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RESEARCH

2018	Accelerated Orthodontic Tooth Movement in Adult Patients by Subsequent Micro- osteoperforations of Cortical Bone
2016	Accelerated Tooth Movement in Adult Patients by Micro-perforations of Cortical Bone
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2011-Present	American Student Dental Association (ASDA)
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2015	Dean's Award for Research Excellence

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2013-2015	Gamma Pi Delta Prosthodontic Honors Society
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ABSTRACT

Title of Thesis: Accelerated Orthodontic Tooth Movement in Adults by Subsequent Micro-osteoperforations of Maxillary Cortical Bone

Robert Laraway Master of Science 2018

Thesis Directed by: Monica Schneider DDS, MS
Clinical Assistant Professor
University of Maryland School of Dentistry, Department of Orthodontics

Objective: Determine if orthodontic tooth movement during space closure is accelerated after subsequent micro-osteoperforations (MOPs).

Methods: Five adults requiring maxillary 1st premolar extractions participated. MOPs were performed unilaterally in the extraction site at the beginning of the study and four weeks later. Canines were retracted bilaterally and space closure was measured after two months.

Results: Overall, the canine retraction rate was 0.34mm greater on the MOP side compared to the control side but showed statistically insignificant differences. When compared to our initial study, which only had one MOP application, canine retraction was 0.24mm greater but, again, was statistically insignificant.

Conclusion: The results of this study show that the experimental side had greater retraction of than the control side. However, the difference was not statistically significant. More studies are needed to study the extent and duration of effects of MOPs on tooth movement in humans.

Accelerated Orthodontic Tooth Movement in Adult Patients by Subsequent Micro-perforations of Maxillary Cortical Bone

by
Robert Laraway

Thesis submitted to the Faculty of the Graduate School of the
University of Maryland, Baltimore in partial fulfillment
of the requirements for the degree of
Master of Science
2018

DEDICATION

This work is dedicated to my wife, Megan and my parents, Kevin and Leslie, for their constant love, encouragement, and support.

AKNOWLEDGEMENTS

Thank you for my mentor, Dr. Monica Schneider for all over her help overseeing the project and for shaping me over the past seven years into the orthodontist that I have become.

Thank you to Dr. Tina Mahmoudi, who took me under her wing during her thesis project and allowed me to gain insight into this study.

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INTRODUCTION

In children and teenager patients, human growth can be utilized to aid in orthodontic and orthopedic treatment of the dental and skeletal malocclusions. However, adult patients have little to no growth remaining. Therefore, orthopedic approaches cannot be utilized, often prolonging treatment and increasing the risk of potential side effects such as gingivitis and periodontitis[1], decalcification, caries[2], and root resorption[3]. In addition to potential side effects, adult's "Oral health related quality of life" (OHrQL) is altered during fixed treatment. There is a decrease in one's personal self-esteem during treatment. Therefore, it is critical to explore safe modalities to accelerate orthodontic treatment time for adults. [4]

In adults with significant dental crowding or protrusion, optimal orthodontic treatment often requires the extractions premolar teeth but treatment requiring premolar extractions is on average six months longer than non-extraction treatment.[5] In order to have an efficient treatment, several factors must be addressed to obtain optimal orthodontic tooth movement (OTM) such as levels of force, duration of force application, and biologic alterations of tissues.

During adult extraction treatment, proper anchorage control and mechanics are critical for an effective treatment. When stationary anchorage is desired in the maxillary arch, temporary anchorage devices (TADs) can be placed in the bone to avoid unwanted side effects when using the dentition as anchorage. To further aid in anchorage control, during extraction space closure, the canine can be retracted prior to the four incisors, referred to as sequential retraction.

The concentration for this study is to provide evidence-based research for osteoperforations of cortical bone in relation to accelerating OTM in adult patients.

LITERATURE REVIEW

With the number of adult patients seeking orthodontic treatment is rapidly increasing, extensive research is being performed to discover an effective approach to accelerate OTM by studying variables such as bracket types, magnitudes of force, pharmacologic therapies, and surgical interventions.

A. Tooth Movement

Tooth movement is limited by physiologic processes where forces are transmitted from the teeth to the periodontal ligament (PDL) within the alveolar bone. Orthodontic tooth movement (OTM) is directly regulated by bone apposition and resorption around the tooth, known as bone remodeling.[6,7] Several hypotheses exist regarding tooth movement: piezoelectric[8,9], mechanotransduction[10,11], bone-bending[12], and pressure-tension[13,14]. Perhaps the most accepted mechanism of tooth movement and bone remodeling is the tension and compression of the PDL due to forces on the tooth causing deposition and resorption of surrounding alveolar bone, respectively.[6,13,14,] Osteoclast cells are responsible for "frontal" alveolar bone resorption whereas osteoblasts stimulate bony apposition on the tension side.[15]

Recent human studies have shown that light, continuous forces by means of a 150g Nickel Titanium (NiTi) coil spring of are optimal; resulting in an average of 0.8 to 1.1mm of OTM per month.[16-20] If forces are too great, undermining resorption may occur,

leading to hyalinization of the PDL, necrosis of the bone, and slower OTM.[21] Through intention reversible injury to the bone, osteoclastic resorption can be induced. This has been referred to as Regional Acceleratory Phenomenon (RAP), which is the basis for most of the accelerated OTM modalities.[22]

B. Regional Acceleratory Phenomenon (RAP)

In 1959, Kole observed that tooth movement is slowed in areas of greater bone mineralization. [23] Consequently, with an intentional injury, the bone metabolism shifts to a more catabolic state. Proliferation of osteoclasts leads to temporary osteopenia, which decreases bone density and bone volume. This process allows the teeth to move in a more elastic environment and thus accelerate OTM.[24]

1. Extent of RAP

Several studies have been performed to study how long the RAP effect exists after injury to the tissue. According to Yaffe et. al, RAP began about 10 days following the noxious stimuli and began to normalize by day 21 in a rat model. [25] Therefore, one can argue that to accelerate OTM for the duration of treatment, the acceleratory procedures should be performed every three to four weeks as the RAP effect begins to diminish.

2. Inflammatory Process

Following an injury to or stress on the PDL, as exists when an orthodontic force is applied to a tooth, there is an increase of blood flow, vascular permeability, and extravasation of cytokines.[17] The pro-inflammatory cytokines seen in crevicular fluid during OTM include IL-1, IL-6, IL-8, IL-11, and TNF-α.[26-29] In addition to the high concentration of cytokines, OTM upregulates prostaglandin and receptor-activator of

nuclear factor kappa-β ligand (RANK-L) release from fibroblasts, which controls inflammation and tissue turnover.[29,30] RANK-L promotes osteoclastogenesis, resulting in a decreased extracellular matrix of bone through a Cathepsin-K pathway.[31] Meanwhile, IL-6 and IL-11 cause a RANK-L independent osteoclastogenesis and increases osteoclastic activity (Kudo Bone 2003).[32] These inflammatory cytokines and RANK-L lead to increased OTM. On the other hand, it has been proven when these cells are depressed, by osteoprotegrin biomarker for example, there is reduced OTM.[33,34]

The tissue responses following an injury or force on the PDL mimic the response to the pathogenic inflammatory disease of periodontitis.[29,35] Due to these similar responses, OTM is accelerated in this diseased state. However, severe side effects such as bone loss and root resorption are evident.[36] Therefore, several proposed techniques attempt to simulate the effects of periodontitis but to do so in a non-pathogenic environment to accelerate OTM such as surgical and non-surgical adjunctive orthodontic therapies.

C. Surgically Facilitated Orthodontic Therapy (SFOT)

Similar to the inflammation processes seen in periodontal disease, tissue injury by means of sterile surgical wounding has be proven to cause RAP through decreasing bone density and increasing bone turnover.[37] Heinrich Kole was perhaps the first to utilize this approach in orthodontic treatment by performing interdental corticotomies to reposition the tooth with the belief that the dense alveolar cortex caused the most resistance to OTM.[23] Since then, a few other approaches to SFOT have been discovered in addition to Kole's "Bony Block" technique such as Osteotomy/Osteogenic Distraction, Piezocision,

Corticotomy Assisted Orthodontic Tooth Movement (CAOT), and Periodontally Accelerated Osteogenic Orthodontics (PAOO).

