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OXFORD

Randomized controlled trial

Accelerating aligner treatment using low-frequency vibration: a single-centre, randomized controlled clinical trial

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Summary

Background: Low-frequency vibrations have been proposed as a means of accelerating tooth movement and reducing orthodontic treatment times.
Objective: To determine any differences in the accuracy of dental movement in patients treated with a low-frequency vibration aligner protocol and/or by reducing the aligner replacement interval with respect to a conventional protocol.
Design: This trial was designed as a single-centre, randomized controlled clinical trial.
Methods: *Participants*: Patients (aged 27.1 ± 9.0 years) who required orthodontic treatment with aligners. *Randomization*: Patients were randomly allocated to three arms as determined by a computer-randomization scheme. Group A were assigned a conventional protocol (aligners replaced every 14 days); group B also used a low-frequency vibration device for 20 minutes per day; group C followed the same vibration protocol but replaced their aligners every 7 days. *Blinding*: The operator who performed the set-up and the one who analysed the data were blinded to the group of the patients. *Outcome:* Pre- and post-treatment digital models were analysed using VAM software to identify the accuracy/imprecision of dental movements. One-way analysis of variance ($P < 0.05$) and the Bonferroni *post hoc* test were used to identify any statistically significant differences between the three arms in terms of the accuracy of tooth movement versus the prescription.
Results: *Numbers analysed:* A total of 45 patients (15 for group) were analysed (i.e. 2286 dental movements). *Outcome:* No statistically significant differences emerged between groups A and C in the upper arch, or among groups A, B, and C in the lower. Group B displayed significantly greater accuracy with respect to group A in upper incisor rotation ($P = 0.016$), and to group C in vestibulolingual ($P = 0.007$) and mesiodistal tipping ($P = 0.029$) of the upper canines, and vestibulolingual tipping of the upper molars ($P = 0.0001$). *Harms:* No adverse events or side-effects were registered.
Conclusions: There was no difference in accuracy between replacing the aligners accompanied by low-frequency vibration every 7 days and replacing them every 14 days without vibration. Moreover, low-frequency vibration seemed to improve the accuracy of a conventional protocol in terms of upper incisor rotation.
Trial registration: The German Clinical Trials Register (DRK00015613).

Introduction

Increasing the speed of tooth movement without compromising accuracy is one of the major challenges in Orthodontics. Numerous methods of speeding up treatment have been proposed, including biomodulator injection, gene therapy, lasers, corticotomy, and vibration (1). Among them, vibration technology has generated particular interest due to its lack of invasiveness and the fact that patients can administer their own treatment at home.

Low-frequency vibrations have long been used in Medicine to promote fracture healing and bone reinforcement in osteoporosis (2). More recently, however, they have been applied in Orthodontics to induce proliferation and differentiation of periodontal cells.

AcceleDent, which has received the CE Mark, is a vibratory orthodontic device that uses low pulsatile forces (0.25 N) through SoftPulse Technology®. Low pulsatile forces, as used by AcceleDent, should stimulate cellular activity during orthodontic treatment when patients gently bite on AcceleDent's mouthpiece for 20 minutes per day. These precisely calibrated micropulses transmit through the roots of teeth to the surrounding bone.

Some *in vitro* and animal studies indicate that the application of low-frequency vibration is also able to increase both the number and activity of osteoclasts in the periodontal ligament, thereby promoting dental movement (15 per cent increase in rate of movement over 21 days in rats using vibrations for 8 minutes per day (3)), as well as reducing capillary obliteration and thereby preventing the formation of hyaline tissue, which in turn lessens the risk of root resorption (4,5). That being said, other studies have failed to confirm that this technology can increase the rate of dental movement in animals (6,7).

Hence, despite the promising results from *in vitro* and animal studies, the efficacy of low-frequency vibrations in humans to this end remains controversial (8,9). Although some studies have not demonstrated any acceleration in fixed orthodontic treatment ascribable to the use of vibration with respect to controls (10–12), several case reports and prospective studies suggest otherwise (13–15). One randomized controlled trial (RCT), using a protocol applying 30 Hz of vibration for 20 minutes per day, which is equivalent to the application of a cyclic force of 0.25 N (25 g), has shown an increase in the rate of canine movement in first premolar extraction space closure cases (16). Nonetheless, a recent RCT (17) showed no evidence of any statistically significant increase in the speed of extraction space closure when a low-frequency vibration protocol was used.

That being said, very few studies into the efficacy of vibration in speeding up fixed orthodontics have thus far been performed, and even fewer on the potential of the association between vibration technology and aligners. The most common aligner protocol, referred to here as the conventional protocol, involves the replacement of aligners with the next in the series after 14 days. This is generally considered the time required to perform the maximum movement they are able to achieve, specifically, 2-degree tipping, 1-degree torque, and 2-degree rotation (18). Although replacing the aligners more frequently would considerably shorten treatment times, it is not yet clear whether this strategy would lead to a loss of accuracy and precision in tooth displacement.

One article on a clinical sample reports that it is possible to replace aligners every 7–10 days if used in conjunction with low-frequency vibration, but as the authors themselves pointed out, this conclusion was based on empirical data obtained without a well-defined, scientifically rigorous protocol (19). A single RCT (20) has been published, which compares the variation of the irregularity index in the anterior teeth with aligners and a 7-day substitution protocol, associating or not with low-frequency vibrations.

Specific objectives or hypotheses

The aim of this study was to determine whether or not there is any difference in the accuracy of tooth movement with respect to a conventional protocol when low-frequency vibrations are associated with aligners replaced every 14 and 7 days.

The null hypothesis was that there would be no significant differences in the accuracy of movements prescribed in the set-up [mesiodistal (MD) tip, vestibulolingual (VL) tip, and rotation] at any tooth type (upper and lower incisors, canines, premolars and molars) whether patients were treated via a conventional protocol in which aligners were replaced every 14 days (group A), whether this protocol was associated with daily application of low-frequency vibrations (group B), or whether daily low-frequency vibrations were used in conjunction with a 7-day aligner replacement protocol (group C).

Materials and methods

Trial design

This prospective three-arm parallel-group randomized clinical trial was approved by the Province of Ferrara Unified Ethics Committee (Protocol 161187) and was conducted in conformity to the Declaration of Helsinki, according to CONSORT guidelines.

