Check for updates

Received: 23 November 2023 | Revised: 10 March 2024 | Accepted: 14 March 2024

DOI: 10.1111/jcpe.13984

ORIGINAL ARTICLE

Journal of Clinical Periodontology WILEY

Minimally invasive non-surgical periodontal therapy of intrabony defects: A prospective multi-centre cohort study

Jaimini Mehta[1] | Marco Montevecchi[2] | Ruben Garcia-Sanchez[1] | Olanrewaju Onabolu[3] | Antonio Liñares[4] | Fernando Eriksson[5] | Carlo Ghezzi[6] | Camilla Donghi[6] | Emily Ming-Chieh Lu[1] | Luigi Nibali[1,7]

[1]Periodontology Unit, Centre for Host Microbiome Interactions, Faculty of Dentistry, Oral & Craniofacial Sciences, King's College London, London, UK

[2]Division of Periodontology and Implantology, Department of Biomedical and Neuromotor Sciences, School of Dentistry and Dental Hygiene, University of Bologna, Bologna, Italy

[3]Private Practice, Claremont Dental Practice, Twickenham & Ten Dental Clapham, London, UK

[4]Unit of Periodontology, School of Medicine and Dentistry, University of Santiago de Compostela, Santiago de Compostela, Spain

[5]Private practice, South Coast Dental Specialists, Dorset, UK

[6]Private practice, "StudioCarloGhezzi", Milan, Italy

[7]'Ravenscourt Dental Practice' & 'The Dentist', London, UK

Correspondence
Luigi Nibali, Centre for Host Microbiome Interactions, King's College London, London, UK.
Email: luigi.nibali@kcl.ac.uk

Abstract

Aim: To assess the potential benefits of minimally invasive non-surgical therapy (MINST) in teeth with intrabony defects and to explore factors associated with the outcomes.

Materials and Methods: A multi-centre trial was conducted in 100 intrabony defects in periodontitis patients in private practice. Steps 1 and 2 periodontal therapy including MINST were provided. Clinical and radiographic data were analysed at baseline and 12 months after treatment, with the primary aim being change in radiographic defect depth at 12 months.

Results: Eighty-four patients completed the 12-month follow up. The mean total radiographic defect depth reduced by 1.42 mm and the defect angle increased by 3° (both $p < .05$). Statistically significant improvements in probing pocket depth (PPD) and clinical attachment level (CAL) were seen at 12 months compared to baseline ($p < .001$). Fifty-six defects (66.7%) achieved pocket closure (PPD ≤ 4 mm) and 49 defects (58.3%) achieved the composite outcome (PPD ≤ 4 mm and CAL gain ≥3 mm). Deeper and narrower angled defects were positively correlated with radiographic and clinical improvements, respectively.

Conclusions: Improvements in clinical and radiographic outcomes were seen after MINST. This study highlights the generalizability and wide applicability of this approach, further supporting its effectiveness in the treatment of intrabony defects. Clinical trial registration: NCT03741374. https://clinicaltrials.gov/study/NCT03741374?cond=minimally%20invasive%20non%20surgical%20therapy&locStr=UK&country=United%20Kingdom&distance=50&rank=2.

KEYWORDS
debridement, intrabony defects, minimally invasive non-surgical therapy (MINST), periodontitis

Clinical Relevance

Scientific rationale for study: The predictability, generalizability and wide applicability of minimally invasive non-surgical therapy (MINST) in intrabony defects remains unclear. Thus, the aim of this study was to assess the effect of MINST in intrabony defects and explore factors influencing treatment response.

This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.
© 2024 The Authors. *Journal of Clinical Periodontology* published by John Wiley & Sons Ltd.

Principal findings: MINST resulted in considerable clinical and radiographic improvements in intrabony defects across different centres and operators. Defect morphology influenced clinical and radiographic outcomes.

Practical implications: The role of MINST in healing intrabony defects should be emphasized as a viable treatment approach. Further research in the form of controlled multi-centre studies should be conducted to validate these findings.

1 | INTRODUCTION

Intrabony defects are associated with periodontal disease progression and tooth loss (Rams et al., 2018). Despite improvements, intrabony defects traditionally persist following Step 1 and Step 2 periodontal therapy (Sanz et al., 2020) because of difficulties in sub-gingival biofilm removal. The presence of uneven bony architecture and unfavourable anatomy such as those found in intrabony defects and furcations are indirectly associated with residual pockets (Papapanou & Tonetti, 2000). It is well established that sites with residual pockets ≥5 mm are at risk of further attachment loss and tooth loss (Claffey & Egelberg, 1995; Matuliene et al., 2008). Because of the increased risk of disease progression associated with intrabony defects, surgical intervention is often needed beyond cause-related therapy to avoid further deterioration of the dentition (Reynolds et al., 2015).

Clinical practice guidelines for the treatment of Stage I–III periodontitis recommend regenerative/reconstructive surgery for residual pockets associated with intrabony defects ≥3 mm deep (Sanz et al., 2020). Studies have shown that the use of biomaterials may not be essential for achieving regeneration (Cortellini et al., 2022; Trombelli et al., 2010). Instead, establishing the best local environment to harness the intrinsic potential of the periodontal tissues has been suggested (Liu et al., 2016). Despite its successes, regenerative surgery is associated with morbidity, complications and high material costs. Outcomes are not always predictable, with clinical failures and incomplete success reported (Needleman et al., 2006). As a result, procedures have transitioned towards more patient-friendly, minimally invasive approaches, a concept derived from medicine.

In periodontology, minimally invasive interventions were first applied to surgical treatment by limiting flap extension to reduce trauma and enhance blood clot stability (Harrel, 1999). These principles have also been applied to non-surgical periodontal therapy with the emergence of minimally invasive non-surgical therapy (MINST). MINST has been proposed as an alternative treatment approach for intrabony defects, aimed at reducing tissue trauma and optimizing wound healing while avoiding surgical incisions and suturing. In a retrospective review of 35 intrabony defects treated with MINST, a 3 mm decrease in radiographic intrabony defect depth was observed. Mean reduction in probing pocket depth (PPD) and clinical attachment level (CAL) gain were 3.12 and 2.78 mm, respectively, while recession increase was minimal (Nibali et al., 2015). Clinical and radiographic improvements achieved at 1 year remained stable throughout 5 years of supportive periodontal therapy. Only 2 of the 21 treated defects exhibited residual PPD > 5 mm, requiring further intervention (Nibali et al., 2018). Other studies have shown similar promising clinical and patient-reported outcomes following MINST (Aimetti et al., 2017; Anoixiadou et al., 2022; Ribeiro et al., 2011).

