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A rodent model using skeletal anchorage and low forces for orthodontic tooth movement

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Introduction: Nonhuman animal models have been used extensively to study orthodontic tooth movement (OTM). However, rodent models have disadvantages, including a reported reduction in bone volume during OTM. The purpose of this study was to determine the viability of a skeletal anchorage and the effect of low force (~3 cN) on interradicular bone volume during OTM. **Methods:** Ninety Sprague-Dawley rats were divided into 5 time points. A miniscrew and a nickel titanium coil spring placed a load of 3 cN (experimental) or 0 cN (sham) on the maxillary first molar in a split-mouth design. Displacement of the first molar and bone volume/total volume (BV/TV) in the interradicular region were quantified. **Results:** The success rate of the miniscrew was 98.9% (89 out of 90). Linear and angular tooth movement increased steadily (mean 0.1 mm/wk, 0.48 mm at 40 days). BV/TV was significantly reduced between the tooth movement and non–tooth movement sides in the 3 cN group: by 13%, 23%, 15%, 23%, and 16% at 3, 7, 14, 28, and 40 days, respectively. **Conclusions:** Our model resulted in efficient OTM without skeletal anchorage failure. BV/TV reduction was lower than in previous reports. This novel validated model is likely to be the basis for future studies. (Am J Orthod Dentofacial Orthop 2019;155:254-63)

Orthodontic patients in general desire shorter orthodontic treatment times. This trend has led to an increased focus on methods for expediting orthodontic tooth movement (OTM). A clear understanding of the biologic processes involved in tooth movement (TM) is crucial for optimization of OTM.[1] In attempts to understand the biologic mechanisms involved, nonhuman animal models have been used extensively in experimental studies of OTM. An acceptable animal model for OTM should allow for constant direction of orthodontic force, an adequate magnitude of orthodontic force, and an accurate method of measuring tooth displacement.[2]

The forces that move teeth most effectively in humans are probably not suitable for rats.[3] According to a systematic review published in 2004, ~20% of rat OTM studies applied forces lower than 20 cN, 27% of the studies used elastomers with unknown forces, 37% used applied forces ranging from 20 cN to 50 cN, and 12% used forces ranging from 50 cN to 100 cN.[4] It has been proposed that the forces used to move teeth in rodents have been excessive and not physiologic, and that forces lower than 25 cN should be used for molar protraction in rats.[3,5] A human canine was moved ~1 mm per month with only 4 kPa (~18 cN) in an 84-day experiment.[6] Scaling the size from human subjects to rats would support that loads of <10 cN could be more appropriate.[3] Thus, it is evident that lower forces should be applied to rodent models; however, developing a traction mechanism that can apply calibrated low forces remains a technical challenge.

One of the surprising findings in rodents subjected to OTM is a dramatic (~70%) reduction in the volume of

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the interradicular bone at 14 to 40 days concomitant with OTM.[7] One study reported that bone volume decreased from ∼60% to ∼15% with OTM in rats with the use of 25 g force.[7] Interestingly, bone volume is restored at later time points of 56 days.[7] It is unclear whether these changes in bone volume are due to the use of excessive forces to move the teeth or whether they accurately reflect the bone physiology in this rat animal model. However, there is no histologic evidence to suggest that rapid bone loss occurs in large animal models, such as dogs.[8] In addition, the results of studies using human radiography suggest that molar protraction results in increased bone volume with associated radiopacity on periapical radiographs and that this newly generated bone hampers TM.[9] Reduced bone volume can accelerate TM, because resistance to TM diminishes. Bone reduction may explain why the results of studies using rats can be misinterpreted, especially when the results of rate of TM are extrapolated to humans.

Published studies of OTM in rats vary considerably in the design of the experimental orthodontic appliance and the forces used to generate OTM.[10] Current rodent models of OTM use the maxillary incisors as an anchorage for moving the first molar in a mesial direction with the use of a nickel titanium (NiTi) coil spring.[5,11,12] This model has disadvantages: It suppresses incisor eruption and alters the vector of the force, causing extrusion of molars because of the continuous eruption of incisors.[13] Ligation to incisors can also lead to repeated dislodgement of the spring; therefore, constant religation, monitoring by study personnel, and sedation of the animals are required.

Recent studies have shown that OTM in rats can be achieved with a force of 3 cN for molar protraction.[5] However, the changes in the bone volume/total volume (BV/TV) in response to this 3 cN force remain unknown. More specifically, is it unknown whether the interradicular bone of the tooth being moved would be altered in a manner that has been previously observed, with rapid declines in bone volume over the duration of TM. The present study was designed to evaluate the BV/TV changes using microscopic computerized tomography (μCT) in the interradicular bone of first and second molars during OTM in a rat model using ∼3 cN force at 5 time points over a 40-day period. The purpose of this study was to provide a better understanding of bone physiology/adaptation in a rodent model with the use of lower forces via a custom-made calibrated coil spring.

MATERIAL AND METHODS

This study was approved by the Institutional Animal Care and Use Committee (IACUC) of the University of Kentucky. A power analysis was performed (SAS version 9.4; SAS Institute, Cary, NC) to determine the number of experimental animals necessary for the study. The main parameter of interest was the change in BV/TV, and we expected to detect a mean difference of 21% between the experimental side and the contralateral side, with expected SDs of 17% and 11%, respectively.[14] The power analysis indicated that with 12 rats in the experimental (3 cN) group and 6 in the sham (0 cN) group (18 rats at each time point, for a total of 90 rats) we would have 83% power to detect a statistically significant difference in BV/TV ($P \leq 0.05$) with the use of a 2-sided *t* test.