Sample size calculation

The following calculation was applied to determine the statistically meaningful number of patients to include: for comparison of three parallel groups via one-way analysis of variance (ANOVA) and to achieve a type 1 error with $\alpha = 0.05$ (5 per cent) and objective power 0.8 (80 per cent)—and therefore a type 2 error of 20 per cent—a minimum of 79 teeth for each tooth per arch would be necessary. Considering that the least numerous tooth type is the canine—two per arch in each patient—the minimum number of patients to be recruited was 40, which was increased to 45 to take into account a possible dropout rate of 10 per cent.

Participants, eligibility criteria, and settings

The 45 subjects were recruited from September 2016 to March 2017 at the University of Ferrara Postgraduate School of Orthodontics Clinic. All had requested aligner treatment with the sole aim of correcting dental alignment. The sample comprised 20 males and 25 females of mean age 27.1 ± 9.0 years (range 14.8–46.9 years). Inclusion and exclusion criteria are listed in Table 1. All subjects gave informed written consent, which was obtained from parents or legal guardians in cases in which the patient was below the age of consent.

Randomization

An external statistician was asked to randomize the sample. Stata statistical software (StataCorp LLC, College Station, Texas, USA) was used to randomly allocate recruited patients to one of the three treatment arms (groups A, B, or C). Stratification was achieved solely by imposing a number of 15 subject per group on the software, so that groups contained an equal number of participants. No other limits were imposed on the stratification process.

Blinding

The operator who performed the set-up was blind to the group that each patient had been assigned to. Both the patients and clinicians were aware of the treatment prescribed, but the operator charged with gathering and analysing the data was blind to the group that each patient belonged to.

Table 1. Sample inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
• Permanent dentition • Age between 14 and 50 y • Complete dentition, or at most 1 missing tooth per quadrant (excluding third molars) • No supernumerary teeth • No tooth shape anomalies • No tooth rotation >35° • No diastems >5 mm • Crowding <5 mm per arch	• Systemic pathologies • Ongoing pharmacological treatment able to influence orthodontic movement (e.g. prostaglandin inhibitors or biphosphonates) • Active periodontal disease • Need for treatment for extraction space closure, distalization, or sagittal correction

Intervention

After collecting pre-treatment records (intra- and extra-oral photographs, panoramic radiograph, teleradiograms, and digital intra-oral scans taken using a Trios scanner (3Shape, Copenhagen, Denmark)), a set-up was planned for each patient using OrthoAnalyzer software (3Shape) for the purposes of treatment using F22 aligners (Sweden & Martina, Due Carrare (PD), Italy). All set-ups were performed by a sole operator.

The treatment staging, i.e. the maximum movement planned for each tooth per aligner, was as follows: up to 2-degree rotation, 2.5-degree each VL and MD tip, and 0.2-mm linear displacement. No auxiliaries of any kind (intra-oral elastics, buttons, chains, etc.) were prescribed, but the F22 system attachments (Grip Points) were used, in addition to anterior and/or posterior interproximal reduction (IPR). The maximum IPR included in the prescription was 0.3 mm per interproximal space, from the mesial sides of the second premolar to the mesial side of the opposite second premolar. The maximum total IPR planned was 2 mm per arch. This was reported in the prescription for each patient and was carried out by a single operator for all patients. IPR was performed manually, with abrasive strips of thickness 0.1 mm and grain 60 μm for stripping, and 15 μm for polishing. The quantity of enamel removed was measured using a dedicated gauge.
The treatment protocols compared in the study were the following:

1. Group A: conventional aligner treatment with aligners replaced every 14 days;
2. Group B: aligners replaced every 14 days + 20 consecutive minutes per day of low-frequency vibration (AcceleDent; OrthoAccel Technologies, Houston, Texas, USA) throughout treatment;
3. Group C: aligners replaced every 7 days + 20 consecutive minutes per day of low-frequency vibration (AcceleDent; OrthoAccel Technologies) throughout treatment.

All patients were instructed to wear their aligners for 22 hours per day, taking them out only during meals and oral hygiene procedures. All patients were examined at monthly check-ups until completion of aligner treatment. During these monthly check-ups, compliance with the vibration protocol was checked via the data recorded on their AcceleDent device. Patients who failed to reach the target 20 minutes were verbally motivated to do so.

Analysis of digital models

For each patient, initial pre-treatment, final post-treatment (upon completion of the aligner series), and ideal final digital models (foreseen by the set-up) were collected, and the respective tooth positions were compared. Models were analysed according to a previously published protocol (21). In brief, a sole operator, blind to the treatment group to which each participant belonged, analysed their digital models using VAM software (Vectra; Canfield Scientific, Fairfield, New Jersey, USA). This package requires the operator to identify 100 anatomical points of interest on the models (Figure 1) from which to calculate the planes, axes, and angles of reference, which, in turn, are used to calculate the tip, torque, and rotation of each tooth (22).

Once each of the 100 anatomical points had been marked, their 3D coordinates were exported, first into a .txt file, and then onto a specifically designed Excel spreadsheet provided by the software developer. This enables extrapolation of the MD tip, VL tip, and rotation values (Figures 2–4) of each tooth with respect to a 3D Cartesian grid parallel to the occlusal reference plane, which was based on the following points (Figure 5):

1. The point at the tip of the mesiovestibular cusp of tooth 16 (maxillary models) or 46 (mandibular models);
2. The point at the tip of the mesiovestibular cusp of tooth 26 (maxillary models) or 36 (mandibular models);
3. The centroid of all occlusal points on the facial axis of the clinical crown (FACC) of teeth 15, 14, 12, 11, 21, 22, 24, and 25 (maxillary models) or 35, 34, 32, 31, 41, 42, 44, and 45 (mandibular models); the canines were excluded from this calculation as their occlusal FACC point is elevated with respect to the occlusal plane of the other teeth.

One month after completion of the analysis of all 270 arches, a random sample of 78 sets of pre-treatment, post-treatment, and ideal models (39 maxillary and 39 mandibular) was selected for repeated measures, i.e. 28.8 per cent of the total sample. Dahlberg's D was calculated to evaluate the random error, and Student's *t*-test for dependent samples to determine whether or not there was any systematic error.