Despite emerging evidence, few studies have been published on MINST, and further clarity is needed regarding its effectiveness. Among the questions still to be answered are the generalizability of findings, as most studies so far have been carried out by the same operators, as well as the potential effect of defect characteristics on clinical and radiographic outcomes. Therefore, the aim of this study was to assess the potential benefits of MINST in teeth with intrabony defects and to explore the potential effects of centre (operator/instruments used), patient and defect characteristics on 12-month outcomes.

2 | MATERIALS AND METHODS

2.1 | Patient population

This was a prospective cohort multi-centre study, carried out by seven specialist periodontists and one hygienist in 11 private practices across the United Kingdom, Italy and Spain. One hundred consecutive patients referred by their general dental practitioners to the study therapists for periodontal treatment were recruited between February 2019 and March 2022. Each patient gave written consent to take part in the study.

The following inclusion criteria were considered for patient recruitment:

- Age between 18 and 70 and diagnosed with periodontitis (Tonetti et al., 2018).
- One or more intrabony defect with PPD and CAL > 5 mm
- Radiographic intrabony defect depth ≥3 mm
- Defect not associated with furcation involvement.

Patients who had undergone periodontal treatment at the study site, defined as a single intrabony defect meeting the inclusion criteria and selected for MINST, within the last 12 months were excluded. Additionally, individuals taking anti-inflammatory, anticoagulant, immunosuppressant medication or systemic antibiotic therapy in the 3 months preceding the baseline examination were also excluded. Patients with medical conditions such as diabetes or transmittable diseases were not included, as were pregnant and breastfeeding women, patients with severe medical or psychiatric conditions, self-reported smokers and former smokers in the past 5 years (including electronic

1600051x, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jcpe.13984 by Test, Wiley Online Library on [04/06/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

cigarettes, vaping or similar) and those with a history of drug or alcohol abuse.

In patients presenting with more than one defect fulfilling the inclusion criteria, the intrabony defect with the deepest PPD was selected as the study site. In case of multiple defects with the same PPD, the treating clinician decided which defect was to be selected.

Ethics approval for the analysis was given by King's College London Research Ethics Committee (reference: CREC18/19-04). For sites outside the United Kingdom, a local ethics application was obtained from the relevant local ethics committee.

2.2 | Examiner calibration

All study examiners underwent a training exercise and intra-examiner calibrations before the start of the study. Duplicate examinations for PPD and recession were performed by each study examiner on five subjects each, at least 15 min apart. Agreements within 1 and 2 mm PPD were achieved in 92.2% and 98.3%, respectively, for double calibration measurements across all examiners. Inter-examiner calibration was not possible for practical reasons.

Duplicate radiographic assessments of bone levels and defect angles were carried out at least 24 h apart by a single masked examiner. Defect morphology estimation was carried out using a combination of clinical and radiographic data. The intraclass correlation coefficient (ICC) was >0.8 for all analysed parameters (Supplemental Material 1), while 100% agreement was achieved for furcation involvement and Peri-Apical Index (PAI) score (Ørstavik et al., 1986).

2.3 | Periodontal treatment and follow-ups

Patients were scheduled to attend at least six visits over a period of approximately 12 months (see flowchart in Supplemental Material 2). All patients received a comprehensive treatment plan, aimed at Steps 1 and 2 periodontal therapy (Sanz et al., 2020), including oral hygiene instructions, risk factor control and supra-gingival instrumentation. Splinting and occlusal adjustment were carried out as part of these steps if considered necessary by the treating clinician (usually in cases of occlusal interferences and mobility Grades II and III). MINST was carried out by eight different operators, including seven periodontists and one hygienist. Sub-gingival instrumentation was carried out in up to four sessions, following a modified MINST protocol (Nibali et al., 2015, 2018) in the study sites, which briefly consisted of the following:

- 2–4× magnification loupes
- Non-adrenaline-containing local anaesthetic infiltration
- Sub-papillary access of the defect to minimize trauma to the soft tissues, especially the most coronal portion of the interdental papilla
- Thorough and gentle debridement of the root surface to the base of the pocket
- Exclusive use of piezo-electric/ultrasonic devices with specific non-diamond thin and delicate tips (PS, PL1, PL2 from EMS, Nyon, Switzerland; Siroperio 1, 2, 3 and 7 from Sirona, Salzburg, Austria; Woodpecker P3 tip, Guilin Woodpecker, Guilin, China; Satelec 10Z from Acteon, UK, depending on what was available in the different study centres)
- Avoidance of 'smoothing' the root surface and performing gingival curettage
- Attempting to stimulate the formation of a stable blood clot by natural filling of the intrabony defect with blood following debridement. Subgingival rinses at the end of treatment were not used.

Patients were seen every 3 months for oral hygiene reviews and supra-gingival debridement. Comprehensive periodontal charting and sub-gingival probing of study sites following MINST occurred at 6 and 12 months.

2.4 | Clinical examination

The following periodontal measurements were taken at six sites per tooth: dischotomous full mouth bleeding score (FMBS) (Guerrero et al., 2005), PPD, recession (REC) of the gingival margin from the cemento-enamel junction (CEJ) and bleeding on probing (FMBS) (Ainamo & Bay, 1975). CAL was calculated as PPD + REC. Tooth mobility (Laster et al., 1975) and furcation involvement (Hamp et al., 1975) were also evaluated. Clinical parameters were assessed by probing using a UNC-15 periodontal probe and furcation involvement by a Nabers probe.

2.5 | Radiographic examination

Periapical radiographs of selected study sites were taken at baseline and at 12 months using the parallel technique with Rinn holders (Updegrave, 1951). Each participating practice used the same setting and exposure time for radiographs taken at both visits. An attempt was made to standardize positioning and minimize distortion of sequential radiographs, although no formal standardization procedures were followed.

Periapical radiographs from all patients included in the study were transferred into a dedicated software measurement system (Emago®, Oral Diagnostic Systems, Amsterdam, Netherlands) and analysed by one examiner (J.M.) in a masked, random order. Linear radiographic measurement analysis at all comparable sites (mesial and distal) was conducted using specific landmarks as shown in Supplemental Material 3 (Nibali et al., 2011).

