CURRICULUM VITAE

NAME: Tina Mahmoudi

EMAIL ADDRESS: tina.mahm@gmail.com

COLLEGIATE INSTITUTIONS ATTENDED

2013- Present	University of Maryland School of Dentistry, Department of Orthodontics Certificate in Orthodontics and M.S. in Biomedical Sciences
2009-2013	University of Maryland School of Dentistry Doctor of Dental Surgery (D.D.S.), May 2013
2006-2008	University of Maryland Baltimore County Bachelor of Science in Biological Sciences (B.S.), May 2008
1994-2001	Baha'i Institute for Higher Education, Iran Bachelor of Science in Dental Sciences (B.D.Sc), May 2001

CLINICAL AND PROFESSIONAL EXPERIENCE

2012	Service Learning/Externship Assignment, Saini Orthodontics, MD
2012	Orthodontic Clerkship Program, University of Maryland School of Dentistry
2002-2008	Orthodontic Chairside Technician, Orthodontic Associates, MD
2002-2003	Orthodontic Lab Technician, Mid-Atlantic Orthodontic Lab, MD

VOLUNTEER WORK

2012	"Habitat for Humanity" Program, University of Maryland School of Dentistry
2012	"Oral Cancer Screening", Lexington Market Health Fair, Baltimore, MD
2012	"Special Olympics Special Smiles", Towson University, MD
2011-2012	"Give Kids A Smile" Program, Maryland Academy of Pediatric Dentistry
2007	Goodwill Store, Nottingham, MD

RESEARCH

2016	Accelerated Tooth Movement in Adult Patients by Micro-perforations of Cortical Bone

PROFESSIONAL MEMBERSHIP

2013- Present	American Association of Orthodontics (AAO)
2013- Present	Mid-Atlantic Society of Orthodontists (MASO)
2013- Present	Maryland State Society of Orthodontics (MSSO)
2011-2012	Academy of General Dentistry (AGD)
2009- Present	American Dental Association (ADA)

AWARDS AND HONORS

2013 Harry E. Kelsey Award for Professional Demeanor

2005-2008 National Dean's List

LICENSURE AND CERTIFICATION

2013- Present Invisalign Certification

2013- Present Maryland State Dental License

2013 North East Regional Board of Dental Examiners (NERB) Certification

ABSTRACT

Title of Thesis: Accelerated Orthodontic Tooth Movement in Adult Patients by Micro-perforations of Cortical Bone

Tina Mahmoudi Masters of Science in Biomedical Sciences, 2016

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

Introduction: The objective of this study was to determine whether micro-osteoperforation of the cortical bone produces accelerated tooth movement during space closure in adult patients.

Methods: Ten healthy adult patients, ages 18 to 44 years old with a malocclusion requiring maxillary first premolar extractions participated in this split-mouth study. Temporary Anchorage Devices (TADs) were placed bilaterally for anchorage control in the maxilla. Micro-osteoperforations were performed unilaterally apical to the extractions site and maxillary canines were distalized using sliding mechanics. Canine retraction rate was measured using: (1) Cone Beam Computed Tomography (CBCT) and (2) Digital models taken before canine distalization at the initiation of the study (T_0) and three months later (T_2).

Results: Each of the research subjects showed varied amount of canine retraction into the extraction space. For the two measurements performed on the initial and final CBCTs, the mean of all patient measurements on the experimental side was 0.44mm less than control for “TAD-U3D” and 0.30mm greater than control for “U5M-U3D”. For the four measurements performed on the initial and final digital models, the mean of all patient measurements on the experimental side was 0.14mm greater than control for “U3 Cusp Tip- U5 Cusp Tip”, 0.24mm less than control for “U5M-U3D”, 0.24mm greater than control for “U2 Midpoint- U3 Cusp Tip”, and 0.18mm greater than control for “U6 MP Cusp Tip- U3 Cusp Tip”. Statistical analysis showed that the amount of canine retraction on the experimental side was not significant when compared with the control side for any of the six measured variables ($P>0.05$).

Conclusion: Our results indicate that 50% of subjects showed faster canine retraction rate on the experimental side when compared to control, however, this difference was not statistically significant. Further studies are necessary to evaluate the effects of micro-osteoperforations on the rate of tooth movement in the orthodontic treatment of adult patients.

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

by

Tina Mahmoudi D.D.S.

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 Biomedical Sciences
2016

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"The root cause of wrongdoing is ignorance, and we must therefore hold fast to the tools of perception and knowledge." -Abdu'l-Bahá

To my daughter, Paurmis,
Thanks for being so patient with me when I barely had time to spend with you. You have brought so much joy and happiness into my world. I am so grateful for every second you are in my life and love you beyond words.

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Master's Thesis

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

Researcher: Tina Mahmoudi DDS
Mentor: Monica Schneider DDS, MS
Research Committee: Monica Schneider DDS, MS
Eung Kwon Pae DDS, MSc, PhD
Bhoomika Ahuja DDS, MS
Glen Minah DDS, MS, PhD

INTRODUCTION

Physical appearance is the foundation on which social acceptance and credibility is built. A beautiful smile is one of the most effective ways of non-verbal communication and one's most important accessory. A first impression is are heavily weighted and assessed by a healthy and attractive smile; therefore, there is a fast growing need to improve it in as little time as possible. Every year, there is an increasing number of adult patients seeking orthodontic treatment and a short treatment time has become a common demand among these patients.

Orthodontic treatment in adult patients frequently takes longer than in adolescent patients due to lack of growth. Lengthier orthodontic treatment time poses several drawbacks such as increased predisposition to dental caries, gingival recession, and root resorption. Therefore, performing research that delivers evidence based treatment modalities and satisfies the adult patient's need for a speedy yet effective result is inevitable.

Dental crowding and/or protrusive dental relationships frequently require the extractions of two maxillary and two mandibular premolars. A critical stage in the correction of dental crowding or protrusion is the retraction of the canine teeth through the first premolar extraction spaces. Variables such as force magnitude, duration, initial tooth displacement, and biologic changes of the periodontium amongst others must be considered to obtain optimal tooth movement. Nonetheless, space closure in adult patients presents unique challenges to practitioners due to age-related changes. These challenges can include but are not limited to reduced bone reactivity to mechanical forces, greater risk of attachment loss, marginal bone loss, greater bone resistance to forces due to medications, etc.

Accurate and precise control of tooth movement can be optimized with the proper use of mechanics; however, the rate of tooth movement depends on the reaction of the surrounding tissue to that force. To date, several techniques have been proposed to accelerate the rate of tooth movement and reduce the treatment time.

The focus of this research project is to address the problem of the treatment duration which is typically longer in adult patients when compared to a younger population. Findings from this study will provide scientific evidence and give more insight about acceleration of tooth movement by performing shallow micro-osteoperforation of cortical bone and whether it can be an accepted approach to accelerate tooth movement.

LITERATURE REVIEW

The duration of the orthodontic treatment is a significant factor to both the patient and the orthodontist. The American Association of Orthodontists has reported that the average length of orthodontic treatment can range between 18 to 30 months depending on treatment modalities and individual patient variation (AAO, 2007). The number of adult patients seeking orthodontic treatment has increased over the years. 20 to 25% of orthodontic patients are reported to be adults. This trend is likely to increase as adult patients are more concerned about esthetics.

A. Orthodontic Tooth Movement

Orthodontic tooth movement occurs in response to orthodontic forces which are not completely regulated by the laws of physics. Therefore, there is no immediate or linear response to the magnitude of the force. Moreover, orthodontic tooth movement is directly associated with bone remodeling and the biological response plays a central role in controlling the rate of orthodontic tooth movement (Sandstedt and Oppenheim, 1930).

The trigger to start the bone remodeling process is still debated and there are different hypothesis on how the remodeling mechanism occurs. One mechanism is the creation of tension and compression forces inside the Periodontal Ligament (PDL) with the assumption that no direct contacts are formed between the tooth root and the alveolar bone.

Direct contact between the tooth root and alveolar bone has been shown by Gottlieb (1938) stating that the contact with the bone is the limiting factor for further tooth movement. Another mechanism triggering bone remodeling is the bone-bending hypothesis (Baumrind, 1969). Baumrind proposed that the bone does not fully stop movement but undergoes deflection during orthodontic tooth movement. The turnover rate of alveolar bone determines the quantity and quality of the orthodontic tooth movement. Osteoclast mediated catabolic activity is the limiting factor in the kinetics of this process. Osteoclasts resorb the cortical lamina dura of the alveolus inducing the bone turnover where new bone apposition is stimulated by the osteoblasts. In order to move teeth faster, the balance between resorption and apposition needs to be modified so that the waiting time for the alveolar cortex to resorb could be accelerated. There are several methods described and studied to accomplish this goal. In all such techniques the basic tenet is to avoid causing irreversible damage to the periodontium while trying to move the teeth faster. Intentional injury of the cortical bone to stimulate a strong and early osteoclastic resorption leading to a faster tooth movement has been one of the most predictable and successful techniques. It has been suggested that the accelerated tooth movement might be due to a demineralization- remineralization process known as the Regional Acceleratory Phenomenon (RAP) (Frost, 1983).

B. Regional Acceleratory Phenomenon (RAP)

Regional Acceleratory Phenomenon (RAP) is a general metabolic shift occurring in the injured region; it leads to accelerated physiologic processes and decreased bone density of the surgical site. RAP can be initiated by any regional noxious stimulus of adequate magnitude. In 1981, Frost observed that surgical wounding of the bone can stimulate bone turnover and decrease bone density of the surgical site. RAP begins within a few days of the surgical procedure and it hits the highest point at one to two months.

Wilcko et al (2001) noted that surgical procedures such as the elevation of buccal and lingual full-thickness flaps with extensive decortications of the buccal and lingual alveolar bone resulted in a physical injury which was responsible for the initiation of a temporary demineralization process. This process of demineralization combined with an increase in localized bone turnover suggests that RAP is taking place. The occurrence of temporary osteopenia (less bone density with the same bone volume) is responsible for the rapid tooth movement as the teeth move in a more elastic and less rigid environment. The main effects of RAP appear to be confined to the region of the noxious stimulus. Areas in proximity to the surgical sites seem to be relatively unaltered by the RAP response (Bogoch et al, 1993). The RAP concept is critical for orthodontists because alveolar mineralization plays a fundamental role in tooth movement. Certainly, when there is the greater mineralization of alveolar bone, tooth movement becomes more difficult (Kole, 1959). Consequently, any stimulus that increases bone turnover and decreases bone density is expected to result in faster tooth movement.

1. Cytokine Expression and Accelerated Orthodontic Tooth Movement

Inflammation is caused by tissue injury; it is characterized by increased blood flow, increased vascular permeability, and accumulation of inflammatory mediators such as cytokines. Cytokines are small cell-derived polypeptides important in cell communication and signaling. The predominant producers of cytokines are helper T-cells and macrophages. The two major types of cytokines are pro-inflammatory and anti-inflammatory. There are several cytokines that play a key role in mediating inflammatory responses including IL-1, TNF- α, IL-6, IL-8, and IL-11. Higher concentration of these inflammatory cytokines have been found in gingival crevicular fluid surrounding the tooth intended to move orthodontically (Alhashimi et al, 2007).

Bone remodeling is an inflammatory phenomenon, cytokines and inflammatory markers like prostaglandin E2 are suggested to have a role in bone resorption in the compression site and bone deposition in the tension site of the periodontal ligament or PDL. Ren et al (2007) reported that soon after forces are applied on a tooth (24 hours), expression of cytokines such as IL-1 β, TNF-α, IL-6, and IL-8 increases. These cytokines stimulate osteoclast differentiation which leads to activation of bone remodeling and tooth movement. Inhibiting the expression of these specific cytokines can lead to a reduced rate of orthodontic tooth movement (Davidovitch et al, 2006).

Teixeira et al (2010) investigated the cytokine expression and tooth movement after performing shallow perforations of approximately 0.25mm in diameter and 0.25 mm in depth in adult Sprague-Dawley rats. This study demonstrated that the shallow perforations of the cortical plate increased the levels of cytokine expression in response to orthodontic forces in the experimental group which indicated increased bone activity. When measuring tooth movement, the authors found that the rate of tooth movement was significantly increased in the experimental group when compared to the control group.

