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Minimally invasive surgical technique and enamel matrix derivative in intra-bony defects. I: clinical outcomes and morbidity

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Abstract

Aims: This case cohort study was designed to evaluate the clinical performance and the intra-operative and post-operative morbidity of the minimally invasive surgical technique (MIST) associated with the application of an enamel matrix derivative (EMD) in the treatment of isolated deep intra-bony defects.

Material and Methods: Forty deep isolated intra-bony defects in 40 patients were surgically accessed with the MIST. This technique was designed to limit the mesio-distal flap extension and the corono-apical flap reflection in order to reduce the surgical trauma and increase flap stability. The incision of the defect-associated papilla was performed according to the principles of the papilla preservation techniques. EMD was applied on the debrided and dried root surfaces. Stable primary closure of the flaps was obtained with modified internal mattress sutures. Surgery was performed with the aid of an operating microscope and microsurgical instruments. Clinical outcomes were collected at baseline and at 1 year. Intra-operative and post-operative morbidity was evaluated with questionnaires.

Results: The 1-year clinical attachment gain was 4.9 ± 1.7 mm ($p < 0.0001$ compared with baseline). This corresponded to a $77.6 \pm 21.9\%$ resolution of the defect. Residual probing pocket depths were 3 ± 0.6 mm. A minimal increase of 0.4 ± 0.7 mm in gingival recession between baseline and 1 year was recorded. No patients experienced intra-operative pain, while only 14 reported a very moderate perception of the hardship of the surgical procedure [7 ± 12 visual-analogue scale (VAS) units, on average]. Primary closure was obtained in all treated sites. At the 1-week follow-up visit, 38 sites (95%) were still closed. Only 12 subjects reported moderate post-operative pain (VAS 19 ± 10) that lasted for 26 ± 17 h.

Conclusions: These data indicate that the minimally invasive surgical technique, in combination with EMD, can be successfully applied in the treatment of isolated deep intra-bony defects, resulting in excellent clinical outcomes with very limited intra- and post-operative morbidity.

Key words: clinical trial; microsurgery; osseous defects; periodontal diseases; periodontal regeneration

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Conflict of interest and source of funding statement

The authors declare that they have no conflict of interests.

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A novel surgical approach for periodontal regeneration, the minimally invasive surgical technique (MIST) has been proposed recently and preliminarily tested in a case cohort of 13 isolated intra-bony defects in combination with an enamel matrix derivative (Cortellini & Tonetti 2007). The clinical rationale for the development of the MIST includes the following issues: (1) reduction of surgical trauma, (2) increase in flap/wound stability, (3) improvement of primary closure of the wound, (4) reduction of surgical chair time, and (5) minimization of intra-operative and post-operative patient discomfort and morbidity. Background foundations for the MIST were the concepts of the

minimally invasive surgery (MIS, Harrel & Rees 1995, Harrel et al. 2005) and the application of the widely tested papilla preservation techniques in combination with passive internal mattress sutures to seal the regenerating wound from the oral environment (Cortellini et al. 1995, 1999). The preliminary case cohort resulted in a clinical attachment level (CAL) gain of 4.8 ± 1.9 mm and an $88.7 \pm 20.7\%$ CAL fill of the intra-bony component of the defects at 1 year. Besides a decrease in the surgical time, there were indications of a decrease in patient morbidity as the post-operative period was uneventful for 77% of the patients. The clinical application of the MIST required the adoption of appropriate devices and instruments, in order to increase the visual acuity and allow for root/defect instrumentation with minimal flap reflection. For these reasons, the MIST is preferably performed with the use of an operating microscope (or high-power magnification loops) and microsurgical instruments (Cortellini & Tonetti 2001, 2005).

A larger study was deemed necessary to confirm the promising outcomes of the preliminary case cohort.

The aims of the present case cohort study were to evaluate the clinical performance and the intra-operative and post-operative morbidity of the ''MIST'' associated with the application of enamel matrix derivative in the treatment of isolated deep intra-bony defects.

Material and Methods

Study population and experimental design

Patients with advanced periodontal disease, in general good health, presenting with at least one deep intra-bony defect were considered to be eligible for this study. Patients were included after completion 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 written informed consent.

