Clin Oral Invest (2006) 10: 55–60
DOI 10.1007/s00784-005-0024-1

ORIGINAL ARTICLE

Stefan-Ioan Stratul · Frank Schwarz · Jürgen Becker · Britta Willershausen · Anton Sculean

Healing of intrabony defects following treatment with an oily calcium hydroxide suspension (Osteoinductal). A controlled clinical study

Received: 21 July 2005 / Accepted: 25 November 2005 / Published online: 20 December 2005

Abstract The purpose of the present clinical study was to evaluate the healing of deep intrabony defects following the application of an oily calcium hydroxide suspension (OCHS). Thirty patients suffering from chronic periodontitis, each of whom displayed one intrabony defect, were randomly treated with access flap surgery (AFS) and the application of OCHS (test) or with AFS alone (control). The following clinical parameters were recorded at baseline and at 6 months after therapy: plaque index, gingival index, bleeding on probing, probing depth (PD), gingival recession, and clinical attachment level (CAL). No differences in any of the investigated parameters were observed at baseline between the two groups. At 6 months after therapy, the test group showed a reduction in mean PD from 7.7±1.5 to 2.9±0.9 mm (P<0.001) and a change in mean CAL from 9.6±2.1 to 5.5±2.5 mm (P<0.001). In the control group, the mean PD was reduced from 6.9±0.9 to 3.7±0.9 mm (P<0.001) and the mean CAL changed from 8.5±2.5 to 6.4±2.7 mm (P<0.001). OCHS resulted in statistically significant higher PD reductions (P<0.01) and CAL gains (P<0.05) than AFS alone. Within the limits of the present study, it can be concluded that: (1) at 6 months after surgery both therapies resulted in statistically significant PD reductions and CAL gains and (2) treatment with OCHS resulted in statistically significant higher CAL gains than treatment with AFS alone.

Keywords Regenerative periodontal therapy · Intrabony defect · Controlled clinical study · Oily calcium hydroxide suspension · Access flap surgery

S.-I. Stratul
Department of Periodontology,
Victor-Babes University of Medicine,
Timisoara, Romania

F. Schwarz · J. Becker
Department of Oral Surgery,
Heinrich Heine University,
Düsseldorf, Germany

B. Willershausen
Department of Conservative Dentistry and Periodontology,
Johannes-Gutenberg University,
Mainz, Germany

A. Sculean (✉)
Department of Periodontology,
Radboud University Medical Center,
P.O. Box 9101, Internal Postal Code 117,
6500 Nijmegen, Philips van Leydenlaan 25,
The Netherlands
e-mail: a.sculean@dent.umcn.nl
Tel.: +31-24-3616371
Fax: +31-24-3614657

Introduction

A major goal of periodontal treatment is to resolve inflammation and thereby arrest disease progression [3]. The results from controlled clinical studies have shown that nonsurgical treatment and various types of conventional surgical treatment may lead to clinically important and statistically significant probing pocket depth reductions and clinical attachment level (CAL) gains [20, 21, 35]. However, histologic studies demonstrated that healing following nonsurgical periodontal therapy and any type of conventional surgical periodontal therapy is mainly characterized by the formation of a long junctional epithelium along the instrumented root surfaces and no predictable regeneration of attachment apparatuses [1, 5, 6, 39, 42]. Ideally, periodontal therapy does not only include arresting the disease but also the regeneration of the tissues that have been lost due to the disease. This includes de novo formation of connective tissue attachment, cementum formation, and the regrowth of alveolar bone [6]. Several treatment modalities, such as the use of guided tissue regeneration (GTR) alone or in combination with different types of bone grafts, root surface demineralization, enamel matrix derivatives (EMDs), or the application of growth factors, have been employed with varying degrees of success to predictably accomplish this goal [2, 16, 22, 23, 28, 29, 32, 40]. Recently, an oily calcium hydroxide suspension (OCHS) has also been supposed to support periodontal regeneration [26]. Calcium hydroxide (CH) is a product of lime slaking from quick lime.

