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ORIGINAL ARTICLE

Long-term stability of regenerative periodontal surgery and orthodontic tooth movement in stage IV periodontitis: 10-year data of a retrospective study

Christina Tietmann[1,2] | **Søren Jepsen**[2] | **Helen Heibrok**[3] | **Sven Wenzel**[1] | **Karin Jepsen**[2]

[1]Private Practice for Periodontology, Aachen, Germany

[2]Department of Periodontology, Operative and Preventive Dentistry, University of Bonn, Bonn, Germany

[3]University of Witten/Herdecke, Witten, Germany

Correspondence
Christina Tietmann, Private Practice for Periodontology, Krefelder Str. 73, 52070 Aachen, Germany.
Email: tietmann@paro-aachen.de

Abstract

Background: This study aimed to evaluate the long-term effectiveness of regenerative treatment of intra-bony defects in combination with consecutive orthodontic therapy (OT) in stage IV periodontitis.

Methods: Twenty-two patients with a total of 256 intra-bony defects were analyzed after regenerative surgery followed by OT initiated 3 months later. Changes in radiographic bone level (rBL) and probing pocket depths (PPD) were evaluated after 1 year (T1), final splinting (T2), and 10 years (T10).

Results: Mean rBL gain was significant with 4.63 mm (±2.43 mm) after 1 year (T1), 4.19 mm (±2.61 mm) at final splinting (T2), and 4.48 mm (±2.62 mm) after 10 years (T10). Mean PPD was significantly reduced from 5.84 mm (±2.05 mm) at baseline to 3.19 mm (±1.23 mm) at T1, to 3.07 mm (±1.23 mm) at T2, and to 2.93 mm (±1.24 mm) at T10. Pocket closure (PPD ≤ 4 mm) was achieved in 90% of all defects. Tooth loss amounted to 4.5%.

Conclusions: Within the limitations of this retrospective study design, these 10-year findings suggest that in motivated and compliant patients with stage IV periodontitis and in need of OT an inter-disciplinary treatment can lead to favorable and stable long-term results.

KEYWORDS

bovine bone mineral, long-term, orthodontic tooth movement, pathologic tooth migration, regenerative periodontal therapy, stage IV periodontitis

1 | INTRODUCTION

Stage IV periodontitis is characterized by similar severity and complexity as stage III periodontitis in terms of attachment loss, vertical bone loss, and periodontal inflammation. However, adding to the severity and complexity in stage IV periodontitis the presence of pathologic tooth migration (PTM)[1] with drifting and flaring of the remaining teeth, hypermobility and secondary occlusal trauma, bite collapse, and masticatory

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dysfunction requires a complex rehabilitation.[2] Patients affected by such a condition are interested to seek orthodontic treatment because of the functional and esthetic changes caused by PTM.[3] An interdisciplinary approach of comprehensive periodontal and orthodontic therapy (OT) is needed to control periodontal infection, reconstruct the defects, and realign the migrated teeth in order to regain and stabilize function and esthetics for the patients.[4,5]

OT with fixed appliances does not seem to have clinically adverse effects on clinical attachment levels in healthy patients or in successfully treated periodontitis patients.[6–8] However, only limited data exist on the combined treatment of periodontal therapy and OT in patients with stage IV periodontitis.[9,10]

The recently published EFP S3 level clinical practical guideline (CPG) for the treatment of stage IV periodontitis[11] gives guidance for these complex interdisciplinary therapies based on explicitly commissioned reviews with regard to quality and strength of evidence. In a structured consensus process a concise treatment algorithm and specific evidence-based and expert-based recommendations were adopted for the interdisciplinary treatment for patients in need of OT diagnosed with stage IV periodontitis (case type 2). As emphasized in the EFP S3 CPG tooth retention should be considered first in the long-term management of stage IV periodontitis. Accordingly, given the value of regenerative procedures in intra-bony defects,[12–17] the EFP S3 CPG recommends the combination of regenerative therapy and consecutive OT in patients with stage IV periodontitis presenting with intra-bony defects and in need of OT.[11] Concerning the timing of OT following periodontal regenerative therapy – based on two recent clinical studies [18,19] – the EFP S3 CPG recommends a time interval between 4 weeks and 6 months.[11]

However, there is still only limited data on the long-term outcomes of such a combined therapy.[20,21] In these two studies, OT was initiated much later (12 months after surgery) and they either reported on a small number of regeneratively treated defects[20] or did not distinguish in their outcomes between defects treated either in a resective or regenerative way before consecutive OT.[21] Thus, although both studies presented encouraging long-term results the effect of a combined regenerative-orthodontic treatment approach in line with the current recommendations cannot be fully appreciated.

Therefore, the aim of this retrospective analysis was to evaluate the long-term effectiveness and stability after 10 years of regenerative treatment of a large number of intra-bony defects at migrated teeth in combination with early consecutive OT in stage IV periodontitis.

2 | MATERIALS AND METHODS

2.1 | Study design and patients

This retrospective analysis included data from a 10-year follow-up of patients presenting with severe periodontitis and PTM (stage IV periodontitis).[2] All of them had been treated by an interdisciplinary approach in a periodontal specialty practice (C.T.) in Aachen, Germany. The interdisciplinary treatment consisted of a comprehensive periodontal therapy including regenerative periodontal surgery and consecutive orthodontic tooth movement in the period of 2001 and 2010 as previously reported for 27 patients after 2–4 years.[18] Twenty-two patients were still available 10 years after regenerative surgery, while 5 patients were lost to follow-up because they had either moved, had returned to their referring dentist, or had died.

The study was conducted in accordance with the Helsinki Declaration (version 2008) and approved by the Ethics committee of the University of Bonn (#16/23). Patients had given their written informed consent for a retrospective evaluation of their clinical and radiographical data.

