

THE IMPACT OF MICRO- OSTEOPERFORATIONS ON THE RATE OF TOOTH MOVEMENT AND ROOT RESORPTION

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CHENNAI

DECLARATION BY CANDIDATE

I hereby declare that this dissertation titled "THE IMPACT OF MICRO OSTEO PERFORATION ON THE RATE OF TOOTH MOVEMENT AND ROOT RESORPTION" is a bonafide and genuine research work carried out by me under the guidance of DR.T.SHOBANA DEVI M.D.S., Reader, Department Of Orthodontics And Dentofacial Orthopaedics, Ragas Dental College and Hospital, Chennai.



DR. BAJATH B

Post Graduate Student

Department Of Orthodontics and

Dentofacial Orthopaedics,

Ragas Dental College and Hospital,

Chennai

Date: 9-2-2019

Place: Chennai

CERTIFICATE

This is to certify that this dissertation titled "THE IMPACT OF MICRO OSTEO PERFORATION ON THE RATE OF TOOTH MOVEMENT AND ROOT RESORPTION" is a bonafide record of work done by Dr. BAJATH B under my guidance during the postgraduate study period 2016-2019.

This dissertation is submitted to THE TAMILNADU Dr.MGR. MEDICAL UNIVERSITY, in partial fulfillment for the degree of MASTER OF DENTAL SURGERY in BRANCH V - Orthodontics And Dentofacial Orthopaedics. It has not been submitted (partially or fully) for the award of any other degree or diploma.

Guided By:



T. Shobhana Devi
9/2/19.

Dr .T.Shobhana Devi, M.D.S
Reader
Department of Orthodontics And
Dentofacial Orthopaedics
Ragas Dental College And Hospital,
Chennai

DEPT. OF ORTHODONTICS
RAGAS DENTAL COLLEGE & HOSPITAL
UTHANDI, CHENNAI-600 119

Head Of The Department:

N.R. Krishnaswamy
9/2/19

Prof.(Dr.)N.R.Krishnaswamy, M.D.S.,
M. Ortho R.C.S (Edin) Dip N.B. (Ortho)
Diplomate-Indian Board Of Orthodontics
Professor and H.O.D
Department of Orthodontics And
Dentofacial Orthopaedics
Ragas Dental College And Hospital,
Chennai

DR. N. R. KRISHNASWAMY
PROFESSOR & HEAD
Dept. of Orthodontics
RAGAS DENTAL COLLEGE & HOSPITAL
2/102, East Coast Road
Uthandi, Chennai-600 119

N.S. Azhagarasan
11/02/2019

Dr .N.S. AZHAGARASAN, M.D.S

Principal

Ragas Dental College And Hospital, Chennai

PRINCIPAL
RAGAS DENTAL COLLEGE AND HOSPITAL
UTHANDI, CHENNAI - 600 119.

THE TAMIL NADU Dr. MGR MEDICAL UNIVERSITY CHENNAI

PLAGIARISM CERTIFICATE

This is to certify the dissertation titled "THE IMPACT OF MICRO OSTEO PERFORATION ON THE RATE OF TOOTH MOVEMENT AND ROOT RESORPTION" of the candidate Dr. BAJATH B, for the award of MASTER OF DENTAL SURGERY in BRANCH V - ORTHODONTICS AND DENTOFACIAL ORTHOPEDICS.

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DR. BAJATH B

Post Graduate Student
Department Of Orthodontics And
Dentofacial Orthopaedics,
Ragas Dental College And Hospital,
Chennai



9/2/19

Dr .T SHOBBANA DEVI, M.D.S

Reader
Department of Orthodontics And
Dentofacial Orthopaedics
Ragas Dental College And Hospital,
Chennai

DEPT. OF ORTHODONTICS
RAGAS DENTAL COLLEGE & HOSPITAL
KEMANDI CHENNAI-600 114

Date: 09/02/19

Place: Chennai

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ABSTRACT

AIM: The purpose of this study was to evaluate the effects of micro osteoperforation on the rate of tooth movement and root resorption.

MATERIALS AND METHODS: 10 adult patients who met the inclusion criteria were selected. All patients received micro osteoperforation (MOPs) at two time intervals. First intervention just before retraction and second intervention after two months. The mean rate of tooth movement was assessed at monthly intervals from study cast. Root resorption (RR) was evaluated 3-dimensionally using pre and post retraction CBCT data.

RESULTS: The mean rate of tooth movement between first and second intervention shows statistically significant value ($P= 0.05$). After the first intervention the tooth moved at the rate of 0.8425 ± 0.04 mm per month and after second intervention tooth movement increased to a rate of 0.9830 ± 0.02 mm per month. Maxillary lateral incisor showed greater root resorption than maxillary centrals and canines.

CONCLUSION: MOPs seem to increase the rate of tooth movement. However repeated interventions are required.

Key Words: Micro-osteoperforations, En-masse Retraction, Temporary anchorage device (TAD) Rate of tooth movement, Acceleration, Root resorption.

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Introduction

INTRODUCTION

Orthodontic tooth movement (OTM) is a biological process that requires the impart of mechanical loading headed for biological signals by periodontal ligament and alveolar bone cells such as osteoblasts, osteocytes and osteoclasts. These cells when exposed to varying degree of magnitude, frequency and duration of mechanical loading express widespread changes¹⁰⁷. Orthodontic tooth movement can occur rapidly or slowly, depending on the physical characteristics of the applied force, and the size and biological response of the periodontal ligament(PDL).

The number of adults seeking orthodontic treatment has dramatically risen and the biological possibilities for tooth movement are reduced to about one-third of those found in children. It is clear that during aging, the bone composition changes, its cells become less reactive, and its metabolism slows¹²².OTM is an aseptic inflammatory process, which involves vascular, and cellular changes inflammatory mediators, including cytokines and neuropeptides, which is crucial in the remodeling of alveolar bone and PDL during orthodontic tooth movement¹¹⁵.

According to Buschang et al. (2012), orthodontic treatment differs from patient to patient, based on individual uniqueness, but on average lasts from 21–27months for non extraction treatment, and 25–35 months for extraction treatment. Orthodontic treatments are often disregarded or not accepted due to their long duration and the negative impact they can have on the patient's physical appearance. This duration is also determined by

problems encountered during treatment, like missing appointments, bracket breakage, poor oral hygiene, and anchorage problems. Prolonged duration of orthodontics is the one of the main reason patient reluctant to undergo treatment¹⁵¹.

Due to difference in the biological activity between young and adult patients treatment duration may prolong in adults. This may not only deter adult patients from seeking orthodontic treatment but also predispose them to root resorption, white spot lesion, caries, and reduced patient compliance. Therefore, the challenge is to decrease the treatment duration without compromising the treatment outcome. With advanced technology, improvement in treatment efficiency can help to alleviate the aforesaid challenges.

The biological concepts behind tooth movement were ignored and research efforts were directed more towards introducing a range of appliances and bracket systems. Orthodontic movement of teeth is a site-specific bone remodeling which consists of coupled bone resorption and bone formation. Bone turnover rate is significant index that indicates quality and quantity of orthodontic tooth movement. The mechanical stimuli generated from the orthodontic appliances results in the alterations in blood flow which create changes in the chemical environment. The chemical changes stimulate the migration of immune cells, which along with native cells such as fibroblasts and osteoblasts, produce inflammatory cytokines¹⁵⁸. Many studies have reported an increase in the activity of inflammatory markers such as

chemokines and cytokines in response to orthodontic forces. All these molecules play an important role in controlling the rate of tooth movement.

The attempt to shorten the treatment time can be divided into different categories, including local or systemic administration of biologic and pharmacological factors. Due to the adverse reactions witnessed with these approaches, the trend has turned towards finding a physical or surgical approach that can accelerate tooth movement. For example, biological agents such as prostaglandin E2 or parathyroid hormone increase the rate of tooth movement, the critical side effects are root resorption and local pain⁷⁸.

The first efforts to move teeth with combined orthodontics and surgery is credited to Kole⁷⁷. He suggested that performing surgical osteotomies in the alveolar process weakens the cortical bone and facilitates orthodontic tooth movement. Harold Frost⁵¹ in 1983 acknowledged that, the molecular dynamics of osteogenesis in stressed bone is based on Regional Acceleratory Phenomenon (RAP) and not on the bony block movement. RAP results in reduced regional bone densities (osteopenia) in healthy tissues, whereas the volume of bone matrix remains stable⁵².

There are many clinical evidences on decortications which accelerate tooth movement 3-4 times faster than conventional techniques. Alveolar corticotomy is promising technique but carry their own negatives. Because it is an invasive surgical technique associated with common risks of morbidity, inflammation, swelling, root resorption, gingival recession, root dehiscence

and fenestration⁸. Patient acceptance can be limited due to expense, the invasive nature and the morbidity of the procedure.

The challenge has been how to locally accelerate bone remodeling in a minimally invasive manner. A new micro-invasive technique called alveocentesis has been developed by PROPEL Orthodontics⁷⁴. They proposed a safe method ie Micro-Osteoperforations (MOP's) to accelerate tooth movement that harnesses and amplifies the patient's normal biological response to orthodontic forces.

Orthodontic force application can sometimes evoke excessive resorption of root cementum, proceeding into the dentin, in the long run shortening the root length—a process called root resorption. Ottolengui (1914) and Ketcham (1927) were the first to report on root resorption. External apical root resorption (EARR), it is an iatrogenic disorder that occurs, unpredictably after orthodontic treatment, where by resorbed apical root portion is replaced by bone. Many orthodontists consider EARR to be an unavoidable pathologic consequence of orthodontic tooth movement¹⁷.

This undesirable side effect is described as being the outcome of a sterile, complex inflammatory process that involves various distinct components including mechanical forces, tooth roots, bone, cells, surrounding matrix, and certain known biological messengers.

Root resorption is believed to be related initially to the force magnitude, and light forces have long been suggested for minimizing this adverse outcome. However, recent reports point out that force magnitude may

not be the most vital etiologic factor responsible for root resorption, and that the severity of this condition is highly related to the routine of force application.

Certain degree of root resorption is required for the radiographic detection using IOPA. To overcome the limitations of two dimensional imaging in clinical practice. CBCT was taken just before and after retraction. The CBCT technique also has benefits of providing images in all three planes. The accuracy and reliability of CBCT is better than the current gold standard (periapical radiograph).¹⁶⁶

The aim of this prospective clinical trial was to evaluate the impact of micro osteoperforation on the rate of tooth movement and root resorption. The primary outcome was to assess the rate of tooth movement. The Secondary outcome was to assess the amount of root resorption following micro osteo perforation.

Review of Literature

REVIEW OF LITERATURE

The review of literature for this study is categorized into seven groups:

1. Role of bone cells
2. Role of mechanical stimuli on bone cells
3. Orthodontic tooth movement
4. En-masse retraction in orthodontics
5. Different Methods to accelerate orthodontic tooth movement
6. Effect of Micro-osteoperforations on tooth movement
7. Root resorption

1. ROLE OF BONE CELLS

K D Cashman (2003)¹⁴ explained about bone cells and their action on remodeling process. Osteoblasts are the cells responsible for formation of type 1 collagen and they develop from pluripotent mesenchymal cells. It has actively synthesizing bone matrix that has many distinctive ultra structural characteristics, including a large nucleus, enlarged Golgi apparatus, and extensive endoplasmic reticulum. Osteoclasts originate from the hemopoietic system, more specifically from the granulocyte–macrophage colony-forming unit for granulocytes and macrophages. Multinucleated osteoclasts, situated either on the surface of cortical or trabecular bone, or within the cortical bone, where they are located at the tip of the remodeling units, are responsible for the resorption of bone at these sites. Osteoclast differentiation and activation are primarily be regulated by the osteoblast and its precursors. Proteolytic

enzymes, especially cathepsins and collagenases, are also synthesized by osteoclasts and are secreted through the ruffled border of bone-resorbing compartment where they digest collagen.

Lynda F Bonewald (2010)⁷⁰ highlighted about the role of osteocytes in bone. Osteocytes lying within the bone matrix descended from the mesenchymal cells through osteoblast proliferation. At the remodeling sites osteocyte can recruit osteoclast cells. Any micro damage or microcrack can result in osteocyte apoptosis. Proapoptotic molecules are elevated in osteocytes immediately at the micro crack region, whereas antiapoptotic molecules are expressed 1 to 2mm away from the micro crack. Apoptotic osteocytes release apoptotic bodies expressing RANKL to recruit osteoclasts.

One of the main function of the osteocyte is act as a mechanosensory cell because of their location in bone and their complex dendritic network. Rapid osteocyte signals in response to shear stress include release of nitric oxide (NO), ATP, and prostaglandin. In bone, NO inhibits resorption and promotes bone formation. Both osteoblasts and osteocytes release NO in response to mechanical strain or fluid-flow shear stress.

Pietrzyk D (2017)¹¹⁶ explained about the action of sclerostin in bone. Sclerostin is formed by osteocytes and transferred by cytoplasmic extensions to osteoblasts, which are located on the surface of bone trabecula. In response to mechanical loads, osteocytes secrete sclerostin through the modulation of the transforming growth factor- β (TGF- β) dependent pathway. Sclerostin is a key molecule that inhibits osteoblast activity. Osteocytes maintain a balance

between osteolysis and osteogenesis through the control of sclerostin secretion. The effect of mechanical forces and micro trauma of bone inhibit the secretion of sclerostin by osteocytes, intensifying the process of bone formation.

