Treatment of Peri-Implantitis with EDTA Decontamination and Application of an Enamel Matrix Protein Derivative – a Report of 3 Cases

Anton Sculean, Péter Windisch, Thorsten Mathias Auschill, Ferenc Döri

The aim of the present case report is to present the four-year results following open flap surgery and additional application of an enamel matrix protein derivative for the treatment of intrabony defects caused by peri-implantitis. Three patients (one female and two males) diagnosed with late peri-implantitis and presenting deep crater like intrabony defects, were treated with open flap debridement (OFD), implant surface decontamination with EDTA and application of an enamel-matrix-protein derivative (EMD). One year after therapy a substantial reduction of probing depth (PD), clinical attachment level (CAL) gain and radiographic bone fill were observed in all three cases. The obtained results were maintained at a stable level for all 3 patients over a period of 4 years. The results of the present case report study indicate that OFD followed by decontamination of the implant surface with EDTA and subsequent application of EMD may result in positive clinical and radiographic results that can be maintained over a period of 4 years.

Key words: peri-implantitis, surgical therapy, enamel matrix protein derivative, case reports

Peri-implantitis is a condition characterized by inflammation of the soft tissues surrounding the osteointegrated implant, bleeding on probing, suppuration and rapid loss of bone (Hämmerle and Lang, 1994; Roos-Jansaker at al, 2003). The lesion is associated with the presence of a subgingival microflora which closely resembles that found in advanced periodontal lesions and contains predominantly Gram-negative anaerobic rods, fusiform bacteria, motile and curved rods and spirochetes (Roos-Jansaker at al, 2003; Mombelli et al, 1987; Leonhardt et al, 1999, 2003). The contaminated implant is frequently surrounded by a crater-like intrabony defect (Roos-Jansaker et al, 2003; Leonhardt et al, 2003; Lindhe et al, 1992; Lang et al, 1993; Schou et al, 1993). During the last decade several treatment protocols have been introduced with varying degree of success for treating peri-implant defects. Different therapeutic modalities such as open flap debridement (OFD), the use of systemically or locally administered antimicrobial agents, decontamination of the exposed implant surface, guided tissue regeneration (GTR), with or without the use of bone grafts, have been shown to result in resolution of the inflammatory lesion and even some bone fill of the intrabony defects (Roos-Jansaker et al, 2003; Leonhardt et al, 2003; Lozada et al, 1990; Goldman et al, 1992; Lehmann et al, 1992, Jovanovic, 1993; Jovanovic et al, 1993; Singh et al, 1993; Hürzeler et al, 1995; Hämmerle et al, 1995; Ericsson et al, 1996; Persson et al, 1996, 1999, 2001a, 2001b; Wetzel et al, 1999; Hall et al, 1999; Deporter et al, 2001; Khoury and Buchmann, 2001; Schou et al, 2003a, 2003b, 2003c). Histologic studies from animals have, however, indicated that while most of the protocols may result in the resolution of the progressive inflammatory lesion, a re-osseointegration does not predictably occur (Jovanovic et al, 1993; Singh et al, 1993; Hürzeler et al, 1995; Ericsson et al, 1996; Persson et al, 1996, 1999, 2001a, 2001b; Wetzel et al, 1999; Hall et al, 1999; Schou et al, 2003a, 2003b, 2003c).

In humans there are only very limited data evaluating different treatment options aiming to recon-

Table 1 Clinical results (in mm) following treatment of peri-implantitis defects with an enamel matrix protein derivative (EMD)