Calculation of mean prescription and imprecision

For each tooth in each patient, the following was calculated for each type of movement:

1. The absolute value of the prescription, i.e. the difference between 'ideal outcome' and 'pre-treatment' measurements, as a measure of the degree of planned movement

$$|\text{Prescription}| = |\text{Ideal Outcome} - \text{Pre-treatment}|$$

2. The absolute value of the imprecision, i.e. the difference between 'ideal' and 'post-treatment' outcomes, as a measure of the degree to which the movement achieved differed from the planned movement.

$$|\text{Imprecision}| = |\text{Ideal Outcome} - \text{Post-treatment}|$$

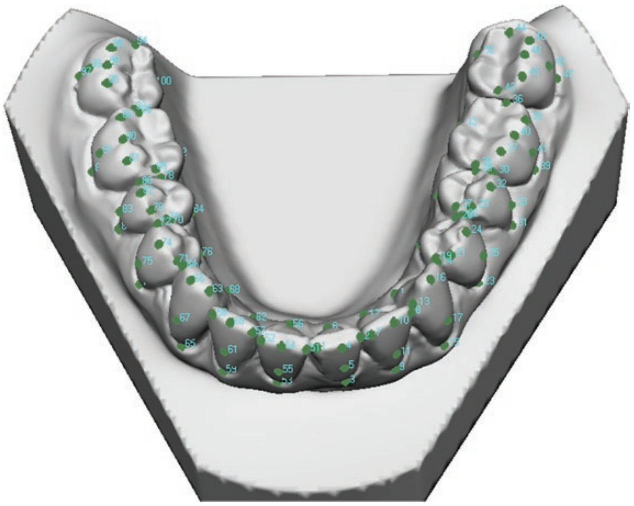

Figure 1. Positioning of the 100 reference points per arch (lower jaw).

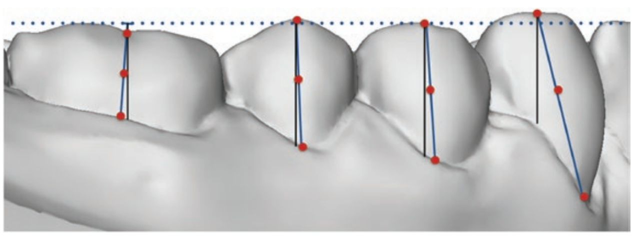

Figure 2. Mesiodistal tipping: mesiodistal inclination of the facial axis of the clinical crown (FACC) with respect to the occlusal plane of reference.

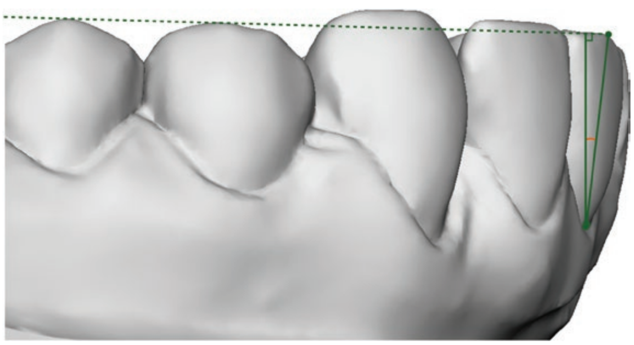

Figure 3. Vestibulolingual tipping: labiolingual inclination of the facial axis of the clinical crown (FACC) with respect to the occlusal plane of reference.

We chose to rely on absolute values for the parameters 'prescription' and 'imprecision', as whether the movement occurred in a clockwise or anti-clockwise (rotation), vestibular or lingual (VL tip), or distal or mesial (MD tip) direction was not taken into consideration.

Subsequently, the 'prescription' and 'imprecision' values were grouped into eight categories on the basis of tooth type (namely upper incisors, upper canines, upper premolars, upper molars, lower incisors, lower canines, lower premolars, and lower molars) and type of movement (MD tipping, VL tipping, and rotation). All movements with a prescription of less than 2 degrees were excluded from the analysis; this method sensitivity threshold had previously been determined by the VAM software method validation study from an analysis of the mean intra-operator error (22) and used in a previously published article (21).

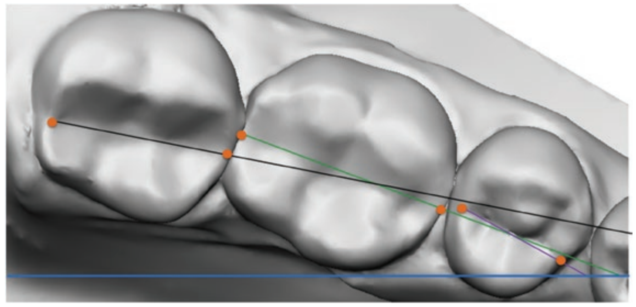

Figure 4. Rotation: the angle between the mesiodistal axis of the tooth and plane *y*.

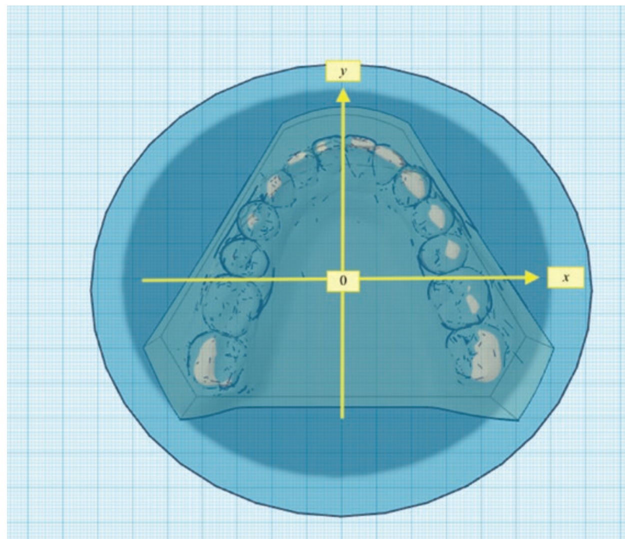

Figure 5. Occlusal plane of reference.

Accuracy calculation

To determine the degree of tooth movement achieved with respect to the prescription, the following formula was applied to each movement of each tooth:

$$\text{Accuracy} = 1 - \frac{\text{Ideal Outcome} - \text{Post-treatment Outcome}}{\text{Ideal Outcome} - \text{Pre-treatment}}$$

which correspond to

$$\text{Accuracy} = 1 - \frac{\text{Imprecision}}{\text{Prescription}}$$

This provided an indicator of accuracy—the closer the value to 1, the more accurate the final position of the tooth with respect to the planned movement.

Comparison among groups and statistical analysis

For each observation group (groups A, B, and C), the mean, standard deviation, and standard error of the means of the prescription, imprecision and accuracy, subdivided by type of tooth and movement, were calculated. One-way ANOVA ($P < 0.05$) and Bonferroni *post hoc* test were used to identify any statistically significant differences in accuracy among the three aligner protocols for each type of tooth and movement.

