Clinical and Radiographic Outcomes of the Modified Minimally Invasive Surgical Technique (M-MIST) With and Without Regenerative Materials. An Initial Randomized Controlled Trial in Intrabony Defects

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Note: The following files were submitted by the author for peer review, but cannot be converted to PDF. You must view these files (e.g. movies) online.

M-MIST.mp4
Clinical and Radiographic Outcomes of the Modified Minimally Invasive Surgical Technique (M-MIST) With and Without Regenerative Materials.

An Initial Randomized Controlled Trial in Intrabony Defects

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Key words: clinical trial, periodontal regeneration, microsurgery, minimally invasive surgery, osseous defects

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Abstract

Aims: this 3-arm study compared the clinical and radiographic efficacy of the modified minimally invasive surgical technique (M-MIST) alone and combined with enamel matrix derivative (EMD) or EMD plus Bone Mineral Derived Xenograph (BMDX), in the treatment of isolated, interdental intrabony defects.

Methods: 45 deep isolated intrabony defects in 45 patients were included, accessed with the M-MIST and randomly assigned to 3 balanced experimental groups. The M-MIST consisted of a small buccal flap without elevation of the defect-associated papilla. After removal of the granulation tissue by sharp dissection and root instrumentation the regenerative material was applied, when indicated, before obtaining primary closure with a single internal modified mattress suture. Surgery was performed with the aid of an operating microscope and microsurgical instruments. Outcomes were evaluated as pocket depth reduction, attachment level gain, radiographic bone fill and patient related outcomes.

Results: Primary wound closure was maintained in all treated sites with the exception of one M-MIST EMD+BMDX site. No patient reported intra-operative or post-operative pain. Within group differences between baseline and 1 year were statistically significant in the 3 groups in terms of PPD reduction, CAL gain and bone fill (P<0.0001). Comparisons among the 3 groups showed no statistically significant difference in any of the measured clinical outcomes. In particular, CAL gains of 4,1±1,4mm were observed in the M-MIST control group, 4,1±1,2mm in the EMD group, and 3,7±1,3mm in the EMD+BMDX one. The percent
radiographic bone fill of the intrabony component was 77±19% in the M-MIST control group, 71±18% in the EMD group and 78±27% in the EMD+BMDX group.

Conclusions: M-MIST with or without regenerative materials resulted in significant clinical and radiographic improvements. While this initial study did not have sufficient power to detect inter-group CAL differences smaller than 0.96 mm, the observed outcomes were remarkably similar and warrant further investigations.
Clinical Relevance

*Scientific rationale for study.* To compare the efficacy of M-MIST to M-MIST with the additional use of regenerative materials in the treatment of intrabony defects.

*Principal findings.* M-MIST alone resulted in excellent clinical and radiographic improvements. Addition of regenerative materials did not provide further improvements. The procedure produced very limited patient discomfort and wound failure was limited to only 1 case.

*Practical implications.* Clinical and radiographic healing following use of M-MIST needs to be confirmed in large multicenter trials.
Introduction

Regeneration is a healing outcome that can occur when the systemic and local conditions are favourable. In periodontal regeneration, the local conditions include the presence of space for the formation of the blood clot at the interface between flap and root surface (Haney et al 1993, Sigurdsson et al 1994, Cortellini et al 1995, Tonetti et al 1996, Wikesjo et al 2003, Kim et al 2004), the stability of the blood clot to maintain a continuity with the root surface avoiding formation of a long junctional epithelium (Linghorne and O’Connel 1950, Hiatt et al 1968, Wikesjo & Nilveus 1990 and Haney et al 1993), and the soft tissue protection to avoid bacterial contamination (Selvig et al. 1992, Tonetti et al 1993, Nowzari et al. 1995, De Sanctis et al. 1996, Sanz et al 2005).

Development of periodontal regenerative medicine in the last 25 years has followed two distinctive, though totally interlaced paths. The interest of researchers has so far focused on regenerative materials and products on one side and on novel surgical approaches on the other side.