Case	Implant type	PD			CAL			Radiographic bone gain	
		Baseline	1 year	4 years	Baseline	1 year	4 years	1 year	4 years
1	ITI (Straumann, Switzerland)	9	2	3	11	4	4	3	3
	Uniplant SP (Sanitaria, Budapest, Hungary)	7	3	3	8	4	5	2.5	2.5
3	Flexiroot (Budapest, Hungary)		8	3	4	9	4	5	3

struct intrabony peri-implant defects (Roos-Jansaker et al, 2003; Leonhardt et al, 2003; Lozada et al, 1990; Goldman et al, 1992; Lehmann et al, 1992; Hämmerle et al, 1995; Deporter et al, 2001; Khoury and Buchmann, 2001). Recent results from animal and human research on periodontal regeneration have shown that the application of an enamel matrix derivative (EMD) onto a previously debrided and conditioned root surface may predictably promote the formation of root cementum and alveolar bone (Hammarström et al, 1997; Heijl et al, 1997; Sculean et al, 1999, 2000a, 2000b, 2000c; Mellonig, 1999; Yukna et al, 2000). Findings from in vitro studies have indicated that EMD may stimulate the differentiation and proliferation not only of periodontal ligament cells (PDL) but also of pre-osteoblasts and osteoblasts (Gestrelius et al,1997a, 1997b; Van der Pauw et al, 2000; Hoang et al, 2000; Lyngstadaas et al, 2001; Haase et al, 2001; Nebgen et al, 1999; Schwartz et al, 2000; Boyan et al, 2000; Sawae et al, 2002; Yoneda et al, 2003; Keila et al, 2004).

A very recent study evaluating the effect of EMD on bone regeneration in rat femurs after drill-hole injury has suggested that EMD may possess an osteo-promoting effect on bone and medullary regeneration (Kawana et al, 2001). Furthermore, it has been demonstrated that EMD acts as a cytostatic agent on cultured epithelial cells and may even inhibit dental plaque vitality and bacterial growth (Kawase et al, 2000; Spahr et al, 2001; Sculean et al, 2001; Arweiler et al, 2002; Newman et al, 2003). Thus, taken together the available data seem to indicate that EMD has a stimulatory effect on a large variety of dental and non-dental tissues including bone and may also influence wound healing by inhibiting or at least retarding epithelial downgrowth. Recent data from an experimental study in rabbits have, however, failed to demonstrate that EMD may contribute to bone formation around titanium implants (Franke Stenport and Johansson, 2003). On the other hand, results from an experimental study in dogs evaluating the effect of EMD and Guided Bone Regeneration (GBR) in dehiscence-type defects around implants have indicated that EMD may positively influence bone healing after GBR around titanium implants (Casati et al, 2002). However, to the best of our knowledge, there are currently no published data reporting on the effect of EMD following its clinical application in intrabony defects associated with peri-implantitis.

The aim of the present case report study was therefore, to evaluate the effect of OFD followed by decontamination of the implant surface with EDTA and application of EMD in the treatment of peri-implantitis intrabony defects.

STUDY DESIGN AND RESULTS

Three patients restored with osseointegrated screw implants were included in this case report (1 woman and 2 men, aged respectively 60, 55 and 50 years at baseline). All three patients were systemically healthy and were non-smokers. The two (male) patients were partially edentulous, whereas the third (female) patient was edentulous in both the maxillary and mandibular arch. Implant type is shown in Table 1. Prior to implant placement two patients (the 2 men) had been treated for

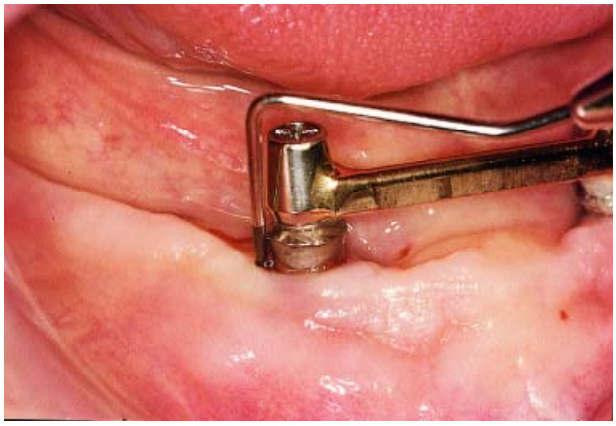

Fig. 1 The preoperative measurements indicated a PD of 9 mm (case 1 from Table 1).