1. Bony Block Concept

    As discussed above, in 1959, Kole observed increased OTM after carrying out osteotomies in the cortical bone around the teeth. He made incisions above the apices of the teeth from the buccal through to the palate and vertically through only the cortical bone between each tooth, essentially creating a block of medullary bone housing each tooth. Kole accredited the increased OTM to the decreased resistance from removing the dense cortical bone. However, in 2001, Wilcko and Wilcko challenged Kole's theory, proposing that the increased OTM was actually a result of the inflammatory cascade and osteoclastogenesis that took place following the flap and osteotomies. [38]

2. Osteotomy with Osteogenic Distraction

    In 1988, Ilizarov adopted the osteotomy technique into dentistry from the early 1900 medical intervention created by Codivilla. Osteotomies are similar to Kole's Bony Block approach except that the bony segments are resected completed through the medullary bone.[39] The osteotomy technique is often paired with osteogenic distraction, in order to move the bone segments. In osteogenic distraction, the cortical bone is split and a distraction screw is attached between the segments of bone to move them towards or away from each other. In 2000, Liou proposed that osteogenic distraction could be

applied to increase OTM by moving teeth through newly formed fibrous bone. The bone distractor was installed, and the segments were moved at a rate of 1mm/day, following a one-week latency period. [40]

Several split mouth studies have confirmed the use of osteogenic distraction to accelerate OTM. Kurt, Kharkhar, and Kumar observed complete canine retraction in 11 days, 12 days, and 20 days respectively. Kurt et. al. measured the canine retraction to be around 0.67mm/day.[41-43] While these three studies observed increased OTM, several studies found serious side effects such as increased root resorption and gingival/pulpal damage, anchorage loss, molar extrusion and mesial tipping of canine.[44]

3. Piezocision

In comparison to the other SFOT techniques, piezocision is unique because it does not require a full thickness flap. Sebaoun made micro-incisions in the alveolar cortex through gingival tunnels. The vibrations from the piezo knife is thought to increase OTM, in addition to the surgical wounding of the bone.[45] Kim et al observed a three-fold increase in OTM of the maxilla and two-fold increase in the mandible after using piezocisions on dogs and Dibart found a two-fold increase in OTM in a rat model. [46,47] Yi and Xiao performed a systematic review including four studies and found weak evidence that piezocision is a safe, effective method to accelerate OTM. However, they concluded that more quality studies are necessary.[48]

4. Corticotomy Assisted Orthodontic Treatment (CAOT)

In CAOT, a periodontist raises a flap and decorticates the alveolus, forming interdental demarcations. The corticotomy-induced RAP increases OTM.[49] This was confirmed in a study by Cho performed on beagle dogs.[50] Vercellotti observed a 65% reduction in treatment time using a piezo saw after flapping the gingiva during their CAOT study.[51] Sanjideh reported a maximum OTM velocity at 22 days after the incision but found the OTM was increased after a second procedure when compared to the side of the mouth where only the initial procedure was performed in foxhound dogs.[52] In the systematic review by Hassan, it was concluded that CAOT is a safe and effective approach for accelerated OTM, increasing space closure and resolving incisor crowding by over 2-fold. [49] However, most human studies are primarily clinical cases so randomized human control trials are needed.[38,51,52]

5. Periodontally Accelerated Osteogenic Orthodontics (PAOO)

First discovered by Wilkco and Wilcko, PAAO claims to reduce orthodontic treatment time by increasing bone remodeling and accelerating OTM. They claim that PAAO causes a PDL-mediated RAP by thinning the bone in the direction of the tooth movement. They observed a premolar extraction site closure of 6-8 weeks with light orthodontic forces.[38] Mathews and Kokich argued that the periosteal release during the surgical gingival flap added to the inflammation and thus increased RAP compared to flapless procedures. Although, this likely would also result in greater patient discomfort.[55]

D. Non-Surgical Approaches to Accelerated OTM

1. Medications

Several medications have been studied over the last decade regarding their effect on OTM. Perhaps the most significant finding is the inhibitory nature of bisphosphonates on osteoclasts and their long-lasting effect on bone metabolism, ultimately slowing OTM. In this same systematic review, Bartzela et. al. also found that non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, have an inhibitory effect on OTM, whereas acetaminophen did not alter OTM. In addition to bisphosphonates and NSAIDs, calcium and estrogen slowed OTM. On the other-hand, corticosteroids, vitamin D, parathyroid hormone, and thyroxin accelerated OTM.[56] Therefore, it is vital that the practitioner has a full medical history prior to commencing orthodontic treatment.

2. Vibration

In the last few years, there has been a strong push by companies such as *Acceledent* and *PROPEL* to gain traction for their vibratory devices - *Aura* and *Vpro5*, respectively. They are both FDA cleared class II medical devices. In a study where 60Hz of vibration was applied to molars, Nashimura found significantly accelerated OTM and less root resorption during expansion with the belief that the vibratory resonance may stimulate RANK-L expression in the PDL.[57] Bowman found a 30% decrease in treatment time of thirty non-extraction class II adult patients.[58] In a systematic review by Jing and Xiao, it

was concluded that 25% of the studies showed accelerated canine retraction while 50% of the studies found no accelerated tooth alignment. The systematic review concluded that more quality research needs to be conducted.[59]

3. Low-level Laser Therapy (LLLT)

The effects of LLLT on OTM were first observed by Saito and Shimizu in 1997, when they irradiated the maxillary mid-palatal suture in rats. They found that LLLT can accelerate bone remodeling by stimulating collagen synthesis and that the application of LLLT may help in the stability of the orthopedic treatment.[60] Cruz studied LLLT in a split mouth study on humans and found that the experimental side had a 30% increase in OTM. Doshi-Mehta found similar results with their split mouth canine retraction study.[61,62] Yasaei concluded that the LLLT increases RANK-L and macrophage colony stimulating factor (M-CSF) that increases osteoclastogenesis and accelerates OTM.[63]

4. Micro-Osteoperforation (MOP)

In micro-osteoperforation (MOP) therapy, no flap is needed. Instead, shallow perforations are made into the cortical bone through the gingiva. The theory of MOPs is very similar to that of the SFOT; however, it does not require the release of an invasive flap.[64] In 2012, The company *PROPEL* coined the term *Alveocentsis*™ to define puncturing the bone for their MOP product line the *Excellerator*, *Excellerator* RT and, later, the *Excellerator* PT (Figure 1). The *Excellerator* line is a FDA-approved Class I medical device

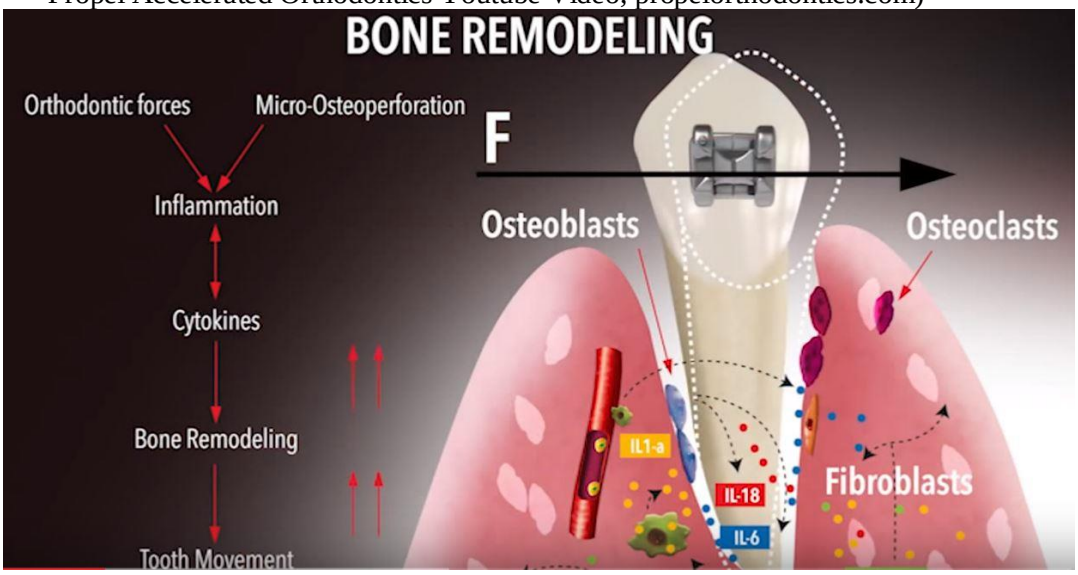
with a sterile stainless-steel tip that can be set to perforate the bone either 3mm, 5mm, or 7mm depending on the clinician's preference (Figure 2).[65]

Figure 1: Propel Excellerator (left), Excellerator RT (middle), and Exellerator PT (right) (adapted from propelorthodontics.com)

Figure 2: Propel Excellarator with depth limiter LED indicator[65]

In 2010, Teixeira studied the effects of MOPs by performing three MOPs in an upside-down triangle pattern in OTM on rats. He discovered an increase in cytokine expression and bone activity when MOPs were combined with orthodontic forces (Figure 3).[26]

Figure 3: Role of Micro-osteoperforations on Bone Remodeling (adapted from Propel Accelerated Orthodontics Youtube Video, propelorthodontics.com)



Later, Alikhani studied the effect of MOPs on humans in a split mouth, blinded study. The subjects had maxillary first premolars extracted and the maxillary canines were retracted with a 100g NiTi coil spring against a TAD. After 28 days, they observed an increase in inflammatory biomarkers and a 2.3x increase in maxillary canine retraction on the experimental site. They concluded that MOP therapy is a safe, effective, and comfortable procedure that accelerates OTM and can reduce treatment time by as much as 62%.[66]

However, several other studies found no clinically significant acceleration in OTM. Swapp et. al believed that MOPs did not cause accelerated OTM on foxhounds because the MOPs only perforated the cortical bone and did not affect the medullary bone.[67] Cramer et. al. believed that the MOPs did not accelerate OTM on seven beagle dogs because the extent of RAP only occurred within 3mm of the MOP.[68] In our initial study, where a single MOP

was performed on ten human subjects, Mahmoudi came to the same conclusion that MOPs did not accelerate OTM, contributing the confounding results to patient variation in biologic response.[69]

E. Summary

As adult orthodontic treatment grows in popularity, the desire for a faster treatment time will be anticipated. Ideally, this accelerated OTM would be consistent, painless, and easily performed. Therefore, MOPs appear to be an ideal alternative to accelerate OTM compared to some of the more invasive techniques like distractions and PAOO. However, several human studies have conflicting results. In the Alikhani study, the space closure was measured 28 days after the MOPs whereas, in our initial single MOP study, the space closure was measured 3 months after the MOP procedure. Therefore, this study will attempt to observe the effect of a "renewed" RAP effect by performing a second MOP procedure after 28 days.

