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Review Article

Minimally Invasive Surgical Approaches in the Treatment of Intrabony Defects. A Literature Review.

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Abstract
The aim of this literature review is to present the minimally invasive surgical techniques for the regeneration of intrabony defects and the impact of these surgical procedures on the clinical outcomes. Less invasive surgical procedures lead to a more uneventful postoperative healing and to reduced patients' morbidity. The introduction of these techniques under the use of magnification tools permits gentle tissue manipulation performing minimal incisions and flap elevations in the field of surgical treatment of intrabony defects. Minimally invasive surgical techniques induce minor surgical trauma and improve the wound stability with favorable results in terms of clinical outcomes and patients' comfort. The defect anatomy, patient-centered factors and the various biomaterials applied are considered. Recent evidence conclude that the adjunctive use of regenerative materials seems to have a less determinant effect on the clinical performance of minimally invasive surgical techniques. In addition, more studies are required to investigate the clinical effectiveness on the treatment of intrabony defects of these surgical techniques compared to the conventional papilla preservation flap techniques.

Keywords
Minimally Invasive Surgery, Tissue Healing, Intrabony Defects, Surgical Trauma

Declaration of Conflicting Interest
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Introduction
Last decades, less invasive surgical procedures that could lead to a more uneventful postoperative healing period and to reduced patients' morbidity was of the most important objectives of the clinicians. The introduction of the operating microscope in surgery served this purpose and gave the surgeons the chance to perform the principles of conventional surgical procedures in a less extensive and more precise way[1,2]. The potential of gentle tissue manipulation under magnification was called minimally invasive surgery[3] and, gradually, the concept of minimal surgical trauma was applied in the field of periodontal surgery[4].

As it is already known, periodontitis extends apically towards the tooth root, causing loss of the periodontal support and alveolar bone destruction. The result is the formation of osseous defects; their morphology depends mainly on the presence of the microbial plaque and local anatomical factors. Infrabony lesions represent vertical defects, in which the base of the pocket is detected apical to the level of the alveolar crest. These lesions may be related to higher risk of progression of periodontal disease, as they tend to present deeper residual pocket depth after non-surgical periodontal therapy [5]. Thus, a variety of surgical approaches and regenerative materials were developed in order to treat the residual defects [6]. Conventional flap surgery in combination with regenerative materials such as membrane

barriers, bone grafts, Enamel Matrix Derivatives, has been proved very effective for the regeneration of intrabony defects [7-9].

Recently, the progress in the field of magnification led to new less invasive periodontal surgery techniques. Minimally invasive surgery techniques are characterised by small incisions, limited flap reflection and suturing for primary wound healing. Based on the principle of papilla preservation techniques [10] which was to maintain the interdental papilla tissue as intact as possible, researchers introduced and evolved new surgical approaches for periodontal regeneration [11-15]. The less invasive surgical procedures demonstrated favorable clinical outcomes in the treatment of intrabony defects, even in esthetic areas [12,16]. In addition, the minimal surgical trauma and the reduced chair time made them better accepted from the patients and improved their perception over surgical procedures. [16] These new perspectives led more clinicians to perform minimally invasive surgical techniques for the treatment of intrabony lesions, when it was indicated.

The aim of this literature review is to present the minimally invasive surgical techniques for the regeneration of intrabony defects and the impact of these surgical procedures on the clinical outcomes.

Minimally Invasive Surgical approach (MIS)

A minimally invasive surgical (MIS) approach was first introduced by Harrel [11,12]. The initial incision is made intrasulcularly around the teeth adjacent to the osseous defect, with the blade parallel to the long axis of the root. Subsequently, an incision, usually on the lingual aspect, is performed in order to connect the two intrasulcular incisions. The interdental papilla is sharply dissected from the underlying bone and small flaps are reflected buccally and lingually. The flaps reflection is followed by the removal of the connective and granulation tissue within the osseous defect. This is performed with the use of a blade and small curettes, as well as with an ultrasonic scaler, which is also used for the initial root debridement. The remaining granulation tissue is shredded and removed with a mechanical instrument and the root planning is refined with finishing burs. In order to obtain primary closure of the wound, a vertical mattress suture is used to close the flaps [11,12,16].

