

Cyclic loading (vibration) accelerates tooth movement in orthodontic patients: A double-blind, randomized controlled trial

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This was a parallel, double-blind, prospective, randomized, controlled trial with the objective to assess the effect of a defined low-level cyclic loading on the rate of orthodontic tooth movement. Overall, 45 orthodontic patients were treated with fixed appliances at the UTHSC San Antonio Orthodontic Department. Inclusion criteria were extraction of maxillary first premolars, maximum maxillary posterior anchorage, and at least 3 mm of extraction space after initial alignment. The enrolled subjects were randomized into two groups, vibration (n = 23) and control (n = 22) using a third-party computer-generated randomization schedule. All care providers, investigators, and patients were blinded to intervention assignment. Cyclic loading was applied to the vibration group for 20 min/day using the AcceleDent[®] device, which delivered a force of 0.25 N (25 g) at a frequency of 30 Hz. The control group was assigned to the same protocol, but the device could not be activated to vibrate. The average monthly rate of maxillary canine retraction into an extraction space was analyzed in all 45 subjects (ITT group). The mean rate of movement was significantly higher for the AcceleDent[®] group with 1.16 mm/month (95% CI: 0.86–1.46) compared to 0.79 mm/month (95% CI: 0.49–1.09) in the control group, with the mean difference of 0.37 mm/month (95% CI: 0.07–0.81, P = 0.05). These results showed that low-level cyclic loading of 0.25 N at 30 Hz increases the rate of tooth movement when applied as an adjunct to orthodontic treatment. (Semin Orthod 2015; ■■■■–■■■.) © 2015 The Authors. Published by Elsevier Inc. All rights reserved.

Introduction

The rate of tooth movement is an important factor determining the duration of orthodontic treatment. Physiologically, the rate of tooth movement reflects the rates of bone turnover and

remodeling. Earlier approaches that have been used in an attempt to accelerate tooth movement include low-energy laser irradiation,¹ magnetic fields,² as well as pharmacological interventions with the injection of prostaglandin E₂³ and vitamin D.⁴ However, adverse events, such as local pain and severe root resorption,⁵ were associated with these treatments. Corticotomy-facilitated orthodontics⁶ has limited clinical use due to the morbidity of the surgery, cost, and insufficient clinical evidence. Shorter treatment time decreases risk of caries, periodontal disease, and root resorption,⁷ but there has been little progress in developing new, non-invasive approaches to accelerate tooth movement and to reduce the duration of treatment.⁸

Low-level mechanical oscillatory signals (vibrations) have been shown to increase the rate of remodeling in mechanical loaded long bones,⁹ which is currently used in the prevention of osteoporosis¹⁰ based on an increase in bone

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metabolism and decrease in bone loss in postmenopausal women.¹¹ There is also compelling evidence from animal studies using cranial suture model^{12,13} and long bone periosteum¹⁴ suggesting that dynamic loading improves bone formation and increases orthodontic tooth movement compared to a static force.¹⁵ While there is an emerging body of evidence that vibration enhances orthodontic tooth movement in animals, the effect of analogous level vibrations on tooth movement in patients had not been investigated. The aim of this study was to determine whether a defined type of vibration, as an adjunct to orthodontic treatment, increases the rate of tooth movement in patients with fixed orthodontic appliances.

Methods

This was a prospective, randomized, controlled, double-blind, parallel group clinical trial conducted at a single center in the United States. Subject enrollment occurred from February 2009 through June 2010. Data analyzed included subject follow-up from the beginning of treatment through the end of space closure. The null hypothesis was that there was no statistically significant difference in the rate of tooth movement with standard orthodontic treatment alone (control group) compared with standard orthodontic treatment plus the vibration applied for 20 min/day (vibration group) by the AcceleDent[®] device (OrthoAccel Technologies, Inc., Bellaire, TX) designed to deliver a cyclical (vibrational) force of 0.25 N (25 g) with a frequency of 30 Hz.