Defect morphology estimation was based on clinical and radiographic data. The following categories were used (as described in Nibali et al., 2023):

Defect extension (assessed based on clinical measurements)

- Extending to mid-buccal (or mid-lingual): CAL on mid-buccal or mid-lingual surface of the affected tooth was ≥5 mm (or when the

1600051x, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jcpe.13984 by Test, Wiley Online Library on [04/06/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

TABLE 1 Baseline characteristics of included patients.

	Patients ($n = 100$)
Age (years)	53 ± 10
BMI	25 ± 5
Gender	
Male	50
Female	50
Ethnicity	
Caucasian	84
Asian	9
Afro-Caribbean	0
Mixed/other	1
Not reported	6
Periodontal diagnosis, stage	
I	0
II	0
III	77 (32 LOC, 45 GEN)
IV	23
Periodontal diagnosis, grade	
A	2
B	35
C	63
Periodontal diagnosis, extent	
Localized	32
Generalized	68
FMPS	37 ± 27%
FMBS	29 ± 24%
No. of PPD ≥ 5 mm	28.5 ± 22.5

Note: Mean ± standard deviation is reported for continuous variables. Frequency is reported for discrete variables.
Abbreviations: BMI, body mass index; FMBS, full-mouth bleeding score; FMPS, full-mouth plaque score; GEN, generalized; LOC, localized; PPD, pocket probing depth.

TABLE 2 Baseline clinical and radiographic defect characteristics.

	Study sites ($n = 100$)
Tooth type	
Incisor	16
Canine	11
Premolar	27
Molar	46
Arch	
Maxilla	34
Mandible	66
Shallow sites (5–6 mm)	12
Deep sites (≥7 mm)	88
Average PPD study site (deepest) (mm)	8.48 ± 1.76
Average CAL study site (deepest) (mm)	9.23 ± 2.04
Average recession study site (deepest) (mm)	0.75 ± 1.15
Average total radiographic defect depth (mm)	9.26 ± 3.65
Average horizontal defect depth (mm)	3.08 ± 2.06
Average intrabony defect depth (mm)	6.27 ± 2.59
Average defect angle	26.9 ± 9.34
Narrow angled (<28°)	52
Wide angled (≥28°)	48

Note: Mean ± standard deviation is reported.
Abbreviations: CAL, clinical attachment level; PPD, probing pocket depth.

radiograph clearly suggested the defect extended to mid-buccal or mid-lingual surfaces);

- Not extending to mid-buccal (or mid-lingual): CAL on mid-buccal or mid-lingual surface of the affected tooth was <5 mm.

2.6 | Statistical analysis and sample size calculation

The primary outcome measure was radiographic total defect depth reduction at 12 months. Secondary outcomes were intrabony defect depth reduction, PPD and CAL change at 12 months. Defect-related data were obtained from clinical measurements recorded at baseline, 6 and 12 months, as well as periapical radiographs taken by the treating clinician at baseline and 12 months post MINST.

The sample size was calculated based on previous observations that narrow-angled defects heal more favourably with greater defect depth reduction (Nibali et al., 2015). Assuming a defect depth reduction of 3 mm for defects with angles <28° (median baseline angle in Nibali et al., 2015) and a reduction of 2 mm for angles ≥28° (SD 2 mm), 84 defects would be required to have 90% power to show such difference between defect angles. Considering 15% drop-out rates, a sample of 100 defects in 100 patients was required. Data from all patients were entered into a spreadsheet and proofed for entry errors. The database was imported into the statistical software package IBM SPSS® 27.0. The statistical significance level was set to 5% throughout with per-protocol analysis reported. Continuous, normally distributed variables are reported as means and standard deviations. Paired *t*-test was used to detect significant changes between baseline and 12 months for the primary outcome using the patient as unit of analysis. Because the before- and after-treatment radiographs were not standardized, a correction factor was calculated using the root or crown length to adjust for vertical distortion and potential variations in radiographic images due to positioning (Liñares et al., 2006).

Descriptive data were presented by pre-specified prognostic baseline factors (age, FMPS, BMI, CAL). Per-protocol univariate analyses were carried out to test associations between potential explanatory variables (age, gender, baseline FMPS, baseline PPD and bleeding on probing (BOP), radiographic parameters, centre, treatment time) and intrabony depth reduction using one-way analysis of variance. Linear regression was then conducted to evaluate the relation of baseline clinical, radiographic and patient characteristics on the changes in intrabony defect depths. Age, baseline plaque score, tooth type, defect depth, angle, extension and centre were included as covariates. Logistic regression was carried out as secondary analysis to test the potential associations between the covariates above and clinical

1600051x, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jcpe.13984 by Test, Wiley Online Library on [04/06/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

TABLE 3 Clinical measurements of all patients that completed the 1-year follow up, across all time points.

Clinical measurements	Baseline	6 months	12 months	Δ 0–12 months	*p*-Value (baseline to 6 months)	*p*-Value (baseline to 12 months)	*p*-Value (6–12 months)
Full-mouth data							
Average PPD (mm)	3.18 ± 0.74	2.51 ± 0.58	2.42 ± 0.55	0.68 ± 0.59	<.001[a]	<.001[a,*]	.035*
Average CAL (mm)	3.68 ± 0.88	3.14 ± 0.69	3.06 ± 0.67	0.56 ± 0.44	<.001[a]	<.00[a]	.090
Number of full-mouth PPDs ≥5 mm	29	10	8	21			
Study sites (1 per patient)							
PPD (mm)	8.40 ± 1.65	4.22 ± 1.35	4.31 ± 1.44	4.17 ± 1.96	<.001[a,*]	<.001[a,*]	.531
Recession (mm)	0.87 ± 1.20	1.29 ± 1.54	1.34 ± 1.51	0.48 ± 1.21	<.001[a,*]	<.001[a,*]	.541
CAL (mm)	9.27 ± 2.00	5.52 ± 2.09	5.67 ± 2.06	3.70 ± 2.06	<.001[a,*]	<.001[a,*]	.446

Note: Mean ± standard deviation is reported.
Abbreviations: CAL, clinical attachment level; PPD, probing pocket depth.
[a]Paired *t*-test.
*Statistically significant difference at the .05 level.

