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Five-year results of a prospective, randomized, controlled study evaluating treatment of intra-bony defects with a natural bone mineral and GTR

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Abstract

Background: Treatment with a natural bone mineral (NBM) and a guided tissue regeneration (GTR) has been shown to promote periodontal regeneration. However, until now there are only very limited data on the long-term clinical results following this regenerative technique.

Aim: To present the 5-year results of a prospective, randomized, controlled clinical study evaluating the treatment of deep intra-bony defects either with open flap debridement (OFD) and a combination of an NBM and GTR (test) or OFD alone (control).

Methods: Nineteen patients diagnosed with advanced chronic periodontitis, and each of whom displayed one intra-bony defect, received randomly the test or the control treatment. Results were evaluated at baseline, at 1 and at 5 years following therapy.

Results: No statistically significant differences in any of the investigated parameters were observed at baseline between the two groups. At 1 year after therapy, the test group showed a reduction in mean probing depth (PD) from 9.1 ± 1.1 to 3.7 ± 0.8 mm ($p < 0.001$) and a change in mean clinical attachment level (CAL) from 10.4 ± 1.3 to 6.4 ± 1.2 mm ($p < 0.001$). At 5 years, mean PD and CAL measured 4.3 ± 0.8 and 6.7 ± 1.6 mm, respectively. At 5 years, both PD and CAL were statistically significantly improved compared with baseline ($p < 0.001$) without statistically significant differences between the 1- and 5-year results. In the control group, mean PD was reduced from 8.9 ± 1.3 to 4.9 ± 1.2 mm ($p < 0.001$) and mean CAL changed from 10.6 ± 1.4 to 8.8 ± 1.5 mm ($p < 0.01$). At 5 years, mean PD and CAL measured 5.6 ± 1.1 and 9.1 ± 1.3 mm, respectively, and were still statistically significantly improved compared with baseline ($p < 0.01$). No statistically significant differences were found between the 1- and 5-year results. The test treatment, at both 1 and 5 years, yielded statistically significantly higher CAL gains than the control one ($p < 0.01$). Compared with baseline, at 5 years a CAL gain of $\geqslant 3$ mm was found in nine defects (90%) of the test group but in none of the defects treated with OFD alone.

Conclusions: It was concluded that (i) treatment of intra-bony defects with OFD+NBM+GTR may result in significantly higher CAL gains than treatment with OFD, and (ii) the clinical results obtained after both treatments can be maintained over a period of 5 years.

Key words: collagen membrane; controlled clinical study; guided tissue regeneration; long-term results; natural bone mineral; open flap debridement; regenerative periodontal therapy

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Regenerative periodontal therapy aims at the restitution of the tooth's supporting periodontal tissues (i.e. new periodontal ligament, new cementum with inserting connective tissue fibers and new bone), which have been lost following injury or periodontal disease (Karring et al. 2003). One method to facilitate periodontal regeneration implies the fill of the intra-bony periodontal defects with a natural bone mineral (NBM) and subsequent coverage of the graft material and the defects by means of a bioresorbable collagen membrane (Camelo et al. 1998, Lundgren & Slotte 1999, Camargo et al. 2000, Mellonig 2000, Sculean et al. 2003a, 2004a, 2005, Tonetti et al. 2004, Liñares et al. 2006). Histological studies in animals and humans have provided evidence that NBM possesses excellent osteoconductive properties and integrates well into bone tissue (Berglundh & Lindhe 1997, Skoglund et al. 1997, Camelo et al. 1998, 2001, Hämmerle et al. 1998, Mellonig 2000, Zitzmann et al. 2001, Paolantonio 2002, Sculean et al. 2003b, 2004a). NBM is very well tolerated and, until now, no adverse reactions such as allergies or rejection of the graft particles related to the material have been reported (Camelo et al. 1998, Richardson et al. 1999, Camargo et al. 2000, Mellonig 2000, Zitzmann et al. 2001, Sculean et al. 2003a, b, 2004a, 2005, Tonetti et al. 2004, Liñares et al. 2006). Findings from controlled clinical studies have indicated that treatment of intra-bony defects with open flap debridement (OFD)+NBM+guided tissue regeneration (GTR) may result in significantly higher clinical attachment level (CAL) gains and osseous fill, compared to that obtained following OFD alone or GTR alone (Camargo et al. 2000, Paolantonio 2002, Sculean et al. 2003a, 2005, Tonetti et al. 2004, Liñares et al. 2006). Although the available data are promising, until now there are still very limited data from controlled clinical studies evaluating the long-term results following treatment of intra-bony defects with OFD+NBM+GTR.