2) ROLE OF MECHANICAL STIMULATION ON BONE CELLS

Daniel P. Nicoletta (2006)¹⁰⁸ investigated osteocyte lacunae tissue strain in cortical bone. Bone modeling and remodeling are controlled at the cellular level through signals mediated by Osteocytes. There are two school of thoughts on relation to role of osteocyte (1) osteocytes are stimulated via the mechanical deformation of the perilacunar bone matrix and (2) osteocytes are stimulated via fluid flow generated shear stresses acting on osteocyte cell processes within the lacunar canaliculi. The osteocyte is attached to the lacuna wall via integrins which are much less stiff than the bone matrix and because of that the strain signal would be attenuated prior to reaching the cell. Fluid flow in bone generates shear stress on mechanical stimulation may provide more stimulation to bone cells.

Laoise M. McNamara (2007)⁹⁸ hypothesis that bone remodeling may be synchronized by signals due to both strain and micro damage. Remodeling stimuli may be generated in response to both micro damage and strain. By incorporating both micro damage and strain as mechano-regulatory stimuli, the creation and refilling of a resorption cavity along the surface of a bone trabecula can be simulated. The initiation of a resorption cavity at the surface proximal to the damage, suggesting that the osteocytes could activate a remodeling cycle but thereafter osteoclasts and osteoblasts regulate refilling.

Lidan You (2008)¹⁶⁹ examined the osteocytes' role in the mechanical regulation of osteoclast formation and activation. He demonstrate that mechanically stimulated osteocytes release soluble factors that can inhibit osteoclastogenesis induced by other supporting cells including bone marrow stromal cells. Mechanically challenged osteocytes can affect the local chemical environment of marrow stromal and pre-osteoblastic cells via secreted signals that alter their ability to induce osteoclast formation. Such a mechanism would allow osteocytes to function as the local mechanotransducers to sense mechanical loading.

Jenneke Klein-Nulend (2013)¹⁰¹ explained about how a mechanical load placed on whole bones is translated and amplified into a mechanical signal that is subsequently sensed by the osteocytes. Osteocytes play a central role in this remodeling process by sensing the external mechanical loads and then transmitting the information to the effector cells, the osteoblasts and/or the osteoclasts, which then maintain the skeletal homeostasis. Osteocytes have cell process and cell body which helps in the mechanosensation. At the same time osteocytes release nitric oxide and prostaglandin, which helps in converting the mechanical loads to biological signal.

Robert T. Brady (2015)³ investigated the role of mechanically stimulated osteocytes and osteoblasts in directing the behavior of bone forming cells. In this study they demonstrated that signaling mechanisms in bone together, act to increase the number of available bone forming cells at a site of loading.

3. ORTHODONTIC TOOTH MOVEMENT

Davidovitch Z (1988)¹⁵⁶ hypothesized that tissue remodeling during orthodontic tooth movement is modulated, at least in part, by factors from the nervous and vascular (immune) systems. The neurotransmitters substance P (SP) and vasoactive intestinal polypeptide (VIP) and the cytokines IL-1 alpha and IL-1 beta were localized immunohistochemically in paradental tissues of cat canines that had been treated by the application of an 80 g tipping force for 1 hour to 14 days. Administration of SP and IL-1 beta to human PDL fibroblasts in vitro for 1 to 60 minutes resulted in significant increases in the levels of the intracellular "second messenger" Cyclic amp, as well as PGE₂, a plasma membrane associated fatty acid these are believed to serve as a local regulator of bone cell activity. The results support the hypothesis that neurotransmitters and cytokines play a regulatory role in orthodontic force-induced alveolar bone remodeling.

S Kyomen (1997)¹³⁹ tested the influences of age related changes in the proliferative activity of PDL cells during experimental tooth movement in rats. Young (6-week old) and adult (14-week old) Wistar strain rats were used in this study. Light (10g) or heavy forces (40g) were applied to the maxillary first molars on day of 1,3,7 and 14. Proliferative activity of PDL cells was evaluated with immunohistochemically. In the control group, cellular activity was significantly greater in the young than in the adult group. Therefore age changes substantially influence the proliferative capacity of the PDL cells and subsequent tooth movement during the initial phase of tooth movement.

Ren Y(2003)¹²² hypothesized that orthodontic procedures seem to be more time consuming in adults than in younger individuals either due to delay in the initial tissue response or because of slow turnover of the bone and periodontal ligament in adults. Orthodontic tooth movement were completed between two groups 30 rats, aged 6 weeks and 9-12 months, respectively. One side of the maxilla, 3 molars together were moved mesially with a standard orthodontic appliance delivering a force of 10 cN. The other side served as a control. The results showed a faster initial tooth movement in younger than in adult animals. Besides a delay in the onset of tooth movement in adult animals, tooth movement could be equally efficient in adults once it has started.

Murray C. Meikle (2006)⁸⁷ investigated on tissue, cellular, and molecular regulation of orthodontic tooth movement. The current evidence suggests that downstream from the initial mechanotransduction event at focal adhesions which link the extracellular matrix to the cytoskeleton, mechanically induced remodeling is mediated by a complex feedback mechanism linking the synthesis of cytokines such as interleukin-1 (IL-1), IL-6, and receptor activator of nuclear factor B ligand by cells of the osteoblast and/or fibroblast lineages. These in turn act in an autocrine/paracrine fashion to regulate the expression of transcription factors, cytokines, growth factors, enzymes, and structural molecules involved in the differentiation, proliferation, and function of mesenchymal and other cell types. In addition orthodontic tooth movement involves alveolar bone bending and remodeling of periodontal tissues.

Blesta A (2006)⁶ investigated the expression of the cytokines like interleukin-1 α and tumor necrosis factor- α in dental tissues during the early phases of orthodontic tooth movement in rats. All maxillary right first molars were moved orthodontically in eighteen male wistar rats, with a force of 0.5 N, for 3 h, 1 d, and 3 d. The left sides served as controls. Parasagittal sections of the maxillary molars and the adjacent tissues were subjected to immune histochemical staining for IL-1 α or TNF- α , and were evaluated with light microscopy. IL-1 α and TNF- α were expressed in the bone and periodontal ligament (PDL) along the roots of the orthodontically moved molars and in the gingiva. Increased expression of both cytokines was observed in the areas after 1 and 3 days of tooth movement.

S Henneman (2008)¹²⁶ described about biological and mechanical signaling path way during orthodontic treatment. The complex cascade of events after the application of an orthodontic force to a tooth introduced a theoretical model to elucidate the strain in the matrix of pdl and alveolar bone immediately after the application of orthodontic force, resulted in a fluid flow in both tissues. As a result of matrix strain cells were deformed. In response to the deformation, fibroblasts and osteoblasts in the PDL as well as osteocytes in the bone are activated. A combination of PDL remodeling, and the localized deposition and resorption of alveolar bone enables the teeth to move.

V. Krishnan (2009)¹⁵⁶ aimed at identifying the nature of the biological response of alveolar bone, periodontal ligament and gingiva during orthodontic tooth movement. Orthodontic tooth movement is produced by mechanical

means which evoke biological responses. The actual performers of this force-induced remodeling are the native cells of the treated teeth and paradental tissues. Other important cellular participants in this remodeling process are derivatives of the neuro-vascular and immune systems. Cells and tissues use mechanosensing, transduction, and response phenomena to respond to applied mechanical forces. This is evident by the aseptic inflammatory reaction, which is initially acute, then becomes chronic a few days after the activation of the orthodontic appliance. Whenever the appliance is reactivated, acute inflammation is re-introduced to the paradental tissues. Hence, it may be suggested that mechano response and inflammation are both essential for achieving effective orthodontic tooth movement. If both mechanisms indeed unfold in concert, orthodontists might be able to accelerate the velocity of tooth movement by utilizing additional external stimuli, like surgical or non surgical methods.

Hyung-Seon Baik (2012)⁵⁴ in this animal study investigated the effect of orthodontic loading on the expression of interleukin-1 α (IL-1 α) and tumor necrosis factor- α (TNF- α) in compressed gingiva. In 24 wistar rats 4 served as control ten samples corticotomy performed either on right or left side and moved orthodontically. The other ten samples molar moved orthodontically by applying 20gm of force. Real time polymerase chain reactions (PCR) of compressed gingiva excised from the euthanized rats were performed. This study concluded that no significant differences in the expression of IL-1 α

between all the groups, but in other hand there is increase in TNF- α in the pressure side gingiva at day 7 after orthodontic loading. The findings imply that gingival tissue may be involved in tissue homeostasis and bone remodeling.

Sarah Alansari (2015)⁹³ reported accelerating techniques can be divided into two main groups: one group stimulates upstream events to indirectly activate downstream target cells, while the other group bypasses the upstream events and directly stimulates downstream target cells. In both approaches, there is a general consensus that the rate of tooth movement is controlled by the rate of bone resorption, which in turn is controlled by osteoclast activity. Therefore, to increase the rate of tooth movement, osteoclasts should be the target of treatment.

Catherine Giannopoulou (2015)²⁸ investigated the variation in the amount of the orthodontically induced tooth movement in humans which include 7 female and 4 males with age range of 11.3 to 28.6yrs. Two premolars in each patient tipped buccally with 1N force for two months and he concluded that rate of tooth movement varied to a large extent between individuals with location whether it is placed in maxilla or mandible. Mean amount of tooth displacement in the maxilla was 3.06 mm and that in the mandible 1.97 mm.

L. Feller (2015)³⁶ stated that in mechano transduction process of converting biomechanical stimuli into intracellular biochemical signal that elicit the tissue responses is complex. Mechanical stresses during orthodontic loads causes c intracellular changes in extra cellular matrix, cytoskeleton and

release of pro inflammatory markers cytokine which helps in bone resorption and formation and facilitate OTM.

Cristina c.teixeira (2017)²¹ explained biphasic theory and the influence of OTM. OTM mainly involves anabolic and catabolic phase Biphasic Theory of Tooth Movement. The biologic response during tooth movement comprises two clearly separated phases. After application of an orthodontic force (a), both the compression and tensile stresses generated by displacement of the tooth cause damage to the PDL, stimulating a perimeter of osteoclastogenesis (b). Once the tooth moves in the direction of the orthodontic force into the space created by osteoclast activity, a perimeter of osteogenesis is formed in roughly in the same area of the alveolar bone where the catabolic response took place.

4. EN-MASS RETRACTION IN ORTHODONTICS

Staggers JA (1991)¹⁴⁷ described that to preserve anchorage canine and incisors were retracted separately. In two step retraction anchorage being taxed twice, as opposed to once with en masse retraction. Pointing out that the posterior segment is unaware of knowing how many teeth are being retracted and it mainly responds according to the force system involved.

R.H.A. Samuels (1993)¹¹² conducted a clinical study on space closure with nickel titanium closed coil spring and elastic modules. The study used sliding mechanics using 19×25ss in 022 slot. Retracted the six anterior teeth against the second bicuspid and first molars to examine the rate of space

closure using 100gms,150gms and 200gms nickel titanium closed coil springs. The result for these springs and elastic module were compared. The 150 and 200gms springs produced a faster rate of space closure than the elastic module or the 100gms spring. No significant difference was noted between the rate of closure for the 150gms and 200gms of closed niti coil springs during anterior retraction.

Samuels RH (1993)¹²⁰ compared the effect of continuous versus intermittent forces using niti coil spring and elastomeric ligation during space closure after premolar extraction. They compared continuous light forces from 150 g nickel-titanium closed coils to heavy intermittent forces from elastomeric ligation that started at 400 to 450 g. The results showed an average space closure of 0.19 mm per week using elastomeric ligation while closed coil niti provided significantly faster average space closure of 0.26 mm per week.

Jack J.G.M. Pilon (1996)¹¹⁷ studied the relationship between the magnitude of a continuous orthodontic force and the rate of bodily tooth movement. Tooth movement was measured directly with a digital caliper twice a week for 16 weeks. Resulting curves were divided in four phases. Large individual differences were found in the rate of tooth movement. No significant differences in the duration of each phase or in the mean rate of tooth movement during each phase were found between the three force groups. Maximum rate of tooth movement was about 2.5 mm per month in all force groups. There were no significant differences in the mesial movement of the anchorage unit between the force groups.

Profit WR (2000)¹¹⁸ recommended separate canine retraction for maximum anchorage, stating that this approach would allow the retraction force to dissipate over the large periodontal ligament area in the anchor unit. They acknowledged, however, that closing the space in two steps rather than in one would take nearly twice as long.

Andrew J Kuhlberg (2001)⁶ described separate canine retraction as less anchorage taxing because the two canines are retracted against several posterior teeth in the anchor unit.

Heo W (2007)⁶² compared degree of anchorage loss between two step retraction versus enmass retraction. There are several commonly used methods of applying this force: these are elastic modules, elastic chain or active modules. Active modules have significant force decay over time. Niti coil springs have the advantage of giving significantly quicker and more consistent rates of space closure.

Madhur Upadhyay (2008)⁹¹ in this trial 40 patients with mean age of 17.6yrs, randomly assigned to two groups. Patient having bidental protrusion and undergone first bicuspid extraction. Enmass retraction using tad as a anchor unit in one group and the other group space closure was done by conventional methods. Group one showed anchorage gain with distalization and intrusion of molar, when compared to conventional method. TAD assisted retraction provides absolute anchorage to allow greater skeletal, dental, and esthetic changes in patients requiring maximum anterior retraction.

Brig SM Londhe (2010)⁵³ studied the efficacy of inclusion of second molar in treatment at the outset to reinforce anchorage. The study successfully quantified the anchorage loss and brought out the advantages of including second molar in treatment at the outset. Not only the anchorage loss is minimized but inclusion of second molar also helps to maximize incisor retraction and helps control angular movement of molar and incisor.

Salma Al-Sibaie (2013)¹²⁸ in this randomized controlled trial Fifty-six participants were analyzed with mean age 22.34 ± 4.56 years. They were randomly distributed into two groups with 28 patients in each group. After first premolar extraction space closure was started using either enmass retraction with TAD or two step retraction using trans palatal arch. In patients with moderate to severe protrusion tad assisted retraction gave superior results than conventional methods

Charushila Vinay Chaudhari (2015)²³ compared rate of space closure and anchorage loss using Niti closed coil spring and elastomeric chains. In 40 patients they divided into two group and rate of anterior retraction was assessed for four months. Mean space closed using niti coil spring 0.91mm and for elastomeric chain 0.61mm. Mean anchorage loss 1.1 mm for niti and 0.82 mm for elastomeric chain.