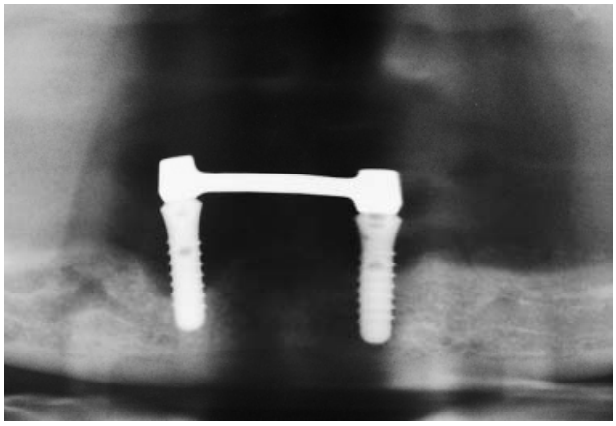

Fig. 2 Preoperative X-ray of a peri-implantitis defect at regio 43 (case 1 from Table 1).

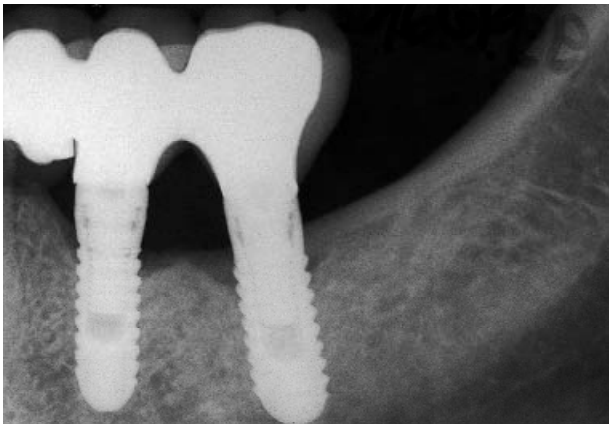

Fig. 3 Preoperative X-ray of case 2 from Table 1.

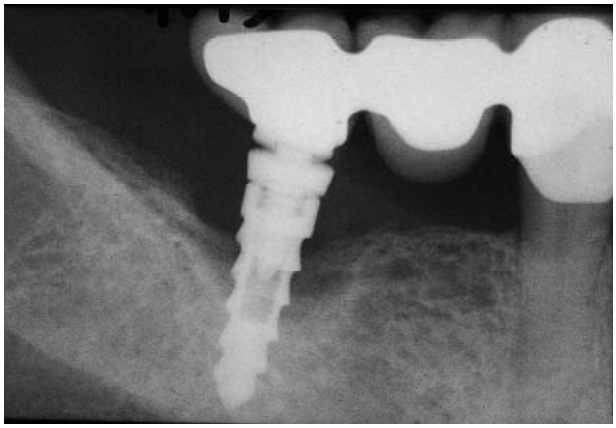

Fig. 4 Preoperative X-ray of case 3 from Table 1.

advanced periodontitis. In all three cases the implants were inserted at least 3 years before the clinical diagnosis of peri-implantitis. Peri-implantitis was defined as: radiographic bone loss amounting 3 threads as compared to the intraoral radiograph 1 year after restoration; an intrabony defect of at least 3 mm as measured on the preoperative radiographs; and bleeding on probing and suppuration from the peri-implant sulci (Figs. 1, 2, 3 and 4). None of the implants showed any signs of mobility as evaluated manually. The clinical measurements revealed probing pocket depths (PD, the distance between the peri-implant mucosal margin and the bottom of the probeable peri-implant pocket) around the implants ranging from (7 to 9 mm) (Fig. 1, Table 1). The level of probeable clinical attachment level (i.e. the distance from the implant shoulder to the bottom of the probeable pocket) was between 8 and 11 mm (Fig. 1, Table 1). All clinical measurements were performed by one investigator (not the surgeon) using the same type of periodontal probe (PCP 12, Hu-Friedy, USA).