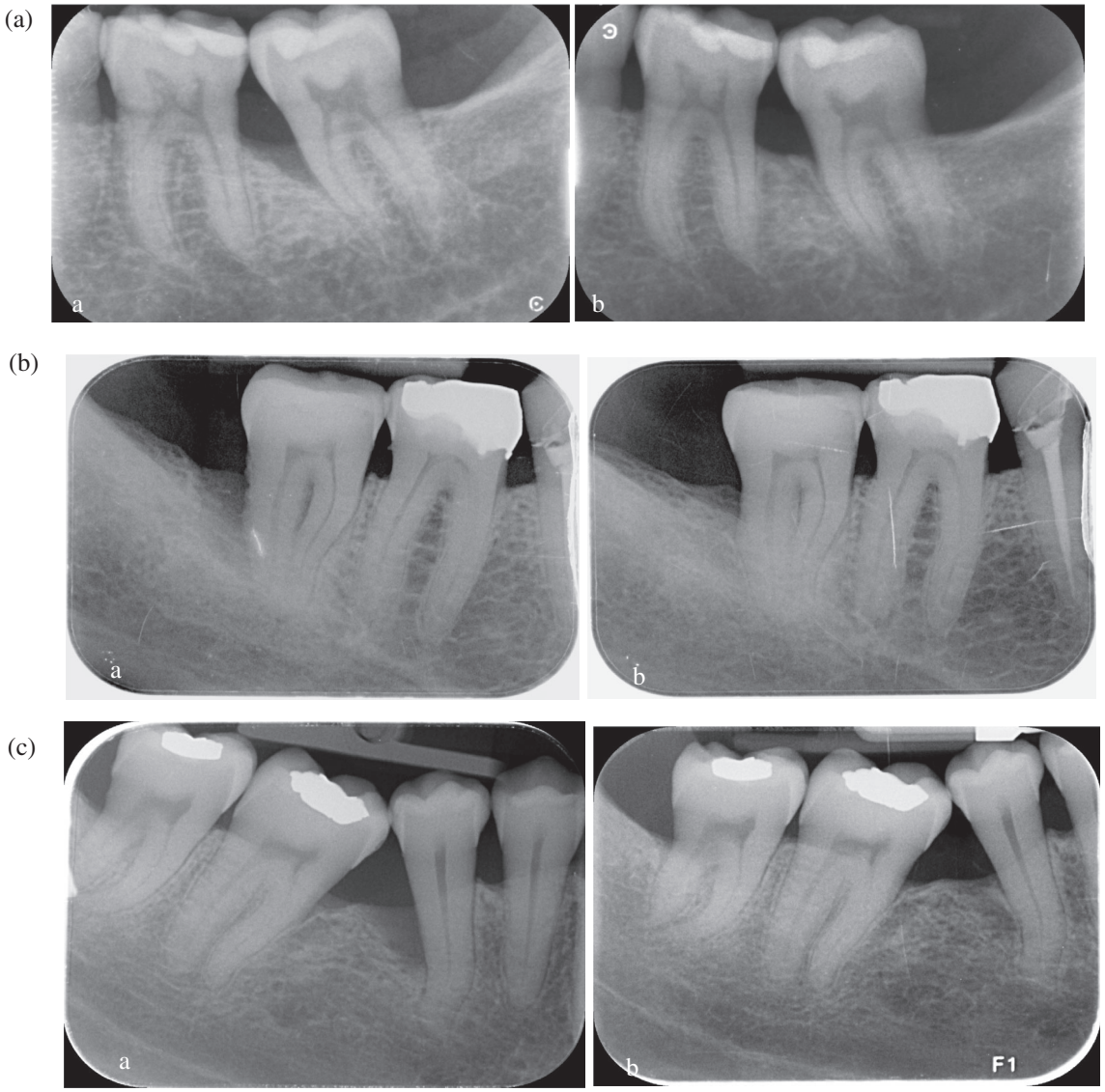


FIGURE 1 Baseline and reassessment (1-year review) radiographic images of the (a) mesial defect on lower left second molar, (b) distal defect on lower right second molar and (c) distal defect on lower right second premolar.

1600051x, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jcpe.13984 by Test, Wiley Online Library on [04/06/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

parameters at 12 months ('pocket closure', e.g., PPD ≤ 4 mm and 'composite outcome' of PPD ≤ 4 mm and CAL gain ≥3 mm).

3 | RESULTS

3.1 | Baseline characteristics

A total of 111 patients meeting the inclusion criteria were invited to participate in the study; 11 declined because of personal reasons. Recruitment continued until 100 patients were enrolled in the study. Eighty-four patients attended the 12-month assessment. Reasons for drop-outs included disruption of treatment due to the COVID-19 pandemic and relocation. Table 1 reports the baseline demographic and clinical characteristics of all patients included in the study, and Table 2 reports clinical and radiographic characteristics of the study sites at baseline. No statistically significant differences were found between baseline characteristics of the 84 intrabony defects that completed the study and the 16 defects lost to follow-up (data not reported). Statistically significant differences were detected among centres for



FIGURE 2 Baseline and 12-month post-operative clinical photographs and radiographs of distal intrabony defect LR2. Baseline probing pocket depth reduced from 12 to 3 mm on the disto-buccal aspect of the lower right lateral incisor after minimally invasive non-surgical treatment and splinting.

TABLE 4 Radiographic measurements at baseline and 12 months (adjusted with correction factor) for the 84 defects that completed the study.

Radiographic measurements	Baseline	12 months	Δ 0–12 months	*p*-Value
Total defect depth CEJ– BD (mm)	9.35 ± 3.65	8.01 ± 2.98	1.42 ± 2.55	<.001[a,*]
Horizontal component CEJ–BC (mm)	3.08 ± 2.06	3.22 ± 1.80	0.01 ± 1.66	.994
Intrabony component BC – BD (mm)	6.27 ± 2.60	4.75 ± 2.09	1.45 ± 1.84	<.001[a,*]
Intrabony angle (°)	27.2 ± 9.50	30.14 ± 11.25	2.90 ± 9.74	4.08[a,*]

Note: Mean ± standard deviation is reported.
Abbreviations: BC, bone crest; BC – BD, depth of the intrabony defect; BD, base of defect; CEJ–BC, distance from CEJ to the bone crest; CEJ–BD, distance from CEJ or restoration margin to base of the defect.
[a]Paired *t*-test.
*Statistically significant difference at .05 level.

1600051x, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jcpe.13984 by Test, Wiley Online Library on [04/06/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

TABLE 5 Regression analysis of variables associated with intrabony defect depth reduction and clinical outcomes of probing pocket depth (PPD) < 5 mm and composite outcome (PPD ≤ 4 mm and clinical attachment level gain ≥3 mm).

