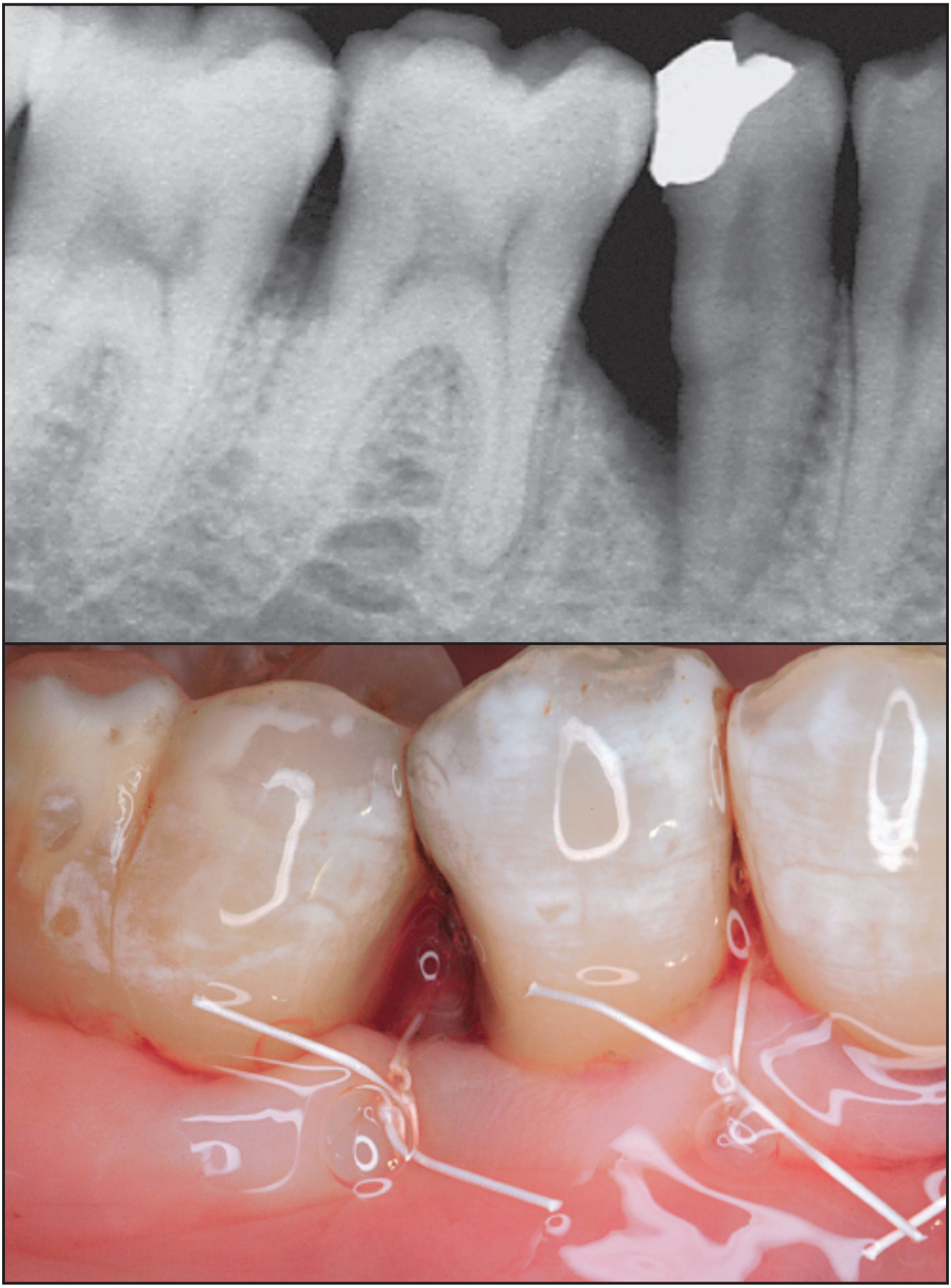
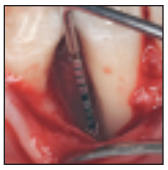


Minimally Invasive Surgical Technique and Enamel Matrix Derivative in Intrabony Defects: 2. Factors Associated with Healing Outcomes