Amy H. Hoch (2017)⁴⁷ in this clinical trial found that there is no difference in anterior en mass retraction and two step retraction, in addition 150gm force using closed niti coil spring is effective in space closure. In both

types additional anchorage devices can be incorporated for the reduction of anchorage loss ,like TPA, TAD, HEADGEAR etc

Joanna Antoszevska-Smith (2017)⁶ compared enmass retraction using TAD and other conventional methods. In this systematic review they stated that TAD provides better anchorage and reduction in treatment duration .TAD provide more incisor retraction than conventional methods, and less anchorage loss in temporary intraoral anchorage devices.

Mumen Z. Rizk (2017)¹⁰⁵ compared enmass retraction and two step retraction during space closure and their effect on treatment duration and root resorption. In this systematic review they stated that En masse retraction is superior in anchorage preservation and incisor retraction if used in conjunction with mini screws when compared to two-step retraction combined with conventional anchorage methods. There is no statistically significant change in root resorption for both groups.

Patricia Pigato Schneider (2018)¹³² in his prospective randomized clinical trial compared two step retraction versus single step retraction. Forty-eight adult patients with bimaxillary protrusion who were planned for orthodontic treatment with extraction of four first premolars were enrolled. All patients were randomly allocated in a 1:1 ratio to either the ER (n -24) group or the TSR (n - 24) group. The findings of the study stated that both methods are efficient to achieve space closure and there is no significant differences in the amount of retraction of incisors and anchorage loss of molars between these

two methods. Magnitudes of incisor and molar tipping were similar between the two space closure methods, with the crowns moving more than the apices.

5. DIFFERENT METHODS TO ACCELERATE ORTHODONTIC TOOTH MOVEMENT

Effects of Pharmacological Agents on Tooth Velocity:

Verna C (2000)¹⁵⁷ experimented on rats undergoing maxillary molar mesial movement, by inducing either hypothyroidism or hyperthyroidism. In rats with high bone turnover, the rate of tooth movement was increased, while it reduced in animals with a low bone turnover group. Examination of histological sections from the jaws of these rats showed root resorption had occurred in both groups, but that it was more pronounced in the low bone turnover group. He claimed that alteration in bone metabolic state affects the rate of tooth movement.

Ali reza sekhavat (2002)¹³⁵ had done a systemic application of misoprostol, PGE1 analog, in rats undergoing tooth movement for 2 weeks. He concluded that (10.0 or 25.0 g/kg/d) of misoprostol significantly increased the velocity of movement without enhancing root resorption.

Abhijith shetty (2015)¹³⁸ evaluated rate of canine tooth movement after locally injecting one milliliters of vit D on the buccal side distal to canine on 7,21st and 47th day. The amount of canine retraction was assessed using

palatal rugae as the reference point. In conclusion the rate of tooth movement less in experimental side than control side.

Thaleia Kouskoura (2017)⁷⁸ provided an overview of recent insights into drug-mediated effects and the use of drugs to influence the rate of tooth movement during orthodontic treatment. During orthodontic tooth movement different biological processes take place at distinct sites of the PDL. Bone resorption and bone formation occur simultaneously at different areas of compression vs areas of tension. The proteoglycan component of the extracellular matrix of the PDL, a hydrated gel, allows the diffusion of free small molecules (such as drugs, hormones) within the pdl and presents a big challenge to the effort of achieving targeted therapeutic interventions at specific sites in pdl. Most of the drugs used can and will influence both biological processes and can furthermore influence other physiological cellular functions.

Woo-Young Jung,(2018) ²⁷ investigated the effect of transmucosal injection of thyroxine in beagle dogs to evaluate the rate of orthodontic tooth movement and osteoclastic activity. The rate of orthodontic tooth movement is higher in thyroxine group when compared to controls. The number of osteoclasts increased markedly in experimental group at 4th week and in 8th week its similar in both groups.

Effects Of Physical Stimuli On Tooth Velocity

Davidovitch Z (1980)³³ determined the usefulness of exogenous electric currents in accelerating orthodontic tooth movement. Two groups of

five cats each were treated by an electric-orthodontic procedure in one maxillary canine for 7 and 14 days, respectively. Teeth treated by force and electricity moved significantly faster than those treated by force alone. It was concluded that orthodontic tooth movement may be accelerated by the use of locally applied electric currents.

Kawasaki K (2000)⁷⁶ analyzed the effects low-energy laser irradiation on tooth movement in rats. 10 g of orthodontic force was applied to rat molars to cause and a Ga-Al-As diode laser was used to irradiate the area around the moved tooth. After 12 days, the amount of tooth movement was measured. Results showed that in the laser irradiation group, the amount of tooth movement was significantly greater (1.3-fold) than that of the non irradiation group in the end of the experiment. The amount of bone formation and rate of cellular proliferation in the tension side and the number of osteoclasts in the pressure side were all significantly increased in the irradiation group when compared with the non irradiation group.

Limpanichkul W (2006)⁸⁴ tested the hypothesis that mechanical forces combined with low-level laser therapy stimulate the rate of orthodontic tooth movement. 12 young adult patients who required retraction of maxillary canines into first premolar extraction spaces using tension coil springs with fixed edgewise appliance was taken in this study. Low level laser therapy was applied on the mucosa buccally, distally and palatally to the canine on the test side and using a pseudo-application on the placebo side. Dental impressions and casts were made at the commencement of the trial and at the end of the

first, second and third months after starting the trial. Measurement of tooth movements was made on each stage model using a stereo microscope. The results showed that there was no significant difference of means of the canine distal movement between the low level laser therapy side and the placebo side for any time periods. The energy density of low level laser therapy (GaAlAs) at the surface level in this study (25 J/cm (2)) was probably too low to express either stimulatory effect or inhibitory effect on the rate of orthodontic tooth movement.

Makoto Nishimura (2008)⁹² evaluated the effects of mechanical stimulation by resonance vibration on tooth movement. The maxillary first molars of 6-week-old male Wistar rats were moved to the buccal side by using an expansive spring for 21 days (control group) with additional vibrational stimulation (60 Hz, 1.0 m/s²) application to the first molars by using a loading vibration system for 8 minutes on days 0, 7, and 14 during orthodontic tooth movement (experimental group). 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.

Hu Long (2013)⁶⁴ Participants in the included studies who require orthodontic treatments. Specifically, they needed the extractions of first premolars and retraction of anterior teeth due to protrusion or dental crowding. They used 780nm of wave length and 5j /cm² of energy. They calculated accumulative moved distance in each month for three months and in first

month is about 0.54mm, second month 1.11mm and third month 1.25mm and they concluded that low level laser therapy accelerates the tooth movement within two to three months

Vinicius Lima de Almeida (2015)³⁵ in this systematic review 5 studies were included and assessed for the rate of tooth movement using low level laser therapy during retraction. Three studies revealed statistically significant differences in induced tooth movement when compared to movement rates between experimental and control groups. The effectiveness of the laser in the maxilla, showing a statistically significant influence of the laser in 3 months, but not in 1 and 2 months. Results in the mandible, showed there is a statistically significant influence of laser in 1 month, but not in 2 and 3 months.

Mohammad Moaffak A. Alsayed Hasana (2017)⁸⁴ evaluated the effect of lasers on crowded maxillary dentition. Laser group received a LLL dose from an 830-nm wavelength Ga-Al-As semiconductor laser device with energy of 2 J/point. The laser was applied to each maxillary incisor's root at four points (two buccal, two palatal). Application was repeated on days 3, 7, 14, and then every 15 days starting from the second month until the end of the leveling and alignment stage. Alignment progress was evaluated on first month, second month and at the end of aligning and leveling. Mean Leveling and alignment improvement percentage was significantly higher in the laser group than in the control group at T1 and T2. At T1, the percentage was $69.41 \pm 15.45\%$ for the laser group compared with $48.85 \pm 17.04\%$ for the control group ($P = .004$). At T2, the laser group LAIP was $89.42 \pm 7.16\%$ compared

with $71.71 \pm 16.18\%$ for the control group and there is no difference in the finishing of alignment.

Peter Miles (2018) ¹¹⁴ assessed the rate of space closure in first bicuspid extraction cases using acceledent devices in ten patients. . Models were taken of the maxillary arch at the start of space closure and just before complete space closure. The space was measured parallel to the occlusal plane from the cusp tips of the teeth mesial and distal to the extraction spaces. The mean rate of tooth movement was slower by 0.13 mm per month on the left side compared with the right side. It was not clinically significant and he concluded that acceledent device has no effect on space closure, only few of them were considered good compliers with the device

Andrew T. Dibiase (2018)⁷ in a randomized clinical trial carried in three hospital included 80 patients and they evaluated rate space closure with acceledent and treatment outcome with fixed appliance. Mean average age of 20yrs and space closure in mandibular arch were evaluated, divided eighty patients into three groups one with acceledent, acceledent sham group and fixed appliance group. The mean rate of tooth movement for control and experimental group was 0.89mm per month irrespective of devices. They stated that a supplementary vibrational force doesn't affect space closure, treatment duration, total no of visits and final outcome of the patient.

Accelerated Tooth Movement By Surgical Means:

Cunningham (1894) ³¹ first proposed the Surgically Facilitated Orthodontic Therapy (SFOT) which is a 100 year old idea that evoked a

succession of surgical refinements designed to (a) accelerated orthodontic tooth movement, (b) limit the quantity and pathologic potential of the foreseeable bacterial load, (c) enhance stability, and (d) reduce the morbidity of orthognathic alternatives.

Cohn-Stock (1921)¹² citing “Angle’s method” removed the palatal bone near the maxillary teeth to facilitate retrusion of single or multiple teeth.

Kretz R (1931)⁷⁹ described a procedure similar to Cunningham’ creating, in effect, a therapeutic fracture of the anterior alveolus. His aggressive manipulation of bone contrasts sharply with modern selective alveolar decortication, a more conservative decortication designed for a proportionate response and a method which prescribes against any aggressive bone manipulation that might compromise vasculature.

Neumann D (1955)¹⁰⁷ quoted that adults, compared with young patients, possess characteristic such as reduced spongy bone, an increase in cortical bone density, a decrease in bone volume, and apical displacement of the marginal bone level, which limit the usefulness of conventional orthodontic treatment. As a result, such problems as marginal bone loss, root exposure, root resorption and extended treatment time often occur in cases involving adults.

Kole H (1959)⁷⁷ brought about decortication of the dentoalveolar process to facilitate orthodontic tooth movement. With some notable refinements, this is the basic technique that is employed today by those who promote the integration of orthodontic therapy and periodontal surgery. The

surgery was limited to the cortex of the dental alveolus, but subapical decortication was inflated by extending buccal and lingual cortical plane incisions until they communicated through the subapical spongiosa. Gross movements with heavy orthodontic forces with active tooth movement were achieved within 6 to 12 weeks and a period of 6 to 8 months of retention offered remarkable stability.

Merrill and Pedersen (1976)¹⁰⁰ claimed that selective alveolar decortications (SAD) limited to the labial alveolar cortex is a reasonable variant where the surgeon may wish to aid simple labial movement and wants to maintain a copious blood supply from the lingual aspect and reflection of lingual mucoperiosteal flaps for labial movement may also contribute to greater stability by producing a more dissipated therapeutic osteopenia.

Generson and Porter (1978)⁵⁵ applied the decortication concept to the treatment of anterior open bites. They departed from aggressive osteotomies and segment mobilization explicitly, stating that “the surgery was done from both the labial and lingual approaches. The bony cuts are made through the cortex. Marrow was able to maintain viability of the osseous segments”. They cite stability and speed as advantages to their technique, and emphasized full thickness (mucoperiosteal) flaps, resecting the neurovascular bundle of the incisive canal. They initiated orthodontic force 3 days after surgery.

Frost HM (1981)⁵¹ found a direct correlation between the severity of bone corticotomy and/or osteotomy and the intensity of the healing response, leading to accelerated bone turnover at the surgical site. This was designated

“Regional Acceleratory Phenomenon” (RAP). RAP was explained as a temporary stage of localized soft and hard-tissue remodeling that resulted in renewal of the injured sites to a normal state through recruitment of osteoclasts and osteoblasts via local intercellular mediator mechanisms involving precursors supporting cells, blood capillaries and lymph.

Suya (1991)¹⁵⁰ revived with “corticotomy-facilitated orthodontics” by reporting his experiences in over 300 patients. He did not connect the buccal and labial incisions, like Kole, but relied on linear interproximal decortication. The style of decortication, divots, lines or other patterns is irrelevant. Only the sum total of therapeutic trauma is significant. Suya’s refinement of Kole’s methods has essentially set the customary for decortication procedures that followed in the modern era.

Liou EJ (1998)⁴⁵ conducted an in-vivo studies based on dental distraction using fifteen orthodontic patients (26 canines, including 15 uppers and 11 lowers) who needed canine retraction and first premolar extraction. At the time of first premolar extraction, the interseptal bone distal to the canine was undermined with a bone bur, grooving vertically inside the extraction socket along the buccal and lingual sides and extending obliquely toward the socket base. Then, a tooth-borne, custom made, intraoral distraction device was placed to distract the canine distally into the extraction space. It was activated 0.5 to 1.0 mm/day immediately after the extraction. Both the upper and lower canines were distracted bodily 6.5 mm into the extraction space within 3 weeks. New alveolar bone was generated and remodeled rapidly in the mesial

periodontal ligament of the canine during and after the distraction. It became mature and identical from the native alveolar bone 3months after distraction. During the distraction, 73% of the first molars did not move mesially and 27% of them moved less than 0.5 mm mesially within 3weeks. The study concluded that the periodontal ligament could be rapidly distracted without complications.

