MICRO-OSTEOPERFORATIONS AND TOOTH MOVEMENT: A RANDOMIZED CONTROLLED CLINICAL TRIAL

NCT Number 02473471

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MATERIAL AND METHODS:

Trial design and any changes after trial Commencement

This study was a split mouth randomized clinical trial with a 1:1 allocation. Methods were not changed after trial initiation.

Participants, eligibility criteria, and settings

Ethical approval was obtained from Institutional Review Board (IRB) at King Abdullah University Hospital /Jordanian University of Science and Technology (JUST) with approval No.: 20150263. This trial was also registered at ClinicalTrials.gov with identifier number: NCT02473471. Participants were recruited from new patients attending the orthodontic department at the Postgraduate Dental Clinics at JUST. The following inclusion criteria were applied: (1) Males and females, (2) ≥ 16 Years old, (3) Class II division 1 malocclusion, (4) Class II canine relationship, (5) Average lower facial height (LFH) and maxillary mandibular plane angle (MMPA); patients with LFH ranging from 53 to 57 percent (55 ± 2) and with MMPA ranging from 23 to 31 degrees (27 ± 4) were only considered based on Eastman cephalometric standards[1]. The exclusion criteria were: (1) diseases/ medications that are likely to affect bone biology, (2) poor oral hygiene, (3) low and high angle cases, (4) previous orthodontic treatment, (5) Evidence of bone loss, (6) active periodontal disease, (7) Smokers. Patients were selected according to the inclusion/ exclusion criteria during the recruitment time. Subsequently, the patients were invited to sign a consent form after clarifying the purpose of the intervention and the associated risks and benefits.

Sample size calculation

The sample size was calculated based on a type I error frequency of 5%. According to the power analysis and assuming a large effect size difference between groups (effect size= 0.8), the power analysis yielded 28 subjects per group at a conventional alpha level ($p = 0.05$) and desired power ($1 - \beta$) of 0.90, yielding a total sample size estimate of 56 subjects. All calculations were performed with the computer application G-Power [2].

Randomization (random number generation, allocation concealment, implementation)

The intervention was randomly allocated to either right or left side with 1:1 allocation ratio. The randomization was accomplished using the permuted random block size of 2 with random generation function in Excel (Microsoft, Washington). Subsequently, the random sequence to either right or left were concealed in opaque envelopes and shuffled before the intervention to increase the unpredictability of the random allocation sequence. Each patient was asked to pick one sealed envelope to assign to the surgical intervention either on the right or the left side. Allocation concealment was aimed to prevent selection bias and protect the assignment sequence until allocation.

Blinding

Blinding of either patient or clinician was not possible. The blinding was ensured at measurement stage (data collection), in which the investigator was blinded of where MOPs were applied to either right or left by coding all digital models.

Interventions

Before the start of orthodontic treatment, subjects were referred to the periodontal department for checking the periodontal condition and for having regular oral care. According to the inclusion criteria, all selected patients were diagnosed with class II div I malocclusion with a treatment plan including extraction of upper first premolar teeth, fixed orthodontic appliance with maximum anchorage support using miniscrews. Included subjects had their orthodontic treatment carried out by the same orthodontic resident, using fixed preadjusted edgewise-orthodontic appliances (3M Gemini Uniteks brackets; 0.022 MBT prescription). The standardized bonding method was applied according to the manufacturer instruction. Miniscrews were used to prevent unwanted tooth movement of posterior teeth during canine retraction. Therefore, after initial leveling and alignment, miniscrews (Aarhus System; American Orthodontics; 1.5 mm width and 8 mm length) were inserted also by one investigator between upper first molars and upper second premolars to be used as direct and indirect anchorage. Direct anchorage was utilized by applying the force directly from miniscrews to canines to prevent mesial movement of posterior teeth during canine retraction.

Indirect anchorage was also applied by passively ligating upper second premolars to miniscrews that might avoid mesial movement of posterior teeth especially at leveling and alignment stage of the orthodontic treatment (Figure 1).

One operator performed Atraumatic extractions of upper first premolars within the same week of miniscrew insertion. After that, leveling and alignment were accomplished until reaching the 0.019x0.025 stainless steel arch wire. The upper canine retraction was started six months after extraction to ensure the complete healing of extraction space [3] (Figure 2).