Results

Baseline data and participant flow

Participant characteristics for each group are reported in Table 2. The groups were homogeneous in terms of mean age and number of aligners in the upper and lower series. However, there was a greater proportion of females (11 out of 15) in group C with respect to the other two. The skeletal and dental characteristics of patients in each group are reported in Supplementary Table 1.

All of the 45 patients recruited completed their prescribed orthodontic treatment, i.e. no dropout occurred (Figure 6).

Recruitment

Collection of all pre-treatment, ideal outcome, and post-treatment records was completed in October 2017. Measurement analysis for paired samples confirmed the absence of systematic error in the measurements of MD tip, VL tip, and rotation (Supplementary Table 2).

Compliance with the vibration device

Patient compliance with the protocol was recorded as follows:

1. Group B: 68.8 ± 21.4 per cent (i.e. 13.7 minutes per day on average)
2. Group C: 76.1 ± 24.5 per cent (i.e. 15.2 minutes per day on average)

Effective sample size

After all teeth with a prescription of less than 2 degrees had been excluded, a total of 740 teeth were available for VL tip analysis, 692 for MD tip, and 854 for rotation—a total of 2286 movements. The size of the sample, subdivided by types of tooth and movement, is reported in Table 3.

Outcomes

Considering all tooth and movement types of the 45 participants, the mean total imprecision was 2.1 ± 0.9 degrees, with respect to a mean prescription of 5.7 ± 2.2 degrees. Table 4 shows the mean prescription, mean imprecision, and accuracy of each type of movement of each tooth type in all 45 participants, irrespective of their group. The movement with the greatest prescription was rotation (mean 8.0 ± 2.6 degrees), and this was associated with a mean imprecision of 2.9 ± 1.0 degrees.

Supplementary Tables 3, 4, and 5 report the mean prescription, mean imprecision, and accuracy of each type of movement of each tooth type in each of the three groups, respectively. In group A, movement of the upper and lower incisors proved to be the most accurate, whereas the least accuracy was found in MD tipping of the canines and upper premolars. Rotation of the canines in both arches displayed the greatest imprecision in absolute values (5.6 ± 5.7 and 5.0 ± 5.6 degrees of the prescription respectively), but these teeth were also subject to the greatest prescribed movements (12.2 ± 9.1 and 12.8 ± 8.9 degrees). In group B too, rotation of the upper and lower canines exhibited the most imprecision, and, together with the lower incisors, the greatest prescription. The greatest accuracy was calculated for rotation of the upper and lower incisors, and the least accuracy for MD tipping of the upper molars. Similarly, in group C the greatest imprecision was registered for rotation of the upper and lower canines; the accuracy at the upper canines was the lowest among those analysed, whereas the highest accuracy was found for rotation of the lower incisors and VL tipping of the upper premolars.

Tables 5 and 6 report the data for the prescription, imprecision, and accuracy among the three groups by tooth type. Statistically significant differences between groups in terms of the accuracy of the same movement of the same tooth are highlighted. The results of multiple comparisons via the Bonferroni *post hoc* test found to be significant are reported in Supplementary Tables 6–8. There was no statistically significant difference in the accuracy of movement of any tooth found in the comparison of groups A and C. However, in four cases, all in the upper jaw, movement was significantly more accurate in group B, specifically:

1. Rotation of the upper incisors: group B was significantly more accurate than group A ($P = 0.016$);
2. VL tipping of the upper canines: significantly more accurate in group B than in group C ($P = 0.007$);

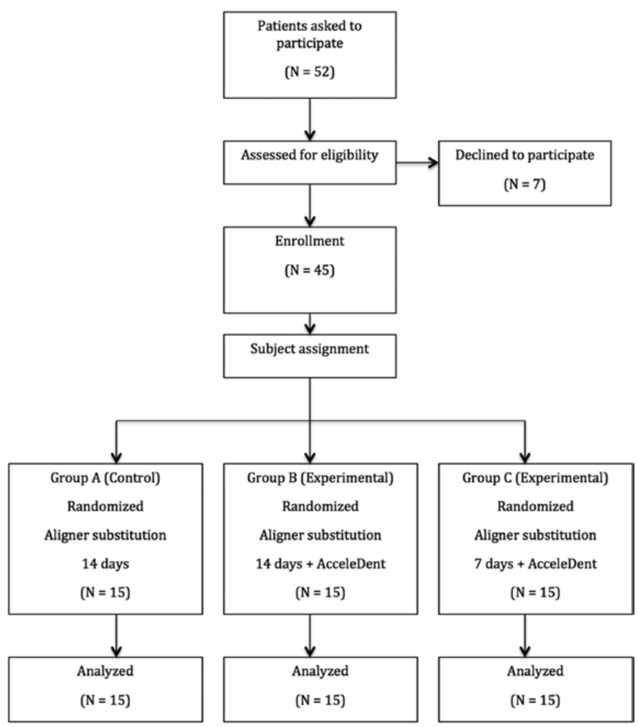

Figure 6. CONSORT diagram showing the flow of subjects in the study.

Table 2. Sample characteristics. M = male; F = female.

Group	*n*°	Age (y)	Gender	*n*° Upper aligners	*n*° Lower aligners
A	15	27.1 ± 8.8	8 M, 7 F	13.5 ± 4.7	12.6 ± 4.9
B	15	26.5 ± 10.7	8 M, 7 F	11.7 ± 4.2	11.5 ± 3.4
C	15	27.4 ± 8.1	4 M, 11 F	11.5 ± 3.9	12.3 ± 3.8
Total	45	27.1 ± 9.1	20 M, 25 F	12.2 ± 4.3	12.1 ± 4.0

3. MD tipping of the upper canines: significantly more accurate in group B than in group C ($P = 0.029$);
4. VL tipping of the upper molars: significantly more accurate in group B than in group C ($P = 0.0001$).

No significant differences in positioning accuracy were found among groups A, B, and C in the lower arch.

Harms

There were no harms experienced by the participants influencing general health of the participants, for any group.

Discussion

Several protocols for shortening the aligner replacement interval have been tested clinically (23), but publications to date have been largely based on case reports or series of weak scientific validity.