PURPOSE OF THE PRESENT STUDY

The specific aim for this research study is: To determine if subsequent micro-osteoperforations produce accelerated orthodontic tooth movement during maxillary 1st premolar extraction space closure in adult patients

HYPOTHESIS

Alternative Hypothesis (H_1): Rate of tooth movement is greater on the experimental side treated with micro-osteoperforations of cortical bone than the control side in adult patients.

Null Hypothesis (H_0): There is no significant difference in the rate of tooth movement between the experimental side treated with micro-osteoperforations of cortical bone and the control side in adult patients.

MATERIALS AND METHODS

The Human Research Protections Office (HRBO) at the University of Maryland Institutional Review Board (IRB) approved this split-mouth clinical trial. This study began in 2015 as a follow-up to our initial single MOP study, which began in 2013 by Dr. Tina Mahmoudi. All patients were recruited from the University of Maryland School of Dentistry Department of Orthodontic graduate clinic. The materials and methods were adopted from our initial single MOP Study.[70]

Study Subjects

Orthodontic resident (R.L) was trained and calibrated by principal investigator (M.S.) for recruitment of patients that met inclusion criteria. Five healthy adult patients between ages 18-44 that met the inclusion criteria (Table 1) were presented with informed consent form approved by the IRB.

Table 1: Inclusion and Exclusion Criteria for Research Subjects

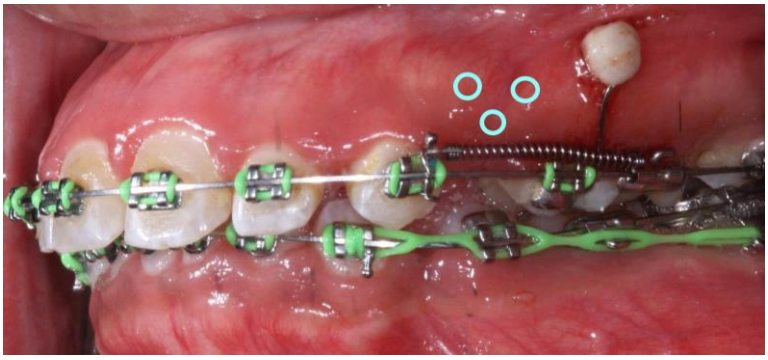
Inclusion Criteria	Exclusion Criteria
Healthy adults ages 18-44	Significant medical history of radiation therapy or immune disorders
No active caries or periodontal disease	Current active periodontal disease
Orthodontic treatment requiring removal of maxillary first premolars	Patients requiring antibiotic prophylaxis for dental treatment

Orthodontic Initial Phase

Unitek Victory Series™ Miniature Metal Brackets (0.022, MBT prescription) or Unitek Clarity Ceramic Brackets with metal slot (0.022, MBT prescription) were bonded (to at least the maxillary canines) and patients had maxillary first premolars extracted bilaterally. Rocky Mountain Orthodontics Dual- Top TADs of 6mm length and 1.6mm diameter were placed bilaterally, interradicular to the maxillary first molar and maxillary second premolar for stationary anchorage. A 0.016x0.022 stainless steel wire was bonded from the TAD to the maxillary first molar for stable indirect anchorage. Space closure was performed using a 0.017x0.025 stainless-steel arch wire (ORMCO). Closed coil nickel titanium coil springs (ORMCO) of 150g of force from the maxillary first molar to maxillary canine were used for sequential retraction by use of conventional sliding mechanics (Figure 4). Three shallow perforations (5-7mm) through keratinized gingival and into cortical bone were performed on the randomly selected experimental side prior to initiation of the previously mentioned canine retraction. One perforation was

performed in the middle of the extraction site and two more perforations placed apical and lateral to that to form a triangle shape of perforations following the pattern from the Teixeira study (Figure 4).

Figure 4: Canine Retraction with Micro-osteoperforations



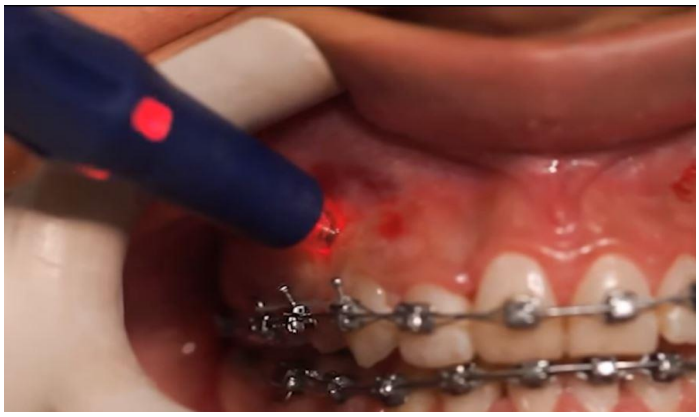
Clinical Micro-Osteoperforation Procedure

A full maxillary cone-beam computed tomography (CBCT) radiograph was obtained for baseline measurements and to confirm proper TAD placement. In addition to the CBCT, intra-oral photographs and alginate impressions for digital casts were taken for baseline measurement at the start of the study (T_0) when the first MOP procedures were performed. The PROPEL® System (Excellerator by Propel Orthodontics) was used to perform the MOPs according to guidelines:

- Apply topical and local infiltrative anesthesia
- Rinse with Chlorhexidine for 30 seconds prior to the procedure
- Perform three micro-osteoperforations of approximately 5mm-7mm in depth and 0.5 mm in diameter distal to the maxillary canines (Figure 5)
- Rinse with Chlorohexidine for 30 seconds after procedure

- Instruct the patient to avoid anti-inflammatory medications during the period of the research

Figure 5: Micro-osteoperforations Performed by PROPEL Excellerator
(adapted from Propel Accelerated Orthodontics Youtube Video, propelorthodontics.com)



Alginate impressions were taken four weeks after T_0 (at T_1), at which a second MOP procedure was performed. Final records (CBCT, intra-oral photographs, and digital models) were taken two months after initial canine retraction and MOP procedure (T_2) (Figure 6).

Figure 6: Maxillary Occlusal Photograph at T_0 (left) and T_2 (right). (MOP performed on right maxilla)

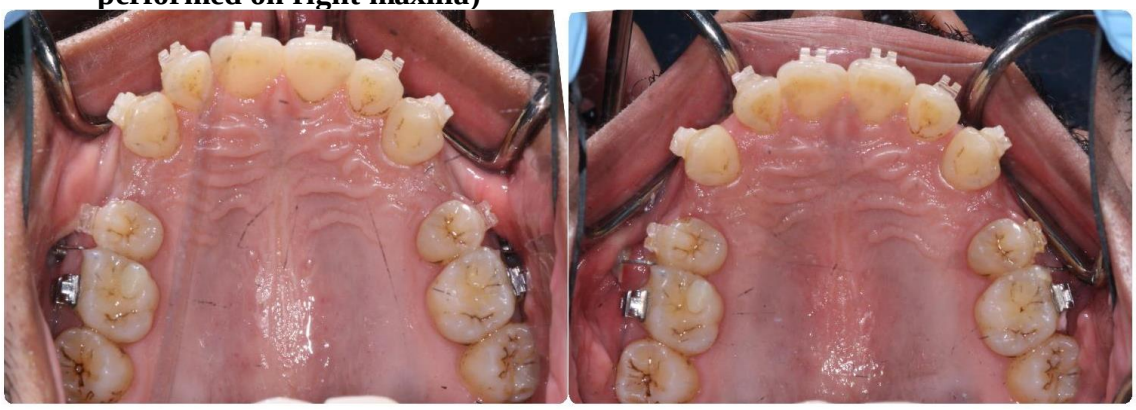


Image acquisition

Cone beam computed tomography (CBCT) image was obtained using the iCAT scanner (Imaging Sciences International, Hatfield, PA, USA) available at The University of Maryland School of Dentistry. To ensure that the voltage, field of resolution, current, field of view (FOV) and patient's position did not affect the measurements obtained from CBCT images, all the CBCT images were taken by the same radiology technician and the CBCT parameters were identical in all of the scans. The scans were taken with the patient's head upright with the following parameters: 120kVp, 47mA, 250-um voxel resolution and 16-cm FOV. Images were taken before the MOP procedure (T_0) and after 2 months of canine retraction (T_2).