Occlusal interferences can decrease the rate of tooth movement [4] , therefore, from day 1 and during weekly follow up period, interferences were checked and if present glass ionomer cement on the lower molars were used to raise the bite.

Clinical Micro-osteoperforations Procedure

MOPs were performed when the canines were ready to be retracted. The patients were asked to rinse their mouth twice by chlorhexidine for 1 minute. Local anesthesia was then given (2% lidocaine with 1:100,000 epinephrine, Septodont, France). MOPs were also performed by one investigator as judged by the randomization process either on the right or left upper canines as the following:

a) MOP with 1.5 mm width and 3 to 4 mm depth inside the bone was applied. MOPs were performed using miniscrews (Aarhus Mini-implant system, American Orthodontics) of 1.5 mm diameter and 6 mm length in 3 points distal to canine.

b) The points of screws insertion were demarcated by bleeding points using the calibrated periodontal probe. One row consisting of 3 holes was made distal to the canine.

c) For standardization of the protocol, the exact location of screw insertion was determined as the following: the first dot was located 3mm distal to canine and 6 mm from the free gingival margin. The second point was marked 5 mm from the first one. The net distances between MOP after insertion of 1.5 mm diameter miniscrews were 3 mm between each

hole and 2 mm away from the contact point and 5 mm away from the free gingival margin (Figure 1).

d) The miniscrew length of 6 mm was used to be inserted 3 to 4 mm deep into the bone and to account for the thickness of the soft tissue of about 2 to 3 mm.

After application of MOP, the extraction space was started to be closed using NiTi close coil spring connecting from the miniscrews between upper second premolar and first molar to power arm extended from the vertical slot of the upper canine bracket (3M Unitek, 9mm, 150g) (see Figure 3). The force was measured by force gauge (Correx, Dentaurum, Germany) at the day of application to ensure the constant and equal amount of force between all subjects and also between experimental and control sides.

After the intervention, the patients were instructed to take analgesics, such acetaminophen/Tylenol, only if necessary. Anti-inflammatory NSAIDs were avoided because of their known effect on tooth movement. Maintaining good oral hygiene and using chlorhexidine 0.2%, twice a day for five days, were recommended.

Outcomes (primary and secondary) and any changes after trial commencement

Primary Outcomes

The rate of tooth movement as primary outcome was determined by indirect measurement of study models and direct intraoral measurement as the following:
Alginate impressions were taken every month and study models were fabricated. The study models were then scanned with Ceramill Map 400- scanner with an accuracy of 0.02 mm (AmannGirrbach, Koblach, Austria) to obtain the three-dimensional (3D) model. By using Ceramill Mind design (CAD: computer-aided design) software (AmannGirrbach, Koblach, Austria), 3D model measurements were obtained. The baseline 3D digital model (M0) was superimposed to 3D digital models of following months (M1: 1st month, M2: 2nd month, M3: 3rd month) to determine the anterioposterior displacement of canines. The stable reference landmark used was the rugae area as recommended by other studies [5-7]. To superimpose two

3D digital models, a generic visualization mesh of the following 3D model was added to the baseline model; and then performs registration of the selected reference points at rugae area (Figure 4-A,B). The best fit matching of the superimposition was evaluated by a color map with a spectrum of colors in which blue color represented the best matching while red represented the worst (Figure 4-C). From buccolingual view, the amount of canine's displacement was measured from the most middle projection from the distal surface of upper canines in baseline model to the most middle projection from the distal surface of upper canines of superimposed transparent models (M1, M2, M3) (Figure 5-A). A reference plane parallel to the bracket slots was used to ensure the standardized orientation of all measurements from buccal view (Figure 5-C). From the occlusal view, the same point was localized at the middle of the distal surface of canines to be parallel to the line of arch anterioposteriorly (Figure 5-B). Additionally, Direct measurement of distance between canine and second premolar in the patient's mouth was done every week using digital caliper (IOS, USA), from upper mesial wing of the canine bracket to upper distal wing of second premolar bracket in both right and left sides parallel to the occlusal plane for 3 months period.

