Regenerative Periodontal Treatment with the Single Flap Approach in Smokers and Nonsmokers

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The present study was performed to evaluate the impact of smoking status on 6-month clinical outcomes of a regenerative procedure based on enamel matrix derivative and deproteinized bovine bone mineral in the treatment of intraosseous defects accessed with buccal single flap approach. A total of 22 defects were selected in smoking (n = 11) and nonsmoking (n = 11) patients. Regenerative treatment resulted in similar clinical attachment level (CAL) gain in both smokers and nonsmokers. A trend toward lower 6-month CAL gain and probing depth reduction was observed in patients smoking 11 to 20 cigarettes per day compared to those smoking 1 to 10 cigarettes per day. Int J Periodontics Restorative Dent 2018;38:e59–e67. doi: 10.11607/prd.3615

In 2007, a simplified surgical technique named the single flap approach (SFA) was introduced for the regenerative treatment of periodontal intraosseous defects. The basic underlying principle of the SFA consists of the elevation of a limited mucoperiosteal flap to allow access to the defect from the buccal or oral aspect only, depending on the main buccal/oral extension of the lesion (as diagnosed preoperatively), preserving the integrity of the interproximal supracrestal gingival tissues. The SFA was shown to be at least as effective as traditional papilla preservation techniques, with successful outcomes being due in part to enhanced wound stability during the early wound healing phase. Several reconstructive/regenerative protocols have been successfully used in combination with the SFA. Among bioactive agents, enamel matrix derivative (EMD) favorably modulates the healing process of the periodontal wound, leading to significantly greater 1-year clinical attachment level (CAL) gain and probing depth (PD) reduction when compared to access flap alone in the treatment of intraosseous lesions. The combination of EMD with deproteinized bovine bone mineral (DBBM) in periodontal regenerative surgery is widely documented in the literature and was shown to ensure a substantial attachment gain.
while limiting the postsurgical recession at challenging defects accessed with SFA.\textsuperscript{7,8}

It is universally recognized that smoking affects the outcomes of periodontal treatment.\textsuperscript{13–15} This is explained by systemic and local effects. Systemically, smoking has been shown to decrease the number of lymphocytes, resulting in an impairment of chemotaxis and phagocytosis. Locally, smoking is associated with reduced proliferation and increased collagenase activity of gingival fibroblasts. Moreover, through several anatomical alterations of the gingival vascular apparatus,\textsuperscript{13,16} smoking is related to an impaired blood perfusion that facilitates the onset of wound dehiscence during the first stages of wound healing.\textsuperscript{17} From a clinical standpoint, smoking patients were shown to experience lower gain in CAL following various periodontal surgical procedures when compared to nonsmokers.\textsuperscript{18} While evidence exists that clinical outcome may be negatively affected by smoking following guided tissue regeneration (GTR) in intraosseous defects,\textsuperscript{19–22} contrasting information is currently available on the effects of smoking status on the outcomes of EMD-based regenerative periodontal surgery. While some studies reported a lower radiographic bone gain\textsuperscript{23} or lower CAL gain and PD reduction\textsuperscript{24} in smokers compared to nonsmokers, other studies did not find a significant effect of smoking on treatment outcomes when smoking status was entered in a multivariate analysis.\textsuperscript{25}

The present study was performed to evaluate the 6-month clinical outcomes of regenerative periodontal surgery with EMD and DBBM at intraosseous periodontal defects accessed with SFA in smoking and nonsmoking patients.

\section*{Materials and Methods}

\subsection*{Experimental and Ethical Design}

The present study is a retrospective analysis of a patient cohort. The study was approved by the Local Ethical Committee of Ferrara, Italy. All clinical procedures were performed in accordance with the Declaration of Helsinki and the Good Clinical Practice Guidelines. Each patient provided written informed consent to surgical treatment.

\subsection*{Study Population}

De-identified clinical data were retrospectively derived from periodontal patients seeking care at the Research Centre for the Study of Periodontal and Peri-Implant Diseases, University of Ferrara, Italy, and one private dental office in Ferrara, Italy.

Patients were included in the analysis if they met the following criteria: (1) diagnosis of moderate or severe periodontitis; (2) presence of at least one interproximal periodontal intraosseous defect with presurgical PD $\geq 5$ mm and radiographic depth (as assessed on a periapical radiograph) $\geq 3$ mm; (3) no extension of the periodontal intraosseous defect on the lingual/palatal side as assessed by preoperative bone sounding; (4) full-mouth plaque score and full-mouth bleeding score $< 20\%$ at the time of the surgical procedure; (5) surgical treatment with buccal SFA in combination of DBBM and EMD; and (7) compliance with the scheduled postsurgical recall sessions. Patients were excluded from the analysis if they met one or more of the following criteria: (1) using medication affecting periodontal status (eg, bisphosphonates, cyclosporine, phenytoin, nifedipine, and other calcium channel blockers or corticosteroids); (2) furcation involvement of the tooth presenting the intraosseous defect; or (3) the treated tooth was a third molar.