The slurry of CH incorporates carbon dioxide from the air and hardens with the formation of calcium carbonate and water. CH is not soluble in organic acids, has a marginal solubility in water and an improved solubility in glycerine or syrup. The saturated aqueous solution exhibits an alkalic pH value of 12.4. Several experimental studies have shown that CH may possess antimicrobial [14, 17] and anti-inflammatory properties [7]. When applied on amputated dental pulp or into the root canal close to the apex, CH has been reported to result in a destruction of the vital tissue, leading to the formation of a necrotic layer and, subsequently, formation of a hard tissue barrier below the exposure site [19, 44]. Additionally, CH also seems to have a positive influence on the healing of periapical lesions [12, 13]. These effects may be mainly due to the alcalic properties of CH leading to a neutralization of the acidic metabolites of macrophages and osteoclasts [47]. However, the CH mechanism used to promote the repair of bone tissues may not only do so by providing rich Ca^{2+} and alkaline environment mineral deposition, but also by stimulating the calcification enzyme activity of osteoblasts [26]. The oily formulation, available under the name Osteoinductal (Osteoinductal GmbH, München, Germany) (OCHS), contains CH, liquid and solid carbohydrate chains, and fatty acids (myristaleinic, oleic, palmitoleinic, gadoleinic, margaric, pentadecanic, myristic, linolenic, stearic, palmitic, arachidic, lauric, and linolic) esterified with glycerol. The oily parts consist of a natural product of porcine origin-oleum pedum, which was demonstrated to have a low cytotoxic effect on human fibroblasts [24], and vaselinum album. So far, there are no data from controlled clinical studies evaluating healing of intrabony defects following treatment with OCHS. Therefore, the aim of this controlled clinical study was to evaluate and compare the healing of advanced intrabony periodontal defects following treatment with access flap surgery (AFS) and the application of OCHS and AFS alone.

Materials and methods

Study population

Thirty patients with chronic periodontitis were included in this parallel-design study (i.e., 15 patients in each group). The patient population comprised 20 men and 10 women (mean age=43±15 years). Patients who reported to smoke only occasionally were not considered as smokers [45]. According to the given definition there were no smokers included in the present study. The study was in accordance with the Helsinki Declaration of 1975, as revised in 1983 and all participants signed informed consent forms. The study protocol was approved by the Ethical Committee of the Victor Babes University of Medicine and Pharmacy of Timisoara, Romania. Criteria needed for inclusion were: (1) no systemic diseases that could influence the outcome of the therapy, (2) a good level of oral hygiene [plaque index (PI) <1] [27], (3) compliance with the maintenance program, and (4) presence of one intrabony defect with a probing depth (PD) of >6 mm and an intrabony component of >3 mm as detected on radiographs. All patients underwent initial periodontal therapy 1 month prior to surgery. The following clinical parameters were assessed 1 week prior to and 6 months after the surgical procedure using a periodontal probe (PCP 12, Hu-Friedy, Chicago, IL, USA): PI [27], gingival index (GI) [27], bleeding on probing (BOP), PD, gingival recession (GR), and CAL. The measurements were made at six aspects per tooth: mesiovestibular, midvestibular, distovestibular, mesiolingual, midlingual, and distolingual. The cemento–enamel junction (CEJ) was used as the reference point. A restoration margin was used as a reference in cases where the CEJ was destroyed due to restorations. All measurements were performed by one previously calibrated examiner who was masked to the specific treatment procedures. The study reports only measurements at the same deepest PD of the selected defect. Pre- and postoperative radiographs were taken using the long-cone parallel technique. After controlling for the depth of the intrabony component and CAL, all patients were randomly assigned to the following treatment groups: (1) AFS and the application of an OCHS (Osteoinductal, Osteoinductal GmbH, München, Germany) (test) and (2) AFS alone (control).

