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Article

Periodontal Outcomes and Digital Data Integration of Orthodontic Treatment with Clear Aligners: A Prospective Pilot Study

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Abstract: Pathologic tooth migration (PTM) is a complication of Stage III and IV periodontitis. This pilot study aims to analyze the periodontal response to orthodontic aligner therapy in stage IV periodontitis patients, by perio charting and digital orthodontic data obtained from intraoral scans. Following periodontal treatment of 21 recruited patients, 11 underwent clear aligner treatment. Periodontal data (Probing Pocket Depth—PPD, Recession Index—REC, Clinical Attachment Loss—CAL) were collected at baseline (T0), after periodontal treatment (T1), and at the end of the orthodontic treatment (T2). Digital data obtained at T1 and T2 were processed with the 3D software Geomagic® Control X™. Occlusograms obtained by the proximity sensors of the scans were converted into differently colored pixelated areas. These results were compared to highlight changes in clinical crown length or occlusal contact areas. The results showed a slight increase in the REC index and a statistically significant reduction of PPD and CAL at T1 and T2. Digital data showed a statistically significant decrease in terms of gingival recessions and clinical crowns at the end of orthodontic treatment. Hard occlusal contacts showed a statistically significant decrease by the end of the orthodontic treatment. The results are comparable to those reported in the scientific literature for fixed orthodontic treatment. Clear aligner treatment could be considered an option in patients with severe periodontitis, promoting final light occlusal contacts.

Keywords: clear aligners; periodontal index; occlusal contacts; tooth movement



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1. Introduction

Periodontitis is a microbial-induced chronic inflammation within tooth-supporting tissues, resulting in progressive attachment loss and alveolar bone resorption. According to the most recent classification, periodontitis is defined with staging and grading [1]. The degree of periodontal tissue breakdown is classified through Stages I to IV based on the severity of clinical attachment loss (CAL) and the number of teeth lost due to periodontitis and denotes the progressively increasing complexity of disease management.

In stage IV periodontitis, the considerable damage to periodontal support is frequently complicated by tooth drifting and flaring, tooth hypermobility due to secondary occlusal trauma, and posterior bite collapse [2]. Pathologic tooth migration (PTM) of anterior teeth is a frequent complication of severe periodontitis, with a prevalence from 30.03 to 55.8% [3,4]. A recent study found that the overall prevalence of PTM was 11.14%; however, when patients with mild periodontitis were excluded, the reported prevalence of PTM was 21.73% [5]. PTM is also a common chief complaint among patients, due to esthetic and functional problems [6].

Orthodontics is a component of the multidisciplinary treatment of periodontitis that aims to re-establish the correct position of flared teeth to restore esthetics and function [7].

Despite the absence of a direct correlation between malocclusion and periodontal breakdown [8], orthodontic treatment is recommended when periodontal health can be worsened by severe crowding, premature contacts, deep bites associated with direct trauma of the periodontal tissues, excessive mobility due to lip interposition [9–11], and premature contacts with occlusal instability [12,13].

Orthodontic forces on the periodontally compromised tooth produce different effects when compared to teeth with an intact periodontium, since the tooth's center of resistance shifts apically, often leading to alveolar bone loss [14], and the moment-to-force ratio for orthodontic tooth movement (OTM) increases with the severity of bone resorption. Controlled tooth movements and appropriate force systems must be delivered according to each individual's anatomic situation. Moreover, it has been demonstrated that the application of light force with a clear aligners system, results in a small amount of linear and angular displacement, even if the predictability of small horizontal, vertical, and sagittal orthodontic movements is likely to occur [15]. Aligner treatment, moreover, reduces posterior occlusal contacts [16], but this condition might not be favored in patients with anterior flaring.