For each nonsmoking patient, a smoking patient (ie, a patient regularly smoking at least 1 cigarette per day despite motivation to quit) was selected by matching the severity (depth of infrabony component) and configuration (bony walls) of the intraosseous defect. Furthermore, smokers were categorized according to daily cigarette exposure (1 to 10 cigarettes per day and 11 to 20 cigarettes per day).

\subsection*{Clinical Procedures}

Presurgical and surgical procedures had been performed by expert periodontal surgeons (L.T., R.F., and L.M.) involved in previous clinical trials on SFA in combination with a regenerative strategy based on DBBM and EMD.\textsuperscript{7,8}

\subsection*{Presurgical Procedures}

Each patient had undergone a single or multiple sessions of scaling
and root planing with ultrasonic mechanical instrumentation (Piezosteril 5, Castellini) and/or area-specific curettes (Gracey curettes, Hu-Friedy), and had received personalized oral hygiene instructions. The surgical phase had been delayed until a minimal residual inflammation (bleeding on probing < 20%) and optimal soft tissue conditions were obtained at the defect site. Moreover, teeth in occlusal trauma and/or with grade II mobility had undergone occlusal adjustment and/or intra- or extra-cortical splinting.

**Surgical Procedures**

All surgeries were performed using ×2.5 or ×3.5 magnifying loupes. The site of surgery was first anesthetized using articaine-epinephrine 1:100,000 avoiding transpapillary infiltrations. Before surgery, transcervical probing (bone sounding) was performed to evaluate defect morphology and extension. The surgical access was performed by the elevation of a buccal mucoperiosteal flap according to the principles of buccal SFA (Figs 1 to 4). Briefly, a sulcular incision was made following the gingival margin of the teeth included in the surgical area. The mesiodistal extension of the flap was kept limited while ensuring access for defect debridement. An oblique or horizontal butt-joint incision was made at the level of the interdental papilla overlying the intraosseous defect. The greater the distance from the tip of the papilla to the underlying bone crest, the more apical (ie, close to the base of the papilla) the buccal incision in the interdental area. A buccal mucoperiosteal envelope flap was elevated using a microsurgical periosteal elevator (P-TROM periosteal elevator, Hu-Friedy), leaving the oral portion of the interdental subcrestal soft tissues undetached. Once defects were debrided using ultrasonic instruments, area-specific curettes (Gracey curettes, Hu-Friedy), and Hirschfeld file scalers (Hu-Friedy), they were treated using EMD (Emdogain gel, Straumann) gel in combination with DBBM (Bio-Oss spongiosa granules, 0.25 to 1.0 mm, Geistlich Pharma) (Figs 5 to 7). The exposed root surface had been treated with 24% EDTA gel for 2 minutes to remove the smear layer. After the surgical area was rinsed with saline, a sandwich technique was applied to treat the defect, as follows: first application of EMD, placement of DBBM mixed with EMD, and second application of EMD on the graft and coronal portion of exposed roots.7,8
Finally, the buccal flap was repositioned and sutured according to the original SFA technique, consisting of a horizontal internal mattress suture at the base of the papilla and a second internal mattress suture (vertical or horizontal) between the most coronal portion of the flap and the most coronal portion of the oral papilla (Fig 8). When necessary (eg, in case of a large, thick interdental papilla), an interrupted suture was performed to ensure primary intention healing at the incision line. Primary flap closure was always obtained at suturing.

**Postsurgical Procedures**

Sutures were removed at 2 weeks after surgery. Patients were prescribed a rescue analgesic (ibuprofen 600 mg) to be used as needed and were asked to abstain from mechanical oral hygiene procedures in the surgical area for 4 weeks. A 0.12% chlorhexidine mouthrinse (10 mL twice per day for 6 weeks) was used from the day of surgery (evening) to support local plaque control. Each patient was enrolled in a monthly recall program for 3 months and was recalled according to individual needs thereafter. Each session had included reinforcement of oral hygiene procedures and professional plaque removal. Subgingival scaling was performed at 6 months after surgery (Figs 9 and 10).
Study Parameters

Immediately before surgery and 6 months after surgery, the following measurements were collected at the site showing the greatest loss of clinical attachment by each periodontal surgeon using a manual standard probe (P-TROM periosteal elevator, Hu-Friedy) with 1-mm increments: PD, measured from the gingival margin to the bottom of the pocket; CAL, measured from the cementoenamel junction (CEJ) to the bottom of the pocket; and interdental recession (iREC), measured from the gingival margin to the CEJ or the apical margin of a restoration.