Secondary Outcomes

Root resorption was evaluated, as a secondary outcome, using the periapical radiographs of the canines before canine retraction and after three months. One operator, using parallax technique made all digital periapical radiographs by the same X-ray machine (RXDC eXTend, Myray, Italy), set up at 7 mA, 60 kV with an exposure time of 0.32 second. DIGORA Optime digital imaging plate system with its phosphor plate films (Soredex, Finland) was used in this study. Intraoral XCP film holders were used (Dentsply Rinn, Elgin, USA). Root resorption was measured using DIGORA for Windows 2.8 software, (Soredex, Finland). All radiographs were calibrated by 15.63 pixels per mm according to the manufacturing instruction. Root resorption in millimeter (mm) was measured by the difference between root length at baseline (R1) and after three months (R2). The reference point was the midpoint of mesial and distal cementoenamel junction (CEJ). The root length was calculated from root apex to the midpoint of cementoenamel junction (CEJ).

Periodontal index and plaque index were also evaluated clinically in both upper

canines and second premolars before canine retraction and after three months according to Löe [8]. Both pain intensity and interference were evaluated using Visual Analog Scale (VAS) from 0 to 10 Numeric Rate Scale (0= no pain, 10= severe pain). The participants filled out a questionnaire to assess the pain intensity immediately, after 1 hour, 12 hours, day 1, day 3, day 5 and day 7 following MOP intervention. Pain interference with daily life was assessed after MOP intervention on 1, 3, 5 and 7 days in which patients were asked to provide their subjective answers of pain during eating, pain awakened them at night, the feeling of discomfort and swelling on the surgical side. Numeric Rate Scale was also used to rate the level of satisfaction (0= not satisfied, 10= very satisfied) and easiness of MOP procedure (0= very easy, 10= very complicated). Moreover, the patients were asked if they were willing to repeat the procedure and recommend to a friend using categorical data (Yes or No). There were no changes to the outcome measures after trial commencement.

Statistical analysis (primary and secondary outcomes, subgroup analyses)

Statistical analysis was accomplished using the Statistical Package for the Social Sciences computer software (SPSS 20.0, SPSS Inc., IL, USA). Probability values equal or less than 0.05 were considered significant. Independent sample t-tests were calculated to analyze the results of the primary outcome and secondary outcomes to compare the difference between MOP and control sides. Similarly, independent sample t-test was performed to compare the amount of root resorption before and after three months in MOP and control sides separately. Chi-square was used for analysis of categorical data including the willingness to repeat the procedure and recommend it to a friend. Descriptive statistics were used to describe the satisfaction and ease of the procedure.

Reliability coefficient (Cronbach's Alpha) was used to evaluate the reliability of measurements of primary outcomes. One examiner did all measurements, and all subjects were randomly selected. Six of 3D superimposed digital models had been chosen randomly. Superimpositions on the rugae area and canine displacement were measured twice within 2-week interval. Reliability coefficient (Cronbach's Alpha) was 0.95, showing excellent superimpositions and measurement agreement.

For intraoral measurements, intra-examiner reliability was done in the lower arch after reaching 0.019x0.025 stainless steel arch wire and teeth were in a passive state; all cases were non-extraction in the lower arch. Six of subjects were selected randomly, and measurements were done twice with the 2-week interval. Measurements were done from the upper mesial wings of the lower canine bracket to the upper distal wing of the lower second premolar bracket. Reliability coefficient (Cronbach's Alpha) was 1.00, indicating excellent measurement agreement.

Figure ligands

Figure 1: Micro-osteoperforations protocol

Figure 2: Diagrams of time events during the study

Figure 3: Clinical Micro-osteoperforations application. A, calibrated periodontal probe to locate the point of miniscrew insertion. B, Three bleeding points. C & D, First MOP application. E, 2nd MOP application. F, Three MOP were visible distal to canines. G, canine retraction by closed coil spring.

Figure 4: 3D digital superimposition. A, registration of 4 reference points at medial and lateral of third rugae area. B, performing registration and best-fit matching. C, best-fit color matching with blue the best match and red the worst.

Figure 5: Measurement of amount of canine retraction **on** 3D digital models. A, buccal view of upper left canines showing measurement tools on the Ceramill mind software. C, occlusal view of the canines showing the measurement tool. The canines in baseline model (Yellow color) and in the 3rd month model (purple color). B, the reference plane parallel to the bracket slots.