C. Surgically Facilitated Orthodontic Therapy (SFOT)

It has been known that surgical wounding of bone increases bone turnover and decreases bone density in the surroundings of the surgical site (RAP). Surgically Facilitated Orthodontic Therapy (SFOT) was first introduced in dental literature in 1892 by Westcott. Subsequently, Heinrich Kole in 1959 suggested that the cortical bone of the alveolus causes the greatest resistance to tooth movement. He described the use of interdental corticotomies to reposition the tooth orthodontically. There are several surgical techniques that are being investigated to increase efficiency of tooth movement and decrease treatment time, these techniques are discussed below.

1. Corticotomy Assisted Orthodontic Treatment (CAOT)

While technological developments provide materials and appliances that can produce a more efficient treatment, the speed of treatment is still controlled by the biological response of bone and periodontal tissues. The concept that orthodontic tooth movement is impaired by the presence of alveolar cortex has been predominant in the surgical community since the end of the 1800s; consequently, it would be necessary to disrupt the cortical bone by a surgical procedure in order to achieve a more efficient tooth movement.

Corticotomy Assisted Orthodontic Treatment (CAOT) is an adjunct procedure for the treatment of adult patients. Patient is usually referred to a periodontist who selectively performs alveolar decortication in forms of lines and dots around the teeth intended to move. Corticotomy induces a transient inflammatory response causing increased bone turnover which is followed by a faster rate of tooth movement and shorter treatment time (Hassan et al, 2010).

Most of the studies investigating the effects of corticotomy on accelerated tooth movement have been carried out by using animal models. These studies have led to the understanding that faster tooth movement after corticotomy is likely to be attributed to RAP.

Cho et al (2007) performed corticotomies and protracted third premolars in beagle dogs for 4 and 8 weeks. This study reported an increase in tooth movement associated with the corticotomies. There was a waiting period before initiating tooth movement in order to minimize the RAP effect associated with the wound healing generated by the tooth extractions.

Vercellotti (2007) reported a significant reduction of orthodontic treatment time of 60-70% after corticotomies were performed by a piezo-surgical micro-saw. Due to the small size of the device, this technique for these osteotomies is more precise; yet, a buccal periodontal flap is still required without much reduction of surgical time and attenuation of post-operative discomfort.

To examine differential tooth movement in mature male foxhounds, Sanjideh et al. (2009), investigated the combined effect of performing the corticotomies simultaneously with tooth extractions, and the effect of performing a second corticotomy after 4 weeks. The authors found that the rate of tooth movement in the corticotomy group was higher until day 22 and then progressively declined. At the time point when tooth movement reached peak velocity, the rate of tooth movement was 85% faster than the movement on the control group. Interestingly, it was also reported that the group that received a second corticotomy showed increased tooth movement when compared to the group with one corticotomy. This study concluded that alveolar corticotomy significantly enhanced tooth movement when orthodontic forces are applied. Although, a second corticotomy after 4 weeks sustained improved velocities on tooth movement for a longer duration, the differences in tooth movement did not appear to justify a second surgical procedure.

In their recent systematic review, Hassan et al. (2015), reported that Corticotomy is a safe and effective method for accelerated orthodontic tooth movement. They also reported that CAOT increases space closure rate, traction of palatally impacted canines, and resolves crowding of incisors by 2-2.5 fold when compared to conventional orthodontic tooth movement.

Overall, corticotomies appear to be effective in accelerating tooth movement however, these procedures are quite invasive and present significant postoperative discomfort to the patients leading to the unwillingness of its use among patients and practitioners.

Unfortunately, reports suggesting accelerated tooth movement rates in human subjects by performing corticotomies are based primarily on clinical case studies and the need for well-designed randomized human control trials is very apparent (Suya 1991, Owen 2001, Wilcko 2001).

2. The "Bony Block" concept

Kole et al (1959), observed rapid tooth movement after performing vertical interproximal cortical incisions and a sub-apical horizontal osteotomy cut from the buccal plate to the palatal plate. He explained that rapid tooth movement was the end result of the "Bony Block" movement concept. The "Bony Block" movement concept describes that movable blocks of bone are created by interdental alveolar corticotomy and through and through osteotomy above the apices of the teeth with the objective that teeth connect only by medullary bone and could potentially move without much restraint. Kole believed that shorter treatment time was due to removal of the mechanical restraint of the cortical bone. However, the "Bony Block" concept was challenged by Wilcko et al. in 2001. Wilcko demonstrated that the movement is not a result of moving the blocks of bone, but rather from a cascade of transient localized reactions in the bony alveolar housing leading to bone healing (Wilcko et al., 2001). A review of several computed tomography scans (CTs) of patients that had gone through corticotomies to accelerate orthodontic tooth movement suggested that the accelerated tooth movement could be credited to an increase in osteoclastic activity and also osteogenic activity localized at the surgical site.

3. Periodontally Accelerated Osteogenic Orthodontics (PAOO)

Wilcko's approach to Periodontally Accelerated Osteogenic Orthodontics (PAOO) or Wilckodontics claims to enhance bone remodeling, accelerate tooth movement, and reduce the duration of treatment. In his recent article, "Accelerating Tooth Movement: The Case for Corticotomy-Induced Orthodontics", Wilcko states that corticotomy surgery provides for a periodontal ligament-mediated acceleration in tooth movement as a result of a stimulated regional acceleratory phenomenon in conjunction with the proper morphologic situation of a thin layer of bone in the direction of movement. Therefore, if the bone is thinned adequately in the direction of the intended tooth movement, premolar site closure can be obtained in 3 to 4 weeks with orthopedic forces or in 6 to 8 weeks with lighter orthodontic forces (Wilcko & Wilcko, 2013).

In his counterpoint to Wilcko's claims, Kokich argues that PAOO needs additional surgery to the bone, along with periosteal release of the flaps to assist in covering the additional bone graft material (Kokich, 2013). The additional releasing of the periosteum adds further inflammation and swelling and will increase the level of patient's discomfort.

4. Osteotomy/Osteogenic Distraction

As the name indicates, in osteotomy, the bony segments are completely resected. In osteogenic distraction, the cortical bone is separated 0.5-1mm away from the teeth to be moved and a bone distractor is screwed to both sides of the alveolar bone to move the bony segment. Osteotomy was first described in literature by Codivilla in 1905 but in 1988 Ilizarov developed the method thoroughly.

Liou et al (2000) proposed that the osteogenic distraction was an orthodontic tooth movement accelerator. According to Liou, tooth movement could be easier when performed through fibrous new bone created by distraction. Liou reported that the first week after activation of the device was the latency period and after that, the distractor could be activated 1 mm/day.

In 2008, Lee investigated the rate of tooth movement in a corticotomy group and an osteogenic distraction group and reported that although the rate of tooth movement was faster in the distraction group, it was not statistically significant.

In three separate split mouth human trials, Iseri, Kumar and Kharkhar performed osteogenic distractions to accelerate canine retraction in extraction cases, with 10, 8 and 6 patients each. Iseri reported 50% faster movement in the distraction side compared to the control side, with a full canine retraction in 8–14 days. Kumar completed canine retraction in 20 days and Kharkhar in 12 days. None of them reported pulpal damage due to stretching of the blood vessels, gingival damage, or root resorption.

Osteogenic distraction can potentially lead to long-term side effects such as molar extrusion, anchorage loss, resistance of the interseptal bone causing mesial tipping of the canine tooth, and pulpal damage. These possible problems have not been fully investigated yet and need to be examined further.

5. Piezocision

Piezocision is another surgical method for accelerated Orthodontic Tooth Movement (OTM). It is a minimally invasive technique that unlike corticotomy does not need flaps.

Sebaoun et al. in 2011 reported using piezo-surgical cortical micro-incisions combined with selective tunneling of the cortical bone that allowed for bone and soft tissue grafting without the need of a periodontal flap. A piezo-electric knife is used in this method instead of a bur; it is claimed that the vibrations of the knife could help with the accelerated tooth movement. Although, piezocision is a less aggressive method than corticotomy, the underlying biological response is believed to be the same as RAP.

In a recent study on dogs, Kim YS et al. (2013), reported 3.26 fold more OTM in the maxilla and 2.45-fold more OTM in the mandible when flapless piezocision or cortical perforations through the soft tissues was used. Dibart et al. (2014) reported that piezocision increased the tooth movement in rats almost twice when compared to the control; 0.6 mm tooth movement was measured after 28 days compared to 0.25 mm without using piezocision.

Unfortunately, there is a lack of human trials investigating the effect of piezocision on orthodontic tooth movement, therefore, caution should be taken when interpreting these results.

D. Non-surgical Approach to Accelerated Orthodontic Tooth Movement

1. Medications

The effects of medications on the rate of tooth movement has been the focus of a few research studies. In a systematic literature review by Bartzela et al (2009), it was reported that administration of Bisphosphonates had a robust inhibitory effect on the rate of OTM; Eicosanoids resulted in increased tooth movement and their inhibition led to a decline. They also concluded that administration of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) had a negative effect on tooth movement, but non-NSAID pain medications such as acetaminophen had no effect; Corticosteroid hormones, Parathyroid hormone, Thyroxin, and Vitamin D3 all increased tooth movement and estrogens and dietary calcium seemed to reduce it.

However, all medications have some reported side effects that limit their application in order to be considered a primary focus when accelerated tooth movement is desired. Therefore, more research is needed to investigate the safety of drug therapy in orthodontics. To this day, there are no medications that can be used safely to increase orthodontic tooth movement.

2. Mechanical Stimulation/Vibration

   a. Low-Level Laser Therapy

Low-Level Laser Therapy (LLLT) has been reported to enhance tooth movement by production of ATP and activation of cytochrome C. Kim et al (2009) reported that immediately after application of low level laser therapy of Gallium Aluminum Arsenide (GaAlAs), wavelength of 808 nm and an output power of 96 mw, levels of fibronectin and type I collagen increased and remained elevated until the end of experiment. They concluded that application of LLLT expedited the turnover of connective tissue during tooth movement.

In 1997, Saito and Shimizu investigated the effects of low-power laser irradiation on bone regeneration in mid-palatal suture during maxillary expansion in rats. Their findings indicate that application of low-intensity laser can accelerate bone regeneration in the mid-palatal suture during rapid palatal expansion and stimulate collagen synthesis. In their report, they conclude that "laser therapy may be of therapeutic benefit in inhibiting relapse and shortening the retention period through acceleration of bone regeneration in the mid-palatal suture". In 2004, Cruz et al. studied the effect of low-intensity laser therapy on orthodontic tooth movement in human and showed that the irradiated canines were retracted 34% faster than the control canines over a period of 2 months. In 2013, Doshi-Mehta et al. investigated the effects of LLLT on canine distalizaiton in a split mouth design. The laser was a semiconductor (GaAlAs) diode emitting infrared radiation and the wavelength used for the study was 808±10nm for 10 seconds. It was applied buccally and palatally to the canine tooth which was distalized after first premolar extraction. The canine tooth was retracted using a NiTi closed coil spring that delivered a constant force of 150g from the first molar to the power arm of the canine bracket. The distance between the first molar and the canine were measured before and six months after the canine distalization on the experimental side and the control side. In their conclusion, they reported that the canine tooth on the side treated with LLLT was distalized 29% faster than the control side in the maxillary arch.

In an article review, Yasaei et al. (2013) reported that LLLT may accelerate the rate of OTM by increasing levels of RANKL in PDL and Macrophage Colony Stimulating Factor (M-CSF) which leads to increased osteoclastic activity and bone remodeling. They also concluded that further research is needed to determine the effect of low-level laser therapy on orthodontic tooth movement with special attention to laser parameters.

b. AcceleDent Aura™

AcceleDent is a non-invasive accessory vibration appliance that delivers pulsatile forces to the teeth. It is an FDA-cleared, class II medical device that is approved to be used as an adjunct to orthodontic treatment and is claimed to accelerate tooth movement. However, there is very limited peer reviewed data investigating AcceleDent and its effects on OTM.