Minimally Invasive Surgical Technique (MIST)

In 2007, Cortellini and Tonetti [17] proposed the minimally invasive surgical technique (MIST) based on the MIS combined with the modified papilla preservation technique (MPPT) or the simplified papilla preservation flap (SPPT) [18]. The width of the interdental space determines the choice of the surgical approach; if it is ⩽ 2 mm the SPPT is used, whereas if it is wider > 2 mm, the MPPT is performed. The SPPT consists of an oblique incision close at the buccal side of the interdental papilla col, while in the MPPT a horizontal incision at the buccal side of the papilla is performed. Two intrasulcular incisions extended buccally and lingually of the two teeth neighboring the defect, are made. The mesio-distal extension of the intrasulcular incisions is as limited as possible and two small full-thickness flaps are reflected in order to expose 1-2 mm of the bone crest. Vertical releasing incisions are made when better reflection of the flaps is demanded. The defect debridement and root planing follow with the use of small curettes and power- driven instruments. Finally, the suturing of the flaps is achieved with a single modified internal mattress suture, while the vertical incisions when performed, are sutured with simple passing sutures. The surgical procedures are performed with an operative microscope [14,16,19].

Modified Minimally Invasive Surgical Technique (M-MIST)

In order to further reduce surgical trauma, Cortellini and Tonetti [15] described the modified minimally invasive surgical technique (M-MIST) in 2009. This technique is an improved and less invasive version of the MIST. As in the MIST, MPPT or SPPT is used to access the defect adjacent to interdental papilla. The interdental incision is extended intrasulcularly at the buccal aspect of the involved teeth. A very small triangular flap is reflected to expose the coronal part of the bone crest. The granulation tissue that fills the defect is moved away with the use of a micro-blade to split it from the interdental tissues. The incisions are not extended to the palatal tissues. After the removal of the granulation tissue underneath the papilla, the defect debridement and root planing is performed using micro curettes and power driven instruments. The access is achieved through a buccal window in order to thoroughly debride the defect and the roots, with respect to the papillary fibrous attachment. Afterwards, a single modified internal mattress is performed to close the flap. All these surgical procedures were carried out with the aid of an operative microscope [15,16].

Single-Flap Approach (SFA)

The same year when M-MIST was introduced by Cortellini and Tonetti (2009), a similar surgical technique was proposed by Trombelli et al. [20]. This technique consists of a limited elevation of a mucoperiosteal flap buccally or lingually, depending on the extension of the defect. Using a periodontal probe, the extension and the morphology of the defect is evaluated. Subsequently, sulcular incisions are performed, following the gingival margin of the teeth neighboring the surgical area. Following the contour of the underlying bone crest, a diagonal or horizontal butt-joint incision is made. The spot of this incision depends on the height of the interdental tissues. Taking this into account, the higher the

interdental papilla is, the more apically the incision is performed, but always at least 1 mm coronal to the bone crest. In this way, an envelope flap, without releasing incisions, is elevated and the supracrestal soft tissues, as well as the rest of the papilla remain undetached. After the reflection of the flap, the debridement of the defect and the instrumentation of the roots follow, using curettes and mechanical instruments. For the reposition of the flap, firstly, a horizontal internal mattress suture is placed, and then a second vertical or horizontal internal mattress suture, in a more coronal spot of the flap and the papilla, is performed to achieve primary closure. The surgical procedure is carried out with the aid of x 2.5 magnifying loupes [20].

Videoscope - Minimally Invasive Surgery (V-MIS)

The principal feature of the minimally invasive surgery techniques is the small incisions and the tiny flaps. Although these techniques limit the surgical trauma, clinicians need to deal with smaller surgical area than the one created in conventional flap access. For this reason, Harrel [11] in 1995 performed the MIS with the aid of surgical telescopes (loupes) and later Cortellini and Tonetti [14] introduced the MIST with the use of the surgical microscope. Nevertheless, the inadequate magnification of the loops and the impractical use of the surgical microscope in clinical practice, made the minimally invasive surgery techniques less acceptable from the clinicians. To overcome this issue, Harrel [21] in 2013 suggested the use of a videoscope flexible insertion tube with a digital camera to better visualize the surgical site. A flow of gas over the end of the videoscope keeps away the blood and debris and prevents the lens from being blurred through the surgical procedure, providing a clear image of the surgical area on the monitor. In addition, a carbon fibre retractor makes the management of the soft tissues easier. The access to the defect is achieved with the MIS, but only a tiny buccal or lingual split thickness flap is performed, without the use of a blunt dissection. The videoscope is placed at the defect and the removal of the granulation tissue, as well as the root debridement follow. These procedures are meticulously performed as the videoscope allows better visualization of the area. Finally, a single modified vertical mattress is positioned at the base of the papilla, while the tip of the papilla is approximated with the use of a wet gauze and finger pressure [13,21].