Sample size was determined based on an expected movement rate of 0.24 mm/week in the control group¹⁶ and a clinically relevant increase over that baseline rate up to 0.35 mm/week in the AcceleDent[®] group, consistent with results from an earlier pilot study.¹⁷ Using the pilot study observed standard deviation of 0.10 mm/week, two-sided alpha (type I error) of 0.05, and 80% power, a sample size of 16 subjects per group (total of 32) was required to detect a statistically significant difference between the groups. This sample yields 95% probability to reveal at least one occurrence of all adverse events that occur at a rate of 17.1% or greater. The sample was increased to 45 subjects to compensate for potentially larger number of dropouts. The study was approved by the IRB and

written informed consent was obtained from all subjects. Trial summary was published on ClinicalTrials.gov. The study protocol was pre-approved by the U.S. Food and Drug Administration (FDA) under an Investigational Device Exemption (IDE-G080191).

Subjects inclusion criteria were age (12–40 years), required extraction of maxillary first premolar(s), space closure with maximum maxillary anchorage, 3 mm of extraction space after initial alignment, and good oral hygiene. Subject exclusion criteria were periodontal disease, prescription medications, use of bisphosphonates, and pregnancy. Subjects were randomly allocated to either the AcceleDent group or the control group that used an appliance with internally disabled vibration. A third-party vendor provided a computer-generated randomization schedule with a block size of 4 and stratified to insure that the number of subjects aged 12–19 years and aged 20–40 years, as well as the number of subjects with “separate canine retraction” versus “en masse retraction” were equally distributed between the groups. Each subject was assigned to the next of the 48 pre-specified numbers for four stratification combinations and the allocation key was kept locked outside the clinic. The device was programmed to the assigned treatment by independent site personnel and both the investigators and the subjects remained blinded to treatment.

All subjects were treated by orthodontic residents under supervision of an investigator/faculty. A routine set of orthodontic records was taken. A 0.022×0.028 in twin brackets (MBT, 3M Unitek, St. Paul, MN) were bonded and the use of AcceleDent[®] started from the beginning of treatment. Patient compliance with the device was tracked using a logbook. After initial alignment, a mini-implant was inserted¹⁸ and immediately loaded with 180 g of force (Fig. 1), which produced a predominantly translatory canine movement, thus avoiding an unstable posterior dental anchorage that would compromise accurate measurements.¹⁹ To avoid excessive occlusal interferences, the bite was opened when necessary using composite build-ups. Separate canine retraction was performed on a 0.018 in stainless steel (SS) arch wire and en masse retraction with a 0.019×0.025 SS arch wire.

Direct measurement of space closure in patients' mouth precludes the analysis of intrarater error at the same appointment. Thus, the