Therefore, the aim of this prospective, randomized-controlled clinical study was to evaluate the 5-year results obtained following the treatment of intra-bony defects with OFD+NBM+GTR (test) or OFD alone (control).

Material and Methods

The study population and the short-term results (1-year data) have been described in detail previously (Sculean et al. 2003a). Briefly, a total of 28 patients (15 females and 13 males) suffering from chronic periodontitis were included in this parallel design study (i.e. 14 patients in each group) after having signed an informed consent form. The study was in accordance with the Helsinki Declaration of 1975, as revised in 1983. However, only 19 patients (10 females and nine males, mean age 45 ± 8.5 years) completed the 5-year evaluation. The other nine patients were lost during follow-up for the following reasons: five patients refused to participate in the evaluation and four patients moved away. Thus, in the following, only the data of the 19 available patients is presented. Before enrollment in the study, all patients received oral hygiene instructions and full-mouth supra and subgingival scaling and root planing with ultrasonic and hand instruments. In all cases, subgingival scaling was performed under local anaesthesia. Three months following initial therapy, re-evaluation of periodontal status was performed and the decision was taken whether the patient fulfilled the following inclusion criteria: (1) no systemic diseases which could influence the outcome of the therapy, (2) a good level of oral hygiene [plaque index (PI) < 1; Löe 1967], (3) compliance with the maintenance program, (4) presence of one intra-bony defect with a probing depth (PD) of at least 6 mm and an intra-bony component of at least 3 mm as detected on the radiographs. If some patients exhibited pockets $\geqslant 6$ mm or molars with deep furcation involvements at other teeth than at those involved in the study, appropriate treatment was rendered based on a comprehensive treatment plan. Patients reporting to smoke more than 10 cigarettes/day were defined as smokers (Tonetti et al. 1996). Patients reporting to smoke only occasionally, were not considered as smokers. There were no smokers in the present patient population.

At the teeth involved in the study, the following clinical parameters were assessed 1 week before and 1 year after the surgical procedure using the same type of periodontal probe (PCP 12, Hu-Friedy, Chicago, IL, USA): plaque index (PI), gingival index (GI; Löe 1967), bleeding on probing (BOP), PD, gingival recession (GR), and CAL. The measurements were made at six sites per tooth: mesiovestibular (mv), midvestibular (v), distovestibular (dv), mesiooral (ml), midoral (l), distooral (dl) by a calibrated investigator who was not the same as the surgeon. The cemento-enamel junction (CEJ) was used as the reference point. In cases where the CEJ was not visible, a restoration margin was used for these measurements. The study reports only measurements at the same, at baseline the deepest, point of the selected defects. Pre- and post-operative radiographs were taken with the long cone paralleling technique.

The defects were randomly assigned before surgery to the two treatment groups with the randomized block approach. Blocking to control for the effects of the prognostic variables INTRA and CAL was used to decrease outcome variability (Fleiss 1986). For allowing randomization, INTRA was estimated before surgery on radiographs and by performing transgingival bone sounding.

Intra-examiner reproducibility

Five patients, each showing 10 teeth (single and multi-rooted) with PDs > 6 mm on at least one aspect of each tooth, were used to calibrate the examiner. The examiner evaluated the patients on two separate occasions, 48 h apart. Calibration was accepted if measurements at baseline and at 48 h were similar to the millimetre at $> 90\%$ level. The examiner was not aware of the surgical procedure to be performed.

Surgical procedure

All operative procedures were performed under local anaesthesia by the same surgeon (A. S.). The surgical procedure was described in detail previously (Sculean et al. 2003a). Briefly, following intra-cervicular incisions, full-thickness mucoperiosteal flaps were raised vestibularly and orally. Vertical releasing incisions were performed only if necessary for a better access, or to achieve a better closure of the surgical site. All granulation tissue was removed from the defects and the roots were thoroughly scaled and planed using hand and ultrasonic instruments. No root surface conditioning was performed.

