MINIMALLY INVASIVE SURGICAL TECHNIQUES IN PERIODONTAL REGENERATION

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ABSTRACT

A review of the current scientific literature was undertaken to evaluate the efficacy of minimally invasive periodontal regenerative surgery in the treatment of periodontal defects. The impact on clinical outcomes, surgical chair-time, side effects and patient morbidity were evaluated.

An electronic search of PUBMED database from January 1987 to December 2011 was undertaken on dental journals using the key-word “minimally invasive surgery”. Cohort studies, retrospective studies and randomized controlled clinical trials referring to treatment of periodontal defects with at least 6 months of follow-up were selected. Quality assessment of the selected studies was done through the Strength of Recommendation Taxonomy Grading (SORT) System.

Ten studies (1 retrospective, 5 cohorts and 4 RCTs) were included. All the studies consistently support the efficacy of minimally invasive surgery in the treatment of periodontal defects in terms of clinical attachment level gain, probing pocket depth reduction and minimal gingival recession. Six studies reporting on side effects and patient morbidity consistently indicate very low levels of pain and discomfort during and after surgery resulting in a reduced intake of pain-killers and very limited interference with daily activities in the post-operative period.

Minimally invasive surgery might be considered a true reality in the field of periodontal regeneration. The observed clinical improvements are consistently associated with very limited morbidity to the patient during the surgical procedure as well as in the post-operative period. Minimally invasive surgery, however, cannot be applied at all cases. A stepwise decisional algorithm should support clinicians in choosing the treatment approach.

INTRODUCTION

In the past decade, a growing interest for more friendly, patient-oriented surgery has urged clinical investigators to focus their interest in the development of less invasive approaches. This interest is well depicted by the increasing number of publications on this subject. A very rough search on PubMed introducing as the keyword “minimally invasive surgery” with no limitations to disciplines, produced 28,386 articles, including 5322 reviews in a time frame between 1973 and 2011. The keyword “minimally invasive dentistry” resulted in 712 articles, including 114 reviews from 1987 to 2011. The keyword “minimally invasive surgery” limited to dentistry produced 464 articles, including 51 reviews from 1994 to 2011.

Keywords: Periodontal surgery, minimally invasive surgery, intrabony defects, periodontal regeneration
Surgical procedures in medicine and in dentistry have undergone radical changes to reduce invasiveness; in parallel, novel instruments and materials have been developed for the inevitable evolution of the surgical armamentarium.

The field of periodontal surgery has been enriched with this peculiar and innovative approach rather recently. Harrel and Rees proposed minimally invasive surgery (MIS) with the aim to produce minimal wounds, minimal flap reflection, and gentle handling of the soft and hard tissues. Cortellini and Tonetti, with the minimally invasive surgical technique (MIST), stressed the aspects of wound and blood clot stability and primary wound closure for blood clot protection, further enforced with the modified minimally invasive surgical technique (M-MIST) that, additionally, incorporated also the concept of space provision for regeneration.

Minimally invasive surgery is a term that describes the use of smaller and more precise surgical procedures that are possible through the use of magnifying instruments, such as operating microscopes and microsurgical instruments and materials. In fact, the development and refinement of the MIS approaches is greatly supported by the use of operative microscopes or magnifying lenses and of microsurgical instruments and materials. Cortellini and Tonetti proposed the use of an operative microscope in periodontal regenerative surgery, reporting an increased capacity to manipulate the soft tissues that resulted in an improved potential for primary closure of the wound from an average 70% of the cases obtained with regular surgery to an excellent 92% obtained with microsurgery. Other authors reported improved outcomes using operative microscopes in different areas of periodontal surgery, from flap surgery to mucogingival surgery.

Periodontal regenerative technologies are applied to improve short- and long-term clinical outcomes of teeth periodontally compromised, presenting with deep pockets and reduced periodontal support. Periodontal regeneration is selected to obtain an increase in the periodontal attachment and bone of a severely compromised tooth, a decrease in pocket depth, and a minimal or no increase in gingival recession. Periodontal regeneration has been shown effective in the treatment of 1-, 2-, and 3-wall intrabony defects or combination thereof, from very deep to very shallow, from very wide to very narrow. Questions of efficacy relate to the added benefit of a treatment modality under ideal experimental conditions (such as those of a highly controlled research center environment). Effectiveness, on the other hand, relates to the benefit that can be achieved in a regular clinical setting where the procedure is likely to be performed in relation to morbidity and adverse events. Besides efficiency considerations, both evidence for efficacy and effectiveness need to be available to provide support for adoption of treatment approaches in clinical practice.