The importance of measurement method

It is necessary to determine that any strategy used to speed up treatment does not compromise results, although quantifying the actual expression of movements planned in the set-up remains another research challenge; some authors have proposed the superimposition of ideal and real post-treatment digital models around anatomical structures like the palatine folds (24), but other studies have shown how the position and conformation of these structures may be altered by certain clinical factors (25). What is more, the palatine folds could only serve as a reference in the upper jaw. An alternative method proposed is the superimposition of digital models based on reference teeth that are not prescribed movement (26), but, once again, changes in the position of these teeth due to mastication forces and/or the presence of the aligner in the mouth (anchorage and/or reactive forces) cannot be ruled out. In contrast, the measurement method proposed by Huanca Ghislanzoni *et al.* (22) have demonstrated reproducibility and a lack of systematic and measurement error for all movements above 2 degrees. This method, based on the mean occlusal plane—calculated as the plane passing through the tips of the mesiovestibular cusps of the first molars and the FACC centroids of all the other teeth (with the exception of the canines)—enables the imprecision caused by tooth movement during orthodontic treatment to be minimized.

Movement accuracy for different tooth types

The cases treated using aligners in this RCT had a mean imprecision in dental positioning of 2.1 ± 0.9 degrees, but not all teeth displayed the same predictability of movement. In particular, the incisors presented the greatest accuracy index, whereas the canines were the teeth less responsive to orthodontic movement with aligners. This is likely due to the particular anatomy of the canine crown (rounded) and root (large and often corticalized, especially in the lower arch), and is in agreement with other articles in the literature. Although profoundly different measurement systems were used, Nguyen and Cheng (27) also reported that the most predictable movement was incisor rotation (60 per cent of that prescribed) and Kravitz *et al.* (28) identified lower canine rotation as the least predictable (36 per cent of the prescription). Only one other study has measured F22 aligner accuracy using the same method (21), and its authors found a greater degree of predictability in premolar and molar tip than we did. However, their results were in line with ours in terms of the

Table 3. Database: sample breakdown. VL = vestibulolingual; MD = mesiodistal.

	VL tip	MD tip	Rotation
	n	*n*	*n*
Upper incisors	115	109	146
Upper canines	82	81	83
Upper premolars	86	85	97
Upper molars	82	80	84
Lower incisors	118	93	157
Lower canines	84	80	85
Lower premolars	92	82	119
Lower molars	81	82	83

Table 4. Mean prescription, mean imprecision, and accuracy in the 45 patients. VL = vestibulolingual; MD = mesiodistal; ROT = rotation.

		Prescription			Imprecision			Accuracy		
		VL tip (°)	MD tip (°)	ROT (°)	VL tip (°)	MD tip (°)	ROT (°)	VL tip (°)	MD tip (°)	ROT(°)
Upper incisors	Mean	4.9	5.1	8.6	1.4	1.6	2.8	0.69	0.65	0.67
	SD	3.2	3.1	5.6	1.2	1.3	2.2	0.20	0.21	0.17
Upper canines	Mean	4.9	5.6	9.8	1.9	2.8	4.0	0.61	0.56	0.60
	SD	2.8	5.4	7.8	1.4	4.5	4.1	0.17	0.22	0.18
Upper premolars	Mean	4.4	3.7	5.8	1.3	1.5	2.3	0.68	0.59	0.60
	SD	2.2	1.5	3.4	0.9	0.8	2.1	0.21	0.19	0.20
Upper molars	Mean	3.3	4.7	4.8	1.2	1.7	1.8	0.64	0.63	0.63
	SD	1.1	1.9	2.4	0.7	1.2	1.7	0.16	0.22	0.17
Lower incisors	Mean	5.1	4.9	9.5	1.4	1.6	2.6	0.70	0.68	0.71
	SD	3.0	2.7	6.5	0.8	1.4	2.3	0.18	0.22	0.18
Lower canines	Mean	5.3	4.7	12.1	1.7	1.8	4.5	0.66	0.61	0.63
	SD	2.9	2.9	8.2	1.2	1.5	4.5	0.18	0.19	0.19
Lower premolars	Mean	4.8	4.4	8.2	1.8	1.6	3.4	0.62	0.64	0.62
	SD	2.4	2.4	6.4	1.2	1.6	4.3	0.19	0.23	0.20
Lower molars	Mean	3.2	4.8	4.8	1.3	1.8	1.8	0.60	0.65	0.60
	SD	0.9	2.6	2.7	0.6	1.7	1.2	0.16	0.20	0.15
Total	Mean	4.5	4.8	8.0	1.5	1.8	2.9	0.65	0.63	0.63
	SD	0.8	0.5	2.6	0.3	0.4	1.0	0.04	0.04	0.04

Table 5. Maxillary arch: mean prescription values, mean imprecision, accuracy, and significance by tooth and movement. VL = vestibulo-lingual; MD = mesiodistal; ROT = rotation.