In the area of materials and products, three different regenerative concepts have been mainly explored: barrier membranes, grafts, and wound healing modifiers, plus many combinations of the aforementioned.

In the area of the surgical approaches, clinical innovation in flap design and handling, has radically changed surgery and has allowed a drastic limitation of interdental wound failure from 100% with conventional flap approaches to less than 10% with the more modern approaches.
The modified minimally invasive surgical technique (M-MIST, Cortellini and Tonetti 2009) has been recently proposed and tested. The M-MIST was designed to: i) improve flap stability; ii) maintain space for regeneration; and iii) preserve an increased portion of the blood supply at the level of the crest and the papilla. The surgical approach consists of a limited interdental incision in which only a buccal triangular flap is elevated, while the papilla is left in place, connected to the root of the crest-associated tooth with its supracrestal fibres. The palatal/lingual tissues are not involved in the surgery. A similar approach used in combination with a bioresorbable barrier, has been recently proposed by Trombelli et al (2009).

The aim of the present 3-arm randomised controlled pilot clinical trial was to initially compare the clinical efficacy of the “modified minimally invasive surgical technique” alone versus the clinical efficacy of the M-MIST combined with two well-recognised regenerative materials, enamel matrix derivative (EMD) alone and in combination with Bone Mineral Derived Xenograph (BMDX), in the treatment of isolated, interdental intrabony defects.
Materials and Methods

Experimental Design

This was a parallel group, randomized, controlled clinical trial comparing the efficacy of 3 treatment modalities in 45 intrabony defects. A single defect was treated in each patient. All the experimental sites were accessed with the modified minimally invasive surgical technique (M-MIST, Cortellini and Tonetti 2009) and carefully debrided. EDTA was applied on the instrumented and dried root surfaces. Enamel matrix derivative (EMD: Emdogain, Institute Straumann AG, Basel, Switzerland) was applied to the debrided root surface in one group (15 defects); EMD plus Bone Mineral Derived Xenograph (BMDX, BioOss, Gestlich, Switzerland) in another group (15 defects). The third group (15 defects) did not receive the application of any regenerative material / device. Flaps were 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-months periodontal supportive care program for 1 year. Clinical and radiographic outcomes were evaluated at 1 year.

Study population

Patients with advanced periodontal disease, in general good health, presenting with at least one isolated deep, predominantly interdental intrabony defect were considered 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 in sites different from the experimental ones was performed, when indicated, before the regenerative treatment. All subjects gave written informed consent. Inclusion/exclusion criteria were as previously reported (Cortellini and Tonetti 2009). Patients were enrolled three months after completion of periodontal therapy, when baseline clinical measurements were recorded.

Sample Size and Randomization

The primary outcome of the study was clinical attachment level gain at 12 months. Changes in probing pocket depths and percentage fill of the radiographic intrabony component of the defect were secondary outcomes. Sample size was set at 15 subjects/treatment arm based on logistic considerations, the results of a previously reported case series (Cortellini and Tonetti 2009) and the pilot nature of this trial.

After verification of the entry criteria, 45 subjects gave informed consent and were enrolled into the study. Subjects were assigned a patient number and were randomly assigned to one of the three treatment regimens. Assignment was performed by a clinical research support infrastructure (ERGOPerio, Genova, Italy) using a custom made program based on balanced random permuted blocks. Furthermore, to reduce the chance of unfavourable splits among groups in terms of key prognostic factors, the randomization process balanced average clinical attachment levels and probing pocket depths. To conceal assignment, opaque envelopes were assigned to the specific subject and were opened during
surgery after defect debridement and EDTA application. Every defect, therefore, received EDTA at the end of defect / root instrumentation.

**Clinical measurements at baseline and at 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 a single calibrated clinician (MT). Full mouth plaque scores (FMPS) were recorded as the percentage of total surfaces (4 aspects per tooth) with the presence of plaque (O Leary 1972). Bleeding on probing (BOP) was assessed dichotomously and full mouth bleeding scores (FMBS) were then calculated (Cortellini et al 1993a)

Probing pocket depth (PPD) and recession of the gingival margin (REC) were recorded to the nearest millimeter at the deepest location of the selected interproximal site. All 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). Clinical attachment levels (CAL) were calculated as the sum of PPD and REC.