Therapy and Postoperative Care

For the surgical procedures the suprastructures were not removed in any of the 3 cases. Following placement of intrasulcular incisions around the neck of the implant abutments full-thickness flaps were reflected on the vestibulars and

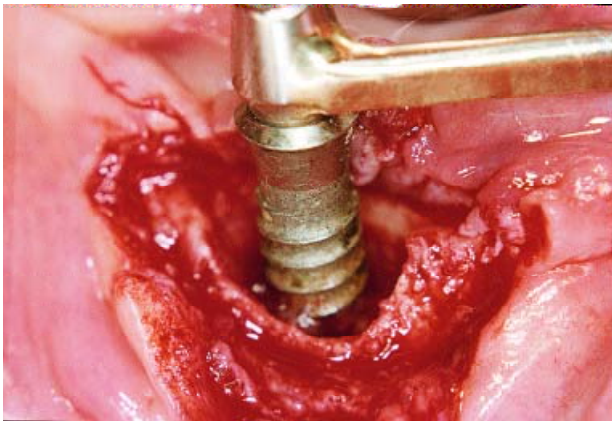

Fig. 5 Following removal of granulation tissue the extent of the intrabony defect is evident (case 1 from Table 1).

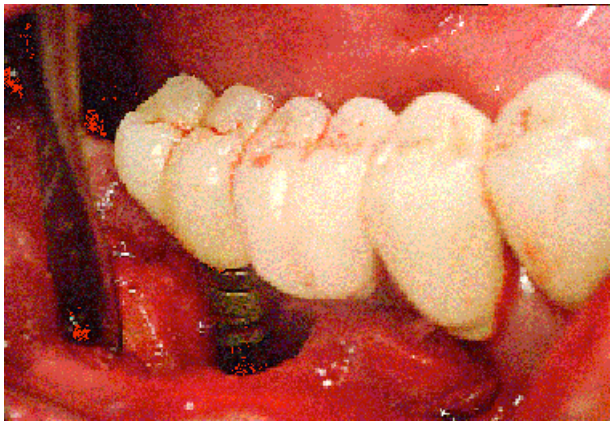

Fig. 6 A deep intrabony defect is visible following removal of granulation tissue (case 3 from Table 1).

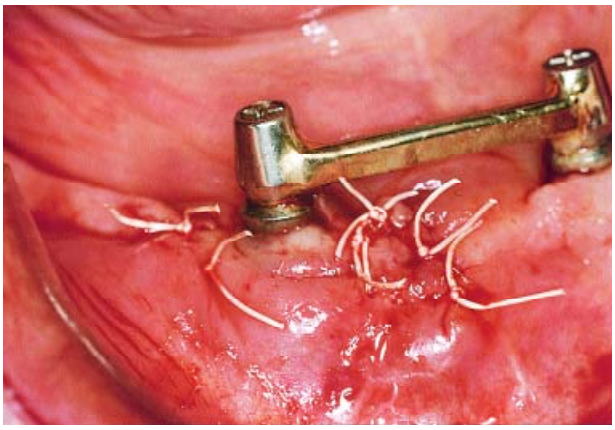

Fig. 7 Flap closure was achieved by means of vertical mattress sutures (case 1 from Table 1).

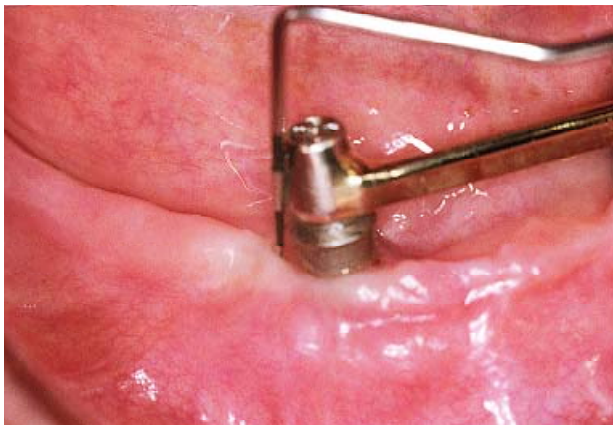

Fig. 8 At 4 years a PD of 3 mm and a CAL of 4 were recorded (case 1 from Table 1).