However, it is mandatory that plaque-induced inflammation be completely suppressed before the application of orthodontic forces, and that proper oral hygiene is maintained [17]. The use of clear aligners may minimize orthodontics-related negative effects on periodontal health, facilitating proper oral hygiene procedures [18], allowing better maintenance of good gingival conditions than fixed appliances [19] and not inducing significant changes in the composition of oral microbioma in the short term [20]; thus, they might be recommended for patients at high risk of developing periodontal issues.

Therefore, this prospective pilot study was conducted to test periodontal indexes in Stage IV periodontitis patients treated with aligner orthodontics as a primary outcome. As a secondary outcome, digital data from intraoral scans were utilized to investigate variation in occlusal contact distribution areas at the end of the treatment, and eventual matching between the clinical periodontal recession index data, in terms of correlation with the clinical crown's length.

2. Materials and Methods

2.1. Sample Selection

This prospective pilot study was performed according to the Declaration of Helsinki guidelines and informed consent from each participant was obtained. The study was approved by the local Ethics Committee (157/2020). Twenty-one patients were referred to the C.I.R. Dental School, University of Turin, between January 2021 and November 2022. All the patients enrolled in the study presented Stage IV–Grade B periodontitis and PTM of the anterior teeth. The average Wits value was 1.8 ± 2.6 mm. Patients' chief complaints were tooth flaring and the misalignment of the frontal teeth.

2.2. Inclusion and Exclusion Criteria

Recent studies examining the inter-disciplinary treatment of periodontitis stage IV suggest that no statistically significant differences between groups can be observed for CAL gain and PPD reduction between early (4 weeks) and late (6 months) commencement of orthodontic treatment after regenerative surgery [21]. Thus, in this trial, we started aligner therapy 9 to 12 weeks after the completion at the Section of Periodontology of the same institution of periodontal non-surgical and surgical treatment, thus reducing the overall treatment time, which seems to have favorable effects on extended inflammation risk [13].

The following inclusion criteria were applied: (1) no residual pocket with probing depth > 4 mm after periodontal treatment; (2) good oral hygiene at home with full-mouth plaque score (FMPS) < 15%; (3) control of the inflammatory component of periodontal disease with full-mouth bleeding score (FMPS) < 15%; [22]; (4) malocclusion within the

orthodontic range (Class I, mild Class II or III, no antero-posterior correction and no orthognatic surgery needed). Patients were excluded if they had any systemic diseases (e.g., uncontrolled diabetes), took medications that would influence treatment (bisphosphonates), had a thin scalloped periodontal phenotype [23,24], smoked more than 10 cigarettes/day, presented tooth mobility degree < 2 mm, and failed to comply with the oral hygiene instructions provided. Eleven patients out of the twenty-one met the inclusion criteria for orthodontic treatment, with 228 teeth located at stabilized severe periodontitis sites, thereby providing 1368 sampling sites for this study.

2.3. Data Collection

The initial periodontal examinations were performed at baseline, before (T0), and after (T1) periodontal treatment. Then, periodontal outcomes were re-evaluated by two experienced examiners at the end of the orthodontic treatment, after an average of a 19-month treatment (T2). Clinical data included assessment of all teeth, except for the third molars, presence/absence of bacterial plaque, presence/absence of bleeding on probing, probing pocket depth (PPD), gingival recession (REC), and attachment loss (CAL) at six sites per tooth, using a manual periodontal probe with 1 mm markings (PCPUNC15, Hu-Friedy®, Chicago, IL, USA).

2.4. Intervention

At T1 and T2, intraoral scans were detected, using the iTero Element 5D (© 2020 Align Technology Inc., San José, CA, USA) scanner. All patients were treated with Clear Aligner Therapy (CAT) using Invisalign® (Align Technology, San Jose, CA, USA) aligners. Materials and features of the aligners were 8th generation, released in 2020 by Align Technology [25].

2.5. Geomagic Analysis

STL files were obtained from MyiTero (<https://bff.cloud.myitero.com>, accessed on 15 December 2022), then exported and managed within Geomagic® Control X™ (Geomagic Qualify (3D Systems(r), Rock Hill, SC, USA) app, so the clinical crown of all teeth was obtained and measured in millimeters, both from the vestibular and the palatal/lingual sides (Figure 1a–d).