Inclusion criteria for the analysis were:

- Successful steps 1 and 2 of periodontal therapy: adequate oral hygiene and control of inflammation: full-mouth plaque score (FMPS) of ≤15% and full-mouth bleeding score (FMBS) of ≤15%
- one- or two-wall intra-bony defects with indication for periodontal regenerative therapy
- PTM due to destruction of periodontal tissues
- orthodontic tooth movement starting 3 months after surgery
- clinical and radiographic data of a continuous follow-up for 10 years after regenerative surgery.

Exclusion criteria were:

- non-compliance to maintenance protocol
- incomplete probing or radiographic data
- additional periodontal or maxillofacial treatment in the areas of interest.

Patients with systemic diseases (i.e., controlled diabetes) and smokers were not excluded.

Based on these criteria, 22 patients with a total of 256 regeneratively treated intra-bony defects and consecutive orthodontic tooth movement were included in the analysis.

2.2 | Treatment

2.2.1 | Regenerative periodontal surgery

Regenerative surgery of teeth with intra-bony defects was performed by one single experienced periodontist (C.T.) after successful anti-infective therapy and orthodontic consultation in the period of 2001–2010. Surgical regenerative procedures were performed under local anesthesia as previously described,[13,18] vertical releasing incisions were avoided by extending flap design to adjacent teeth, apical split flap preparation was only performed if needed for primary tension-free flap closure. After debridement of the defect the biomaterial was chosen depending on the configuration of the intra-bony defect. To prevent a soft-tissue collapse into the defect a bone filler was used (DBBMc, Bio Oss Collagen; Geistlich, Wolhusen, Switzerland). If the graft material was at risk for dislocation in non-contained defects, a collagen membrane (Bio GidePerio; Geistlich, Wolhusen, Switzerland) was applied without pin or suture fixation. Enamel matrix derivative (EMD, Emdogain; Straumann, Basel, Switzerland) was applied in contained defects to enhance periodontal wound healing. Primary tension-free closure of the coronally positioned flap was achieved by modified horizontal mattress sutures and additional single interrupted sutures for papilla adaptation (6-0 Monofilament single sutures Premilene USP6/0-DS13, B. Braun, Tuttlingen, Germany; Seralene USP6/0-DS12 SeragWiessner, Naila, Germany; SeraleneUSP6/0-DS15; SeragWiessner, Naila, Germany).

A strict anti-infective protocol postoperatively was advised to the patient including the rinse with 0.2% chlorhexidine solution three times a day and abstention from mechanical tooth cleaning in the surgically treated areas for 4 weeks or until complete wound healing. Antibiotics were prescribed at the discretion of the surgeon.

Sutures were removed after 10–14 days depending on individual wound healing progression.

2.2.2 | Orthodontic therapy

Early orthodontic consultation was performed within the context of step 2 of periodontal therapy to define the individual interdisciplinary treatment options. For best stabilization of the clot and graft during and after regenerative therapy, the type of splinting was chosen with regard to the grade of tooth mobility.[22] In cases of increased tooth mobility (>grade II) of multiple adjacent teeth, passive fixed orthodontic appliances were inserted prior to periodontal surgery. This applied to nine patients. Otherwise, if not needed during surgery for stabilization, removable acrylic splints or semi-permanent lingual retainers were used to facilitate best stabilization of the blood clot and graft after regenerative surgery.

Active orthodontic tooth movements with low forces and moments started 3 months after periodontal regenerative surgery, using fixed orthodontic appliances (straight-wire-technique) in all patients performed by one and the same experienced orthodontist. In brief, orthodontic movement was started with a 0.012 nickel-titanium (Ni-Ti) wire, followed by the alignment with the sequence of 0.014 Ni-Ti, 0.016 Ni-Ti, 0.018 Ni-Ti, and 0.016*0.016 stainless steel wire. A 0.0175-inch seven time twist flex in the upper jaw and a 0.0155 inch seven time twist flex in the lower jaw were used as fixed retainers and controlled on a regular basis.

Active OT was considered completed when the predefined treatment goals for aesthetic and function in each patient had been achieved. Time span of active orthodontic tooth movements was determined by the individual extent of treatment needs of the patient and varied from 10 to 31 months with a mean duration of 22 months.

Stabilization of treatment outcomes was accomplished either by fixed bonded retainers (10 patients), removable splints (9 patients) which also served as a night-guard because of bruxism, or a combination of both (3 patients).

2.2.3 | Supportive periodontal therapy

After periodontal surgery, supportive periodontal therapy (SPT) started with a tight interval of 4 weeks up to 3 months during the period of OT. Control of inflammation was accomplished by cautious professional tooth cleaning and oral hygiene reinforcement with particular emphasis on teeth undergoing orthodontic intrusive movements.

After completion of active OT periodontal supportive care was provided corresponding to individual patient's need with a minimum recall interval of three times a year during the observation period of 10 years.

2.3 | Outcomes

2.3.1 | Clinical and radiographic measurements

Clinical and radiographic measurements were assessed as previously described.[18] In brief, probing pocket depths (PPD) at four sites per tooth and periapical radiographs were taken preoperatively. During surgery, the tooth site measured with the most advanced bone loss mesially or

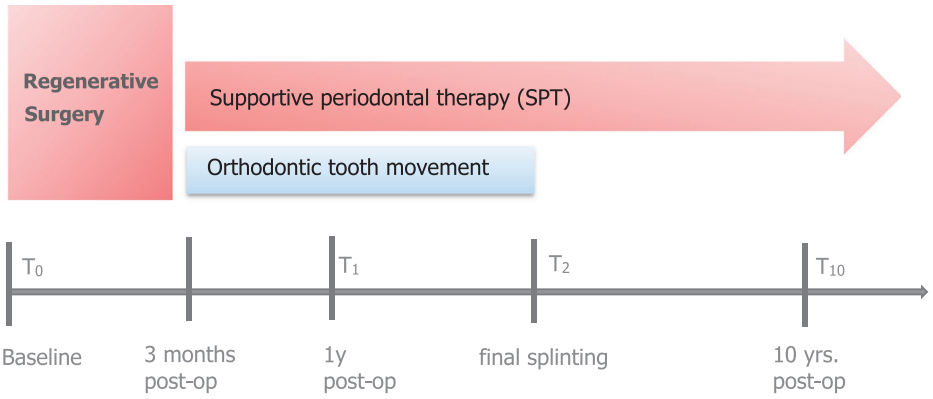

FIGURE 1 Chronical sequence of treatment and examinations (T_0, T_1, T_2, T_{10}).