In rodents, the rate of skeletal growth increases from week 1 through week 5 and then declines at skeletal maturity (∼11-13.0 weeks).[15] Therefore, this study used male Sprague-Dawley rats (n = 90; Charles River Laboratories, Wilmington, Mass) aged 12-14 weeks with an average weight of 500 g. Rats were acclimatized to the facility for 1 week after arrival. Rats were then divided into 5 time points based on the duration of the application of force (3, 7, 14, 28, or 40 days). A force of 0 cN (n = 6 rats in each group) or 3 cN (n = 12 rats in each group) was applied to the maxillary first molar of each rat. The side to which the force was applied (right or left) was randomly selected for each animal, with an equal number of animals per side.

Rats were sedated with the use of ketamine (50 mg/kg) and xylazine (5 mg/kg) administered by intraperitoneal injection. Baytril (enrofloxacin, 5 mg/kg) and meloxicam (2-4 mg/kg) were administered subcutaneously. A 2-mm biopsy punch was used to remove gingival tissue at the distopalatal gingival margin of the maxillary incisor, and an indent (∼0.3 mm) was placed with a high-speed electrical dental handpiece using a no 2 size round bur under water irrigation. The indent was placed to obtain a point of access and to prevent slippage during insertion. A 1.2 mm × 4 mm self-threading Stryker titanium screw (Stryker-Leibinger, Hamilton, Ont, Canada) was inserted into the alveolar bone ∼12 mm from the mesial aspect of the first permanent molar by hand with the use of a miniscrewdriver (Fig 1, *A* and *B*). The screws were placed only in monocortical bone, on a shelf lateral to the incisor tooth, and without any contact with the incisor. In our initial experiments, we refined the placement of the screw by viewing the μCT images of the defect left after the screw was removed at the end of the experiment. Thickness of the bone is ∼1 mm. Because the miniscrews do not have a collar like miniscrew implants used in clinical practice, they were inserted ∼1 mm in to the bone with threads extending outside the bone to facilitate securing the nickel-

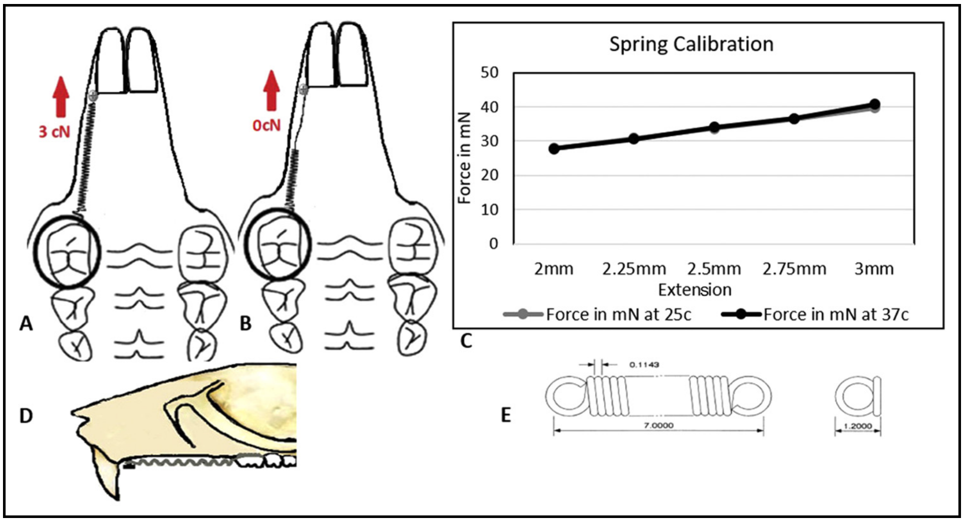

Fig 1. Appliances and custom-made coil spring dimensions and calibration. **A,** Activated coil spring in the 3 cN group. **B,** Nonactivated coil spring in the 0 cN group. **C,** Force exerted by custom-made coil spring at different activation lengths at 25°C and 37°C. Force levels overlap at both temperatures until 2.75 mm of extension. **D,** Lateral view of appliances. **E,** Dimensions of custom-made coil spring.

titanium (NiTi) coil placement with the stainless steel ligature.

A custom-manufactured NiTi coil spring (Motion Dynamics, Fruitport, Mich), designed to exert 0.0066 lb of force (3 g, 2.94 cN) at a length of 0.374 in (9.4 mm) with an original length of 7 mm, was secured to the first molar on one side and to the miniscrew on the other side with a 0.008-in stainless steel ligature wire (Fig 1, *A* and *B*). Planned extension was 2.5 mm to exert the desired force of ~3 cN. The springs were tested and calibrated at room temperature by Motion Dynamics and retested by the University of Kentucky Mechanical Engineering Department at room temperature and at 37°C (Fig 1, *C*). Intraorally, a periodontal probe was used to measure the length of the entire spring (Fig 1, *D*) at the desired extension (eyelet to eyelet). The rats were allowed to recover from anesthesia; the reversal agent atipamezole (1 mg/kg) was administered if necessary. All the springs and screws were stable except for 1 miniscrew, which was loose in the 40-day sham group but still supported the spring. Appliances were examined under inhalation anesthesia (isoflurane) at 3 days in the 7-day group and at 7 days in the 14-day group. Because no appliance failures were observed in these 2 groups, appliance checks were performed infrequently in the 28-day and 40-day groups so that the stress induced by repeated anesthesia could be avoided. The animals were fed with a moistened chow and gel diet so that any discomfort after insertion of the orthodontic appliance insertion or the risk of appliance displacement could be minimized.