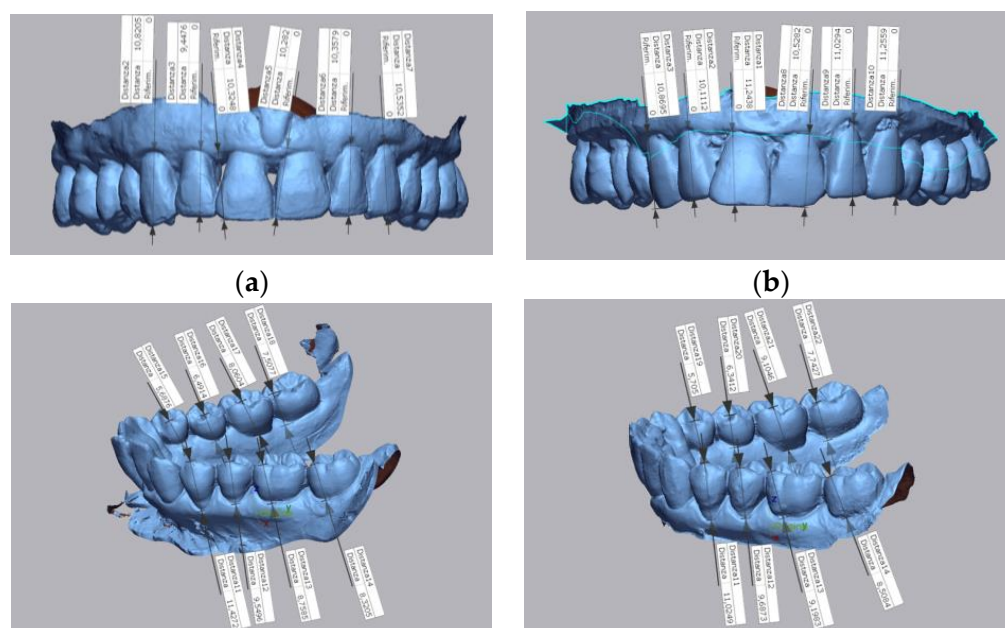


Figure 1. (a–d) Examples of upper and lower arches, pre and post treatment, respectively, were managed with Geomagic® Control X™ software. Schematic illustrations of linear measurements (mm)

were considered in the study: upper and lower, central and lateral incisors, distance between medium point on the incisal edge and the most gingival point among distal, central, and mesial site, both on vestibular and lingual–palatal side; upper and lower cuspids: distance between higher cusp’s point and the most gingival point among distal, central, and mesial sites, both on vestibular and lingual–palatal side; upper and lower premolars: vestibular cusp apex and vestibular gingival margin of the gingival margin among distal, central and mesial sites, both on vestibular and lingual–palatal side; lingual cusp apex and apical lingual point of the gingival margin; upper and lower molars: mesio-buccal cusp apex and most apical buccal point of the gingival margin among distal, central and mesial sites; mesio lingual cusp apex and most apical lingual point from among the distal, central and mesial sites.

2.6. ImageJ Analysis

Drawing STL files from MyiTero (<https://bff.cloud.myitero.com> accessed on 15 December 2022), the occlusal contacts’ images of the upper and lower arches were evaluated and collected, before and after orthodontic treatment. Occlusal contacts were analyzed according to the Occlusal Clearance legend [26], which determines the distance between opposing teeth to survey occlusal contact collisions in terms of tenths of millimeters (Figure 2a–c).