Minimally Invasive Surgical Techniques (MISTs) and Periodontal Regeneration of Intrabony Defects

The successful regeneration of intrabony defects depends mainly on two factors: the surgical technique and the selected biomaterials [9]. Since the MISTs have been introduced in periodontal regenerative surgery, they have been combined with a variety of biomaterials such as the enamel matrix derivatives, bone grafts (demineralised freeze-dried bone allografts (DFDBA), xenografts) alone or with barrier membranes, as well as with growth factors and Platelet Rich Fibrin (PRF) [14,20,22-27]. Several clinical studies have been conducted aiming to evaluate the effectiveness of MISTs with or without the adjunctive use of biomaterials and define the best treatment modality for intrabony defects.

Enamel matrix derivative (Emdogain, EMD) has been, widely, used for the regeneration of intrabony defects alone or in combination with other biomaterials and different surgical techniques leading to various clinical outcomes [28]. Harrel et al. [25,29], in two studies with an 11-month and a 6-year follow-up, evaluated the use of enamel matrix proteins used in conjunction with MIS approach. One hundred sixty sites of intrabony defects in sixteen patients were treated and the results showed significant improvement in probing depths and clinical attachment level compared to baseline. Specifically, at 11 months the change in pocket depth (PD), clinical attachment level (CAL) and recession (REC) was 3.56, 3.57 and 0.01 mm, respectively, while at 6 years, the differences were not statistically significant. The authors concluded that the clinical outcomes remained stable over the 6 year-period and underlined the favorable results for the patients' aesthetics as they observed minimal gingival recession.

In a series of studies, Cortellini and Tonetti [14,19,30] evaluated the clinical effectiveness and the patient perception of the MISTs in conjunction with the application of EMD in the treatment of isolated and of multiple adjacent deep intra-bony defects. The clinical outcomes were assessed at the 1-year follow-up, the single defects resulted in CAL gains of 4.9 ± 1.7 mm, associated with 3 ± 0.6mm of residual probing depth and 0.4 ± 0.7mm increase of REC [14,19] whilst the multiple defects resulted in CAL gains of 4.4 ± 1.4 mm, associated with 2.5 ± 0.6mm of residual probing depth and a 0.2 ± 0.6mm increase of REC [30] .The authors concluded that MISTs combined with EMD can be applied successfully in these defects and it is an advantageous procedure in terms of patient morbidity. On the other hand, in a randomized-controlled trial when MISTs alone were compared to MISTs + EMD and MISTs + EMD + bone mineral derived xenograph (BMDX) for the treatment of isolated inter-dental intrabony defects, it was shown that the additional application of regenerative materials did not improve the results although, as it was emphasized, the power of the study was limited to detect a difference of 0.96 mm [31].

In a randomized, prospective, controlled clinical study, Ribeiro et al. [32] compared MISTs + EMD and MISTs alone for treatment of intrabony defects in a group of 14 patients. Similar and significant results in terms of changes in CAL, PD, REC and radiographic parameters were demonstrated in the two groups, at 3 and 6 months of follow-up. Thus, it was shown that in this type of bony defects EMD did not

offer an additional benefit to MISTs.

Videoscope assisted minimally invasive surgery (V-MIS) in combination with EMD and DFDBA was also performed for the regenerative treatment of 1-, 2- and 3-walled defects [13,33]. These studies demonstrated statistically significant improvements of the clinical measures compared to baseline at 6, 12, and 36 months, postoperatively [13,33,34]. It is worth reporting that V-MIS led to minimal REC and, in some cases, the soft tissue height increased compared to baseline. These results could be explained by the fact that with the videoscope tiny incisions and more effective root debridement can be ensured [13].

Moreover, MISTs were applied in conjunction with guided tissue regeneration (GTR) and a hydroxyapatite (HA)-based biomaterial [20,35]. Twenty-four intraosseous defects were treated with MISTs + HA/GTR or MISTs alone and the clinical outcomes, in terms of CAL gain, PD reduction and REC increase were assessed at 6 months. It was concluded that MISTs with and without HA/GTR should be considered as a valuable minimally invasive approach in the treatment of deep intraosseous periodontal defects.