	Linear regression	Logistic regression	
	p-Value (standardized beta) for intrabony defect depth reduction	*p*-Value (OR, 95% CI) for PPD < 5 mm at 12 months	*p*-Value (OR, 95% CI) for composite outcome at 12 months
Age (years)	.848 (0.03)	.147 (0.96, 0.92–1.01)	.525 (0.98, 0.94–1.03)
Plaque score	.371 (−0.06)	.407 (1.01, 0.99–1.03)	.081 (1.02, 0.99–1.04)
Tooth type	.572 (−0.15)	.355 (0.70, 0.33–1.48)	.216 (0.63, 0.30–1.30)
Intrabony defect depth	<.001* (−0.87)	.569 (1.07, 0.84–1.37)	.249 (0.88, 0.70–1.10)
Defect angle (narrow vs. wide)	.952 (0.02)	.043* (0.28, 0.81–0.96)	.239 (0.49, 0.15–1.60)
Defect extension	.846 (0.08)	.546 (1.45, 0.43–4.85)	.817 (0.87, 0.27–2.79)
Centre	.436 (−0.04)	.960 (0.99, 0.85–1.17)	.083 (0.87, 0.74–1.02)
R^2	.302	.172	.207

Abbreviations: CI, confidence interval; OR, odds ratio.
*Statistically significant difference at the .05 level. Nagelkerke R^2 is presented for the logistic regressions.

baseline plaque score ($p < .001$) and radiographic defect depth ($p = .028$).

Average treatment time per study site was 10 min.

3.2 | Treatment outcomes

Reductions in full-mouth mean PPD, CAL and the number of PPDs ≥ 5 mm were detected between baseline and both 6- and 12-month examinations ($p < .001$) (Table 3). Statistically significant improvements in baseline PPD, CAL and REC were seen in the study sites at 6 and 12 months ($p < .001$), while no differences were detected in any of the clinical parameters between 6- and 12-month follow-ups (Table 3). Figures 1 and 2 show considerable post-treatment radiographic improvements, with partial to complete resolution of these defects between baseline and 12 months.

Following MINST, 67% and 79% of defects achieved 'pocket closure' (PPD ≤ 4 mm and PPD ≤ 5 mm, respectively), whereas 58% of study sites achieved the composite outcome of PPD ≤ 4 mm and CAL gain ≥3 mm at 12 months (Trombelli et al., 2020). Also, 54% of defects reached the outcome 'pocket closure' combined with no BOP at 12 months. The percentage of 'pocket closure' at 12 months was identical for both shallower (PPD < 7 mm) and deeper (PPD ≥ 7 mm) sites (66.7% for both).

Minor differences were found between raw and adjusted radiographic measurements (after application of the correction factor), suggesting that only minimal distortion occurred despite non-standardized radiographs. Statistically significant reductions were seen in radiographic intrabony component and overall defect depth and an increase in radiographic angle between baseline and both 6-month and 12-month follow-ups (all $p < .001$, Table 4). Mean radiographic total defect depth reduction and intrabony defect depth reduction were 1.42 and 1.45 mm, respectively, while the suprabony component remained almost the same. Defect angle changed from 27.2° at baseline to 30.1° at reassessment.

3.3 | Factors affecting treatment outcomes

Supplemental Material 4 reports the associations between explanatory variables and clinical and radiographic outcomes. Deeper baseline total defect depth and narrower angled defects (<28°) were statistically significantly associated with greater intrabony defect depth reductions. Narrower angled defects achieved almost twice more intrabony defect depth reduction than wider angled defects (1.87 and 0.99 mm, respectively) ($p = .036$). Staging and grading were not associated with the study outcomes.

Linear regression revealed that the initial radiographic defect depth was statistically significantly associated with defect depth reduction at 12 months (Table 5). Logistic regression revealed that narrow-angled defects were significantly associated with pocket closure ($p = .043$). No factors reached statistical significance with the composite outcome (Table 5).

4 | DISCUSSION

To our knowledge, this is the first multi-centre study to analyse clinical and radiographic outcomes of intrabony defects treated with MINST. The main findings of this study showed significant clinical and radiographic improvements at 12 months, including a reduction of approximately 1.5 mm in radiographic measurements.

These findings agree with the outcomes reported in previous single-centre studies on MINST, providing additional confirmation that an atraumatic technique, which minimizes tissue damage and trauma while promoting gingival margin stability and reducing

1600051x, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jcpe.13984 by Test, Wiley Online Library on [04/06/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

chairside time, can substantially improve intrabony defects. In a retrospective study of 35 treated defects in 23 patients, the mean intrabony defect reduction of 2.93 mm at 1 year was detected, which is just over double the reduction observed in this study (Nibali et al., 2015). Slightly deeper baseline intrabony defect depths of mean 6.7 mm were included, while the corresponding value in this study was 6.2 mm. It has been well established that deeper intrabony defects respond more favourably to regenerative surgery (Nibali et al., 2021), which appears to be consistent with outcomes detected following MINST in this study and in the literature (Nibali et al., 2015; Nibali et al., 2018). Furthermore, comparisons of this study's findings with two randomized controlled trials found similar mean reductions of 1.9 mm (Anoixiadou et al., 2022) and 2.1 mm radiographic defect fill (Aimetti et al., 2017) in the MINST test group at 12 months. Radiographically, the average defect angle changed from 27.2° at baseline to 30.1° at reassessment in the present study. Although statistically significant, the 3° increase was much smaller than the 16° (Nibali et al., 2015) and 7.6° increase in defect angle (Anoixiadou et al., 2022) reported in previous studies. The differences observed across studies could potentially be attributed to smaller sample sizes, the efficacy of a single operator and heterogenous study designs.

The clinical findings in this study are in keeping with results from other studies exploring the effects of MINST in intrabony defects. After 12 months, 84 defects presented with a mean PPD reduction of 4.17 mm, CAL gain of 3.70 mm and REC increase of 0.48 mm. The results in this study are almost identical to or even slightly better than observations reported elsewhere (Anoixiadou et al., 2022). In contrast to a previous retrospective study conducted in a smaller patient cohort (Nibali et al., 2015), which found a mean reduction of 3.12 mm PPD, 2.78 mm CAL gain and 0.28 mm increase in REC at 12 months, this study found greater clinical improvements.

Furthermore, the outcomes achieved in this study with MINST seem to be consistent with those achieved through periodontal regeneration. In a randomized controlled trial comparing MINST and minimally invasive surgery, there were no statistical differences observed in PPD, CAL and REC (Ribeiro et al., 2023). A non-inferiority randomized controlled trial comparing M-MIST (modified minimally invasive surgical technique) and MINST is currently under way, but the results are yet to be published (Nibali et al., 2019).