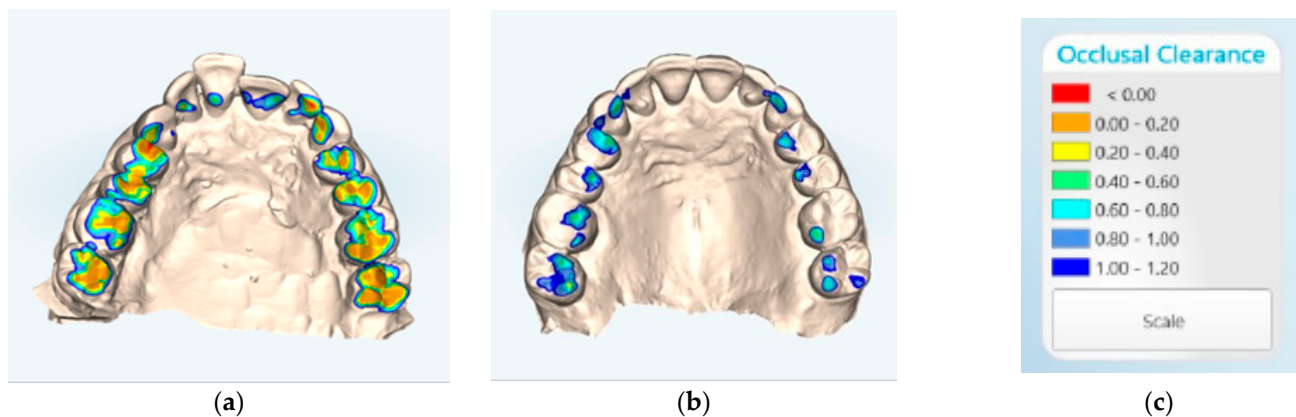


Figure 2. Examples of upper arches, pre (a) and post (b) treatment, respectively, with occlusal contacts exported into MyiTero scans. Occlusal Clearance Scale (c).

These occlusal images were then imported in ImageJ (<https://imagej.nih.gov/ij/index.html>, accessed on 28 November 2023) (Figure 3a,b). Contact colors analyzed are depicted in ImageJ, and were red, green, and blue, in decreasing order of occlusal proximity to the opposite arch, respectively. The differently colored pixels were counted to determine pre and post treatment of occlusal contacts’ areas.

2.7. Statistical Analysis

The normality assumption of the data was evaluated with the Shapiro–Wilk test. Homoscedasticity and autocorrelation of the variables were assessed using the Breusch–Pagan and Durbin–Watson tests. Multiple regression modeling was performed to estimate the difference in time (T1–T0), adjusting for side, arch, and tooth type. Estimates with std. error show the mean difference between times. In total, 95%CI was used to explain estimate variability. Descriptive values were shown, considering the main indicators of distribution and variability. The level of significance was set at $p < 0.05$. The sample size calculation is based on the parameter $\alpha = 0.05$. Subjects were enrolled for the study in order to detect 80% of statistical power. The study was able to detect a MD (mean difference) $\geq |0.35|$ between time (T1 and T0), which can be considered an efficient cut-off for the included variables in this specific context. Statistical analyses were conducted using the R statistical package (version 3.5.3, R Core Team, Foundation for Statistical Computing, Vienna, Austria).