Image and Digital Cast Analyses

To perform more accurate measurements and avoid superimposition of the contralateral side on the CBCT, single-sided lateral cephalograms were generated. Anatomage Invivo5 3D software was used to create right and left side two dimensional cephalometric radiographic images from the initial and final CBCTs for each subject.

The dependent variable measured was:

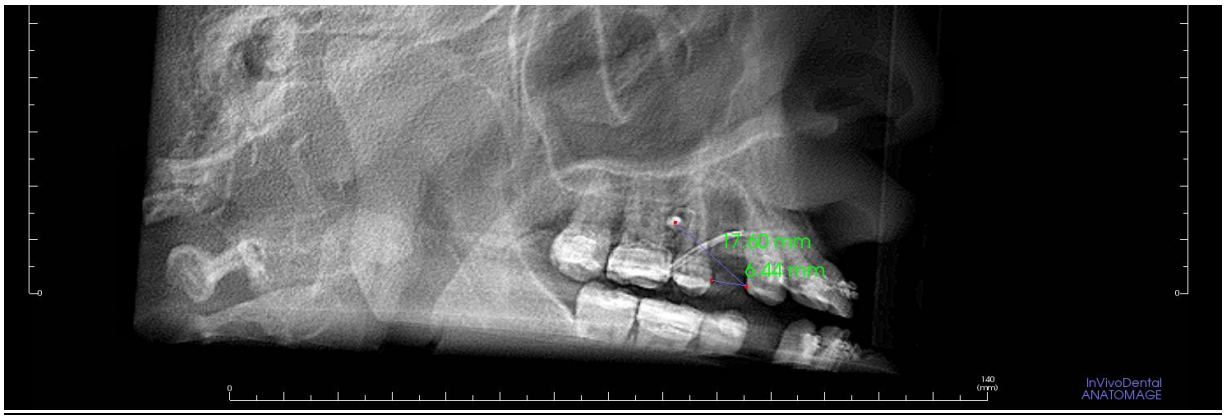
- Amount of maxillary first premolar extraction site closure through canine retraction.

Two measurements on the control and experimental sides were performed on the unilateral cephalograms at T_0 and T_2:

1. The distance in millimeters between the TAD and the most distal curvature of the maxillary canine (TAD-U3D).
2. The distance in millimeters between the most distal of the curvature of the maxillary canine and the most mesial curvature of the maxillary second premolar (U3D-U5M).

The TAD was used as a stable superimposition landmark. All the landmarks were identified and measurement by two separate operators who were blinded as to which side the experimental procedures were performed (Figure 7). Abbreviations of all measurements can be found in Table 2.

Figure 7: Two CBCT Measurements Performed on Unilateral Cephalograms



Alginate impressions for plaster casts were taken at the initial and final appointments (T_0, T_1 and T_2). The casts were scanned, digitized, and measured using OrthoCAD 3.5.0.38 (Cadent ^{TM}). These digital casts were used to measure the amount of maxillary 1st premolar extraction site closure through maxillary canine retraction. Three separate measurements were performed on the digital casts at T_0 and T_2 by two separate operators

who were blinded as to which side the experimental procedures were performed. The three measurements used for the study were (Figure 8):

1. The distance in millimeters between the cusp tip of the maxillary canine to mesiopalatal cusp tip of maxillary first molar (U6 cusp -U3 cusp).

2. The distance in millimeters between the distal wall of the maxillary canine to the mesial wall of the maxillary second premolar (U3D-U5M).

3. The distance in millimeters between the cusp tip of the maxillary canine to buccal cusp tip of maxillary second premolar at T_0 and T_2 (U3 cusp -U5 cusp).

Abbreviations of all measurements is seen in Table 2

Figure 8: Three Measurements Performed Bilaterally on Digital Models (MOP performed on right side)

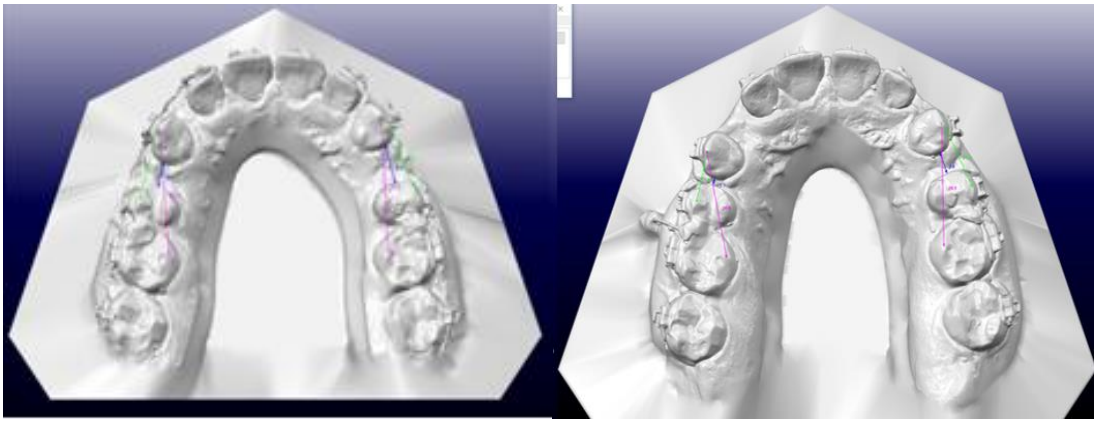


Table 2: Abbreviations and Measurements

	Abbreviation	Measurement
CBCT	TAD-U3D (mm)	The distance between the TAD to the most outer point of the distal curvature of the maxillary canine
	U3D-U5M (mm)	The distance between the most outer point of the mesial curvature of the maxillary 2nd premolar and the distal most outer point of the curvature of the maxillary canine
Digital Cast	U3 Cusp-U6 Cusp (mm)	The distance between the cusp tip of the maxillary canine to mesiopalatal cusp tip of maxillary 1st molar
	U3D-U5M (mm)	The distance between the distal wall of the maxillary canine to the mesial wall of the maxillary 2nd premolar
	U3 Cusp- U5 Cusp (mm)	The distance between the cusp tip of the maxillary canine to buccal cusp tip of maxillary 2nd premolar

Comparison to Initial Single MOP Study

The mean differences between T_0 and T_2 on both the experimental and control sides for the four common measurements were compared to those of our initial study by Dr. Mahmoudi where the MOPs were only performed at T_0 but not at T_1 and final records taken 3 months after T_0 rather than after 2 months as in this current study.

Statistical Analysis

All the acquired data was analyzed using MYSTAT software version 12 by SYSTAT. Paired Student t-test were performed for the five measurements to compare the average rate of space closure on the experimental side and the control side. A paired student t-test was also used to compare the means of this study to means of the initial single MOP study. Statistical significance was determined by p-value <0.05.

When comparing the results to those of the initial single MOP study, four measurements were in common: CBCT U3D-U5M, CBCT U3 cusp-U5 cusp, Digital Cast U3 Cusp-U5 Cusp, and Digital Cast U3D-U5M. The mean measurement for the control side was subtracted from the propel side for each measurement category and these differences were compared to those differences of the initial single MOP study.

RESULTS

Five healthy adult patients between the ages of 18 and 44 were recruited from the Orthodontic Department at the University of Maryland School of Dentistry. These patients required the extraction of at least the maxillary first premolars as part of their orthodontic treatments. All five patients completed the research study with no loss of appointments and good oral hygiene. All subjects exhibited no changes in medical history including avoidance of anti-inflammatory medications.

The age range of subjects was between 20 years of age and 26 years of age with a mean age of 22.2 years. Three subjects were male and two were female. Two subjects were African-American, two were Caucasian, and one was Hispanic. The demographics for the patients can be seen in Table 3.

Table 3: Subject Demographics

Subject #	Gender	Age	Ethnicity
1	F	24	African-American
2	M	20	Hispanic
3	F	20	Caucasian
4	M	26	Caucasian
5	M	21	African-American

For all five measurements categories (two CBCT and three digital cast measurements), the two examiners measurements were averaged, and one tailed statistical t-test performed for the difference between T_0 and T_2 on each measurement category to evaluate significance of space closure between the control and experimental sides.

A. CBCT Measurements:

1. **TAD – U3D:** The average measurements of examiner 1 and 2 are seen in Table 4. The mean of these averages showed that control side had 0.013mm greater space closure after two months than the experimental side. However, this difference is not significant (Table 5 and Figure 9).