Skinner (2000)¹⁴³ stated that just before World War II, Bichlmayr described a corticotomy for patients older than 16 years, to accelerate tooth movement and reduce relapse for maxillary protrusion. This was employed with canine retraction after first bicuspid extraction, by excision of the buccal and lingual cortical plates at the extraction site.

Hajji SS (2000)⁵⁸ investigated the efficacy of a technique combining orthodontics with alveolar corticotomy + grafting as an effective treatment for class I and II malocclusions in comparison with conventional, non-surgical orthodontic non-extraction and extraction therapies. He found that there were no differences between the RAP or AOO procedure and traditional non extraction treatments, except that treatment was three to four times faster in the corticotomy assisted group and B point increased significantly due to the alveolar augmentation.

Wilcko (2001)¹⁶³ demonstrated two case reports (24-year old man with a Class I severely crowded malocclusion and an overly constricted maxilla with concomitant posterior cross-bites and a 17-year old female with a Class I moderately to severely crowded malocclusion). Surgical technique included buccal and lingual full-thickness flaps, selective partial decortication of the

cortical plates, concomitant bone grafting/augmentation, and primary flap closure. From bonding to debonding, both cases were completed in approximately 6 months and 2 weeks. The canine and premolars in this area were expanded buccally by more than 3mm and an increase in the buccolingual thickness of the overlying buccal bone. Additionally, a preexisting fenestration on the buccal of the first premolar was covered. Both of these findings lend credence to the incorporation of the bone augmentation procedure into the corticotomy surgery because this made it possible to complete the orthodontic treatment with a more intact periodontium.

Seher Sayın (2004)¹³⁴ evaluated the effects of rapid canine distalization on dentoalveolar tissues during the rapid distalization of canine teeth with semi rigid, individual tooth-borne distractors on 43 canine teeth in 18 (seven male and 11 female) patients who required first premolar extractions. The mean age of the patients was 16.7 years. The second premolars and first molars were used as anchor units. The -distractors were activated 0.25 mm three times a day, and the canines were distalized efficiently an average of three weeks. Results showed quick canine distalization with the PDL distraction reduces the treatment time, and both the upper and lower canines can be distalized successfully in three weeks with controlled distal tipping.

Iseri H (2005)⁶⁹ evaluated the effects of dentoalveolar distraction. The study consisted of 20 maxillary canines in 10 growing or adult subjects. First premolars were extracted and the dentoalveolar distraction surgical procedure was performed, and a custom made intraoral, rigid, tooth-borne distraction

device was placed. The canines moved rapidly into the extraction sites in 8 to 14 days, at a rate of 0.8 mm per day. Results concluded that the dentoalveolar distraction procedure is an innovative method that reduces overall orthodontic treatment time by nearly 50%, with no unfavorable effects on surrounding structures.

Iino (2006)⁶⁸ published case report of adult bimaxillary protrusion treated with corticotomy-facilitated orthodontics and titanium miniplates. The maxillary first premolars and mandibular second premolars were extracted at the same time, a corticotomy was performed on the cortical bone of the lingual and buccal sides in the maxillary anterior as well as the mandibular anterior and posterior regions. Leveling was initiated immediately after the corticotomy. The extraction spaces were closed with conventional orthodontic force (approximately 1N per side). The edgewise appliance was adjusted once every 2 weeks. The total treatment time was 1 year.

Lee JK (2007)⁸³ compared the treatment outcomes of orthodontic treatment, anterior segmental osteotomy and corticotomy assisted orthodontic treatment for resolution of bimaxillary dentoalveolar protrusion. 65 Korean adult female were divided as: group 1 (orthodontic treatment), group 2 (corticotomy-assisted orthodontic treatment with skeletal anchorage in the maxilla and anterior segmental osteotomy in the mandible), group 3 (anterior segmental osteotomy in the maxilla and mandible). The findings revealed that orthodontic treatment or corticotomy-assisted orthodontic treatment is indicated for those with severe incisor proclination with normal basal bone

position. Although corticotomy assisted orthodontics advantageous for adult patients those concerned with treatment duration and anterior segmental osteotomy is recommended for bimaxillary dentoalveolar protrusion patients with a gummy smile, basal bone prognathism, relatively normal incisor inclination and relatively underdeveloped chin.

Sebaoun JD (2008)³⁶ investigate the alveolar response to corticotomy as a function of time and proximity to the surgical injury in a rat model. Maxillary buccal and lingual cortical plates were injured in 36 healthy adult rats adjacent to the upper left first molars. Twenty-four animals were euthanized at 3, 7, or 11 weeks. In one group, the maxillae were removed and stripped of soft tissues, and histo-morphometric analysis was performed to study alveolar spongiosa and periodontal ligament (PDL) modeling dynamics. Catabolic activity was analyzed with TRAP cells. Anabolic activity measured using fluorescent bone stain At 3 weeks, the surgery group had significantly ($P < 0.05$) less calcified spongiosa bone surface, greater periodontal ligament surface, higher osteoclast number, and greater lamina dura apposition width. The catabolic activity(osteoclast count) and anabolic activity (apposition rate) were three-fold greater, calcified spongiosa decreased by two-fold, and PDL surface increased by two-fold. This tissue turnover dissipated to a steady state postoperatively in week 11. The impact of the injury was localized to the area immediately adjacent to the decortication injury. So selective alveolar decortication helps in increasing the tissue turn over.

Thomas Wilcko (2008) ⁸⁹ named the new interpretation of the rapid movement as “bone matrix transportation” had made it possible to design a surgical approach, which permits extraction space closure in 3 to 4 weeks. This protocol allows conventional OTM 300% to 400% faster, increases the envelope of movement 2- to 3- fold and alveolar augmentation (periodontally accelerated osteogenic orthodontics or PAOO), and increase alveolar volume providing an alternative to bicuspid extraction. He emphasized that “Mobilization” of any outlined single-tooth blocks of bone (luxation) is totally contraindicated and can lead to intra pulpal and intra osseous morbidity and will not increase the rate of tooth movement.

Su Jung Kim (2009) ¹⁴⁹ developed an interesting technique that is often contrasted with flap reflection methods. Although it does not allow the surgeon to imagine periodontal pathosis, and may indeed aggravate preexisting lesions, they successfully used a method of transmucosal incision “corticision”, wherein a reinforced scalpel is used as a thin chisel to separate the interproximal cortices trans-mucosally, without a surgical flap reflection.

Wilcko MT (2009) ¹⁶² discussed in a study that demineralization of a thin layer of bone over a root prominence after corticotomy surgery can optimize the response to applied orthodontic forces. This physiologic response is consistent with the regional acceleratory phenomenon process. This was substantiated with computerized tomographic and histological evaluations. Orthodontics was combined with full-thickness flap reflection, selective alveolar decortication, ostectomy, and bone grafting to accomplish complete

orthodontic treatment. The accelerated osteogenic orthodontics technique provides for efficient and stable orthodontic tooth movement.

Aboul-Ela SM (2011)³ evaluated miniscrew implant-supported maxillary canine retraction with corticotomy-facilitated orthodontics. Corticotomy-facilitated orthodontics was randomly assigned to 1 side of the maxillary arch at the canine premolar region, and the other side served as the control. By using mini screws as anchorage, canine retraction was initiated via closed nickel-titanium coil springs applying 150 g of force per side. Over a 4-month follow-up period: rate of tooth movement, molar anchorage loss, plaque index, gingival index, probing depth, attachment loss, and gingival recession were examined. The average daily rate of canine retraction was significantly higher on the corticotomy than the control side by 2 times during the first 2 months after the corticotomy surgery.

Hechang Huang (2014)⁶⁵ summarized the molecular mechanism behind the accelerated orthodontic tooth movement. It mainly involves on the alveolar modeling and remodeling, which in turn enhance the activity of osteoclast, osteoblasts, and osteocyte, which are controlled by prostoglandins and cytokines for increased bone modeling and remodeling. Osteoclast plays a crucial role in accelerated orthodontic tooth movement. Osteoblastic cell-derived cytokines M-CSF and the RANKL/OPG ratio determine osteoclast formation and function during any accelerated procedures. M-CSF and increase the RANKL/OPG ratio directly or indirectly through changes in blood flow and hypoxia, and tissue damage, promoting the production of cytokines

including VEGF, TNF-a, interferon-b, matrix metalloproteinase, and others. Osteocytes are abundant in bone cells, may also mediate the effects of that accelerate tooth movement by inducing osteoclast. Osteoblast helps in maintaining normal bone density and mass in alveolar process.

Fleming PS,(2015) ³⁷ in cochrane review assessed the effects of surgically assisted orthodontics in OTM and duration of treatment. In these review four clinical trials which includes 47 patients age ranges between 11 to 33 years. In the primary outcome, increase in rate of tooth movement in surgically assisted orthodontics in comparison with conventional method. In four of the three trials which compared rate of tooth movement for one month period, there is over all increase about 0.61mm more tooth movement compared to conventional methods. Two trials assessed rate of orthodontic tooth movement over a three month period, the surgical intervention resulted in 2.03 mm more tooth movement after three months of treatment.

Donald J. Ferguson (2015) ⁴⁹ reviewed the scope of treatment offered by periodontally accelerated osteogenic orthodontics. PAOO treatment expands the possibility of conventional orthodontic treatment in the adult 2-fold to 3-fold in most spatial dimensions. PAOO may offer a possible alternative, When orthognathic surgery is judged too expensive or risky, PAOO should be considered for solving imbalances secondary to alveolar deficiencies in the vertical and transverse dimensions.

Alaa M. H. Alfawal (2018) ³ evaluated the effectiveness of two minimally invasive surgical procedures in the acceleration of canine retraction:

piezocision and laser-assisted flapless corticotomy. 36 Class II division I patients (12 males, 24 females; age range: 15 to 27 years) requiring first upper premolars extraction followed by canine retraction are participated in this study. The rate of canine retraction was significantly greater in the experimental side than in the control side in both groups by two-fold in the first month and 1.5-fold in the second month.

Omar Gibreal (2018) ⁵⁶ evaluated the effectiveness of flapless piezocision-assisted corticotomies in accelerating lower anterior teeth alignment. Thirty-six patients (mean age 20.32 ± 1.96 years) in need of orthodontic treatment with a fixed orthodontic appliance randomly allocated to control and experimental group. After first premolar extraction, five radiographic-guided micro incisions and localized piezoelectric corticotomies were performed on the labial surfaces of the alveolar bone involving the six anterior teeth in order to accelerate alignment for patients in the experimental group, control group received conventional orthodontic treatment. Overall alignment time was measured at the same time little's irregularity index was calculated every month. Overall alignment time was reduced by 59% in the experimental group compared to the control group.

6) Effect Of Mico-Osteoperforations On Tooth Movement:

C.C. Teixeira (2010)²¹ hypothesized that stimulating the expression of inflammatory cytokines, through small perforations of cortical bone, increases the rate of bone remodeling and tooth movement. Forty-eight rats were divided into four groups: 50-Cn force applied to the maxillary first molar (O),force

application plus soft tissue flap (OF), force application plus flap plus 3small perforations of the cortical plate (OFP), and a control group ©. From the 92 cytokines studied, the expression of 37 cytokines increased significantly in all experimental groups, with 21 cytokines showing the highest levels in the OFP group. After 28 days, micro computed tomography, light and fluorescent microscopy, and immuno histochemistry confirmed higher numbers of osteoclasts and bone remodeling activity in the OFP group accompanied by generalized osteoporosity and increased rate of tooth movement.

E. Khoo(2014)⁴² discussed that researchers from the Consortium for Translational Orthodontic Research (CTOR) at New York University College of Dentistry have been able to develop a technique to increase the rate of tooth movement, applying the same biological principles activated during bone remodeling. Taking advantage of this bone repair mechanism, NYU researchers developed a method called Alveocentesis to accelerate tooth movement. Micro-osteoperforations are created in the alveolar bone adjacent to the teeth that need to be moved, under local anesthesia, without the need to raise any flap. This method moves teeth at least twice as fast as the normal rate shown in both animal and human studies. As seen in these case series, the use of conservative osteoperforations may prove to be a useful technique for accelerating tooth movement.

Mani Alikhani (2013)⁹³ conducted a split mouth study on the effect of micro osteoperforations on the rate of tooth movement and the expression of inflammatory markers. Micro-osteoperforations significantly increased the rate

of tooth movement by 2.3-fold; this was accompanied by a significant increase in the levels of inflammatory markers. The patients did not report significant pain or discomfort during or after the procedure, or any other complications. They concluded that micro-osteoperforations is an effective, comfortable, and safe procedure to accelerate tooth movement and significantly reduce the duration of orthodontic treatment.

Hu Long (2013)⁶⁴ in this systematic review evaluated the effectiveness of interventions on accelerating orthodontic tooth movement for which data bases of PubMed, Embase, Science Citation Index, CENTRAL and SINGLE from January 1990 to August 2011 were searched that assessed the effectiveness of interventions on accelerating orthodontic tooth movement. Assessed interventions (low-level laser therapy, corticotomy, electrical current, pulsed electromagnetic fields and dentoalveolar or periodontal distraction)

The systematic review revealed that:

1. Out of all procedures Corticotomy is efficient and safe procedure to accelerate orthodontic tooth movement.
2. Low-level laser therapy is safe but unsuccessful to accelerate orthodontic tooth movement.
3. Current evidence does not disclose whether electrical current and pulsed electromagnetic fields are effective in accelerating orthodontic tooth movement.
4. Dentoalveolar or periodontal distraction is promising in accelerating orthodontic tooth movement but lacks in evidence.