The inclusion criteria were as follows:

1. *Absence of relevant medical conditions*: Patients with uncontrolled or poorly controlled diabetes, unstable, or life-threatening conditions, or requiring antibiotic prophylaxis were excluded.
2. *Smoking status*: Only light smokers were included (< 10 cigarettes/day).
3. *Defect anatomy*: Presence of at least one tooth with probing pocket depth (PPD) and CAL loss of at least 5 mm associated with an intra-bony defect of at least 2 mm.
4. *Good oral hygiene*: Full-mouth plaque score $\leqslant 25\%$.
5. *Low levels of residual infection*: Full-mouth bleeding score $\leqslant 25\%$.
6. *Compliance*: Only patients with optimal compliance, as assessed during the cause-related phase of therapy, were selected.
7. *Endodontic status*: Teeth had to be vital or properly treated with root canal therapy.

Forty intra-bony defects in 40 subjects (mean age 48.3 ± 9.8, range 31–74 years, 14 males, and five smokers), who met the admission criteria, were consecutively included in this case cohort.

Three months after completion of periodontal therapy, baseline clinical measurements were recorded. The experimental sites were accessed with the MIST and carefully debrided. Measurements were taken during surgery to characterize the defect anatomy Cortellini et al. 1993a, b). EDTA and EMD (Emdogain, Institute Straumann AG, Basel, Switzerland) were applied on the instrumented and dried root surfaces and flaps were sutured with modified internal mattress sutures (Tonetti et al. 2002). A questionnaire was given to the patients at the end of surgery, with questions about the subjective perception of the surgical procedure as described previously (Tonetti et al. 2004). At the 1-week follow-up visit, a second questionnaire was given to patients with questions about the first post-operative week. Patients were enrolled in a stringent post-operative supportive care programme with weekly recalls for 6 weeks, and then included in a 3-month periodontal supportive care programme for 1 year. Outcome measures were taken at 1 year.

Clinical measurements at baseline and at the 1-year follow-up visit

The following clinical parameters were evaluated at baseline before regenerative therapy and at the 1-year follow-up visit by an independent clinician. Full-mouth plaque scores (FMPS) were recorded as the percentage of total surfaces (four aspects per tooth), which revealed the presence of plaque (O'Leary et al. 1972). Bleeding on probing (BOP) was assessed dichotomously and full-mouth bleeding scores (FMBS) were then calculated (Cortellini et al. 1993a)

PPD and recession of the gingival margin (REC) were recorded to the nearest millimetre at the deepest location of the selected inter-proximal site. All PD measurements and BOP were taken with a pressure-sensitive manual periodontal probe at 0.3 N (Brodontic probe equipped with a PCP-UNC 15 tip, Hu-Friedy, Chicago, IL, USA). CAL were calculated as the sum of PPD and REC. The radiographic defect angle of each defect was measured on a periapical radiograph, as described previously (Tonetti et al. 1993a). Tooth hyper-mobility was evaluated at baseline and at the 1-year follow-up visit according to a clinical score ranging from 0 to 3, where degree 0 represented physiologic mobility, degree 1 the mobility of the tooth $\leqslant 1$ mm in the horizontal direction, degree 2 the mobility of the tooth > 1 mm in the horizontal direction, and degree 3 the mobility of the tooth in the vertical direction as well (Nyman & Lindhe 1997).

Clinical characterization of the intra-bony defects

Defect morphology was characterized intra-surgically in terms of the distance between the cemento-enamel junction and the bottom of the defect (CEJ–BD) and the total depth of the intra-bony component of the defect (INFRA), essentially as described previously (Cortellini et al. 1993b). The depth of the 3-, 2-, and 1-wall sub-components, as well as the extension of the buccal and lingual/palatal bone dehiscences were also measured. Corticalization of the defects was classified as markedly corticalized, regularly cribriform, or very cancellous. Bleeding tendency of the defects was dichotomously recorded, as present or absent after completion of defect debridement.

Surgical and post-surgical variables

The chair time of each surgical procedure was calculated, starting from injection of

local anaesthesia and ending at completion of sutures. The number of teeth and the number of inter-proximal spaces involved in the procedure as well as the use of vertical releasing incision(s) and their position (mesial/distal buccal/lingual) were recorded. Primary closure of the flaps was evaluated at completion of surgery and at weekly recalls for a period of 6 weeks, along with the presence/absence of root sensitivity, oedema, haematoma, suppuration, granulation tissue, and any other post-surgical complication.

