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Research article

An in vivo evaluation of clear aligners for optimal orthodontic force and movement to determine high-efficacy and periodontal-friendly aligner staging

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A R T I C L E I N F O

Keywords:
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A B S T R A C T

Objectives: To investigate the effect of aligner displacement on tooth movement and periodontal health to improve the efficiency of aligner treatment and explore the mechanism in vivo.
Methods: A two-tooth site was established by a finite element (FE) model to virtually evaluate aligner staging. A randomized controlled experiment was conducted when the tooth sites in beagles were treated with fixed or aligner appliances with different movement and force, and tooth movement and internal structure were recorded during the alignment. After sacrificing five dogs, bone-periodontal ligament (PDL)-tooth specimens were removed and processed to conduct uniaxial compression and tensile tests as well as micro-CT imaging and histological analysis.
Results: Three displacements of 0.25, 0.35 and 0.45 mm were obtained from FE analysis and applied in beagles. In general, aligners had poorer performance on movement compared to fixed systems in vivo, but the aligner with a staging of 0.35 mm had the highest accuracy (67.46%) ($P < 0.01$). Loaded with severe force, fixed sites exhibited tissue damage due to excess force and rapid movement, while aligners showed better safety. The PDL under a 0.35-mm aligner treatment had the highest elastic modulus in the biomechanical test (551.4275 and 1298.305 kPa) ($P < 0.05$).
Conclusions: Compared to fixed appliances, aligners achieve slightly slower movement but better periodontal condition. Aligners with an interval of 0.35 mm have the highest accuracy and best PDL biomechanical and biological capacities, achieving the most effective and safest movement. Even with complexity of oral cavity and lack of evaluation of other factors, these results provide insight into faster displacement as a method to improve the efficacy of aligners.

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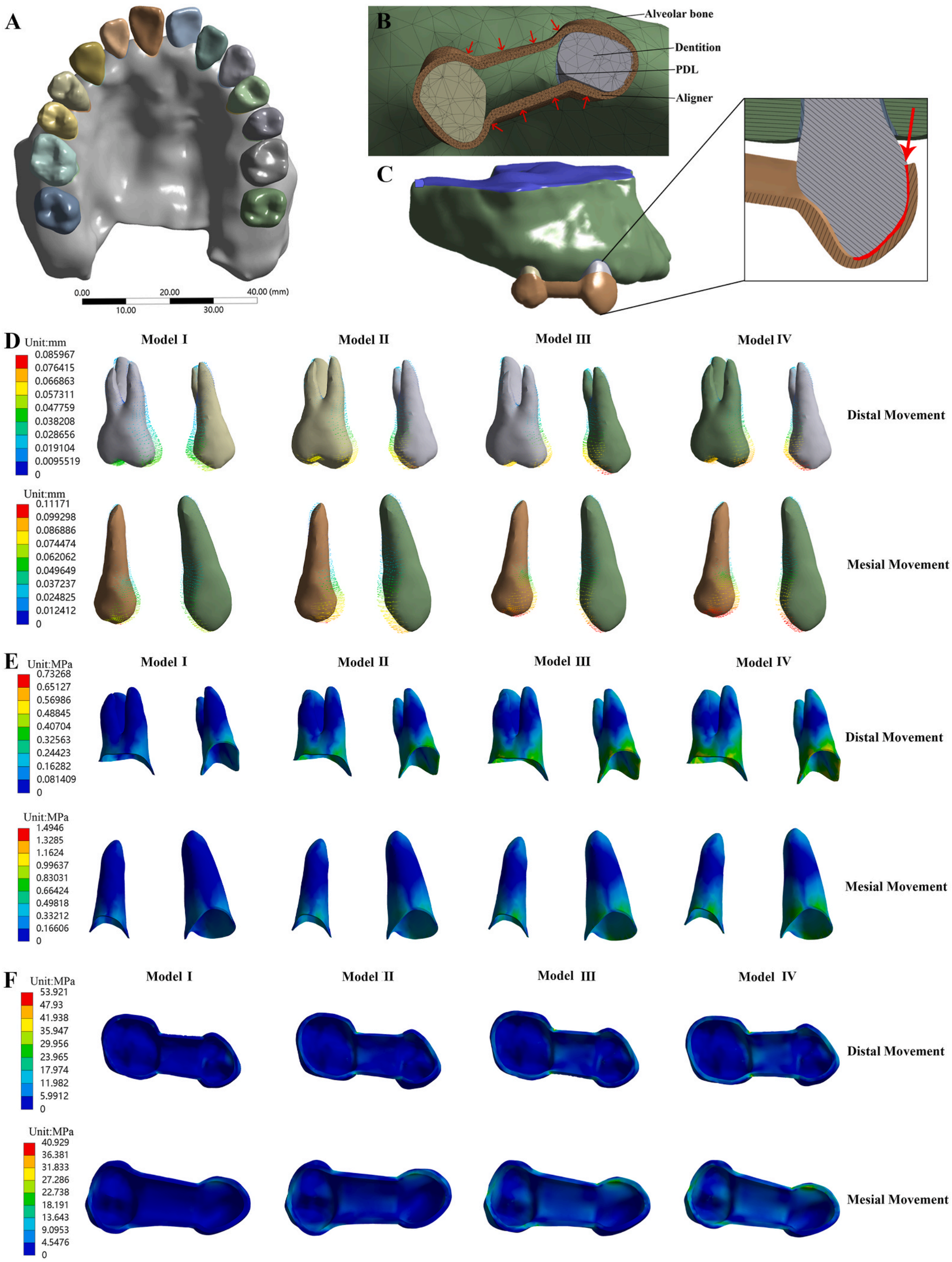

Fig. 1. Finite element model with premolar distal and mesial movements. (A) The basic meshed finite element models based on cone-beam computed tomography (CBCT) scanning to establish a maxilla arch model. (B) The separation of teeth, aligner, periodontal ligament (PDL), alveolar bone and their assembly body. (C) The simplified maxilla finite element model. The blue top shows the range of the fixed boundary part in the ANSYS software. The right magnification indicates that the pre-constructed aligner with applied load produces an overlap (the red line) between aligner and the unmoved tooth. (D) Instantaneous displacement of teeth on each side of the extraction space in the distal and mesial movement groups with an aligner staging of 0.25 mm, 0.35 mm, 0.45 mm or 0.50 mm. The solid regions indicate the original location of teeth, while the dotted regions show instantaneous displacement caused by different aligner displacements. (E) Hydrostatic stress nephograms of the PDL in the distal and mesial movement groups with different aligner displacements. (F) Stress nephograms from the inner side of the dentition in the distal and mesial movement groups with various aligner displacements. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

1. Introduction

Since its original development in 1997 with the Invisalign® technology [1], clear aligner treatment is gaining popularity due to esthetics and comfort [2,3]. However, ten years after Invisalign was introduced, researchers began to quantify how well clear aligners move teeth by superimposing digital models, indicating that the accuracy of aligners is generally less than 50% [4–6]. Considering the growing consumer demand and worldwide use of clear aligners to treat misaligned teeth, several concerns regarding the efficiency and safety of the aligner system in controlling tooth movement remain [7].