In 2008, Nishimura et al. measured the effects of vibration forces on tooth movement in rats. Vibration at a frequency of 60Hz was applied to the molar teeth of the subjects undergoing "standard orthodontics" to move them buccally by expansion. At the end of their 21-day experiment, they reported that the group that received vibration showed significantly faster tooth movement and a trend toward decreased root resorption compared to the static-force group. They stated in their conclusion that “The application of resonance vibration might accelerate orthodontic tooth movement via enhanced RANKL expression in the periodontal ligament without additional damage to periodontal tissues such as root resorption”.

In a clinical report, Bowman (2014) used AcceleDent during initial leveling and aligning of the teeth of 30 Class II non-extraction adult subjects who were undergoing orthodontic treatment and observed a 30% reduction in treatment compared to two control groups. Kau et al (2011), used an AcceleDent prototype and reported 3mm/month of tooth movement in the maxillary arch and 2.1mm/month in the mandibular arch.

In another clinical report, Orton-Gibbs (2015) states that the successful incorporation of AcceleDent into an orthodontic practice can significantly reduce treatment time, making it an attractive adjunct for both patients and clinicians.

Since the data supporting the use of AcceleDent and its effectiveness in the orthodontic tooth movement is mainly based on clinical reports, further studies and well-designed randomized controlled trials are needed to better understand the true effects of the pulsatile forces on the rate of OTM.

3. Flapless micro-osteoperforations of the cortical bone

Another less invasive alternative to accelerate tooth movement is micro-osteoperforations of cortical bone. In the micro-osteoperforations procedure, limited and shallow perforations of the buccal cortical plates are performed. Teixeira et al. (2010) investigated the cytokine expression and tooth movement after performing shallow perforations of approximately 0.25mm in diameter and 0.25 mm in depth in adult Sprague-Dawley rats. This study demonstrated that the shallow perforations of the cortical plate increased the levels of cytokine expression in response to orthodontic forces in the experimental group, which indicated increased bone activity. They reported that limited shallow perforations of the buccal cortical plate would be as sufficient to accelerate bone remodeling; therefore, leading to an increased rate of tooth movement. The authors found that the rate of tooth movement was significantly increased in the experimental group when compared to the control group. A major advantage of this less invasive method to improve the rate of tooth movement is that it required no elevation of periodontal flap. Hence, shallow micro-osteoperforations of cortical bone seems to be a more accepted approach that could be used routinely by the orthodontist without the need of referrals. Also, it would considerably reduce the surgical time and minimize post-operative patient discomfort.

In 2013, Alikhani et al. reported that micro-osteoperforation is an effective, comfortable, and safe procedure to accelerate tooth movement.

In one of the most recent studies performed to investigate the effects of both flapless micro-osteoperforation and a corticision on the rate of orthodontic tooth movement in rats, Tsai et al (Nov. 2015), observed no differences between these two minimally invasive, flapless procedures. They reported that both flapless surgical techniques increased osteoclastic activity and bone remodeling, and therefore faster orthodontic tooth movement for at least 2 weeks in rats.

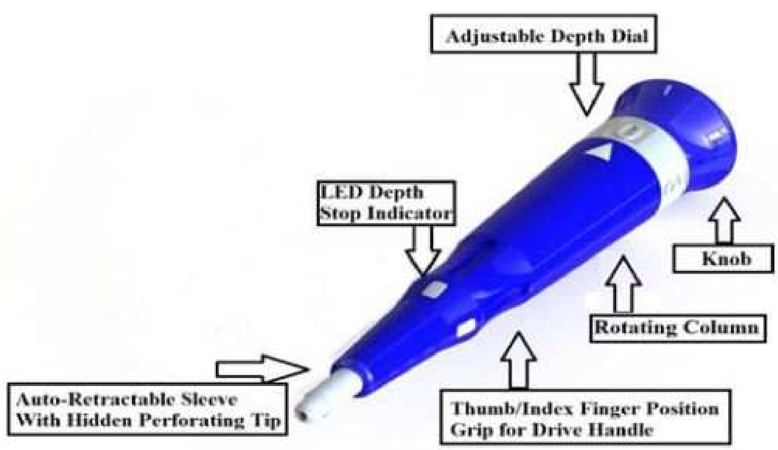
a. Propel Accelerated Orthodontics

Alveocentesis™ translates to "puncturing bone" and is one of minimally invasive methods to increase the OTM and reduce the treatment time. It was introduced by Propel Orthodontics in 2012. Excellerator and Excellerator RT are the two types of devices presented by Propel Orthodontics. Their Excellerator instrument, Propel, is a Class I FDA-registered medical device indicated to be used with any orthodontic treatment technique (Figure 1). It is a ready-to-use sterile disposable device with a surgical-grade stainless steel tip that could be adjusted by the healthcare professional to perform micro-osteoperforations of the bone to depths of 3mm, 5mm, and 7mm depending on where in the mouth the perforations are to be made (Figure 2).

Figure 1- Propel Excellerator (on the left) and Excellerator RT (on the right)

(adapted from www.propelorthodontics.com)

Figure 2- Propel Excellarator with depth limiter LED indicator

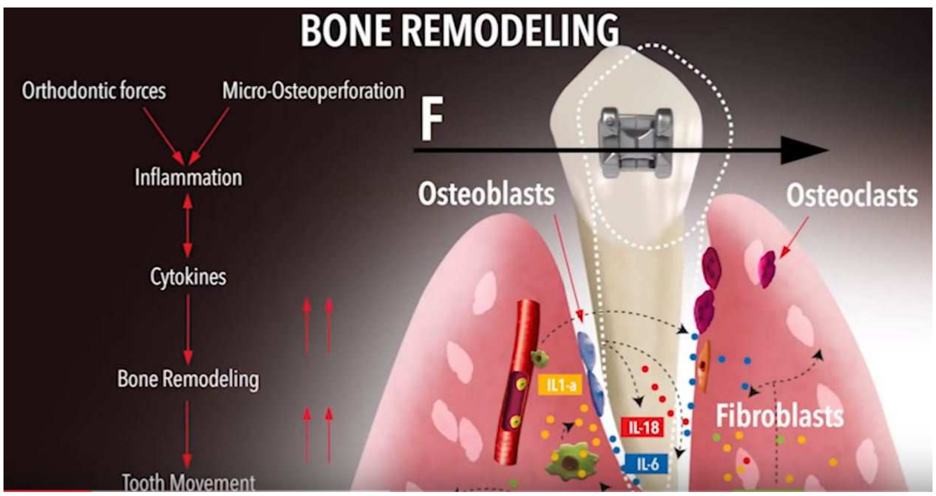


(adapted from J. Nicozisis, “Accelerated Orthodontics with Alveocentesis” Research Report,

Clinical Orthodontics, December 2012)

The Propel device uses RAP; the micro-osteoperforations create a localized area of trauma, which leads to activation of an inflammatory process. The expression of the cytokines such as IL-1 β, TNF-α, IL-6, and IL-8 stimulate and up-regulate a receptor on the surface of osteoblasts named Receptor Activator of Nuclear Factor-Kappa B Ligand (RANK-L) or Osteoclast Differentiation Factor which both lead to activation of bone remodeling and tooth movement (Udagawa et al, 1999) (Figure 3).

Figure 3- Role of Micro-osteoperforations in Inflammatory Processes and the Cytokine Cascade



(adapted from Propel Accelerated Orthodontics Youtube Video, propelorthodontics.com)

In 2013, Alikhani et al performed a single center single blinded study to investigate the effect of micro-osteoperforations on the rate of tooth movement in human subjects. In their study, they divided twenty adults with Class II Division 1 malocclusion into control and experimental groups. The control group did not receive micro-osteoperforations, and the experimental group received micro-osteoperforations on 1 side of the maxilla using the Excellerator propel device. They used a Niti closed coil spring, delivering a constant force of 100g to distalize the maxillary canine into the extraction site. The spring was anchored to a temporary anchorage device (TAD) that was placed distal to the second premolar on one side, and to the canine bracket using a power arm through the vertical slot on the other side. To monitor the rate of tooth movement, they took alginate impressions at the beginning of the study, immediately before canine retraction, and 28 days after canine retraction. The distance between the canine and the lateral incisor was measured before and after canine retraction by a digital caliper. According to their report, micro-osteoperforations significantly increased the rate of tooth movement by 2.3-fold; this was accompanied by a significant elevation in the levels of inflammatory markers. Moreover, the patients participating in the study did not report any significant pain, discomfort, or any other complications during or after the procedure. They concluded their study by stating that the micro-osteoperforations are a safe and effective way to accelerate tooth movement and can reduce the orthodontic treatment time.

However, this was the only study investigating micro-osteoperforations performed by the Propel device on human and further research needs to be performed to support their findings.

E. Summary

Although Alikhani's report on accelerated tooth movement in 2013 seems very promising, they had a small sample size and a short research period. Therefore, lack of sufficient research about the effectiveness of micro-osteoperforations in accelerating the tooth movement in orthodontic patients is still evident. This study intends to further examine the effectiveness of using micro-osteoperforations as a flapless and minimally invasive procedure to enhance orthodontic tooth movement in adult patients.

PURPOSE OF THE PRESENT STUDY

The specific aim for this research study is:

- To determine whether micro-osteoperforations produce accelerated orthodontic tooth movement during space closure in adult patients.

HYPOTHESIS

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

PRINCIPAL STUDY

A. Material and Methods

Approval to conduct this split-mouth pilot study was obtained from the Human Research Protections Office (HRPO) of University of Maryland Institutional Review Board (IRB) in 2013. Patients were recruited from the University of Maryland Orthodontic Graduate Clinic.

1. Procedures:

   a. Study Subjects

   One orthodontic resident (T.M.) was trained and calibrated by the principal investigator (M.S.) and was responsible to recruit patients who met the inclusion criteria and were willing to participate in the study. Ten healthy adult patients between the ages of 18 to 44 seeking orthodontic treatment at the University of Maryland Graduate Orthodontic Clinic met the inclusion criteria and were willing to take part in the study. The informed consent form was presented and risks and benefits of the procedure explained to the subjects by one of the members of the research team (T.M.) and their signatures obtained. All of these patients required extraction of bilateral maxillary first premolars and subsequent maxillary canine retraction to close the extraction space as part of their orthodontic treatment. The inclusion and exclusion criteria are summarized in the table 1.