Surgical approach (MIST)

The surgical approach was as described previously (Cortellini & Tonetti 2007). In brief, the defect-associated inter-dental papilla was accessed either with the simplified papilla preservation flap (SPPF, Cortellini et al. 1999) or the modified papilla preservation technique (MPPT Cortellini et al. 1995) according to indications. The inter-dental intra-sulcular incision (SPPF or MPPT) was extended to the buccal and lingual aspects of the two teeth neighbouring the defect, limiting as much as possible their mesio-distal extension to allow the reflection of a very small full-thickness flap to expose 1–2 mm of the defect-associated residual bone crest. When possible, only the defect-associated papilla was accessed and vertical-releasing incisions were avoided. When the position of the residual buccal/lingual bony wall(s) was deep and difficult or impossible to reach with the above-described minimal incision of the defect-associated inter-dental space, the flap(s) was (were) further extended mesially or distally involving one extra inter-dental space to obtain a larger flap reflection. Vertical-releasing incisions were performed when flap reflection caused tension at the extremities of the flap(s). The vertical-releasing incisions were always kept very short and within the attached gingiva, never involving the muco-gingival junction. Periosteal incisions were not performed.

Defect debridement and EMD application

The defects were debrided with a combined use of mini curettes (Gracey, Hu-Friedy, Chicago, IL, USA) and power-driven instruments (Soniflex Lux, Kavo, Germany) and the roots were carefully planed. During the instrumentation, the flaps were slightly reflected, carefully protected with periosteal elevators, and frequently irrigated with saline. At the end of instrumentation, EDTA was applied on the instrumented and dried root surfaces for 2 min. After that, the defect area was carefully rinsed with saline and finally EMD was applied on the dried root surface. When the defect showed bleeding tendency, care was taken to reduce bleeding in order to be able to apply EMD on dried root/bone surfaces. This was generally accomplished by compacting a wet sterile gauge into the defect for 3–4 min. Then, the flaps were re-positioned.

Flap suturing technique

The suturing approach in most of the instances consisted of a single modified internal mattress suture applied at the defect-associated inter-dental area to reach primary closure of the papilla in the absence of any tension (Cortellini & Tonetti 2001, 2005). When a second inter-dental space had been accessed, the same suturing technique was used to obtain primary closure in this area. Vertical-releasing incisions were sutured with interrupted passing sutures. The buccal and lingual flaps were re-positioned at their original level, without any coronal displacement to avoid any additional tension in the healing area.

All the surgical procedures were performed with the aid of an operating microscope (Global Protege, St. Louis, MO, USA) at a magnification of X4–X16 (Cortellini & Tonetti 2001, 2005). Microsurgical instruments were utilized, whenever needed, as a complement to the normal periodontal set of instruments. Incisions were carried out using delaminating microsurgical blades (M6900, Advanced Surgical Technologies, Sacramento, CA USA). 6-0 e-PTFE (Gore-tex, WL Gore & Associates, Flagstaff AZ, USA) sutures were preferred to obtain primary closure of the inter-dental tissues.

Control of tooth mobility

Teeth that were found to be hypermobile at baseline were splinted either before or immediately after the surgical procedure (Cortellini et al. 2001). Splinting was carried out between the experimental tooth and the neighbouring teeth with the aid of a composite resin. Splinting was performed before surgery for teeth that were severely hypermobile (Miller grade II or greater). In other instances, mobility was re-evaluated at the end of surgery and the splint was applied when mobility was clearly increased with respect to the baseline value.

Post-operative period

A protocol for the control of bacterial contamination consisting of doxicycline (100 mg b.i.d. for 1 week), 0.12% chlorhexidine mouth rinsing three times per day, and weekly prophylaxis was prescribed (Tonetti et al. 2002). Patients were requested to avoid brushing, flossing, and chewing in the treated area for periods of 3–4 weeks. At the end of this period, patients resumed full-oral hygiene. At the end of the ''early healing phase'', patients were placed on a 3-months recall system for 1 year.

Evaluation of intra-operative and post-operative morbidity

Patient perceptions of intra-operative and post-operative morbidity were evaluated with a questionnaire administered upon completion of the procedure (hardship of the procedure and pain) and at suture removal (pain, discomfort, use of pain killers, interferences with daily activities, and adverse events). Responses were quantified with a VAS of 100 mm as described previously (Cortellini et al. 2001, Tonetti et al. 2004).

Data analysis

Data were expressed as means ± standard deviation (SD) of 40 defects in 40 patients. No data points were missing. Comparisons between baseline and 1-year data were made using the Student *t*-test ($\alpha = 0.05$). CAL gains, residual pocket depth, and the position of the gingival margin were the primary outcome variables. Percentage fill of the baseline intra-bony component of the defect was calculated as: CAL% = (CAL gains)/INFRA × 100.