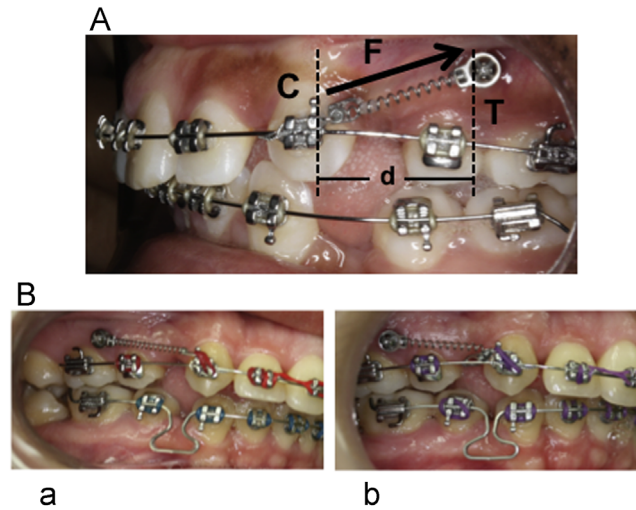


Figure 1. (A) Orthodontic appliance for separate canine retraction: C, canine being retracted; T, TAD (Tomaspin, Dentaaurum, Ispringen, Germany) with a diameter of 1.6 mm and a length of 9 mm was inserted between the maxillary second premolar and the first molar, under local anesthetic and was immediately loaded; F, retraction force of 180 g (measured by Dontrix[®] gauge, American Orthodontics, Sheboygan, Wisconsin) was applied with a nickel-titanium coil spring between the TAD and the canine bracket; d, distance measured parallel to the occlusal plane using a digital caliper prior to each coil spring activation or reactivation. An average value from two measurements was entered at each visit, which were approximately 4 weeks apart. The spring was truncated as needed and re-tied to deliver 180 g of force. (B) Representative example of retraction mechanics for space closure. (a) Activated coil spring in place at the beginning of space closure. (b) One month later, the space opened mesial to the canine.

intra-rater and inter-rater reliability was tested by making measurements on 12 different quadrants of typodonts with mounted mini screws and bonded brackets. The intra-rater reliability was tested for each rater 1 and rater 2 by comparing repeated measurements with a 1-week interval between them, and the inter-rater reliability was tested by comparing the average of the assessments of two independent raters who each conducted two assessments of each quadrant. Intraclass correlation coefficients (ICCs) were calculated with ICC model 2.1 for intra-rater reliability and ICC model 2.2 for inter-rater reliability.

As a primary outcome measure, the average monthly rates of tooth movement in the AcceleDent and control groups were analyzed for the intent-to-treat (ITT) and the per-protocol (PP) treatment populations, using a general linear model that accounted for age (12–19 versus 20–40 years), gender, and type of retraction. The monthly rate of tooth movement was calculated for each subject and each quadrant by calculating the total distance the cuspid moved, while the TAD was stable and dividing it by the total length

of time that the TAD was stable during the space closure. If any level of TAD mobility was observed, it was considered loose and the last month's measurement was excluded. If a TAD continued to fail after two attempts of reinsertion in the proximity of the original site, the measurements were discontinued (Fig. 2). The subject's data were included in the analysis if there were at least three consecutive stable TAD measurements recorded.

Results

Baseline demographic and clinical characteristics analysis showed that there was no difference between the AcceleDent and control groups with respect to age, ethnicity, or weight. Of 45 subjects enrolled in the study (ITT group), 39 were represented in the PP group (Fig. 2). Six subjects were excluded from the PP group for the following reasons: pregnancy ($n = 1$), extraction space less than 3 mm after initial alignment ($n = 1$), and no stable TAD distance measurements [TAD failure due to poor oral hygiene ($n = 4$)]. The retraction was