Current approaches, however, are technique sensitive and burdened by a significant amount of clinical failures or incomplete success. We know today that most of the failures of regenerative therapy have an explanation in terms of negative patient factors, suboptimal use of surgical approaches and materials, and insufficient clinical skill and experience of the surgeon. Clinical success requires application of meticulous diagnostic and treatment strategies.

Development of periodontal regenerative medicine in the past 25 years has followed 2 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.

The aim of this article was to review the current scientific literature concerning minimally invasive periodontal regenerative surgery, highlighting its strengths and weaknesses and to propose a clinical step-by-step approach to the treatment of periodontal defects based on flow charts supported by current evidence.

MINIMALLY INVASIVE SURGICAL TECHNIQUES

The first technical proposal in periodontal regenerative surgery was MIS. The authors suggested the use of MIS in combination with bone grafting material covered with a bioresorbable vicryl mesh to treat isolated and multiple intrabony defects. The technique consists of an initial intrasulcular incision around the teeth neighboring the defect, followed by an incision between the teeth, usually on the lingual aspect, to connect the preliminary intrasulcular ones. The papilla is sharply dissected from the underlying bone and small buccal and lingual flaps are carefully reflected. The connective tissue within the osseous defect is dissected with a blade and removed with curettes and ultrasonic instruments, and the root debrided. The authors suggested finalizing root planing with finishing burs. Root conditioning with citric acid is also suggested, followed by placement of Decalcified Freeze Dried Bone Allograft (DFDBA) mixed with tetracycline hydrochloric acid to fill or slightly overfill the defect. Overfilling should not exceed the extent of space made available by the dissection of the connective tissue under the papilla. An unsutured vicryl mesh is positioned to help holding the graft in place. The flap is sutured with vertical parallel mattress sutures to obtain primary closure.

Cortellini and Tonetti proposed MIST in combination with enamel matrix derivative (EMD) to treat isolated intrabony defects. MIST incorporates many concepts of MIS, introducing, however, some modifications. In the MIST approach, the defect-associated interdental papilla is accessed either with the simplified papilla preservation flap (SPPF) in narrow interdental spaces or the modified papilla preservation technique (MPPT) in large interdental spaces (Figs. 1 and 2).
Figure 1. (A) MIST approach to the upper right second premolar presenting with a 9-mm distal pocket. (B) The isolated distal intrabony defect is 6 mm deep and 40° wide. (C) Access to the defect has been gained through a very short buccal incision and a minimal flap reflection to expose the bone crest of the 3-wall intrabony defect. (D) The interdental papilla, dissected according to the principle of the MPPT, has been raised toward the palatal side. A short vertical incision has been traced on the mesial edge of the palatal flap to improve flap reflection. (E) A single modified internal mattress suture is positioned to seal the wound, following the delivery of amelogenins. (F) At 1 year, the treated site presents with a 3-mm sulcus. (G) The 1-year radiograph shows the complete resolution of the intrabony component of the defect.

Figure 2. (A) MIST approach to an isolated 8-mm pocket at the mesial aspect of the first lower right molar. (B) The pocket is associated with a narrow intrabony defect 5 mm deep. (C) Three months before regeneration, endodontic therapy has been provided to treat the periapical lesions. (D) Minimal buccal flap reflection and the elevation of the interdental papilla according to the SPPF design provides full access to the 3-wall intrabony component. (E) The wound has been stabilized with a single modified internal mattress suture. No regenerative materials have been positioned in the treated site. (F) The 1-year 3-mm sulcus and the definitive crown. (G) The 1-year radiograph shows the resolution of the intrabony component of the defect and of the periapical lesion.

The SPPF is a diagonal incision traced as close as possible to the buccal side of the papilla col, whereas the MPPT is a horizontal incision traced on the buccal side of the papilla. Intratruncular incisions are performed from the interdental side to the buccal and lingual sides of the teeth neighboring the defect; tiny buccal and lingual flaps are elevated to expose the residual bone crest. Periosteal incisions are performed only if needed to improve flap reflection. The soft tissue is sharply dissected from the osseous defect and debridement and root planing are performed with a combination of mini-curettes and power air-driven instruments. EDTA is applied to the air-dried root surface for 2 minutes, then carefully washed away and EMD is applied on the air-dried root surface. The suturing approach is based on the use of a single internal
modified mattress suture. Additional sutures can be applied to further increase primary closure, when needed.