On digital photographs taken as perpendicular as possible to the long axis of the tooth presenting the intraosseous defect before surgery, using dedicated software (NIS-Elements version 4.2, Nikon Instruments), an examiner (A.S.) assessed the buccal recession (bREC), measured from the CEJ to the gingival margin (bREC was recorded as 0 when the gingival margin was located coronal to the CEJ). To account for photographic magnification, bREC was compared with the increments of a periodontal probe (UNC15, Hu-Friedy) depicted in the same photograph. Measurements were rounded to the nearest 0.1 mm. All measurements were repeated on photographs taken at the 6-month visit.

Immediately after completion of root and defect debridement, the following defect-related measurements were taken (in millimeters) using a periodontal probe (P-TROM periosteal elevator, Hu-Friedy): severity of bone loss (CEJ-BD), measured as the distance between the CEJ and the base of the defect; intrabony component (IBD), measured as the distance between the most coronal point of the alveolar crest and the base of the defect; suprabony component (CEJ-BC), measured as the distance between the CEJ and the most coronal extension of the interproximal bone crest; and buccal dehiscence (bCEJ-BC), measured as the distance between the CEJ and the most coronal extension of the buccal bone crest. The morphology of the intraosseous defect (ie, number of bony walls) was recorded as follows: (1) mainly 1-wall; (2) mainly 2-wall; or (3) mainly 3-wall.

At suture removal, performed 2 weeks after surgery, the early wound healing of the incision at the level of the interdental papilla overlying the intraosseous defect was evaluated according to the early healing index (EHI). EHI assessments were performed on digital photographs showing different views of the interdental papilla by a trained and calibrated examiner (A.S.) who was involved in previous clinical trials using the same type of evaluations.

Statistical Analyses

Data were entered in a unique database file (STATISTICA software version 7.1, StatSoft Italia). The patient was the statistical unit. The primary outcome variable was the 6-month change in CAL. Data were expressed as mean ± SD. Within-group comparisons (presurgery vs 6 months) were performed with Wilcoxon test. Intergroup comparisons were performed with Fisher exact test, chi-square test, and Mann-Whitney U test. The level of statistical significance was fixed at 0.05.

Results

Study Population

A total of 22 patients (14 men and 8 women; mean age: 50.2 ± 11.4 years, range: 29 to 68 years; 11 smokers, 11 nonsmokers), each contributing one periodontal intraosseous defect, were included for the analysis. Patient characteristics at the presurgical visit are summarized in Table 1. In smokers, daily cigarette consumption was 9.4 ± 5.6 (range: 2 to 20) cigarettes per day, and duration of the smoking habit was 21.9 ± 6.4 years (range: 8 to 30 years). In the smoker group, the number of patients smoking 1 to 10 or more than 10 cigarettes per day was 6 and 5, respectively.

Defect and site characteristics at the presurgical visit are summarized

### Table 1 Patient-Related Characteristics in Smokers and Nonsmokers

|                        | Nonsmokers (n = 11) | Smokers (n = 11) | P  
|------------------------|---------------------|-----------------|----
| Age (y) (mean ± SD)    | 56.8 ± 9.1          | 43.6 ± 9.8      | .007
| Sex (men/women)        | 6/5                 | 8/3             | .659
| Diabetes mellitus      | 0/11                | 0/11            | 1  
| (diabetics/nondiabetics)|                    |                 |    

in Tables 2 and 3. A similar distribution of defects according to dental arch and tooth type was observed between groups (Table 2). In smokers and nonsmokers, IBD was 5.2 ± 2.4 mm and 5.6 ± 2.4 mm, respectively, and no significant differences in presurgical probing parameters (Table 3) and defect morphology (Table 2) were observed between groups.

### Clinical Outcomes

At 2 weeks, smokers and nonsmokers showed a significantly different patient distribution according to EHI (Table 4) (P = .009). In particular, the number of sites showing optimal wound healing (EHI = 1) was 5 (45.5%) in nonsmokers and 0 for smokers. On the other hand, the number of sites with incomplete flap closure (EHI = 4) was 5 (45.5%) in smokers and 2 (18.2%) in nonsmokers.