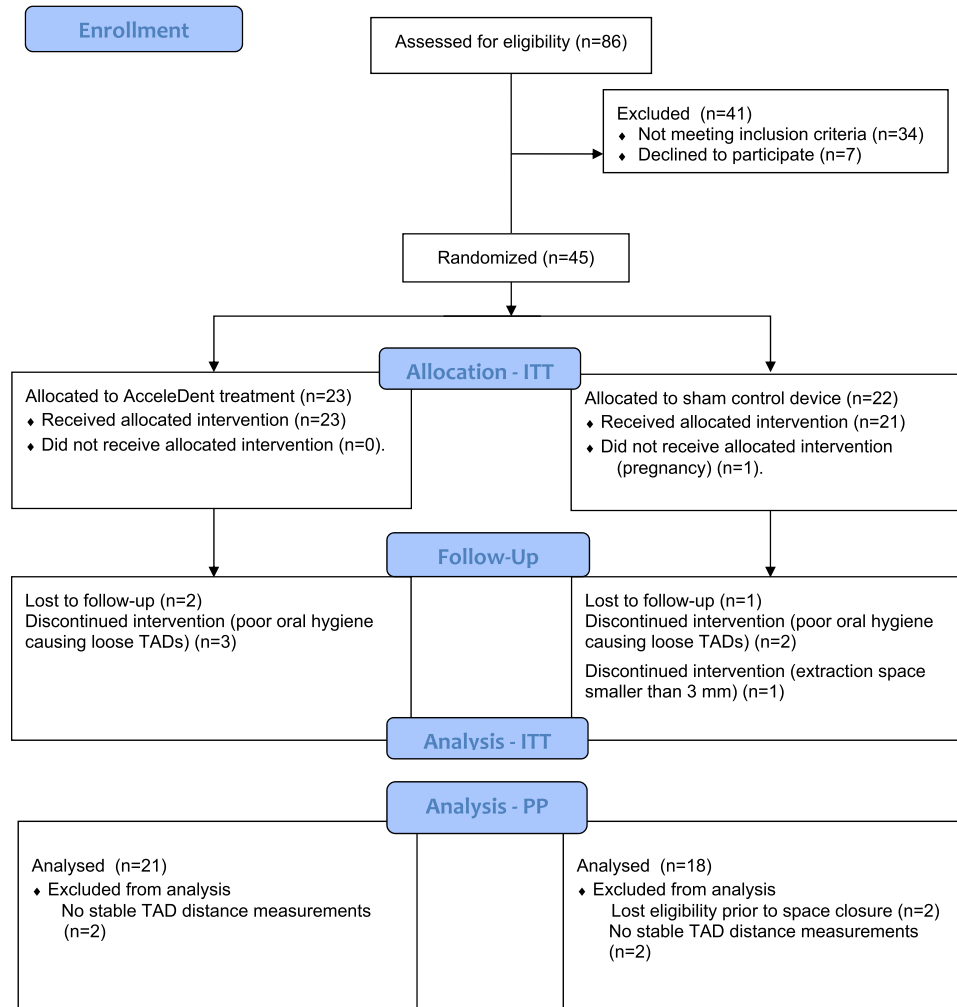


Figure 2. Patient flow diagram (CONSORT format) describing subjects enrolled and included in analyses. The number of subjects excluded from analysis in each group (listed in the Analysis—PP boxes) does not correspond to the total number of lost to follow-up and discontinued intervention subjects (listed in the Follow-Up boxes). This is because some of the subjects with discontinued intervention had fulfilled the requirement of at least three consecutive measurements being taken prior to discontinuation, thus remaining in the analysis group.

bilateral in 35 patients, and an average rate was calculated for each subject. The canine moved by translation, as demonstrated by the reversal lines in bone and mathematical analysis (Fig. 3). The results of the error analysis showed that the ICC was 0.98 for rater 1 (95% CI: 0.93–0.99), 0.96 for rater 2 (95% CI: 0.87–0.99), and the ICC for the average assessments between the two raters was 0.94 (95% CI: 0.80–0.98), indicating that there was no significant intra-rater and inter-rater differences that biased the tooth movement measurements.

The ITT analysis of the primary outcome is presented in the Table. The average monthly rate of tooth movement in the AcceleDent group was 1.16 mm/month (95% CI: 0.86–1.46), which was significantly faster ($48.1 \pm 7.1\%$) compared to 0.79 mm/month (95% CI: 0.49–1.09) in the control group, with the mean difference of 0.37 mm/month (95% CI: 0.07–0.81, $P = 0.05$). The PP analysis also demonstrated significantly faster movement of the retracting cuspids when vibration was applied ($P = 0.02$, Table). The emphasis in interpretation of the