Table 1- Inclusion and Exclusion Criteria

Inclusion Criteria	**Exclusion Criteria**
Healthy adult patients ages 18-44	Medical history of immune disorders or radiation therapy
Minor to moderate crowding (up to 6mm)	Severe crowding (greater than 6mm)
No current active periodnotal disease	Current active periodontal disease
Orthodontic treatment plan requiring removal of bilateral first maxillary premolars	Patients who require prophylactic antibiotics

Within-patient comparisons were made to reduce bias originated from biological differences among individuals. Since bone regional acceleratory phenomenon has been shown to be restricted to the area of the stimulus, we expected that the experimental procedure to affect mainly the treatment side without causing any significant effect to the control side.

b. Orthodontic Initial Phase

Patients were bonded with 0.022 slot Unitek brackets (Victory Series™ Miniature Metal Bracket System or Clarity Ceramic Brackets with metal slot) and were referred for extraction of the maxillary first premolars. After the initial leveling and alignment stage, TADs were placed bilaterally mesial to the maxillary first molars (between the maxillary second premolar and first molar roots) in order to maintain adequate anchorage. RMO Dual-Top Temporary Anchorage Device of 1.6mm of diameter and 6mm in length was used in this study. A 0.016x0.022 stainless steel section of wire was used to connect the maxillary first molars to the TAD for stabilization and acted as indirect anchorage. Following the initial phase of leveling and aligning, space closure was performed using a 0.017x0.025 stainless steel maxillary arch wire. Canine retraction was carried out by conventional sliding mechanics; 150g of force was delivered using nickel titanium coil springs. Small shallow perforations of cortical bone were performed on the randomly selected experimental side prior to initiation of canine retraction.

c. Clinical Micro-osteoperforation Procedure

Before initiation of the micro-osteoperforation procedure, a full maxillary CBCT was obtained to evaluate TAD placement and location of canine crown and root. Intra-oral photographs and alginate impressions for digital study models were also taken before starting the canine retraction (T_0), at the next adjustment appointment (T_1), and at the conclusion of the study (T_2). The impressions were poured up immediately with Whip Mix orthodontic stone, labeled, dated, and scanned by OrthoCast model lab. The CBCT and digital models provided a baseline for future measurements. The investigator performed manual micro-osteoperforation using the PROPEL® System (Propel Orthodontics, the Excellerator) adhering to the following protocol (Figures 4 and 5):

- Rinse with Chlorhexidine Digluconate 0.2% w/v Antiseptic mouthwash for 60 seconds prior to the procedure
- Apply local infiltrative anesthesia
- Perform three micro-osteoperforations of approximately 5mm in depth and 0.25 mm in diameter distal to the maxillary canines

- Rinse with Chlorexidine Digluconate 0.2% w/v Antiseptic mouthwash for 60 seconds after the procedure is performed
- Advise patient to take Tylenol in case of experiencing any discomfort and avoid taking anti-inflammatory medications such as Ibuprofen during the period of the study

Figure 4- Three Micro-osteoperforations Performed at the Extraction Site

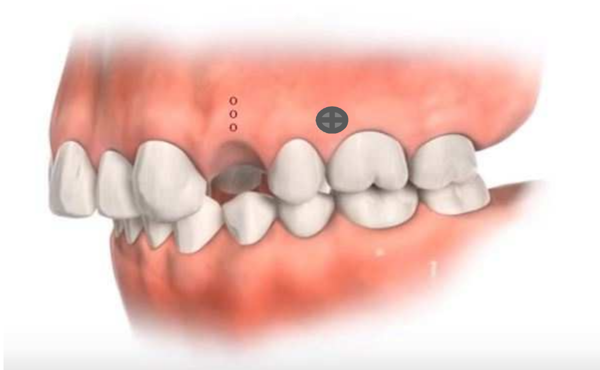


Figure 5- Micro-osteoperforations Performed by Propel Excellerator – Depth Limiter LED Indicator

(adapted from Propel Accelerated Orthodontics Youtube Video, propelorthodontics.com)

Canine retraction was performed using a 0.017 x 0.025 stainless steel working arch wire. Nickel titanium closed coil springs (Sentalloy® -GAC International) were placed from the canine bracket hook to the first molar bilaterally (Figure 6). The force from the coil spring was measured with a Correx gram force gauge to deliver 150g of force which is the adequate force magnitude for retraction. The force produced by the coil was checked and the appliances were examined for any distortion or change in position at each visit. Final records (CBCT, intra-oral photographs, and digital models) were taken three months after initial tooth movement (T2) (Figure 7).

Figure 6 – Initiation of Canine Retraction Using Bilaterall NiTi Coil Springs

Figure 7- Final Records Taken Three Months after Initiation of Canine Retraction

d. Image acquisition

Cone Beam Computed Tomography 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 measurements obtained from CBCT images, all the CBCT images were taken by the same person and the CBCT parameters and patient's position were identical in all 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 both before the micro-osteoperforation procedure (T_0) and after three months of canine retraction at the conclusion of the study (T_2).

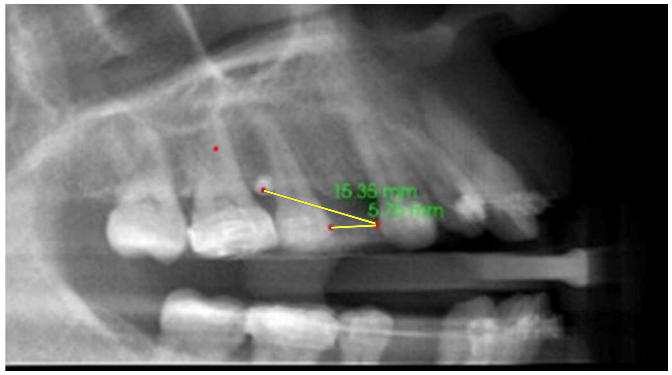
e. Image and Digital Model Analyses

To perform more accurate measurements and avoid superimposition, only one-sided cephalograms were used in this study. Anatomage Invivo5 3D software was used to create right and left side cephalometric x-rays from the initial and final CBCTs for each subject. To quantify the distance of tooth movement in millimeters, the following measurements were recorded: 1) The distance in millimeters from the TAD to the most outer point of the distal curvature of the maxillary canine on both sides, indicated as “TAD-U3D (mm)”.

2) The distance from the most outer point of the mesial curvature of the maxillary second premolar to the distal most outer point of the curvature of the maxillary canine on both sides, indicated as “U5M-U3D (mm)”.

The TAD was used as a superimposition landmark. All the landmarks were digitized and measurements were performed by two separate operators who were blinded to the experimental procedures involved (Figure 8).

Figure 8- Two CBCT Measurements Performed on Unilateral Cephalograms Using Anatomage Invivo5 3D



Alginate models taken at the initial and final appointments (T_0 and T_2) were scanned and digitized using OrthoCAD 3.5.0.38 (Cadent [TM]). The scanned models were used to measure the maxillary canine movement. Two sets of four separate measurements were performed at T_0 and T_2 by two different examiners who were blinded to the study and an average of the two measurements was taken and used in the statistical analysis.

The four measurements used for the study were:

1) The distance in millimeters from the cusp tip of the maxillary canine to buccal cusp tip of maxillary second premolar at T_0 and T_2 on both sides, indicated as "U3 Cusp Tip-U5 Cusp Tip (mm)".

2) The distance in millimeters from the distal wall of the maxillary canine to the mesial wall of the maxillary second premolar (the extraction space) at T_0 and T_2 on both sides, indicated as "U5M-U3D (mm)".

3) The distance in millimeters from a midpoint on the incisal edge of the maxillary lateral incisor to the maxillary canine cusp tip at T_0 and T_2 on both sides, indicated as “U2 Midpoint-U3 Cusp Tip (mm)”.

4) The distance in millimeters from the mesio-palatal cusp tip of the maxillary first molar to the maxillary canine cusp tip at T_0 and T_2 on both sides, indicated as “U6 MP Cusp Tip-U3 Cusp Tip (mm)”.

All digital model measurements were made using OrthoCAD Software Version 3.5.0.38 (Cadent ™) (Figure 9). Abbreviation of all the measurements is summarized in table 2.

Figure 9- Four Measurements Performed Bilaterally on Digital Models Using OrthoCAD at T_0 and T_2

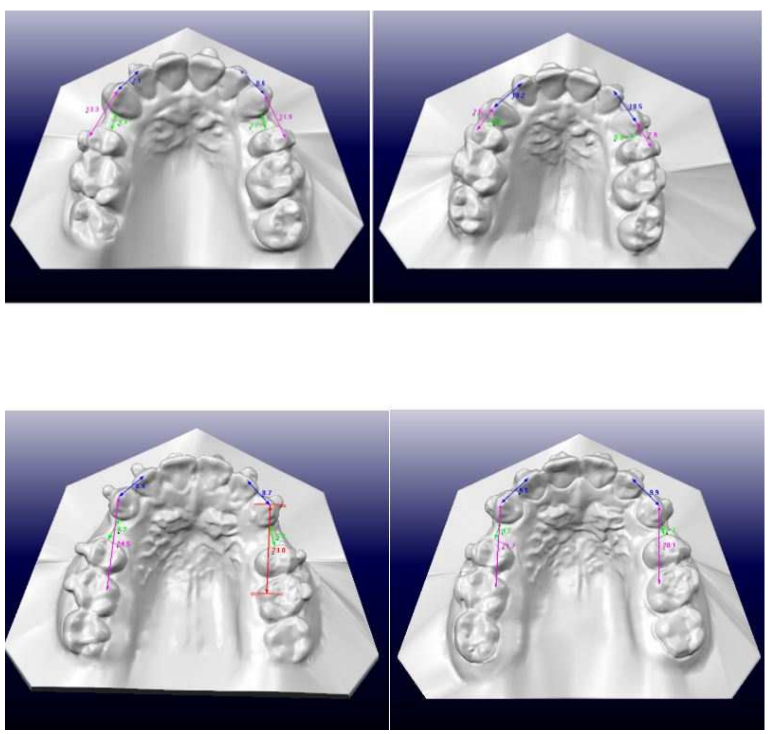


Table 2- Abbreviations and Measurements

	Abbreviation	Measurement
Anatomage Invivo 5 3D	TAD-U3D (mm)	The distance from the TAD to the most outer point of the distal curvature of the maxillary canine
	U5M-U3D (mm)	The distance from 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
OrthoCAD 3.5 Cadent ™	U3 Cusp Tip-U5 Cusp Tip (mm)	The distance from the cusp tip of the maxillary canine to buccal cusp tip of maxillary 2nd premolar
	U5M-U3D (mm)	The distance from the distal wall of the maxillary canine to the mesial wall of the maxillary 2nd premolar
	U2 Midpoint-U3 Cusp Tip (mm)	The distance from a midpoint on the incisal edge of the maxillary lateral incisor to the maxillary canine cusp tip
	U6 MP Cusp Tip- U3 Cusp Tip (mm)	The distance from the mesio-palatal cusp tip of the maxillary first molar to the cusp tip of the maxillary canine

2. Statistical Analysis

All the acquired data was analyzed using the STATA software version 10. Skewness and Kurtosis for normality were examined for each of the six measurements (two CBCT measurements and four digital model measurements) and all the parameters showed normal distribution (See Appendix D).

In addition, intra-examiner reliability was tested for each of the six measurements performed by each examiner using Student t-tests to compare the compatibility between their measurements. Six random patients were chosen for each measurement and the $P < 0.05$ was considered to be significant for statistical inferences.

Paired Student t-tests were performed for the six measurement to compare the average rate of space closure in the experimental side, the side treated with micro-osteoperforations using the Propel device, and the control side. One-tailed P values were also calculated and $P<0.05$ was determined to be as the level of statistical significance. A group difference was expressed by mean ± 1 standard deviation (SD).

B. Results

Fourteen healthy adult patients between the ages of 18-44 were initially recruited from University of Maryland School of Dentistry, Orthodontic Department's patient pool. All of these patients had a malocclusion that required extraction of maxillary first premolars as part of their treatment plan. Four patients did not initiate the study due to various reasons, the original treatment plan was changed for three of them and one moved to another state. The ten remaining subjects initiated the experimental phase and completed the study with no loss to follow-up. All patients maintained good oral hygiene throughout the study and took no medications including anti-inflammatory analgesics before and during the period of the study.

The age range of the study subjects was from 18 to 37 years old with the mean of 25.5. Eight subjects were females and two were males. Six subjects were African American, two were Caucasian, one was Asian, and one was Hispanic. The demographic distribution of the study subjects is summarized in table 3.

Table 3- Demographic Distribution of Patients

Subject Number (10)	Gender	Age (years)	Ethnicity
1	F	26	Caucasion
2	F	28	African American
3	F	24	Asian
4	M	33	Caucasion
5	F	18	Hispanic
6	F	37	African American
7	F	21	African American
8	F	25	African American
9	M	19	African American
10	F	23	African American

Canine retraction was initiated on both sides of the mouth after the initial phase of leveling and aligning. After bilateral TAD placement, an initial CBCT and digital study models were taken (T_0). The experimental side received three micro-osteoperforations between the canine and the second premolar using the Propel Excellerator instrument while the control side did not receive any. A final CBCT and digital models were taken three months later (T_2). Canine retraction was measured on each patient on both experimental and control side by two calibrated examiners at T_0 and T_2 on CBCTs and digital models. An average of the two obtained measurements for each category was then used for statistical analysis. Canine retraction was measured bilaterally on the CBCTs at T_0 and T_2 using Anatomage Invivo5 3D software in two ways:

1) From TAD to the outermost distal curvature of the canine tooth (TAD-U3D).