Mani Alikhani (2015)⁹⁴ hypothesized that controlled micro-trauma in the form of micro-osteoperforations (mops) will increase the expression of inflammatory markers that are usually expressed during orthodontic treatment and that this increased response will accelerate both bone resorption and tooth movement.

Chi-Yang Tsaia (2015)¹⁵¹ in this animal study : Forty-five 8-week-old male Sprague-Dawley rats were divided into the following groups: micro-osteoperforation and orthodontic force (MOP + F), corticision and orthodontic force (C + F), and orthodontic force only (F, control) and evaluated the effects on rate of orthodontic tooth movement, total duration was 6 weeks and maxillary first premolar is pulled forward with 50gm of force. There is significant increase in osteoclast cells, reduction in bone density and bone fraction volume in mop and corticision. The distance of tooth movement in the C + F (1.43 ± 0.38 mm) and MOP + F (1.39 ± 0.49 mm) groups was significantly greater than that in the control group (0.93 ± 0.49 mm). Rats subjected to both micro-osteoperforation and corticision showed significant declines in BMD at 3rd and 6th weeks. Reduced bone mineralization may indicate a highly active bone catabolism. Furthermore, this indicates that the RAP occurred after the two surgical operations , the RAP was observed within 2 weeks after flapless micro-osteoperforation and corticision in rats. The limited duration of the RAP indicates that second or third surgical intervention may be required for re inducing RAP and ensuring rapid orthodontic tooth movement.

Tracy Cheung (2016)²⁴ in this animal study Six male Sprague Dawley rats underwent orthodontic force application for tooth movement on both sides of the maxillary dentition and received mini-implant–facilitated mops on only the left maxilla and control on right side . On average, the MOP side (0.54 ± 0.13 mm) showed a 1.86-fold increase in tooth movement compared with the control side (0.29 ± 0.15 mm. In micro ct it shows significant reduction in bone volume fraction in mop side than control side.

Yamile Zamora Escobar(2017)⁴⁶ compared canine distalization using micro osteo perforation in ten young patients. After leveling and aligning tad was placed between the inter radicular area between first molar and second premolar. Microosteo perforation was performed on extraction site and 150 gm of force was applied using e chain and changed every 15 days. Other side of the patient was control side and normal conventional retraction carried out. He found that there is increase in rate of tooth movement by 41 percentage when compared with control side.

Masood Feizbakhsh (2018)⁹⁵ evaluate the effect of MOP in canine retraction. The average rate of tooth movement in the interventional side was 1.3 mm and in the control group was 0.64 mm in 28 days. Micro osteoperforations significantly increased the rate of tooth movement by more than 2-fold when compared to the control side.

Sonal Attri (2018)¹⁴⁵ investigated rate of tooth movement and pain perception in conventional fixed appliance therapy with micro osteo perforation. 2 arm parallel randomized controlled trial consisting of 33 females

and 27 males requiring en-masse retraction following first premolar extractions. Three interventions are placed in the extraction area in equal distance with depth of 3mm and 1.5mm wide for every 28 days directly in the gingival tissue. Mean rate of space closure in the group which received MOP was 0.89 (0.17) mm/month in the maxilla (right) and 0.88 (0.21) mm/month in the maxilla (left) and 0.80 (0.19) mm/month in the mandible (right) and 0.73 (0.1) mm/month in the mandible (left). in the control group, mean rate of space closure was 0.63 (0.11) mm/month in the maxilla (right) and 0.53 (0.19) mm/month in the maxilla (left); 0.53 (0.1) mm/month in the mandible (right) and 0.49 (0.1) mm/month in the mandible (left). There is no significant difference in pain perception. This randomized clinical trial concluded that practitioners could consider using MOPs as a minimally invasive tool if acceleration of OTM is required

Saritha Sivarajan (2018) ¹⁴² investigated the effect of micro osteoperforation (MOP) on mini-implant supported canine retraction using fixed appliances. Thirty subjects (seven males and 23 females) with a mean age of 22.2 (3.72) years were randomized into three groups: Group 1 (MOP 4-weekly maxilla/8-weekly mandible, Group 2 (MOP 8-weekly maxilla/12-weekly mandible, and Group 3 (MOP 12-weekly maxilla/4-weekly mandible, measured at 4-week intervals over 16 weeks. Mean overall canine retraction was 4.16 (1.62) mm with MOP and 3.06 (1.64) mm without MOP. In this study they conclude that MOP was associated with statistically significantly increased overall canine retraction of 1.1 mm over a 16-week period of study.

There were only diminutive differences in tooth movement when intervals of 4, 8, and 12 week MOP were used.

7) Root resorption

Pongsri brudvik and per rygh (1993)¹⁷ in his electron microscopic investigation he concluded that OIRR is associated with local trauma ,over compression of pdl .In this study he studied more detailed about the root surface during the initial penetration of cells into precementum and mineralized cementum .This study concluded that initial root resorption occurs at the periphery of the necrotic pdl, where mononucleated cells not stained by tartrate resistant acid phosphatase (trap),these trap cells are the first cells to penetrate the root surface.

Pongsribrudvik and per rygh (1994)⁵ in this transmission electron microscopic study he found cells responsible for resorption , mono-nucleated macrophage-like cells were responsible for removal of the necrotic tissue and also for resorption of the surface parts of the root cementum. Mngc showed many morphological traits similar to the observed odontoclasts and osteoclasts. Multi-nucleated clast-like cells with ruffled border were only found in resorption lacunae and bone.

Edward F. Harris (2000)⁴¹ stated that root resorption is common a consequence during orthodontic treatment. It is normal and constant remodeling process that occurs due to oral micro traumas. Irreversible root shortening occurs due to excessive forces, reversible resorption corrected by appositional repair. OIRR occurs adjacent to the hyalinized tissue during and

after the removal of hyalinization. Intrusion causes more root resorption and the biomechanics which we used and cortical bone plays major role in root resorption, but persons genotype had strong correlation with root resorption.

GR Segal (2004)⁴⁶ in his meta analysis more than 10 studies are included. Pre orthodontic and post orthodontic xrays and amount of apical displacement were noted. Many studies states that longer the treatment duration cause more root resorption. He concluded that the amount of total apical displacement of root apex and longer duration causes root resorption .In addition the patients with predisposed factors may result in increased EARR.

Shaza K. Abass (2007)¹²⁵ investigated factors among individuals in their susceptibility to orthodontic resorption. Root resorption factors related to patients or treatments such as the type of malocclusion, appliance used, the nature of force, duration of treatment, missing teeth, trauma, systemic factors, habits, and gender, however these factors couldn't explain on certain individuals. Depending on the genetic background, reaction to the orthodontic force varies. G genetic variation accounts for approximately 64%. This polymorphism marker lies close to TNFRSF11A gene, suggesting that it closely linked one contributes to the susceptibility to EARR. The TNFRSF11A gene codes for RANK, an essential signaling molecule in osteoclast differentiation and function.

Lam L. Cheng (2010)⁸ studied the root resorption craters with 4 or 8 weeks of retention after 4 weeks of continuous light or heavy orthodontic force application. Four patients divided in to two groups who requires first bicuspid

extraction. The maxillary left and right first premolars were loaded with light (25 g) or heavy (225 g) orthodontic force for 4 weeks. After 4 or 8 weeks of retention, the maxillary first premolars were extracted. Less root resorption was repaired by new cementum after heavy orthodontic force application and short retention time. The reparative processes depend on time, with longer retention time yielding the most amount of repair. Reparative processes seemed to commence at the central part of the resorption cavity and expand to the periphery. He concluded that Root resorption cavities have the potential to repair regardless of the orthodontic force magnitude.

Belinda weltman (2010)¹⁶¹ in his systematic review he evaluated the root resorption as an outcome of orthodontic tooth movement. This study suggests during orthodontic treatment increase in incidence of root resorption and there might be chance because of heavy forces. Root resorption not associated with arch wire sequencing, bracket prescription and self ligation. Pause in orthodontic treatment about two to three months helps in total decrease in root resorption.

Yan huang (2010)⁶⁷ compared the root shortening between en mass retraction and two step retraction. 52 patients were selected either with class I or class II malocclusion which requires first premolar extraction. After initial alignment and leveling retracted either using enmass or two step method using closed niti coil spring of 150 gm force. There is an increase in treatment duration in two step method, but the amount of resorption is not significant in both methods. . The average root shortening of maxillary central and lateral

incisors was 0.43 ± 0.12 mm and 0.58 ± 0.10 mm, respectively, and that of mandibular central and lateral incisors was 0.23 ± 0.07 mm and 0.22 ± 0.06 mm, respectively.

Henrik Lund (2012)⁸⁸ investigated the severity of root resorption using cbct. 152 patients (65 boys, 87 girls) with mean age 15.2yrs involved in this study. CBCT is taken on three occasions before treatment, six months after treatment, and after completing the treatment. At the 6-month control, the highest frequencies of root shortening >1 mm were found at both roots of upper two-rooted premolars (29.5%), lateral incisors (upper 16.5%, lower 16%), and upper, single-rooted premolars (16%). Few roots had shortenings >2 mm, and none had shortening >4 mm. At endpoint, the highest frequencies of root shortenings exceeding >1 mm were found at lateral incisors (upper 56.3%, lower 43.1%), followed by upper central incisors (41.4%). Root shortenings >4 mm were found in 2.6% of upper incisors and in the palatal root of two-rooted upper premolars. CBCT technique thus can provide more valid and accurate information about root resorption.

Marina G. Roscoe (2015)¹²³ in a systematic review assessed the association between orthodontic force system and root resorption. 10 to 70 patients were selected. This study concluded that a positive correlation exists between increased force level and root resorption. A stop in the tooth movement is beneficial for the cementum to repair.

V Krishnan (2017)⁸¹ states that proper medical history and assessment of predisposing factors, like root morphology and shape and careful planning

and execution of orthodontic mechanics may reduce the incidence of root resorption to an extent. In between mid treatment radiograph has to be taken to identify root resorption if required adequate rest period has to be given to promote the anatomic repair of root.

Alexander Dudic (2017)⁴⁰ investigated the amount cervical root resorption and its associated factors. 30 subjects (20 females, 10 males) with an age range of 11.3 to 43.0 years were included in this split mouth study. 59 premolars were moved buccally for two months with 1n force. Contralateral 58 premolars served as control. Teeth were extracted and scanned with micro ct and volumetric evaluation done. Higher amount of cervical root resorption was detected in the orthodontically moved teeth (0.00055 mm³) compared to controls (0.00003 mm³; teeth located in mandible shows more resorption than maxilla and the resorption was correlated with amount of tooth movement.

Tiffany Teen Yu Huang (2017)⁶⁶ the null hypothesis of his was to there is no significant difference in root resorption by gradually increasing or decreasing the force generated by magnets. Twenty maxillary first premolars from 10 patients were subjected to ascending (25– 225 g, magnets in attraction) and descending (225 to 25 g, magnets in repulsion) buccal forces using a split mouth over an 8-week period. Polyvinyl impression taken at 0,4 and 8th week then teeth were extracted and scanned with micro ct and volumetric evaluation done. OIRR with ascending force was 1.20 mm³, and with descending force was 1.25 mm³. He states that there is no difference between orthodontically in ascending or descending forces and the buccal side shows more OIRR.

Amal Alkebsi (2018)² assessed the effect of micro-osteoperforations on the rate of tooth movement during canine retraction in adults with Class II malocclusion. When a tooth subjected to orthodontic force the periodontal ligament undergoes compression between alveolar bone and tooth in the direction of force. When heavy forces are applied pdl get injured and hyalinization occurs. In some studies it is reported that remodeling of the pdl is closely associated with resorption. Macrophage that appear initially in necrotic area converted in to multinucleated giant cells (odontoclast cells) that attacks cementum and dentin. During the removal hyalinized layer it also lead to removal of cementoid layer actually protecting layer. This cause raw cemental surface that can be easily attacked by odontoclasts. Resorption occurs most commonly in apical third the main reason was fulcrum is occlusal to the apical half of the root and the differences in the direction of the periodontal fibers apical third is covered by cellular cementum and increase in number of blood vessels toward the apex of the roots which makes it more liable to trauma and cell injury reactions Macrophage colony stimulating factor is essential for the proliferation and differentiation osteoclasts. OPG/RANKL/RANK system is a key mediator in osteoclastogenesis.

Donald J. Ferguson (2018)⁴⁹ compared root resorption of maxillary central incisor followed by with corticotomy and without corticotomy. Sample consist of totally 54 patients divided in to two groups, non extraction with corticotomy and without corticotomy. Edgewise 022 slot used for the treatment. Periapical radiograph taken before treatment and after treatment

using paralleling technique to assess root resorption. In this study root resorption is greater in conventional group than corticotomy group. This may be due to in corticotomy group, increased tissue turn over and there by reducing the hyalinization.

Emmanuel Chan (2018)²² investigated the effects of micro-osteoperforations on orthodontic root resorption with micro computed tomography. Study involving 20 patients s (8 male, 12 female)who required therapeutic extraction of first premolar .this was split mouth study, mop procedure done on one side and 17*25 tma spring with 150gm buccal tipping force on first premolar applied for 28 days. After 28 days first premolar extracted and micro computed tomography scanning was done to assess the root volume. In this study, micro-osteoperforations were associated with greater root resorption crater volumes compared with the controls. Premolars treated with micro osteoperforation demonstrated greater root resorption in all 4 surfaces than the control side. Histological studies shows that rap decreases the hyalinization period and there by reducing root resorption. So that the surgically assisted accelerated tooth movements on root resorption has been unclear.

Linn Haugland (2018)⁶¹ in a systemic review and meta analysis studied the effects of effects on OIIRR of biologic factors and adjunctive therapies in human and animal subjects.9 human and 36 animal studies were included in this study and he stated that administration of fluoride, thyroxine and steroids

decreased OIIRR but corticotomy increases the OIRR. The effect of OIRR increased with increased exposure of cortical bone and higher volume.