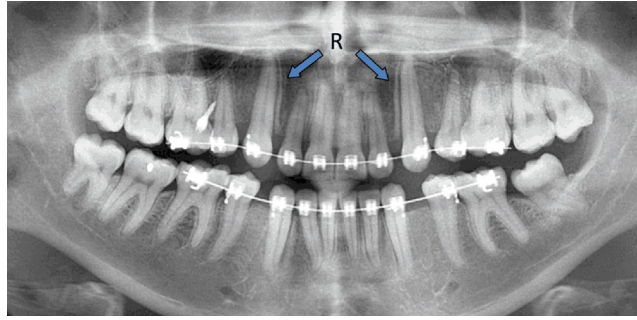


Figure 3. Representative panoramic radiograph during space closure. R, the reversal lines at the mesial aspects of distally moved canines. These lines, which indicate the onset of new bone formation on the tension side of the periodontium, are parallel with the outline of the root surface, indicating predominantly translational movement. With the difference of 0.004 in between the slot size and wire diameter and the mesio-distal bracket width 0.125 in, the tipping component during closing of 5.3 mm (the average extraction space size in this study) was minimal and clinically insignificant, resulting in almost pure translational movement with the center of rotation at 9.48 m above the canine root apex. Translational tooth movement resulted in uniform, non-traumatic stress levels across the periodontium, thus eliminating excessive stresses in the apical and coronal regions.

results is placed on the ITT analysis to minimize bias in assessing the primary outcome. After enrollment and randomization, some subjects were withdrawn from the ITT group for various reasons and excluding these subjects could introduce a bias in statistical analysis.

The most common adverse side effect in both groups was loosening of TADs, which was reported in three subjects in the AcceleDent group and two subjects in the control group. A TAD was considered loose if any detectable level of mobility was observed clinically. Additional harms/safety-related outcomes analyzed in this study included the effect of vibration on root resorption and other potential harmful effects (such as pain, discomfort, and headache), as well as subjects' perception of the ease of use of the device. Because of space limitations, the results of these outcomes will be reported elsewhere (manuscript in preparation). These outcomes generally indicated that the AcceleDent® is safe and convenient for patients' daily use.

Discussion

The design of this study and the mechanics used maximized the reproducibility of orthodontic force application and measurement of tooth movement, while minimizing the variables associated with the loss of posterior anchorage. A recent systematic review²⁰ revealed lack of quality randomized clinical trials that would allow for an evidence-based approach in clinical use of techniques for accelerated tooth movement. The present study fully adheres to the CONSORT guidelines and CONSORT 2010 checklist²¹ for conducting and reporting randomized clinical trials and provides evidence for the positive effect of cyclic loading on the rate of orthodontic tooth movement.

Relatively constant and reproducible retraction force of 180 g was used, reported to be within an optimal range for canine retraction.²² The sliding mechanics produced a translatory canine movement²³ with a negligible component of tipping (Fig. 3). The applied force level of

Table. Average rate (mm/month) of tooth movement during space closure.

| ITT ^a | | | | PP ^a | | | |
|---------------------|--------------|---------------|---------|---------------------|--------------|---------------|---------|
| Treatment | Mean (SE) | 95% CI | P value | Treatment | Mean (SE) | 95% CI | P value |
| AcceleDent (N = 23) | 1.16 (0.153) | 0.86–1.46 | | AcceleDent (N = 21) | 1.25 (0.117) | 1.01–1.49 | |
| Control (N = 22) | 0.79 (0.150) | 0.49–1.09 | | Control (N = 18) | 0.89 (0.118) | 0.63–1.15 | |
| Mean difference | 0.37 (0.217) | –0.07 to 0.81 | 0.05 | Mean difference | 0.36 (0.181) | –0.01 to 0.73 | 0.02 |

^aP values for the individual covariates included in the general linear model for ITT were 0.97 (age), 0.28 (type of retraction), and 0.093 (gender). Corresponding P values for PP were 0.88 (age), 0.02 (type of retraction), and 0.03 (gender).