Periapical radiographs were taken at baseline and 1-year as previously described (Tonetti et al 1993b). The baseline radiographic defect angle; the distance between the cemento-enamel junction and the bottom of the defect (X-ray CEJ-BD); the distance between the cemento-enamel junction and the interdental bone crest (X-ray CEJ-BC) were performed on high resolution scanned radiographs (8 bit, 1200 dpi) using the program ImageJ (NIH, Bethesda, USA). The radiographic
infrabony component (X-ray INFRA) was calculated as (CEJ BD) – (CEJ BC).

Primary closure of the flaps and early healing events were evaluated at completion of surgery and at weekly recalls for a period of 6 weeks.

Clinical characterization of the infrabony defects

Defect morphology was characterized after flap elevation and debridement in terms of distance between the cemento-enamel junction and the bottom of the defect (CEJ-BD) and total depth of the infrabony component of the defect (INFRA), essentially as previously described (Cortellini et al 1993b). The defects were described as 1, 2, 3-wall or combination defects.

Surgical and patient outcomes

Surgical time was measured with a chronograph, starting at delivery of local anesthesia through the completion of sutures. Primary closure of the flap was checked with magnification at the end of surgery and weekly for 6 weeks. The presence of a discontinuity in the soft tissues was registered as wound failure.

Patients were asked at the end of surgery to report about intra-operative pain and personal feeling of the hardship of the procedure. A visual-analog scale (VAS) 10 cm long was used to indicate the intensity (0=no pain/hardship; 10=unbearable pain/hardship). Patients were asked at week one for their experience with post-operative pain and discomfort using a standard questionnaire; pain intensity was quantified with a VAS essentially as described (Cortellini et al 2001, Tonetti et al
Surgical approach (M-MIST)

All the surgical procedures were performed as previously described (Cortellini and Tonetti 2009, Video Clip 1) with the aid of an operating microscope (Global Protege, St Louis, Mo) at a magnification of 4X to 16X (Cortellini & Tonetti 2001, 2005). The defect-associated interdental papilla was surgically approached either with a diagonal incision following the pattern of the simplified papilla preservation flap when the width of the interdental space was 2mm or narrower (SPPF, Cortellini et al 1999) or with a horizontal incision according to the modified papilla preservation technique at interdental sites wider than 2mm (MPPT, Cortellini et al 1995). Flap elevation was limited to the buccal flap. No interdental and/or lingual intrasulcular incisions were performed. The supra-crestal interdental tissues, therefore, i) remained attached to the root cement of the crest-associated tooth with its supracrestal fibers, ii) maintained continuity with the palatal tissue and iii) were not elevated or displaced. After removal of the granulation tissue by careful dissection and root debridement, the root surface was chemically conditioned with a 2-minute application of an EDTA gel (Preph-gel, Straumann AG, Basel, Switzerland). The randomization envelope was opened and treatment continued based on the assignment.

A single modified internal mattress suture was positioned at the defect-associated interdental area (6-0 or 7-0 e-PTFE Gore-tex, WL Gore & Associates, Flagstaff AZ, USA). In the control group, that did not receive any regenerative
materials, the suture was tightened to reach primary closure of the defect-associated papilla (Cortellini & Tonetti 2001, 2005, 2007).

In the two test groups that received additional regenerative materials the suture was left loose. In the EMD test group, EMD was applied on the rinsed and air-dried root surface. In the EMD BMDX test group the xenograph was mixed with EMD on a sterile plate. EMD was applied on the rinsed and air-dried root surface and the mixture of EMD and BMDX was positioned into the defect with a sterile instrument with no attempt to tightly pack the material into the defect or to overfill it. When the regenerative materials were properly in place the suture was tightened to reach primary closure of the defect-associated papilla.