Orthodontic tooth movement relies on coordinated tissue resorption and formation in the surrounding structure [8]. If the amount of force regenerated from clear aligners is not adequate, the intended tooth movement cannot be achieved; however, if clear aligners move a lot, the excess orthodontic force may lead to damage of periodontal ligaments and related adjacent tissues [9]. Efficient alignment with a reduced time period and healthy periodontium can be ensured only by using an ideal orthodontic force with aligners to achieve proper movement. However, how to evaluate force generated from clear aligner and to improve its efficacy is a difficulty for orthodontists [10]. As previously reported, clear aligner therapy often requires the use of auxiliaries (attachments, altered aligner geometries, inter-arch elastics,etc.) to improve the efficacy of orthodontic movement [11,12]. Optimized attachments on first molars play a role on preserving molar anchorage and vertical rectangular attachments on canines are beneficial in achieving more predictable incisor tooth movement [13]. As for aligner displacement, one of potential factors affecting aligners' effectiveness, previously suggested desired movement ranges from 0.25 mm to 0.33 mm, and the most common clinical staging (displacement per aligner) is 0.25 mm [1]. As an emerging orthodontic appliance, clear aligners have a completely different force loading system from fixed appliances [14], and few laboratory studies have focused on maximum staging of aligners.

Although more complex clinical cases with aligners are in process, more basic animal and three-dimensional (3D) models should be constructed to elucidate the mechanisms behind tooth movement, aiming to improve movement efficacy. Finite element (FE) analysis is an effective tool that has been widely used in biomechanics to calculate initial tooth movement instantly after force loading and to analyze the stress and strain response of external forces in the intrinsic structure [15]. A FE study of anterior teeth showed the optimal orthodontic displacement depended on periodontal conditions of patients according to stress distribution in the periodontal ligament (PDL) [16]. However, computer virtual technology is not as persuasive as a comprehensive study in vivo, suggesting that FE analysis should only provide pre-lab auxiliary evidence. The exploration of tooth movement beyond the limit is not practical or ethical when applying to humans. Therefore, beagle, as a large animal model, is the most conventional model established to study orthodontic mechanisms because the animal tooth size limits the application of orthodontic systems, and the beagle bone density and periodontal tissue are close to those of humans [17].

We constructed a 3D FE model to mimic movement and stress modes of clear aligners with distinct displacements, and an in vivo beagle model was established to obtain ideal displacement of aligners to accomplish faster and safer movement at the same time. The purpose of the present study was to comprehensively evaluate the effect of aligner systems on movement and stress modes in both FE and beagle models as well as to explore clinical staging to obtain high-efficacy and periodontal-friendly staging for aligners, thereby providing orthodontists additional knowledge of clear aligners.

2. Materials and methods

2.1. Finite element models

A 3D FE model of the maxillary dentition with teeth, bone-PDL and alveolar bone was built using Mimics 21.0 (Materialise NV, Leuven, Belgium) based on a cone-beam computed tomography (CBCT) scanning of a male patient treated at the Department of Pedodontics, West China Hospital of Stomatology, Sichuan University. Through thresholding, region growing and 3D calculation, an anatomically accurate 3D maxillary model was imported into 3ds MAX 2020 (Autodesk, San Rafael, USA) (Fig. 1A). The Ogden 3rd model and normalized-based relaxation function regarded PDL as a nonlinear material with both super-elasticity and viscoelasticity as previously reported [18–20] (Tables 1–3). And parameters of the Ogden 3rd model mainly refer to a previous article [21]. A PDL model with a thickness of 0.25 mm was then created through Boolean operation. These models were configured in Geomagic Wrap 2020 (3D System, Rock Hill, USA) and SOLIDWORKS 2020 (Dassault Systèmes, Concord, USA), and they were then imported into ANSYS workbench 2020 R2 (ANSYS, Canonsburg, USA). The teeth, PDL and maxilla were separated from the whole tissues to monitor movement and stress separately as a basis for the following FE analyses. To simplify the analysis, the maxilla was considered as a whole. All parts other than the PDL part were assumed to be homogeneous, isotropic, and linearly elastic materials in the model.

2.2. Two-tooth site analysis

The maxillary dentition was divided into four groups, including the individual distal and mesial direction movement of two

Table 1
Parameters of normalized-based relaxation function.

I	G(I)	K(I)	TAU(I)
1	0.0276968	0	0.13927
2	0.0976967	0	10.41900

premolars [4,22]. Aligner shape was developed by matting dental crown surfaces with a thickness of 0.75 mm to generate the assembly body (Fig. 1B). With regard to loading and boundary conditions, set the top of the maxilla as a fixed constraint (Fig. 1C). The "Bounded" relationship was used to join the maxilla-PDL and the PDL-teeth. The "Frictionless" relationship was used to join the teeth-appliance. All other software-determined contact relationships are deleted. Orthodontic force is applied to teeth by setting the contact surface between the unmoved tooth and the aligner in ANSYS software without penetration, forcing the aligner to deform; thus the aligner can exert force to the teeth from mesial direction to distal direction (Fig. 1C). The maxillary first or second premolar distal or mesial tipping movement was set as 0.25 mm, 0.35 mm, 0.45 mm and 0.50 mm towards the static first molar or canine to generate Models I, II, III and IV, respectively. The hydrostatic stress nephograms of the PDL of the maxillary premolars and corresponding aligners as well as the instant displacement of the maxillary premolars were analyzed under the above conditions.

2.3. Animal preparation

Five 12-month-old male beagle dogs, weighing 12.34–13.62 kg, were supplied by Chengdu Dossy Biological Technology Company, China. The beagles were housed and fed according to previous studies [23]. Seven teeth were extracted from each beagle after general anesthesia. Clinical examinations and imaging were performed weekly throughout the entire experiment, and periapical radiographs were taken every six weeks until the end of the experiment. All protocols in this study were in accordance with institutional guidelines on animal welfare and were approved by the Institutional Laboratory Animal Care and Use Committee of Sichuan University (permit no. WCHSIRB-D-2022-325).

2.4. Tooth site design

Seven teeth in each beagle were carefully extracted after anesthesia to provide space for tooth movement. Because these extracted teeth had small cone-shaped crowns that were difficult for adding attachments, second or third premolars with appropriate crown-to-root ratios were selected as the moving teeth. The large canines and first molars, which have solid roots, functioned as anchorage teeth. To simulate every moving situation in human as fully as possible, half of the moving teeth were mesial third premolars, and the other half were distal second premolars. There were six tooth movement sites in each beagle (Fig. 2A) as follows: right maxillary second premolar moving to right maxillary first molar (upper right site, URS); left maxillary third premolar moving to left maxillary canine (upper left site, ULS); bilateral mandibular second premolars moving to bilateral mandibular canines (lower right canine site, LRCS; and lower left canine site, LLCS); and bilateral mandibular third premolars moving to bilateral mandibular first molars (lower right molar site, LRMS; and lower left molar site, LLMS).