oral side to expose the peri-implant defects. The granulation tissue was removed by means of hand instruments (Gracey curettes, Hu-Friedy, USA) (Figs. 5 and 6). None of the implant surfaces was mechanically instrumented. A 24% EDTA gel (Biora, Malmö, Sweden) was applied for 2 min. to decontaminate the surfaces (Blomlöf and Lindskog, 1995; Blomlöf et al, 1997). The defects and the adjacent mucoperiosteal flaps were then thoroughly rinsed with sterile saline in order to remove all EDTA residues. Following the decontamination procedure the defects were filled up with EMD (Emdogain, Biora, Malmö, Sweden) that was always freshly mixed before each surgical procedure. Finally, the flaps were repositioned coronally to completely cover the defects and carefully adapted around the neck of the implants by means of vertical mattress sutures (Fig. 7). The postoperative care consisted of an antibiotic regimen (3 x daily 250 mg of metronidazole and 3 x daily 375 mg of amoxicillin) (Van Winkelhoff et al, 1989) for 10 days and 0.2% chlorhexidine digluconate rinses twice daily for 4 weeks. The sutures were removed at 14 days after surgery. Recall appointments associated with full mouth professional supragingival tooth/implant cleaning were performed monthly for the first year following surgery. Twelve months after surgery the patients were enrolled in a maintenance programme consisting of recall appointments on a 3-months basis.

Healing was uneventful in all three cases. The patients tolerated the surgical procedure well. No adverse reaction associated with the postoperative medication occurred. One year after surgery, the clinical measurements indicated a PD reduction and a CAL gain in all 3 cases (Fig. 8). The radiographic evaluation indicated a bone fill in all 3 defects (Figs. 9, 10 and 11). No differences were found between the 1 and 4-year evaluation period.

DISCUSSION

The results of the present case report have shown that treatment of deep peri-implant intrabony defects by means of OFD, implant surface decontamination with EDTA and application of EMD may result in significant clinical improvements as evidenced by PD reduction, CAL gain, and radiographic bone fill. Furthermore, the obtained results were maintained at a stable level over a period of 4 years in all three cases. When interpreting the present findings it has to be taken into consideration that the present cases are, to the best of our knowledge, the first published data on the treatment of peri-implantitis defects following EDTA decontamination and application of EMD and thus, a comparison with other reports evaluating the same treatment protocol is not possible. However, it should be noted that until now, most clinical data on the various treatment protocols for the treatment of peri-implantitis defects originate from case reports or case series (Lozada et al, 1990, Zablotsky, 1992; Goldman et al, 1992; Lehmann et al, 1992; Hämmerle et al, 1995; Deporter et al, 2001, Khoury et al, 2001; Roos-Jansaker et al, 2003; Leonhardt et al, 2003).

Successful bone fill in both early and late peri-implant defects has been reported following treatment with guided tissue regeneration (GTR) alone, autogenous bone grafts and other bone grafts and substitutes alone, or in combination with GTR (Goldman et al, 1992; Lehmann et al, 1992; Hämmerle et al, 1995; Deporter et al, 2001; Khoury and Buchmann, 2001; Roos-Jansaker et al, 2003; Leonhardt et al, 2003). The results of a very recent literature review have indicated that clinically, treatment of peri-implantitis defects with