Surgical procedure

All operative procedures were performed under local anesthesia by the same surgeon. Following intracrevicular incisions, full thickness mucoperiosteal flaps were raised vestibularly and orally. Vertical releasing incisions were performed only if necessary for better access or to achieve 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 ultrasound instruments. No root surface conditioning was performed. During surgery the following measurements were made: distance from the CEJ to the bottom of the defect (CEJ-BD) and distance from the CEJ to the most coronal extension of the alveolar bone crest (CEJ-BC). The intrabony component (INTRA, BC-BD) of the defects was defined as CEJ-BD minus CEJ-BC. At the test sites, bleeding into the defects was reduced to a minimum and the sites were subsequently filled with OCHS, starting from the bottom of the defect. Care was taken to obtain direct contact between OCHS and the adjacent alveolar bone without interposition of a blood clot. Defects were slightly overfilled, as the OCHS has a creamy consistency and tends to leak from the defect. Finally, the mucoperiosteal flaps were repositioned coronally and fixed with vertical or horizontal mattress sutures. Where possible, sutures were put in position before filling the defects with the OCHS to prevent the possible leakage of the material. The same surgical protocol was also used for the control sites; however, the OCHS was not applied.

Table 1 Configuration and distribution of the treated defects

	Test (n=15)	Control (n=15)
1 wall	4	5
2 walls	10	10
Circular	1	–

Table 2 Baseline defect characteristics (mean±SD)

Treatment	CAL (mm)	CEJ-BD (mm)	CEJ-BC (mm)	INTRA (mm)
Test (n=15)	5.5±2.5	10.1±2.3	4.3±1.6	5.8±1.4
Control (n=15)	6.4±2.7	9.4±2.0	4.5±1.6	5.0±0.9

Postoperative care

All patients received peri- and postoperative antibiotic medication for 1 week (3× 500 mg amoxicillin/day). Additionally, postoperative care consisted of rinsing with 0.2% chlorhexidine (PlakOut, Santa Balanos, Greece) twice a day for 4 weeks. 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. Neither probing nor subgingival instrumentation was performed during the first 6 months after the surgery.

Statistical analysis

The statistical analysis was performed using a commercially available software program [Statistical Package for the Social Sciences (SPSS) 11.0, SPSS, Chicago, IL, USA]. The primary outcome variable was CAL. In the calculations, only the deepest PD per tooth was taken into consideration. For the statistical evaluation of the changes from baseline to 6 months after surgery, the Wilcoxon signed-rank test was used. For comparisons between the groups, the Mann–Whitney U test was used. For the given input values (CAL and SD of both groups, a level of significance of alpha=0.05, and a sample size of 15), a power (1-β) of 0.75 was computed for a two-sided null hypothesis H_0.

Table 3 Mean (±SD) PI, GI, and BOP at baseline and after 6 months (n=15 patients in each group)

	Test	Control
PI		
Baseline	0.7±0.6	0.8±0.7
6 months	0.6±0.4	0.7±0.5
GI		
Baseline	1.7±0.9	1.8±0.6
6 months	0.8±0.6	0.9±0.6
BOP		
Baseline	68%	63%
6 months	28%	26%

Table 4 Clinical parameters at baseline and 6 months after surgery for the test and control groups (n=15 patients in each group)

	Baseline	6 months	Difference	Significance
Probing depth				
Test	7.7±1.5	2.9±0.9	4.8±0.8	P<0.001
Control	6.9±0.9	3.7±0.9	3.3±1.5	P<0.001
			P<0.01	
Gingival recession				
Test	1.9±1.4	2.8±1.9	0.7±1.1	P<0.01
Control	1.5±1.9	2.7±2.5	1.2±1.6	P<0.05
			n.s.	
Clinical attachment level				
Test	9.6±2.1	5.5±2.5	3.9±1.2	P<0.001
Control	8.5±2.5	6.4±2.7	2.1±2.3	P<0.01
			P<0.05	

Results

At the baseline examination, there were no statistically significant differences in any of the investigated parameters. The configuration of the defects is shown in Table 1. The depth of the intrabony component as measured during surgery is presented in Table 2. The postoperative healing was uneventful in both groups. No complications, such as allergic reactions, abscesses, or infections, were observed throughout the study period. However, minor postoperative swelling appeared to be reduced in the test group as compared to the control group. The mean PI, GI, and BOP for both groups at baseline and after 6 months are summarized in Table 3. In both groups, mean PI values remained low throughout the study period. There were no statistically significant differences within or between groups. In both groups the GI and BOP improvement was statistically significant as compared to the baseline (P<0.01). However, at 6 months after surgery, the difference between the groups was statistically not significant. The mean PD, GR, and CAL in both groups at baseline and after 6 months are summarized in Table 4. In