At each time point, the 18 rats were killed by means of IACUC-approved methods. The maxillas were removed and fixed in 4% neutral-buffered formalin for 24 hours and stored in 70% ethanol. Three-dimensional (3D) imaging was performed with the use of a μCT 40 scanner (Scanco Medical, Brüttisellen, Switzerland) after appliance removal. High-resolution images were acquired at 55 KvP (145 μA), 8 W, and a field of view (FOV) of 20.5 mm. Three-dimensional reconstructions were generated with the use of the Ondemand3D Application (Cybermed, Tustin, Calif).

Micro-CT image orientation and measurement of linear and angular tooth displacement are shown in Figures 2 and 3. We measured the BV/TV values of the interradicular bone of the first and second molars on either side of both experimental and sham animals. Clear and reproducible orientation was obtained by adjusting the axial, coronal, and sagittal planes. In the coronal plane (Fig 4, *A*), the sagittal axis was aligned with the long axis of the first molar. When the specimen was viewed in the sagittal plane, the transverse axis was aligned parallel to the alveolar ridge, and a line was drawn parallel to the transverse axis at the apex of the mesial root. The perpendicular line connecting the transverse axis and the parallel line at the apex of the mesial root were trisected to represent the one-quarter root, the mid-root, and the three-quarter root levels as tagged image file format (TIFF) images (Fig 4, *B* and *C*) were obtained. These TIFF images were imported into the microscopy imaging software program Bioquant Osteo (Bioquant Image Analysis Corp, Nashville, Tenn), and

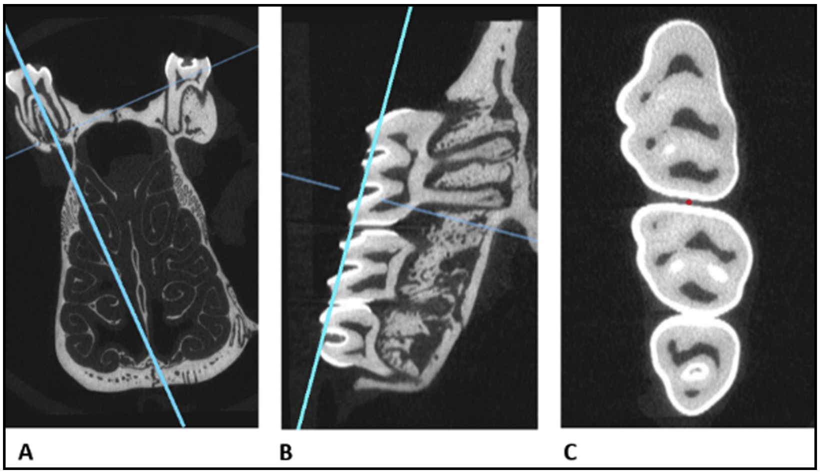

Fig 2. Linear measurement recorded between nearest contact points of first and second molars. Reproducible orientation was achieved with the use of anatomic landmarks. **A,** Sagittal axis aligned with long axis of second molar. **B,** Transverse axis aligned with occlusal table of second and third molars. **C,** Occlusal plane was moved apically to find closest distance between the teeth.

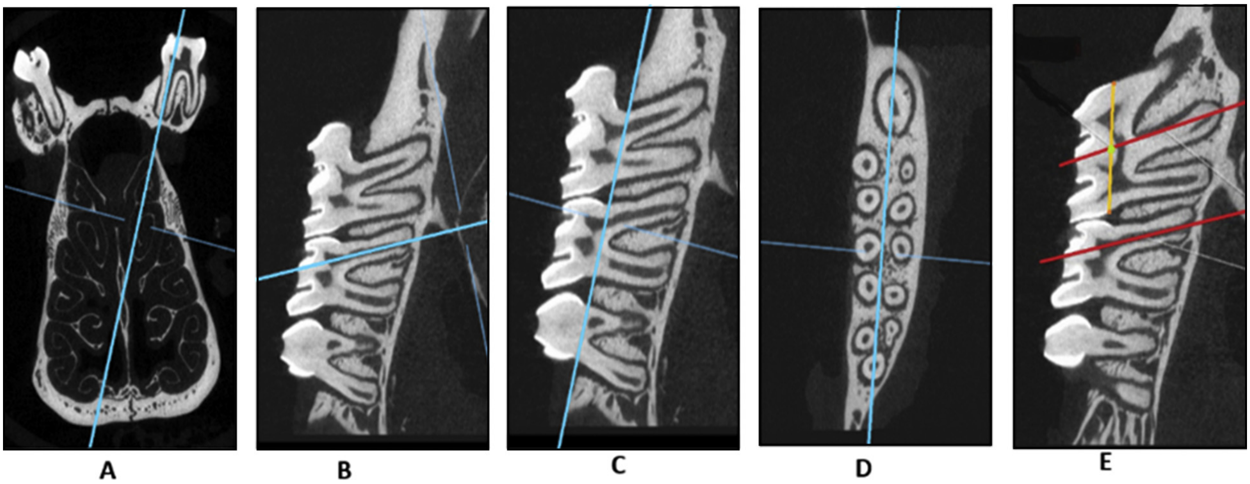

Fig 3. The angular measurement was made in the sagittal plane to determine relative tipping of the first molar. **A** and **B,** Sagittal and coronal axes aligned with mesiopalatal root of second molar. **C,** Transverse axis aligned with alveolar ridge apex. **D,** Sagittal axis reoriented to bisect the alveolar ridge buccolingually. **E,** The first ray of the angle was aligned to the long axis of the mesiopalatal root of the second molar. The second ray was drawn from the midpoint of a line connecting mesial and distal cementoenamel junction of the first molar to the tip of the mesiopalatal root of the first molar. The difference in angulation between experimental and control sides was taken to represent angular displacement of the first molar during OTM.

the BV/TV of the interradicular region of the first and second molars were determined (Fig 4, *D-G*).