One of this study's strengths is the exploration of the association between estimated defect characteristics and healing outcomes, which could lead to better clinical applications of MINST. Deeper and narrower defects showed greater clinical and radiographic improvements, consistent with findings from previous studies on MINST (Nibali et al., 2015, 2018) and periodontal regeneration (Nibali et al., 2020, 2021; Tsitoura et al., 2004). The current study was powered on a difference of radiographic bone gain between narrower and wider angled defects (threshold <28°). It is interesting to note that a statistically significant difference was observed in this outcome, albeit of a smaller magnitude (1.87 vs. 0.99 mm) than what was originally hypothesized (3 vs. 2 mm). Defect depth, narrow angle and increased number of walls are all correlated, as usually the deepest part of the defect is narrower and associated with the greatest number of residual walls. While there was a clear association between initial defect depth and intrabony defect reduction, we must acknowledge that this may be in part due to the issues of mathematical coupling and regression to the mean (Tu et al., 2005) rather than some specific biological characteristics typical of deeper defects. Many regenerative studies have also highlighted greater chances of treatment success in defects with a greater number of residual walls (Rosling et al., 1976; Tonetti et al., 2002). It is worth noting that radiographic estimations of defect morphology are often inconsistent with intra-surgical findings (Nibali et al., 2023).

While significant centre effects have been observed following regenerative therapy with enamel matrix derivative (Tonetti et al., 2002) and guided tissue regeneration membranes (Cortellini et al., 2001), no statistically significant associations between centre and study outcomes were detected in the present study. However, variations in success rates among operators in achieving the composite outcome ranged from 25% to 100% ($p = .038$). This variation may be influenced by various factors, including the patients' social backgrounds, type of periodontal disease, response to therapy, as well as differences in technical ability, clinician experience and instruments used (Tonetti et al., 2002). Ultrasonic/piezo-electric instruments included different makes of slimline tips, depending on availability in the participating practices. While some of these instruments have been used in previous studies investigating MINST, it is very difficult to speculate on the effect of individual instruments on outcomes at this stage.

The outcomes of periodontal therapy are dependent on mechanisms of wound healing. It is hypothesized that wound healing after MINST is not too dissimilar from the healing observed after surgical regenerative therapy (Nibali et al., 2018). Despite the radiographic improvements seen following regeneration of intrabony defects, 'bone fill' does not prove formation of new cementum with inserting collagen fibres. Furthermore, it has been shown that despite new bone formation, junctional epithelium (JE) can be interposed between new bone and root surfaces (Caton & Zander, 1976). Bone fill or remodelling appears to take place after MINST, as evidenced by a radiographic reduction in intrabony defect depth; however, histological studies are required to determine whether true regeneration occurs (Nibali et al., 2015). Given that almost no change occurred in the suprabony component in this study, the discrepancy between the 3.70 mm CAL gain and 1.45 mm intrabony defect depth reduction could be explained by the attachment gain deriving from reconstruction of the intrabony component and formation of long JE. Furthermore, the mechanism of healing following MINST is supported by studies showing that biomaterials are not necessary for regeneration when the intrinsic potential of the periodontal tissues are optimized (Liu et al., 2016). This may occur when the molecular regenerative potential of intrabony defects is used to its full potential (Koidou et al., 2022; Santamaria et al., 2023). Further studies are needed to evaluate the exact mechanisms of healing following MINST to enable clinicians to modify techniques and optimize treatment outcomes.

The main limitations of this study are the lack of control group, the exclusion of smokers which limit the generalizability of findings and the use of non-standardized radiographs. However, the possible

1600051x, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jcpe.13984 by Test, Wiley Online Library on [04/06/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

distortions of radiographic images were minimal, and there were no statistically significant differences in any parameter after the application of the correction factor. Radiographic findings in this study are further strengthened by the analysis being conducted by a single masked examiner who underwent several calibration steps. In addition, defect morphology and its influence on treatment outcome could not be fully ascertained because of the non-surgical nature of the treatment provided. Another limitation is the different number of cases treated across operators (ranging from a minimum of 6 to a maximum of 35). Furthermore, in patients presenting with multiple eligible defects, clinicians selected the study site, potentially introducing selection bias by favouring defects expected to have a more positive response to MINST. Further studies are required to assess the factors that influence treatment response and long-term stability of outcomes and to assess the wider generalizability of these findings.

5 | CONCLUSIONS

In summary, this multi-centre prospective cohort study confirms, on a larger scale, the effectiveness of MINST without adjuncts as the sole therapy of intrabony defects during Step 2 of periodontal treatment. MINST appears to demonstrate favourable clinical outcomes with minimal treatment time and adverse events. However, there is no doubt that to obtain the clinical endpoint of PPD < 5 mm with no bleeding on probing, surgical intervention might be necessary in some cases.

AUTHOR CONTRIBUTIONS

L.N. contributed to the conception and design of the study and wrote the first draft of the research protocol. All authors discussed and formulated the final research design. L.N., M.M., R.G-S., O.O., A.L., F.E., C.G., C.D. and E.M-C.L. contributed to patient recruitment and treatment. L.N. and J.M. contributed to data collection, analysis, drafting of the manuscript and its revisions. All authors contributed to interpretation of data, critical revision of the manuscript and approval of the final manuscript.

ACKNOWLEDGEMENTS

The authors are grateful to Dr Haniyen Moaven for her valuable contribution to data entry in this study.

FUNDING INFORMATION

No specific funding was obtained for the conduct of this study.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest in connection with this article.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Jaimini Mehta https://orcid.org/0000-0003-2804-7356
Marco Montevecchi https://orcid.org/0000-0001-7312-802X
Antonio Liñares https://orcid.org/0000-0003-1611-5884
Emily Ming-Chieh Lu https://orcid.org/0000-0002-7074-1846
Luigi Nibali https://orcid.org/0000-0002-7750-5010

REFERENCES

Aimetti, M., Ferrarotti, F., Mariani, G. M., & Romano, F. (2017). A novel flapless approach versus minimally invasive surgery in periodontal regeneration with enamel matrix derivative proteins: A 24-month randomized controlled clinical trial. *Clinical Oral Investigations*, *21*(1), 327–337. https://doi.org/10.1007/s00784-016-1795-2

Ainamo, J., & Bay, I. (1975). Problems and proposals for recording gingivitis and plaque. *International Dental Journal*, *25*(4), 229–235.