Aikaterini Samandara (2018)¹²⁹ in his systematic review, evaluated orthodontically induced root resorption using CBCT. At the end of orthodontic tooth movement a mean average of 0.86mm of root resorption was found. Based on this study, CBCT seems to be a reliable tool for assessing OIRR during or post orthodontic treatment.

Material and Methods

MATERIAL AND METHODS

Patient selection

Inclusion and Exclusion criteria Patient data

Armamentarium

Method- Procedure for MOP

Radiograph evaluation and measurements

Statistics

The prospective clinical study was approved by the Institutional Review Board of Ragas Dental College.

Patient selection

Patients who reported to the Department of Orthodontics at Ragas Dental College and Hospital, Chennai, India, between August 2017 and November 2017 were screened for the study. 40 adult subjects were screened for the study of which 14 who met the inclusion criteria were enrolled for this prospective clinical study. The procedure was explained to the subjects. Out of which 10 subjects (3 males & 7 females) were willing to undergo additional procedure which may influence the duration of treatment were included. The skeletal and dental characteristics of the patients are plotted as shown in (Table 1).

Criteria for sample selection Inclusion criteria

1. Angles Class I malocclusion
2. Adult patients between the age of 18-25 years
3. Extraction of all first four premolars
4. Thick periodontal biotype
5. No history of active bone loss or periodontal disease
6. No smoking
7. Good oral hygiene

Exclusion criteria

1. Long term use of antibiotics, anti inflammatory drugs
2. Systemic diseases
3. Previous orthodontic treatment
4. Severe gingival recession
5. Root resorption

TABLE 1: COMPARISON OF THE SKELETAL AND DENTAL CHARACTERISTICS OF THE PATIENTS

	MOP GROUP MEAN	STANDARD DEVIATION
SNA(°)	82 ⁰	±2
SNB(°)	79 ⁰	±2
ANB(°)	3 ⁰	±1
GoGn-SN(°)	34 ⁰	±2
U1-NA(°)	32 ⁰	±3
L1-NB(°)	38 ⁰	±2
U1-SN(°)	119 ⁰	±3
IMPA(°)	105 ⁰	±4
Overjet(mm)	6 mm	±1

Patient data

Subjects included in the study had Angles Class I malocclusion with arch length tooth size discrepancy that required the removal of all four first bicuspid. A written consent was obtained from the patients who met the inclusion criteria.

ARMAMENTARIUM:

- ROTH prescription brackets 0.022” slot(American orthodontics)
- MOP device* [fig.4](Propel)
- Nickel Titanium closed coil springs (medium Sentalloy 200gms , G&H Orthodontics) [fig.2]
- Disposable 26 gauge needle and syringe [fig.1]
- Local anesthetic (2%lidocaine with 1:100,000 epinephrine) and topical anesthetic spray [fig.1]
- 1.5x8mm TAD (ORTHO ONE) [fig.7]
- Alginate impression material
- Dental stone
- Chlorhexidine mouth rinse (0.12%) [fig.1]
- Digital vernier calliper [fig.5]
- Dontrix gauge [fig.6]
- CBCT root measurement [fig.8]

Figure 1: Armamentarium



Figure 2: NiTi closed coil spring (medium sentalloy* 200gms)



FIGURE 3: 0.019 X 0.025 SS WIRE WITH SOLDERED HOOKS

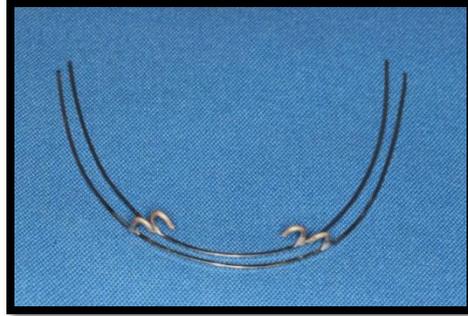


Figure 4: MOP DEVICE (PROPEL SECOND GENERATION)



FIGURE 5: DIGITAL VERNIER CALLIPER



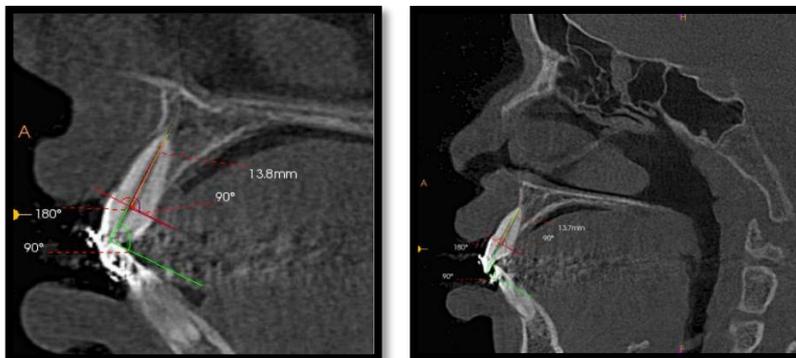
FIGURE 6: DONTRIX GAUGE



Figure 7: TAD



Figure 8: ROOT MEASUREMENT IN CBCT



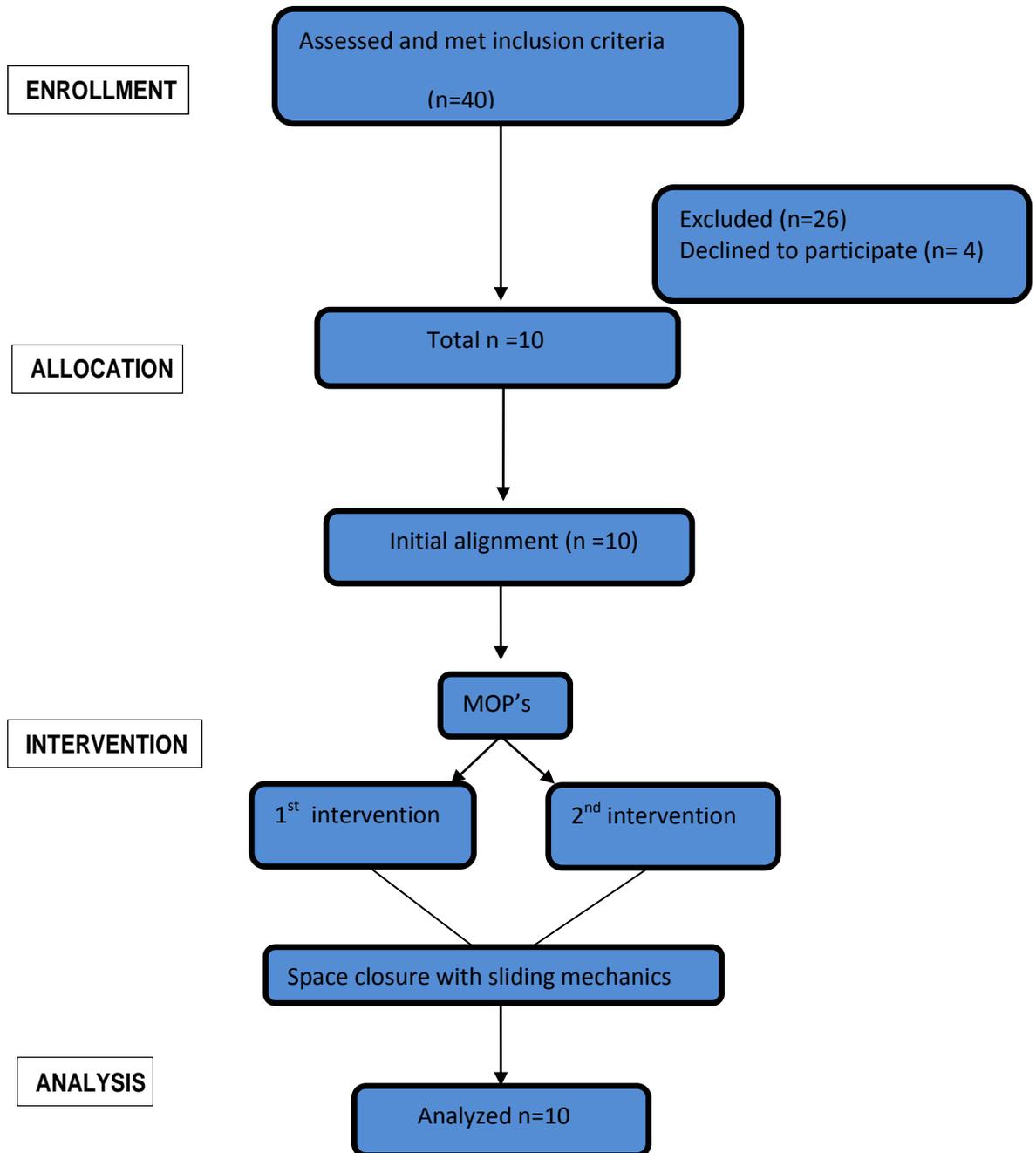
Method:

All Patients were bonded with ROTH prescription brackets (0.022" slot). All four first bicuspid were extracted before leveling and aligning. Both the arches were aligned and leveled till a 19×25 stainless steel wire fitted passively in the bracket slot. A 0.019" x 0.025" SS working wire soldered with brass hooks between the lateral incisor and the canine for anterior retraction were placed in the upper and lower arch. A 1.5×8mm miniscrew was placed between first molar and second premolar before retraction in all quadrants (figure 7). The sequential progression of treatment in shown in Figure 8.

A panoramic x ray was taken after leveling and aligning to evaluate the root proximity and root morphology. The patient was asked to rinse with chlorhexidine mouthrinse before the procedure. After the application of topical local anesthetic spray, the buccal mucosa of the maxillary and mandibular arch was infiltrated with 2ml of 2% lignocaine. All patients received three MOPs between each tooth starting from distal of canine to the distal of contralateral canine in both the arches (fig.10,11) using a disposable second generation MOP device by PROPEL Orthodontics (Ossing, NY). Each perforation with a depth of 3mm, 5mm, 7mm were given from the attached gingiva to the apex. The device has got a retractable sheath to keep the soft tissue taut and to prevent any damage to soft tissue. Line marks on sleeve indicate depth at 3mm, 5mm, and 7mm.

The MOPs was repeated after two months to evaluate the effect of second intervention on rate of tooth movement. At the end of four months the study was concluded. En masse retraction of the anterior segment was carried out, with 19×25 SS wire with soldered brass hooks using 200gm caliberated Niti closed coil spring. The Niti closed coil spring was placed from the soldered hook to the TAD. Any distortion of the coil springs were checked and replaced immediately if distorted. The sequence of events during the study is summarized in Table 2.

Chart 1: CONSORT diagram showing the flow of participants through the trial



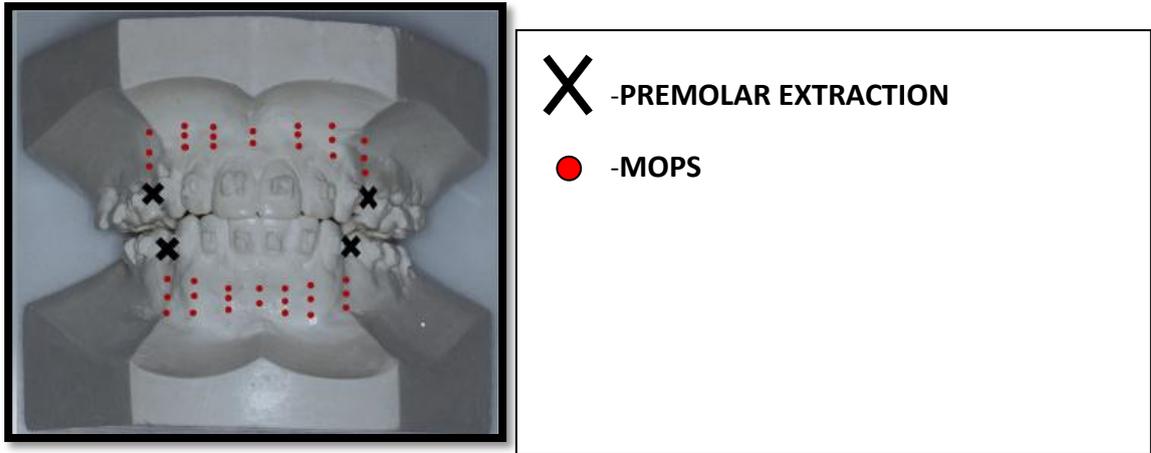


FIGURE 9: EXPERIMENTAL MODEL

MAXILLA



MANDIBLE



FIGURE 10,11; MOP PROCEDURE

TABLE 2: SEQUENCE OF EVENTS DURING THE STUDY

EVENTS	TIME (MONTH)
Extraction of first bicuspid	1
Levelling and aligning	0-6
Extraction of third molars	NIL
Placement of 19X25 stainless steel with soldered hooks	6
TAD placement	6
MOP (upper and lower arch)	6
2nd intervention	8
Monitoring tooth movement	6-10

Measurements

Measurements were made from study cast taken before retraction and at the end of every month for four months. The distance between the maximum contour of the mesial of second premolar to the maximum contour of distal of canine was measured using a digital caliper. Two reviewers independently assessed the cast using a digital caliper to the nearest two digits. Prior to the commence of measurement, they were calibrated and all definition, land mark and measuring methods were briefed. Their measurements were consistent and with good inter/ intra observer agreement. The average sum of two observation was taken with final value and used throughout the study. CBCT was taken before and after retraction to evaluate RR.

Root length was measured using CBCT data. Reference lines are long axis of the tooth, CEJ and tip of the tooth (figure 11). In sagittal section, of each tooth two lines are constructed, one along the CEJ and the other line on the incisal edges which is parallel to each other. The long axis of the tooth is drawn bisecting these two lines. Root length was measured from CEJ to tip of the root apex.