Statistical analysis

Statistical analyses were performed with the use of SAS version 9.4 (SAS Institute), and all tests were 2 sided with statistical significance set at $P \leq 0.05$. Linear mixed-effects modeling with random subject effects was used to account for correlation between outcomes from the same animal. Pearson correlation coefficient was determined to assess associations between TM and BV/TV. The intraclass correlation coefficients of angular and linear measurements were calculated from multiple

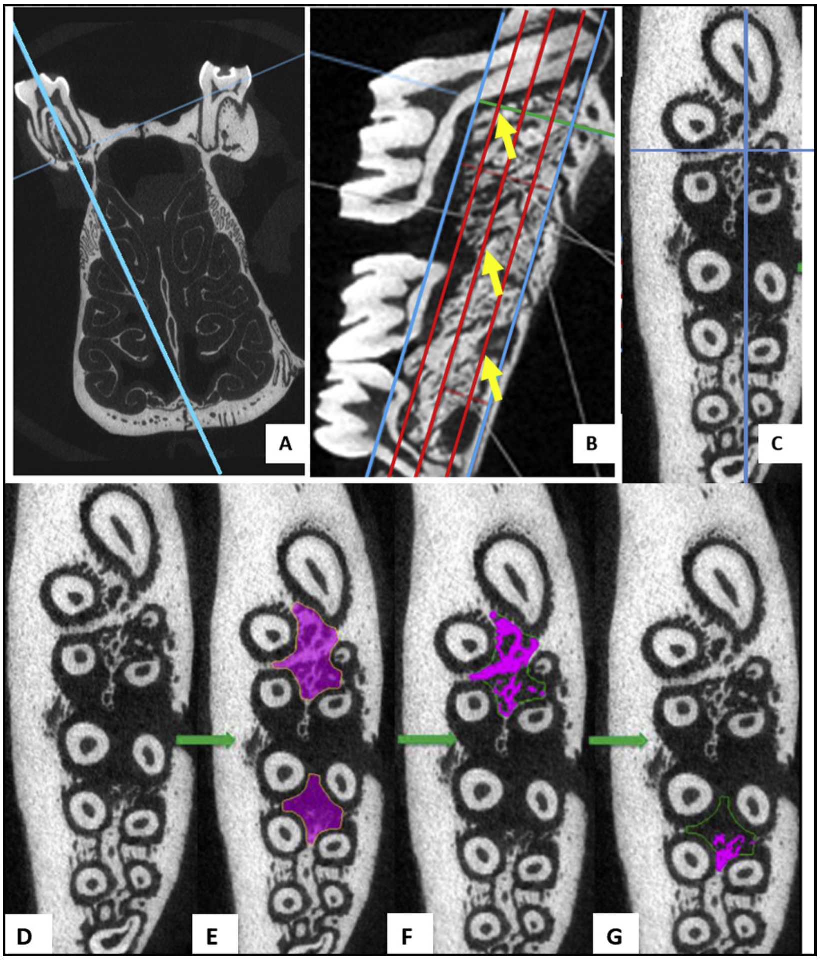

Fig 4. Orientation of μCT image and measurement of BV/TV. **A,** Alignment of sagittal axis with the long axis of the first molar. **B,** Alignment of transverse axis parallel to the alveolar ridge, and a line drawn parallel to the transverse axis at the apex of the mesial root. The perpendicular line connecting the transverse axis and the parallel line at the apex of the mesial root were trisected to represent the one-quarter root, the mid-root, and the three-quarter root levels. **C,** The transverse axis in the sagittal plane was then moved toward the apex of the mesial root, and the corresponding images in the axial plane at the one-quarter root, the mid-root, and the three-quarter root levels were obtained as TIFF images. **D-G,** Defining region of interest and measurement of BV/TV in the interradicular region of first molar and second molars.

paired measurements made 2 weeks apart in 3 randomly selected animals per group.