distally (distance between the cemento-enamel junction or restoration to the bottom of the defect) became the target site. Intra-operative bone level (BL) was used for calibration of the pre-operative periapical radiograph by using the overall tooth length as a reference length, as previously described.[13]

After calibration, the radiographs were analyzed using ImageJ Software (Version 1.43u, National Institutes of Health, Bethesda, Maryland, USA) by a trained and calibrated examiner (H.H.) who was not involved in the surgeries.

Complete clinical and radiographic data at all time-points were obtained from 256 defects in 22 patients. PPD was recorded at baseline and every year during supportive periodontal care, radiographic BL (rBL) at baseline (T_0), 1 year (T_1), at final splinting (T_2), and 10 years (T_{10}) after surgery. (Figure 1).

2.4 | Statistical analysis

All statistical analyses were performed using the statistical software R, version 3.6.3 (R Core Team, 2020).[23] Change of rBL was the primary outcome parameter, change in PPD and frequency of pocket closure (sites with PPD≤4 mm) served as secondary outcomes. Descriptive analysis was outlined for rBL and pocket probing depth (PPD) with change over time for the four time points T_0, T_1, T_2, and T_{10} on defect and patient level and for the most severe defect per patient by means and standard deviations per defect as well as per patient.

Comparisons of rBL and PPD between time points were analyzed by a Wilcoxon signed-rank test; a Wilcoxon signed-rank test for clustered data was used to take possible clustering within patient into account.[24]

To compare the BL gain and pocket closures between time points a logistic regression with time as fixed and patient and defect as random effects was run.

To explore the effect of explanatory variables "smoking", "full-mouth-bleeding and plaque scores" at T_{10} a multilevel analysis was conducted using a mixed effect linear regression with patient as random factor and "radiographic bone at baseline" as covariate. *p*-values were derived with the Satterthwaite method.[25] The level of significance of each test was set to 0.05. Starting from the minimal model with rBL at T_0 as only fixed effect, first models were run with only one more fixed effect included. Variables were only retained if significant and interaction term was only tested if the main effect was significant. Then, only variables were added if they showed a significant improvement of the model.

Since adjunctive antibiotic treatment had not shown any additional effect as previously described,[18] no further statistical investigation of the 10-year data was performed.

Statistical analyses of the clinical and radiographic data were performed by an independent expert biostatistician.

3 | RESULTS

3.1 | Patient and defect characteristics

For all 22 patients included in this analysis data up to 10 years postoperatively was available. All of them were diagnosed with stage IV periodontitis and -based on calculation of percentage bone loss/age baseline – with Grade C except for three patients with Grade B. The collection of the 10-year follow-up data were completed by April 2022. All of the patients had shown full adherence to the scheduled appointments of supportive therapy during the observation period of 10 years. The number of defects per patient ranged from 4 to 15 with an average of 11 defects. In total, 34.2% were one-wall defects while 65.8% were two-wall defects. At baseline, mean radiographic BL of 268 defects was 8.33 ± 2.45 mm. Tooth loss at T_2 amounted to 1.2%

TABLE 1 Patient and defect characteristics at baseline (T_0).

***N* patients**	**22**	
Female sex	59.1% (13)	
Mean age (range)	43.9 (29–62) years	
Smokers	9.1% of patients (8.21% of all defects)	
N defects	268 baseline	256 complete cases 10 years
Single-rooted teeth	165/61.57%	165/64.45%
Multi-rooted teeth	103/38.43%	91/35.55%
Mean bone level all	8.33 ± 2.45 mm	8.32 ± 2.49 mm
Two wall defects	176/65.47%	171/66,80%
One wall defects	92/34.33%	85/33,20%
DBBMc	90/33.58%	
DBBMC + CM	62/23.13%	
DBBMC + EMD	46/17.2%	
DBBMc + CM + EMD	35/13%	
EMD	35/13%	

Abbreviations: CM, collagen membrane; DBBMc, collagenous demineralized bovine bone mineral; EMD, enamel matrix derivative.

(3 teeth in two patients) and at T_{10} to 4.5% (12 teeth in eight patients) due to endodontic complications (5 teeth) and root fracture (7 teeth). No tooth loss was observed at T_1. Hence, complete observation data at T_{10} were present for 256 defects with a mean radiographic BL at baseline of 8.32 ± 2.49 mm. DBBMc alone was used in 33.58% of the defects, whereas in 23.13% of the defects DBBMc + CM was applied, DBBMc + EMD was used in 17.2% of the defects and DBBMc + CM + EMD in 13.0% of defects. EMD alone was applied in 13% of the defects. Patient and defect characteristics are presented in Table 1.

3.2 | Outcomes

Surgeries and soft tissue healing were generally uneventful. None of the patients developed any major complications. There were no allergic reactions, suppuration, or abscesses. Minor complications such as postoperative swelling and pain in the surgically treated area resolved within a few days after surgery. In the rare case of wound dehiscencies, no further complications of wound healing could be observed following reinforcement of postoperative intensive clinical care. Representative examples of treated patients included in the present analysis are illustrated in Figures 2 and 3.