0.25 N represents an approximately 70-fold reduction of the level of 18 N used in clinical trials in patients with osteoporosis,²⁴ and it is based on the difference in the mass of the maxilla compared to the whole skeleton (since no similar studies applying pre-defined levels of cyclic force to the alveolar bone have been reported). The 0.25 N force imposes peak to peak accelerations of less than 0.003 g (1 g = earth's gravitational field), which is over 300 times lower than the level of 1 g demonstrated to be safe and not produce any detrimental skeletal resonances.²⁴ This extremely low force did not produce any significant discomfort or adverse effects for the patients. The monthly rate of canine retraction for the control group was 0.79 mm/month, which compares favorably with earlier reports.^{16,25} The effect of vibrations in the AcceleDent group was 48.1% above this established baseline value, which demonstrates a significant clinical benefit. The results from analysis of harms and safety-related outcomes showed that the AcceleDent[®] is safe and convenient for patient's use.

A recent study using the Tooth Masseur device in orthodontic patients²⁶ reported no effect on the rate of tooth movement. This is contrary to our results, and those from medical clinical trials and animal models, most likely because the Tooth Masseur was never intended or designed to accelerate tooth movement: its output frequency is four times higher compared to our study, while the force is about four times lower. Another study reported that micro-osteoperforation increased the tooth movement by 2.3-fold, measured during the period of initial 28 days of canine retraction into a first bicuspid extraction space.²⁷ These results are consistent with studies using other invasive procedures, such as corticotomy⁶ and similar surgical interventions. A recent systematic review and meta-analysis (which did not include vibration) revealed some evidence for effectiveness of low laser therapy and corticotomy and only a weak or no evidence for the effectiveness of interseptal bone reduction, photobiomodulation, and pulsed electromagnetic fields.²⁸

While loosening or potential drift of some TADs cannot be excluded, it is important to note that only a relatively small number of subjects had TAD failures, which were distributed

similarly between the groups (three in the AcceleDent, two in the control), with an overall failure rate of 11.1% that is smaller than the reported average TAD failure rate of 13.5%.²⁹ Furthermore, the loading conditions in the present study were markedly different from the single study where a total average drift of 0.4 mm (0.044 mm/month) was reported in seven out of 16 patients over the course of 9 months of space closure, using an excessive retraction force of 400 g per side.³⁰ The accuracy of our technique, using a TAD as a reference point, has advantage over most other techniques (e.g., using the palatal rugae or an adjacent tooth that can move being pulled by trans-septal fibers), since it avoids several intermediate steps in making a cast and its 2-D image and overlying a grid or drawing lines, with each step introducing additional errors. Measuring space closure from lateral cephalograms can introduce considerable magnification, angulation, and landmark recognition errors. Using casts and custom reference templates is more accurate method for measuring 3-D tooth movement^{31,32} that is particularly suitable for space closure by segmented arch technique where canine is not engaged into an arch wire, and its side effects are difficult to control. Employing sliding mechanics with a tight bracket-wire interface in this study minimized a chance for the second order tipping, rotational, and vertical displacements. This allowed us to use a direct, highly reproducible, and accurate one-step measuring technique and focus on the effect of vibration on a single, reproducible type of tooth movement—the translation of canine during space closure.

Vibrational loading stimulates bone remodeling,^{9,10} but the biological mechanism underlying this effect is not understood. Mechanical loading initiates signaling pathways in bone^{33,34} and osteocytes were identified as mechano-responsive cells during orthodontic tooth movement,³⁵ in which signals can be triggered by fluid shear stress, bone microfractures, or bone bending, all of which occur during vibrations. Early responses in osteocytes are followed by differentiation of osteoblasts³⁶ and stimulation of other bone genes.³⁷ Future studies should address the question whether cyclic loading, as an adjunct to orthodontic stress, activates known or new signaling pathways underlying the faster tooth movement.

Conclusion

The application of cyclic loading (vibration) of 0.25 N (25 g) at the frequency of 30 Hz, as an adjunct to treatment with a fixed orthodontic appliance, significantly increases the rate of orthodontic tooth movement.

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