RESULTS

A pilot study with 6 rats was conducted to optimize anesthesia and surgical techniques. No animals died prematurely or were eliminated of the 90 study animals. No drastic weight loss was reported; in fact, all rats steadily gained weight throughout the experiment, suggesting that the appliance did not interfere with feeding and that pain control was adequate. Appliances remained intact, and no loss or loosening of the miniscrew was noted for up to 28 days. One miniscrew was found to be loose but still supporting the coil spring in a 40-day 0 cN group animal. Tooth movement steadily increased at an average of 0.1 mm per week from 3 days to 40 days in the experimental (3 cN) group. The linear TM was statistically significant ($P < 0.01$) between experimental (3 cN) and sham (0 cN) rats at all time points (Fig 5, *A*). Angular TM increased through 28 days but had decreased in the 40-day group; the difference in angular TM between experimental and sham animals was statistically significant only in the 28-day group ($P = 0.01$;

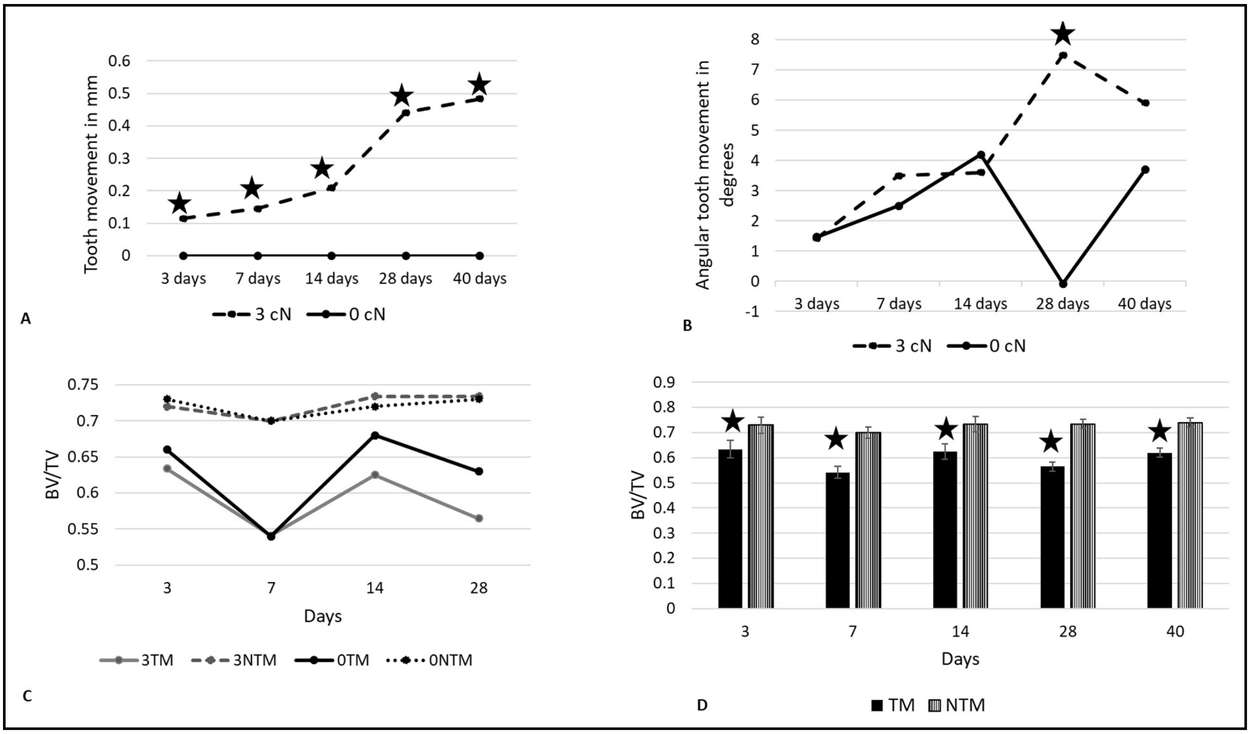

Fig 5. Tooth displacement and BV/TV reduction. **A,** Linear tooth movement at different time point in the 3 cN and 0 cN groups. *Star*, statistical significance between the 3 cN and 0 cN groups. The associated *P* values were 0.002, 0.001, 0.01, 0.0002, and 0.0005 at 3, 7, 14, 28, and 40 days, respectively. **B,** Angular tooth movement at different time point in the 3 cN and 0 cN groups. The associated *P* value at 28 days was 0.01. **C,** BV/TV of the 3 cN and 0 cN groups at different time points in the interradicular region of first molar on the tooth movement (TM) and non–tooth movement (NTM) sides. The overall reduction in BV/TV between the TM and NTM sides in the experimental (3 cN) group was statistically significant ($P < 0.05$) at all time points. BV/TV was lower on the TM side of sham (0 cN) rats than on the NTM side. The difference was statistically significant at the one-quarter and mid-root level at 7 days in the 0 cN group, with *P* values of 0.0004 and 0.0046, respectively. **D,** Comparison of BV/TV at TM and NTM sides of the 3 cN group at different time points, depicting that with OTM there is less bone.

Fig 5, *B*). The intraclass correlation coefficient of the linear TM measurements was 0.99 and of the angular was 0.62.

At the interradicular region of the first maxillary molar, BV/TV was lower on the TM side/appliance side than on the contralateral (non-TM) side of experimental (3 cN) and sham (0 cN) rats at all time points in all groups (Fig 5, *C*). The overall reduction in BV/TV between the TM ande non-TM sides in the experimental (3 cN) group was statistically significant ($P < 0.05$) at all time points (Fig 5, *D*). Similarly, BV/TV was lower on the appliance side of sham (0 cN) rats than on the contralateral side. A similar trend was also observed at the interradicular region of the second molar. The estimated means of BV/TV (Figs 5 and 6) demonstrate reductions at the different time points. The mean percentage reduction in BV/TV between the TM side and the non-TM side of the experimental (3 cN) group was 18%, and it was 12.5%, 22.8%, 15%, 23%, and 16% at 3, 7, 14, 28, and 40 days, respectively (Fig 5, *D*). When the TM side of the 3 cN group and the appliance side of the 0 cN group were compared, the experimental (3 cN) group exhibited a statistically significant reduction in BV/TV at only the mid-root level (18%; $P = 0.004$) at 28 days and both the one-quarter root level (27%; $P = 0.0071$) and the mid-root root level (14%; $P = 0.0087$) at 40 days. At the first molar in experimental (3 cN) animals, a statistically significant reduction in BV/TV from baseline was observed at the three-quarter root level (22.5%; $P = 0.0004$) at 3 days, at all root levels at 7 days (one-quarter, 28%; mid-root, 21%; three-quarter, 16%; $P < 0.004$), and at the one-quarter (21%) and one-half (14.8%) root levels at 14 days (21%, 14.8%; $P < 0.0330$), 28 days (33%,25%; $P < 0.0007$), and 40 days (31%, 12.6%;