Results

Patient and defect characteristics at baseline

Full-mouth plaque scores and full-mouth bleeding scores at baseline were

Table 1. Baseline patient and defect characteristics ($N = 40$)

Variables	Mean ± SD	Minimum	Maximum
FMPS (%)	13.1 ± 5.1	6	24
FMBS (%)	8.8 ± 3.3	2	15
PPD (mm)	8.2 ± 1.9	5	12
REC (mm)	1.8 ± 1.6	0	7
CAL (mm)	10 ± 2.9	5	17
CEJ–BD (mm)	10.9 ± 3	6	18
INFRA (mm)	6.5 ± 2.3	3	12
3 wall (mm)	3.5 ± 2.1	0	8
2 wall (mm)	2 ± 1.5	0	6
1 wall (mm)	1.1 ± 1.2	0	4
X-Ray angle (°)	30 ± 7.5	15	47

FMPS, full-mouth plaque scores; FMBS, full-mouth bleeding scores; PPD, probing pocket depth; REC, recession of the gingival margin; CAL, clinical attachment level; CEJ–BD, cemento-enamel junction and the bottom of the defect; INFRA, intra-bony component of the defect.

Table 2. Surgical parameters ($N = 40$)

Variables	Mean ± SD	*N* (%)	Minimum–Maximum
Number of teeth involved in surgery	2.4 ± 0.7	–	1–4
Number of interdental spaces involved	1.6 ± 0.6	–	0–3
Periosteal incision	–	–	–
Vertical releasing incision (buccal)	–	16 (40%)	–
Vertical releasing incision (lingual)	–	9 (22.5%)	–
Surgical time (min.)	55.7 ± 8.8	–	41–70
Flap closure at the end of surgery	–	40 (100%)	–

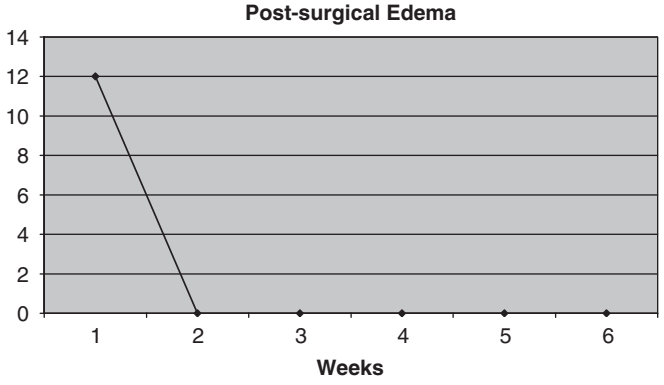

Fig. 1. Number of sites that presented with edema in the operated area at weekly examinations (weeks 1–6).

13.1 ± 5.1% and 8.8 ± 3.3%, respectively (Table 1). CAL of 10 ± 2.9 mm and PPD of 8.2 ± 1.9 mm on average were recorded (Table 1). The radiographic defect angle was 30 ± 7.5°. The distance from the CEJ–BD was 10.9 ± 3 mm, and the INFRA was 6.5 ± 2.3 mm (Table 1). Eighteen teeth were found to be hypermobile (eight presenting with Miller degree 1, 7 with degree 2, and 2 with degree 3 mobility). Thirteen teeth were splinted at baseline (six before surgery and seven immediately after surgery).

Surgical parameters (Table 2)

The simplified papilla preservation flap was used in 14 sites, while the modified papilla preservation technique was applied in 21 cases; five sites were accessed with a crestal linear incision. An incision restricted to the defect-associated papilla was performed in 16 cases. The flap was further extended buccally and/or lingually in 23 sites and only in one case it involved three interproximal spaces. A vertical-releasing incision was performed in 17 cases to help flap reflection. The average surgical chair-time was 55.7 ± 8.8 min. (range 41–70 min.).

Evaluation of the surgical procedure and the post-operative period

Patient perception of the procedure was very favorable. Twenty-six patients found it easy to cope with the surgical procedure, while only 14 reported a very limited degree of hardship of the surgical procedure (7 ± 12 VAS units on average, range 3–38, with 0 = easy to cope with and 100 = difficult to cope with). No one reported intra-operative pain. In all the treated sites, primary closure was obtained at completion of the surgical procedure. At the 1-week follow-up visit, 95% of the sites were closed: only two sites, both accessed with MPPT, presented with a small inter-dental gap between the two edges of the papilla. At week 2, the papillae found open at week 1 were fully closed (100% full inter-dental closure). All the sites remained closed during the following 5 weeks of the early healing period. A slight oedema was recorded in 12 (30%) of the cases at week 1. The oedema was fully resolved at week 2 in all the sites (Fig. 1). No post-surgical haematoma, suppuration, flap dehiscence, presence of granulation tissue, or other complications were noted in any of the treated sites. Root sensitivity was not a frequent occurrence in this study group (Fig. 2). It was reported at week 1 by eight patients (20%) and decreased in the following weeks. At week 6, only one patient still reported some root sensitivity.