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This case cohort study was designed to evaluate the healing response of a minimally invasive surgical technique (MIST) in combination with enamel matrix derivative (EMD) in isolated deep intrabony defects. Forty deep intrabony defects were surgically accessed with the MIST. This technique was designed to limit the flap extent and reflection to reduce surgical trauma and increase flap stability. EMD was applied on the dried root surfaces. Surgery was performed with the aid of an operating microscope and microsurgical instruments. The 1-year clinical attachment level gain was 4.9 ± 1.7 mm. Seventy percent of defects gained ≥ 4 mm. Clinical attachment level gain was significantly associated with the depth of the three-wall component of the defect, with the intraoperative bleeding tendency of the defect, and with its interaction with the baseline amount of bone loss. Defect morphology and bleeding tendency seem to influence clinical outcomes from the use of MIST in combination with EMD. (Int J Periodontics Restorative Dent 2009;29:257–265.)

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In the last 20 years, membranes, demineralized freeze-dried bone allograft, enamel matrix derivative (EMD), and combinations of membranes and fillers[1–6] have been successfully used in periodontal regenerative treatment of deep intrabony defects. A significant amount of variability in clinical results, however, has been consistently observed and explained in terms of differences in patient populations, defect morphology, surgical strategies, and operative protocols.

Patient-associated factors, such as the level of self-performed oral hygiene, residual periodontal infections, and smoking habits, have been found to consistently influence the clinical outcomes of various regenerative strategies and materials.[4,7–12] Among defect-associated factors, the indicators of defect severity, including pocket depth, attachment loss, bone loss, and depth of the intrabony component of the defect, have been found to be consistently associated with the amounts of clinical attachment gained with all tested regenerative procedures.[4,7,9,10,13–15] Some morphologic characteristics of the defects, however, appear to be more approach-specific.

The defect angle (as assessed radiographically) has been found to affect clinical attachment level (CAL) gains when nonresorbable and resorbable barrier membranes[7,13,16] and EMD[11,17] are used, whereas defect angle did not show a significant impact on CAL gains when the defects were treated with titanium-reinforced expanded polytetrafluoroethylene membranes[9] or with resorbable membranes in combination with deproteinized bovine bone mineral.[18] Similarly, the number of residual bony walls did not seem to affect regeneration with barrier membranes alone[7,9,15] or in conjunction with deproteinized bovine bone mineral[4] but was significantly associated with outcomes following application of EMD in gel form.[11] Defect characteristics assessed during surgery, such as intraoperative bleeding tendency from the defect walls, have been found to negatively affect the final outcome of EMD-treated intrabony defects.[11]

Observations from the cited studies have been used to develop clinical decision trees based on the morphology of the defect for the selection of the regenerative strategy, indicating the use of self-supporting (ie, titanium-reinforced) or supported membranes (ie, in combination with a filler material) in non–space-maintaining defects, such as one-wall and/or wider defects, and the application of EMD or resorbable barrier membranes in the inherently more supportive two- to three-wall and/or narrower defects.[19–22]

Surgical factors seem to greatly impact clinical outcomes as well. The different regenerative approaches are associated with clinical complications, the most frequent being flap dehiscence and exposure of the regenerative material, which is frequently observed with the use of barrier membranes and combined therapies.[4,10,13,15,23–26] The cited postsurgical complications were found to negatively influence the gain of clinical attachment. Reduced postoperative complications have been observed following the application of EMD.[11,27] In a controlled clinical trial, the absence of surgical complications was associated with improved outcomes.[27]

The design of the surgical access and suturing technique in regenerative therapy has dramatically evolved in the last 20 years, from the use of conventional access flaps[13,23] sutured with external mattress sutures to the application of papilla preservation techniques associated with double-layer or single-layer internal mattress sutures to obtain a stable seal of the wound in the absence of tension.[28–30] The use of operating microscopes and microsurgical instruments has also been proposed to enhance the ability of the surgeon to properly handle the soft and hard tissues as well as the devices and materials involved in the regenerative treatment.[20,21]

Recently, several authors have proposed the use of minimally invasive approaches in isolated[31–34] or multiple defects.[35,36] Among these, a minimally invasive surgical technique (MIST) was proposed and tested in a preliminary case series.[34] Its main clinical objectives included a reduction of surgical trauma, an increase of flap/wound stability, stable primary closure of the wound, a reduction in surgical time, and minimal intraoperative and postoperative patient discomfort and morbidity. MIST was then tested in a case cohort; the clinical and patient outcomes of this case cohort study are reported elsewhere.[37]

The specific aim of the present study was to identify defect factors associated with the 1-year changes in terms of CAL following application of the MIST in combination with EMD for the treatment of isolated deep intrabony defects.