The post-operative regimen was as previously described (Tonetti et al 2002, Cortellini and Tonetti 2009). Patients were requested to avoid brushing, flossing and chewing in the treated area. At week 1, sutures were removed and patients resumed careful tooth-brushing with a soft tooth-brush (Vitis Surgical, Barcelona, Spain). Patients resumed interdental cleaning after 3 to 4 weeks. At week 4, patients performed full oral hygiene and resumed mastication in the treated area. Weekly prophylaxis was delivered for 6 weeks. At the end of the “early healing phase”, patients were placed on a 3-months recall system for 1 year.

Data analysis

Clinical attachment level gains (CAL gains), residual PPD, position of the gingival margin and radiographic bone gain were the outcome variables. Data within each
group were expressed as means ± standard deviation of 15 defects in 15 patients. All calculations were performed using the software Stata version 11.1 (College Station, Texas, USA). Post-hoc power analysis was calculated using the program G*Power 3.1 (Faul et al 2007).

Comparisons between baseline and 1 year measurements within each group were performed applying the paired Student t-test (α=0.05). Comparisons among the experimental groups at baseline and at 1 year were performed applying the ANOVA. Radiographic percent fill of the baseline intrabony component of the defect was calculated as: Bone fill% = (X-ray Bone Gain)/ X-ray INFRA * 100.
Results

Experimental population and surgical approach

Forty-five subjects were enrolled in this 3-arm randomized controlled clinical trial. The M-MIST alone was applied in 15 subjects (mean age 48.9±7.9, range 34 to 59 years, 6 females, 1 smoker). The M-MIST plus EMD was applied in 15 subjects (mean age 47.2±8.5, range 34 to 64 years, 8 females, 2 smokers). The M-MIST plus EMD-BMDX was applied in 15 subjects (mean age 53.5±11.9, range 28 to 71 years, 7 females, 2 smokers). No subject discontinued participation in the study and no data points were missing for analysis (Figure 1).

Baseline subject and defect characteristics are described in Table 1. The defect morphology of the 3 groups was well matched in terms of width of the defect and number of residual bony walls. The defects were mainly combinations of 3, 2 and 1-wall components. A 1-wall component was present in the majority of sites (9 sites in the M-MIST group and 10 sites in the other two). No differences were detected in any of the baseline clinical measurements among the 3 groups.

Postoperative course and early healing phase

The surgical time was rather short for all the 3 procedures. The shortest was recorded by M-MIST alone (average time 52.9±5.6 minutes, min 45', max 63'), followed by the M-MIST EMD (average time 54.2±7.4 minutes, min. 42', max. 67'). Slightly more time was required for M-MIST EMD+BMDX that accounted for 58.9±6.2 minutes, on average (min 45', max 63'). The difference among groups reached statistical significance (P=0.036, analysis of variance).
Primary closure was obtained in all treated sites at completion of surgery. All the treated sites remained closed during the 6 weeks of early healing period with the exception of one M-MIST EMD+BMDX site that presented at suture removal (week 1) with a slight discontinuity of the interdental wound on the side of the defect-associated tooth. Few BMDX granules were surfacing the soft tissues and were carefully removed. At week 2 the gap appeared closed. No oedema or haematoma was noted in any of the treated sites.

None of the patients reported intra-operative pain or personal feeling of hardship of the procedure at the end of surgery. At 1 week none of the patients reported having experienced post-operative pain. Slight discomfort was reported by 3 patients of the M-MIST group (average VAS value 10.7±2.1), by 2 patients of the M-MIST EMD (average VAS value 11.5±0.7) group and by 4 patients of the M-MIST EMD+BMDX one (average VAS value 12.3±3.1). Few patients needed pain control medications (ibuprofen): 3 patients from the control group (average number of 600 mg pills 0.4±0.7, max 2), 4 patients from the EMD group (average 0.3±0.6, max 2), 4 patients from the EMD+BMDX group (average 0.5±1, max 3).