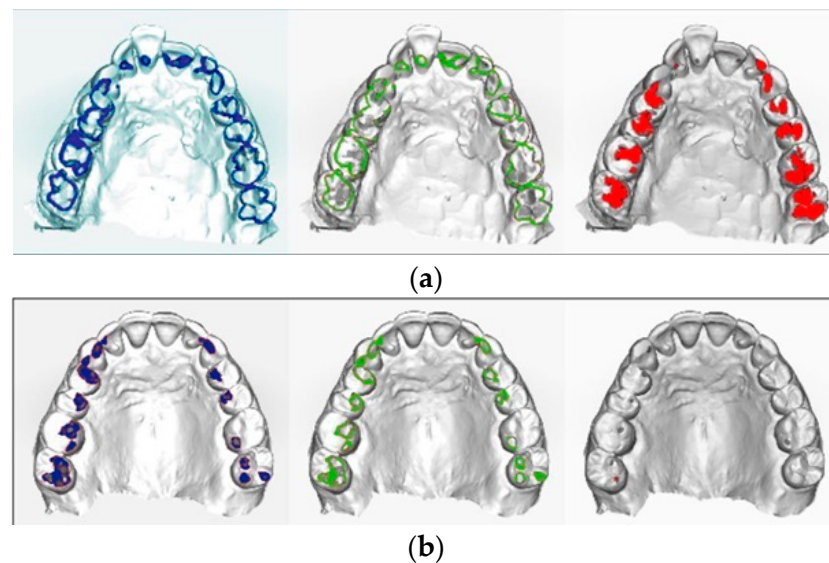


Figure 3. (a,b) Examples of upper arches: pre (a) and post (b) treatment, respectively, with occlusal contacts exported into ImageJ software. Blue, green, and red colors are in increasing order of occlusal proximity to the opposite arch, respectively.

3. Results

The records of 228 teeth of 11 patients (4 men and 7 women; mean age 50.7 ± 12.4), meeting the inclusion criteria for orthodontic therapy, were analyzed. In total, 168 sampling sites and respective measurements for the periodontal indices were provided for each patient at each time point. Periodontal indices data were measured for all sites at T0, T1, and T2 with periodontal charting. The results are shown as a percentage of sites affected by statistically significant differences, and sorted per anterior (from 1.3 to 2.3 and from 3.3 to 4.3) or posterior (from 1.4 to 1.7, from 2.4 to 2.7, from 3.4 to 3.7, from 4.4 to 4.7) teeth and time points (Tables 1–3). The estimated values reported in the Supplementary Material Tables' highlighted mean differences between T1 and T0 and between T2 and T0, stratified per site, measure, and tooth (Tables S1–S3). The patients presented pathological tooth migrations with flaring of the incisors, resulting in increased overjet (4.9 ± 1.7 mm) and overbite (4.4 ± 2.7 mm).

Table 1. (a) T0 was used as reference. The percentage of sites refers to statistically significant changes for the REC index only and is related to all 168 sites sampled. The minimum and maximum values refer to statistically significant measurements only. (b) T1 was used as reference. The percentage of sites refers to statistically significant changes for REC index only and is related to the total of 168 sites sampled. The minimum and maximum values refer to statistically significant measurements only.

| (a) Tooth | Measure | Percentage | Time | Estimate Minimum Value (mm) | Estimate Maximum Value (mm) |
|-----------------|---------|------------|------|-----------------------------|-----------------------------|
| Anterior teeth | REC | 1.38% | T2 | 1.32 | 1.32 |
| Posterior teeth | REC | 1.78% | T2 | 0.78 | 1.17 |
| (b) Tooth | Measure | Percentage | Time | Estimate Minimum Value (mm) | Estimate Maximum Value (mm) |
| Anterior Teeth | REC | 2.97% | T2 | 1.22 | 1.55 |
| Posterior teeth | REC | 1.19% | T2 | 0.75 | 0.89 |
| Posterior teeth | REC | 0.59% | T2 | −1.40 | −1.40 |

Table 2. (a) T0 was used as reference. The percentage of sites refers to statistically significant changes only for CAL index; it is related to all 168 sites sampled. The minimum and maximum values refer to statistically significant measurements only. (b) T1 was used as reference. The percentage of sites refers to statistically significant changes only for CAL index; it is related to the total of 168 sites sampled. The minimum and maximum values refer to statistically significant measurements only.