Method and materials

Study population and experimental procedures

The details of the patient population are described elsewhere.[37] All subjects had: (*1*) advanced periodontal disease but were in good general health; (*2*) at least one tooth with probing pocket depth and CAL loss of at least 5 mm associated with an intrabony defect of at least 2 mm; (*3*) full-mouth plaque scores (FMPS) ≤ 25%; (*4*) full-mouth bleeding scores (FMBS) ≤ 25%; (*5*) demonstrated a good level of compliance; and (*6*) teeth that were vital or had been properly treated with root canal therapy. Heavy smokers (> 10 cigarettes/day) were excluded. All subjects had received a cycle of cause-related therapy consisting of scaling and root planing, motivation, and oral hygiene instructions. Flap surgery for pocket elimination was performed, when indicated, in the remaining portions of the dentition of each patient before the regenerative treatment. All subjects gave informed written consent. Forty intrabony

defects in 40 subjects that met the admission criteria were consecutively included in this cohort.

Three months after completion of periodontal therapy, baseline clinical measurements were recorded, including FMPS, FMBS, probing depth (PD), and recession of the gingival margin (REC). The experimental sites were accessed with the MIST and carefully debrided. The procedure is described in detail elsewhere.[37] Measurements were made during surgery to characterize the defect anatomy, including the distance from the cementoenamel junction to the bottom of the defect (CEJ-BD), the total depth of the intrabony component of the defect (INFRA[38]), and the bleeding tendency of the defect. When the defect showed bleeding tendency, bleeding was controlled by compacting wet, sterile gauze into the defect for 3 to 4 minutes. The root surface was cleansed with an ethylenediaminetetraacetic acid gel and EMD (Emdogain, Institut Straumann) was applied on the instrumented and dried root surfaces. Flaps were repositioned and sutured with modified internal mattress sutures. Patients were enrolled in a stringent postoperative supportive care program with weekly recalls for 6 weeks and then included in a 3-month periodontal supportive care program for 1 year. Outcome measures were obtained at 1 year.

Periapical radiographs of the experimental sites were taken at baseline and at the 1-year follow-up.

Data analysis

Data were expressed as means ± standard deviations of 40 defects in 40 patients. No data points were missing. Comparisons between baseline and 1-year CAL, PD, and REC values were made using the paired Student *t* test ($\alpha = .05$). Averages and 95% confidence intervals (CIs) were calculated for the differences between baseline and 1-year CAL, PD, and REC values. Percentage fill of the baseline intrabony component of the defect was calculated as ([CAL gain]/INFRA) × 100.

A multivariate linear regression analysis was carried out to predict changes in CAL (as a continuous variable) 1 year after the use of the MIST and application of EMD according to an a priori hypothesis; the selected variables were jointly entered in the model. The model included only variables related to defect morphology. As postulated in the a priori hypothesis, variables indicative of defect severity (CEJ-BD), the depth of the three-wall subcomponent, the radiographic defect angle as a descriptor of the defect morphology, and the bleeding tendency of the defect were entered into the model, along with the interaction between bleeding tendency of the defect and CEJ-BD. The variable CEJ-BD was selected as an indicator of disease severity[36]; because it is highly correlated with CAL and INFRA, it can be used alone as a variable in a relatively small sample. The bleeding tendency of the defect was included following the observation that it was significantly greater in sites with greater baseline periodontal destruction (greater CEJ-BD or greater CAL). Patient-related variables were not considered, since those that could influence the outcomes had been controlled during cause-related therapy and heavy smokers and patients with poor oral hygiene or high levels of residual infection had been excluded.