Cephalometric landmarks identified on radiographs which includes:

Landmarks

Cranial Base superimposition:

- 1) Posterior nasal spine (PNS)
- 2) Anterior nasal spine (ANS)
- 3) A point
- 4) B point
- 5) Pogonion (Pog)
- 6) Gonion (Go)
- 7) Pterygomaxillary fissure (Ptv)
- 8) Orbitale (Or)
- 9) Sella (S)
- 10) Nasion (N)

Maxillary regional superimposition:

- 1) Maxillary incisor tip (U1 tip)
- 2) Maxillary incisor root apex (U1 apex)
- 3) Maxillary mesial buccal cusp tip (U6 tip)
- 4) Maxillary mesial root apex (U6 apex)

Mandibular regional superimposition:

- 1) Mandibular incisor tip (L1 tip)
- 2) Mandibular incisor root apex (L1 apex)
- 3) Mandibular mesial buccal cusp tip (L6 tip)
- 4) Mandibular mesial root apex (L6 apex)

STATISTICAL ANALYSIS

All statistical analysis was performed by using SPSS statistical package for social service (version 23.0, IBM IL, USA). Mean and standard deviation calculation for each outcome variables measured in lateral cephalograms. The descriptive statistics for the outcome variables are presented. Comparison within the groups at different time intervals were assessed by analysis and variance (ANOVA). Multiple comparison analysis was performed with differences in the rate of space closure between maxillary and mandibular were also assessed. $P < 0.05$ was set as the level of significance.

Results

RESULTS

Ten patients who met the inclusion and exclusion criteria participated in this clinical trial

The study was designed to evaluate the following:

- 1) Rate of tooth movement during anterior en-masse retraction with multiple micro-osteoperforations
- 2) Root resorption, if any

The rate of tooth movement was assessed from measurements on study casts using a digital caliper taken at monthly intervals.

Over all rate of tooth movement in monthly intervals (Table 3, Graph 1):

1. The mean rate of tooth movement was 0.946mm/month in maxilla and 0.879mm/month in mandible.
2. The over all rate of tooth movement was 0.912mm/month.
3. Mean rate of tooth movement during
 - First month - 0.8350mm
 - Second month - 0.8505mm
 - Third month - 0.905mm
 - Fourth month -1.061mm

Comparison of rate of tooth movement in the maxilla and mandible at monthly intervals:

1. There was no statistical significant difference in the rate of tooth movement in maxilla and mandible.(Table 4& Graph 2)
2. In paired sample test month 3rd and month 4th shows statistically significant than month 1&2 and month 2 & 3.(Table 5)
3. Paired sample test of maxillary and mandibular rate of tooth movement shows significant increase in the month 3 and 4. (Table 5).
4. The mean rate of tooth movement 0.946mm in maxilla and 0.879mm in mandible. Mean rate of tooth movement was faster in maxilla than mandible and it was clinically significant.(Table 7).
5. Table 7 shows paired sample statistics of maxilla and mandible after adding correlation and significance, shows no significant variation in the rate of tooth movement between maxilla and mandible.
6. Multiple comparison between each month shows no significant difference with other month (Table 8).
7. In descriptive ANOVA test no statistically significant difference between the groups and within the group.(Table 10)
8. When compared between first intervention and second intervention there is increase in rate of tooth movement after second intervention (Graph 3).
9. Table 11 shows significant difference in the rate of tooth movement between first and second intervention. Mean rate of tooth movement after first intervention was 0.8425mm and for the second intervention 0.983mm.

**COMPARISON OF EXTERNAL APICAL ROOT RESORPTION IN
MAXILLARY ANTERIOR TOOTH (Table 11)**

1. Root length was measure and compared between the pre retraction and post retraction CBCT, between pre and post but between teeth, maxillary lateral incisor showed statistical significance compared to maxillary central incisors and canines.

Tables and Graphs

TABLE 3: OVERALL RATE OF TOOTH MOVEMENT AT MONTHLY INTERVALS

Descriptive Statistics					
	N	Minimum	Maximum	Mean	Std. Deviation
M1	20	.52	1.70	.8350	±.30980
M2	20	.40	1.70	.8505	±.33081
M3	20	.4	1.7	.905	±.3332
M4	20	.60	2.24	1.0610	±.35774
Valid N (listwise)	20				

TABLE 4: RATE OF TOOTH MOVEMENT IN MAXILLA AND MANDIBLE

Descriptive Statistics						
		N	Minimum	Maximum	Mean	Std. Deviation
Mandible	M1	10	.52	1.19	.7840	±.28175
	M2	10	.40	1.70	.8600	±.41419
	M3	10	.4	1.1	.810	±.2558
	M4	10	.70	1.40	1.0630	±.22015
	Valid N (listwise)	10				
Maxilla	M1	10	.55	1.70	.8860	±.34271
	M2	10	.60	1.27	.8410	±.24347
	M3	10	.5	1.7	1.000	±.3859
	M4	10	.60	2.24	1.0590	±.47085
	Valid N (listwise)	10				

TABLE 5: PAIRED SAMPLES STATISTICS

Paired sample statistics after adding correlation and p value					
		Mean	Std. Deviation	Correlation	Significance P value
Pair 1	M1	.8350	±.30980	.134	.572
	M2	.8505	±.33081		
Pair 2	M2	.8505	±.33081	.286	.222
	M3	.905	±.3332		
Pair 3	M3	.905	±.3332	.706	.001
	M4	1.0610	±.35774		

TABLE 6 ; PAIRED SAMPLES TEST

		Paired differences					
		Mean	Std. Deviation	95% Confidence Interval of the Difference		df	Significance P value
				Lower	Upper		
Pair 1	M1 - M2	-.01550	±.42176	-.21289	.18189	19	0.871
Pair 2	M2 - M3	-.05450	±.39689	-.24025	.13125	19	0.546
Pair 3	M3 - M4	-.15600	±.26609	-.28053	-.03147	19	0.017

TABLE 7; PAIRED SAMPLES STATISTICS OF MAXILLA AND MANDIBLE -, AFTER ADDING CORRELATION & SIGNIFICANCE

			Mean	Std. Deviation	Correlation	Significance P value
Mandible	Pair 1	M1	.7840	±.28175	-.303	.395
		M2	.8600	± .41419		
	Pair 2	M2	.8600	± .41419	-.038	.918
		M3	.810	± .2558		
	Pair 3	M3	.810	± .2558	.619	.056
		M4	1.0630	± .22015		
Maxilla	Pair 1	M1	.8860	± .34271	.785	.007
		M2	.8410	± .24347		
	Pair 2	M2	.8410	± .24347	.771	.009
		M3	1.000	± .3859		
	Pair 3	M3	1.000	± .3859	.788	.007
		M4	1.0590	± .47085		

TABLE 8: PAIRED SAMPLE TEST

			Paired differences				t	df	Significance P value
			Mean	Std. Deviation	95% Confidence Interval of the Difference				
					lower	Upper			
Mandible	Pair 1	M1 - M2	-.07600	.56718	-.48174	.32974	-.424	9	.682
	Pair 2	M2 - M3	.05000	.49497	-.30408	.40408	.319	9	.757
	Pair 3	M3 - M4	-.25300	.21024	-.40340	.10260	-3.805	9	.004
Maxilla	Pair 1	M1 - M2	.04500	.21376	-.10792	.19792	.666	9	.522
	Pair 2	M2 - M3	-.15900	.25155	-.33895	.02095	-1.999	9	.077
	Pair 3	M3 - M4	-.05900	.29046	-.26678	.14878	-.642	9	.537

TABLE-9 DESCRIPTIVES

	N	Mean	Std. Deviation	95% Confidence Interval for Mean		Minimum	Maximum
				Lower Bound	Upper Bound		
M1	20	.8350	.30980	.6900	.9800	.52	1.70
M2	20	.8505	.33081	.6957	1.0053	.40	1.70
M3	20	.9050	.33321	.7491	1.0609	.40	1.70
M4	20	1.061	.35774	.8936	1.2284	.60	2.24
Total	80	.9129	.33908	.8374	.9883	.40	2.24

TABLE 10 :POST HOC & ANOVA

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	.639	3	.213	1.918	.134
Within Groups	8.444	76	.111		
Total	9.083	79			

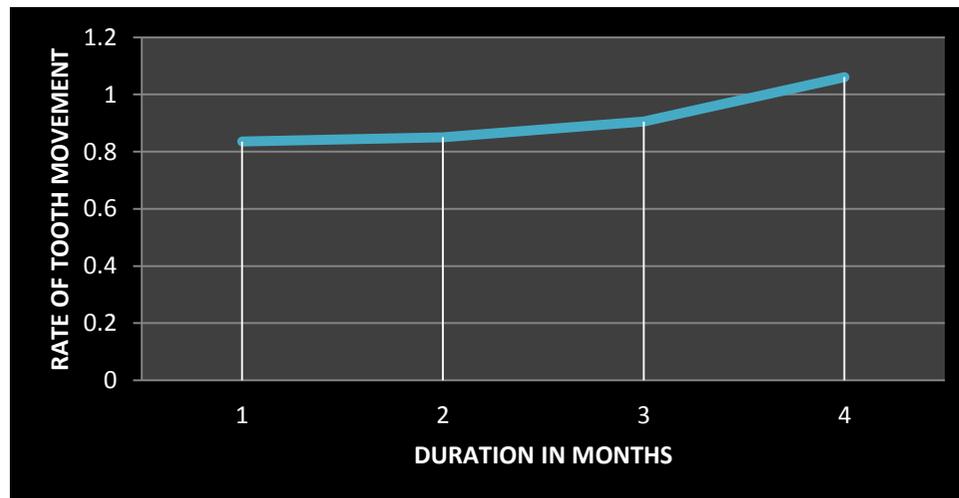
TABLE-10 Comparison of rate of tooth movement between two interventions

	Mean \pm SD	t-value	P – value
First intervention	0.8425\pm0.04	-3.72751	0.0325*
Second intervention	0.9830\pm 0.02		

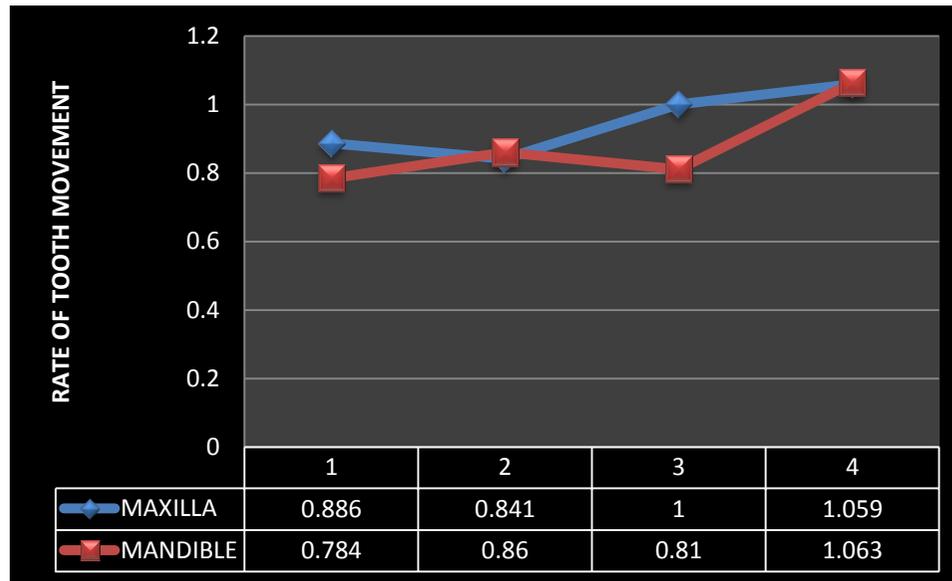
***statistically significant**

t –test

GRAPH 1: OVERALL RATE OF TOOTH MOVEMENT



GRAPH 2 COMPARISON OF RATE OF TOOTH MOVEMENT BETWEEN MAXILLA AND MANDIBLE



GRAPH 3: COMPARISON OF RATE OF TOOTH MOVEMENT BETWEEN FIRST INTERVENTION AND SECOND INTERVENTION

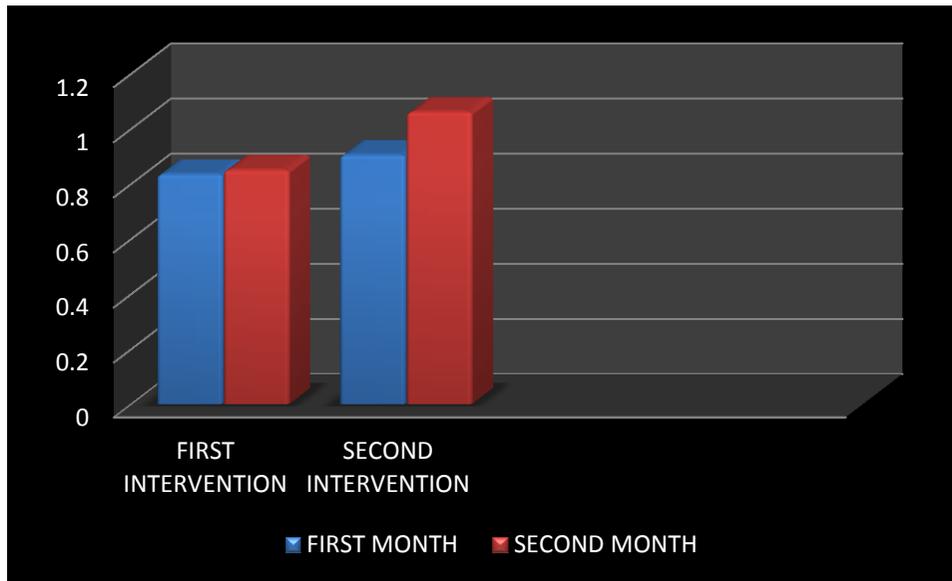


Table 11 COMPARISON OF EXTERNAL APICAL ROOT RESORPTION ON PRE PRERETRACTION AND POST RETRACTION

Tooth number	Before retraction Mean± SD (mm)	After retraction Mean± SD(mm)	t- value	P – value
11	12.46 ± 1.15	11.96 ± 1.25	0.65473	0.2655
12	11.46 ± 1.51	10.68 ± 1.50	0.81632	0.028*
13	16.8 ± 1.23	16.26 ± 1.36	0.65601	0.2651
21	12.66 ± 1.28	12.18 + 1.26	0.59445	0.2843
22	11.4 ± 1.29	10.82± 1.26	0.71643	0.0470*
23	16.64 ± 1.29	16.28 ± 1.32	0.43402	0.3378