2.5. Orthodontic tool

In a total of 30 sites, conventional orthodontic devices and invisible removable aligners were installed on the premolars to exert light (Group A/D), moderate (Group B/E) and severe force (Group C/F), resulting in six groups on the basis of force and appliance types (Fig. 2B–D).

Coronal preparation was conducted to increase retention on premolars to keep the devices in place. Silicone rubber impression and casts were precisely made. The resin was applied to shape the coronal contour into a column and firmly bond the welded bands. Shallow cavities about 0.5 mm deep were prepared on the buccal surfaces of bands as reference marks for measurement. Secondly, a wire (0.018 in x 0.025 in) was inserted between the buccal tubes of premolars and anchorage teeth (canines or first molars) to guide the direction of tooth movement (Fig. 2E). A linear elastic chain was placed, and the force was measured using an orthodontic dynamometer (Zahoransky AG, Germany) to ensure that the magnitude of the load was always 80 g in Group A and 120 g in Group B (Fig. 2B). Severe force (Group C) was generated by a screw in the buccal side of the bone with a coil spring, providing a total force of 200 g to cause maximal movement beyond the capacity of healthy periodontal tissue (Fig. 2C). Finally, aligners with different displacements of 0.25 mm, 0.35 mm and 0.45 mm were digitally designed and fabricated on the basis of a cast scan. STL files were imported after designing aligners to exert light (Group D), moderate (Group E) and severe (Group F) force with Romexis 3D Ortho Studio (Planmeca Oy, Finland). Polyethylene terephthalate glycol (PET-G)-modified materials were used to create 0.75-mm thick clear aligners (Fig. 2D).

2.6. Grouping

The tooth sites were characterized in four different ways as follows: 1) light, moderate and severe force with fixed orthodontic tools (Group A, B and C) and with clear aligners (Group D, E and F); 2) specific sites as described in detail above (URS, ULS, LRCS, LLCS, LRMS and LLMS); 3) two randomly selected beagles were sacrificed at Week 6 and Week 10 after alignment (Beagles I and II), and the

Table 2
Parameters of 3rd Ogden model.

μ_1 (MPa)	μ_2 (MPa)	μ_3 (MPa)	α_1	α_2	α_3
0.33811	1.33143	−1.40954	1.99878	4.00283	−2.00581

remaining three beagles were sacrificed at Week 14 after alignment (Beagles III, IV and V); and 4) sites were divided into the Isodynamic Group (to compare fixed/aligner at different time points) and Equidistance Group (to compare aligners of different displacements with the same total movement) according to different purposes of the experiments (Table 4). Eighteen tooth site designs were set and then beagles were divided by lots with simple randomization method.

For the Isodynamic Group, the fixed and removable appliances exerted force of equal level in the same or identical tooth sites (i.e., URS and ULS; LRCS and LLCS; and LRMS and LLMS). For example, Group A corresponded to Group D at different end time points of application of orthodontic load. Similarly, Group B corresponded to Group E and Group C corresponded to Group F to compare moderate and severe forces, respectively.

For the Equidistance Group, clear aligners with different displacements of 0.25 mm, 0.35 mm and 0.45 mm moved teeth to reach to a total displacement of 3.50 mm within 14 weeks. Each aligner was worn for 1 week to gradually move misaligned teeth to planned positions. Similar to the Isodynamic Group, identical or similar tooth sites were matched.

2.7. Movement measurement

The distances between the reference marks of gingival margin of the tube or attachment on the anchorage and moving teeth were measured every three weeks with an electronic Vernier caliper (Dentaurum, Ispringen, Germany). Each distance was measured twice by the same observer, and the mean value was used. In addition, silicone rubber impressions and casts of every aligner site were precisely made at the time points of both pre- and posttreatments to provide superimposition digital models in Mimics 21.0 (Materialise NV, Leuven, Belgium). Romexis 3D Ortho Studio (Planmeca Oy, Finland) was used to create a color-coded legend according to displacements (Fig. 3H). The percentage of accurate tooth movement was determined by the following equation: Accuracy = 100% − [(|predicted-achieved|/|predicted|)*100%].

2.8. Specimen division and Micro-CT scans

Five beagles were randomly selected for various site designs and humanely sacrificed with intravenous injections of pentobarbital (50 mg per kilogram) at 6, 10 and 14 weeks after tooth alignment, and the jaws were then removed. Tooth specimens were harvested anterior to the canine and distal to the first molar immediately after the beagles were sacrificed. These specimens were divided further according to experimental tooth sites, namely, moving teeth-to-anchorage specimens. Micro-CT scans of specimens were performed from apical and coronal views (Fig. 4G and H). The PDL widths were evaluated at two levels (middle and apical) in different directions and were analyzed to compare differences (Fig. 4I and J).

2.9. Histological staining

Some isolated teeth with periodontal tissues were fixed in 4% paraformaldehyde overnight at 4 °C and decalcified with 10% ethylenediaminetetraacetic acid (EDTA) at 37 °C for 10 months. The teeth were then dehydrated in ethanol, embedded in paraffin and cut into consecutive sections (5-μm thickness). Sections were stained with hematoxylin and eosin (H&E) to analyze bone and PDL-like tissue regeneration. Change in periodontal tissue sections was examined under an optical microscope and recorded by acquiring digital photos.

2.10. Periodontal ligament biomechanical testing

Fourteen specimens with teeth and bone were individually collected with a dental lathe (Shixin, China). Transverse sections (approximately 2 mm thick) were cut perpendicularly to the root longitudinal axis using a rotating blade saw with a speed of 500 r/min. From each root, one experimental sample was obtained from the cervical portion for the uniaxial compression test (UCT), and two samples were obtained from the middle portion for the uniaxial tensile test (UTT) (Fig. 5A). Prior to testing, ligament width and tooth perimeter were obtained with a sliding caliper (Dentaurum, Ispringen, Germany). Slices were then extracted from these sections (6 × 6 × 2 mm) using a dental low-speed hand piece. The UCT and UTT were conducted using a Universal Material Testing Machine (Zwick Z010, Ulm, Germany). The alveolar bone and dentin sides of the specimens were fixed using two custom-made clamps (Fig. 5A). Before the mechanical testing, all samples were preconditioned by applying 10 tensile-compression cycles with linear loading and unloading at 0.2 mm/min, as previously reported [24,25]. The value of the preconditioning cycle was selected based on the repeatability of the mechanical response of the PDL. The specimens were subjected to a compressive force vertically to the dentin surface at a loading speed of 0.1 mN/s [26]. Then unloaded stress at the reduction rate of 0.25 mN/s until the indenter left the surface. A tensile force was exerted by clamping the bony part of the specimen at a speed of 0.3 mm/s until a fracture failure of the PDL (Fig. 5A). The force and

Table 3
Material parameters of for the finite element model.