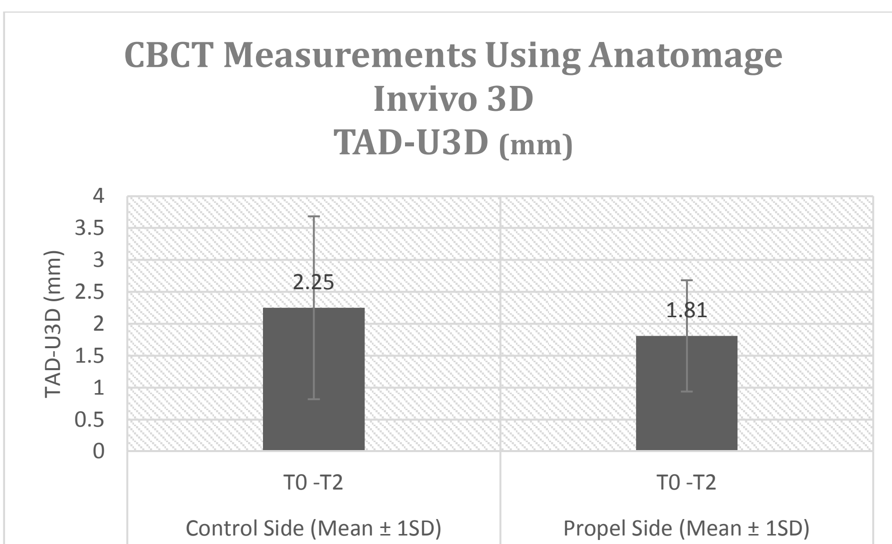
2) From the outermost mesial curvature of the second premolar to the outermost distal curvature of the canine tooth (U5M-U3D).

For the first measured variable (TAD-U3D), the amount of tooth movement in millimeters measured from the TAD to the distal curvature of the canine tooth shows that the mean of all patient measurements on the Propel side is 0.44mm less than the control side. However, there was no significant difference between the Propel side and the Control side (table 4 & Fig 10).

Table 4- Descriptive Statistics (Anatomage Invivo5 3D, TAD-U3D Measurements)

Variable	N	Mean	S.D.	S.E.	[95% conf. Interval]		t	p- value
Control Side T0-T2 TAD- U3D (mm)	10	2.25	1.43	0.45	1.22	3.28	0.92	0.19
Propel Side TAD-U3D (mm)	10	1.81	0.87	0.27	1.18	2.43		
Degrees of Freedom = 9								*= Significant (P<0.05)

Figure 10- CBCT Measurements Using Anatomage Invivo 3D (TAD-U3D)

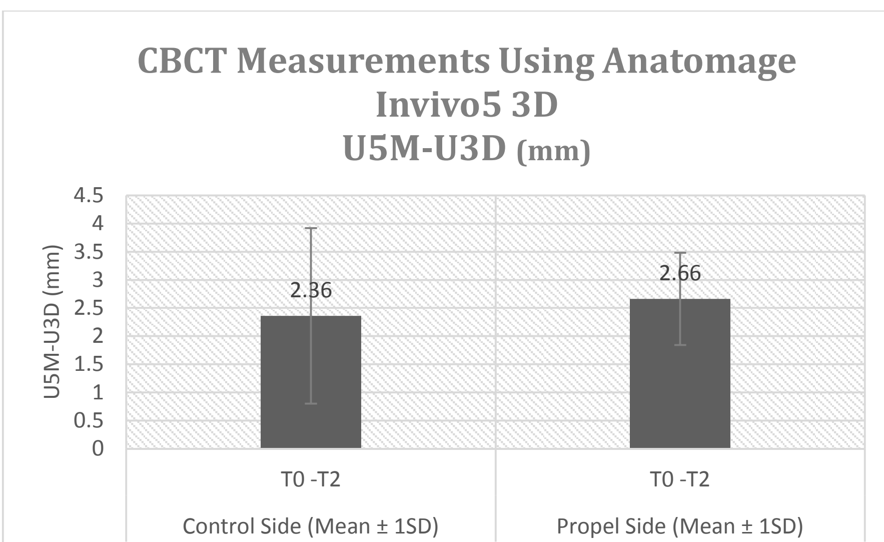


For the second measured variable (U5M-U3D), the amount of tooth movement in millimeters measured from the outermost mesial curvature of the second premolar to the outermost distal curvature of the canine tooth shows that the mean of all patient measurements on the Propel side is 0.30mm greater than the control side. However, there was no significant difference between the Propel side and the Control side (table 5 & Fig 11).

Table 5- Descriptive Statistics (Anatomage Invivo5 3D, U5M-U3D Measurements)

Variable	N	Mean	S.D.	S.E.	[95% conf. Interval]		t	p- value
Control Side T_0-T_2 U5M-U3D (mm)	10	2.36	1.56	0.49	1.24	3.47	-0.62	0.72
Propel Side T_0-T_2 U5M-U3D (mm)	10	2.66	0.82	0.26	2.07	3.25		
Degrees of Freedom = 9								*= Significant (P<0.05)

Figure 11 – CBCT Measurements Using Anatomage Invivo 3D (U5M-U3D)



Canine retraction was also measured on the digital models using OrthoCAD 3.5 (Cadent ™) software at T_0 and T_2 in four ways:

1) From the cusp tip of the canine to the cusp tip of the second premolar (U3 Cusp Tip- U5 Cusp Tip).

2) From the outermost mesial curvature of the second premolar to the outermost distal curvature of the canine (U5M-U3D).

3) From a midpoint on the incisal edge of the lateral incisor to cusp tip of the canine (U2 Midpoint- U3 Cusp Tip).

4) From the mesio-palatal cusp tip of the maxillary first molar to the maxillary canine cusp tip (U6 MP Cusp Tip-U3 Cusp Tip).

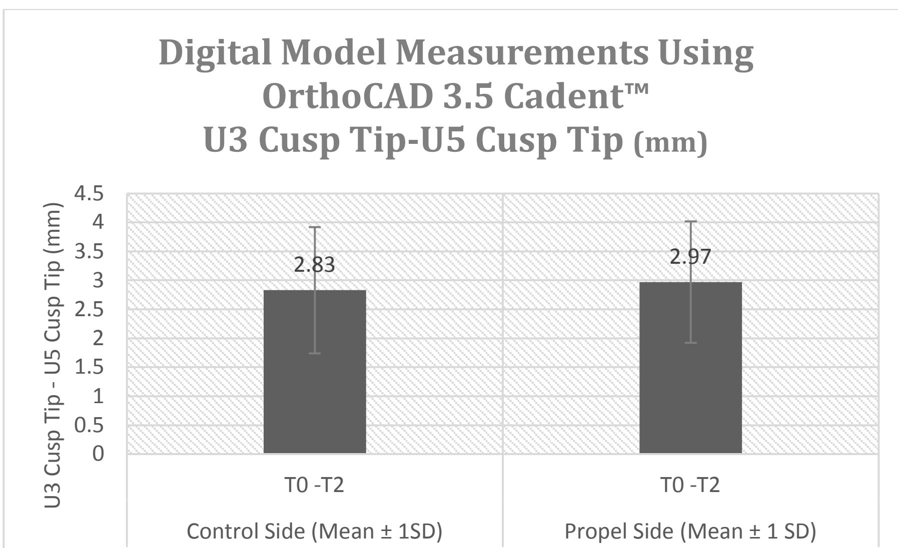
Comparisons were made for each category at T_0 and T_2 on both experimental and control sides.

For the first measured variable (U3 Cusp Tip- U5 Cusp Tip), the amount of tooth movement in millimeters measured from the cusp tip of the canine to the cusp tip of the second premolar shows that the mean of all patient measurements on the Propel side is 0.14mm greater than the control side in average. However, there was no significant difference between the Propel side and the Control side (table 6& Fig 12).

Table 6- Descriptive Statistics (OrthoCAD, U3 Cusp tip- U5 cusp tip Measurements)

Variable	N	Mean	SD	S.E.	[95% conf. Interval]		t	p-value
Control Side, T_0-T_2 U3 cusp tip -U5 cusp tip (mm)	10	2.83	1.09	0.34	2.04	3.62	-0.4	0.65
Propel Side, T_0-T_2 U3 cusp tip -U5 cusp tip (mm)	10	2.97	1.05	0.33	2.21	3.73		
Degrees of Freedom = 9								*= Significant (P<0.05)

Figure 12- Digital Model Measurements Using OrthoCAD 3.5 Cadent ™ (U3 Cusp Tip-U5 Cusp Tip)

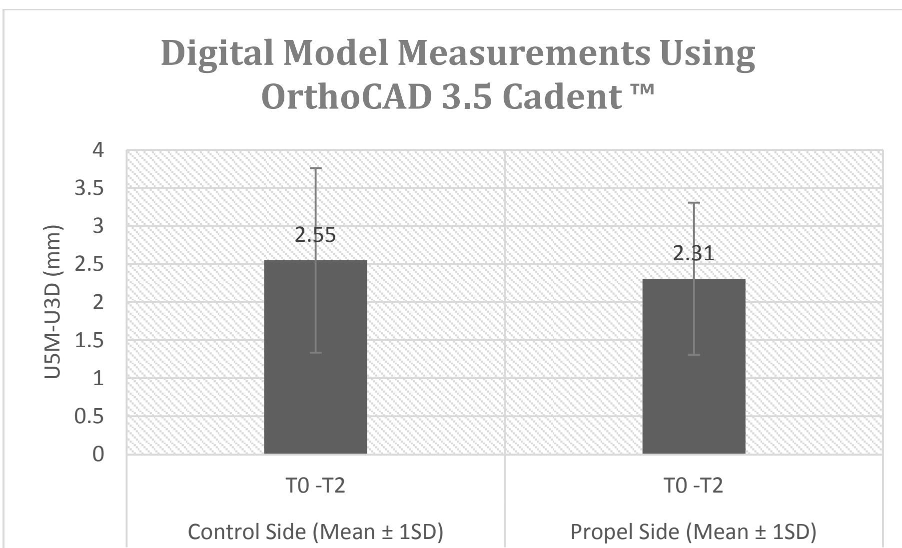


For the second measured variable (U5M-U3D), the amount of tooth movement in millimeters measured from the outermost mesial curvature of the second premolar to the outermost distal curvature of the canine shows that the mean of all patient measurements on the Propel side is 0.24mm less than the control side in average. However, there was no significant difference between the Propel side and the Control side (table 7& Fig 13).

Table 7- Descriptive Statistics (OrthoCAD, U5M-U3D Measurements)

Variable	N	Mean	S.D.	S.E.	[95% conf. Interval]		t	p-value
Control Side T0-T2 U5M-U3D (mm)	10	2.55	1.21	0.38	1.68	3.42	0.68	0.25
Propel Side T0-T2 U5M-U3D (mm)	10	2.31	1.00	0.31	1.59	3.03		
Degrees of Freedom = 9								*= Significant (P<0.05)

Figure 13- Digital Model Measurements Using OrthoCAD 3.5 Cadent ™ (U5M-U3D)

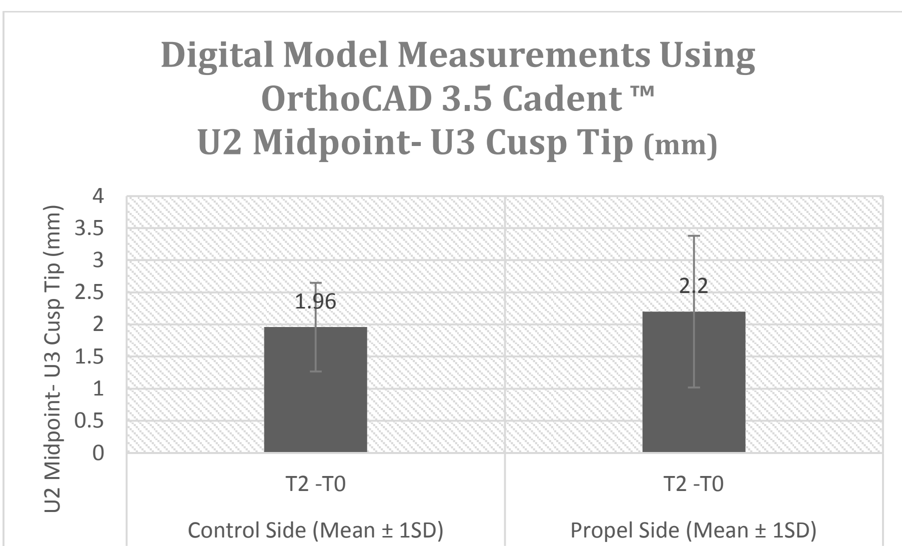


For the third measured variable (U2 Midpoint- U3 Cusp Tip), the amount of tooth movement in millimeters measured from a midpoint on the incisal edge of the lateral incisor to cusp tip of the canine shows that the mean of all patient measurements on the Propel side is 0.24mm greater than the control side in average. However, there was no significant difference between the Propel side and the Control side ($p \geq 0.05$) (table 8& Fig 14).