| (a) Tooth | Measure | Percentage | Time | Estimate Minimum Value (mm) | Estimate Maximum Value (mm) |
|-----------------|---------|------------|------|-----------------------------|-----------------------------|
| Anterior teeth | CAL | 10.71% | T1 | −1.44 | −3.22 |
| Posterior teeth | CAL | 13.54% | T1 | −1.00 | −3.60 |
| Anterior teeth | CAL | 5.95% | T2 | −1.67 | −3.00 |
| Posterior teeth | CAL | 13.54% | T2 | −1.15 | −3.18 |
| Posterior tooth | CAL | 0.59% | T2 | 3.85 | 3.85 |
| (b) Tooth | Measure | Percentage | Time | Estimate Minimum Value (mm) | Estimate Maximum Value (mm) |
| Posterior tooth | CAL | 0.59% | T2 | 1.22 | 1.22 |
| Posterior tooth | CAL | 0.59% | T2 | −1.40 | −1.40 |

Table 3. (a) T0 was used as reference. The percentage of sites refers to statistically significant changes only for PPD index and is related to all 168 sites sampled. The minimum and maximum values refer to statistically significant measurements only. (b) T1 was used as reference. The percentage of sites refers to statistically significant changes for the PPD index only and is related to all 168 sites sampled. The minimum and maximum values refer to statistically significant measurements only.

| (a) Tooth | Measure | Percentage | Time | Estimate Minimum Value (mm) | Estimate Maximum Value (mm) |
|-----------------|---------|------------|------|-----------------------------|-----------------------------|
| Anterior teeth | PPD | 15.47% | T1 | −0.67 | −2.89 |
| Posterior teeth | PPD | 17.85% | T1 | −0.67 | −3.60 |
| Anterior teeth | PPD | 22.02% | T2 | −0.78 | −3.22 |
| Posterior teeth | PPD | 30.35% | T2 | −0.78 | −3.88 |
| (b) Tooth | Measure | Percentage | Time | Estimate Minimum Value (mm) | Estimate Maximum Value (mm) |
| Anterior teeth | PPD | 4.76% | T2 | −0.67 | −1.00 |
| Posterior teeth | PPD | 2.38% | T2 | −0.66 | −1.76 |

3.1. Periodontal Indexes

3.1.1. Gingival Recession (REC)

When analyzing data to establish gingival recession (REC) with respect to T0 in the anterior area, 1 site showed a significant worsening at T2 (1.38%). In the posterior area, a significant worsening was indicated at 3 sites (1.78%) at T2. All the remaining measurements (both at T1 and at T2) showed no statistically significant difference with respect to T0.

The evaluation of data after orthodontic treatment with respect to T1 showed a significant worsening of recession, ranging from 0.75 to 1.55 mm, at 5 sites (2.97%) in the anterior area, 2 sites (1.19%) in the posterior areas, and a recession improvement in the posterior area (0.59%) (Table 1).

3.1.2. Clinical Attachment Loss (CAL)

For clinical attachment loss (CAL) a general reduction, deemed a clinical improvement, was observed after periodontal treatment in the anterior area; 18 sites (10.71%) at T1 and 10 sites (5.95%) at T2 showed a statistically significant reduction. In the posterior area, CAL was statistically significantly reduced at 13 sites (7.73%) at T1 and 13 sites (7.73%) at T2.

The evaluation of data after orthodontic treatment, with respect to T1, showed a statistically significant improvement of attachment loss on 1 vestibular site (0.59%) and a worsening on 1 site (0.59%) (Table 2).

3.1.3. Probing Pocket Depth (PPD)

When probing pocket depth (PPD), an overall reduction was highlighted. In the anterior area, the PPD decrease was significant at 37 sites (22.02%) at T2 and 26 sites (15.47%) at T1, with respect to T0. For the posterior areas, the overall reduction of PD measurements was significant at 30 sites (17.85%) at T1, and 51 sites (30.35%) at T2 with respect to T0.

The evaluation of data after orthodontic treatment, with respect to T1, confirmed a statistically significant improvement in probing depth, ranging from 0.66 to 1.76 mm at 12 sites (7.14%) (Table 3).