Part	Young's Modulus (MPa)	Poisson's Ratio
Tooth	20,000	0.30
Maxilla	13,700	0.26
Transparent Appliance	585.3	0.30

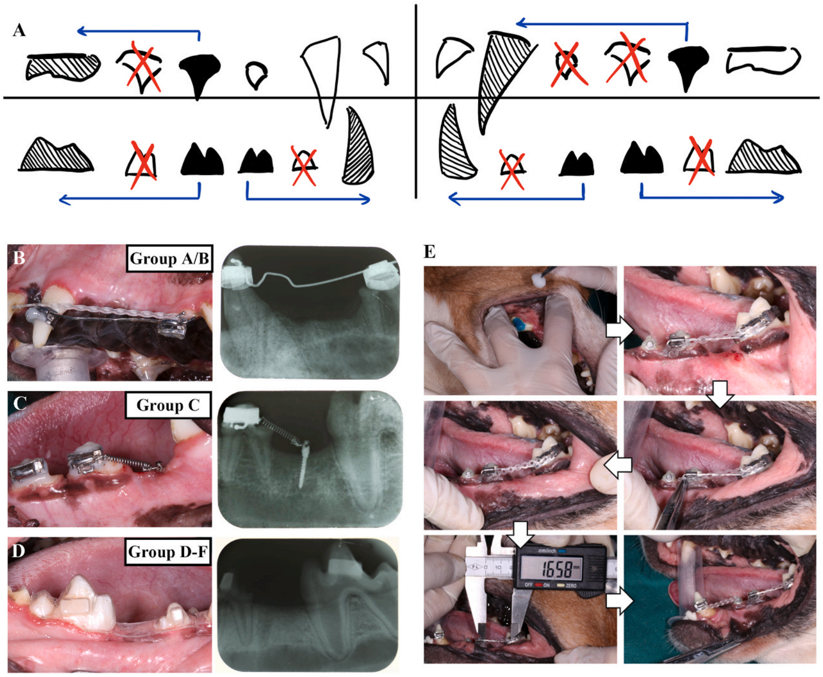

Fig. 2. Orthodontic tool design. (A) Schematic diagram of the six tooth movement sites in each beagle. Arrows on sites indicate directions of tooth movement. Every site includes a moving tooth (black; premolars) and an anchorage tooth (striped; canines or molars). Some premolars (red cross) were extracted to create movement space. (B) Fixed orthodontic systems exerting light and moderate force with bands, wire and elastic chain. The initial X-ray is shown beside the image. (C) Fixed orthodontic systems exerting severe force with coil spring and screw. The initial X-ray is shown beside the image. (D) A clear aligner moving the third premolar toward the molar in the LLMS. The initial X-ray is shown beside the image. (E) The entire process of wearing fixed orthodontic appliance included bonding the bands, applying force with a linear elastic chain and examining with an orthodontic dynamometer. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 4
Site groupings in five beagles.

Beagle	Treatment Period (weeks)	URS	ULS	LRCS	LLCS	LRMS	LLMS
I	6	E	B	D	A	E	B
II	10	F	C	D	A	F	C
III	14	D	A	E	F	D	F
IV	14	E	B	D	F	D	E
V	14	E	F	D	E	D	F

All tooth sites and their division into Groups A-F. The Isodynamic Group was comprised of the green groups (A + D) to compare light force, yellow groups (B + E) to compare moderate force and red groups (C + F) to compare severe force. The Equidistance Group included three beagles with a 14-week treatment period and is indicated by white boxs.

displacement data of the PDL respectively were converted to stress (S) and strain (λ) by using the relation $S = Fl_0/A_0l$ and $\lambda = l/l_0$, where F, A_0 and l, are the applied force, the width of initial cross section and the deformed length of the PDL. The stress-strain curves were obtained from the experimental load-displacement data. The elastic modulus (EM) was obtained by using the relation $EM = S/\lambda$. The variation in EM and the ultimate strain of the PDL values at the end time points of the moving teeth were analyzed.

2.11. Statistical analysis

All data were analyzed using SPSS software (version 21.0; IBM, NY, USA). Each variable was measured three times. To check the normality of data distribution, the Shapiro-Wilk test was performed ($p > 0.05$). Since data was normally distributed, the differences between the groups were analyzed using the one-way ANOVA followed by the Tukey HSD post-hoc test. Paired samples *t*-test was used to find the differences between fixed and aligner groups. $P < 0.05$ was considered to indicate a statistically significant difference.