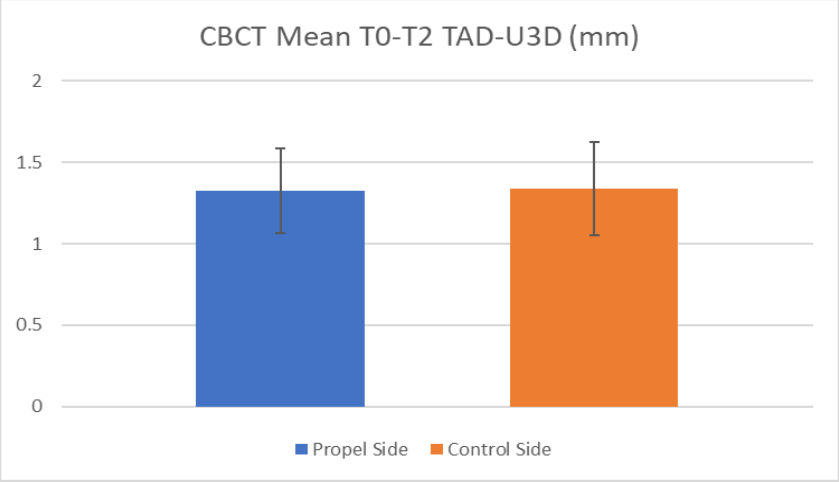
Table 4: CBCT Measurements, TAD-U3D (mm)

	MOP side	**Control side**
Average of Examiner 1& Examiner 2 Values	**TAD- U3D (mm)**	**TAD- U3D (mm)**
	T_0 -T_2	**T_0 -T_2**
Patient #1	1.99	1.565
Patient #2	1.79	2.115
Patient #3	0.65	0.57
Patient #4	1.38	0.8
Patient #5	0.83	1.64

Table 5: Descriptive Statistics (CBCT, TAD-U3D Measurements)

Variable	N	Mean (mm)	Std. Dev.	Std. Err.	p- Value
MOP Side T_0-T_2 TAD-U3D	5	1.33	0.583	0.261	0.481
Control Side T_0-T_2 TAD-U3D	5	1.34	0.638	0.285	
Diff.	5	-0.013	-0.055	-0.024	
Not Significant (p≥0.05), *= Significant (P<0.05)					

Figure 9: CBCT Mean Measurements (TAD-U3D)



2. **U3D - U5M:** The average measurements of examiner 1 and 2 are seen in Table 6. The mean of these averages showed that experimental side had 0.29mm greater space closure after two months than the control side. However, this difference is not significant (Table 7 and Figure 10).

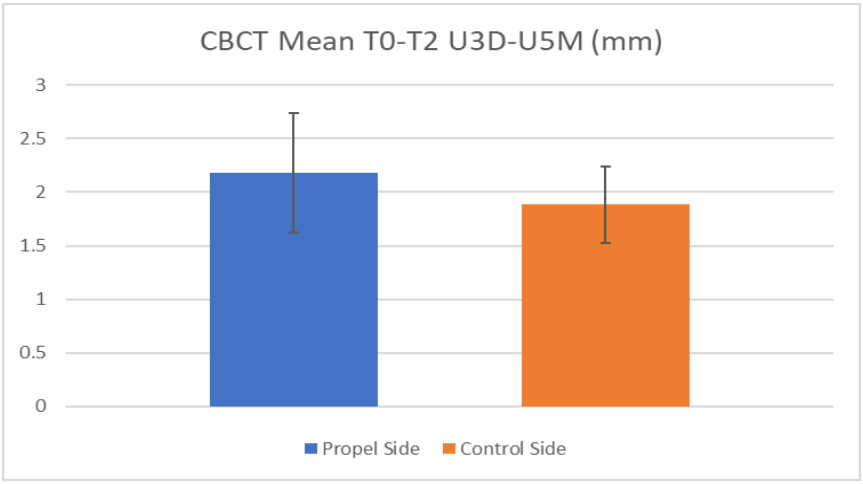
Table 6: CBCT Measurements, U3D-U5M (mm)

	MOP side	Control side
Average of Examiner 1& Examiner 2 Values	**U3D- U5D (mm)**	**U3D- U5D (mm)**
	T_0 -T_2	**T_0 -T_2**
Patient #1	3.085	2.285
Patient #2	3.87	3.105
Patient #3	1.12	1.395
Patient #4	1.755	1.16
Patient #5	1.07	1.48

Table 7: Descriptive Statistics (CBCT, U3D-U5M Measurements)

Variable	N	Mean (mm)	Std. Dev.	Std. Err.	p- Value
MOP Side T_2-T_0 U3D-U5M	5	2.18	1.25	0.557	0.163
Control Side T_2-T_0 U3D-U5M	5	1.89	0.803	0.359	
Diff.	5	0.29	0.447	0.198	
Not Significant (p≥0.05), *= Significant (P<0.05)					

Figure 10: CBCT Mean Measurements (U3D-U5M)



B. Digital Cast Measurements:

1. U6 Cusp – U3 Cusp: The average measurements of examiner 1 and 2 are seen in Table 8. The mean of these averages showed that experimental side had 0.52mm greater space closure after two months than the control side. However, this difference is not significant (Table 9 and Figure 11).

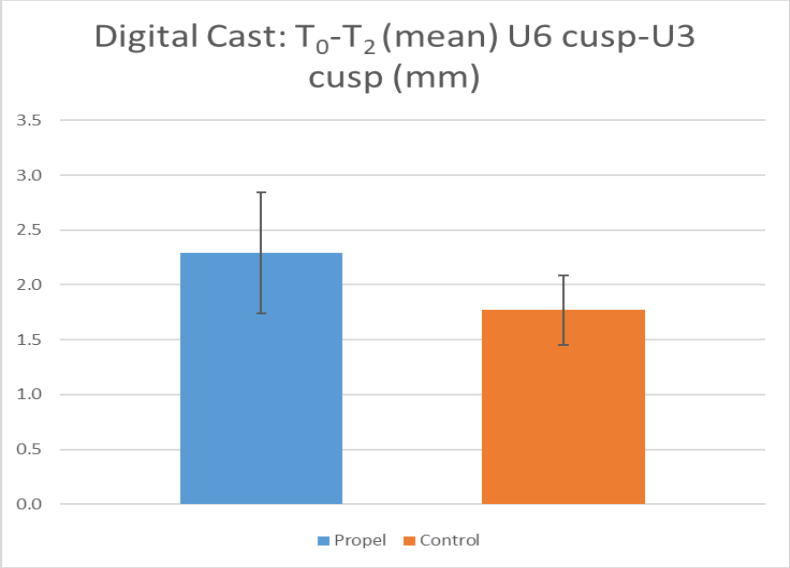
Table 8: Digital Cast Measurements, U6 Cusp - U3 Cusp (mm)

	MOP side	**Control side**
Average of Examiner 1 & Examiner 2 Values	**U6 Cusp- U3 cusp (mm)**	**U6 Cusp- U3 cusp (mm)**
	T_0 -T_2	**T_0 -T_2**
Patient #1	3.5	2.35
Patient #2	3.65	2.2
Patient #3	0.9	2.3
Patient #4	1.4	1.1
Patient #5	2	0.9

Table 9: Descriptive Statistics (Digital Cast, U6 Cusp - U3 cusp Measurements)

Variable	**N**	**Mean (mm)**	**Std. Dev.**	**Std. Err.**	**p- Value**
MOP Side T0-T2 U6 Cusp - U3 Cusp	5	2.29	1.240	0.553	0.185
Control Side T0-T2 U6 Cusp - U3 Cusp	5	1.77	0.709	0.317	
Diff.	5	0.52	0.531	0.236	
Not Significant ($p \geq 0.05$), *= Significant ($P < 0.05$)					

Figure 11: Digital Cast Mean Measurements (U6 Cusp -U3 Cusp)



2. **U3D – U5M:** The average measurements of examiner 1 and 2 are seen in Table 10. The mean of these averages showed that experimental side had 0.43 mm greater space closure after two months than the control side. However, this difference is not significant (Table 11 and Figure 12).