Cortellini et al. proposed the application of a single MIS technique to treat multiple adjacent defects. The surgical modification includes an extension of the flap to all the teeth involved by osseous defects. The larger flap is minimally reflected in accordance with the previously described principles. The rest of the procedure is unmodified.

More recently, Cortellini & Tonetti proposed M-MIST (Figs. 3 and 4). The surgical approach consists of a tiny interdental access in which only buccal intrasulcular incisions are performed and connected with a buccal horizontal incision of the papilla performed as close as possible to the papilla tip.

Figure 3. (A) Upper right lateral incisor presenting with an 8-mm mesial pocket accessed with a M-MIST approach. (B) The radiograph shows a narrow intrabony defect. (C) The interdental incision is slightly diagonal (SPPF-like approach). (D) A very tiny buccal flap has been raised to uncover the buccal crest. The interdental papilla has not been elevated and the granulation tissue has been carved away from under the interdental tissues. (E) A 6-mm combined intrabony defect is evident. (F) The surgical wound has been sealed with a single modified internal mattress suture and an additional passing suture. No regenerative materials have been used in this site. (G) The 1-year photograph reporting a 3-mm sulcus and no gingival recession. (H) Radiographic resolution of the defect at 1 year.
The tiny buccal triangular flap is elevated to expose the residual buccal bone crest. The papillary tissues are left untouched, carefully preserving the supracrestal attachment apparatus to the root cementum of the crest-associated tooth. Access to the defect is gained through the tiny buccal "window." The soft tissue filling the defect (ie, the so-called granulation tissue) is sharply dissected from the papillary supracrestal connective tissue and removed with mini-curettes. In other words, the soft tissue filling the osseous defect is "carved" away from under the papilla. Then the root surface is carefully debrided with mini-curettes and power-driven air instruments avoiding any trauma to the supracrestal fibers of the defect-associated papilla. The palatal tissues are not surgically accessed. The suturing approach is based on the use of a single internal modified mattress suture. Additional sutures can be applied to further increase primary closure, when needed. M-MIST cannot be applied to all periodontal defects. Its limits are the access to the diseased root surface. Whenever a defect extending to the lingual/palatal side of a root is difficult to debride, the authors suggest raising the papilla and performing a MIST approach.

**Technical implications**

The previously cited studies propose 2 different minimally invasive approaches to intrabony defects. The MIS and the MIST\(^4,24\) include the elevation of the interdental papillary tissues to uncover the interdental space, gaining complete access to the intrabony defect (Figs. 1 and 2), whereas the M-MIST\(^5\) proposes an approach in which the access to the defect is gained through the elevation of a small buccal flap, without elevation of the interdental papilla (Figs. 3 and 4). The major problem to overcome in applying minimally invasive surgery is the problem of visibility and manipulation of the surgical field. This issue is clearly enhanced in the M-MIST approach. High magnification and direct optimal illumination can help in solving the problem. Traditionally we are taught to raise large flaps to completely and exceedingly expose the area of interest. In reality, our limits to defect visibility are the residual bony walls that surround the defect. The elevation of a flap to the edge of the residual bony walls should therefore be sufficient to gain visibility of the defect: over-reflection of the flaps does not increase our ability to look into the defect; however, the minimal flap reflection narrows the angle of vision and especially the light penetration into the surgical field. In addition, the soft tissue manipulation during instrumenta-
tion requires more care, as the flaps, not fully reflected, lay very close to the working field. Small instruments, such as small periosteal elevators and tiny tissue players, are mandatory, as well as their gentle application to soft and hard tissues. Micro-blades, mini-curettes, and mini-scissors allow for a full control of the incision, debridement, and refinement of the surgical area, and sutures from 6-0 to 8-0 are mandatory for the wound closure.

**Clinical studies and outcomes**

Cohort studies and randomized controlled clinical trials reporting outcomes on the application of minimally invasive surgical approaches are shown in Tables 1 and 2.