The analysis of the primary outcome-change in radiographic BL over time of 256 defects revealed a significant gain in rBL with 4.63 mm (±2.43 mm) ($p < 0.0001$) at T_1, 4.19 mm (±2.61 mm) at T_2 ($p < 0.0001$) and 4.48 mm (±2.62 mm) ($p < 0.0001$) at T_{10}. Change in radiographic BL on patient level was comparable to the analyzed data on defect level. When looking at the deepest defect per patient rBL gain was even more evident ($p < 0.0001$) (Table 2A and B; Figure 4A–C).[26]

As previously reported,[18] different treatment modalities did not show any impact on rBL change over time (Figure 4D).

Mean PPD was significantly reduced at T_1, with further reduction at T_2 and T_{10} ($p < 0.0001$). Mean PPD reduction was even more pronounced when looking at the deepest defect and statistically significant ($p < 0.0001$) at all time points. The frequency of sites with PPD ≤ 4 mm improved from 33% at baseline (T_0) to 87% at T_1, to 86% at T_2, and remained stable with 90% at T_{10} (Table 2C and D).

A multilevel analysis showed that only smoking ($p = 0.017$) was significant when added as a single variable to the minimal model only containing rBL at baseline, however, not in interaction with the rBL at T_0 ($p = 0.564$). Adding other variables such as plaque at T_{10} or BOP at T_{10} did not show any significant improvement. For smokers the change of rBL was on average less from T_0 to T_{10} ($p = 0.017$). The results of the final model are presented as Table A1 in the appendix.

4 | DISCUSSION

The 10-year data of this retrospective clinical cohort study reveal the long-term effectiveness of a combined regenerative and orthodontic treatment in patients with stage IV periodontitis.

TABLE 2 (a) Mean radiographic bone level (rBL) ± standard deviation (mm) and confidence intervals (CI in the format mean) over time (T_0 = baseline, T_1 = 1 year, T_2 = final splinting, T_{10} = 10 years) calculated for patients and defects with different length of follow-up (b) *p*-values for testing rBL between time points (statistics Wilcoxon signed-rank test from the R-library coin version 1.3.1 [Hothorn et al., 2008]) (c) Frequency distribution of residual PPD for all defects $N = 256$, complete observation time (d) *p*-values for testing proportion of pocket closure (pc) between time points (statistics: Logistic regression with time as fixed and patient and defect as random effects)

(a)	*N*	T_0	T_1	T_2	T_{10}
rBL per defect ($n = 268$)	268	8.33 ± 2.45 CI (8.03, 8.62)	3.66 ± 1.92 CI (3.42, 3.89)	NA ± NA	NA ± NA
rBL per defect in complete cases ($n = 256$)	256	8.32 ± 2.49 CI (8.01, 8.62)	3.69 ± 1.94 CI (3.45, 3.93)	4.13 ± 2.01 CI (3.88, 4.38)	3.84 ± 2.10 CI (3.59, 4.10)
rBL per patient ($n = 22$)	22	8.36 ± 1.24 CI (7.81, 8.91)	3.53 ± 1.30 CI (2.95, 4.10)	4.02 ± 1.24 CI (3.47, 4.57)	3.64 ± 1.29 CI (3.07, 4.22)
rBL deepest defect per patient ($n = 22$)	22	12.27 ± 3.09 CI (10.90, 13.64)	5.15 ± 2.49 CI (4.05, 6.26)	5.35 ± 2.49 CI (4.11, 6.59)	5.48 ± 2.76 CI (4.26, 6.71)

(b)	*p*-Values for testing BL between time points				
	$T_0.T_1$	$T_1.T_2$	$T_2.T_{10}$	$T_0.T_{10}$	$T_1.T_{10}$
rBL per defect, complete cases ($n = 256$)	1.31e−05	0.018	0.012	1.55e−05	0.97
rBL per patient ($n = 22$)	4.77e−07	0.0042	0.074	4.77e−07	0.42
rBL deepest defect per patient ($n = 22$)	4.77e−07	0.51	1.00	4.77e−07	0.40

(c) PPD (mm)	Baseline T_0	T_1	T_2	T_{10}
≤4	85 (33.20%)	223 (87.11%)	220 (85.94%)	230 (89.84%)
5	27 (10.55%)	18 (7.03%)	18 (7.03%)	12 (4.69%)
6	48 (18.75%)	10 (3.91%)	17 (6.64%)	11 (4.30%)
7	37 (14.45%)	2 (0.78%)	0 (0.00%)	0 (0.00%)
8	38 (14.84%)	3 (1.17%)	1 (0.39%)	2 (0.78%)
9	9 (3.52%)	0 (0.00%)	0 (0.00%)	1 (0.39%)
10	6 (2.34%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
11	6 (2.34%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

(d) Comparison	*p*-Value
pc0 – pc1	<1e−05
pc0 – pc2	<1e−05
pc0 – pc10	<1e−05
pc1 – pc2	0.262
pc1 – pc10	0.649
pc2 – pc10	0.117

Regenerative periodontal treatment with consecutive early orthodontic tooth movement led to significant rBL gain 10 years postoperatively, as demonstrated by mean rBL gain of 4.48 mm as well as pocket closure in 90% in a large number of teeth severely compromised by intrabony defects and PTM. The long-term data compare well with the results of our former report with data of 2–4 years observation time[18] and are a proof for the feasibility of successful retention of the natural dentition in an adequate state of health and function. While the mean radiographic bone gain at final splinting T_2 dropped slightly to 4.19 mm, it advanced again to 4.48 mm at T_{10}. The slightly reduced mean bone gain at T_2 may be explained by the fact that bone remodeling due to orthodontic tooth movements is still not accomplished at final splinting. However, the clinical findings of a continuous pocket reduction from baseline