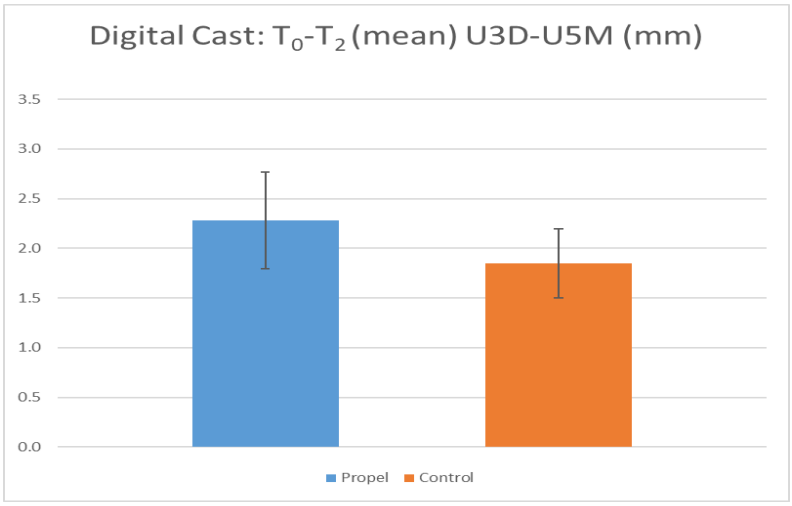
Table 10: Digital Cast Measurements, U3D-U5M (mm)

	MOP side	**Control side**
Average of Examiner 1& Examiner 2 Values	**U3D-U5M (mm)**	**U3D-U5M (mm)**
	T_0 -T_2	**T_0 -T_2**
Patient #1	**3**	**2.95**
Patient #2	**3.75**	**2.3**
Patient #3	**1**	**1.65**
Patient #4	**1.75**	**1.35**
Patient #5	**1.9**	**1**

Table 11: Descriptive Statistics (Digital Cast, U3D-U5M Measurements)

Variable	N	Mean (mm)	Std. Dev.	Std. Err.	p- Value
MOP Side T0-T2 U3D-U5M	5	2.28	1.090	0.487	0.148
Control Side T0-T2 U3D-U5M	5	1.85	0.779	0.348	
Diff.	5	0.43	0.311	0.139	
Not Significant (p≥0.05), *= Significant (P<0.05)					

Figure 12: Digital Cast Mean Measurements (U3D-U5M)



3. **U3 Cusp – U5 Cusp:** The average measurements of examiner 1 and 2 are seen in Table 12. The mean of these averages showed that experimental side had 0.50 mm greater space closure after two months than the control side. However, this difference is not significant (Table 13 and Figure 13).

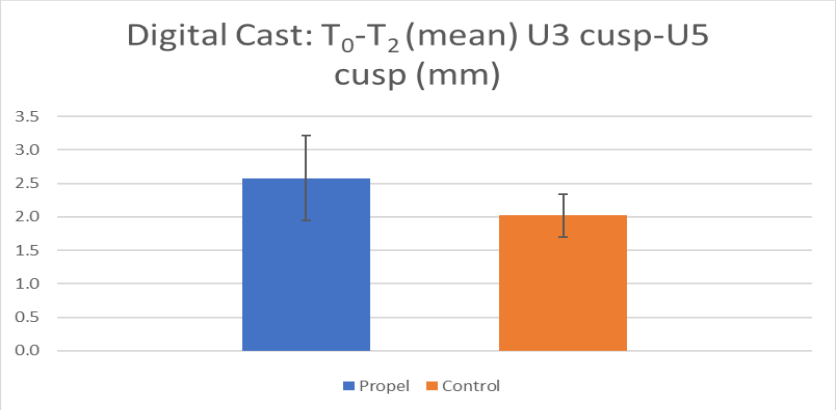
Table 12: Digital Cast Measurements, U3 Cusp Tip- U5 Cusp Tip (mm)

	MOP side	Control side
Average of Examiner 1 & Examiner 2 Values	**U3 cusp - U5 cusp (mm)**	**U3 cusp - U5 cusp (mm)**
	T_0 -T_2	**T_0 -T_2**
Patient #1	3.25	2.65
Patient #2	4.75	3
Patient #3	1.25	1.9
Patient #4	1.7	1.4
Patient #5	1.95	1.45

Table 13: Descriptive Statistics (Digital Cast, U3 Cusp tip- U5 cusp tip Measurements)

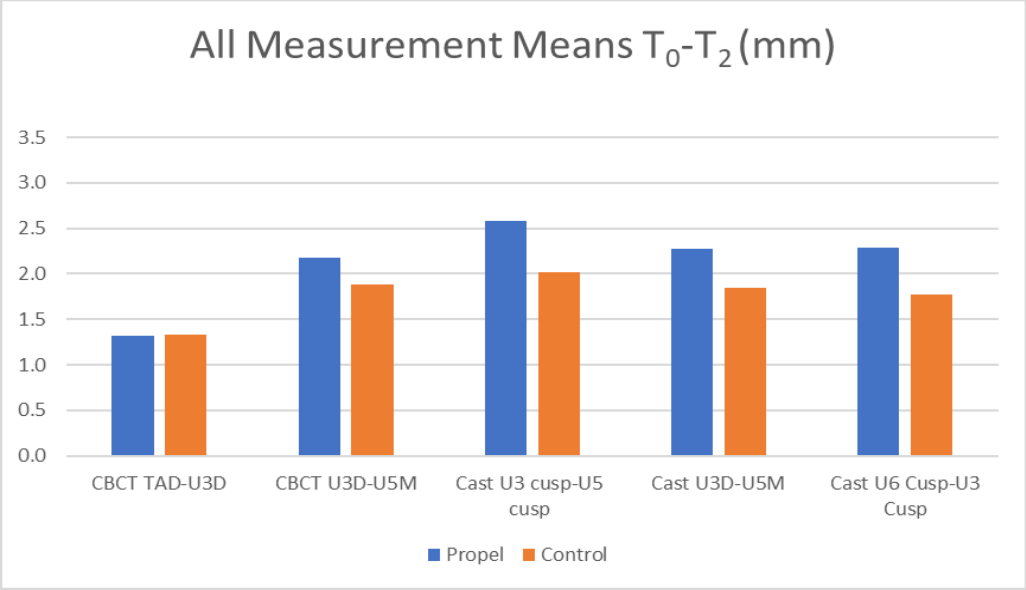
Variable	N	Mean (mm)	Std. Dev.	Std. Err.	p-Value
MOP Side T0-T2 U3 Cusp - U5 Cusp	5	2.58	1.420	0.636	0.131
Control Side T0-T2 U3 Cusp - U5 Cusp	5	2.08	0.718	0.321	
Diff.	5	0.5	0.702	0.315	
Not Significant (p≥0.05), *= Significant (P<0.05)					

Figure 13: Digital Cast Mean Measurements (U3 Cusp -U5 Cusp)



Overall, three subjects showed more canine retraction in all five measurements, one subject showed less canine retraction in all five measurements (figure 14), and one subject showed less canine retraction on the experimental side than on the control side according to the CBCT measurements but had the opposite trend on the digital cast measurements. When all five measurement categories were averaged together, the experimental side showed 0.34 mm more canine retraction than the control side.

Figure 14: All Measurements Mean T_0-T_2



C. Comparison to Initial Singe MOP Study

When comparing the results to those of the initial single MOP study by Dr. Mahmoudi, four measurements were in common: CBCT U3D-U5M, CBCT U3 cusp – U5 cusp, Digital Cast U3 Cusp – U5 Cusp, and Digital Cast U3D-U5M. This study showed 0.24mm greater canine retraction rate in just two months when all common

measurement categories were averaged and compared to our initial single MOP study of 3 months (Table 14).

Table 14: Descriptive Statistics (Comparison of Study to Initial Single MOP Study)

Variable	Control Minus MOP Mean Difference	
	Current Study	Single MOP Study
CBCT U3D-U5M (mm)	0.29	0.44
CBCT U3D-TAD (mm)	-0.013	-0.3
Digital Cast U3D-U5M (mm)	0.43	-0.24
Digital Cast U3Cusp-U5Cusp (mm)	0.5	-0.14
Mean	0.30	0.06
Standard Deviation	0.23	0.34
p-value	0.117	

DISCUSSION

The purpose of this study was to determine if subsequent micro-osteoperforations (MOPs) accelerate orthodontic tooth movement (OTM) during maxillary 1st premolar extraction space closure in adults. Five healthy adult patients between 18 and 44 years of age with dental malocclusions requiring the extraction of the maxillary first premolars were recruited for this split mouth study. Following the extractions and alignment with fixed appliances, three MOPs were performed to the cortical bone in the extraction space on one side. Both maxillary canines were then retracted with 150g NiTi closed coil springs to maxillary first molars that were indirectly anchored to temporary anchorage devices (TADs). Initial records included intra-oral photographs, a CBCT, and digital models. After four weeks of canine retraction following the first round of MOPs, the three MOPs were performed again on the experimental side. After another four weeks,

final records including intra-oral photographs, a CBCT, and digital models were taken. The amount of space closure through canine retraction by the end of the study was compared between the experimental and control sides. It must be understood that, while the goal of canine retraction in this study is through pure bodily translation, on a 17x25 SS wire, a degree of crown tipping does occur. Therefore, the amount of space closure may be magnified at the crown as opposed to the center of resistance.

Assessment of Effect of Micro-osteoperforations

Using CBCT, two variables were used to measure the amount of canine retraction: 1) the distance between the TAD to the most outer point of the distal curvature of the maxillary canine and 2) the distance between the most outer point of the mesial curvature of the maxillary 2nd premolar and the distal most outer point of the curvature of the maxillary canine. These measurements were taken at T_0 and T_2. Three of five subjects showed greater space closure on the experimental side. However, the average of all patients showed greater space closure on the experimental side. This was not statistically significant the null hypothesis was not rejected.