Results

Clinical outcomes

Details of the study population and clinical results were published previously.[37] In brief, 40 intrabony defects in 40 subjects (mean age 48.3 ± 9.8 years; range, 31 to 74 years; 14 men and 26 women; five smokers) were treated with the MIST + EMD. Average FMPS and FMBS were 13.1% ± 5.1% and 8.8% ± 3.3%, respectively. Defects presented with mean PD of 8.2 ± 1.9 mm, mean CAL of 10.0 ± 2.9 mm, and mean REC of 1.8 ± 1.6 mm. The mean intrabony component of the defects was 6.5 ± 2.3 mm. At 1 year, a CAL gain of 4.9 ± 1.7 mm (range, 3 to 9 mm; 95% CI, 4.3 to 5.4 mm) was associated with a residual PD of 3.0 ± 0.6 mm and a very limited increase of 0.4 ± 0.7 mm in REC (95% CI, 0.1 to 0.6 mm). Changes between baseline and 1 year in CAL and PD were clinically and statistically highly significant (mean PD change: 5.2 ± 1.7 mm, 95% CI, 4.7 to 5.8 mm; $P < .0001$). Changes in REC also reached statistical significance ($P = .017$).

The data were stratified into four classes of CAL gain (Table 1). No sites lost attachment and no sites gained less than 3 mm of attachment, whereas 70% of sites gained 4 mm or more. The

Table 1 Baseline defect characteristics stratified by CAL gain as observed at 1 year after regenerative surgery

Baseline characteristics	CAL gain at 1 year			
	< 3 mm	3 mm	4–5 mm	≥ 6 mm
N (%)	0	12 (30.0%)	13 (32.5%)	15 (37.5%)
PD	–	6.3 ± 0.9	7.8 ± 1.0	10.1 ± 1.2
CAL	–	7.8 ± 2.1	8.9 ± 1.7	12.6 ± 2.3
CEJ-BD	–	9.0 ± 2.5	10.1 ± 2.0	13.1 ± 2.6
INFRA	–	5.0 ± 1.5	5.8 ± 1.5	8.3 ± 2.3
Three-wall	–	1.9 ± 1.6	3.3 ± 1.6	4.8 ± 1.9
Two-wall	–	1.4 ± 1.4	1.8 ± 1.1	2.5 ± 1.8
One-wall	–	1.7 ± 1.4	0.7 ± 0.8	1.0 ± 1.2
Defect angle (deg)	–	31.9 ± 7.9	31.5 ± 7.1	27.1 ± 7.1
Intraoperative defect - bleeding (prevalence)		17%	31%	67%

PD = probing depth; CAL = clinical attachment level; CEJ-BD = distance from cementoenamel junction to the bottom of the defect; INFRA = intrabony component of the defect.

baseline characteristics of the defects clustered according to the different classes of CAL gain show that larger amounts of CAL gains were obtained in more severe defects, described in terms of PD, CAL, and bone loss, and intrabony component depth.

The 1-year mean resolution of the defects was 77.6% ± 21.9% (range, 33.3% to 133.3%), and 12 sites (30%) reached 100% of the baseline intrabony component. Defect resolution ranging from 50% to 99% was observed in 26 sites (65%), while only two sites failed to reach 50% fill of the baseline intrabony component.

Figure 1 depicts a patient treated with the MIST + EMD method.

Multivariate analysis

The multivariate analysis carried out to predict changes in CAL at 1 year after the application of MIST and EMD generated a highly statistically significant model ($P < .0001$) that explained 71% of the observed variability in CAL gains (Table 2). CAL gain was significantly associated with: (*1*) the bleeding tendency of the debrided defect during surgery, ie, bleeding defects resulted in greater amounts of CAL gain; (*2*) the interaction between the bleeding tendency of the defect and CEJ-BD, ie, deeper defects that bled showed the greatest amounts of CAL gain; and (*3*) the baseline depth of the three-wall intrabony subcomponent, ie, deeper three-wall components were associated with greater CAL gains. The baseline radiographic defect angle did not reach statistical significance.

A subgroup analysis of 16 defects without a one-wall superficial component of the defect showed an overall tendency toward improved outcomes with respect to the total population in terms of CAL gain (5.1 ± 1.5 mm) and percent fill of the intrabony component of the defect (84.2% ± 27.1%).