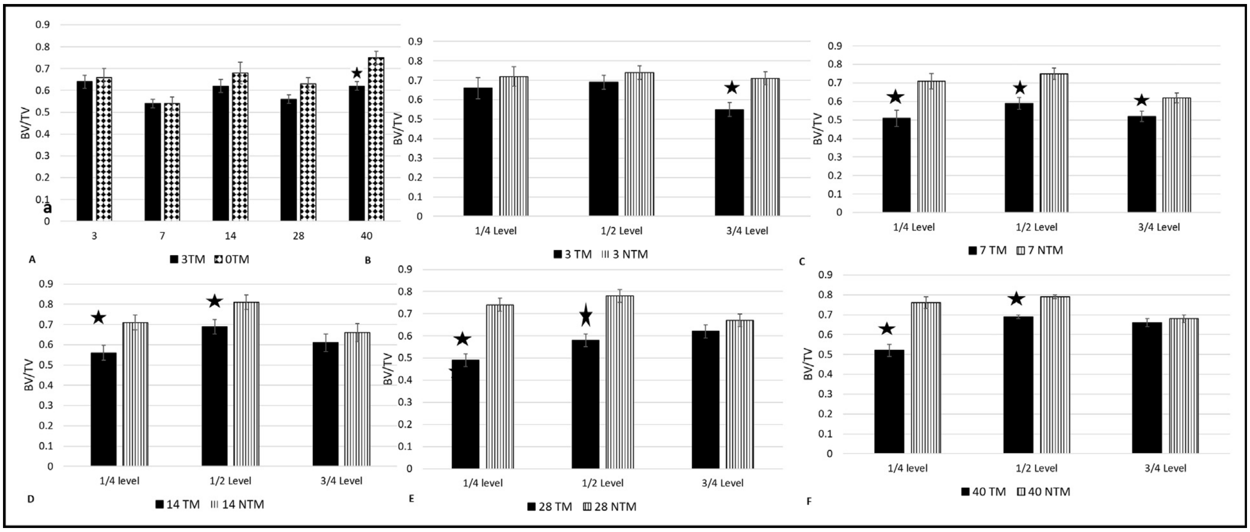

Fig 6. A, BV/TV comparison between TM sides of the 3 cN and 0 cN groups with all levels combined. Statistically significant (*star*) at 40 days, with $P = 0.0045$. **B-F,** BV/TV comparison between TM and NTM sides of the experimental 3 cN animals at different levels of the mesial root of the maxillary first molar at 3, 7, 14, 28, and 40 days. The associated statistical values are **(B)** $P = 0.0004$ at the three-quarter root level at 3 days, **(C)** $P < 0.004$ at all root levels at 7 days, and **(D)** $P < 0.033$, **(E)** $P < 0.0007$, and **(F)** $P < 0.0006$ at the one-quarter and mid-root root levels at 14, 28, and 40 days, respectively.

$P < 0.0006$; Fig 6, *C-F*). The representative linear and angular tooth displacements are shown in Figure 7.

BV/TV values were lower on the appliance side of sham (0 cN) rats than on the contralateral side (non-TM). The difference was 9.5%, 22%, 5.5%, and 13.6% at 3, 7, 14, 28, and 40 days. The difference in reduction was statistically significant at 7 days, especially at the one-quarter root level (37%; $P = 0.0004$) and at the mid-root level of the first molar (16%; $P = 0.0046$). The differences between the experimental (3 cN) and sham (0 cN) groups in BV/TV on the non-TM side were not statistically significant.

DISCUSSION

This study aimed to determine the viability of a skeletal anchorage, quantify the amount of TM achieved, and determine the effect of low calibrated force (~3 cN) on interradicular BV/TV in response to OTM. The miniscrew success rate (98.9%) was very high. Efficient TM was obtained with skeletal anchorage and a force of ~3 cN. The reported reduction in BV/TV was lower than that reported in previous rat OTM studies.