Using the digital casts, three variables were used to measure the amount of canine retraction: 1) the distance between the cusp tip of the maxillary canine to mesiopalatal cusp tip of maxillary 1st molar, 2) the distance between the distal wall of the maxillary canine to the mesial wall of the maxillary 2nd premolar, and 3) the distance between the cusp tip of the maxillary canine to buccal cusp tip of maxillary 2nd premolar. These measurements were taken at T_0 and T_2. In four of the five patients, the space closure was greater on the side with the MOPs. In this study, the average of all patients showed

greater space closure on the experimental side, but this was not statistically significant; and, thus, the null hypothesis was not rejected.

Interestingly, the one subject that showed more canine retraction on the control side was the only subject that did not have extractions on the mandibular arch and had a full cusp Class II Division I malocclusion with a deep bite. Perhaps, there was additional friction between the lingual of the maxillary canine and the facial surface and bracket of the mandibular canine and this friction could lead to slowed canine retraction.

With all five of this study's measurement categories relating to the amount of first premolar extraction space closure through canine retraction, one subject had disagreeing results with accelerated space closure on the MOP side on the digital cast measurements; yet, a slower space closure on the MOP side on the CBCT measurements. Perhaps one explanation was the precision of the measuring. Using the Invivo Anatomage software to measure the CBCTs once the lateral cephalograms were created, the image could not be zoomed during measuring. Another possible explanation could be the TADs tipping and extruding during heavy force load, although all TADs were verified stable throughout the study.[71] For the TAD-U3 measurement in this subject, perhaps the TAD on the control side extruded over the study, making the measurement shorter.

Comparison to Initial Single MOP Study

To determine if subsequent MOPs accelerateded tooth movement greater than a single round of MOPs, the results were compared to our initial study by Dr. Mahmoudi. In that study, MOPs were performed only at T_0 and space closure was measured after three months. The amount of space closure through canine retraction by the end of this study was compared between the experimental and control sides. Then, the average

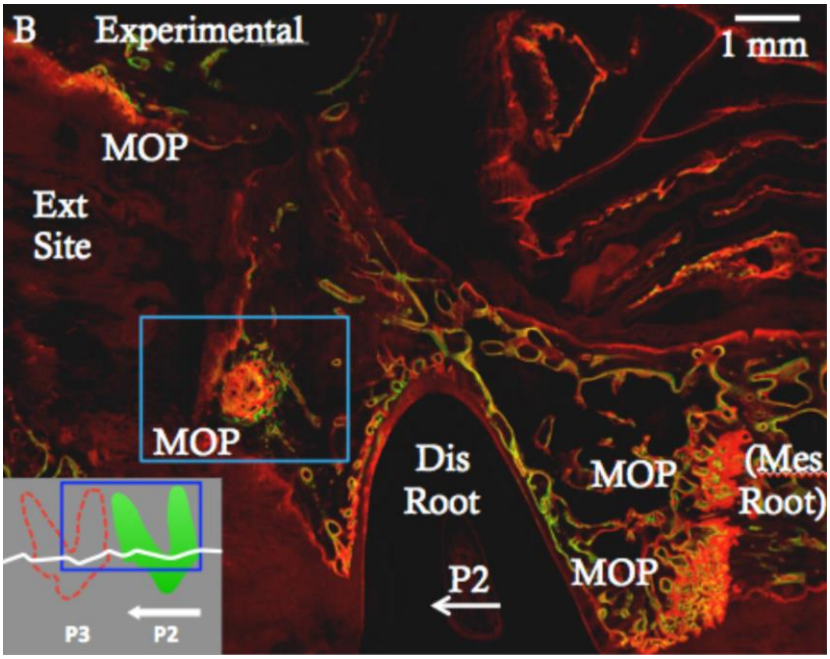
difference of space closure between the MOP and control sides in this study was compared to that of the pilot study. When comparing the means, the second round of MOPs did increase the amount of canine retraction. However, this was not statistically significant. Although the initial single MOP study was three months in length and this study only two months long.

Clinical Suggestions

While the biologic effects associated with the inflammatory cascade following MOPs have been proven, numerous studies have had confounding results whether OTM is accelerated. In theory, the MOP should induce a regional acceleratory phenomenon (RAP), resulting in greater tooth movement. However, this study concluded with inconsistent results. Perhaps, this is due to the extent of inflammatory response from the MOP. While MOPs are considered less invasive, this may also reduce the amount of insult to the gingival and osseous tissue, thus limiting the extent of inflammation. In addition, PROPEL instructions claim that there is an osteoclastic response between 6-10mm from MOP. The extent of bone demineralization by MOPs was studied in a recent orthodontic resident thesis from Texas A&M. MOPs were performed on beagle dog maxillae and the bone remodeling process was evaluated histologically. It was concluded that a majority of the bone mineralization occurred within the MOP hole itself and only extended up to 1mm from the circumference of the MOP hole, perhaps due to microfractures (Figure 15).[68] This limited extend of MOP effect was also found in a thesis by VanGermt, who found acellular bone within 0.8mm of the MOP border and bone density changes only within 1.5mm of the MOP border.[72] Cramer believes this

increase in acellular bone around the MOP may even restrict OTM due to its resistance to demineralization.[68]

Figure 15: Fluorescent Sections of MOP in Beagles (from Cramer[68])



In order to take full advantage of the RAP induced by the MOPs, it is recommended that the MOP be performed within 1.5 mm of the limiting tooth which can increase risk of damage to the root and technique sensitivity, according to Cramer. [68] In addition, PROPEL has changed its protocol to include performing MOPs mesial and distal to tooth intending to move rather than just on the side of the tooth that it is moving towards. Perhaps revealing that orthodontists were not achieving the reduction of treatment time expected or advertised.

Research Limitations

This study found that there is a trend towards faster canine retraction on the MOP side compared to the control side, but this proved neither statistically nor clinically significant. However, a small sample size and other variables may have influenced the results. Ideally, this study would have included over 25 subjects. But, due to the recent tendency away from extraction therapy in orthodontics, recruiting subjects to meet the inclusion criteria proved difficult. Also, while the age range included subjects from 18-44, all five subjects in this study were between the ages of 20 and 26 years of age.

While the split-mouth study design minimizes inter-subject variability, the quality and quantity of bone in the extraction site on each side within each subject may be inconsistent. Even though the maxillary 1st premolars were extracted several months prior to this initiation of the MOPs, the level of bony trauma from the extractions could not guarantee the same volume of bone through which the canine must be retracted, thus adding a variable to this study.

Future Studies

In future MOP studies, a larger sample size should be utilized. In an attempt to minimize the amount of canine crown tipping during retraction, a retraction hook could be added. The coil spring could then be attached from the TAD to the hook, reducing the distance of force application from the canine's center of resistance. In addition, the bone volume and density of the extraction site and around the canine could be evaluated on the control and experimental sides using the initial and final CBCTs. It would also be

clinically relevant to study the effects of MOPs on the mandible, lingual cortical bone, in addition to other orthodontic tooth movements such as alignment, intrusion, extrusion, etc.

CONCLUSIONS

The purpose of this study was to determine if subsequent micro-osteoperforations (MOPs) accelerate orthodontic tooth movement (OTM) during maxillary 1st premolar extraction space closure in adults. Under the limitations of this study, canine retraction was 0.34mm greater after two months of performing MOPs at 1-month intervals compared to the control side but this was neither statistically nor clinically significant. MOPs have been proven to cause an increase in inflammation in the cortical bone, but the extent of the RAP associated with the inflammation needs further investigation and the applications of MOPs should be revised accordingly as several studies regarding the acceleration of OTM after MOPs is contradicting.