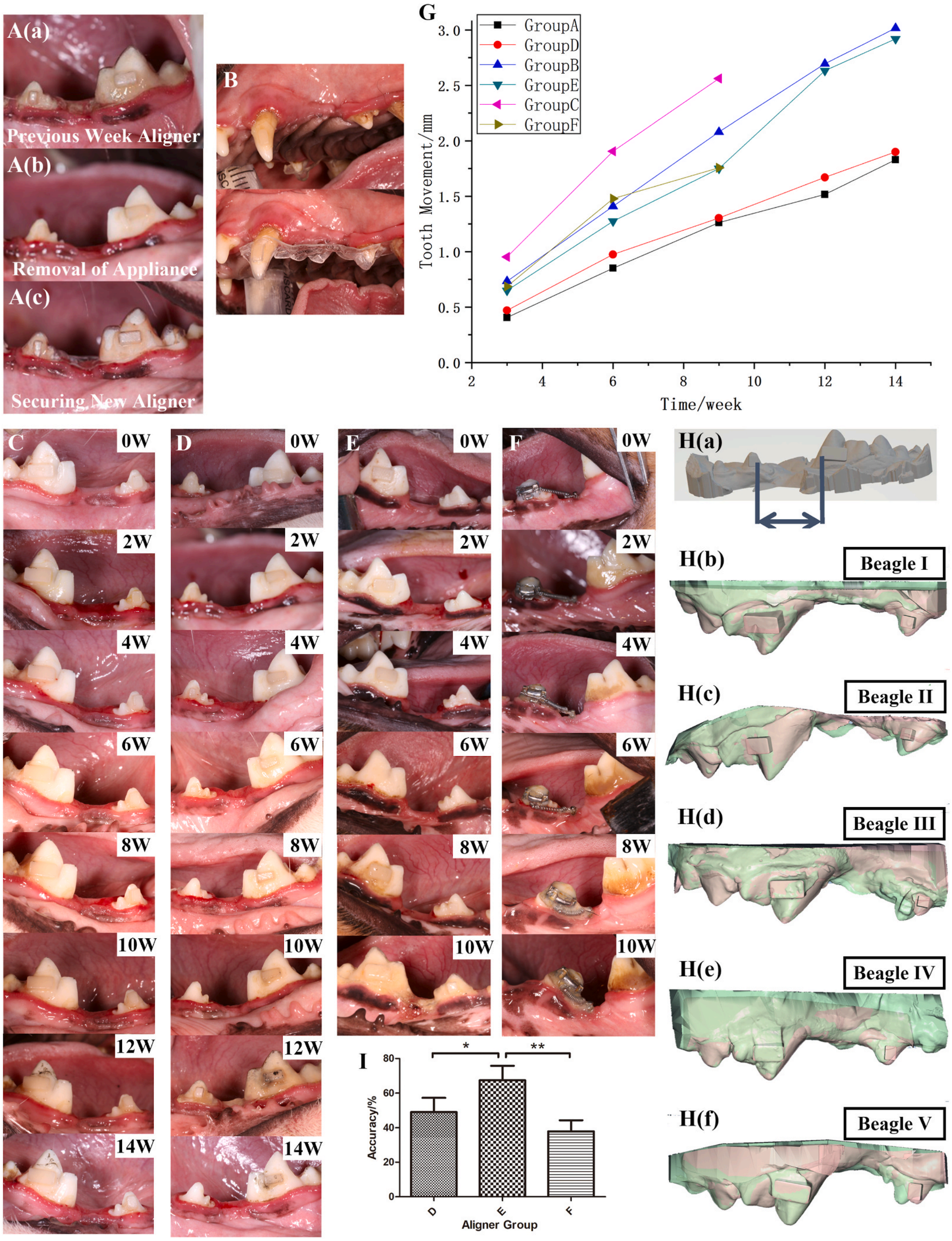

Fig. 3. Orthodontic records with tooth displacement and aligner accuracy. (A) The follow-up visits for the aligner treatment involved the following processes: (a) aligner remaining from previous week; (b) removal of the appliance; and (c) securing the new aligner for the next week. (B) The 0.45-mm-staging aligner became unfit in the ULS of Beagle V at treatment Week 5. (C–D) Record of orthodontic process in the LRMS and LLMS of beagle V comparing Group D and F in the Equidistance Group. (E–F) Record of orthodontic process in the LRMS and LLMS of beagle II comparing Group F and C in the Isodynamic Group. (G) The displacements of moving teeth loaded with light, moderate and severe force were measured every three weeks. (H) The digital models were superimposed to compute differences between the predicted and achieved tooth positions using best-fit surface-based registration. a: Measurement example. b–f: Superimposition of the tooth site of the pretreatment model (white) and posttreatment model (green) for the URS in five beagles (I to V). (I) Accuracy of tooth movement in aligner groups. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

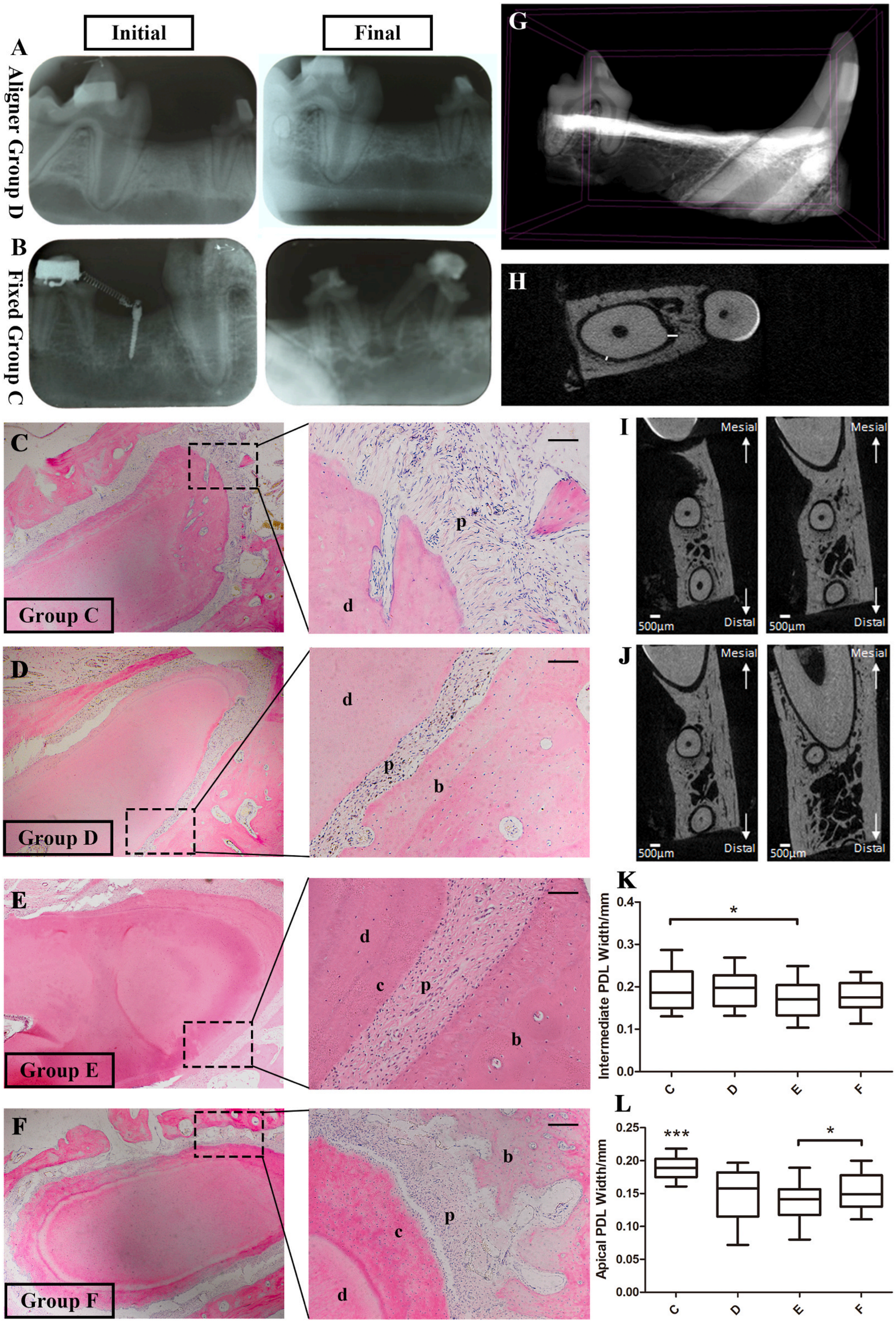

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Fig. 4. Health of periodontal tissue after tooth movement. (A) Radiographs of a tooth site in Group D showing that the site with an aligner attachment at Week 1 resulted in healthy periodontal tissue after tipping movement at the end of the experiment. (B) Radiographs of a tooth site in Group C showing that the site with a screw and a coil spring to exert severe force at Week 1 resulted in a widened periodontal ligament and disappearance of the lamina dura around the mesial root due to excess force and rapid movement. (C–F) HE staining of tissues in Groups C, D, E and F, respectively (b, bone; p, periodontal ligament; d, dental root; and c, cementum). (G) Micro-CT evaluation of each group at the end of the treatment showed three-dimensional reconstruction of the tooth site region in one lower right canine site (LRCS). (H) An example of the cross-sectional tooth slice and the measurement of periodontal ligament width, showing the minimum and maximum (white lines). (I) Sliced image used to measure the intermediate parts of the mesial and distal roots of the moving premolar. (J) Sliced image used to measure the apical parts of the mesial and distal roots of the moving premolar. (K) Quantification of the PDL width from the intermediate parts of the moving premolar in Groups C–F. (L) Quantification of the PDL width from the apical parts of the moving premolar in Groups C–F.