Table 1 refers to studies in which the interdental papillary tissues have been elevated to uncover the interdental space completely (MIS and MIST). This approach is supported by a retrospective study,\(^25\) 4 cohort studies,\(^1,4,12,24\) and 2 controlled studies.\(^26,27\)

Ribeiro et al\(^26\) investigated the impact of EMD proteins on the outcome of an MIST in the treatment of 30 intrabony defects in 30 patients. The defects were randomly assigned to treatment with MIST plus EMD or MIST alone. Significant pocket reductions, clinical attachment gains, and minimal changes in gingival recession were obtained at 3 and 6 months in both groups. No clinically or statistically significant differences were found between the 2 groups in terms of clinical and radiographic evaluations at any time. The authors concluded that the use of EMD did not provide superior benefits on the outcome of the minimally invasive surgical approach for the treatment of intrabony defects (Figs. 1 and 2).

Table 2 reports studies in which the access to the defect was gained through the elevation of a small buccal flap, without elevation of the interdental papilla. This approach is supported by a cohort study\(^5\) and 2 controlled studies.\(^28,29\)

Cortellini and Tonetti\(^28\) designed a 3-armed randomized controlled clinical trial to compare the clinical efficacy of the “modified minimally invasive surgical technique” alone versus M-MIST combined with amelogenins (EMD) and amelogenins plus bone mineral–derived xenograph (BMDX), in the treatment of isolated, interdental intrabony defects. The study was performed on 45 deep isolated intrabony defects accessed with the M-MIST and randomly assigned to 3 experimental groups: 15 to M-MIST alone, 15 to M-MIST+EMD, and 15 to M-MIST+EMD-BMDX. Differences between baseline and 1 year were statistically significant in the 3 groups in terms of probing pocket depth (PPD) reduction, as well as in terms of clinical attachment level (CAL) gain (P > .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 ± 1.4 mm were observed in the M-MIST control group, 4.1 ± 1.2 mm in the EMD group, and 3.7 ± 1.3 mm in the EMD+BMDX group. 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. The authors concluded that the M-MIST is efficacious in the treatment of intrabony defects with or without the additional use of regenerative materials (Figs. 3 and 4).

An independent study\(^29\) reported similar outcomes with the single-flap approach (SFA). This study evaluated the adjunctive significance.\(^93\)
### TABLE 1. Clinical studies in which the interdental papillary tissues have been elevated to uncover the interdental space completely

<table>
<thead>
<tr>
<th>MIS / MIST</th>
<th>Type of study (quality of evidence)</th>
<th>Interventions</th>
<th>No. pax</th>
<th>No. defects</th>
<th>CAL gain</th>
<th>PD reduction</th>
<th>Residual PD</th>
<th>Δ REC</th>
<th>Patient outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harrel et al 1999&lt;sup&gt;19&lt;/sup&gt;</td>
<td>Retrospective (Level 3)</td>
<td>MIS+DFDBA+Vycril</td>
<td>87</td>
<td>194</td>
<td>4.87±0.27 23pax (60)</td>
<td>4.58±0.26</td>
<td>—</td>
<td>—</td>
<td>NO</td>
</tr>
<tr>
<td>Harrel et al 2005&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Case cohort (Level 2)</td>
<td>MIS+EMD+DFDBA* (*if deemed indicated)</td>
<td>16</td>
<td>160</td>
<td>3.57±1.75 3.56±1.31</td>
<td>3.1±0.75</td>
<td>0.01</td>
<td>NO</td>
<td></td>
</tr>
<tr>
<td>Cortellini &amp; Tonetti 2007&lt;sup&gt;24&lt;/sup&gt;</td>
<td>Case cohort (Level 2)</td>
<td>MIST+EMD</td>
<td>13</td>
<td>13</td>
<td>4.8±1.9 4.8±1.8</td>
<td>2.9±0.8</td>
<td>0.1±0.9</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>Cortellini &amp; Tonetti 2007&lt;sup&gt;24&lt;/sup&gt;</td>
<td>Case cohort (Level 2)</td>
<td>MIST+EMD</td>
<td>40</td>
<td>40</td>
<td>4.9±1.7 5.2±1.7</td>
<td>3±0.6</td>
<td>0.4±0.7</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>Cortellini et al 2008&lt;sup&gt;23&lt;/sup&gt;</td>
<td>Case cohort (Level 2)</td>
<td>MIST+EMD</td>
<td>20</td>
<td>44</td>
<td>4.4±1.4 4.6±1.3</td>
<td>2.5±0.6</td>
<td>0.2±0.6</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>Ribeiro et al 2011&lt;sup&gt;26&lt;/sup&gt;</td>
<td>RCT (Level 1)</td>
<td>MIST MIST+EMD</td>
<td>15</td>
<td>14</td>
<td>2.82±1.19* 3.02±1.94*</td>
<td>3.55±0.88* 3.56±2.07*</td>
<td>3.57±0.81* 3.53±1.12*</td>
<td>0.54±0.58* 0.46±0.87*</td>
<td>NO</td>
</tr>
<tr>
<td>Ribeiro et al 2011&lt;sup&gt;27&lt;/sup&gt;</td>
<td>RCT (Level 1)</td>
<td>MIST MINST (RPL)</td>
<td>14</td>
<td>14</td>
<td>2.85±1.19* 2.56±1.12*</td>
<td>3.51±0.90* 3.13±0.67*</td>
<td>3.56±0.84* 3.21±0.85*</td>
<td>0.48±0.51* 0.45±0.46*</td>
<td>YES</td>
</tr>
</tbody>
</table>