Anoixiadou, S., Parashis, A., & Vouros, I. (2022). Enamel matrix derivative as an adjunct to minimally invasive non-surgical treatment of intrabony defects: A randomized clinical trial. *Journal of Clinical Periodontology*, *49*(2), 134–143. https://doi.org/10.1111/jcpe.13567

Caton, J., & Zander, H. A. (1976). Osseous repair of an infrabony pocket without new attachment of connective tissue. *Journal of Clinical Periodontology*, *3*(1), 54–58. https://doi.org/10.1111/j.1600-051X.1976.tb01850.x

Claffey, N., & Egelberg, J. (1995). Clinical indicators of probing attachment loss following initial periodontal treatment in advanced periodontitis patients. *Journal of Clinical Periodontology*, *22*(9), 690–696. https://doi.org/10.1111/j.1600-051X.1995.tb00828.x

Cortellini, P., Cortellini, S., Bonaccini, D., & Tonetti, M. S. (2022). Modified minimally invasive surgical technique in human intrabony defects with or without regenerative materials—10-year follow-up of a randomized clinical trial: Tooth retention, periodontitis recurrence, and costs. *Journal of Clinical Periodontology*, *49*(6), 528–536. https://doi.org/10.1111/jcpe.13627

Cortellini, P., Tonetti, M. S., Lang, N. P., Suvan, J. E., Zucchelli, G., Vangsted, T., Silvestri, M., Rossi, R., McClain, P., Fonzar, A., Dubravec, D., & Adriaens, P. (2001). The simplified papilla preservation flap in the regenerative treatment of deep intrabony defects: Clinical outcomes and postoperative morbidity. *Journal of Periodontology*, *72*(12), 1702–1712. https://doi.org/10.1902/jop.2001.72.12.1702

Guerrero, A., Griffiths, G. S., Nibali, L., Suvan, J., Moles, D. R., Laurell, L., & Tonetti, M. S. (2005). Adjunctive benefits of systemic amoxicillin and metronidazole in non-surgical treatment of generalized aggressive periodontitis: A randomized placebo-controlled clinical trial. *Journal of Clinical Periodontology*, *32*(10), 1096–1107. https://doi.org/10.1111/j.1600-051X.2005.00814.x

Hamp, S.-E., Nyman, S., & Lindhe, J. (1975). Periodontal treatment of multi rooted teeth. *Journal of Clinical Periodontology*, *2*(3), 126–3553. https://doi.org/10.1111/j.1600-051X.1975.tb01734.x

Harrel, S. K. (1999). A minimally invasive surgical approach for periodontal regeneration: Surgical technique and observations. *Journal of Periodontology*, *70*(12), 1547–1557. https://doi.org/10.1902/jop.1999.70.12.1547

Koidou, V. P., Hagi-Pavli, E., Cross, S., Nibali, L., & Donos, N. (2022). Molecular profiling of intrabony defects' gingival crevicular fluid. *Journal of Periodontal Research*, *57*(1), 152–161. https://doi.org/10.1111/jre.12948

Laster, L., Laudenback, K., & Stoller, N. (1975). An evaluation of clinical tooth mobility measurements. *Journal of Periodontology*, *46*(10), 603–607. https://doi.org/10.1902/jop.1975.46.10.603

Liñares, A., Cortellini, P., Lang, N. P., Suvan, J., & Tonetti, M. S. (2006). Guided tissue regeneration/deproteinized bovine bone mineral or papilla preservation flaps alone for treatment of intrabony defects. II: Radiographic predictors and outcomes. *Journal of Clinical Periodontology*, *33*(5), 351–358. https://doi.org/10.1111/j.1600-051X.2006.00911.x

1600051x, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jcpe.13984 by Test, Wiley Online Library on [04/06/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Liu, S., Hu, B., Zhang, Y., Li, W., & Song, J. (2016). Minimally invasive surgery combined with regenerative biomaterials in treating intra-bony defects: A meta-analysis. *PLoS One*, *11*(1), e0147001. https://doi.org/10.1371/journal.pone.0147001

Matuliene, G., Pjetursson, B. E., Salvi, G. E., Schmidlin, K., Brägger, U., Zwahlen, M., & Lang, N. P. (2008). Influence of residual pockets on progression of periodontitis and tooth loss: Results after 11 years of maintenance. *Journal of Clinical Periodontology*, *35*(8), 685–695. https://doi.org/10.1111/j.1600-051X.2008.01245.x

Needleman, I., Worthington, H. V., Giedrys-Leeper, E., & Tucker, R. (2006). Guided tissue regeneration for periodontal infra-bony defects. *Cochrane Database of Systematic Reviews*, *19*(2), CD001724. https://doi.org/10.1002/14651858.CD001724.pub2

Nibali, L., Koidou, V., Salomone, S., Hamborg, T., Allaker, R., Ezra, R., Zou, L., Tsakos, G., Gkranias, N., & Donos, N. (2019). Minimally invasive non-surgical vs. surgical approach for periodontal intrabony defects: A randomised controlled trial. *Trials*, *20*(1), 461. https://doi.org/10.1186/s13063-019-3544-8

Nibali, L., Koidou, V. P., Nieri, M., Barbato, L., Pagliaro, U., & Cairo, F. (2020). Regenerative surgery versus access flap for the treatment of intra-bony periodontal defects: A systematic review and meta-analysis. *Journal of Clinical Periodontology*, *47*, 320–351. https://doi.org/10.1111/jcpe.13237

Nibali, L., Mehta, J., Al-Shemeri, D., Anoixiadou, S., Parashis, A., & Vouros, I. (2023). Association between defect morphology and healing of intrabony defects treated with minimally invasive non-surgical therapy: A pilot exploratory analysis of two cohorts. *Journal of Periodontal Research*, *58*(4), 708–714. https://doi.org/10.1111/jre.13119

Nibali, L., Pometti, D., Chen, T.-T., & Tu, Y.-K. (2015). Minimally invasive non-surgical approach for the treatment of periodontal intrabony defects: A retrospective analysis. *Journal of Clinical Periodontology*, *42*(9), 853–859. https://doi.org/10.1111/jcpe.12443

Nibali, L., Pometti, D., Tu, Y. K., & Donos, N. (2011). Clinical and radiographic outcomes following non-surgical therapy of periodontal infrabony defects: A retrospective study. *Journal of Clinical Periodontology*, *38*(1), 50–57. https://doi.org/10.1111/j.1600-051X.2010.01648.x