Table 5 Frequency distribution of CAL gain in the test and control groups (n=15 patients in each group)

CAL gain (mm)	Test		Control	
	N°	%	N°	%
−1			3	20.0
1			4	26.7
2	2	13.3	1	6.7
3	3	20.0	3	20.0
4	6	40.0	1	6.7
5	2	13.3	2	13.3
6	2	13.3	1	6.7

particular, at 6 months after therapy, the test group showed a reduction in mean PD from 7.7±1.5 to 2.9±0.9 mm (P<0.001), and a change in mean CAL from 9.6±2.1 to 5.5±2.5 mm (P<0.001). In the control group, the mean PD was reduced from 6.9±0.9 to 3.7±0.9 mm (P<0.001), and the mean CAL changed from 8.5±2.5 to 6.4±2.7 mm (P<0.001). OCHS resulted in statistically significant higher PD reductions (P<0.01) and CAL gains (P<0.05) than AFS alone. The frequency distribution of CAL gains in both treatment groups is shown in Table 5. In particular, in the test group, 66.6% of the sites (n=10 defects) gained at least 4 mm of CAL. In contrast, a CAL gain of 4 mm or more was measured in four defects (26.7%) in the control group (Table 5).

Discussion

The results of the present study have indicated that treatment of intrabony defects with both OCHS and AFS resulted in statistically significant and clinically important reductions of PD and gains of CAL at 6 months after surgery. However, the test treatment resulted in statistically significant higher PD reductions and CAL gains than the control treatment. From a clinical point of view, it should also be noted that postoperative healing was uneventful in all patients. Because there were no signs of any allergic reactions, abscesses, or infections, it might be suggested that OCHS was well tolerated. Furthermore, the observation that postoperative swelling tended to be lower in the OCHS-treated than in the AFS-treated group might be explained by the anti-inflammatory properties noted for CH [7]. However, one problem encountered during the surgical procedure was the low consistency of OCHS which in turn might result in the mucoperiosteal flap having poor resistance to collapsing into the intrabony defect, allowing undesirable cell types to enter the secluded wound area [23, 43, 48]. Indeed, this flap collapse may have implications on the outcome of treatment in a manner similar to that observed following the application of enamel matrix proteins (EMD) [38, 39]. In this context, the collapse may be prevented by means of implantation of additional bone grafts or bone graft substitutes into the defect to support the OCHS in preserving its original position. Further studies are necessary to clarify this issue. When interpreting the present results, it has to be noted that mean CAL gain as observed 6 months postoperatively was 3.9±1.2 mm in the OCHS group and 2.1±2.3 mm in the AFS group. In this context, it needs to be pointed out that these are the first data evaluating the use of OCHS for the treatment of intrabony periodontal defects. Therefore, a comparison with other studies is not possible. However, the CAL gains noted in the OCHS group seemed to be within the range of other well-documented regenerative treatment procedures [9–11, 25, 30, 31, 34, 46]. Mean CAL gain as observed following GTR treatment using nonbioabsorbable membranes (i.e., expanded polytetrafluorethylene) was 3.7±1.7 mm, which did not differ from that obtained with bioabsorbable barrier materials (i.e., polylactid acid, collagen) with 3.6±1.5 mm. In particular, CAL gains of 2–3 mm were observed in 29.2% of the defects, while CAL gains of 4–5 mm were reported in 35.4% of the defects, and CAL gains of 6 mm or more were reported in 24.9% of the defects [9–11, 25, 30, 31, 34, 46]. The CAL gain noted in the OCHS group might also be compared with previously published clinical data on EMD. Hejil et al. [18] reported CAL gains of 2.1 mm 8 months postoperatively and 2.3 mm 16 months postoperatively (baseline CAL=9.4 mm, INTRA=4.8 mm). There was a statistically significant difference between EMD- and placebo-treated sites. Similarly, Pontoriero et al. [33] reported a mean CAL gain of 2.9 mm for EMD-treated sites after 1 year, with a statistically significant difference between EMD- and placebo-treated sites (baseline CAL=9.1 mm, INTRA=4.2 mm); Froum et al. [15] reported a 4.26-mm CAL gain (baseline CAL was not reported, INTRA=5.63 mm); and Sculean et al. [41] reported a 3.4-mm CAL gain (baseline CAL=10.6, INTRA=3.8 mm). The mean CAL gain of 2.1±2.3 mm obtained in the control group is also in agreement with most of the reported results [4, 11, 36, 37]. However, slight differences noted in these data may be explained by baseline defect depths and configurations. Indeed, it is well documented that the postoperative PD reduction and CAL gain obtained after any type of conventional or regenerative periodontal treatment is dependent upon the initial defect depth (i.e., the deeper the defect, the higher the CAL gain) [8, 21, 35]. In this context, it must also be emphasized that even though mean initial PD, CAL, and INTRA were statistically not significant between both groups, mean values tended to be higher in the OCHS group. Accordingly, it is impossible to estimate to what extent this difference might also have influenced the higher mean CAL gains following the application of OCHS. Nevertheless, the present data seem to indicate that OCHS might be successfully used for treatment of intrabony periodontal defects. In this context, however, it is important to realize that the presented clinical results need to be supported by extended histologic evidence. It is still unclear to what extent the CAL gains obtained following application of OCHS represent real periodontal regeneration rather than defect fill without new connective tissue attachment. Also, the stability of the obtained CAL gains over time has to be evaluated in further clinical studies.