EMD, enamel matrix derivative; MIS, minimally invasive surgery; MIST, minimally invasive surgical technique; MINST, minimally invasive nonsurgical technique (RPL with the aid of a microscope).
DFDBA, Decalcified Freeze Dried Bone Allograft
*No statistical difference.

### TABLE 2. Clinical studies in which the access to the defect was gained through the elevation of a small buccal flap, without elevation of the interdental papilla

<table>
<thead>
<tr>
<th>M-MIST / SFA</th>
<th>Type of study (quality of evidence)</th>
<th>Interventions</th>
<th>No. pax</th>
<th>No. defects</th>
<th>CAL gain</th>
<th>PD reduction</th>
<th>Residual PD</th>
<th>Δ REC</th>
<th>Patient outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortellini &amp; Tonetti 2009&lt;sup&gt;25&lt;/sup&gt;</td>
<td>Case cohort (Level 2)</td>
<td>M-MIST+EMD</td>
<td>15</td>
<td>15</td>
<td>4.5±1.4</td>
<td>4.6±1.5</td>
<td>3.07±0.6</td>
<td>0.07±0.3</td>
<td>YES</td>
</tr>
<tr>
<td>Cortellini &amp; Tonetti 2011&lt;sup&gt;18&lt;/sup&gt;</td>
<td>RCT (Level 1)</td>
<td>M-MIST M-MIST+EMD M-MIST+EMD+BioOss</td>
<td>15</td>
<td>15</td>
<td>4.1±1.4* 4.1±1.2* 3.7±1.3*</td>
<td>44±1.6* 44±1.2* 40±1.3*</td>
<td>3.1±0.6* 3.4±0.6* 3.3±0.6*</td>
<td>0.3±0.6* 0.3±0.5* 0.3±0.7*</td>
<td>YES</td>
</tr>
<tr>
<td>Trombetti et al 2010&lt;sup&gt;29&lt;/sup&gt;</td>
<td>RCT (Level 1)</td>
<td>SFA SFA+HA+GTR</td>
<td>12</td>
<td>12</td>
<td>4.4±1.5* 4.7±2.5*</td>
<td>5.3±1.5* 5.3±2.4*</td>
<td>3.3±0.6* 3.8±1.3*</td>
<td>0.8±0.8* 0.4±1.4*</td>
<td>NO</td>
</tr>
</tbody>
</table>

CAL, clinical attachment; GTR, resorbable collagen membrane; HA, hydroxyapatite; M-MIST, modified minimally invasive surgical technique; PD, probing depth; REC, recession; SFA, single-flap approach.
*No statistical difference.
The effect of hydroxyapatite (HA) biomaterial protected with a resorbable collagen membrane (GTR) in the management of intraosseous periodontal defects accessed with SFA compared with SFA alone. Twenty-four intraosseous defects in 24 patients were randomly allocated to treatment with SFA or SFA + HA/GTR. There were no statistically significant or clinical differences in clinical attachment gain (4.7 ± 2.5 versus 4.4 ± 1.5 mm), probing depth reduction (5.3 ± 2.4 versus 5.3 ± 1.5 mm), or gingival recession increase (0.4 ± 1.4 versus 0.8 ± 0.8 mm) between the SFA + HA/GTR and SFA groups. The authors concluded that SFA with and without HA/GTR seems to be a valuable minimally invasive approach in the treatment of deep intraosseous periodontal defects.