			Prescription			Imprecision			Accuracy		
			VL tip	MD tip	ROT	VL tip	MD tip	ROT	VL tip	MD tip	ROT
Upper incisors	Group A	Mean	5.7	4.7	8.8	1.5	1.5	3.2	0.71	0.66	0.62*
		SD	4.5	2.8	6.3	1.6	1.3	2.8	0.22	0.21	0.20
	Group B	Mean	4.3	4.8	8.2	1.2	1.6	2.3	0.68	0.64	0.72*
		SD	2.0	2.8	4.4	0.8	1.2	1.8	0.20	0.20	0.16
	Group C	Mean	4.9	5.9	8.9	1.5	1.8	2.8	0.68	0.65	0.66
		SD	2.7	3.6	5.9	1.0	1.3	1.9	0.18	0.24	0.13
	Total	Mean	4.9	5.1	8.6	1.4	1.6	2.8	0.69	0.65	0.67
		SD	3.2	3.1	5.6	1.2	1.3	2.2	0.20	0.21	0.17
Upper canines	Group A	Mean	4.8	8.3	12.2	2.0	4.5	5.6	0.61	0.54	0.60
		SD	3.2	8.4	9.1	1.9	7.3	5.7	0.18	0.24	0.20
	Group B	Mean	5.6	4.4	8.8	1.8	1.7	3.3	0.67*	0.65*	0.62
		SD	3.2	2.3	8.5	1.4	2.0	3.5	0.16	0.24	0.16
	Group C	Mean	4.0	4.2	8.4	1.8	2.1	3.1	0.54*	0.49*	0.59
		SD	1.8	1.4	5.0	0.9	0.9	1.8	0.13	0.12	0.17
	Total	Mean	4.9	5.6	9.8	1.9	2.8	4.0	0.61	0.56	0.60
		SD	2.8	5.4	7.8	1.4	4.5	4.1	0.17	0.22	0.18
Upper premolars	Group A	Mean	3.7	3.4	6.2	1.1	1.6	3.0	0.68	0.54	0.56
		SD	1.3	1.1	3.8	0.8	0.9	3.2	0.24	0.23	0.24
	Group B	Mean	5.4	3.8	5.7	1.7	1.2	1.9	0.66	0.66	0.65
		SD	2.9	1.4	3.3	1.2	0.6	1.4	0.19	0.18	0.17
	Group C	Mean	3.9	4.0	5.6	1.1	1.7	2.2	0.71	0.57	0.58
		SD	1.4	1.7	3.2	0.6	0.8	1.3	0.17	0.15	0.17
	Total	Mean	4.4	3.7	5.8	1.3	1.5	2.3	0.68	0.59	0.60
		SD	2.2	1.5	3.4	0.9	0.8	2.1	0.21	0.19	0.20
Upper molars	Group A	Mean	3.0	4.2	4.8	1.1	1.4	1.9	0.64	0.66	0.64
		SD	0.8	1.7	2.4	0.5	1.2	2.0	0.14	0.22	0.20
	Group B	Mean	3.4	4.9	5.7	0.9	2.2	2.3	0.71*	0.55	0.62
		SD	1.0	2.0	3.1	0.5	1.3	1.9	0.15	0.21	0.16
	Group C	Mean	3.6	5.2	3.9	1.6	1.6	1.3	0.55*	0.64	0.64
		SD	1.5	2.0	1.2	0.8	0.9	0.6	0.16	0.23	0.16
	Total	Mean	3.3	4.7	4.8	1.2	1.7	1.8	0.64	0.63	0.63
		SD	1.1	1.9	2.4	0.7	1.2	1.7	0.16	0.22	0.17

*$P < 0.05$

difficulty in predicting canine and lower premolar rotation (54 per cent of that prescribed). Nonetheless, the fact that their study was retrospective and considered a smaller patient sample makes meaningful comparison difficult.

Comparison among groups

Associating vibration (20 consecutive minutes per day) with the conventional protocol, in which aligners were replaced every 14 days, had no effect on the accuracy of tooth movement, with the exception of upper incisor rotation, which was significantly more accurate in group B (+10 per cent). Furthermore, when this vibration protocol was combined with a 7-day aligner replacement schedule, there was no statistically significant difference in movement accuracy to that achieved by the conventional protocol without vibration.

That being said, there were several significant differences between the 7-day and 14-day + vibration protocols. In particular, the accuracy of replacing the aligners every 14, rather than 7, days led to an increase in accuracy of between 13 and 16 per cent; significant improvements were registered for MD tipping and VL tipping of the upper canines, and VL tipping of the upper molars.

In our sample, adding low-frequency vibration to the aligner protocol enabled us to reduce treatment time by 50 per cent without compromising accuracy. This seems to align with the research, that pulsating forces are clinically shown to stimulate the cellular activity in orthodontic treatment. One possible explanation for this observation is that tooth movement rate may be permitted by vibratory stimulation of the periodontium, as suggested by animal models (3) and in some *in vivo* (15) studies with fixed appliances. However, a lack of clear scientific evidence in this regard makes further *in vitro* and *in vivo* studies necessary to clarify the molecular and cellular effects of vibration appliances on the periodontal ligament.

In this specific experimental model, the use of the vibratory orthodontic device may have had a further effect on the aligner treatment by increasing mechanical efficiency, predictability, and tracking. Indeed, it is well known that good aligner fit, i.e. intimate contact between aligner and tooth, is essential to the success of treatment; it may be that gripping the vibration device between the arches on a daily basis may have improved the accuracy of tooth movement, thereby enabling us to reduce the aligner replacement interval. In other words, the mechanical effect exerted by biting down on the device combined with the vibration may have improved the contact between aligner and teeth, and thereby improved upon the outcome that would be possible due to stimulation of the bone metabolism alone. However, at this stage such an effect is merely hypothetical and will require further investigation.

Table 6. Mandibular arch: mean prescription values, mean imprecision, accuracy, and significance by tooth and movemsent. VL = vestibulolingual; MD = mesiodistal; ROT = rotation.

			Prescription			Imprecision			Accuracy		
			VL tip	MD tip	ROT	VL tip	MD tip	ROT	VL tip	MD tip	ROT
Lower incisor	Group A	Mean	4.7	4.1	8.5	1.4	1.2	2.4	0.68	0.71	0.70
		SD	3.5	1.6	6.2	1.0	0.9	1.9	0.22	0.22	0.20
	Group B	Mean	5.1	5.5	9.3	1.3	2.0	2.6	0.73	0.64	0.71
		SD	2.7	2.9	5.9	0.9	1.9	2.6	0.17	0.27	0.18
	Group C	Mean	5.5	4.8	10.8	1.5	1.4	2.8	0.69	0.69	0.71
		SD	2.6	2.9	7.2	0.6	1.0	2.4	0.15	0.15	0.16
	Total	Mean	5.1	4.9	9.5	1.4	1.6	2.6	0.70	0.68	0.71
		SD	3.0	2.7	6.5	0.8	1.4	2.3	0.18	0.22	0.18
Lower canines	Group A	Mean	4.9	5.3	12.8	1.6	2.2	5.0	0.68	0.60	0.65
		SD	2.7	3.8	8.9	1.2	1.9	5.6	0.19	0.17	0.17
	Group B	Mean	6.6	4.3	13.2	2.2	1.5	4.8	0.65	0.64	0.63
		SD	3.5	2.3	8.7	1.4	1.6	4.6	0.17	0.23	0.21
	Group C	Mean	4.4	4.4	10.5	1.4	1.7	3.7	0.66	0.59	0.62
		SD	1.7	1.9	6.9	0.7	0.7	2.8	0.18	0.13	0.18
	Total	Mean	5.3	4.7	12.1	1.7	1.8	4.5	0.66	0.61	0.63
		SD	2.9	2.9	8.2	1.2	1.5	4.5	0.18	0.19	0.19
Lower premolars	Group A	Mean	4.9	5.2	9.2	1.9	1.9	4.0	0.60	0.64	0.60
		SD	2.7	3.1	7.8	1.2	1.9	6.3	0.17	0.24	0.23
	Group B	Mean	5.4	3.8	7.8	1.8	1.4	3.0	0.66	0.63	0.65
		SD	2.7	1.2	5.6	1.3	1.0	2.8	0.24	0.23	0.20
	Group C	Mean	3.9	4.1	7.6	1.6	1.5	3.1	0.59	0.64	0.60
		SD	1.5	2.0	5.5	0.9	1.7	2.9	0.13	0.23	0.17
	Total	Mean	4.8	4.4	8.2	1.8	1.6	3.4	0.62	0.64	0.62
		SD	2.4	2.4	6.4	1.2	1.6	4.3	0.19	0.23	0.20
Lower molars	Group A	Mean	3.0	5.3	4.6	1.1	1.9	2.0	0.62	0.67	0.57
		SD	1.1	3.2	3.0	0.7	2.0	1.7	0.19	0.17	0.18
	Group B	Mean	3.5	4.4	5.4	1.3	1.6	1.7	0.62	0.66	0.64
		SD	0.9	1.5	3.1	0.6	1.2	0.8	0.18	0.23	0.15
	Group C	Mean	3.0	4.7	4.5	1.4	1.9	1.9	0.55	0.63	0.58
		SD	0.6	2.9	1.6	0.4	1.8	0.8	0.09	0.19	0.12
	Total	Mean	3.2	4.8	4.8	1.3	1.8	1.8	0.60	0.65	0.60
		SD	0.9	2.6	2.7	0.6	1.7	1.2	0.16	0.20	0.15