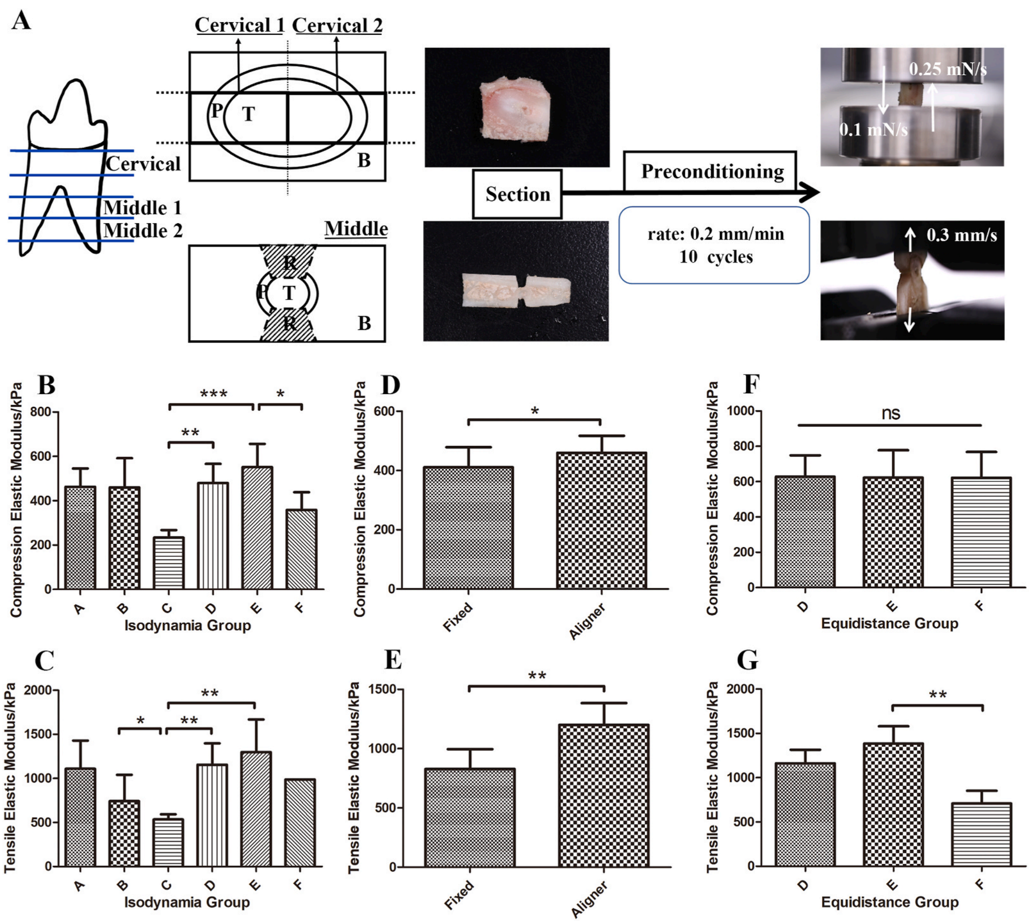

Fig. 5. Compression and tensile testing with different treatments. (A) Schematic diagram of preparing specimens and testing conditions in biomechanical tests. The left part shows the procedure used to obtain tooth specimens and generating cervical and middle parts (B, bone; P, periodontal ligament; T, tooth; and R, removed parts). The middle part shows sections for use in biomechanical compression and tensile tests. The right part shows preconditioning, loading and unloading conditions in two tests. (B–C) Differences in the elastic modulus in the compression and tensile tests within the Isodynamic Group. (D–E) Differences in the elastic modulus between fixed orthodontic tools and clear aligners in the compression and tensile tests. (F–G) Differences in the elastic modulus in the compression and tensile tests within the Equidistance Group.

3. Results

We successfully created hydrostatic stress nephograms of the PDL and aligner in two premolar moving sites for Models I, II, II and IV with intervals of 0.25 mm, 0.35 mm, 0.45 mm and 0.50 mm, respectively (Fig. 1D–F). In all models, the movement direction of the crown and root was opposite, and the major displacement was at the dental cusps, which indicated that an aligner at a staging greater than 0.25 mm was sufficient to trigger tipping movement. The real-time instantaneous displacement increased with the staging increasing from 0.25 mm to 0.50 mm (Fig. 1D). Among the four models and two sites, the distal movement of the first premolar was the smallest, and the mesial movement of the second premolar was the largest (Table 5). With corresponding instantaneous displacement, the PDL under compression and tension displayed a hydrostatic stress nephogram. In general, the stresses on the PDL of the first premolars were much less than those of the second premolars (Fig. 1E). In both the distal and mesial directions, the stress on the PDL and aligner increased as the staging of the aligner increased. With a staging of 0.25 mm, 0.35 mm, 0.45 mm and 0.50 mm, the maximum stresses on the PDL of distal moving first premolars were 0.3442, 0.5033, 0.6352, and 0.7327 MPa, respectively, and those of mesial moving second premolars were 0.5731, 0.9348, 1.2597 and 1.4946 MPa, respectively (Table 6). Because the stress resulting from 0.50-mm staging was higher than the limit for the PDL in beagle, 0.50-mm staging was excluded. In general, the stresses of the aligners on the first premolar groups were more than those on the second premolar groups, which disagreed with previous findings of stress on the PDL (Fig. 1F). Importantly, the stresses on the aligners in all models were within the limit of the PET-G material. For subsequent animal experiments, staging distances of 0.25 mm, 0.35 mm and 0.45 mm were used.

All animals tolerated the experiment procedure favorably. All elastic chains were replaced after using the orthodontic dynamometer, and all coil springs were examined weekly. Most aligner sites finished the expected treatment (Fig. 3Aa–c). However, a series of aligners at the 0.45-mm interval became unfit for the ULS in beagle V at Week 5 (Fig. 3B), which was rectified by stepping back to the fourth aligner and continuing the procedure. Other experimental devices remained in place and intact until they were removed. Most of the half-mandibles were set as the matched groups for control variables. One of the comparisons in the Equidistance Group through Week 14 and one in the Isodynamic Group through Week 10 were organized to show intraoral changes directly (Fig. 3C–F).