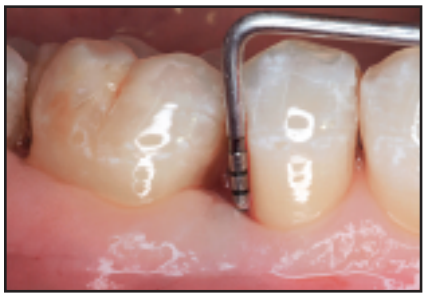
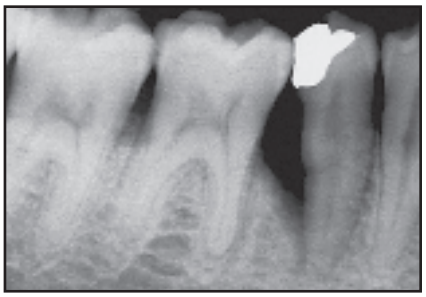


Fig 1a (left) *Preoperative clinical view of the mandibular right second premolar. The tooth presents with a distal pocket that is 12 mm deep.*

Fig 1b (right) *Baseline radiograph shows a deep and narrow intrabony defect reaching the apical third of the root.*



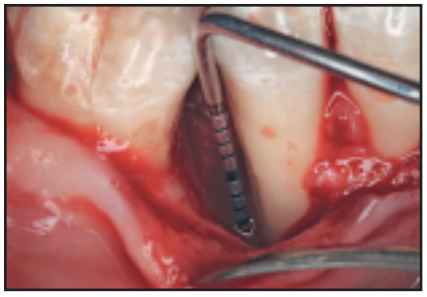
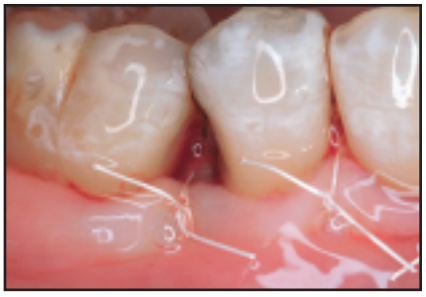


Fig 1c (left) *Intraoperative view. The two- to three-wall intrabony defect is 12 mm deep. The total bone loss on the distal side amounts to 18 mm. An MIST approach was used to expose the residual bone contour and minimize flap reflection.*

Fig 1d (right) *An internal modified mattress suture was applied to close the defect-associated interdental papillae.*



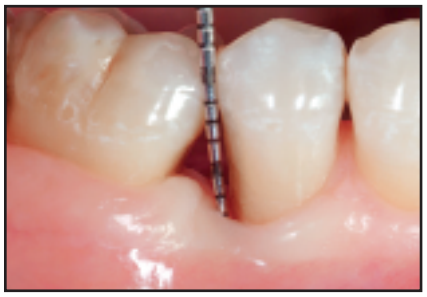


Fig 1e (left) *A 3-mm probing depth was measured at 1 year.*

Fig 1f (right) *The 1-year radiograph shows the resolution of the intrabony component of the defect.*

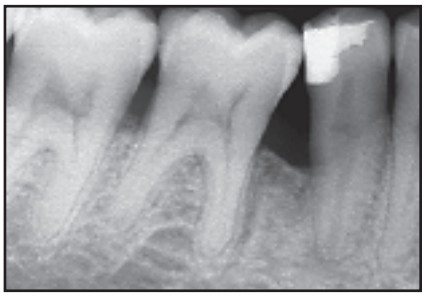


Table 2 Multivariate analysis

Variable	Estimate	SE	t ratio	Prob > |t|
Intercept	3.78	1.07	3.53	0.0012
CEJ-BD (mm)	0.06	0.08	0.75	0.4558
Bleeding tendency after debridement	–4.40	1.40	–3.15	0.0034
CEJ-BD × bleeding tendency	0.46	0.12	3.87	0.0005
Depth three-wall component (mm)	0.29	0.08	3.44	0.0015
Radiographic angle (deg)	–0.04	0.02	–1.67	0.1050

The tested outcome was change in CAL (as a continuous variable) between baseline and 1 year. The model was highly significant ($P < .001$; $R^2 = 0.71$).