Nibali, L., Sultan, D., Arena, C., Pelekos, G., Lin, G. H., & Tonetti, M. (2021). Periodontal infrabony defects: Systematic review of healing by defect morphology following regenerative surgery. *Journal of Clinical Periodontology*, *48*, 100–113. https://doi.org/10.1111/jcpe.13381

Nibali, L., Yeh, Y., Pometti, D., & Tu, Y. (2018). Long-term stability of intrabony defects treated with minimally invasive non-surgical therapy. *Journal of Clinical Periodontology*, *45*(12), 1458–1464. https://doi.org/10.1111/jcpe.13021

Ørstavik, D., Kerekes, K., & Eriksen, H. M. (1986). The periapical index: A scoring system for radiographic assessment of apical periodontitis. *Dental Traumatology*, *2*(1), 20–34. https://doi.org/10.1111/j.1600-9657.1986.tb00119.x

Papapanou, P. N., & Tonetti, M. S. (2000). Diagnosis and epidemiology of periodontal osseous lesions. *Periodontology 2000*, *22*(1), 8–21. https://doi.org/10.1034/j.1600-0757.2000.2220102.x

Rams, T. E., Listgarten, M. A., & Slots, J. (2018). Radiographic alveolar bone morphology and progressive periodontitis. *Journal of Periodontology*, *89*(4), 424–430. https://doi.org/10.1002/JPER.17-0279

Reynolds, M. A., Kao, R. T., Camargo, P. M., Caton, J. G., Clem, D. S., Fiorellini, J. P., Geisinger, M. L., Mills, M. P., Nares, S., & Nevins, M. L. (2015). Periodontal regeneration – Intrabony defects: A consensus report from the AAP regeneration workshop. *Journal of Periodontology*, *86*(2S), S105–S107. https://doi.org/10.1902/jop.2015.140378

Ribeiro, F. V., Casarin, R. C. V., Palma, M. A. G., Júnior, F. H. N., Sallum, E. A., & Casati, M. Z. (2011). Clinical and patient-centered outcomes after minimally invasive non-surgical or surgical approaches for the treatment of intrabony defects: A randomized clinical trial. *Journal of Periodontology*, *82*(9), 1256–1266. https://doi.org/10.1902/jop.2011.100680

Ribeiro, F. V., Mehta, J. J., Monteiro, M. F., Moore, J., Casati, M. Z., & Nibali, L. (2023). Minimal invasiveness in nonsurgical periodontal therapy. *Periodontology 2000*, *91*(1), 7–19. https://doi.org/10.1111/prd.12476

Rosling, B., Nyman, S., & Lindhe, J. (1976). The effect of systematic plaque control on bone regeneration in infrabony pockets. *Journal of Clinical Periodontology*, *3*(1), 38–53. https://doi.org/10.1111/j.1600-051X.1976.tb01849.x

Santamaria, P., Sari, A., & Nibali, L. (2023). Molecular profiling of gingival crevicular fluid fails to distinguish between infrabony and suprabony periodontal defects. *Journal of Clinical Periodontology*, *50*(10), 1315–1325. https://doi.org/10.1111/jcpe.13849

Sanz, M., Herrera, D., Kebschull, M., Chapple, I., Jepsen, S., Beglundh, T., Sculean, A., Tonetti, M. S., & EFP Workshop Participants and Methodological Consultants. (2020). Treatment of stage I-III periodontitis-the EFP S3 level clinical practice guideline. *Journal of Clinical Periodontology*, *47*(S22), 4–60. https://doi.org/10.1111/jcpe.13290

Tonetti, M. S., Greenwell, H., & Kornman, K. S. (2018). Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. *Journal of Clinical Periodontology*, *1*(45), S149–S161. https://doi.org/10.1002/JPER.18-0006

Tonetti, M. S., Lang, N. P., Cortellini, P., Suvan, J. E., Adriaens, P., Dubravec, D., Fonzar, A., Fourmousis, I., Mayfield, L., Rossi, R., Silvestri, M., Tiedemann, C., Topoll, H., Vangsted, T., & Wallkamm, B. (2002). Enamel matrix proteins in the regenerative therapy of deep intrabony defects. *Journal of Clinical Periodontology*, *29*(4), 317–325. https://doi.org/10.1034/j.1600-051X.2002.290407.x

Trombelli, L., Farina, R., Vecchiatini, R., Maietti, E., & Simonelli, A. (2020). A simplified composite outcome measure to assess the effect of periodontal regenerative treatment in intraosseous defects. *Journal of Periodontology*, *91*(6), 723–731. https://doi.org/10.1002/JPER.19-0127

Trombelli, L., Simonelli, A., Pramstraller, M., Wikesjö, U. M. E., & Farina, R. (2010). Single flap approach with and without guided tissue regeneration and a hydroxyapatite biomaterial in the management of intraosseous periodontal defects. *Journal of Periodontology*, *81*(9), 1256–1263. https://doi.org/10.1902/jop.2010.100113

Tsitoura, E., Tucker, R., Suvan, J., Laurell, L., Cortellini, P., & Tonetti, M. (2004). Baseline radiographic defect angle of the intrabony defect as a prognostic indicator in regenerative periodontal surgery with enamel matrix derivative. *Journal of Clinical Periodontology*, *31*(8), 643–647. https://doi.org/10.1111/j.1600-051X.2004.00555.x

Tu, Y. K., Baelum, V., & Gilthorpe, M. S. (2005). The relationship between baseline value and its change: Problems in categorization and the proposal of a new method. *European Journal of Oral Sciences*, *113*(4), 279–288. https://doi.org/10.1111/j.1600-0722.2005.00229.x

Updegrave, W. J. (1951). The paralleling extension-cone technique in intraoral dental radiography. *Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology*, *4*(10), 1250–1261. https://doi.org/10.1016/0030-4220(51)90084-9

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Mehta, J., Montevecchi, M., Garcia-Sanchez, R., Onabolu, O., Liñares, A., Eriksson, F., Ghezzi, C., Donghi, C., Lu, E. M.-C., & Nibali, L. (2024). Minimally invasive non-surgical periodontal therapy of intrabony defects: A prospective multi-centre cohort study. *Journal of Clinical Periodontology*, 1–10. https://doi.org/10.1111/jcpe.13984

1600051x, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jcpe.13984 by Test, Wiley Online Library on [04/06/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License