We recorded the movement of premolars loaded with light, moderate and severe force every three weeks and at the last week (Table 7). The tooth-displacement curve indicated average moving distance at measurement time points (Fig. 3G). The average total distances with fixed orthodontic systems were greater than those with aligners at the same level of force ($P < 0.05$). At the end of the experiment, Group B (which had an elastic chain of 120 g) had an average movement of 3.02 cm, which was more effective than all of the aligner groups ($P < 0.05$). The movement with screws and coil springs loaded with severe force was almost twice that of the aligners with a displacement of 0.45 mm at Week 9 ($P < 0.05$).

We superimposed digital pre-and posttreatment models of 21 aligner sites, except for one incomplete impression (Fig. 3H). A multipoint locating method demonstrated that the mean accuracy of aligners for all sites was 51.44% in five beagles and 49.59% in beagles III-V. At Week 14, the highest accuracy (67.46%) was achieved in aligners with a displacement of 0.35 mm ($P < 0.01$), which was significantly higher than the lowest accuracy (37.88%) in Group F ($P < 0.05$). In addition, Group D had an accuracy of 49.00% ($P < 0.05$) (Fig. 3I).

The moving teeth mostly suffered from inclination due to difficulty of bodily movement (Fig. 4A). Periodontal tissue destruction resulted from rapid tooth movement, and periapical radiographs indicated severe excessive force on the LLMS of beagle II with a screw and spring (Fig. 4B). H&E staining, which provided a histological overview of bone and cementum at the formed and resorbed regions, indicated mineral formation and resorption at Week 10 of treatment (Fig. 4C–F). In Group C, which used the maximum force, severe resorption was observed in widened regions of the PDL complex (Fig. 4C), and the force produced by aligners with 0.25- and 0.35-mm staging resulted in intact and healthy PDL structure (Fig. 4D and E).

We evaluated the PDL width in reconstructed micro-CT models and cross-section slices (Fig. 4I and J). For the intermediate PDL, the micro-CT images showed differences only between Groups C and E ($P < 0.05$). The average PDL width of Group C was the longest, which was 0.1951 mm, and the average PDL width of Group E was the shortest, which was 0.1705 mm (Fig. 4K). Group C had the longest apical PDL width (average of 0.1895 mm), and it was significantly different compared to the apical PDL widths of the other groups (0.1472 mm, 0.1384 mm and 0.1539 mm) ($P < 0.001$). Among the aligner sites, the group with a staging of 0.25 mm showed no differences from those with a staging of 0.35 mm or 0.45 mm, but the latter two groups were slightly different from each other ($P < 0.05$) (Fig. 4L).

Of the 42 compression and 42 tensile specimens from the 21 tooth sites tested, 9 specimens were excluded due to tooth fracture, which resulted in 38 compression and 37 tensile specimens. Within the Isodynamic Group, Group C had the lowest EM in both the UCT and UTT (233.815 and 533.710 kPa, respectively) ($P < 0.05$), and Group E had the highest EM in both the UCT and UTT (551.4275 and 1298.305 kPa, respectively) ($P < 0.05$) (Fig. 5B and C). More specifically, the aligner group had higher EM values in both the UCT and UTT (459.736 kPa and 1200.578 kPa, respectively) compared to fixed orthodontic tools (410.912 kPa and 827.815 kPa, respectively) ($P < 0.05$) (Fig. 5D and E). Within the Equidistance Group, there were no obvious differences in the EM for the UCT among the three aligners with different displacements ($P > 0.05$) (Fig. 5F). However, the EM for the UTT was similar between the Equidistance Group and Isodynamic Group with the highest EM in Group E and the lowest EM in Group F ($P < 0.01$) (Fig. 5G).

4. Discussion

An ideal orthodontic force minimizes tissue damage and maximizes the speed of tooth movement. Despite the increasing demand for invisible orthodontics and aesthetic considerations, previous studies have reported a mean overall accuracy of 41–50% in patients treated with Invisalign, which is less than that with fixed appliances, leaving some doubt among clinicians about the suitability of Invisalign [6]. It has been reported that 70–80% of patients may require additional aligners to improve efficiency [27]. The type and position of attachments are also essential for intrusion achievement [28], but mesial and distal movement, as one of major tooth

Table 5
Instantaneous displacement of distal and mesial moving premolars.

Instantaneous Displacement (mm)	Model I	Model II	Model III	Model IV
Distal Movement	0.0565	0.0733	0.0820	0.0860
Mesial Movement	0.0765	0.0936	0.1046	0.1117

Table 6
Maximum stress on PDL and aligner of distal and mesial moving premolars.

Max Stress (MPa)	Group	Model I	Model II	Model III	Model IV
On PDL	Distal Movement	0.3442	0.5033	0.6352	0.7327
	Mesial Movement	0.5731	0.9348	1.2597	1.4946
On Aligner	Distal Movement	19.0410	36.6600	49.9890	53.9210
	Mesial Movement	10.8470	18.0890	28.0830	40.9290

Table 7
Distances of moving teeth subjected to light, moderate and severe force every three weeks. (Unit: mm).

Force	Sites and Weeks	3	6	9	12	14
Light force	Fixed site (I-LLCS)	0.41	0.85			
	Aligner site (I-LRCS)	0.50	0.92			
	Fixed site (II-LLCS)	0.42	0.87	1.33		
	Aligner site (II-LRCS)	0.48	0.94	1.27		
	Fixed site (III-ULS)	0.39	0.84	1.19	1.52	1.83
	Aligner site (III-URS)	0.43	1.06	1.34	1.67	1.90
Average-light	Fixed site	0.41	0.85	1.26	1.52	1.83
	Aligner site	0.47	0.97	1.30	1.67	1.90
	Ideal aligner site	0.75	1.50	2.25	3.00	3.50
	Realization ratio for aligner	0.63	0.65	0.58	0.56	0.54
Moderate force	Fixed site (I-ULS)	0.74	1.49			
	Aligner site (I-URS)	0.66	1.41			
	Fixed site (I-LLMS)	0.64	1.28			
	Aligner site (I-LRMS)	0.57	1.25			
	Fixed site (IV-ULS)	0.82	1.46	2.08	2.70	3.02
	Aligner site (IV-URS)	0.72	1.16	1.75	2.63	2.92
Average-moderate	Fixed site	0.73	1.41	2.08	2.70	3.02
	Aligner site	0.65	1.27	1.75	2.63	2.92
	Ideal aligner site	1.05	2.10	3.15	4.20	4.90
	Realization ratio for aligner	0.62	0.61	0.56	0.63	0.60
Severe force	Fixed site (II-ULS)	0.73	1.43	2.20		
	Aligner site (II-URS)	0.63	1.51	1.90		
	Fixed site (II-LLMS)	1.18	2.38	2.93		
	Aligner site (II-LRMS)	0.74	1.45	1.62		
Average-severe	Fixed site	0.95	1.91	2.56		
	Aligner site	0.69	1.48	1.76		
	Ideal aligner site	1.35	2.70	4.05		
	Realization ratio for aligner	0.51	0.55	0.43		

movements in alignment, was ignored. Distalization with aligners can be achieved with the sequential movement of the posterior teeth, which means the main movement occurs on the specific tooth in every alignment stage [10]. Therefore, we chose two-tooth site model in the study, instead of the whole dentition like most studies established.