Appendix A: CBCT Graphs

Figure 16 – Average of Examiners 1 and 2: CBCT T_0-T_2 TAD to U3

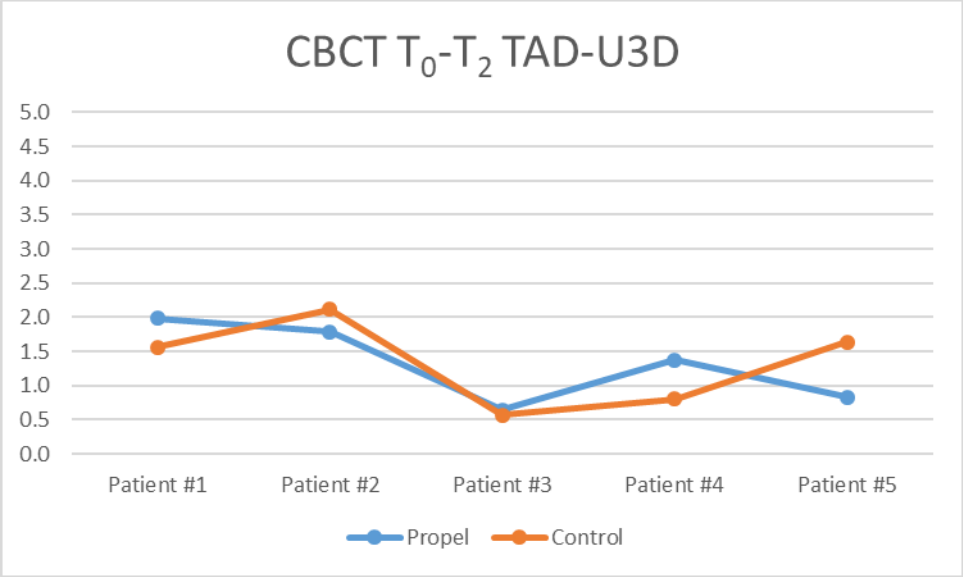
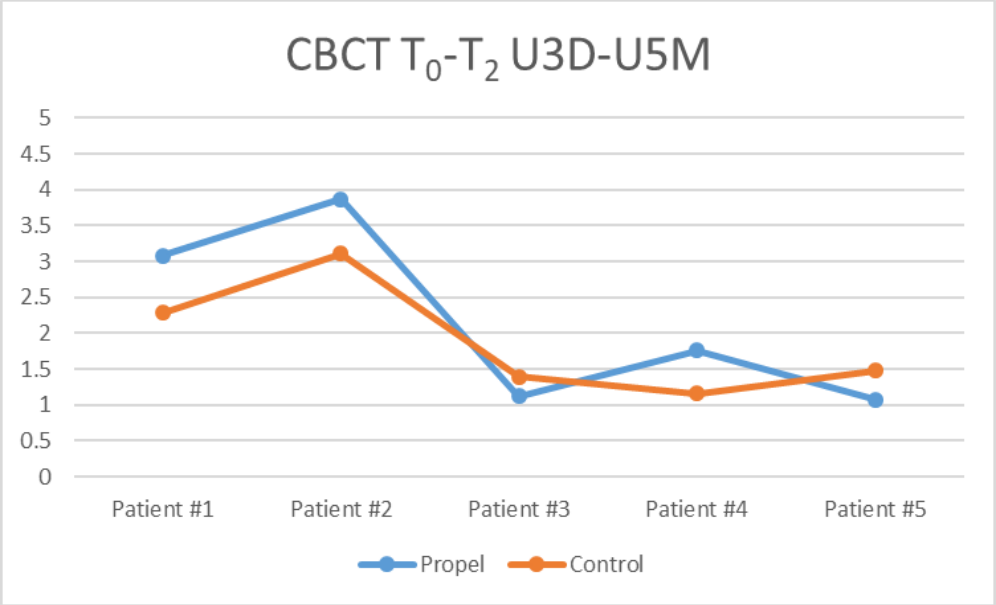


Figure 17– Average of Examiners 1 and 2: CBCT T_0-T_2 U3D to U5M



Appendix B: Digital Cast Graphs

Figure 18 - Average of Examiners 1 and 2: Digital Cast T_0-T_2 U6 Cusp to U3 Cusp

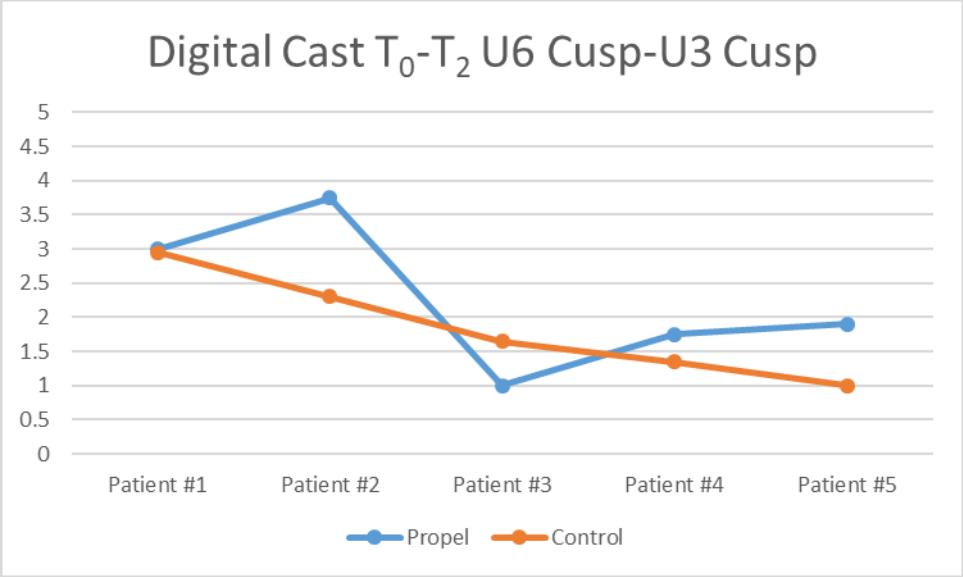


Figure 19 - Average of Examiners 1 and 2: Digital Cast T_0-T_2 U3D to U5M

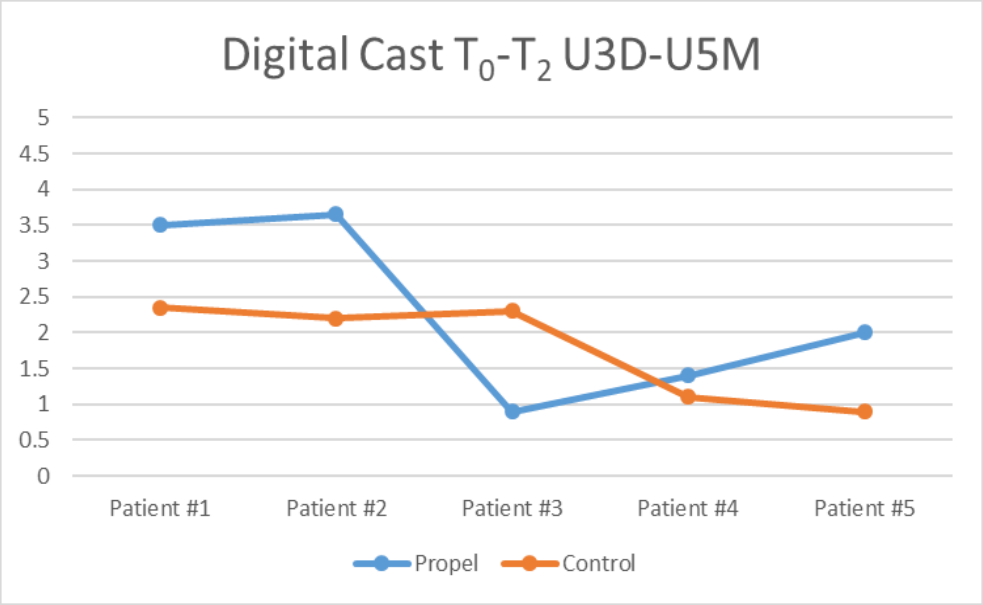
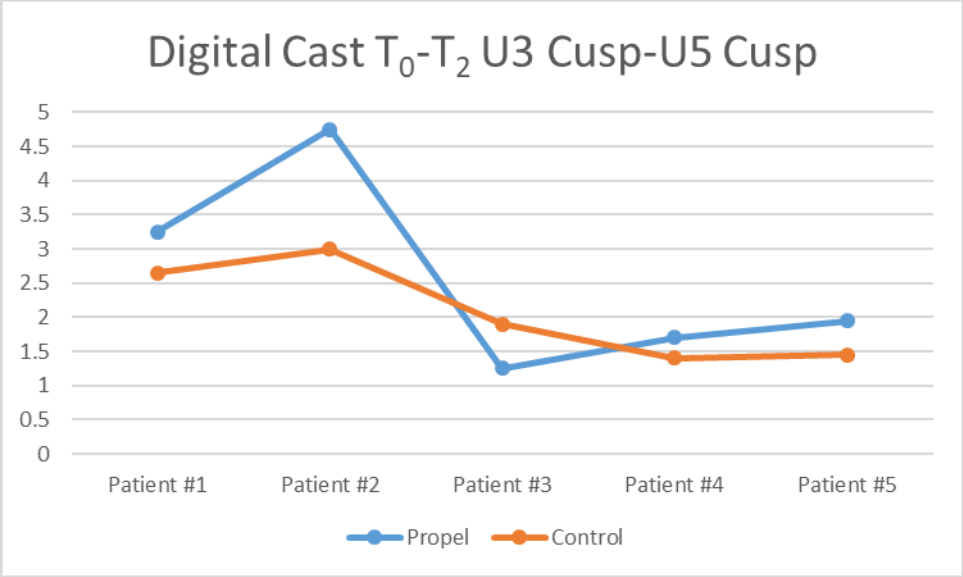


Figure 20 – Average of Examiners 1 and 2: Digital Cast T_0-T_2 U3 Cusp to U5 Cusp



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