The prevalence and extent of post-operative pain is presented in Table 3. Twenty-eight patients (70%) did not experience any post-operative pain. The 12 subjects reporting pain described it as being very moderate (VAS 19 ± 10, with 0 = no pain and 100 = unbearable pain). In these patients, pain lasted for 26 ± 17 h, on average. Home consumption of analgesic tablets was 1 ± 2 on average (range 1–11). Twenty-three patients did not use any pain killer in addition to the first two compulsory tablets that were taken in the practice immediately after the surgery and 6 h later.

Seven of the 12 patients (17.5%) reporting pain also experienced some discomfort (VAS 28 ± 11, with 0 = no discomfort and 100 = unbearable discomfort) that lasted 36 ± 17 h, on average.

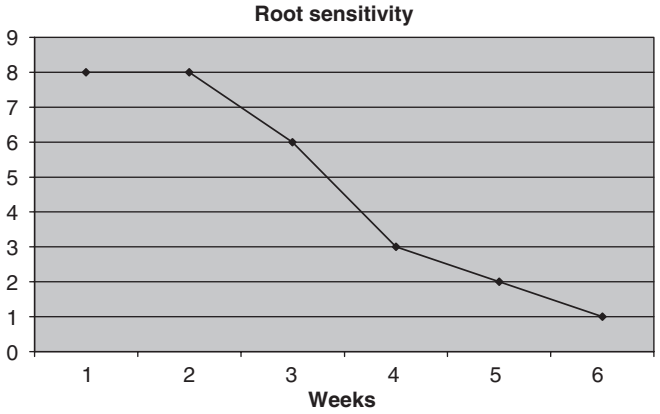

Fig. 2. Number of patients who experienced root sensitivity in the operated area at weekly examinations (weeks 1–6).

Table 3. Subject experience in terms of post-operative pain

	N (%)	Mean ± SD	Minimum–Maximum
Subjects reporting pain	12 (30%)		
Intensity of pain (VAS units)		19 ± 10	8–35
Duration of pain (hours)		26 ± 17	8–60
Number of analgesic tablets		1 ± 2	1–11

VAS units, visual analogic scale units (with 0 = no pain and 100 = unbearable pain).

Table 4. Clinical outcomes at baseline and 1 year after treatment ($N = 40$)

Variables	Baseline	1 year	Difference	Significance (p)*
PPD (mm)	8.2 ± 1.9	3 ± 0.6	5.2 ± 1.7	<0.0001
REC (mm)	1.8 ± 1.6	2.2 ± 1.9	0.4 ± 0.7	0.017
CAL (mm)	10 ± 2.9	5.1 ± 2	4.9 ± 1.7	<0.0001

*Paired *t*-test.

PPD, probing pocket depth; REC, recession of the gingival margin; CAL, clinical attachment level.

Only three patients reported some interference with daily activities (work and sport activities) for 1–3 days.

One-year clinical outcomes

The 40 patients presented at the 1-year follow-up visit with FMPS and FMBS of 11.4 ± 3.8% (range 6–20%) and 6.2 ± 2% (range 2–11%), respectively. The differences in FMPS and FMBS between baseline and 1 year were statistically significant ($p < 0.0001$).

The 1-year CAL was 5.1 ± 2 mm, with a CAL gain of 4.9 ± 1.7 mm (range 3–9 mm, Table 4). Differences in CAL between baseline and 1 year were clinically and statistically highly significant ($p < 0.0001$).

To characterize the distribution of the observed CAL gain among the different sites, data were stratified into four classes of CAL gain (Table 5). The stratified data show that no sites lost attachment, and no sites gained < 3 mm of attachment, while 70% of the sites gained 4 mm or more.

The 1-year per cent resolution of the defect was 77.6 ± 21.9% (range of 33.3–133.3%), and reached at least 100% of the baseline intra-bony component in 12 sites (30%). A per cent defect resolution ranging from 50% to 99% was observed in 27 sites (67.5%), while only one failed to reach the 50% fill of the baseline intra-bony component.