Interestingly, the reported randomized clinical trials performed using minimally invasive approaches (with or without papilla elevation) report no differences in terms of clinical outcomes between the minimally invasive control flap approach and the test in which a regenerative material/product was introduced under the flap. The reported outcomes raise a series of hypotheses that focus on the intrinsic healing potential of a wound when ideal conditions are provided with the surgical approach. In other words, the outcomes of these studies challenge clinicians with the possibility to obtain substantial clinical improvements without the use of products or materials applying surgical techniques that do enhance “per se” blood clot and wound stability. In particular, the advanced flap design of the M-MIST greatly enhances the potential to provide space and stability for regeneration by leaving the interdental papillary soft tissues attached to the root surface of the crest-associated tooth and by avoiding any palatal flap elevation. The interdental soft tissues are the stable “roof” of a room where the blood fills in and forms a clot. The hanging papilla prevents the collapse of the soft tissues, maintaining thereby space for regeneration. The anatomic bone deficiencies are potentially supplemented by the peculiar flap design that provides additional “soft tissue walls” to the missing bony walls improving stability; walls of the “room” are the residual bony walls, the root surface and the buccal/lingual soft tissues. The minimal flap extension and elevation also minimizes the damages to the vascular system, favoring the healing process of the tiny soft tissues.

Postoperative period and local side effects

From the very beginning of the “guided tissue regeneration era,” it was apparent the frequent occurrence of complications, in particular, the adoption of amelogenins largely reduced the prevalence of complications.16,39,42 The development of minimally invasive surgery has greatly reduced the amount of complications and side effects in the postoperative period.

Primary closure of the flap was reported in 100% of cases treated with MIST and maintained in 95% of the cases at 1 week in single sites4,24 and in 100% of the cases in treatment of multiple sites.23 Edema was noted in few cases.4,23,24 No postsurgical haematoma, suppuration, flap dehiscence, presence of granulation tissue, or other complications were reported in any of the treated sites.4,23,24 Root sensitivity was not a frequent occurrence. It was reported at 1 week by about 20% of the patients and rapidly decreased in the following weeks; at week 6, only 1 patient still reported some root sensitivity.24 Ribeiro et al24 reported that the extent of root hypersensitivity and edema was very discreet and no patients developed hematoma.

When applying the M-MIST, Cortellini & Tonetti3 reported primary closure obtained and maintained in 100% of the cases. In a second controlled study,28 one M-MIST/EMDX site presented at suture removal (week 1) with a slight discontinuity of the interdental wound. At week 2, the gap appeared closed.

No edema, hematoma, or suppuration was noted in any of the treated sites.5,28

Surgical and postsurgical patient morbidity

Patients treated with MIST and EMD were questioned at the end of surgery and at week 1 about the intraoperative and postoperative periods and reported no pain.3 Three patients reported very limited discomfort in the first 2 days of the first postoperative week. Seventy-seven percent of the patients described the first postoperative week as uneventful, reporting that they had no feeling of having been surgically treated after the second postoperative day.

In a large case cohort using MIST and EMD,24 none of the patients declared intraoperative pain or discomfort and 70% did not experience any postsurgical pain. The 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 hours, on average. Home consumption of analgesic tablets was 1 ± 2, on average. Twenty-three patients did not use any pain killer in addition to the first 2 compulsory tablets that were administered in the practice immediately after the surgery and 6 hours later. Seven (17.5%) of the 12 patients reporting pain also experienced some discomfort (VAS 28 ± 11, with 0 = no discomfort and 100 = unbearable discomfort) that lasted 36 ± 17 hours, on average. Only 3 patients reported some
**Table 3. Historical comparison among clinical studies performed with the use of conventional versus minimally invasive surgery**