*$P < 0.05$

Compliance

Naturally, any effects of vibration protocols will depend on patient compliance. As Kau *et al*. (14) reported that real patient compliance with the vibrating device is far lower than that perceived by the patient (67 versus 80 per cent respectively), we made use of the FastTrack Usage Report, which captures compliance on each device. Although patients were asked to apply vibration for 20 consecutive minutes each day, these recordings revealed that group B participants used it for 13.7 minutes per day on average, whereas the corresponding figure in group C was 15.2 minutes. This confirms that it is difficult to persuade patients to comply consistently over long periods of time, although a means of objective measurement may help the clinician identify which patients would benefit from constant motivation.

Limitations

There are certain limitations to this study. The first is the trial registration, which was obtained retrospectively, after the study was completed. The registration with a public international trial register is recommended before the beginning of patient recruitment. The second is the sample size. Even if the sample size was statistically adequate, larger groups would have provided more generalizable results. Another one is the blinding procedure; although the operator who performed the set-ups and analysed the data was blind to the study group, the clinician who treated the patients was necessarily aware of the prescribed treatment for both test and control groups. Moreover, despite the reported accuracy and reproducibility of the method, measurement was based on a mean occlusal plane of reference traced through the centroids of the FACCs of all teeth except for the canines; this plane may undergo subtle variation during orthodontic treatment due to tooth movement. Another limitation is the control group; group A patients were not provided with an inactive vibration device as in other studies (16). A recent RCT suggests that there is no statistically significant difference in the final irregularity index in patients treated with aligners by substituting them every 7 days, whether using a low-frequency vibration or a non-vibrating bite (20). That being said, gripping even a sham device between the teeth for 20 minutes per day may conceivably improve aligner fit (as discussed earlier), and therefore nullify the meaningfulness of the control; a further study would determine whether or not an inactive device is in fact able to influence the accuracy of orthodontic movement achieved using aligners.

Another useful addition for comparative purposes would be a group in which patients were not given any device designed to accelerate dental movement and instructed to replace their aligners every 7 days. Indeed, although the comparisons between groups A and B, and B and C each enabled assessment of the effect of a single variable (vibration or not, and aligner replacement time reduction, respectively), a comparison between groups A and C shows the cumulative effect of both. To separate the variables will be useful for better understanding the rule of the vibrating device.

Implications

The results of this RCT indicate that a vibration device can statistically significantly improve the accuracy of upper incisor rotation (the aligner replacement time remaining the same). Moreover, the precision of canine and upper molar tip expression was significantly greater when the aligners, accompanied by the same vibration protocol, were replaced less frequently (every 14 days with respect to every 7 days). This improvement, of between 10 and 16 per cent, may, however, not be clinically significant, especially in cases of slight crowding.

Furthermore, even though a means of reducing aligner treatment time without compromising its accuracy would certainly be of benefit to both patients and clinicians, the root response to low-frequency vibration also needs to be examined in detail to rule out the risk of iatrogenic damage. Indeed, it has been reported that aligner treatment is associated with a lower risk of root resorption with respect to fixed multi-bracket orthodontics (29), and it would be interesting to discover whether more frequent aligner replacement (every 7 days) and/or low-frequency vibration may alter this important outcome.

Conclusions

1. There was no statistically significant difference in the accuracy of dental movement achieved by protocols involving a conventional 14-day F22 aligner replacement interval + no vibration and a 7-day aligner replacement interval + low-frequency vibration applied for 20 minutes a day throughout treatment.
2. Adding 20 minutes per day of low-frequency vibration (30 Hz, 0.25 N) to a conventional 14-day F22 aligner protocol improves the accuracy of upper incisor rotation by 10 per cent.
3. A protocol involving 20 minutes per day of low-frequency vibration (30 Hz, 0.25 N) and a conventional 14-day F22 aligner protocol improves the accuracy of VL and MD tipping of the upper canines and VL tipping of the upper molars between 13 and 16 per cent with respect to one in which aligners are replaced every 7 days.

Supplementary material

Supplementary material is available at the *European Journal of Orthodontics* online.

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Conflict of interest

None to declare.