3.2. Clinical Crown (CC)

Clinical crown length, digitally measured in millimeters, before (T1) and after (T2) of the orthodontic treatment, showed an average increase in the anterior area of 0.2 mm ± 0.18 mm after aligner therapy, which is not a statistically significant result. In the posterior area, a significant decrease in clinical crown size was found, and it was, on average, 0.29 mm ($p = 0.049$) (Table 4), so that any clear correlation between scanner measurements and periodontal charting could be confirmed, but a mere slight trend in these results matching was pointed out.

Table 4. Scan digital data measurements. Multiple regression analyses stratified per teeth. T1 was used as reference.

| Clinical Crown Size (mm) | Time | Estimate | Std.Error | p Value | 95% Lower | 95% Upper |
|-------------------------------------|------|----------|-----------|--------------|-----------|-----------|
| Anterior Teeth (incisors, cuspids) | T2 | 0.2 | 0.18 | 0.28 | −0.16 | 0.55 |
| Posterior Teeth (premolars, molars) | T2 | 0.29 | 0.15 | 0.049 | 0.001 | 0.57 |

3.3. Occlusal Contacts

Analyzing occlusal contact areas by pixel number (Table 5), with ImageJ software (<https://imagej.nih.gov/ij/index.html>, accessed on 15 December 2022), the red pixel number representing hard inter-arches contacts decreased significantly, while green and blue pixels, representing light contacts, increased, even if not in a significant way (Figure 3a,b).

Table 5. Occlusal contact areas were measured as the difference in number of differently colored pixels, at the beginning (T1) and at the end (T2) of the orthodontic treatment. Multiple regression analyses are stratified by color. T1 was used as reference.

| Pixel Color | Time | Estimate (Pixel Number) | Std.Error | p Value | 95% Lower | 95% Upper |
|-------------|------|-------------------------|-----------|---------------|------------|-----------|
| BLUE | T2 | 18,084 | 16,015 | 0.27 | −13,305.58 | 49,473.48 |
| GREEN | T2 | 1046.7 | 1854 | 0.58 | −2587.11 | 4680.59 |
| RED | T2 | −7117 | 2764 | 0.0144 | −12,534.14 | −1700.07 |

4. Discussion

In this prospective pilot study, we investigated how CAT could affect severe periodontal conditions in perio patients with pathologic tooth migration (PTM), previously treated with non-surgical and surgical periodontal treatments.

An interdisciplinary approach, combining periodontal and orthodontic treatment, is needed to re-establish proper esthetics and function in stage IV periodontitis patients with PTM [27,28]. Application of orthodontics forces requires complete inflammation removal

and a strict oral hygiene protocol. Indeed, all patients underwent orthodontic therapy at the end of the active periodontal treatment and followed a strict periodontal maintenance program [29]. As previously observed in a study carried out on aggressive periodontitis patients [30], orthodontic treatment could lead to a slight improvement in some periodontal outcomes. Moreover, teeth alignment and leveling facilitate hygiene procedures, giving the option to access all teeth surfaces and maintain good oral health easily [18,31,32].

Our results showed the maintenance of good periodontal health at the end of orthodontic treatment with clear aligners in the short term. In addition, forces and strengths were applied widely within 1 N limits, mainly on periodontally compromised teeth [33]. Considering all these aspects together is essential to avoid further damaging effects on periodontal tissues due to orthodontic-induced inflammation [34].

Previous studies have displayed satisfactory clinical results with aligners, showing a good percentage of randomly chosen cases complied with the American Board of Orthodontics–Objective Grading System (ABO-OGS) score [35] when treatments were conducted by expert clinicians [36,37].

A recent systematic review with meta-analysis [38] compared the outcomes of CAT compared to braces; it showed robust evidence, based on “ABO scores and proportion of treated cases with ‘acceptable’ finishing quality (ABO-OGS score < 30)”, and did not favor aligners treatment. However, focusing our attention on PTM, ABO components such as alignment, marginal ridges, and interproximal contacts produced very similar results for both CAT and fixed braces appliances.