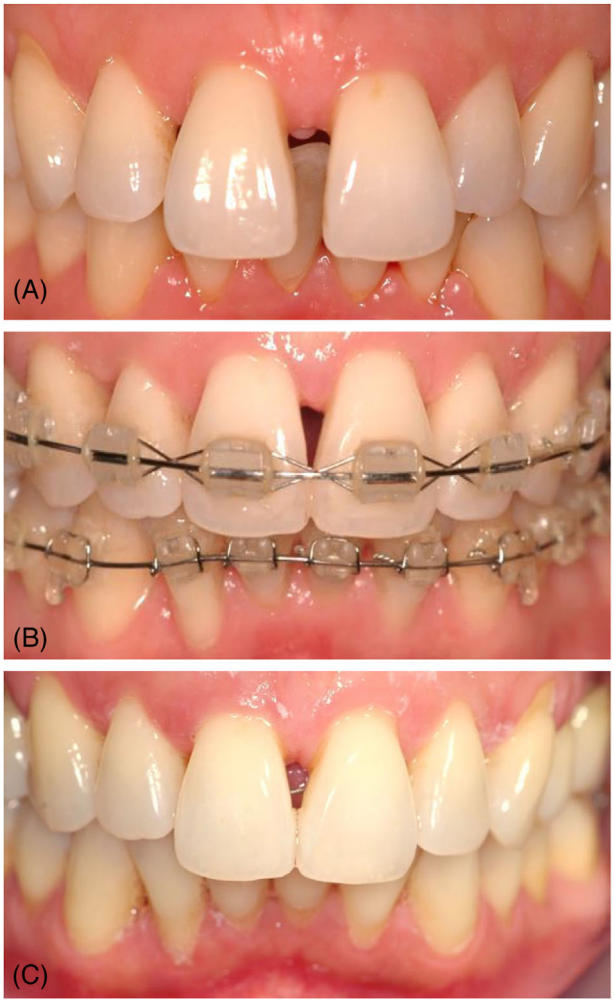

FIGURE 2 Clinical situation of a 35-year-old patient diagnosed with stage IV periodontitis with pathological tooth migration (spacing and flaring) (A) after step 1 and 2 of periodontal therapy (T0 = baseline), (B) 1 year after regenerative surgery (T1), (C) 10 years after regenerative therapy (T10).

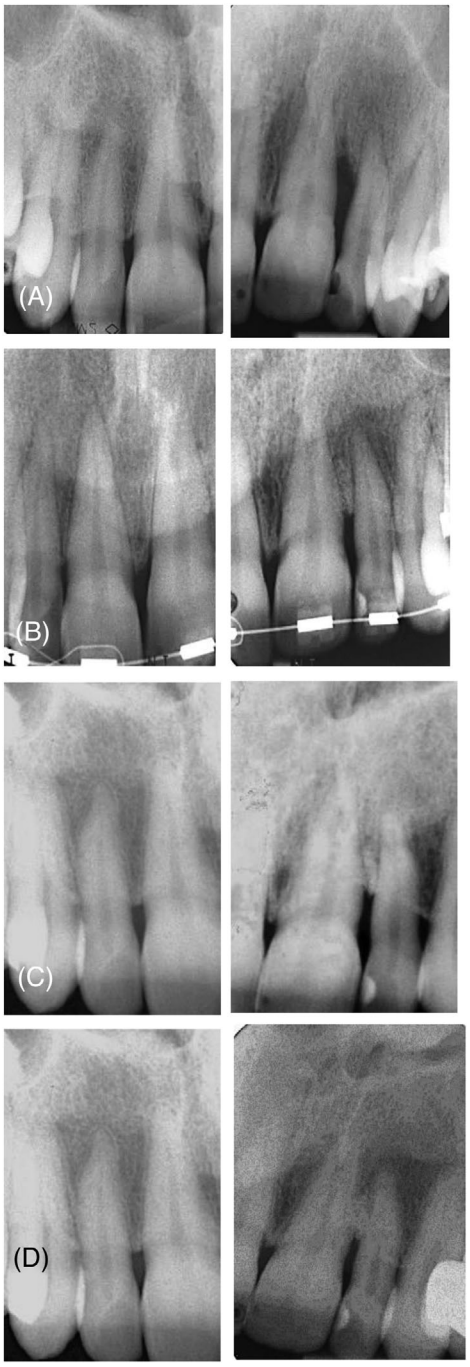

FIGURE 3 (A–D): Radiographical situation of 48-year-old patient diagnosed with stage IV periodontitis (A) after step 1 and 2 of periodontal therapy (T0 = baseline), (B) 1 year after regenerative therapy (T1), (C) at final splinting (T2), (D) 10 years after regenerative therapy (T10).

to T_1, to T_2 and to T_{10} underline the benefit of the combined regenerative-OT. Mean PPD reduction and pocket closure at final splinting in this study are similar to the data of the mid-term follow up of 2–4 years as previously reported.[18] The long-term effectiveness of this combined regenerative therapy and orthodontic treatment is shown by further improvement of rBL and pocket closure at 10 years. The low number of sites with residual deeper pockets could be maintained by regular re-instrumentation during SPT visits. This indicates that, in the setting of a specialized practice, a good prognosis even for severely periodontally compromised patients can be achieved if compliant with SPT and adequate oral hygiene.[27]

The present study analyzing the stability and long-term effectiveness of regenerative periodontal therapy combined with early orthodontic tooth movement is -to our knowledge- the study with the largest number of defects and longest observation time of this kind of interdisciplinary treatment approach published so far. The high number of participants and defects treated in the setting of a private practice strengthen the generalizability of the results. Adding to the strengths of the study, the radiographs were evaluated by the same blinded exam-