<table>
<thead>
<tr>
<th>Regenerative approach</th>
<th>No. of patients</th>
<th>Chair time, min</th>
<th>Interference with daily activity</th>
<th>Subjects with postoperative discomfort</th>
<th>Subjects with postoperative pain</th>
<th>Pain intensity</th>
<th>N of pain killers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortellini &amp; Tonetti 2011</td>
<td>56</td>
<td>99±46</td>
<td>35.7%</td>
<td>53.6%</td>
<td>46%</td>
<td>28.1±2.5</td>
<td>4.1±2.5</td>
</tr>
<tr>
<td>Cortellini et al. 2007</td>
<td>83</td>
<td>89±34</td>
<td>29.5%</td>
<td>41.5%</td>
<td>50%</td>
<td>28±20</td>
<td>4.3±4.5</td>
</tr>
<tr>
<td>Tonetti et al. 2004</td>
<td>40</td>
<td>58±11</td>
<td>7.5%</td>
<td>17.5%</td>
<td>30%</td>
<td>19±10</td>
<td>19±4.2</td>
</tr>
<tr>
<td>Cortellini &amp; Tonetti 2011</td>
<td>15</td>
<td>54±27.4</td>
<td>0</td>
<td>13.3%</td>
<td>0</td>
<td>0±0.6</td>
<td>0.3±0.6</td>
</tr>
</tbody>
</table>

The table reports the chair-time measured from delivery of anesthesia to completion of the regenerative surgical procedures, in minutes; the percentage of subjects reporting postoperative interference with daily activities, discomfort and pain, as questioned at 1-week recall visit; the intensity of pain measured with a visual analogic scale (VAS); the number of pain killers taken in addition to the 2 compulsory tablets. None of the patients reported intraoperative or significant postoperative pain. Three patients reported slight discomfort in the first 2 days after surgery. Fourteen of 15 described the first postoperative week as uneventful, reporting that they had no feeling of having been surgically treated after the second postoperative day.

In a controlled study on the additional benefit of EMD or EMD/BMDX to M-MIST alone,28 none of the patients reported experiencing intraoperative or postoperative 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 group (VAS 11.5 ± 0.7), and by 4 patients of the M-MIST EMD/BMDX group (VAS 12.3 ± 3.1). Few patients needed pain control medications: 3 patients from the control group (average number of tablets 0.4 ± 0.7, maximum 2), 4 patients from the M-MIST group (average 0.3 ± 0.6, maximum 2), and 4 patients from the EMD/BMDX group (average 0.5 ± 1.0, maximum 3).

In a second case-cohort study with MIST and EMD,23 14 patients did not experience any postoperative pain. The 6 subjects reporting pain described it as being very mild (VAS 19 ± 9). In these patients, pain lasted for 21 ± 5 hours, on average. Home consumption of pain killers was 0.9 ± 1.0. Nine patients did not use any analgesic in addition to the first 2 compulsory tablets. Ten patients experienced mild discomfort (VAS 21 ± 10) that lasted 20 ± 9 hours, on average. Only 4 patients reported some interference with daily activities (work and sport activities) for 1 to 3 days.

Ribeiro et al.,22 applying MIST and EMD, reported that the extent of discomfort/pain experienced during therapy was very limited. In addition, the extent of discomfort during the first postoperative week was very discreet, and no patients developed high fever or an interference with daily activities. The quantity of analgesic medication taken by patients was minimal (lower than 1 analgesic medication per patient).

In a case-cohort study in which defects were treated with MIST and EMD,23 none of the patients reported intraoperative or significant postoperative pain. Three patients reported very limited discomfort in the first 2 days after surgery. Fourteen of 15 described the first postoperative week as uneventful, reporting that they had no feeling of having been surgically treated after the second postoperative day.

In a controlled study on the additional benefit of EMD or EMD/BMDX to M-MIST alone,28 none of the patients reported experiencing intraoperative or postoperative 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 group (VAS 11.5 ± 0.7), and by 4 patients of the M-MIST EMD/BMDX group (VAS 12.3 ± 3.1). Few patients needed pain control medications: 3 patients from the control group (average number of tablets 0.4 ± 0.7, maximum 2), 4 patients from the M-MIST group (average 0.3 ± 0.6, maximum 2), and 4 patients from the EMD/BMDX group (average 0.5 ± 1.0, maximum 3).