During surgery the following measurements were made: distance from the cemento-enamel junction to the bottom of the defect (CEJ–BD), distance from the CEJ to the most coronal extension of the alveolar bone crest (CEJ–BC). The intra-bony component

(INTRA) of the defects was defined as (CEJ–BD)–(CEJ–BC).

At the test sites, the defects were filled with bovine porous bone mineral granules of particle size 0.25–1.0 mm NBM (BioOss®, Geistlich, Wolhusen, Switzerland). Care was taken not to overfill the defects. Following grafting, a bioresorbable collagen membrane of porcine origin (BioGide Perio®, Geistlich) was trimmed and adapted over the entire defect, so as to cover 2–3 mm of the surrounding alveolar bone and to ensure stability of the graft material. No sutures or pins were used for membrane fixation or stabilization. Finally, the mucoperiosteal flaps were repositioned coronally and fixed with vertical or horizontal mattress sutures.

The same surgical protocol was also used for the control sites, without the use of NBM or GTR.

Post-operative care

Immediately after surgery all patients received antibiotics for 1 week (3×500 mg Amoxicillin/day). The post-operative care consisted of 0.2% chlorhexidine rinses twice a day for 4 weeks and the administration of analgesics (2×600 mg ibuprofen/day for 3 days). The sutures were removed 14 days after the surgery. Recall appointments were scheduled every second week during the first 2 months after surgery, and monthly following the rest of the observation period of 1 year. Neither probing nor subgingival instrumentation was performed during the first year after surgery. After the first year and during the rest of the observation period of 5 years, patients were recalled every 3 months. The recall appointments consisted mainly of reinforcement of oral hygiene measures and professional supragingival tooth cleaning.

Statistical analysis

The statistical analysis was performed using a commercially available software program (SPSS® for Windows, 2003 Chicago, IL, USA). In the statistical evaluation, only the baseline, 1- and the 5-year data of the 19 available patients have been considered. The primary outcome variable was the CAL. In the calculations, the deepest site per tooth was included. For the statistical evaluation of the changes from baseline to 1 year, the paired *t*-test was used. For the comparisons between the groups, the unpaired *t*-test was used. The α error was set at 0.05. The power of the study, given 1 mm as a significant difference between the groups, was calculated to be 0.65.

Table 1. Plaque index (PI), gingival index (GI) and bleeding on probing (BOP) at baseline at 1 and at 5 years following treatment with test or control

Parameter	Treatment	Baseline	1 year	*p* value	5 years	*p* value
PI						
	Test ($n = 10$)					
	Mean (± SD)	0.8 ± 0.4	0.9 ± 0.4	NS	1.2 ± 0.8	NS
	Control ($n = 9$)					
	Mean (± SD)	0.7 ± 0.5	0.7 ± 0.5	NS	1.1 ± 0.7	NS
GI						
	Test ($n = 10$)					
	Mean (± SD)	1.7 ± 0.5	0.6 ± 0.4	<0.001	1.0 ± 1.0	NS
	Control ($n = 9$)					
	Mean (± SD)	1.8 ± 0.8	0.8 ± 0.6	<0.001	1.1 ± 0.9	NS
BOP						
	Test ($n = 10$)					
	Mean (± SD)	53%	34%	<0.001	38%	NS
	Control ($n = 9$)					
	Mean (± SD)	49%	36%	<0.001	40%	NS

No significant differences between the test and control group were found.

Results

The post-operative healing was considered as generally uneventful. Minor complications were related to usual post-operative swelling and occurred within the first days after surgery. None of the patients reported any adverse reactions to the antibiotics or analgesics used. In both groups, all patients reported a high degree of satisfaction with the provided treatment, which was related to the possibility of maintaining the teeth. The PI, GI and BOP for both treatment groups at baseline and after 1 and 5 years are summarized in Table 1. Mean PI did not reveal a statistically significant difference between the two groups at baseline and after 1 and 5 years. Although at 5 years the PI increased slightly in both treatment groups, this difference was not found to be statistically significant compared with the baseline or to the 1-year results. A statistically significant difference was observed in both treatment goups, when comparing the 1 and 5 years GI and BOP to the baseline values ($p < 0.001$). However, no statistically significant differences between the two groups in GI and BOP were observed at 1 and 5 years (Table 1).

The distribution of the defects according to their configuration is presented in Table 2. No differences in the distribution of the defects were found between the two groups.