1-year clinical outcomes

At 1 year, the 3 groups presented with low levels of FMPS and FMBS, shallow residual pockets, significant amounts of CAL gains and limited increase in gingival recession (table 2). Differences between baseline and 1 year were statistically significant in the 3 groups in terms of PPD reduction (P<0.0001 for all groups, t-test) as well as in terms of CAL gain (P<0.0001 for all groups, t-test). Minor changes in the position of the gingival margin occurred between baseline
and 1 year in the 3 groups (average recession increase of 0.3mm): the difference between baseline and 1 year was not statistically significant in the M-MIST and in the M-MIST EMD+BMDX groups, while reached statistical significance in the M-MIST EMD one (P=0.02).

Comparisons among the 3 groups showed no statistically significant difference in any of the measured clinical outcomes (analysis of variance, table 2). In particular, CAL gains of 4.1±1.4mm were observed in the M-MIST control group, 4.1±1.2mm in the EMD group, and 3.7±1.3mm in the EMD+BMDX one.

The frequency distribution of gains in CAL is reported in table 3. None of the sites gained less than 2mm of attachment, while 73.3% of the M-MIST group, 60% of the EMD group, and 46.6% of the EMD+BMDX group gained 4mm or more.

Bone changes were measured on scanned radiographs (table 4). The 3 groups gained a substantial amount of bone at 1 year as compared to baseline. The percent bone fill of the intrabony component was 77±19% in the M-MIST control group, 71±18% in the EMD group and 78±27% in the EMD+BMDX group. Differences among groups were not statistically significant.
Discussion

In this trial the Modified Minimally Invasive Technique alone resulted in pocket depth reductions, clinical attachment level gains and radiographic bone fill better than the reported ranges with access flap surgery in intrabony defects (Tu et al 2009). In particular, these cases expressed a very high clinical healing potential that resulted in the almost complete resolution of the intrabony defects (77±19% radiographic bone fill), good amounts of CAL gains (4.1±1.4mm) and stability of the gingival margin. Wound failure was observed in only one instance (2.2%) treated with EMD + BMDX, and complications and morbidity were minimal.

The additional application of regenerative materials (EMD or EMD plus Bone Mineral Derived Xenograph) did not improve the results as expected from the current literature utilizing more conventional papilla-preservation surgery (Trombelli and Farina 2008). While the power of this initial study to detect a true difference was limited to a difference of 0.96 mm, the fact that the outcomes among the 3 groups could not be discriminated is interesting and raises a series of hypotheses that focus on the intrinsic healing potential of the surgical approach. The M-MIST was designed to optimize wound and blood clot stability, flap margin blood perfusion and provide a stable space for regeneration (Cortellini and Tonetti 2009). The importance of these factors has been systematically assessed in pre-clinical studies and specific solutions have been introduced in periodontal regenerative surgery by progressively evolving flap designs (Cortellini et al 1994, 1999, Cortellini and Tonetti 2001, 2007, 2009).

As previously indicated, the M-MIST is not always applicable (Cortellini et al
When a defect wraps around the lingual aspect of a tooth, elevation of the interdental soft tissues becomes necessary and a Minimally Invasive Surgical Technique (MIST) becomes the preferred approach.

Independent full-scale clinical trials are needed to confirm the results of the present study. It is also important to determine the exact nature of the healing observed following application of M-MIST as the clinical healing observed in this study does not necessarily equate to periodontal regeneration. If such research will confirm these results and provide histological evidence of periodontal regeneration, M-MIST may become the procedure of choice for the treatment of interdental intrabony defects.

Acknowledgements

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Table 1. Baseline patient and defect characteristics of the 3 experimental groups (N=45).