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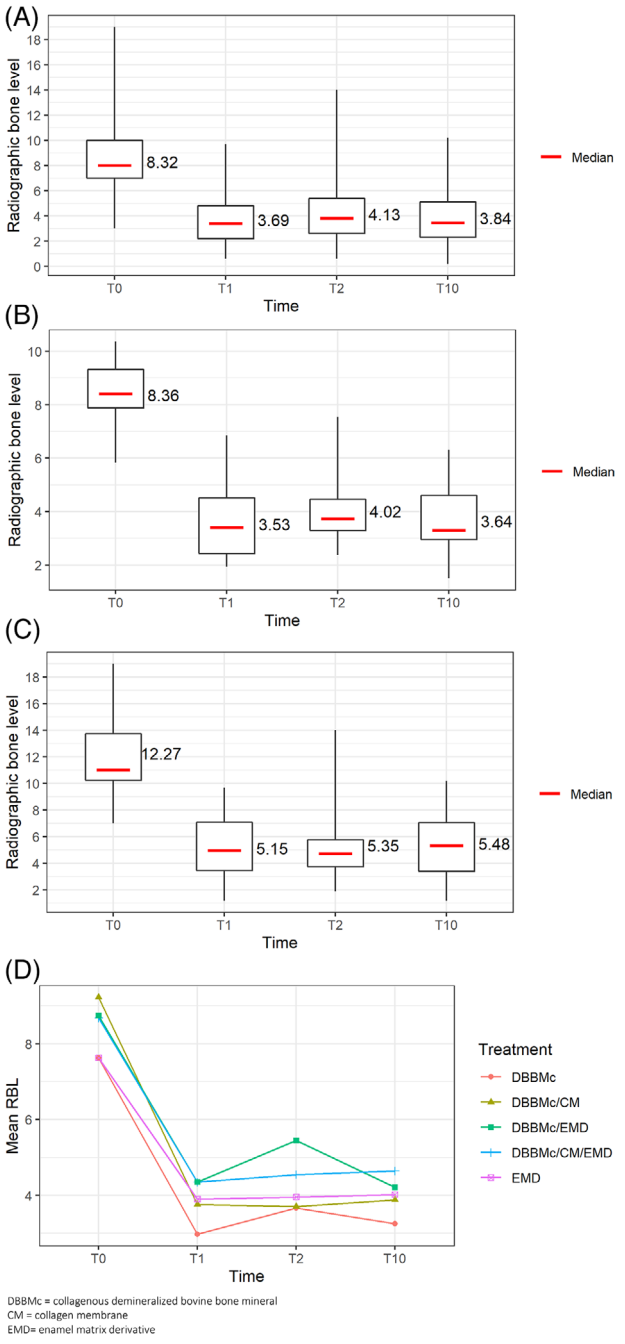

FIGURE 4 (A–D) Box plots showing mean changes in radiographic bone level over time (256 defects in 22 patients) (A) at defect level (B) at patient level, average over all defects (C) at deepest defect per patient $n = 22$ (D) for different treatment modalities. CM, collagen membrane; DBBMc, collagenous demineralized bovine bone mineral; EMD, enamel matrix derivative.

iner, data analysis was performed by an independent expert statistician, both not being involved in the clinical phases of the study. Furthermore, the study was conducted independently and not funded by industry.

However, the present study also has inherent limitations, primarily due its retrospective study design and a missing comparison group. Therefore, the study has to be regarded as a large-scale feasibility study for the design of further prospective randomized clinical trials.

Possible sources of bias, such as orthodontically induced root resorption, the use of radio-opaque bone fillers, measurement errors of rBL due to change of tooth position have been discussed previously in great detail.[18]

The present results cannot be easily compared to those of previously published studies because of differences in study protocols with regard to regenerative procedures, patient and defect selection, choice of outcome measures, time points between regenerative and OT and lengths of follow-up.

However, the protocol of our study and the observed long-term tooth retention by this combined periodontal-regenerative and orthodontic treatment are in line with and in support of the recently published EFP S3 clinical practice guideline (CPG) on the treatment of stage IV periodontitis.[9–11] According to the evidence-based CPG there is a clear recommendation for orthodontic treatment of regeneratively treated intra-bony defects since this combined treatment significantly improves periodontal outcomes and significantly reduces inflammation as long as guidelines of regenerative periodontal treatment[16] and sequences of therapeutic interventions are followed.[11] Based on the recommendation of the evidence-based EFP-S3 level CPG for the treatment of stage IV periodontitis,[11] inflammation has to be under control before, during, and after OT, as it was accomplished in the present study by a rigorous supportive care program over a long period of time.

There is only one earlier study reporting 10-year data following the interdisciplinary treatment of regenerative periodontal therapy and consecutive orthodontic tooth movements which can serve as a direct comparison,[20] however, with a far smaller number of regeneratively treated defects ($n = 36$) compared to our study ($n = 256$). The authors focused on clinical parameters and not on rBL gain. They reported a mean PPD reduction of 3.2 mm and pocket closure of 83% at the 10-year follow-up which is comparable to 2.9 mm mean PPD reduction and 90% of pocket closure observed in the present study. A second long-term follow-up with an average of 11 years[21] on the combined perio/orthodontic therapy did not distinguish in their outcomes between resectively and regeneratively treated defects. Mean PPD reduction was therefore much less with 1.6 mm. However, the observed pocket closure of 87% reveals the same tendency for stability of treatment outcomes as in our study for successful combined periodontal/regenerative and OT. A major difference between these two studies and the present one is the time point of orthodontic intervention (12 months vs. 3 months after periodontal surgery). A

reduced overall treatment time should be viewed as an advantage.

Early orthodontic tooth movements, 3 months after regenerative surgical therapy in this study, did not have a negative impact on long-term outcomes in patients with stage IV periodontitis. This is not only in agreement with the 1-year findings of a multi-center randomized clinical trial on timing of OT – early versus late-stating that there is no adverse effect of early application of orthodontic forces after regenerative therapy – thus reducing overall treatment time[19] and the according CPG recommendation,[11] but indicates that early OT does not preclude but may even support favorable long-term outcomes.