Table 2. Distribution and configuration of treated defects

	Test ($n = 10$)	Control ($n = 9$)
1–2 wall	2	1
2 wall	7	7
3 wall	1	1

Baseline defect characteristics are presented in Table 3. There were no statistically significant differences in any of the baseline defect characteristics between test and control groups.

The clinical results at 1 and at 5 years after treatment are presented in Tables 4–6.

No statistically significant differences in any of the investigated parameters were observed at baseline between the two groups. At 1 year after therapy, the test group showed a reduction in mean PD from 9.1 ± 1.1 to 3.7 ± 0.8 mm ($p < 0.001$) and a change in mean CAL from 10.4 ± 1.3 to 6.4 ± 1.2 mm ($p < 0.001$). At 5 years, mean PD and CAL measured 4.3 ± 0.8 and 6.7 ± 1.6 mm, respectively. At 5 years, both PD and CAL were statistically significantly improved compared with baseline ($p < 0.001$) without statistically significant differences between the 1- and 5-year results. In the control group, mean PD was reduced from 8.9 ± 1.3 to 4.9 ± 1.2 mm ($p < 0.001$) and mean CAL changed from 10.6 ± 1.4 to 8.8 ± 1.5 mm ($p < 0.01$). At 5 years, mean PD and CAL measured 5.6 ± 1.1 and 9.1 ± 1.3 mm, respectively, and were still statistically significantly improved compared with baseline ($p < 0.01$). No statistically significant

Table 3. Baseline defect characteristics expressed in millimetre (mean ± SD)

Treatment	PD (mm)	GR (mm)	CAL (mm)	CEJ–BD (mm)	CEJ–BC (mm)	INTRA (mm)
Test ($n = 10$)	9.1 ± 1.1	1.4 ± 1.5	10.4 ± 1.3	11.1 ± 1.1	7.1 ± 1.4	4.0 ± 1.4
Control ($n = 9$)	8.9 ± 1.3	1.7 ± 1.2	10.6 ± 1.4	11.3 ± 1.2	7.2 ± 1.4	4.1 ± 1.3

PD, probing depth; GR, gingival recession; CAL, clinical attachment level; CEJ–BD, cemento-enamel junction to the bottom of the defect; CEJ–BC, distance from the CEJ to the most coronal extension of the alveolar bone crest.

Table 4. Clinical parameters at baseline and 1 year for the test and control groups

	Baseline	1 year	Difference	Significance
Probing depth				
Test ($n = 10$)	9.1 ± 1.1	3.7 ± 0.8	5.4 ± 1.5	$p < 0.001$
Control ($n = 9$)	8.9 ± 1.3	4.9 ± 1.2	4.0 ± 0.9	$p < 0.001$
			$p \leqslant 0.05$	
Gingival recession				
Test ($n = 10$)	1.4 ± 1.5	2.7 ± 1.7	1.3 ± 1.3	< 0.01
Control ($n = 9$)	1.7 ± 1.2	3.9 ± 1.4	2.2 ± 0.8	< 0.01
Clinical attachment level				
Test ($n = 10$)	10.4 ± 1.3	6.4 ± 1.2	4.0 ± 1.0	$p < 0.001$
Control ($n = 9$)	10.6 ± 1.4	8.8 ± 1.5	1.8 ± 0.8	$p < 0.01$
			$p < 0.01$	

Table 5. Clinical parameters at baseline and 5 years for the test and control groups

	Baseline	5 years	Difference	Significance
Probing depth				
Test ($n = 10$)	9.1 ± 1.1	4.3 ± 0.8	4.8 ± 1.6	$p < 0.001$
Control ($n = 9$)	8.9 ± 1.3	5.6 ± 1.1	3.3 ± 1.4	$p < 0.001$
			$p \leqslant 0.05$	
Gingival recession				
Test ($n = 10$)	1.4 ± 1.5	2.4 ± 1.4	1.1 ± 1.2	< 0.01
Control ($n = 9$)	1.7 ± 1.2	3.7 ± 1.2	2.0 ± 0.8	< 0.01
			NS	
Clinical attachment level				
Test ($n = 10$)	10.4 ± 1.3	6.7 ± 1.6	3.7 ± 1.1	$p < 0.001$
Control ($n = 9$)	10.6 ± 1.4	9.1 ± 1.3	1.4 ± 0.7	$p < 0.01$
			$p < 0.01$	