Conversely, the same systematic review and meta-analysis based on the PAR index, revealed no significant differences between aligners and braces, with the exception of significant differences in the PAR components for the upper anterior and overbite, which favored braces [38].

On this basis, CAT would seem not to severely worsen periodontal indices with respect to the end of the periodontal treatment, contributing to reduced PPD in the anterior and posterior areas with periodontal maintenance therapy [39,40].

In this study, the REC data showed a slight increase after CAT for anterior areas and overall changes (increase and decrease) in the posterior areas, even if not statistically significant, consistent with previous evaluations in the literature [41], thus confirming a trend of continuous increments in gingival recessions after treatment, ranging to around 7% at the end of treatment, as Renkema et al. (2013) illustrate in their retrospective study [41].

Both at the end of the periodontal treatment (T1) and of CAT (T2), a statistically significant overall improvement for CAL was observed in this study, above all at the mesial and distal sites. Unsurprisingly, this data confirms the efficacy of periodontal treatment, but also suggests that the CAL may benefit from orthodontic therapy, due to the final greater interproximal stability of adjacent teeth.

Interproximal contact point (CP) strength determines the maintenance of the interdental papilla in severe periodontitis patients [42]. Moreover, CP distance from the alveolar bone crest is also a determining factor in the presence of an interdental papilla. Since orthodontic movements can change the position of the CP, the papilla can be reshaped and stabilized inside interproximal spaces [43].

Clinical crown (CC) length measured on STL files increased after orthodontic treatment in the anterior area (not statistically significant) and on premolars and molars (statistically significant). Conversely, for the same teeth, the periodontal charting did not highlight any recession increase accordingly; this could be due to the poor reliability and overall difficulty reading the millimeter scale on the perio probe in posterior areas [44,45]. Scan measurements, instead, were found to be a reliable means to detect changes in clinical crown height [46].

The occlusograms obtained from intraoral scans at the beginning and at the end of CAT showed that hard inter-arches contacts after orthodontic treatment decreased significantly, and light inter-arches contacts increased at the same time. This may suggest that OTM with aligners could promote light occlusal contacts. Moreover, according to a recent systematic

review [13], the long-term prognosis of pathologically migrated teeth could be enhanced by a harmonious occlusion with balanced occlusal contacts, even if a retention appliance was used in the vast majority of studies included in this review, representing a possible confounding factor. Therefore, light occlusal contacts would be able to decrease the occlusal trauma-associated risks.

Moreover, the virtual planning of OTM, with reduced linear and angular movement velocity, can result in minimizing periodontium tissue distress [37,47] with aligners in patients with a healthy reduced periodontium.

5. Conclusions

Within the limitations of this pilot study, with the small number of patients involved, the periodontal indexes of stabilized stage IV periodontitis patients treated with clear aligner therapy experienced partial improvement in terms of clinical attachment and probing depth.

The correlation between the clinical and digital data was poor but was confirmed for the anterior area, although it was not consistent for posterior areas. Therefore, the possible application of digital intraoral scans as adjunctive diagnostic data in periodontal evaluation should be investigated further.

Occlusal contacts of CAT patients were lightened after the end of orthodontic treatment, but a reduction in periodontal risk was associated with occlusal trauma. In addition, the stability of orthodontic results over time should be a topic for further research on larger samples.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/app14010116/s1>.

Author Contributions: S.R. and T.C. Conceptualization, S.R. and T.C. Methodology, S.R. Validation, S.R., E.M. and A.S. Investigation, S.R. and E.M. Data Curation, G.C. Formal Analysis, S.R. Writing—Original Draft Preparation, S.R., T.C. and A.D. Writing—Review and Editing. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of Comitato Etico Interaziendale A.o.U and Città della Salute e della Scienza di Torino (protocol code number is 0071268 and the approval date is 24 July 2020).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author. The data are not publicly available due to privacy policies.

Conflicts of Interest: Author T.C. has received fees and grants from Align technology outside the present study and in any case irrelevant to the present study. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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