MISTs were also been evaluated with growth factors. In a randomized, controlled, two armed study, Mishra et al.[26] assessed the impact of the addition of a recombinant human platelet derived growth factor (rhPDGF-BB) gel on the efficacy of MISTs. The results of the study showed significant PD reductions and CAL gains from baseline in both the groups, MISTs alone and MISTs + rhPDGF-BB, but no statistically significant inter-group differences were observed, at 6 months postoperatively. Thus, the improvement in clinical and radiographic parameters was attributed to the performed surgical technique. Recently, another randomized clinical trial conducted to investigate the outcomes of MISTs with or without PRF for the treatment of isolated intrabony defects led to similar results concerning the additional use of growth factors [27]. Although the thirty-six defects treated in thirty-six patients showed comparable improvement in clinical and radiographic parameters at the 6-month follow-up, the authors concluded that, due to the limitations of the study design such as the small sample size, and the short observation period, the use of PRF could not be excluded.

Discussion

Minimally invasive surgical techniques gave a new perspective in periodontal regeneration of isolated and multiple intrabony defects aiming to reduce the invasiveness of the surgery and the patients' morbidity and chair time. The use of microsurgical instruments and high magnification [36], as well as the introduction of videoscope [21], made the single flap MISTs a feasible treatment modality in isolated 1-, 2- and 3-wall interproximal defects, which can be accessed and effectively debrided through a buccal or lingual flap window [13,15,20]. Nevertheless, even with the aid of magnification, the tiny unilateral flap elevation often enough isn't adequate to access the defects that extend to the opposite side of the buccal or lingual flap [15,20]. In these cases, the flap design has to be modified to a double flap MISTs with the elevation of the interdental papilla and even vertical incisions for the adequate exposure of the defect [14,16,19]. The double flap MISTs was considered suitable for the approach of intrabony defects with pure 3-wall, or shallow 2- and/or 1-wall subcomponents [19]. Though, in cases that severe defects are extended in almost all the sides of the tooth and/or a deep buccal/lingual bone dehiscence is present, a larger flap reflection and possibly vertical or periosteal incisions are demanded for the complete exposure of the defect and the application of the selected regenerative biomaterials [6,16]. Thus, it seems that the extension of the defect determines the choice between single or double flap MISTs and their limitations over deeper and more extensive defects.

The less, as possible, increase of REC after periodontal surgery of intraosseous defects is a great challenge for the operators, aiming to fulfil the patients' demands over aesthetics, especially when the defect concerns the anterior aesthetic zone. The limited surgical trauma and the gentle manipulation of the soft tissue with MISTs led to minimal [14,19] and even not significant recession of the gingival margin compared to the baseline values [13,15,20]. This is in accordance with the results of the meta-analysis by Clementini et al. [37], demonstrating a mere and not statistically significant REC increase, using the MISTs principles. In a case series, in order to maintain the gingival margin stable after the surgical treatment of vertical defects, the authors performed an atraumatic caused-related therapy and subsequently a papilla preservation flap (PPF) technique in combination with a coronally advanced envelope-type buccal flap. After 1 year the shift of the gingival margin was nor statistically neither clinically significant [38]. Subsequently, both the MISTs and conventional PPF techniques can be considered that they impair less the patients' aesthetics and therefore have to be preferred over the traditional flap designs [39]. Nevertheless, there is need to clarify if MISTs could demonstrate the same aesthetic outcomes in all types of defects. Some studies indicated that neither the morphology of the defect [13,15,40] nor the gingival biotype [40] could be considered as predictors for increased recession, whenever MISTs were performed. In their study, Farina et al. [40] concluded that the apical shift of the gingival margin after the periodontal surgery is depended on the presurgical interproximal PD and suggested the additive use of biomaterials in deep defects located in aesthetic areas. Cosyn et al. (2012) [24], in contrast, claimed that non-supportive defects and a thin-scalloped gingival biotype related to greater postsurgical REC increase. Thus, more studies are necessary to determine the risk factors that may compromise the patients' aesthetics after the periodontal surgical treatment.