In Table 3 are reported some surgical and postsurgical parameters from 4 studies. Two studies were performed applying the traditional large papilla preservation flaps with bioresorbable barriers37 or amelogenins.43 The other 2 studies were performed using the minimally invasive surgeries in combination with amelogenins.24,28 This historical comparison clearly evidences differences in most of the parameters among the 4 studies. Surgical chair-time was the longest when large papilla preservation flaps and barriers were applied, shorter when large papilla preservation flaps were combined with amelogenins, by far the shortest when M-MIST and amelogenins were used. The number of subjects reporting postoperative interference with daily activities, discomfort, and pain was...
A step-by-step surgical approach based on evidence and on clinical experience has been built up to help clinicians in planning the proper regenerative approach to periodontal defects. The following clinical flow charts were developed, also taking into account the scientific contributions on surgical and postsurgical events, such as chair time, side effects, and postoperative pain. In other words, the idea is to apply to a given periodontal defect the best performing procedure with the minimum load of intra- and postoperative side effects and morbidity.

Clinical Strategies

Periodontal regeneration in intrabony defects has been successfully attempted with a variety of different regenerative materials and surgical approaches. Controlled clinical trials report added benefits in terms of clinical attachment level gain as compared with open flap debridement alone.15-17 However, comparisons among some of the cited regenerative approaches failed to demonstrate a clear superiority of one of the tested materials. The existing evidence, therefore, does not support the choice of one superior approach among the different regenerative strategies.

From a clinical standpoint, clear-cut differences are to be highlighted among the various surgical proposals. The traditional papilla preservation flaps20,21 were designed as wide and very mobile flaps to allow for ample access to the defects, for perfect visibility of the surgical field, for easy allocation of biomaterials, and for the coronal positioning of soft tissues to cover barriers and biomaterials often overfilling the defects. The MIS1 and the MIST,4,24 on the contrary, were designed to reduce flap extension and mobility as much as possible, so as to increase blood clot and wound stability and reduce invasiveness and patient morbidity. A further development of the surgical approach ended into the M-MIST,5,28 where only a tiny buccal flap is elevated. It is clear that such a flap is not designed to allow for the positioning of a barrier, but easily allows for the use of biologicals or grafts.
The suturing approach is chosen according to the type of regenerative strategy applied (Flow chart 4. Strength of recommendation B). It will consist of a single internal modified mattress suture when an M-MIST or an MIST approach is chosen and amelogenins alone are applied.4,5,23,24,28 It will consist of a combination of 2 internal mattress sutures applied at the defect associated with the interdental area to reach primary closure of the papilla in the absence of any tension when a large papilla preservation flap with a periosteal incision is used in association with a barrier or a graft or a combination.7,18,20-22

The surgical procedure is preferably performed with the aid of magnification, such as loops or an operating microscope.6-8 Microsurgical instruments and materials should be used to complement the normal periodontal set.

Postsurgical and early home care protocols are directly derived from the experiences developed by running many controlled clinical trials (strength of recommendation A).22,36-40,43 An empirical protocol for the control of bacterial contamination consisting of doxycycline (100 mg twice a day for 1 week), 0.12% chlorhexidine mouth rinsing 3 times per day, and weekly prophylaxis is prescribed. Sutures are removed after 1 week. Patients are requested to avoid normal brushing, flossing, and chewing in the treated area for periods of 6 to 10 weeks. A postsurgical soft toothbrush soaked in chlorhexidine is adopted from week 1 to gently wipe the treated area. Nonresorbable membranes are removed after 6 weeks. Patients can resume full oral hygiene and chewing function in the treated area 2 to 4 weeks after membrane removal or when bioresorbable membranes are fully resorbed. Patients treated with amelogenins resume full oral hygiene after a period of 4 to 5 weeks. At the end of the “early healing phase,” patients are placed on a 3-month recall system.
A general suggestion to avoid any invasive clinical maneuver, such as hard subgingival instrumentation, restorative dentistry, orthodontics, and additional surgery, for a period of about 9 months is also part of a strategy that is aimed at optimizing the clinical outcomes of periodontal regeneration.

CONCLUSIONS
Minimally invasive surgery might be considered a true reality in the field of periodontal regeneration. Cohort studies and randomized controlled clinical trials have demonstrated its potential to greatly improve the periodontal conditions of sites associated with intrabony defects, proving its efficacy. These clinical improvements are consistently associated with very limited morbidity to the patient during the surgical procedure, as well as in the postoperative period. Chair time required to perform such a surgery is by far shorter than the chair time required for more conventional surgical approaches. Minimally invasive surgery, however, cannot be applied in all cases. A stepwise decisional algorithm should support clinicians in choosing the proper approach.

REFERENCES