Within the limits of the present study, it can be concluded that: (1) at 6 months after surgery both therapies resulted in statistically significant PD reductions and CAL gains, and (2) treatment with OCHS resulted in statistically significant higher CAL gains than treatment with AFS alone.

References

1. Aukhil I, Schaberg TV, Greco GW, Simpson DM (1988) Surgical versus non-surgical treatment and recurrent periodontal disease in beagle dogs. J Clin Periodontol 15:99–105
2. Brunsvold MA, Mellonig JT (1993) Bone grafts and periodontal regeneration. Periodontol 2000 1:80–91
3. Caffesse RG, Mota LF, Morrison EC (1995) The rationale for periodontal therapy. Periodontol 2000 9:7–13

4. Camargo PM, Lekovic V, Weinlaender M, Nedic M, Vasilic N, Wolinsky LE, Kenney EB (2000) A controlled re-entry study on the effectiveness of bovine porous bone mineral used in combination with a collagen membrane of porcine origin in the treatment of intrabony defects in humans. J Clin Periodontol 27:889–896
5. Caton J, Nyman S, Zander H (1980) Histometric evaluation of periodontal surgery. II. Connective tissue attachment levels after four regenerative procedures. J Clin Periodontol 7:224–231
6. Caton JG, Greenstein G (1993) Factors related to periodontal regeneration. Periodontol 2000 1:9–15
7. Charles P, Nathalie S, Carine D, Alexandru G (2004) Calcium hydroxide and treatment of inflammatory inter-radicular bone resorption of non-vital deciduous molars. Rev Belge Med Dent 59:163–169
8. Cortellini P, Pini Prato G, Tonetti MS (1993) Periodontal regeneration of human infrabony defects. I. Clinical measures. J Periodontol 64:254–260
9. Cortellini P, Pini Prato G, Tonetti MS (1995) Periodontal regeneration of human intrabony defects with titanium reinforced membranes. A controlled clinical trial. J Periodontol 66:797–803
10. Cortellini P, Pini Prato G, Tonetti MS (1996) Periodontal regeneration of human intrabony defects with bioresorbable membranes. A controlled clinical trial. J Periodontol 67:217–223
11. Cortellini P, Carnevale G, Sanz M, Tonetti MS (1998) Treatment of deep and shallow intrabony defects. A multicenter randomized controlled clinical trial. J Clin Periodontol 25:981–987
12. De Moor RJ, De Witte AM (2002) Periapical lesions accidentally filled with calcium hydroxide. Int Endod J 35:946–958
13. De Rossi A, Silva LA, Leonardo MR, Rocha LB, Rossi MA (2005) Effect of rotary or manual instrumentation, with or without a calcium hydroxide/1% chlorhexidine intracanal dressing, on the healing of experimentally induced chronic periapical lesions. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 99:628–636
14. Evanov C, Liewehr F, Buxton TB, Joyce AP (2004) Antibacterial efficacy of calcium hydroxide and chlorhexidine gluconate irrigants at 37 degrees C and 46 degrees C. J Endod 30:653–657
15. Froum SJ, Weinberg MA, Rosenberg E, Tarnow D (2001) A comparative study utilizing open flap debridement with and without enamel matrix derivative in the treatment of periodontal intrabony defects: a 12-month re-entry study. J Periodontol 72:25–34
16. Gottlow J, Nyman S, Karring T, Lindhe J (1984) New attachment formation as the result of controlled tissue regeneration. J Clin Periodontol 11:494–503
17. Haenni S, Schmidlin PR, Mueller B, Sener B, Zehnder M (2003) Chemical and antimicrobial properties of calcium hydroxide mixed with irrigating solutions. Int Endod J 36:100–105
18. Heijl L, Heden G, Svardstrom G, Ostgren A (1997) Enamel matrix derivative (EMDOGAIN) in the treatment of intrabony periodontal defects. J Clin Periodontol 24:705–714
19. Holland R, de Mello W, Nery MJ, Bernabe PF, de Souza V (1977) Reaction of human periapical tissue to pulp extirpation and immediate root canal filling with calcium hydroxide. J Endod 3:63–67
20. Isidor F, Karring T, Nyman S, Lindhe J (1985) New attachment–reattachment following reconstructive periodontal surgery. J Clin Periodontol 12:728–735
21. Kaldahl WB, Kalkwarf KL, Patil KD, Molvar MP, Dyer JK (1996) Long-term evaluation of periodontal therapy: I. Response to 4 therapeutic modalities. J Periodontol 67:93–102