### Changes in probing parameters and their 6-month values are reported in Table 3.

The procedure resulted in significant change in CAL, from 10.0 ± 1.9 mm to 5.5 ± 1.9 mm in smokers (P = .003) and from 10.1 ± 2.5 mm to 6.5 ± 2.0 mm in nonsmokers (P = .003). The 6-month CAL gain was not significantly different between groups.

Also, PD was significantly reduced from 8.4 ± 1.6 mm to 3.1 ±

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### Table 2 Defect and Site Characteristics in Smokers and Nonsmokers

<table>
<thead>
<tr>
<th></th>
<th>Nonsmokers (n = 11)</th>
<th>Smokers (n = 11)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dental arch (maxilla/mandible)</td>
<td>6/5</td>
<td>5/6</td>
<td>.671</td>
</tr>
<tr>
<td>Tooth type (incisor/canine/premolar/molar)</td>
<td>1/2/6/1</td>
<td>1/3/5/2</td>
<td>.843</td>
</tr>
<tr>
<td>IBD (mm) (mean ± SD; minimum–maximum)</td>
<td>5.6 ± 2.4 (2–10)</td>
<td>5.2 ± 2.4 (2–10)</td>
<td>.652</td>
</tr>
<tr>
<td>CEJ-BD (mm) (mean ± SD; minimum–maximum)</td>
<td>9.6 ± 3.6 (4–16)</td>
<td>9.7 ± 2.5 (6–14)</td>
<td>.949</td>
</tr>
<tr>
<td>CEJ-BC (mm) (mean ± SD; minimum–maximum)</td>
<td>4.0 ± 1.5 (2–6)</td>
<td>4.5 ± 1.5 (2–7)</td>
<td>.478</td>
</tr>
<tr>
<td>bCEJ-BC (mm) (mean ± SD; minimum–maximum)</td>
<td>4.7 ± 2.7 (2–12)</td>
<td>4.3 ± 2.1 (1–7)</td>
<td>1</td>
</tr>
<tr>
<td>Defect configuration</td>
<td>Mainly 1-wall/mainly 2-wall (n)</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Mainly 3-wall (n)</td>
<td>6</td>
<td>3</td>
</tr>
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0.5 mm in smokers (P = .003) and from 7.7 ± 1.2 mm to 3.6 ± 0.9 mm in nonsmokers (P = .003), with a significant difference between groups (P = .028). At 6 months, PD was similar (P = .151) in smokers and nonsmokers. These results were paralleled by a mean increase in bREC of 0.5 mm in both groups, which was significant only in nonsmokers (P = .028). In both groups, iREC did not show significant variations at 6 months compared to before surgery.

Eight patients in the smoker group and seven patients in the nonsmoker group showed a 6-month PD ≤ 4 mm, CAL gain ≥ 3 mm, and iREC and bREC increases ≤ 1 mm.

When clinical outcomes were evaluated in smokers with different daily cigarette consumption, a trend toward lower 6-month CAL gain and PD reduction was observed in patients smoking 11 to 20 cigarettes per day compared to those smoking 1 to 10 cigarettes per day (Table 5).

### Discussion

This retrospective cohort study was performed to evaluate the 6-month clinical outcomes of a regenerative procedure based on EMD and DBBM in the treatment of intraosseous defects accessed with buccal SFA. A total of 22 defects in 11 smokers (6 light smokers, 5 heavy smokers; mean daily cigarette consumption: 9.4 ± 5.6) and 11 nonsmokers were selected and included for analysis. When compared to nonsmokers, smokers showed a significantly lower quality of early wound healing and a similar postsurgery gain in CAL, residual PD, and increase in gingival recession.

At 2 weeks, smokers showed a significantly lower number of sites with optimal wound healing and a higher number of sites with incomplete flap closure when compared to nonsmokers (0% vs 45.5% and 45.5% vs 18.2%, respectively), indicating a detrimental effect of smoking on early wound healing. This finding can be explained, at least in part, by the alterations of the gingival vascular apparatus induced by smoke, which in turn may have impaired blood perfusion. Blood perfusion was demonstrated to be a key determinant of the early healing of mucoperiosteal flaps, and its impairment is frequently associated with wound dehiscence.