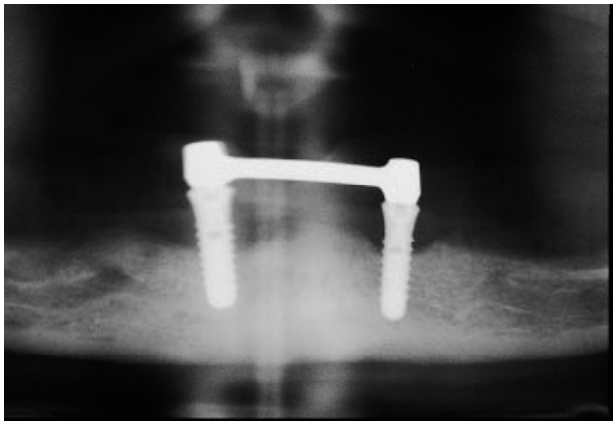

Fig. 9 The X-ray at 4 years following surgical treatment with EMD demonstrates a fill of the intrabony defect component (case 1 from Table 1).

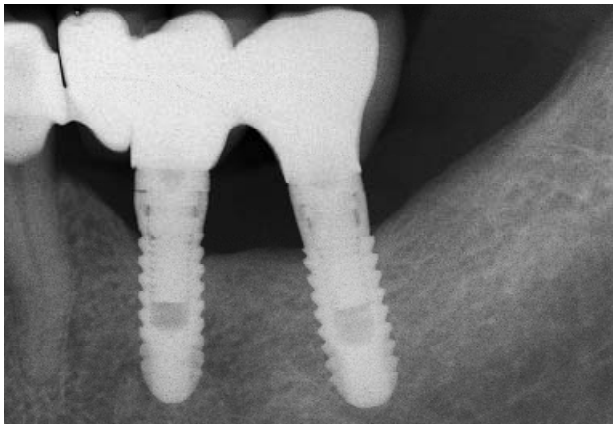

Fig. 10 At 4 years after surgery with EMD the radiographs indicates a defect fill (case 2 from Table 1).

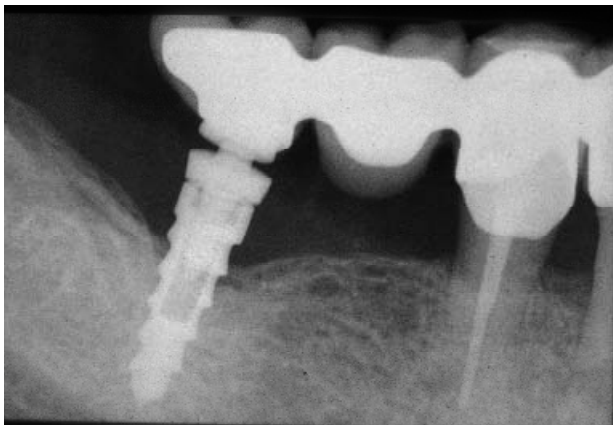

Fig. 11 At 4 years following treatment with EMD some defect fill can be observed on the intraoral radiograph (case 3 from Table 1).