Residual probing depths were 3 ± 0.6 mm, with an average pocket depth reduction of 5.2 ± 1.7 mm (Table 4). The differences between baseline and 1-year probing depths were clinically and statistically highly significant ($p < 0.0001$). Only six sites showed a residual probing depth of 4 mm; all the other sites resulted in a 1-year PPD of 3 mm or less.

A very limited increase of 0.4 ± 0.7 mm in gingival recession between baseline and 1 year was recorded (Table 4). This difference was statistically significant ($p = 0.017$).

Hyper-mobility was detected on 18 teeth at baseline. Four of the 18 baseline hyper-mobile teeth, presenting with a degree 1 at baseline, showed normal mobility (degree 0) at 1 year. A reduction in mobility from degrees 2 to 1 was recorded in seven teeth, while two showed a reduction from degrees 3 to 1. The other teeth did not show any change in mobility between baseline and 1 year.

Discussion

The present case cohort study was designed to assess the clinical performance and the intra-operative and post-operative morbidity of a MIST in combination with an enamel matrix derivative in the regenerative treatment of deep, isolated intra-bony defects.

The treated population of deep intra-bony defects resulted in 1-year CAL gains of 4.9 ± 1.7 mm, associated with 3 ± 0.6 mm of residual probing depth and 0.4 ± 0.7 mm increase of gingival recession (Table 4). The clinical outcomes reported clearly demonstrate the potential of the proposed clinical approach in changing the anatomy of deep pockets associated with isolated deep intra-bony defects into shallow crevices, preventing a relevant apical shift of the gingival margin. This healing pattern favourably compares with that of the most successful regenerative approaches so far published in the last decade (Cortellini & Tonetti 2000, Needleman et al. 2002, Murphy & Gunsolley 2003). The evaluation of the clinical improvements in terms of CAL gain shows that in this defect population, no sites lost attachment and no sites gained less than 3 mm of CAL (Table 5). The majority of sites (70%) gained 4 mm or more at 1 year and 37.5% of the sites more than 6 mm. In addition, the percent resolution of the intra-bony component of the defects was extremely satisfactory, with a 78 ± 22 CAL% fill. Using the Ellegaard & Loe (1971), criteria resolution of the

Table 5. Frequency distribution of clinical attachment level gains at 1 year

	< 2 mm	3 mm	4–5 mm	⩾ 6 mm
N (%)	0	12 (30%)	13 (32.5%)	15 (37.5%)

intra-bony component of the defect was either complete (30%) or satisfactory (67.5%) in 39 out of 40 treated sites. Only one site showed an unsatisfactory resolution of 33.33%. The consistency of these data clearly sets the outcomes of this case cohort in the top percentiles in terms of both CAL gains and defect resolution (Cortellini & Tonetti 2000, Rosen et al. 2000). The reported outcomes were obtained in a patient population where the patient-associated factors, such as bacterial plaque, residual periodontal infection, and smoke had been controlled through the delivery of optimal non-surgical periodontal therapy and smoking cessation protocols, in order to reduce the negative impact of the cited factors (Tonetti et al. 1993b, 1995, 1996).

The proposed surgical approach was designed to minimize flap elevation and reflection and resulted in minimal intra-operative and post-operative flap mobility (Cortellini & Tonetti 2007). The post-operative wound stability played a possible positive role in the healing process. A study on dogs (Hiatt et al. 1968) demonstrated that wound integrity in the early healing phase is primarily dependent on the stability of the flaps and on the suturing technique. In an experimental dog model, Wikesjo & Nilveus (1990) and Haney et al. (1993) demonstrated that the fibrin clot and early wound stability play fundamental roles in periodontal wound healing.

In the present study, an improved stability of the healing area was attempted with a modified surgical approach designed to minimize flap mobility and consequent wound tension and to improve the gingival seal on top of the healing area. Primary closure was obtained in all the sites and was maintained at week 1 in 95% of the cases. From weeks 2–6, all sites were fully sealed.

The limited surgical trauma and the stability of the flaps also accounted for the absence of significant post-surgical local side effects. In fact, no post-surgical hematoma, suppuration, flap dehiscence, presence of granulation tissue, or other complications were noted in any of the treated sites. In only 12 (30%) cases was a slight oedema recorded at week 1. The oedema was fully resolved at week 2 in all the sites (Fig. 1). Root sensitivity was reported at week 1 by eight patients (20%) and rapidly decreased in the following weeks (Fig. 2). At week 6, only one patient still mentioned some root sensitivity. This could be the result of the very limited extension of the surgical flap and the associated minimal increase in gingival recession observed in the treated sites. These data are consistently more favourable with respect to the same data reported in a previous EMD study (Tonetti et al. 2004) and in a barrier membrane study (Cortellini et al. 2001) in which conventional papilla preservation approaches associated with a more ample flap elevation and reflection were applied.