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Figure 1

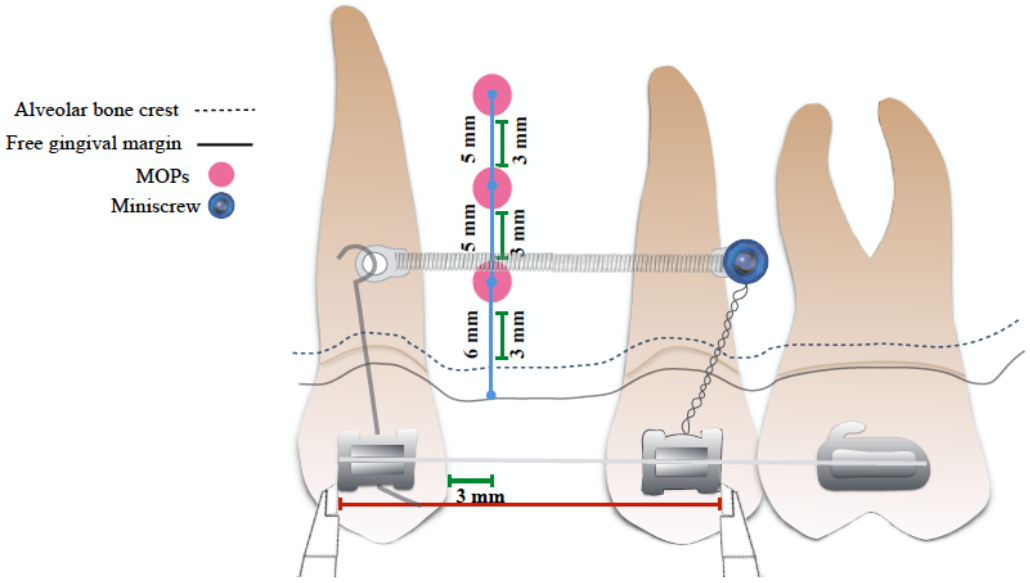

Figure 2

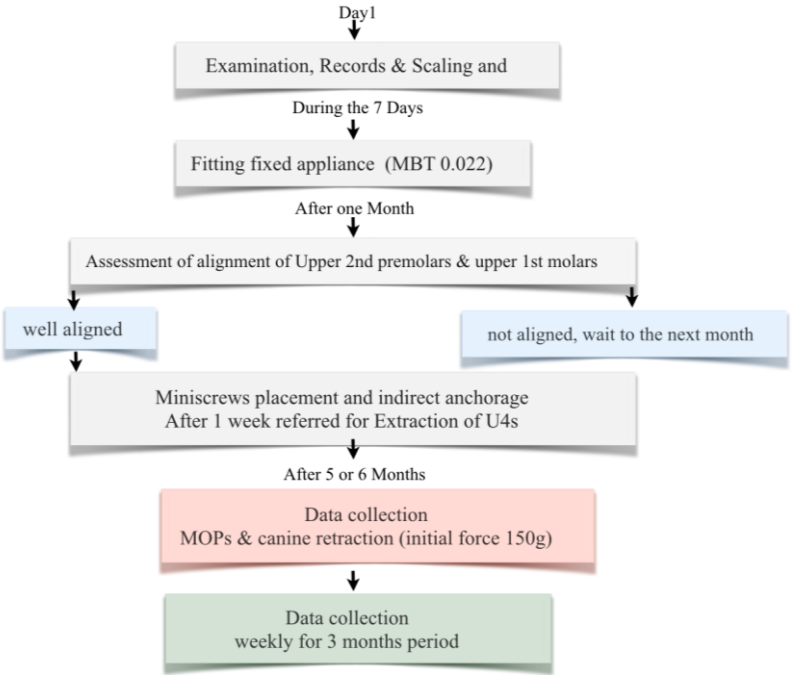