Discussion

The treatment of 40 deep intrabony defects with the MIST in combination with EMD resulted in 1-year mean CAL gains of 4.9 ± 1.7 mm, associated with 3.0 ± 0.6 mm of residual PD and 0.4 ± 0.7 mm of increase in REC.[37] In this cohort, no sites lost attachment and no sites gained less than 3 mm of attachment. The majority of sites (70%) gained 4 mm or more of attachment at 1 year, and 37.5% of sites gained 6 mm or more. The reported outcomes were obtained in a patient population where the relevant patient-associated factors such as bacterial plaque, residual periodontal infection, and smoking habits were under optimal control.[4,7–12]

Analysis of the baseline defect characteristics according to stratified classes of CAL gain (Table 1) and the results of the multivariate analysis (Table 2) allows for some interesting considerations. The largest amounts of CAL gain were obtained in sites that had been severely compromised by periodontal destruction. This observation is consistent with the data reported in many different regenerative studies.[4,7,9,10,13–15] The present study confirms the evidence that regenerative therapy is a treatment modality that can change the prognosis of severely compromised teeth, resulting in sizable amounts of CAL gain and PD reduction.

Defect morphology, described in terms of residual bony walls, was also found to affect the final outcomes. Larger amounts of CAL gain were observed in sites with deeper three-wall and two-wall subcomponents. In particular, the multivariate analysis (Table 2) showed a statistically significant correlation between the 1-year gain of CAL and the depth of the three-wall subcomponent. This confirms the observations of a previous EMD study[11] and other studies reporting on the application of nonresorbable and resorbable barrier membranes.[7,13,16] The more favorable outcomes in the three-wall intrabony subcomponents are generally explained in terms of greater support provided by the residual bony walls to the barriers and/or the repositioned gingival flaps.[7] The larger number of residual bony walls could also positively affect the blood clot stability, which is perceived as relevant for early healing events.[39–42] Another relevant finding of the present study is the evidence of improved outcomes in deep defects with an intraoperative bleeding tendency. In a previous EMD trial,[11] reduced CAL gains were observed at bleeding defects. This different response could be explained by the different intraoperative protocol for EMD application. In the present study, special care was taken to apply EMD on dried root and bone surfaces. When a defect showed a tendency to bleed, bleeding was controlled with compaction of wet, sterile gauze into the defect for a few minutes. After the gauze was removed, the area was carefully rinsed with saline and gently dried with air spray, and EMD was applied immediately. It may be that EMD is rapidly washed away in bleeding defects and thus fails to reach the root surfaces and the defect walls, thereby reducing the expression of its regenerative potential in bleeding defects. In contrast, when a dried root surface is

present for EMD application, the potential for regeneration of bleeding defects seems to be greater than that seen at nonbleeding sites. These observations suggest the need to adopt a protocol for EMD delivery on dried root and bone surfaces.

An interesting and novel observation was the interaction between the bleeding tendency of the defect and the severity of the bone destruction (CEJ-BD), which was highly significant. In this population, greater CAL gains were associated with increasing CEJ-BD depth in defects classified as bleeding. This was not seen in the nonbleeding defects. In other words, the bleeding tendency of the defects accounted for improved outcomes, and the improved outcomes, as expected, were correlated with the severity of the defects: the deeper defects gained more attachment. In fact, the observation of the lack of correlation between the severity of the defects and CAL gain in nonbleeding sites was unexpected. This might give rise to a series of hypotheses on the potential for regeneration expressed in bleeding or nonbleeding sites. Are bleeding defects better "providers" for regeneration? Do they support faster angiogenesis? Could this finding support a clinical effort to make nonbleeding sites bleed with additional bone instrumentation? The data from this paper do not allow definitive answers, but they raise questions regarding a potentially relevant issue. Further research is needed to explore this area.

In conclusion, the application of the minimally invasive surgical technique in combination with enamel matrix derivative proved to be an efficacious surgical approach for the treatment of deep intrabony defects with a prevalent three-wall and two-wall morphology. The results were not significantly influenced by the radiographic defect angle and were more favorable in deep, bleeding defects, provided that bleeding was controlled during application of the enamel matrix derivative.

Acknowledgments

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