The accuracy needed for gentle soft tissue handling, for careful defect/root debridement, for EMD placement, and for precise suturing to seal the wound was, at least in part, obtained by the use of an operating microscope and micro-surgical instruments (Cortellini & Tonetti 2001, 2005). The augmented visual acuity and the optimal field illumination provided by the microscope, along with the skill and experience of the surgeon, are probably key factors for the very limited surgical trauma and optimal healing pattern of the treated cases. The minimal flap elevation end extension required a minimal amount of sutures to close the wound. In 16 cases, the incision was restricted to the defect-associated papilla and a single modified internal mattress suture was applied. The flap was further extended buccally and/or lingually in 23 sites, requiring a second inter-proximal suture, and only in 1 case it involved three inter-proximal spaces. An additional suture was applied in the 17 cases that required a vertical-releasing incision to flap reflection.

The surgical chair time of this regenerative approach was very short (55.7 ± 8.8 min. on average, range 41–70 min.). In 24 surgeries, the chair time was shorter than 60 min. and only one reached 70 min. This favourably compares with 80 ± 34 min. of the cited EMD study and with 98.7 ± 45.7 min. of the barrier membrane study (Cortellini et al. 2001, Tonetti et al. 2004). It should be underlined that chair-time is influenced not only by the extension of the flap but also by the complexity of the procedure and the experience and skill of the operator. In this group of defects, few required a longer chair-time (up to 70 min.) due to the overall complex morphology of the defects.

The short surgical time and the limited surgical trauma probably could explain, at least in part, the limited intra-operative and post-operative patient morbidity observed in this case series.

In conclusion, this case cohort indicates that the MIST is an effective surgical approach for the treatment of isolated deep intra-bony defects in combination with EMD, reaching outcomes comparable with those of more conventional regenerative approaches, and may present important advantages in terms of reduction of surgical chair time and patient morbidity.

References

Cortellini, P., Pini Prato, G. & Tonetti, M. S. (1995) The modified papilla preservation technique. A new surgical approach for inter-proximal regenerative procedures. *Journal of Periodontology* **66**, 261–266.

Cortellini, P., Pini Prato, G. & Tonetti, M. S. (1999) The simplified papilla preservation flap. A novel surgical approach for the management of soft tissues in regenerative procedures. *International Journal of Periodontics and Restorative Dentistry* **19**, 589–599.

Cortellini, P., Pini-Prato, G. P. & Tonetti, M. S. (1993a) Periodontal regeneration of human infrabony defects. I. Clinical measures. *Journal of Periodontology* **64**, 254–260.

Cortellini, P., Pini-Prato, G. P. & Tonetti, M. S. (1993b) Periodontal regeneration of human infrabony defects. II. Re-entry procedures and bone measures. *Journal of Periodontology* **64**, 261–268.

Cortellini, P. & Tonetti, M. S. (2000) Focus on intrabony defects: guided tissue regeneration. *Periodontology 2000* **22**, 104–132.

Cortellini, P. & Tonetti, M. S. (2001) Micro-surgical approach to periodontal regeneration. Initial evaluation in a case cohort. *Journal of Periodontology* **72**, 559–569.

Cortellini, P. & Tonetti, M. S. (2005) Clinical performance of a regenerative strategy for intrabony defects. Scientific evidence and clinical experience. *Journal of Periodontology* **76**, 341–350.

Cortellini, P. & Tonetti, M. S. (2007) a minimally invasive surgical technique (MIST) with enamel matrix derivate in the regenerative treatment of intrabony defects: a novel approach to limit morbidity. *Journal of Clinical Periodontology* **34**, 87–93.

Cortellini, P., Tonetti, M. S., Lang, N. P., Suvan, J. E., Zucchelli, G., Vangsted, T., Silvestri, M., Rossi, R., McClain, P., Fonzar, A., Dubravec, D. & Adriaens, P. (2001) The simplified papilla preservation flap in the regenerative treatment of deep intrabony defects: clinical outcomes and postoperative morbidity. *Journal of Periodontology* **72**, 1702–1712.

Ellegaard, B. & Loe, H. (1971) New attachment of periodontal tissues after treatment of

intrabony lesions. *Journal of Periodontology* **42**, 648–652.