GTR may lead to bone fill and improved soft tissue conditions (Roos-Jansaker et al, 2003). The analyzed data have also indicated that the longer the membranes were covered the more bone fill was obtained (Roos-Jansaker et al, 2003). On the other hand, membrane exposure with subsequent inflammation and infection was a frequent complication associated with the application of barrier membranes (Khoury et al, 2001; Roos-Jansaker et al, 2003). Data analysis has also suggested that the longer an exposed membrane was left in place, the smaller the obtained bone fill (Roos-Jansaker et al, 2003). The available data do not indicate a superiority of the combinated approach when comparing the results obtained following treatment with bone grafts or bone substitutes alone, or GTR alone (Roos-Jansaker et al, 2003).
Another important aspect which may have a significant influence upon the healing process is the decontamination of the implant surfaces (Roos-Jansaker et al, 2003). However, the recommended detoxification agent varies greatly within the studies (e.g. abrasive sodium carbonate air-powder, citric acid, chlorhexidine, sterile saline, delmopinol or hydroxyperoxide) (Goldman et al, 1992; Jovanovic, 1993; Jovanovic et al 1993; Singh et al, 1993, Hämmerle et al, 1995; Hürzeler et al, 1995; Ericsson et al, 1996; Persson et al, 1996, 1999, 2001a, 2001b; Wetzel et al, 1999; Deporter et al, 2001; Khoury et al, 2001; Roos-Jansaker et al, 2003; Leonhardt et al, 2003; Schou et al, 2003a, 2003b, 2003c). In the present report the implant surfaces were treated in all three cases with ETDA. The rationale behind the use of EDTA was based on earlier reports that have indicated that EDTA may predictably remove the smear layer from bacterial contaminated root surfaces and has no necrotizing effects upon the surrounding soft and hard tissues which was frequently the case when using more aggressive agents such as citric or phosphoric acid (Blomlöf and Lindskog, 1995; Blomlöf et al, 1997). However, based on the findings from the present case reports no conclusions can be drawn regarding the suitability of EDTA as a decontaminating agent for peri-implantitis affected implant surfaces. Further studies are needed in order to elucidate this issue.
The positive clinical and radiographic results obtained in all three treated cases might be explained by the results of previous in vitro and histological studies which have indicated that EMD may influence the proliferation of osteoblasts and enhance healing in bone defects (Nebgen et al, 1999; Schwartz et al, 2000; Boyan et al, 2000; Kawana et al, 2001; Sawae et al, 2002; Yoneda et al, 2003). In this context it is worth noting the results of an in vitro study evaluating the response of osteoblasts at 3 stages of osteogenic maturation to EMD, which has suggested that EMD may affect early states of osteoblastic maturation by stimulating proliferation, and as cells mature in the lineage, by enhancing differentiation (Schwartz et al, 2000). A very recent study investigating the in vitro effects of EMD on rat bone marrow stromal cells (BMSC) has demonstrated that EMD increased the osteogenic capacity of bone marrow, as evidenced by approximately a three-fold increase in BMSC cell number and approximately two-fold increase in alkaline phosphatase (ALP) activity and mineralized nodule formation (Keila et al, 2004). Furthermore, results from an experimental study in rats evaluating the effects of EMD on bone regeneration in rat femurs after drill-hole injury, suggested that EMD possesses an osteo-promotive effect on bone and medullary regeneration during wound healing of injured long bones (Kawana et al, 2001). It should, however, be kept in mind that the reports regarding the potential role of EMD for enhancing healing of bone defects are controversial. While some reports have shown a clear osteo-promotive effect of EMD (Nebgen et al, 1999; Boyan et al, 2000; Schwartz et al, 2000; Kawana et al, 2001; Sawae et al, 2002; Yoneda et al, 2003), others have failed to show any additional bone formation around titanium implants following application of EMD (Franke Stenport et al, 2003).
Moreover, the findings of a very recent study in rats evaluating the effect of guided bone regeneration (GBR) in combination with or without deproteinized bovine bone mineral (DBBM) and/or EMD on the healing of critical-size calvarial defects have failed to demonstrate any significant benefit to enhance the potential for complete healing provided by the GBR procedure (Donos et al, 2004). On the other hand, it is also important to mention the results of recent studies, which have shown that EMD possesses a strong antibacterial activity which in turn, may also influence the healing process (Spahr et al, 2001; Sculean et al, 2001; Arweiler et al, 2002; Newman et al,

2003). Therefore, it could be speculated that the positive clinical results might also be attributed to the antibacterial effect of EMD. Finally, it is important to emphasize that although the presented results are positive, they represent observations made in three single cases and consequently they need to be interpreted with caution. It would thus be of clinical significance to know how a simple OFD procedure without EMD, would perform in such cases. Regarding this issue it should, however, be emphasized that hitherto there are only very sparse data (limited to single case reports) evaluating treatment of peri-implantitis with OFD alone (Zablotsky, 1992; Roos-Jansaker et al, 2003). Thus, further controlled histological and clinical studies are warranted to explore the potential of the presented treatment protocol in the therapy of peri-implantitis.

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