References

1. Andrade, I. Jr, Sousa, A.B. and da Silva, G.G. (2014) New therapeutic modalities to modulate orthodontic tooth movement. *Dental Press Journal of Orthodontics*, 19, 123–133.
2. Suzuki, A., Takayama, T., Suzuki, N., Kojima, T., Ota, N., Asano, S. and Ito, K. (2009) Daily low-intensity pulsed ultrasound stimulates production of bone morphogenetic protein in ROS 17/2.8 cells. *Journal of Oral Science*, 51, 29–36.
3. Nishimura, M., Chiba, M., Ohashi, T., Sato, M., Shimizu, Y., Igarashi, K. and Mitani, H. (2008) Periodontal tissue activation by vibration: intermittent stimulation by resonance vibration accelerates experimental tooth movement in rats. *American Journal of Orthodontics and Dentofacial Orthopedics*, 133, 572–583.
4. Xue, H., *et al*. (2013) Low-intensity pulsed ultrasound accelerates tooth movement via activation of the BMP-2 signaling pathway. *PLos One*, 8, e68926.
5. Zhang, C., Li, J., Zhang, L., Zhou, Y., Hou, W., Quan, H., Li, X., Chen, Y. and Yu, H. (2012) Effects of mechanical vibration on proliferation and osteogenic differentiation of human periodontal ligament stem cells. *Archives of Oral Biology*, 57, 1395–1407.
6. Yadav, S., Dobie, T., Assefnia, A., Gupta, H., Kalajzic, Z. and Nanda, R. (2015) Effect of low-frequency mechanical vibration on orthodontic tooth movement. *American Journal of Orthodontics and Dentofacial Orthopedics*, 148, 440–449.
7. Kalajzic, Z., Peluso, E.B., Utreja, A., Dyment, N., Nihara, J., Xu, M., Chen, J., Uribe, F. and Wadhwa, S. (2014) Effect of cyclical forces on the periodontal ligament and alveolar bone remodeling during orthodontic tooth movement. *Angle Orthodontist*, 84, 297–303.
8. Miles, P. (2017) Accelerated orthodontic treatment—what's the evidence? *Australian Dental Journal*, 62(suppl 1), 63–70.
9. Aldrees, A.M. (2016) Do customized orthodontic appliances and vibration devices provide more efficient treatment than conventional methods? *Korean Journal of Orthodontics*, 46, 180–185.
10. Miles, P., Smith, H., Weyant, R. and Rinchuse, D.J. (2012) The effects of a vibrational appliance on tooth movement and patient discomfort: a prospective randomised clinical trial. *Australian Orthodontic Journal*, 28, 213–218.
11. Woodhouse, N.R., DiBiase, A.T., Johnson, N., Slipper, C., Grant, J., Alsaleh, M., Donaldson, A.N. and Cobourne, M.T. (2015) Supplemental vibrational force during orthodontic alignment: a randomized trial. *Journal of Dental Research*, 94, 682–689.
12. Miles, P., and Fisher, E. (2016) Assessment of the changes in arch perimeter and irregularity in the mandibular arch during initial alignment with the AcceleDent Aura appliance vs no appliance in adolescents: a single-blind randomized clinical trial. *American Journal of Orthodontics and Dentofacial Orthopedics*, 150, 928–936.
13. Kau, C.H. (2009) A novel device in orthodontics. *Aesthetic Dentistry Today*, 3:42–43.
14. Kau, C.H., Nguyen, J.T. and English, J.D. (2010) The clinical evaluation of a novel cyclical force generating device in orthodontics. *Orthodontic Practice*, 1:1–4.
15. Bowman, S.J. (2014) The effect of vibration on the rate of leveling and alignment. *Journal of Clinical Orthodontics*, 48, 678–688.
16. Pavlin, D., Anthony, R., Raj, V. and Gakunga, P.T. (2015) Cyclic loading (vibration) accelerates tooth movement in orthodontic patients: a double-blind, randomized controlled trial. *Seminars in Orthodontics*, 21:187–194
17. DiBiase, A.T., Woodhouse, N.R., Papageorgiou, S.N., Johnson, N., Slipper, C., Grant, J., Alsaleh, M., Khaja, Y. and Cobourne, M.T. (2018) Effects of supplemental vibrational force on space closure, treatment duration, and occlusal outcome: a multicenter randomized clinical trial. *American Journal of Orthodontics and Dentofacial Orthopedics*, 153, 469–480.e4.

18. Ojima, K., Dan, C., Kumagai, Y. and Schupp, W. (2016) Invisalign treatment accelerated by photobiomodulation. *Journal of Clinical Orthodontics*, 50, 309–317; quiz 319.
19. Orton-Gibbs, S., and Kim, N.Y. (2015) Clinical experience with the use of pulsatile forces to accelerate treatment. *Journal of Clinical Orthodontics*, 49, 557–573.
20. Katchooi, M., Cohanim, B., Tai, S., Bayirli, B., Spiekerman, C. and Huang, G. (2018) Effect of supplemental vibration on orthodontic treatment with aligners: a randomized trial. *American Journal of Orthodontics and Dentofacial Orthopedics*, 153, 336–346.
21. Lombardo, L., Arreghini, A., Ramina, F., Huanca Ghislanzoni, L.T. and Siciliani, G. (2017) Predictability of orthodontic movement with orthodontic aligners: a retrospective study. *Progress in Orthodontics*, 18, 35.
22. Huanca Ghislanzoni, L.T., Lineberger, M., Cevidanes, L.H., Mapelli, A., Sforza, C. and McNamara, J.A., Jr (2013) Evaluation of tip and torque on virtual study models: a validation study. *Progress in Orthodontics*, 14:19.
23. Ojima, K., Dan, C., Nishiyama, R., Ohtsuka, S. and Schupp, W. (2014) Accelerated extraction treatment with Invisalign. *Journal of clinical orthodontics*, 48, 487–499.
24. Miller, R.J., Kuo, E. and Choi, W. (2003) Validation of align technology's treat III digital model superimposition tool and its case application. *Orthodontics and Craniofacial Research*, 6(suppl 1), 143–149.
25. Ali, B., Shaikh, A. and Fida, M. (2016) Stability of palatal rugae as a forensic marker in orthodontically treated cases. *Journal of Forensic Sciences*, 61, 1351–1355.
26. Kravitz, N.D., Kusnoto, B., BeGole, E., Obrez, A. and Agran, B. (2009) How well does Invisalign work? A prospective clinical study evaluating the efficacy of tooth movement with Invisalign. *American Journal of Orthodontics and Dentofacial Orthopedics*, 135, 27–35.
27. Nguyen, C.V. and Chen, J. (2006) Three-dimensional superimposition tool. In O.C. Tuncay (ed.), *The Invisalign System*. Quintessence Publishing, New Malden, UK, Chapter 14, pp. 12–32.
28. Kravitz, N.D., Kusnoto, B., Agran, B. and Viana, G. (2008) Influence of attachments and interproximal reduction on the accuracy of canine rotation with Invisalign. A prospective clinical study. *Angle Orthodontist*, 78, 682–687.
29. Elhaddaoui, R., Qoraich, H.S., Bahije, L. and Zaoui, F. (2017) Orthodontic aligners and root resorption: a systematic review. *International Orthodontics*, 15, 1–12.