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<tr>
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<th>M-MIST (N=15)</th>
<th>M-MIST+EMD (N=15)</th>
<th>M-MIST + EMD BMDX (N=15)</th>
<th>Significance</th>
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<tr>
<td>FMPS (%)</td>
<td>13.6±4.9</td>
<td>12.5±3.7</td>
<td>14.4±6.0</td>
<td>P=0.659</td>
</tr>
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<td>FMBS (%)</td>
<td>10.3±4.4</td>
<td>10.4±3.4</td>
<td>10.7±4.1</td>
<td>P=0.964</td>
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<td>PD (mm)</td>
<td>7.5±1.6</td>
<td>7.8±0.9</td>
<td>7.3±1.2</td>
<td>P=0.521</td>
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<td>REC (mm)</td>
<td>2.1±1.4</td>
<td>2.1±1.4</td>
<td>2.9±1.8</td>
<td>P=0.307</td>
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<tr>
<td>CAL (mm)</td>
<td>9.6±2.0</td>
<td>9.9±1.3</td>
<td>10.1±2.4</td>
<td>P=0.758</td>
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<td>INFRA (mm)</td>
<td>5.2±1.1</td>
<td>5.3±1.0</td>
<td>5.2±1.4</td>
<td>P=0.935</td>
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<tr>
<td>CEJ BD (mm)</td>
<td>10.5±2.4</td>
<td>10.5±1.5</td>
<td>10.9±2.2</td>
<td>P=0.852</td>
</tr>
<tr>
<td>CEJ BC (mm)</td>
<td>5.3±1.8</td>
<td>5.2±1.6</td>
<td>5.7±1.8</td>
<td>P=0.733</td>
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<td>3 wall</td>
<td>2.8±1</td>
<td>2.9±0.8</td>
<td>2.9±0.9</td>
<td>P=0.897</td>
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<td>2 wall</td>
<td>1.5±0.9</td>
<td>1.5±0.5</td>
<td>1.5±0.8</td>
<td>P=0.963</td>
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<td>1 wall</td>
<td>0.9±0.8</td>
<td>0.9±0.7</td>
<td>0.8±0.7</td>
<td>P=0.961</td>
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<td>X-ray angle °</td>
<td>35.2±7.2</td>
<td>30.4±5.4</td>
<td>32.8±9.1</td>
<td>P=0.218</td>
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Table 2. Clinical outcomes at 1 year (N=45).

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<thead>
<tr>
<th></th>
<th>M-MIST (N=15)</th>
<th>M-MIST+EMD (N=15)</th>
<th>M-MIST + EMD BMDX (N=15)</th>
<th>Significance</th>
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<tr>
<td>FMPS (%)</td>
<td>10,2±4,4</td>
<td>9,9±4,0</td>
<td>10,6±4,8</td>
<td>P=0,925</td>
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<td>FMBS (%)</td>
<td>7,0±5,2</td>
<td>5,7±3,0</td>
<td>7,0±3,6</td>
<td>P=0,605</td>
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<td>PD (mm)</td>
<td>3,1±0,6</td>
<td>3,4±0,6</td>
<td>3,3±0,6</td>
<td>P=0,327</td>
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<td>REC (mm)</td>
<td>2,4±1,4</td>
<td>2,3±1,4</td>
<td>3,1±2,1</td>
<td>P=0,354</td>
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<td>CAL (mm)</td>
<td>5,5±1,6</td>
<td>5,7±1,7</td>
<td>6,4±2,4</td>
<td>P=0,397</td>
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<td>Delta PD (mm)</td>
<td>4,4±1,6</td>
<td>4,4±1,2</td>
<td>4,0±1,3</td>
<td>P=0,657</td>
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<tr>
<td>Delta REC (mm)</td>
<td>-0,3±0,6</td>
<td>-0,3±0,5</td>
<td>-0,3±0,7</td>
<td>P=1</td>
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<td>CAL Gain (mm)</td>
<td>4,1±1,4</td>
<td>4,1±1,2</td>
<td>3,7±1,3</td>
<td>P=0,639</td>
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Table 3. Frequency distribution of CAL gains at 1 year (N=45).

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<th>Cal Changes (mm)</th>
<th>N of sites</th>
<th>M-MIST (15)</th>
<th>M-MIST+EMD (15)</th>
<th>M-MIST + EMD BMDX (15)</th>
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<tr>
<td>0-1 mm</td>
<td>0</td>
<td>0</td>
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<td>2-3 mm</td>
<td>4</td>
<td>6</td>
<td>8</td>
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<td>4-5 mm</td>
<td>9</td>
<td>7</td>
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<td>≥6 mm</td>
<td>2</td>
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Table 4. Baseline radiographic measurements and 1-year radiographic outcomes (N=45).