At the same time, only few studies have reported on the association between aligner staging and tooth movement. Previous studies based on clinical cases and treatment outcome with a staging of 0.25 mm were limited due to ethical standards for testing on human, which prevented exploration of optimal staging for aligners. It is generally believed that the desired movement is approximately 0.30 mm [29], but Nickel et al. reported that 0.063 mm per day (0.441 mm per week) is the average maximum mean rate of tooth movement [30]. Ma et al. analyzed the stress value with different axial inclinations of anterior teeth and found that the optimal displacement for periodontal disease patients needed to descend to 0.10–0.18 mm to avoid the strain at the top of the alveolar crest [16]. These studies prompted us to investigate the maximal staging for achieving maximal tooth movement and good periodontal status. Unlike these mentioned studies, we established two-tooth sites in FE and beagles considering the essence of tooth movement in aligner. To the best of our knowledge, this is the first attempt to systematically investigate the effect of aligner staging on tooth movement as well as the biomechanical and biological property changes of periodontal tissues.

As a virtual method, we used FE analysis to establish a two-tooth simplified model to analyze maximal stress and specific sites of the stress concentration on the PDL and aligner. As the aligner staging increased, instantaneous tooth displacement as well as the stress on the aligner and PDL increased. It has been previously demonstrated that 1 MPa was an optimal applied stress under a fixed appliance [30]. Therefore, the stress on the PDL in Model IV was far beyond the limit, which indicated that a staging of 0.50 mm was greater than the margin of tooth movement with aligners. Thus, we selected aligners with a staging of 0.25 mm, 0.35 mm or 0.45 mm for use in vivo experiments subsequently.

The movement curve indicated that fixed appliances and aligners achieved similar movement under a light force, but the movement of fixed systems was significantly better compared to that achieved with aligners under moderate and heavy forces. It has previously been reported that most tooth movements achieve approximately 1 mm per month [31]. The displacement in the present study was slightly less, which may have been due to a low crown-root ratio in beagle. The superimposed pre- and posttreatment models indicated that the aligner with 0.35-mm staging was superior with an accuracy of 67.46%, which was higher than the previously reported highest accuracy of 47.1% with lingual movement [4]. However, several factors may affect the movement of teeth during aligner treatment, such as healing time after extraction [31], thermoplastic material property, modification type [32] and species. Nonetheless, this high accuracy could be explained by the increasing staging of the aligner.

The greater force within the limit produces more movement regardless of using fixed orthodontic tools or aligners. In the present study, imaging indicated that excess force resulting from micro-screw anchorages widened the PDL and caused the lamina dura to disappear, and microscopic imaging indicated inflammation and slower movement with excess force. In the micro-CT reconstruction models, Group C had the greatest width at both the intermediate and apical regions, and some root resorption occurred with orthodontic tooth movement under heavy force in Group C. Group F also showed bone resorption, but it was not as severe as that in Group C. Other sites showed acceptable safety with new bone formation and mild inflammation after subjected to gentle force exerted by aligners. However, various conditions may be related to increased root resorption, including duration of the applied force, warranting additional research to investigate these conditions. The PDL may be utilized to assess periodontal health status. In the UTT and UCT, which were used to test the specimen's biomechanical properties of the PDL, the group with a staging of 0.35 mm showed a significant advantage over the other two groups. The EM of the group with a staging of 0.45 mm was significantly decreased, which indicated that a staging of 0.35 mm was close to the fusion point of the highest movement distance and the best biocompatibility as previously speculated [29].

The biomechanical experiments in the present study had several limitations. First, each tooth root was cut into three slices of the same thickness, but the EM and PDL widths may have varied from the cervical to apical specimens [33]. Moreover, the apical specimens were not used in this study due to the radial direction of the fibers. The micro-CT slices indicated that the thickness of the mesial and distal regions were homogenous but that of the buccal and palatal regions was heterogeneous. Therefore, the mesial and distal regions of the PDL were subjected to biomechanical testing. Secondly, the sample size was insufficient. As mentioned previously, only two specimens were assessed by the UCT and UTT in the Isodynamic Group, which was divided into six groups. Moreover, Group F had a limited sample size ($n = 1$) due to tooth fracture during testing. Therefore, it is essential to study compression and tensile properties with more tooth specimens in the future. Thirdly, a lack of standardization of procedures followed to determine the desired effects may have introduced bias in the present study [34]. The PDL is a complex connective tissue loaded with occlusal force from varieties of directions. However, the results of the present study only reflected the mechanical response of the bone-PDL-tooth complex and not the whole intact PDL. Finally, the acquired data were based on laboratory simulation conditions and cannot be directly applied to biological mechanisms of tooth movement within the PDL.

Large animal models provide reliable evidence when studying orthodontic mechanisms preclinically [17]. The present study was the first study to investigate aligners using beagle models. Considering the difficulty of complex movement conducted on beagles, we simplified complex malocclusions into mesial and distal direction tipping movements in beagles, but we will focus on other unpredictable movements, including rotation of the lower canines [22], in the future. It is also unrealistic to measure a subjective comfort degree on beagles, encouraging us to explore clinical application on human for further development in aligners.

There are several limitations in this study. First, this study is focused on two premolars moving distally or mesially, and other tooth movements remain unclear. Second, a species difference between humans and beagles would produce discrepancy in results. Third, tooth movement is affected by many factors including action time, auxiliary, and oral and maxillofacial muscle occlusion. These results of preliminary finite element and animal need to be used in clinical practice to verify its efficacy.

5. Conclusions

The present study utilized an established FE model to evaluate the effect of aligner staging on displacement and stress, providing a reference for staging selection in vivo. In beagles, aligners generally had poorer performance with regard to movement compared to fixed orthodontic systems, but aligners with a 0.35-mm interval had the highest accuracy. When loaded with severe force, fixed sites exhibited tissue damage, but aligner sites showed better safety with only unfitting teeth movement. Root resorption as a result of pressure only occurred in groups under heavy force, indicating the necessity to control the appliance force. A staging of 0.35 mm was safe and effective, indicating that it may be used to improve the present clinical staging of 0.25 mm. The present study emphasizes the importance of continuing studies to expand the method of improving the accuracy of clear aligners. However, the structure of oral cavity is extremely complex and there may be other factors to affect the treatment effect of clear aligner. The further clinical research needed to be undertaken.

Author contribution statement

Yuru Wang: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Jie Chen: Conceived and designed the experiments; Performed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Siwen Qin: Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Xue Han; Xiutian Sima: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data.

Lijun Liao: Analyzed and interpreted the data.

Weihua Guo: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

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Data availability statement

Data will be made available on request.

Declaration of interest's statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e15317.

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