Figure 3

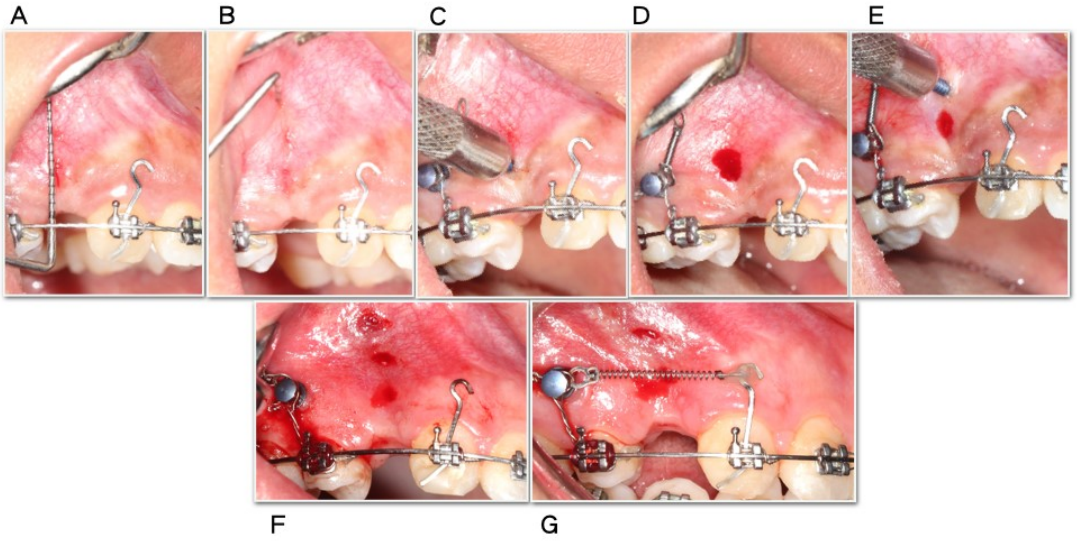

Figure 4

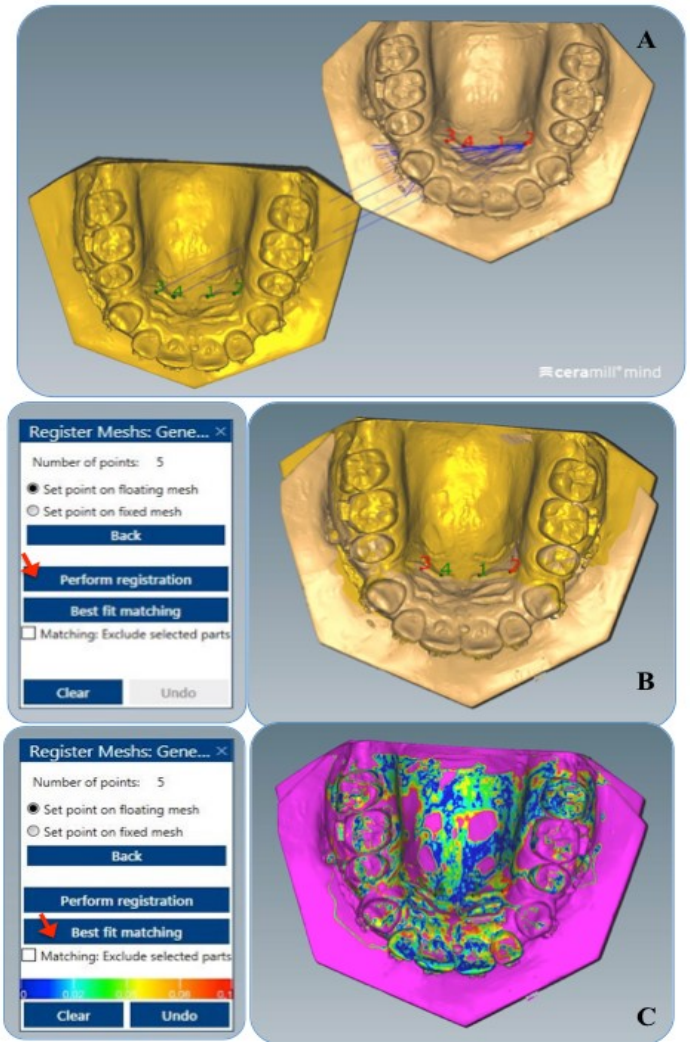
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Figure 5