Table 8- Descriptive Statistics (OrthoCAD, U2 Midpoint- U3 Cusp tip Measurements)

Variable	N	Mean	S.D.	S.E.	[95% conf. Interval]		t	p-value
Control Side T2- T0 U2 Midpoint-U3 cusp tip (mm)	10	1.96	0.69	0.21	1.46	2.45	-0.8	0.77
Propel Side T2- T0 U2 Midpoint-U3 cusp tip (mm)	10	2.20	1.18	0.37	1.36	3.04		
Degrees of Freedom = 9								*= Significant (P<0.05)

Figure 14- Digital Model Measurements Using OrthoCAD 3.5 Cadent ™ (U2 Midpoint- U3 Cusp Tip)

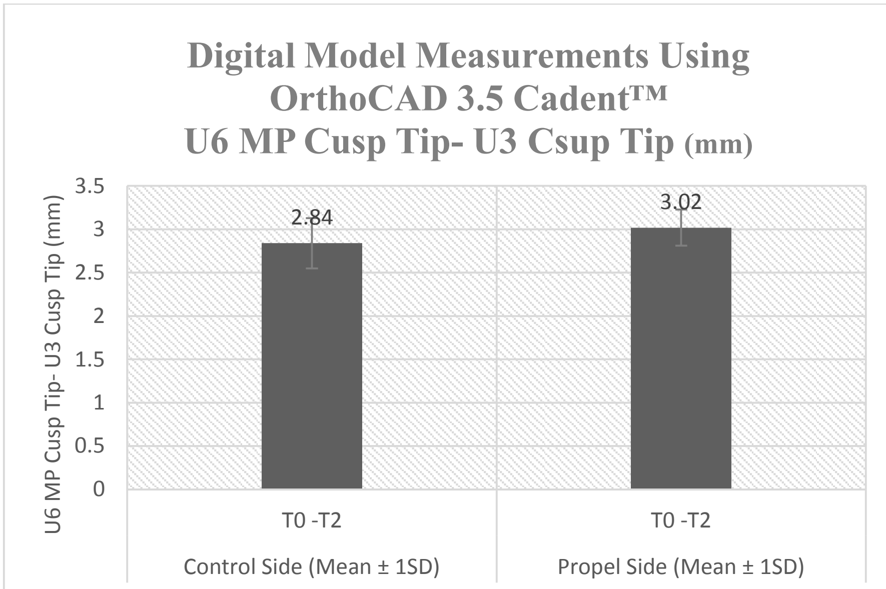


For the fourth measured variable (U6 MP Cusp Tip- U3 Cusp Tip), the amount of tooth movement in millimeters measured from the mesio-palatal cusp tip of the first molar to the cusp tip of the canine shows that the mean of all patient measurements on the Propel side is 0.18mm greater than the control side in average. However, there was no significant difference between the Propel side and the Control side (Table 9& Fig 15).

Table 9- Descriptive Statistics (OrthoCAD, U6 MP Cusp Tip- U3 Cusp Tip Measurements)

Variable	N	Mean	S.D.	S.E.	[95% conf. Interval]		t	p-value
Control Side T_2- T_0 U6 MP Cusp Tip- U3cusp tip (mm)	10	2.84	0.93	0.29	2.16	3.51	-0.53	0.69
Propel Side T_2- T_0 U6 MP Cusp Tip- U3cusp tip (mm)	10	3.02	0.67	0.21	2.54	3.50		
Degrees of Freedom = 9								*= Significant (P<0.05)

Figure 15- Digital Model Measurements Using OrthoCAD 3.5 Cadent ™ (U6 MP Cusp Tip-U3 Cusp Tip)



Five study subjects, four female patients and one male patient, showed more canine retraction on the experimental side than the control side but the overall amount of canine retraction on the experimental side with micro-osteoperforations was not statistically significant when compared with the control side ($P>0.05$).

The intra-examiner reliability showed no significant difference between the measurements obtained from the first examiner versus the second examiner for each of the six measurement (See Appendix C).

DISCUSSION

A. Assessment of the Effect of Micro-osteoperforations

The objective of this study was to determine whether micro-osteoperforation of the cortical bone produces accelerated tooth movement during space closure in adult patients. A split mouth study was designed to explore the effects of micro-osteoperforations of the bone in ten healthy adult patients, ages 18 to 44 years old with a malocclusion requiring maxillary first premolar extractions. Temporary Anchorage Devices (TADs) were placed bilaterally for anchorage in the maxilla, micro-osteoperforations were performed only on one side using the Excellerator Propel device and both upper canines were distalized using NiTi closed coil springs delivering 150g of force. The amount of canine retraction was measured using CBCTs and digital OrthoCAD models were taken at the initiation and conclusion of the study. The results of this clinical trial indicate that five study subjects showed more canine retraction on the experimental side but the overall rate of canine retraction was not significantly different between the experimental side and the control side for all the measured variables. Thus, the null hypothesis was not rejected.

In Rapid Acceleratory Phenomenon (RAP), surgical wounding of the cortical bone increases its turnover and decreases its density in the surroundings of the surgical site. Therefore, the rate of bone remodeling is increased. Bone remodeling is an inflammatory phenomenon that depends on the expression of cytokines and inflammatory markers. After forces are applied on a tooth, expression of cytokines such as IL-1 β, TNF-α, IL-6, and IL-8 increases which in turn leads to osteoclast differentiation and activation of bone remodeling and tooth movement (Ren et al., 2007). In 2010, Teixeira et al. performed shallow perforations of approximately 0.25mm in diameter and 0.25 mm in depth in adult rats and found that the shallow perforations of the cortical plate increased the levels of inflammatory markers and bone metabolism. They concluded that micro-osteoperforations increased the rate of tooth movement in the experimental group when compared to the control group. Although there are a few animal research studies reporting an increase in the rate of tooth movement when micro-osteoperforations of the bone are performed, there has not been any testimony on human clinical trials until 2013 when Alikhani et al. reported that micro-osteoperforations can increase the rate of canine retraction by more than 2-fold. They also concluded that micro-osteoperforation is an effective and safe procedure to accelerate tooth movement in humans. However, their study was the only one investigating the micro-osteoperforations performed by the Propel device and their sample size was small. For these reasons, further investigation of this method seems necessary.

A split-mouth study was first introduced by Ramjford in the late sixties, it was then adopted and used widely in healthcare related research studies because of its efficiency in terms of sample size since the patients act as their own controls (Pandis et al, 2013). In an attempt to eliminate inter-subject variability and due to a smaller sample size, a split-mouth study was designed for this clinical research project. Six different measurements were performed on each side of the mouth, the experimental and the control, by two calibrated examiners and an average of the two measurements was used for the statistical analysis.

Using CBCT (Anatomage Invivo5), the two variables mentioned below were measured at T_0 and T_2 on each side of the mouth: 1) the distance in millimeters between the TAD and the most outer-point of the distal curvature of the maxillary canine and 2) the distance in millimeters from the most outer-point of the mesial curvature of the maxillary second premolar to the distal most outer-point of the curvature of the maxillary canine. To compare canine retraction, comparisons were made between the experimental (micro-osteoperforations performed using Propel) side and the control side (no micro-osteoperforations). A variety of responses were observed between the different subjects. Those patients who responded favorably to the experiment were both males and females from different ethnicities aging from 18 to 37 years old with the mean age of 26.1 (See Appendix A).

After performing the statistical analysis, it was concluded that the retraction of the canine tooth on the experimental side was not statistically different from the control side and the null hypothesis was not rejected. (Table 1 and 2). Comparisons were also made for four variables measured on the digital models at T_0 and T_2 on both sides of the mouth using OrthoCAD software: 1) the distance in millimeters from the cusp tip of the maxillary canine to buccal cusp tip of maxillary second premolar 2) the distance in millimeters from the distal wall of the maxillary canine to the mesial wall of the maxillary second premolar (the extraction space) 3) the distance in millimeters from a midpoint on the incisal edge of the maxillary lateral incisor to the maxillary canine cusp tip and 4) The distance from the mesio-palatal cusp tip of the maxillary first molar to the cusp tip of the maxillary canine.

Again, each of the research subjects responded differently to the micro-osteoperforations with varied amount of canine retraction into the extraction space; patients who showed more canine retraction on the experimental side were males and females from different ethnicity groups aging 23 to 37 years old with the mean age of 27.5 (See Appendix B). The overall amount of canine retraction was not statistically different between the experimental side and the control side at T_2 for any of the four measured variables, therefore the null hypothesis was not rejected. (Table 3, 4, and 5).

Research supports the role of inflammation in accelerating the orthodontic tooth movement but the findings of this research study is in line with one of the latest systematic review performed by Rozen et al in 2015 that investigates the most recent publications on accelerated tooth movement methods. In their conclusion, they determined that all the studies that have been produced on this timely topic in the recent years (since 2011) have "potentially invalidating evidence and description of new methods"; for that reason, there is a need for more research studies and a new systematic review on adjunct procedures including accelerated tooth movement by Propel.

B. Clinical Suggestions

For many adult patients with malocclusion who can benefit from orthodontic treatment, the duration of the treatment is one of the major factors in their decision-making. The longer treatment time can discourage an adult patient from seeking orthodontic treatment and in turn encourage him/her to seek alternative, unnecessary, and less than ideal treatment options such as veneers, implants, etc. As a result, orthodontic treatment options need to be more appealing to the busy adult patients in terms of time and efficiency. Research has shown that bone remodeling is an inflammatory phenomenon; inflammatory markers are the main factors in bone resorption on the compression site and bone deposition in the tension site of the PDL. Injuring the cortical bone can induce an inflammatory response and cause increased bone turnover followed by a faster rate of tooth movement and shorter treatment time (Hassan et al. 2010). Thus, there is an imperative need to finding new methods that can incorporate the benefits of the cortical bone response to inflammation, shorten the orthodontic treatment time, and appeal to the adult patient population. There are many different, innovative, and appealing orthodontic methods suggested by the competing manufacturers to reduce the treatment time in adult patients; however, a great practitioner must carefully examine each method, know their limitations, and be cautious when interpreting and conveying that knowledge to his/her patients. Propel Orthodontics advocates considerably faster tooth movement and shorter treatment time in adult patients when the Propel Excellerator and Propel Excellerator RT are used to perform micro-osteoperforations in the cortical bone, but there has been only one research study supporting their statement. In this study, our population did not replicate the findings noted by Alikhani et al. (2013) and no significant differences were observed between the experimental and the control side when the amount of canine retraction was considered. It is arguable that perhaps a larger sample size may alter the results.

The biological response of the cortical bone to force can be different in individuals leading to variable amount of tooth movement in each study subject. There could be possible factors leading to some of the study subjects showing accelerated tooth movement when the propel device is used; for example, the purpose of using the Propel device is to create a "localized" area of trauma that leads to activation of an inflammatory process (RAP) and accelerated tooth movement but it is not clear if the inflammation actually stays localized or spreads. These biological factors that can potentially alter the result of the study are yet to be determined and discussed. At this time, the evidence is not compelling and one cannot recommend micro-osteoperforations as an effective method to reduce the treatment time in adult patients. More research is needed to obtain a better understanding of the effects of micro-osteoperforations on the rate of orthodontic tooth movement. A keen clinician needs to judiciously select and cater the best treatment option for each patient.

C. Research Limitations

The results of this study show that the rate of canine retraction on the experimental side where micro-osteoperforations of the cortical bone were performed with Propel device did not appear to be different from the control side where micro-osteoperforations were not performed.