Table 6. Clinical parameters at 1 and 5 years for the test and control groups

	1 year	5 years	Difference	Significance
Probing depth				
Test ($n = 10$)	3.7 ± 0.8	4.3 ± 0.8	0.6 ± 0.7	NS
Control ($n = 9$)	4.9 ± 1.2	5.6 ± 1.1	0.6 ± 0.7	NS
			NS	
Gingival recession				
Test ($n = 10$)	2.7 ± 1.7	2.4 ± 1.4	− 0.3 ± 0.5	NS
Control ($n = 9$)	3.9 ± 1.4	3.7 ± 1.2	− 0.2 ± 1.2	NS
			NS	
Clinical attachment level				
Test ($n = 10$)	6.4 ± 1.2	6.7 ± 1.6	− 0.3 ± 0.6	NS
Control ($n = 9$)	8.8 ± 1.5	9.1 ± 1.3	− 0.3 ± 0.5	NS
			NS	

differences were found between the 1- and 5-year results. The test treatment, at both 1 and 5 years, yielded statistically significantly higher CAL gains than the control one ($p < 0.01$). Compared with baseline, a CAL gain of $\geqslant 3$ mm was found at 5 years in nine defects (90%) of the test group but in none of the defects treated with OFD alone (Table 7). In the test group, two defects lost 2 and 1 mm, respectively, of the CAL gained at 1 year. A CAL loss of 1 mm was measured at three defects of the control group.

Table 7. Frequency distribution of clinical attachment level (CAL) gain after 5 years in the test and control group

CAL gain (mm)	Test ($n = 10$)		Control ($n = 9$)	
	no.	%	no.	%
0	0	0	1	11
1	0	0	3	33
2	1	10	5	56
3	4	40		
4	3	30		
5	1	10		
6	1	10		

Discussion

The results of this study demonstrated that the treatment of deep intra-bony defects with both the combination of OFD+NBM+GTR and OFD alone may lead to clinically and statistically significant PD reductions and CAL gains. The clinical results measured at 1 year were maintained in both groups over a period of 5 years. However, treatment with OFD+NBM+GTR, at both 1 and 5 years, has led to statistically significantly higher PD reductions and CAL gains than treatment with OFD alone. In the present study, mean CAL gain obtained at 1 year measured 4.0 mm in the test and 1.8 mm in the control group, respectively. These 1-year results are in agreement with previous reports evaluating the same treatments using a comparable study design (Camargo et al. 2000, Tonetti et al. 2004). In the mentioned studies, treatment with OFD+NBM+GTR resulted in a mean CAL gain of 3.2 mm and of 3.3 mm, respectively, while treatment with OFD alone yielded a significantly lower mean CAL gain varying from 1.7 mm (Camargo et al. 2000) to 2.5 mm (Tonetti et al. 2004). The mean of 1.8 mm of CAL gain obtained at 1 year in the control group is in agreement with most of the reported results (Cortellini et al. 1996, Camargo et al. 2000, Sculean et al. 2004b, Tonetti et al. 2004). Slight differences in the results may be explained with baseline defect depth and configuration and/or differences in the surgical technique. Data from controlled clinical studies have provided evidence that the clinical outcome following any type of regenerative or conventional periodontal surgery is strongly influenced by initial defect depth and configuration (i.e. the

deeper the defect, the higher the CAL gain; Cortellini et al. 1998, Tonetti et al. 2004, Tsitoura et al. 2004, Liñares et al. 2006). Moreover, it should also be pointed that recent data from clinical studies, which have suggested that the use of special flap designs intended to completely maintain the soft tissues surrounding the bony defects and ensure primary wound closure, may additionally improve the outcome of regenerative and even conventional periodontal surgery (Tonetti et al. 2002, 2004, Cortellini & Tonetti 2005).