22. Karring T, Nyman S, Gottlow J, Laurell L (1993) Development of the biological concept of guided tissue regeneration—animal and human studies. Periodontol 2000 1:26–35
23. Karring T, Lindhe J, Cortellini P (1997) Regenerative periodontal therapy. In: Lindhe J, Karring T, Lang NP (eds) Clinical periodontology and implant dentistry, 3rd edn. Munksgaard, Copenhagen, pp 597–646
24. Klaiber B, Mittermayer C, Kaden P, Schwechten I (1981) Determination of the toxicity of root canal filling materials and their separate components in cell cultures. Dtsch Zahnarztl Z 36:212–216
25. Laurell L, Falk H, Fornell J, Johard G, Gottlow J (1994) Clinical use of a bioresorbable matrix barrier in guided tissue regeneration therapy. Case series. J Periodontol 65:967–975
26. Liang Y, Wang J, Yu S (2000) Mechanisms of bone repairment in periapical diseases: studies on adjusting bone metabolism with calcium hydroxide in vitro. Zhonghua Kou Qiang Yi Xue Za Zhi 35:112–114
27. Löe H (1967) The gingival index, the plaque index and the retention index systems. J Periodontol 38:610–616 (Suppl)
28. Lowenguth RA, Blieden TM (1993) Periodontal regeneration: root surface demineralization. Periodontol 2000 1:54–68
29. Lynch SE, Williams RC, Polson AM, Howell TH, Reddy MS, Zappa UE, Antoniades HN (1989) A combination of platelet-derived and insulin-like growth factors enhances periodontal regeneration. J Clin Periodontol 16:545–548
30. Mattson JS, McLey LL, Jabro MH (1995) Treatment of intrabony defects with collagen membrane barriers. Case reports. J Periodontol 66:635–645
31. Mellado JR, Salkin LM, Freedman AL, Stein MD (1995) A comparative study of ePTFE periodontal membranes with and without decalcified freeze-dried bone allografts for the regeneration of interproximal intraosseous defects. J Periodontol 66:751–755
32. Nyman S, Lindhe J, Karring T, Rylander H (1982) New attachment following surgical treatment of human periodontal disease. J Clin Periodontol 9:290–296
33. Pontoriero R, Wennstrom J, Lindhe J (1999) The use of barrier membranes and enamel matrix proteins in the treatment of angular bone defects. A prospective controlled clinical study. J Clin Periodontol 26:833–840
34. Proestakis G, Bratthall G, Soderholm G, Kullendorff B, Grondahl K, Rohlin M, Attstrom R (1992) Guided tissue regeneration in the treatment of infrabony defects on maxillary premolars. A pilot study. J Clin Periodontol 19:766–773
35. Ramfjord SP, Caffesse RG, Morrison EC, Hill RW, Kerry GJ, Appleberry EA, Nissle RR, Stults DL (1987) 4 modalities of periodontal treatment compared over 5 years. J Clin Periodontol 14:445–452
36. Sculean A, Chiantella GC, Windisch P, Donos N (2000) Clinical and histologic evaluation of human intrabony defects treated with an enamel matrix protein derivative (Emdogain). Int J Periodontics Restorative Dent 20:374–381
37. Sculean A, Donos N, Brecx M, Reich E, Karring T (2000) Treatment of intrabony defects with guided tissue regeneration and enamel-matrix-proteins. An experimental study in monkeys. J Clin Periodontol 27:466–472
38. Sculean A, Windisch P, Chiantella GC, Donos N, Brecx M, Reich E (2001) Treatment of intrabony defects with enamel matrix proteins and guided tissue regeneration. A prospective controlled clinical study. J Clin Periodontol 28:397–403
39. Sculean A, Berakdar M, Chiantella GC, Donos N, Arweiler NB, Brecx M (2003) Healing of intrabony defects following treatment with a bovine-derived xenograft and collagen membrane. A controlled clinical study. J Clin Periodontol 30:73–80
40. Sculean A, Windisch P, Keglevich T, Gera I (2003) Histologic evaluation of human intrabony defects following non-surgical periodontal therapy with and without application of an enamel matrix protein derivative. J Periodontol 74:153–160
41. Sculean A, Chiantella GC, Windisch P, Arweiler NB, Brecx M, Gera I (2005) Healing of intra-bony defects following treatment with a composite bovine-derived xenograft (Bio-Oss Collagen) in combination with a collagen membrane (Bio-Gide PERIO). J Clin Periodontol 32:720–724