The goal of the study was to minimize the effects of factors that could change the outcome of this study; for example, healthy adult patients ages 18-44 years old with similar malocclusion were selected in an attempt to eliminate the biological factors that allow for faster tooth movement in the younger age groups and homogenize the age-related influences involved in the rate of tooth movement but one can argue that the biology of tooth movement in the selected age group can still be different for each subject; for instance, the rate of tooth movement can be faster in an 18 year old in comparison to a 44 year old. Similarly, efforts were made to minimize the operator- related errors in detection of the canine and second premolar cusp tips but in some study subjects with attrition, it was challenging to completely eliminate these type of errors.

Furthermore, an attempt was made to achieve bodily movement of the canine using standard mechanics but during the clinical exam, the retraction of the canine was not completely bodily and some rotation and tipping had occurred on both sides of the mouth. The amount of canine rotation and tipping was not quantified in this study but if measured, it could potentially alter the results. Also, TADs were placed bilaterally to eliminate mesial drifting of the first molars, but no further measures were taken to eliminate the possible mesial drift of the second premolars.

Moreover, it is plausible that there are other variables that could not be accounted for in the subjects showing more or equal canine retraction on the control side; these factors that could potentially affect the rate of tooth movement can include but are not limited to: gender and hormonal changes, forces of occlusion, and patient's health issues requiring medication therapy that were not disclosed during the period of the research study.

D. Future Studies

Future studies can include the effects of a second micro-osteoperforation on the rate of tooth movement, changes in the bone density during treatment with micro-osteoperforations, effects of sexual hormonal changes in the rate of tooth movement, and comparative study of friction between self-ligating brackets and conventional brackets when micro-osteoperforations are performed.

CONCLUSIONS

The purpose of the present study was to determine whether micro-osteoperforations of the cortical bone increase rate of tooth movement in adult patients.

The results of this split mouth study indicate that 50% of the study subjects showed more canine retraction on the experimental side when compared to the control side but the increase in the rate of tooth movement was not significantly different in the overall sample.

Although, micro-osteoperforations can cause an inflammatory response in the cortical bone, additional research studies are necessary to evaluate and confirm their positive effect on the rate of tooth movement in the orthodontic treatment of adult patients. Therefore, a skilled clinician should be judicious when introducing micro-osteoperforations of the bone to their adult patient as an effective method to decrease treatment time.

Appendix A – CBCT Measurements Using Anatomage Invivo5 3D (Raw Data)

Table 1- CBCT Measurements, TAD-U3D (mm)

Anatomage Invivo5 3D Measurements (Average of Examiner 1& Examiner 2 Values)	Control Side TAD-U3D (mm)	Propel Side TAD-U3D (mm)
	T0-T2	T0-T2
Patient #1	1.69	3.25
Patient #2	3.15	2.45
Patient #3	1.29	2.87
Patient #4	1.96	1.66
Patient #5	1.60	0.82
Patient #6	2.46	2.06
Patient #7	2.08	0.83
Patient #8	3.01	1.96
Patient #9	2.13	1.48
Patient #10	0.41	0.72

Table 2- CBCT Measurements, U5M-U3D (mm)

Anatomage Invivo5 3D Measurements (Average of Examiner 1& Examiner 2 Values)	Control Side U5M-U3D (mm)	Propel Side U5M-U3D (mm)
	T0-T2	T0-T2
Patient #1	1.54	3.86
Patient #2	3.09	2.99
Patient #3	0.91	2.72
Patient #4	3.26	2.62
Patient #5	1.13	1.75
Patient #6	3.54	4.08
Patient #7	2.54	1.65
Patient #8	5.61	2.57
Patient #9	1.53	2.63
Patient #10	0.45	1.80

Appendix B – Digital Model Measurements Using OrthoCAD 3.5 Cadent™ (Raw Data)

Table 1- Digital Model Measurements, U3 Cusp Tip- U5 Cusp Tip (mm)

OrthoCAD 3.5 Cadent ™ Measurements (Average of Examiner 1& Examiner 2 Values)	Control Side U3 Cusp Tip-U5 Cusp Tip (mm)	Propel Side U3 Cusp Tip-U5 Cusp Tip (mm)
	T0-T2	T0-T2
Patient #1	2.35	2.95
Patient #2	3.15	2.55
Patient #3	1.55	3.55
Patient #4	4.25	5.55
Patient #5	1.96	2.85
Patient #6	4.15	3.40
Patient #7	3.00	2.15
Patient #8	4.25	2.75
Patient #9	2.30	2.25
Patient #10	1.40	1.75

Table 2- Digital Model Measurements, U5M-U3D (mm)

OrthoCAD 3.5 Cadent ™ Measurements (Average of Examiner 1& Examiner 2 Values)	Control Side U5M-U3D (mm)	Propel Side U5M-U3D (mm)
	T0-T2	T0-T2
Patient #1	2.20	2.70
Patient #2	3.75	2.30
Patient #3	0.70	2.15
Patient #4	3.75	4.50
Patient #5	1.65	1.20
Patient #6	3.55	3.35
Patient #7	3.15	1.45
Patient #8	3.85	2.30
Patient #9	2.05	1.45
Patient #10	0.90	1.75

Table 3- Digital Model Measurements, U2 Midpoint- U3 Cusp Tip (mm)

OrthoCAD 3.5 Cadent ™ Measurements (Average of Examiner 1& Examiner 2 Values)	Control Side U2 Midpoint- U3 Cusp Tip (mm)	Propel Side U2 Midpoint- U3 Cusp Tip (mm)
	T2-T0	T2-T0
Patient #1	2.30	0.65
Patient #2	1.55	1.05
Patient #3	3.15	3.65
Patient #4	2.00	2.70
Patient #5	1.55	2.40
Patient #6	3.15	3.75
Patient #7	1.20	0.90
Patient #8	1.55	3.55
Patient #9	1.55	1.70
Patient #10	1.60	1.70

Table 4- Digital Model Measurements, U6 MP Cusp Tip- U3 Cusp Tip (mm)

OrthoCAD 3.5 Cadent ™ Measurements (Average of Examiner 1& Examiner 2 Values)	Control Side U6 MP Cusp Tip- U3 Cusp Tip-U3 (mm)	Propel Side U6 MP Cusp Tip- U3 Cusp Tip (mm)
	T_0-T_2	T_0-T_2
Patient #1	2.60	3.10
Patient #2	2.65	2.45
Patient #3	1.50	3.4
Patient #4	4.20	4.25
Patient #5	2.30	3.60
Patient #6	3.05	3.65
Patient #7	2.80	2.70
Patient #8	4.60	2.40
Patient #9	2.70	2.25
Patient #10	2.00	2.45

Appendix C – Intra-Examiner Reliability t-test (Raw Data and Statistical Analysis)

Table 1- CBCT Intra-Examiner Reliability t-test Raw Data (TAD-U3D)

Anatomage Measurements	**Examiner 1- Control Side**	**Examiner 2- Control Side**
for Intra-examiner Reliability Test	**TAD- Distal of Max. Canine (mm)**	**TAD- Distal of Max. Canine (mm)**
	T_2	**T_2**
Patient #2	**12.75**	**12.99**
Patient #3	**11.4**	**12.55**
Patient #5	**8.75**	**8.94**
Patient #7	**13.02**	**13.11**
Patient #8	**12.35**	**12.91**
Patient #10	**19.74**	**19.64**

Table 2- CBCT Intra-Examiner Reliability t-test Statistical Analysis (TAD-U3D)

Variable	N	Mean	S.D.	S.E.	[95% conf. Interval]		t	p-value
Examiner 2 Control Side (T2)	6	13.35	3.46	1.41	9.72	16.99	1.95	0.054
Examiner 1 Control Side (T2)	6	13.00	3.64	1.48	9.17	16.82		
Degrees of Freedom = 5						*= Significant (P<0.05)		

Table 3- CBCT Intra-Examiner Reliability t-test Raw Data (U5M-U3D)

Anatomage Measurements for Intra-examiner Reliability Test	**Examiner 1- Propel Side**	**Examiner 2- Propel Side**
	Mesial of Max. 2nd Premolar-Distal of Max. Canine (mm)	**Mesial of Max. 2nd Premolar-Distal of Max. Canine (mm)**
	T_0	**T_0**
Patient #2	**6.17**	**6.75**
Patient #3	**3.08**	**3.55**
Patient #5	**1.72**	**1.87**
Patient #7	**6.66**	**6.62**
Patient #8	**8.03**	**7.9**
Patient #10	**7.89**	**8.31**

Table 4- CBCT Intra-Examiner Reliability t-test Statistical Analysis (U5M-U3D)

Variable	N	Mean	S.D.	S.E.	[95% conf. Interval]		t	p-value
Examiner 2 Propel Side (T2)	6	5.83	2.56	1.04	3.14	8.52	2.03	0.05
Examiner 1 Propel Side (T2)	6	5.59	2.60	1.06	2.85	8.32		
Degrees of Freedom = 5								*= Significant (P<0.05)

Table 5- Digital Model Intra-Examiner Reliability t-test Raw Data (U3 Cusp Tip- U5 Cusp Tip)

OrthoCAD Measurements	Examiner 1- Propel Side	Examiner 2- Propel Side
for Intra-examiner Reliability Test	U3 cusp tip- U5 cusp tip (mm)	U3 cusp tip- U5 cusp tip (mm)
	T_0	T_0
Patient #2	**14.5**	**15**
Patient #3	**12**	**11.7**
Patient #5	**11.1**	**10**
Patient #7	**15.6**	**14.8**
Patient #8	**16.7**	**16.9**
Patient #10	**18.4**	**18.5**

Table 6- Digital Model Intra-Examiner Reliability t-test Statistical Analysis (U3 Cusp Tip- U5 Cusp Tip)

Variable	N	Mean	S.D.	S.E.	[95% conf. Interval]		t	p-value
Examiner 2 Propel Side (T2)	6	14.48	3.16	1.29	11.15	17.80	-0.92	0.80
Examiner 1 Propel Side (T2)	6	14.71	2.78	1.13	11.79	17.63		
Degrees of Freedom =5								*= Significant (P<0.05)

Table 7- Digital Model Intra-Examiner Reliability t-test Raw Data (U5M-U3D)

OrthoCAD Measurements	**Examiner 1- Control Side**	**Examiner 2- Control Side**
for Intra-examiner Reliability Test	**U5M-U3D (mm)**	**U5M-U3D (mm)**
	T_2	**T_2**
Patient #2	**3.6**	**4.4**
Patient #3	**0.4**	**0.6**
Patient #5	**0**	**0.4**
Patient #7	**2.6**	**2.7**
Patient #8	**3.5**	**3.3**
Patient #10	**8.8**	**8.9**

Table 8- Digital Model Intra-Examiner Reliability t-test Statistical Analysis (U5M-U3D)

Variable	N	Mean	S.D.	S.E.	[95% conf. Interval]		t	p- value
Examiner 2 Control Side (T2)	6	3.38	3.11	1.27	0.11	6.65	1.68	0.07
Examiner 1 Control Side (T2)	6	3.15	3.16	1.29	-0.16	6.46		
Degrees of Freedom = 5								*= Significant (P<0.05)

Table 9- Digital Model Intra-Examiner Reliability t-test Raw Data (U2 Midpoint- U3 Cusp Tip)

OrthoCAD Measurements	**Examiner 1- Control Side**	**Examiner 2- Control Side**
for Intra-examiner Reliability Test	**U2 midpoint- U3 cusp tip (mm)**	**U2 midpoint- U3 cusp tip (mm)**
	T_2	**T_2**
Patient #2	**10.7**	**10.8**
Patient #3	**14.4**	**14.3**
Patient #5	**9.9**	**9.9**
Patient #7	**9.8**	**9.9**
Patient #8	**11.2**	**12**
Patient #10	**10.8**	**11.5**

Table 10- Digital Model Intra-Examiner Reliability t-test Statistical Analysis (U2 Midpoint- U3 Cusp Tip)