The application of MISTs in the treatment of intrabony defects induced subtle postoperative pain and decreased the patients' morbidity [37]. The less invasiveness and the minimal surgical trauma caused by MISTs approach reduced the patients' discomfort and need for painkillers consumption, irrespective of the type of regenerative materials applied [6]. Moreover, the perception of the post-surgical pain and the amount of analgesics intake by the patients, as well as the overall chair time found to be significantly lower for the MISTs procedures in comparison with the conventional surgical techniques [6,40]. In addition to the favorable patient-centered outcomes, a low percentage of postoperative adverse effects was documented during the healing period [19,34,41]. Primary wound closure was achieved in all cases, after the surgical procedure with MISTs for the treatment of both single and multiple sites of defects. One week later, the rate of wound closure remained high at 95% and 100%, respectively [19,30]. In their study, Trombelli et al. (2009) [20], noted the absence of membrane exposure in patients treated with bioresorbable membranes and bone graft, although two smokers were included. This was another benefit of MISTs, which increased their effectiveness in the treatment of intrabony defects, as membrane exposure has been proved to jeopardize the clinical outcomes of regenerative therapy [20,42]. The mild postoperative pain and the low morbidity rendered MIS a patient-friendly procedure and improved their perception over surgical treatment.

The successful application of MISTs requires the use of magnification instruments for the adequate visualization of the surgical field [12,14,21]. Although the operative microscope and the videoscope can serve this purpose better than the loupes, their cost could be a major consideration for the clinicians [13,21]. Moreover, the surgical procedure under high magnification and the delicate manipulations of soft tissues, render MISTs as clinically sensitive techniques and demand the clinicians' clinical skills and experience in order to be efficient.

Defect anatomy is another factor that its effect on the clinical performance of MISTs has to be further investigated. In particular, intrabony defects with more residual bony walls are associated with greater CAL gain and decreased percentage of failure in the clinical outcomes when MISTs were performed [24,43]. Inconsistently with these results, in their study Harrel et al. [13] used MISTs with the aid of videoscope and concluded that the number of residual bony walls did not have a significant impact on the gain of CAL. Concerning the influence of the depth and the angle of the defects in the effectiveness of MISTs, the findings are also contradictory. Specifically, Cortellini et al. [30] claimed that defects with wider radiographic angle at the baseline demonstrated less CAL gain, while the depth of the 3-wall subcomponent did not seem to affect the clinical results. On the contrary, in another study of the same authors the relation between defect angle and CAL gain was not found significant, while deeper 2- and 3-wall subcomponents showed more favorable clinical outcomes in terms of CAL gain [43]. The differences in the results of these studies, can be attributed to the small number of the participant patients. Thus, more studies with greater sample size are needed to clarify whether the defect anatomy can play a role as a determinant in the treatment of intrabony defects with MISTs.

Patient factors, like poor oral hygiene and smoking, have been established to have a negative impact on the clinical outcomes of periodontal regeneration procedures [44,45]. Although most of the studies, in which MISTs were performed, included patients with well controlled full mouth plaque and bleeding scores, the presence of plaque was related with reduced CAL gain after the periodontal surgery treatment. In addition, the occurrence of postoperative complications and the non-compliance with the scheduled recall sessions were also predictors for failures in CAL and vertical radiographic bone gains [23,24]. It remains questionable if smoking can influence the clinical efficacy of MISTs. Trombelli et al (2018) [46], observed similar outcomes in terms of CAL gain, residual PD and REC increase between smokers and non-smokers, but significantly better early wound healing for the non-smokers group. Nevertheless, these clinical results seem to be inferior for heavy smokers (>10 cigarettes per day). The inclusion of light smokers and the small sample size can be considered as limitations of this study and more investigations are needed for firm conclusions.