Our study is the first to use skeletal anchorage combined with a low force. With the exception of one miniscrew in a 40-day sham (0 cN) rat, all screws (n = 89) remained intact during the experimental period. The high success rate in our study could be attributed to the use of low force (~3 cN) and strategic miniscrew placement with adequate primary stability. In this study, we did not need to trim the mandibular incisors to ensure that they were out of occlusion and not at risk of breaking the appliance.[11] Neither did we pin incisors to prevent further eruption, nor extract mandibular first molars to prevent damage to the appliance.[16,17] All of these methods interfere with the normal masticatory process of the animal. Some recent studies have attempted to use skeletal anchorage instead of incisor anchorage in a rat model of OTM. A miniscrew (1.4 mm × 6.0 mm) along with incisors was used to protract maxillary molars.[18] The report of that study did not state the miniscrew failure rate, but 7 of the 30 animals were eliminated because of appliance failure or premature death of the animals. Longer screws can perforate the nasal cavity and cause bleeding in these obligate nasal breathers, causing death, which we observed in our pilot study. A success rate of 92% at 4 weeks and 80% at 8 weeks was reported with the use of a Stryker miniscrew (1.2 mm × 3.0 mm) and a force of ~30 g.[13] In our study, the placement of an appropriately sized miniscrew at an optimal site in the rat maxilla and the use of low force levels not anchored to the incisor allowed for normal physiologic eruption of incisors. Lack of failure/readjustment of the traction mechanism offered important advantages in obtaining

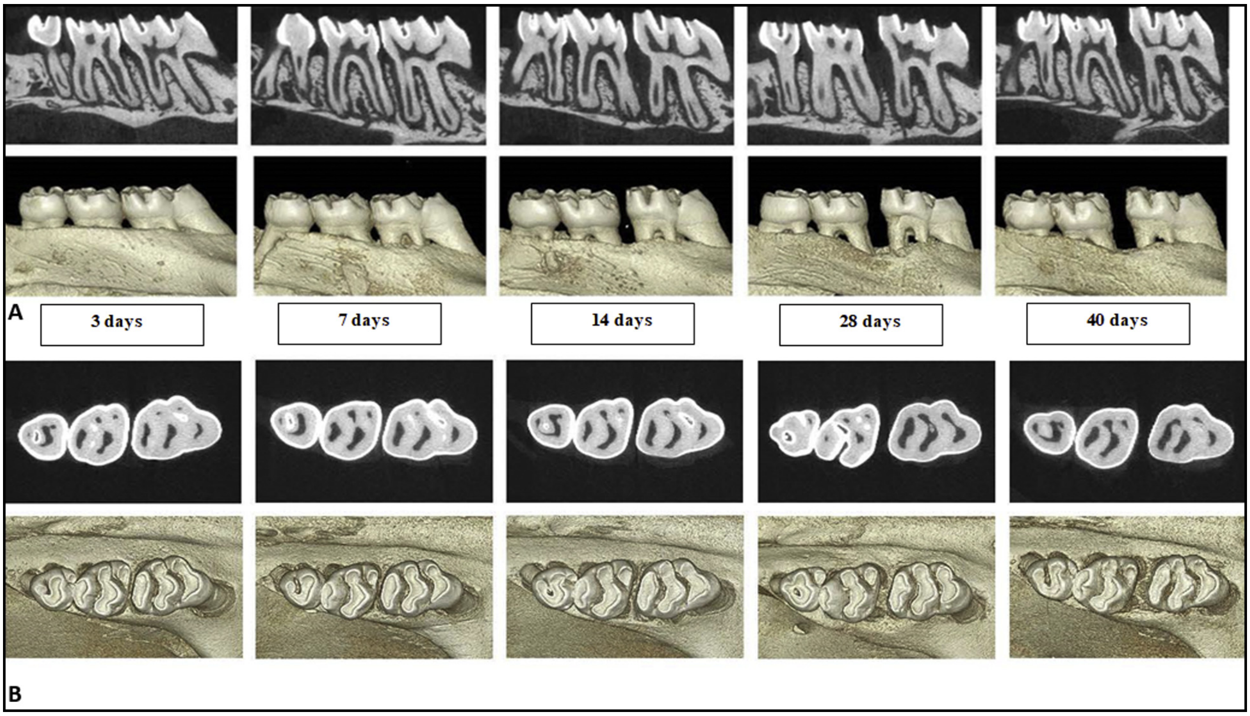

Fig 7. Micro-CT images showing the linear and angular tooth displacements at different time points. **A,** Pictorial representation of mean angular tooth movement at each time point. **B,** Pictorial representation of mean linear tooth movement at each time point.

an appropriate and constant force vector with fewer visits to the animal housing location by study personnel.

In the present study, a physiologic force (~3 cN) was exerted by custom-made NiTi coil springs. Commercial orthodontic springs, although easily available, exert higher forces which are probably excessive in a rodent model. The use of custom-made calibrated springs, although difficult to obtain and needing to be custom fabricated, allowed the application of calibrated and optimal force.

Several methods have been used to measure OTM in rats. Some studies have used feeler gauges and Vernier calipers to measure minute tooth displacements and are probably inaccurate for measuring fractions of a millimeter.[19,20] Other studies used 2D radiological imaging and cone-beam CT (CBCT) to measure OTM.[10,11] In the present study, linear and angular TMs were measured with the use of μCT images in a 3D software program. The amount of TM generated by our appliance is similar to that achieved by studies using much higher (10-100 g) forces (Fig 7). The amount of TM (0.2 ± 0.1 mm) obtained with a force of 3 cN with skeletal anchorage at 14 days is similar to the TM (0.192 ± 0.054 mm) obtained with a force of 100 cN at 14 days.[5] In fact, the amount of TM (0.4 ± 0.2 mm) obtained in our study at 28 days is larger than the amount (0.292 ± 0.048 mm) obtained at 28 days with a force of 100 cN.[5] This finding suggest that the force level may also alter the amount of TM, ie, that a lower force generates larger amounts of OTM. The OTM of 0.29 ± 0.15 mm with the use of a force of 25 cN[21] and OTM of 0.21 mm with a force of 60 cN[22] at 21 days are similar to the TM obtained in the present study at 14 days (0.20 ± 0.12 mm). Similarly, the OTM achieved by this study at 14 days (0.20 ± 0.12 mm) is close to the OTM (0.23 ± 0.043 mm) achieved at 14 days with a force of 30 g.[23] This finding suggests that low forces of ~3 cN with skeletal anchorage can produce effective TM. It is likely that these forces are not excessive in the magnitude of stress/strain to the periodontal ligament and bone.