Variable	N	Mean	S.D.	S.E.	[95% conf. Interval]		t	p- value
Examiner 2 Control Side (T2)	6	11.4	1.65	0.67	9.66	13.13	1.7	0.07
Examiner 1 Control Side (T2)	6	11.13	1.68	0.68	9.36	12.90		
Degrees of Freedom = 5						*= Significant (P<0.05)		

Table 11- Digital Model Intra-Examiner Reliability t-test Raw Data (U6 MP Cusp Tip- U3 Cusp Tip)

Anatomage Measurements for Intra-examiner Reliability Test	**Examiner 1- Propel Side**	**Examiner 2- Propel Side**
	U6 MP Cusp Tip- U3 Cusp Tip (mm)	**U6 MP Cusp Tip- U3 Cusp Tip (mm)**
	$\mathbf{T_0}$	$\mathbf{T_0}$
Patient #2	**22.7**	**22.7**
Patient #3	**20.7**	**20.6**
Patient #5	**19.6**	**19.7**
Patient #7	**23.9**	**24.5**
Patient #8	**24.9**	**24.8**
Patient #10	**28.9**	**29**

Table 12- Digital Model Intra-Examiner Reliability t-test Statistical Analysis (U6 MP Cusp Tip- U3 Cusp Tip)

Variable	N	Mean	S.D.	S.E.	[95% conf. Interval]		t	p- value
Examiner 2 Propel Side (T0)	6	23.55	3.35	1.37	19.97	26.92	0.93	0.19
Examiner 1 Propel Side (T0)	6	23.45	3.31	1.35	20.02	27.07		
Degrees of Freedom = 5						*= Significant (P<0.05)		

Appendix D – Skewness/Kurtosis Tests for Normality

Table 1- CBCT (TAD-U3D)

Variable	Observations	Pr (Skewness)	Pr (Kurtosis)	------------ Joint --------------	
				adjchi2(2)	prob>chi2
TAD-U3D (mm)	10	0.19	1.12	4.28	1.11

Figure 1- Normality Graph (TAD-U3D)

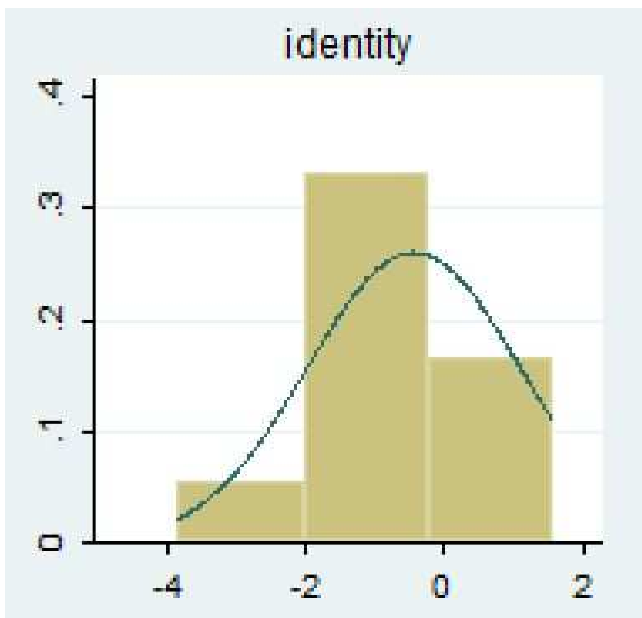


Table 2- CBCT (U5M-U3D)

Variable	Observations	Pr (Skewness)	Pr (Kurtosis)	------------- joint--------------	
				adjchi2(2)	prob>chi2
U5M-U3D (mm)	10	0.14	0.29	3.67	0.15

Figure 2- Normality Graph (U5M-U3D)

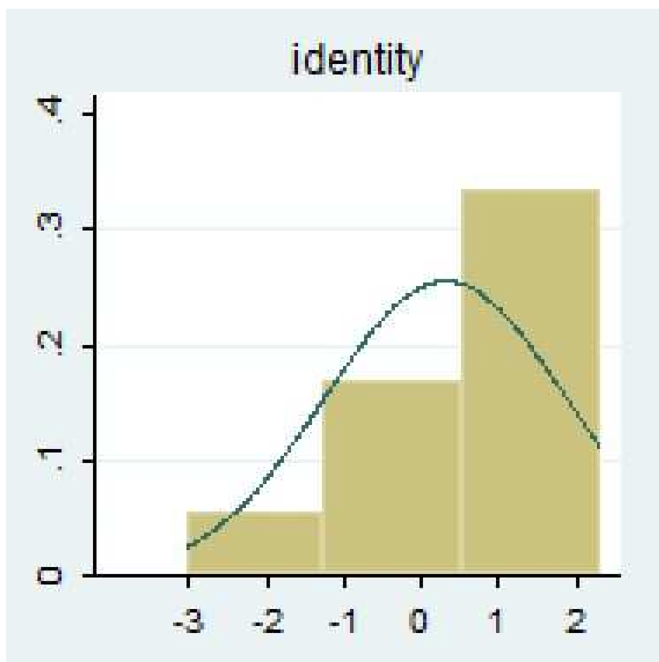


Table 3- Digital Model (U3 Cusp Tip- U5 Cusp Tip)

Variable	Observations	Pr (Skewness)	Pr (Kurtosis)	------------- joint -------------	
				adjchi2(2)	prob>chi2
U3 Cusp Tip -U5 Cusp Tip (mm)	10	0.74	0.64	0.32	0.85

Figure 3- Normality Graph (U3 Cusp Tip- U5 Cusp Tip)

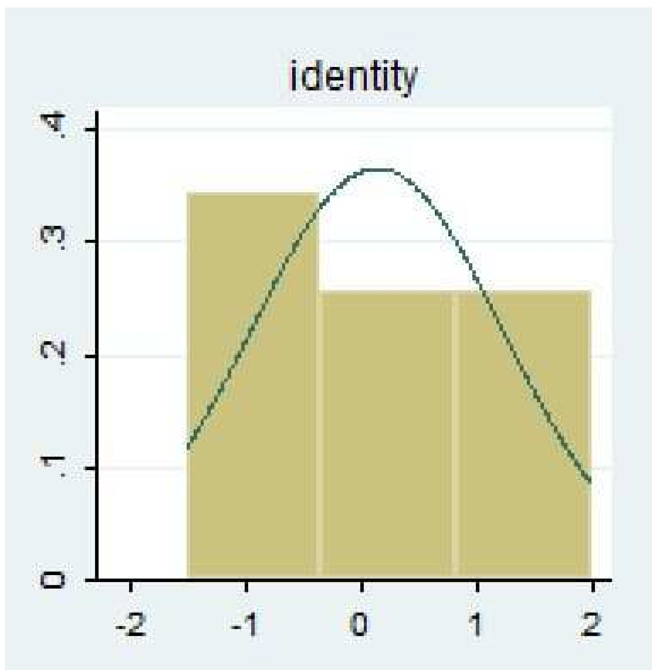


Table 4- Digital Model (U5M-U3D)

Variable	Observations	Pr (Skewness)	Pr (Kurtosis)	------------- joint-------------- adjchi2(2)	prob>chi2
U5M-U3D (mm)	10	0.96	0.22	1.73	0.42

Figure 4- Normality Graph (U5M-U3D)

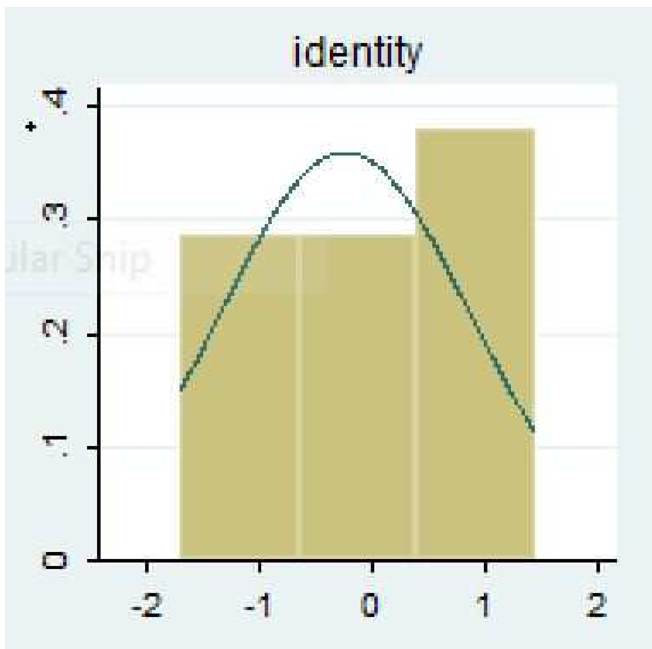


Table 5- Digital Model (U2 Midpoint- U3 Cusp Tip)

Variable	Observations	Pr (Skewness)	Pr (Kurtosis)	------------ Joint -------------	
				adjchi2(2)	prob>chi2
U2 Midpoint- U3 Cusp Tip (mm)	10	0.70	0.23	1.82	0.40

Figure 5- Normality Graph (U2 Midpoint- U3 Cusp Tip)

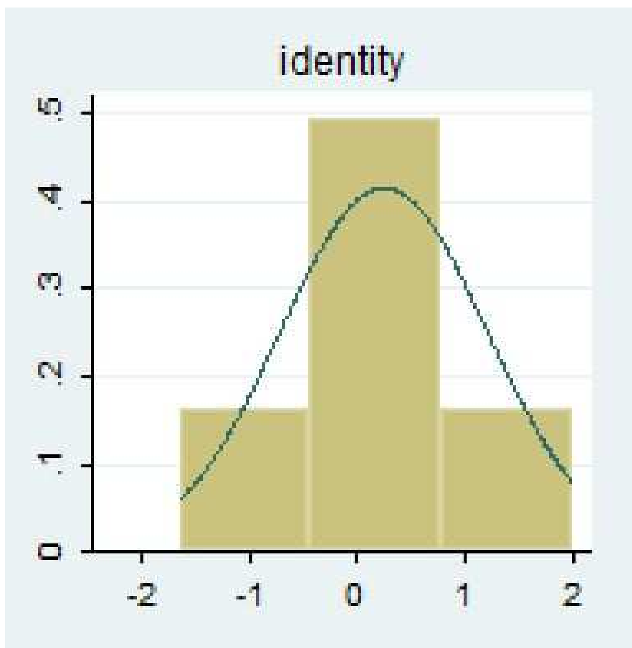
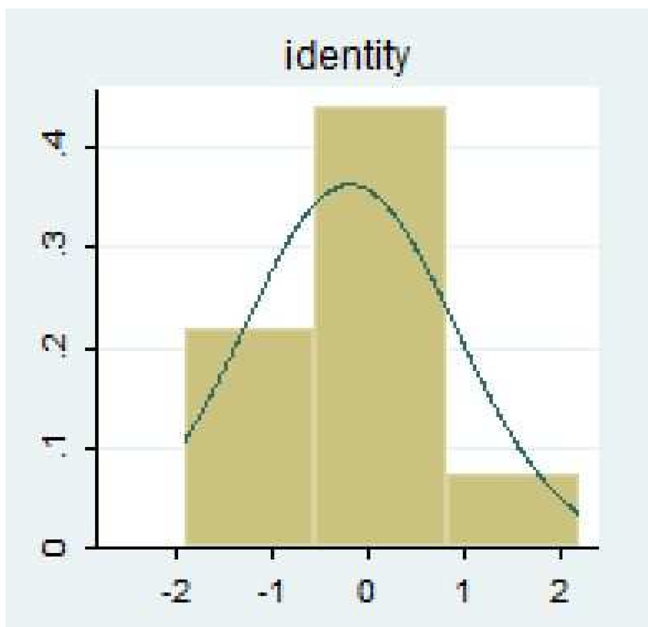


Table 6- Digital Model (U6 MP Cusp Tip- U3 Cusp Tip)

Variable	Observations	Pr (Skewness)	Pr (Kurtosis)	------------ Joint ------------- adjchi2(2)	prob>chi2
U6 MP Cusp Tip- U3 Cusp Tip (mm)	10	0.252	0.145	3.85	0.145

Figure 6- Normality Graph ((U6 MP Cusp Tip- U3 Cusp Tip)



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