The last decades, conventional surgical techniques in conjunction with various biomaterials have been widely used for the regeneration of bone defects that remain after the cause related therapy, with significant benefits in terms of defect filling and periodontal attachment gain [9,47,48]. MISTs have been successfully combined with biologically active materials such as amelogenins [14,19,25,29,30,32] and growth factors [26,40], bone replacement grafts [23,24], PRF [27] or in conjunction with two [13,20,31,33,35] or more [31] different biomaterials for the periodontal regeneration of intrabony defects. Cortellini in 2012 [16] proposed different regenerative strategies with MISTs depending on the defect morphology. Thus, the single flap MISTs can be applied in any defect anatomy either alone or combined with EMD. In addition, the double flap MISTs suggested to be performed in conjunction with EMD for the treatment of self-supporting defects and with EMD and graft for non-containing defects. Nevertheless, the additional use of regenerative materials does not seem to significantly improve the clinical outcomes of MISTs, as it is resulted from the available randomized clinical trials (RCTs) [26,27,31,32,35]. In a meta-analysis of 4 RCTs, the mean difference between the MISTs plus biomaterials and MISTs alone group in terms of CAL gains, PD reduction and REC increase was 0.24 mm (95%CI: -0.32–0.71, p=0.32), 0.20 mm (95%CI: -0.26–0.66, p =0.40) and 0.03 mm (95%CI: -0.22–0.28, p=0.81), respectively [49]. None of these differences was found

to be statistically significant, confirming the fact that extra additives to MISTs do not provide further clinical benefits. On the contrary, the impact of biomaterials is important when they are combined with conventional surgical techniques [9]. Although, papilla preservation flap techniques improved the clinical performance of conservative surgery in the treatment of intrabony defects [39], regenerative periodontal therapy still leads to significantly superior clinical outcomes [9]. The regenerative potential of MISTs as a stand-alone protocol in the treatment of intrabony defects may be a consequence of the primary wound closure and the optimal wound and blood clot stability [14,19,20]. In addition, the integrity of the interdental tissues can ensure the necessary blood supply and space for the formation of the blood clot [15,20]. These factors have been documented in experimental studies to be the determinants for periodontal regeneration and the clinical efficacy of MISTs can be attributed to them [50-52]. Though, the small sample sizes of the available RCTs and the short follow-up periods do not allow the extrapolation of definitive conclusions.

A practical question would be if the evolved flap design of MISTs could be considered more conducive in the surgical treatment of intrabony defects in comparison with the conventional papilla preservation flap techniques. This was the main objective of two RCTs comparing the effectiveness of the single flap MISTs with a double flap PPF technique with or without the use of regenerative materials [40,53]. In two groups of fourteen patients, Trombelli et al. [53]. compared buccal MISTs and SPPT/MPPT for the treatment of intrabony defects. Although the MISTs group demonstrated significant greater CAL gain and PD reduction than the PPF group at a 6-month follow-up, these values were not statistically significant, when the comparison was adjusted to the presurgical CAL and PD ones of the two groups. Both CAL gain and PD reduction were significantly different for the two groups compared to the baseline. REC increase was similar for the two groups at 6 months, but statistically significantly greater only for the MISTs group compared to the baseline. Authors had to take into account that the two groups were different concerning the age, number of smokers, pocket depth and bleeding score positive sites, though it was considered to have a significant impact only on the PD reduction. In another randomized controlled trial, Schincaglia et al. [54] assessed clinically and radiographically the efficacy of a single buccal or oral flap elevation MIS technique and a double flap papilla preservation technique (SPPT, MPPT), combined with a recombinant human platelet derived growth factor (rhPDGF-BB) and ß-tricalcium phosphate (ß-TCP), in the treatment of 1-,2-, and 3-wall defects. The two groups demonstrated significant changes in CAL, PD, REC and radiographic parameters at a 6-month follow up, but they were not significantly different between the two groups. Although the CAL gain and PD reduction were slightly greater for the MISTs group, it included significantly fewer 1 -wall defects than the PPF one. Nevertheless, the patients from MISTs group reported significantly lesser postoperative pain and painkillers consumption, while the early wound healing was better. This is attributed to the less invasiveness and the limited flap extension of MISTs that provide minimal trauma and better wound stability [40]. It can be concluded that MISTs are at least as effective as the conventional PPF techniques, though this conclusion has to be further examined in more studies that will directly compare these techniques.

Conclusion

Minimally invasive surgical techniques decreased significantly the surgical trauma in soft tissues and the rates of wound failure after the periodontal surgery. As a consequence, many favorable clinical outcomes were observed in studies in which MISTs were applicated, while patients' perception of periodontal surgery was improved. The adjunctive use of regenerative materials seems to have a less determinant effect on the clinical performance of MISTs. It is critical for the clinicians to estimate adequately the defect morphology in order to perform the most suitable surgical technique. Finally, more studies are required to evaluate the potential superiority of MISTs over the conventional ones.

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