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<tr>
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<th>M-MIST+EMD (N=15)</th>
<th>M-MIST + EMD BMDX (N=15)</th>
<th>Significance</th>
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<tbody>
<tr>
<td>CEJ-BD 0 (mm)</td>
<td>9,0±1,7</td>
<td>9,3±2,0</td>
<td>10,5±2,1</td>
<td>P=0,102</td>
</tr>
<tr>
<td>INFRA (mm)</td>
<td>4,7±1,0</td>
<td>4,7±1,3</td>
<td>4,5±1,3</td>
<td>P=0,128</td>
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<tr>
<td>CEJ-BD 1 (mm)</td>
<td>5,5±1,3</td>
<td>6,0±1,5</td>
<td>7,2±2,1</td>
<td>P=0,025</td>
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<tr>
<td>Bone gain (mm)</td>
<td>3,5±1,0</td>
<td>3,3±1,2</td>
<td>3,3±1,1</td>
<td>P=0,815</td>
</tr>
<tr>
<td>Bone fill (%)</td>
<td>77±19</td>
<td>71±18</td>
<td>78±27</td>
<td>P=0,603</td>
</tr>
</tbody>
</table>
References


Legends to Figures

Figure 1. Consort diagram showing the study layout.

Figure 2a. Site treated with M-MIST alone. Lower right lateral incisor presenting with a preoperative PD of 6mm and a CAL of 11mm

Figure 2b. Preoperative radiograph showing the presence of an interdental intrabony defect

Figure 2c. Elevation of a M-MIST buccal flap and defect debridement. Note the untouched interdental papilla.

Figure 2d. Primary closure of the defect associated papilla was obtained with an internal modified mattress suture.

Figure 2e. The 1 year photograph shows a 3mm residual PD and a CAL of 8mm. No gingival recession occurred.

Figure 2f. Complete radiographic resolution of the intrabony component at 1 year.

Figure 3a. Site treated with M-MIST and EMD. Lower left second bicuspid presenting with a preoperative PD of 8mm and a CAL of 9mm

Figure 3b. Preoperative radiograph showing the presence of a deep interdental intrabony defect

Figure 3c. After the elevation of a tiny buccal flap the defect has been debrided. Note the untouched interdental papilla.
Figure 3d. EMD has been applied on the air dried root surface and primary closure has been provided with an internal modified mattress suture.

Figure 3e. The 1 year photograph shows a 2mm residual PD and a CAL of 5mm.

Figure 3f. The 1 year radiograph shows the almost complete resolution of the intrabony defect.

Figure 4a. Site treated with M-MIST and EMD plus BMDX. Upper left central incisor presenting with a preoperative PD of 11mm and a CAL of 13mm

Figure 4b. Preoperative radiograph showing the presence of a deep interdental intrabony defect

Figure 4c. After the elevation of a buccal flap the 2 wall defect has been debrided. Note the untouched interdental papilla.

Figure 4d. EMD plus BMDX has been applied on the air dried root surface and primary closure of the wide interdental papilla has been obtained with an internal modified mattress suture and an additional passing suture.

Figure 4e. Postoperative radiograph showing the BMDX grafted to fill the intrabony component of the defect.

Figure 4f. The 1 year photograph shows the nice preservation of the interdental soft tissues.

Figure 4g. The 1 year radiograph shows the complete resolution of the intrabony defect. BMDX particles are clearly detectable within the bone structure.
Figure 1. Consort diagram

Enrollment (n=45)

M-MIST (n=45)

Allocated to intervention M-MIST alone (n=15)

1 year analysis (n=15)

Allocated to intervention M-MIST+EMD (n=15)

1 year analysis (n=15)

Allocated to intervention M-MIST+EMD-BMDX (n=15)

1 year analysis (n=15)