Haney, J. M., Nilveus, R. E., McMillan, P. J. & Wikesjo, U. M. E. (1993) Periodontal repair in dogs: expanded polytetrafluorethylene barrier membrane support wound stabilisation and enhance bone regeneration. *Journal of Periodontology* **64**, 883–890.

Harrel, S. K. & Rees, T. D. (1995) Granulation tissue removal in routine and minimally invasive surgical procedures. *Compendium of Continuing Education Dentistry* **16**, 960–967.

Harrel, S. K., Wilson Jr, T. G. & Nunn, M. E. (2005) Prospective assessment of the use of enamel matrix proteins with minimally invasive surgery. *Journal of Periodontology* **76**, 380–384.

Hiatt, W. H., Stallard, R. E., Butler, E. D. & Badget, B. (1968) Repair following mucoperiosteal flap surgery with full gingival retention. *Journal of Periodontology* **39**, 11–16.

Murphy, K. G. & Gunsolley, J. C. (2003) Guided tissue regeneration for the treatment of periodontal intrabony and furcation defects. A systematic review. *Annals of Periodontology* **8**, 266–302.

Needleman, I., Tucker, R., Giedrys-Leeper, E. & Worthington, H. (2002) A systematic review of guided tissue regeneration for periodontal infrabony defects. *Journal of Periodontal Research* **37**, 380–388.

Nyman, S & Lindhe, J (1997) *Examination of Patients with Periodontal Disease. Textbook Clinical Periodontology and Implant Dentistry. Chapter 12*, 3rd edition, pp. 383–395. Copenhagen: Munksgaard.

O'Leary, T. J., Drake, R. B. & Naylor, J. E. (1972) The plaque control record. *Journal of Periodontology* **43**, 38.

Rosen, P. S., Reynolds, M. A. & Bowers, G. M. (2000) The treatment of intrabony defects with bone grafts. *Periodontology 2000* **22**, 88–103.

Tonetti, M., Pini-Prato, G. & Cortellini, P. (1993b) Periodontal regeneration of human infrabony defects. IV. Determinants of the healing response. *Journal of Periodontology* **64**, 934–940.

Tonetti, M., Pini-Prato, G. & Cortellini, P. (1995) Effect of cigarette smoking on periodontal healing following GTR in infrabony defects. A preliminary retrospective study. *Journal of Clinical Periodontology* **22**, 229–234.

Tonetti, M., Pini-Prato, G. & Cortellini, P. (1996) Factors affecting the healing response of intrabony defects following guided tissue regeneration and access flap surgery. *Journal of Clinical Periodontology* **23**, 548–556.

Tonetti, M. S., Fourmousis, I., Suvan, J., Cortellini, P., Bragger, U. & Lang, N. P. (2004) Healing, post-operative morbidity and patient perception of outcomes following regenerative therapy of deep intrabony defects. *Journal of Clinical Periodontology* **31**, 1092–1098.

Tonetti, M. S., Lang, N. P., Cortellini, P., Suvan, J. E., Adriaens, P., Dubravec, D., Fonzar, A., Fourmousis, J., Mayfield, L., Rossi, R., Silvestri, M., Tiedemann, C., Topoll, H., Vangsted, T. & Walkamm, B. (2002) Enamel matrix proteins I the regenerative therapy of deep intrabony defects. A multicenter randomized controlled clinical trial. *Journal of Clinical Periodontology* **29**, 317–325.

Tonetti, M. S., Pini-Prato, G. P., Williams, R. C. & Cortellini, P. (1993a) Periodontal regeneration of human infrabony defects. III. Diagnostic strategies to detect bone gain. *Journal of Periodontology* **64**, 269–277.

Wikesjo, U. M. E. & Nilveus, R. (1990) Periodontal repair in dogs: effect of wound stabilisation on healing. *Journal of Periodontology* **61**, 719–724.

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Clinical Relevance

Scientific rationale for the study: There is a need to develop surgical approaches able to favour wound stability and primary closure of the flaps in order to improve the healing potential of regenerative therapy, and to reduce the intra-operative patient perception of the hardship of the procedure and the post-operative morbidity.

Principal findings: Application of MIST and EMD resulted in remarkable clinical improvements, with the complete resolution of 30% of the treated intra-bony defects. Few patients reported minimal post-operative pain and discomfort.

Practical implications: The MIST in combination with EMD can be successfully applied in the treatment of isolated deep intrabony defects. Clinicians could find advantages in applying such a minimal invasive procedure, when indicated, reducing patient morbidity.