Retention of teeth—as strongly recommended being the first line of treatment strategy by the EFP CPG for stage IV periodontitis[11]—was possible over 10 years in our study with only 4.5% of tooth loss due to non-periodontal reasons, in particular, due to root fracture and endodontic lesions. This is in line with 2.7% of tooth loss due to root fracture as reported in a previous study.[20] The primary outcome of our study—change of rBL—has not been investigated in previous long-term studies[20,21] or cannot be compared due to the lack of distinction between resective or regenerative periodontal therapy before orthodontic tooth movements.[21]

As already stated in our former report[18] the comparison of two independent retrospective cohort studies with regeneratively treated intra-bony defects in the same practice with the same protocol, including surgical procedures, outcome measures and follow-up with and without orthodontic tooth movement[13] was in favor of the combined therapy. With all limitations of such an indirect comparison using a "historical control group," it was remarkable to observe—when now looking at the 10-year follow-up in both cohort groups- that the improvements with regard to mean BL gain in the present study with combined perio/orthodontic therapy were even higher (4.48 mm, 256 defects) than in the cohort, where patients did not undergo OT (3.9 mm, 226 defects). The same applies to PPD reduction with 2.91 mm in the present study and 2.28 mm in the group without OT at the 10-year follow-up. Since the baseline characteristics of the treated defects with regard to mean PPD were similar in both cohorts these findings seem to indicate a possible "stimulating" effect of orthodontic tooth movement in the early healing phase on the regenerative outcomes, as previously suggested by pre-clinical investigations.[28–30] However, this observation should be interpreted with great caution. Further preclinical trials and well controlled clinical research are warranted to decode the effects of mechanical loading after regenerative procedures.

5 | CONCLUSION

Within the limitations of the retrospective study design, the present results suggest that the combination of regenerative treatment and consecutive early OT in patients with stage IV periodontitis well adherent to a strict maintenance protocol can lead to favorable and stable long-term results after 10 years. These findings are in line with and support the current recommendations for this clinical case type 2 of stage IV periodontitis and at the same time provide a promising long-term perspective that has not been available so far.

In the future, well planned prospective randomized clinical trials that also include patient-related and orthodontic outcome measures will further refine the most suitable protocol for the combined regenerative and orthodontic treatment of patients with stage IV periodontitis.

AUTHOR CONTRIBUTIONS

Christina Tietmann conceived the idea of the study, performed the surgeries, interpretation of the results, and manuscript writing. Karin Jepsen and Søren Jepsen contributed to supervision, interpretation of the results, and writing/revising of the manuscript. Helen Heibrok collected the data. Sven Wenzel contributed by supervising the supportive care program. All authors critically reviewed and approved the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest with regard to this study.

DATA AVAILABILITY STATEMENT

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

ETHICS STATEMENT

The study was conducted in accordance with the Declaration of Helsinki (version 2008) and was approved by the Ethical committee of the University of Bonn (#16/23).

ORCID

Christina Tietmann https://orcid.org/0000-0002-7667-762X

Søren Jepsen https://orcid.org/0000-0002-4160-5837
Karin Jepsen https://orcid.org/0000-0002-1015-3145