42. Sculean A, Stavropoulos A, Berakdar M, Windisch P, Karring T, Brecx M (2005) Formation of human cementum following different modalities of regenerative therapy. Clin Oral Investig 9:58–64
43. Selvig KA, Kersten BG, Wikesjo UM (1993) Surgical treatment of intrabony periodontal defects using expanded polytetrafluoroethylene barrier membranes: influence of defect configuration on healing response. J Periodontol 64:730–733
44. Tepel J, Darwisch el Sawaf M, Hoppe W (1994) Reaction of inflamed periapical tissue to intracanal medicaments and root canal sealers. Endod Dent Traumatol 10:233–238
45. Tonetti MS, Pini-Prato G, Cortellini P (1995) Effect of cigarette smoking on periodontal healing following GTR in infrabony defects. A preliminary retrospective study. J Clin Periodontol 22:229–234
46. Tonetti MS, Pini Prato G, Stalpers G, Cortellini P (1996) Guided tissue regeneration of deep intrabony defects in strategically important prosthetic abutments. Int J Periodontics Restorative Dent 16:378–387
47. Tronstad L (1988) Root resorption-etiology, terminology and clinical manifestations. Endod Dent Traumatol 4:241–252
48. Wikesjö UM, Selvig KA (1999) Periodontal wound healing and regeneration. Periodontol 2000 19:21–39