The angular measurements obtained in this study revealed tipping TM. This movement can be attributed to the anatomy of rat molars and the point of force application relative to the center of resistance, which is located apically. Although some studies have used a specially designed appliance to produce bodily TM in rats, they reported that some tipping TM still occurred.[3] This tipping is one of the limitations of using a rat model of OTM. The use of a reliable skeletal anchor resulted in efficient TM and a vector of force application that is more likely to result in predictable TM in a mesial direction with minimal rotation force. We did observe slight rotation of the molar in the mesial direction in some rats; this rotation could be attributed to the fact that the spring lay toward the buccal surface of the molar rather than at the buccolingual center of the tooth. Accurately measuring this angular TM was challenging, primarily because of anatomic variation in the root morphology both between animals and within the same animal between two sides of the split-mouth design. However, it was clear that the type of TM was a tipping and not a bodily translation, even though the force was applied as apically as possible with the traction mechanism described.

Our study design assumed that the experimental side of any given animal was anatomically identical to the contralateral side regarding the first and second molars. More specifically, we expected that the angulation of the root structures of these 2 teeth would be similar to those of the contralateral teeth. Although most samples were consistent in this regard, outliers in the data suggest that the morphology was not bilaterally symmetric before the force was applied. The difference in angulation noted between the contralateral and experimental sides in the sham group demonstrated asymmetry and points out the challenges involved in using reliable landmarks to measure angular tooth displacements. Another notable anatomic variation that affected our results was root fusion, which occurred in 6 of the 90 animals.

Current research on expedited TM relies on in vivo experiments with appropriate animal models; such experiments allow researchers to obtain evidence-based results for current treatment practices. The dramatic reduction in BV/TV found in previous rat OTM studies complicates the extrapolation of the results from these models to humans. In the present study, lower BV/TV values were reported in the interradicular region of the first and second molars on the experimental side than on the contralateral control side. Interestingly, the 0 cN sham group also exhibited lower BV/TV values on the appliance side (at a force of 0 cN) than on the contralateral side with no appliance. This reduction in BV/TV could be due to resorption caused by the stainless steel ligature secured around the first molar. This finding stresses the importance of using a sham group for comparison. However, the absence of a statistically significant difference in BV/TV between the non-TM sides at forces of 0 cN and 3 cN suggests that it may be possible to eliminate the need for a separate control group in rat OTM studies and demonstrates that the contralateral side can be used as a control side in a split-mouth design with a skeletal anchor and low force. Although the results of our study show lower BV/TV values on the experimental side than on the control side, the amount of bone loss is lower than the amounts obtained in other published studies.[7]

Coil springs delivering forces lower than 3 cN are very challenging to fabricate and calibrate; thus, calibrated lower forces may be difficult to generate even though they are required in, for example, a mouse model. Compared with a 70% reduction in BV/TV at 28 days with the application of 25 g of force, we found ~23% reduction at the same time point.[7] The reduction in BV/TV of 15% at 14 days found in the present study was less than the reduction in BV/TV of ~55% with a force of 25 g and of ~24% with a force of 10 g at 14 days.[24,25] In contrast to the use of a rodent model, a study using a dog model found no statistically significant differences between treatment and control groups in BV/TV.[8]

Although histologic analyses are the criterion standard for measuring BV/TV, μCT, with higher resolution, is a valid and reliable method of measuring BV/TV in a nondestructive manner.[26] In addition, μCT offers the flexibility necessary for designing a method of measuring BV/TV at various levels of a specimen. The region of interest and the orientation of images used to measure BV/TV varies considerably in reports of rat OTM studies. Although these differences complicate the comparison of BV/TV between studies, we overcame the difference by measuring BV/TV at 3 separate levels of the mesial root of the maxillary first molar. Also, the difference in BV/TV at various levels implies the need to measure it at various levels or to specify at what level the BV/TV measurement is obtained.

Some of the limitations of using a rat model of OTM are tipping type of TM and reduction in BV/TV at the second molar probably owing to constant distal drift and at the TM side of both 3 cN and 0 cN groups. Despite these drawbacks, the rat model is still considered to be appropriate for studies of short-term effects of OTM and gene expression levels. The use of larger animal models may yield more relevant information, especially regarding the rate of expedited TM that can be extrapolated to humans. However, given its economy in terms of animal husbandry and personnel time, the rodent model is attractive.

CONCLUSIONS

Skeletal anchorage offers important advantages in obtaining an appropriate force vector, minimizing animal husbandry and personnel time, and achieving predictable and efficient TM in a rodent OTM model.

Efficient TM was achieved with a rat model of OTM by using low force with a skeletal anchorage. If lower force produces similar TM, there is no reason to use high force; in fact, cellular and molecular responses may be altered by unnecessarily high, possibly traumatic, forces. No dramatic reduction in BV/TV was found with the application of low forces. We developed and validated an OTM model in rats with skeletal anchorage and low calibrated forces. Such a model has not been previously described in published studies. Given the advantages of this model, it is likely that it will be adopted for future studies.

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