REFERENCES

1. Brunsvold MA. Pathologic tooth migration. *J Periodontol*. 2005;76:859-866. doi:10.1902/jop.2005.76.6.859
2. Papapanou PN, Sanz M, Buduneli N, et al. Periodontitis: consensus report of workgroup 2 of the 2017 World Workshop on the classification of periodontal and peri-implant diseases and conditions. *J Clin Periodontol*. 2018;45(suppl 2):162-170. doi:10.1111/jcpe.12946
3. Hirschfeld J, Reichhardt E, Sharma P, et al. Interest in orthodontic tooth alignment in adult patients affected by periodontitis: a questionnaire-based cross-sectional pilot study. *J Periodontol*. 2019;90:957-965. doi:10.1002/jop.18-0578
4. Cardaropoli D, Gaveglio L, Abou-Arraj RV. Orthodontic movement and periodontal defects: rationale, timing, and clinical implications. *Semin Orthod*. 2014;20:177-187.
5. Sanz M, Martin C. Tooth movement in the periodontally compromised patient. In: Lang NP, Lindhe J, eds. *Clinical periodontology and implant dentistry*. Wiley; 2015:1297-1324.
6. Bollen AM, Cunha-Cruz J, Bakko DW, Huang G, Hujoel P. The effects of orthodontic therapy on periodontal health: a systematic review of controlled evidence. *J Am Dent Assoc*. 2008;139(4):413-422. doi:10.14219/jada.archive.2008.0184
7. Papageorgiou S, Papadelli A, Eliades T. Effect of orthodontic treatment on periodontal clinical attachment: a systematic review and meta-analysis. *Euro J Orthod*. 2018;40(2):176-194. doi:10.1093/ejo/cjx052
8. Martin C, Celis B, Ambrosio N, Bollain J, Antonouglou GN, Figuero E. Effect of orthodontic therapy in periodontitis and non-periodontitis patients: a systematic review with meta-analysis. *J Clin Periodontol*. 2021;49(suppl 24):72-101. doi:10.1111/jcpe.13487
9. Papageorgiou S, Antonoglou G, Michelogiannakis D, Kakali L, Eliades T, Madianos P. Effect of periodontal-orthodontic treatment of teeth with pathological tooth flaring, drifting, and elongation in patients with severe periodontitis: a systematic review with meta-analysis. *J Clin Periodontol*. 2021;49(suppl 24):102-120. doi:10.1111/jcpe.13529
10. Kloukos D, Roccuzzo A, Stahli A, Sculean A, Katsaros C, Salvi GE. Effect of combined periodontal and orthodontic treatment of tilted molars and teeth with intra-bony and furcation defects in stage-IV periodontitis patients: a systematic review. *J Clin Periodontol*. 2021;49(suppl 24):5121-5148. doi:10.1111/jcpe.13509
11. Herrera D, Sanz M, Kebschull M, et al. Treatment of stage IV periodontitis: the EFP S3 level clinical practice guideline. *J Clin Periodontol*. 2022;49(suppl 24):124-171. doi:10.1111/jcpe.13639
12. Cortellini P, Tonetti MS. Clinical concepts for regenerative therapy in intrabony defects. *Periodontol 2000*. 2015;68(1):282-307. doi:10.1111/prd.12048
13. Bröseler F, Tietmann C, Hinz AK, Jepsen S. Long-term results of periodontal therapy: a retrospective cohort study. *J Clin Periodontol*. 2017;44:520-529. doi:10.1111/jcpe.12723
14. Nibali L, Koidou V, Nieri M, Barbato L, Pagliaro U, Cairo F. Regenerative surgery versus access flap for the treatment of intrabony periodontal defects. A systematic review and meta-analysis. *J Clin Periodontol*. 2020;47(suppl 22):320-351. doi:10.1111/jcpe.13237
15. Nibali L, Sultan D, Arena C, Pelekos G, Lin GH, onetti M. Periodontal infrabony defects: systematic review of healing by defect morphology following regenerative surgery. *J Clin Periodontol*. 2021;48:101-114. doi:10.1111/jcpe.13381
16. Sanz M, Herrera D, Kebschull M, et al. Treatment of stage I-III periodontitis- the EFP S3 level clinical practice guideline. *J Clin Periodontol*. 2020;47(suppl 22):4-60. doi:10.1111/jcpe.13290
17. Stavropoulos A, Bertl K, Spinelli L, Sculean A, Cortellini P, onetti M. Medium- and long-term clinical benefits of periodontal regenerative/reconstructive procedures in intrabony defects: systematic review and network meta-analysis of randomized controlled clinical studies. *J Clin Periodontol*. 2021;48(3):410-430. doi:10.1111/jcpe.13409
18. Tietmann C, Bröseler F, Axelrad T, Jepsen K, Jepsen S. Regenerative periodontal surgery and orthodontic tooth movements in stage IV periodontitis: a retrospective practice-based cohort study. *J Clin Periodontol*. 2021;48(5):668-678. doi:10.1111/jcpe.13442
19. Jepsen K, Tietmann C, Kutschera E, et al. The effect of timing of orthodontic therapy on the outcomes of regenerative periodontal surgery in patients with stage IV periodontitis: a multicenter randomized trial. *J Clin Periodontol*. 2021;48(10):1282-1292. doi:10.1111/jcpe.13528
20. Roccuzzo M, Marchese S, Dalmasso P, Roccuzzo A. Periodontal regeneration and treatment of severely periodontally compromised teeth: 10-year results of a prospective study. *Int J Periodontics Restorative Dent*. 2018;38(6):801-809. doi:10.11607/prd.3756
21. Aimetti M, Garbo D, Ercoli E, Grigorie MM, Citterio F, Romano F. Long-term prognosis of severely compromised teeth following combined periodontal and orthodontic treatment: a retrospective study. *Int J Periodontics Restorative Dent*. 2020;40(1):95-102. doi:10.11607/prd.4523
22. OťLeary TJ. Tooth mobility. *Dent Clin North Am*. 1969;13(3):567-579.
23. R Core Team. *R: a language and environment for statistical computing. R foundation for statistical Computing* 2020; https://www.R-project.org/
24. Rosner B, Glynn R, Lee ML. The Wilcoxon signed rank test for paired comparisons of clustered data. *Biometrics*. 2006;62(1):185-192. doi:10.1111/j.1541-0420.2005.00389.x
25. Fai AH, Cornelius PL. Approximate F-tests of multiple degree of freedom hypotheses in generalized least squares analyses of unbalanced split-plot experiments. *J Statist Comput Simul*. 1996;54(4):363-378. doi:10.1080/009496596088111740
26. Hothorn T, Hornik K, van den Weil MA, Zeileis A. Implementing a class of permutation tests: the coin package. *Jof Statistical Software*. 2008;28(8):1-23. doi:10.18637/jss.v028.i08
27. Franke M, Bröseler F, Tietmann C. Patient-related evaluation after systematic periodontal therapy – A clinical study on periodontal health-related quality of life (PHQoL). *Oral Healt Prevent Dent*. 2015;13:163-168. https://do.org/10.3290/j.ahpd.a32340
28. Nemcovsky CE, Beny L, Shanberger S, Feldman-Herman S, Vardimon A. Bone apposition in surgical bony defects following orthodontic movement: a comparative histomorphometric study between root- and periodontal ligament-damaged and periodontally intact rat molars. *J Periodontol*. 2004;75(7):1013-1019. doi:10.1902/jop.2004.75.7.1013

29. Vardimon AD, Nemcovsky CE, Dre E. Orthodontic tooth movement enhances bone healing of surgical bony defects in rats. *J Periodontol*. 2001;72(7):858-864. doi:10.1902/jop.2001.72.7.858
30. Diedrich P, Fritz U, Kinzinger G, Angelakis J. Movement of periodontally affected teeth after guided tissue regeneration (GTR) – an experimental pilot study in animals. *J Orofac Orthop*. 2003;64(3):214-227. doi:10.1007/s00056-003-0240-8

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APPENDIX

TABLE A1 Results from final model for the change of radiographic bone level from T_0 to T_{10}.

	Estimate (SE)	*p*-Value
Fixed effects		
(Intercept)	−1.00 (0.46)	0.031
rBl at T0	0.69 (0.05)	<0.0001
Smoking	−1.99 (0.76)	0.017
Random effects:		
Patient standard deviation	0.836	
Residual standard deviation	1.76	
R2:		
R2m/R2c	0.474/0.571	