, Paolantonio et al. [15] observed an average PAL gain of 5.0 mm, while Camargo et al. [1] found a PAL gain of 3.3 mm after surgery. The somewhat lower values of PAL gain obtained in the study of Camargo et al. [1] and the present study, when compared with the results reported by Paolantonio et al. [15], may be attributed to the fact that the latter study included only patients who did not smoke.

The present study suffers from the fact that each of the two treating centers performed only one of the two treatment modalities (i.e., in Aarhus only PLA/PGA copolymer membranes were placed, while in Mainz the porcine collagen type-1 membrane was used). However, all surgeries and all the controls in each center were made

by one (the same) experienced surgeon. Therefore, it seems reasonable to anticipate that the lack of treatment randomization between the centers may have influenced the results only insignificantly.

Conclusion

In conclusion, the results of the present study corroborate the view that the membrane material is not a critical factor for the outcome of GTR treatment of intrabony defects with bioresorbable membranes.

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