<table>
<thead>
<tr>
<th>EHI</th>
<th>Nonsmokers (n = 11)</th>
<th>Smokers (n = 11)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 – Complete flap closure, no fibrin line in the interproximal area</td>
<td>5</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>2 – Complete flap closure, fine fibrin line in the interproximal area</td>
<td>4</td>
<td>2</td>
<td>.009</td>
</tr>
<tr>
<td>3 – Complete flap closure, fibrin clot in the interproximal area</td>
<td>0</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>4 – Incomplete flap closure, partial necrosis of the interproximal tissue</td>
<td>2</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>5 – Incomplete flap closure, complete necrosis of the interproximal tissue</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

### Table 4 Distribution of Smokers and Nonsmokers According to Early Healing Index (EHI) as Assessed at 2 Weeks Following Surgery

<table>
<thead>
<tr>
<th>Cigarettes/day (n)</th>
<th>Patients (n)</th>
<th>CAL gain (mm; mean ± SD)</th>
<th>PD reduction (mm; mean ± SD)</th>
<th>iREC changea (mm; mean ± SD)</th>
<th>bREC changea (mm; mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–10</td>
<td>6</td>
<td>5.2 ± 2.3</td>
<td>5.7 ± 1.6</td>
<td>-0.5 ± 2.1</td>
<td>-0.7 ± 0.8</td>
</tr>
<tr>
<td>11–20</td>
<td>5</td>
<td>3.8 ± 1.1</td>
<td>4.8 ± 0.4</td>
<td>-1.0 ± 1.2</td>
<td>-0.4 ± 0.9</td>
</tr>
</tbody>
</table>

*a A negative value indicates an increase in recession.

CAL = clinical attachment level; PD = probing depth; iREC = interdental recession; bREC = buccal recession.
In smokers and nonsmokers, treatment with EMD and DBBM at defects accessed with buccal SFA resulted in substantial CAL gain, with no significant intergroup difference. The magnitude of treatment effect is consistent with previous clinical trials investigating the use of EMD and DBBM in the treatment of intraosseous defects accessed with SFA.7,8 This finding contrasts with several studies that showed a detrimental effect of smoking on the outcomes of regenerative periodontal surgery based on GTR provision.19–22,27 It must be considered that all the studies showing a negative effect of smoking on the regenerative outcome were based on the use of a resorbable (polylactic acid)/nonresorbable (ePTFE) membrane device in association with a conventional, double-flap approach.19–22,27 It can be hypothesized that SFA and the use of EMD might have counterbalanced the documented negative impact of smoking on the 6-month clinical outcomes of regenerative periodontal surgery. In this respect, in the SFA the surgical wound is restricted to one aspect (buccal or oral) and kept as limited as possible mesiodistally. These technical aspects may limit the vascular impairment caused by flap elevation, enhancing conditions for optimal wound stability. Moreover, the repositioning of the flap on the undetached papilla allows for the stability of the blood clot, promoting a better quality of early wound healing.5,28 In standardized periodontal defects experimentally created in rat molars, Azuma et al.28 demonstrated that the elevation of a single flap with limited mesiodistal extension is associated with a smaller area of inflammatory infiltrate and a lower amount of neutrophils, more rapid colonization of the elevated gingival tissues by fibroblasts, and greater connective tissue area occupied by type III collagen during early post-operative healing when compared to wide double flaps. On the other hand, a beneficial effect of EMD on the early healing of supracrestal soft tissue has been previously demonstrated in preclinical and clinical29 studies.

Another explanation for the lack of effect of smoking status can be related to the inclusive definition of smoker patient adopted in this study. A patient who smoked at least 1 cigarette per day was considered a smoker. The inclusion of light smokers may have mitigated, at least in part, the negative effect of smoking on the clinical outcomes. This hypothesis seems to be corroborated by data presented in Table 5, where patients smoking more than 10 cigarettes per day showed a clear tendency toward a lower CAL gain and PD reduction compared to patients smoking 1 to 10 cigarettes per day.

Although PD reduction was significantly greater in smokers, treatment resulted in a similarly maintainable residual PD in both groups. On average, gingival recession on the buccal or interdental aspect was limited and not significantly different between smokers and nonsmokers. The present findings are in contrast with previous studies reporting a greater extent of gingival recession following different types of periodontal surgeries in smokers.18–20 As for the magnitude of the recession, when considering the clinical conditions of the defects included in this study (mean presurgical PD of about 8 mm and bCEJ-BC of about 4 mm), the mean increase in bREC of 0.5 mm is consistent with the prediction model constructed by Farina et al.9 These data reinforce the use of an EMD/DBBM combination at sites accessed with buccal SFA to minimize the extent of postsurgical gingival recession irrespective of smoking status.

Conclusions

The results of the present study indicate that treatment of intraosseous defects with buccal SFA in association with EMD and DBBM may lead to substantial CAL gain and limited residual PD over the short term (6 months) in smokers and nonsmokers. The data suggest that a regenerative strategy based on a minimally invasive approach such as SFA and the combined use of amelogenins and xenograft is also a suitable treatment when dealing with intraosseous lesions in patients with moderate daily cigarette consumption.

Acknowledgments

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