When comparing the 1-year to the 5-year results, it has to be noted that in both groups a slight, statistically insignificant loss of mean CAL was measured between the 1- and 5-year evaluation period. This slight loss of mean CAL may probably be attributed to the CAL loss that occurred in both groups at some of the defects (i.e. two defects treated with the test therapy lost 2 and 1 mm, respectively, while three defects from the control group lost 1 mm each). This loss of CAL may probably be explained in both treatment groups by the slightly higher values of PI compared with those measured at baseline or at 1 year. Although at 5 years the increase in mean PI, GI and BOP did not reach statistical significance compared with the 1-year values, it cannot be excluded that the plaque accumulation might have led to inflammation and loss of CAL. Results from controlled clinical studies have shown that the stability of gained clinical attachment following conventional and regenerative periodontal therapy is dependent upon stringent oral hygiene and compliance with a supportive periodontal care program (Tonetti et al. 1996, Cortellini & Tonetti 2004, Sculean et al. 2004b). It should be kept in mind that for the time being, only very limited data on the long-term outcome following treatment of intrabony periodontal defects with NBM+GTR are available, and thus direct comparisons are difficult. However, the results obtained in the test group compare well to those from a recent case report study evaluating the 5-year results following the treatment of intra-bony periodontal defects with NBM impregnated in gentamicin sulphate and subsequent coverage with a PLA/PGA bioresorbable membrane (Stavropoulos & Karring 2005). In the mentioned study, the authors reported a CAL gain of 3.8 ± 1.8 mm at 1 year and of 4.1 ± 1.6 mm at 5 years, respectively. There were no statistically significant differences between the 1- and 5-year data, thus indicating long-term stability of the obtained results.

On the other hand, it has to be noted that in the present follow-up study only 19 out of the originally 28 patients were included, which in turn resulted in a lower statistical power (i.e. 0.65). Therefore, it is unknown to what extent the lack of those nine patients might have influenced the 5-year results. Further studies, including a higher number of patients and defects, are warranted to confirm the present findings.

Another important factor that was demonstrated to strongly influence the outcome of regenerative periodontal treatment was smoking. However, because none of the 19 patients was a smoker, no conclusion could be drawn regarding this issue. When addressing the clinical relevance of the present findings, it is important to point out that compared with baseline, a CAL gain of $\geqslant 3$ mm was found at 5 years in nine defects (90%) of the test group but in none of the defects treated with OFD alone. As the limiting factors for the outcome of surgical therapy such as plaque and infection control, operator variability, and smoking were reduced to a minimum, it is most likely that the significantly higher CAL gains obtained in the test group are due to the regenerative materials used. Moreover, based on previous histologic findings from humans it may be assumed that the clinical improvements obtained in the test group represent not only a defect fill but also, at least in part, a regeneration process characterized by the formation of cementum, periodontal ligament and bone (Camelo et al. 1998, Mellonig 2000, Sculean et al. 2004a). On the other hand, it is important to note that also the clinical improvements obtained in the OFD group were maintained over a 5-year period. These results corroborate previous histological and clinical findings, which indicate that a site treated with a conventional surgical approach is not more prone to losing further attachment than a site treated with a regenerative approach, or even a healthy site (Magnusson et al. 1983, Tonetti et al. 1996, Kostopoulos & Karring 2004, Sculean et al. 2004b). Therefore, it is important to emphasize that from a clinical point of view, the main role of regenerative periodontal surgery is to achieve more support for the tooth and not to increase the stability against further progression of periodontal disease (Tonetti et al. 1996).

In conclusion, within their limits the present findings indicate that (i) treatment of intra-bony defects with OFD+NBM+GTR may result in significantly higher CAL gains than treatment with OFD, and (ii) the clinical results obtained after both treatments can be maintained over a period of 5 years.

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Clinical Relevance

Scientific rationale for the study: Treatment with an NBM and a GTR has been shown to promote periodontal regeneration. Till date, there are very limited data on the long-term clinical results following this regenerative technique. In this report, the 5-year results of a prospective, controlled clinical study evaluating the treatment of deep intra-bony defects with either OFD and a combination of a NBM and GTR (test) or OFD alone (control) are presented.

Principal findings: Both treatments showed, at 1 and at 5 years, statistically significant improvements in terms of PD reduction and CAL gain compared with baseline. There were no statistically significant differences in any of the two groups between the 1- and 5-year results. However, the test treatment, at both 1 and 5 years, yielded statistically significantly higher CAL gains than the control one ($p < 0.01$). Compared with baseline, a CAL gain of $\geqslant 3$ mm was found at 5 years in nine defects (90%) of the test group but in none of the defects treated with OFD alone.

Practical implications: Although treatment of intra-bony defects with OFD+NBM+GTR may result in significantly higher CAL gains than treatment with OFD, the clinical results obtained with both treatments can be maintained over a period of 5 years.