*Statistically significant

Representative cases

PRETREATMENT INTRA ORAL PHOTOGRAPHS



AFTER ALIGNMENT AND LEVELLING



MICRO-OSTEOPERFORATIONS IN MAXILLARY & MANDIBULAR ARCH

1ST INTERVENTION



2ND INTERVENTION AFTER 2 MONTHS



RETRACTION MECHANICS

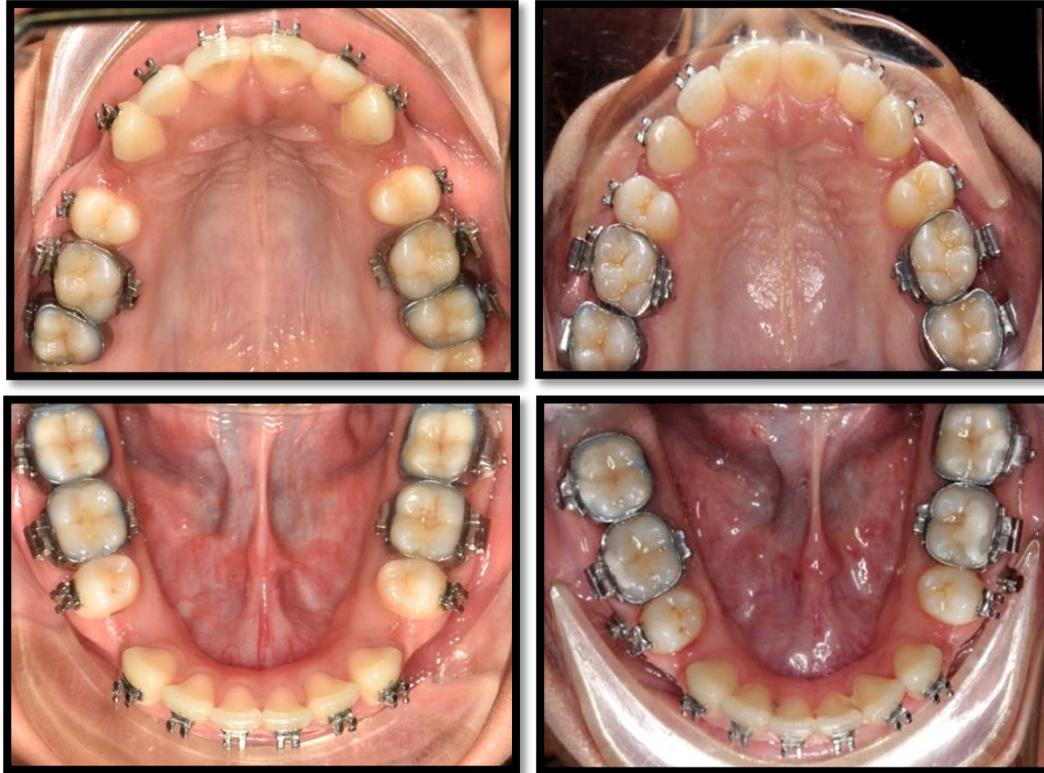


**MOP GROUP
AFTER - 4 MONTHS**



PRE RETRACTION

AFTER 4 MONTHS



LATERAL CEPHALOGRAM



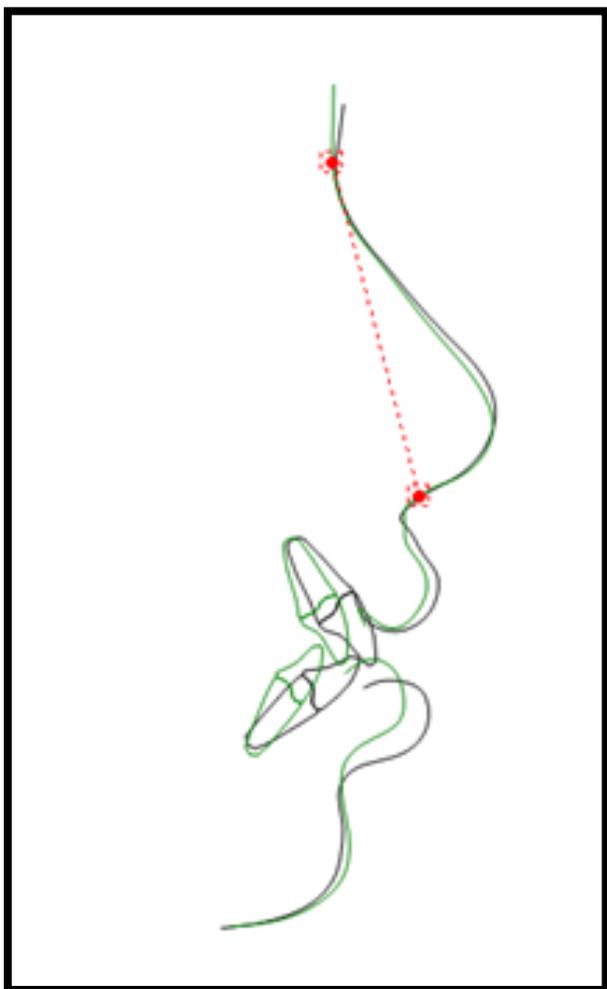
PRETREATMENT



PRE RETRACTION



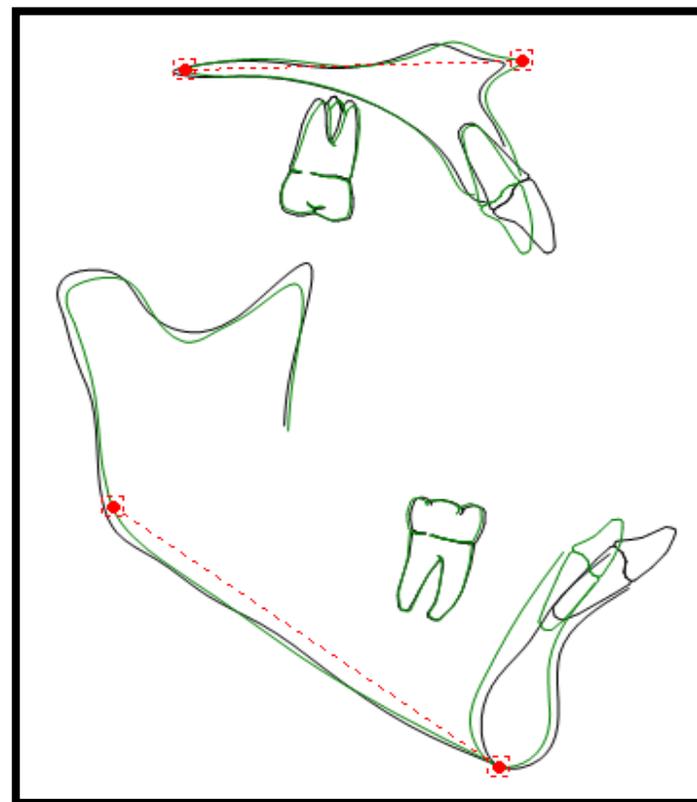
POST RETRACTION



PROFILE SUPERIMPOSITION

PRE RETRACTION AND POST RETRACTION

SUPERIMPOSITION ON PALATAL PLANE



SUPERIMPOSITION ON CORPUS AXIS

**PRE AND POST RETRACTION COMPARISION OF SKELETAL AND
DENTAL PARAMETERS**

CEPHALOMETRIC VARIABLES	PRE RETRACTION	POST RETRACTION
SNA (°)	85°	83°
SNB (°)	82°	82°
ANB (°)	3°	1°
SN- GoGn (°)	33°	28°
UI to NA (mm)	8 mm	4 mm
UI to NA (°)	37°	24°
UI to SN (°)	119°	107°
LI to NB (mm)	9 mm	7 mm
LI to NB (°)	38°	25°
LI to Mnd. Plane (°)	106°	99°
Overjet	6 mm	2 mm
U6 to Ptv	30 mm	29 mm

Discussion

DISCUSSION

Accelerated tooth movement bone remodeling has attracted considerable scientific interest, with an increase in the number of adults seeking orthodontic treatment. It is well known fact that biological activity is increased in younger individuals compared to adults, as a result the treatment duration is prolonged in adults. Some of the iatrogenic effects of prolonged treatment duration are decalcification and root resorption. Prolonged orthodontic treatment is challenging both for the patients and orthodontists and is neither desired nor hygienic. **Aliki Tsihlaki**⁵ reported that the mean duration of comprehensive orthodontic treatment on average requires less than 2 years to complete. So the main focus in treating adult patient is to reduce the treatment duration and minimize the iatrogenic effects.

Histologically, it has been found that when forces are applied, four distinct phases of tooth movement occurs. First initial displacement phase into PDL space, second lag phase / hyalinization phase formed in the PDL and in the third post lags phase tooth moves slowly with significant resorption of adjacent alveolar bone and finally acceleration phase. By minimizing the hyalinization phase /lag phase tooth movement can be accelerated and treatment duration reduced¹³.

The sequence of biological events after loading of orthodontic force occurs as (1) fluid flow changes and matrix strain (2) strain on mechano receptor cells (3) cell activation and (4) tissue remodeling leading to tooth

movement. The mechanoreceptor cells in periodontal tissue include osteocytes and bone lining osteoblasts in alveolar bone and fibroblasts in periodontal ligament (PDL).

Orthodontic tooth movement is characterized by the rapid organization of compression and pressure zones within the PDL and depends on the physical characteristics of the applied force and the biological response of the ligament⁸⁰.

OTM mainly depends on the rate of bone remodeling. It is an aseptic inflammatory response which involves a cascade of events. It has been shown that compressive force induces bone matrix deformation and microcracks; and the accumulation of microscopic cracks in the bone matrix may induce additional damage to osteocytes in the microcrack region. Microcracks are more rampant on the pressure-side than on the tension-side of the tooth, and it has been hypothesized that microcracks were the first damage induced by the orthodontic force to induce osteocyte apoptosis and bone remodeling.¹⁰⁷

Bentolila¹⁵⁴ et al. demonstrated that it is possible to stimulate the activation of intracortical remodeling in rats by creating micro damage within the cortex. **Murshid sakhr**¹²⁷ stated that microcracks may play a role in the commencement of bone resorption on the pressure side of the tooth under the compressive force of orthodontic loading. Decades ago, osteocytes were considered inactive placeholder cells within the bone matrix. Recent data have shown that osteocytes are not passive cells, but instead, they are metabolically active and multifunctional. Several functions have been

anticipated for osteocytes, including osteolysis, regulation of mineralization, and mineral metabolism; they also act as mechano-sensory cells to perceive mechanical stimuli produced from the mechanical loading of bones, and they are regulators of osteoblast and osteoclast function during bone remodeling.

Frost⁵¹ originally proposed that remodeling would occur to repair micro damage in bone. He suggested that interruption of canalicular connections that occurred when cracks crossed them could provide the stimulus to initiate remodeling.

M. Alikhani⁹³ stated that increasing the magnitude of orthodontic force cannot enhance the biological response, and therefore, it cannot be warranted as a methodology to amplify the rate of tooth movement. To increase the rate of tooth movement, the saturation of the biological response must be overcome by supplementary methods.

Many studies evaluated the effectiveness of invasive and non invasive methods for accelerating orthodontic tooth movement. Current evidence revealed that electrical current and pulsed electromagnetic fields are ineffective in accelerating orthodontic tooth movement¹¹⁴. However dentoalveolar or periodontal distraction is promising in accelerating orthodontic tooth movement but lacks convincing evidence. Although invasive procedures like corticotomy and piezocision are relatively safe and are effective to accelerate OTM, because of its invasiveness and morbidity, patients are reluctant to undergo such procedures.

Uribe et al⁵⁰ evaluated perception of patients', parents', and orthodontists 'perspectives on orthodontic treatment duration and techniques for accelerating the rate of tooth movement. The majority of orthodontists deemed a reduction of 20% to 40% in treatment time to be attractive for using alternative techniques to enhance the rate of orthodontic tooth movement. The invasiveness of the procedure was inversely related to its acceptance in all groups. Therefore, the challenge is how to accelerate orthodontic tooth movement in a minimally invasive way?

In an animal study **Hideki kitaura**⁶³ et al reported that IL-12 and IFN- γ strongly inhibit osteoclast formation and orthodontic tooth movement. Similarly, animals that are deficient in chemokine receptor2 (ccl2), which is a receptor for ccl2, or deficient in ccl3, demonstrate a significant reduction in orthodontic tooth movement and number of osteoclasts. Therefore inhibiting inflammatory markers decreases the rate of tooth movement. Increasing the activity of inflammatory markers should significantly increase the rate of tooth movement.

In an animal study **Alikhani et al**⁹⁴ concluded that rate of tooth movement increased significantly, with tooth movement occurring two folds as fast in the MOP group compared with control group because cytokine expression increased in GCF significantly 24hrs after force application in the MOP side than control side.

The outcome of human clinical trial also concluded that pro inflammatory cytokines are crucial mediators of orthodontic tooth movement.

These pro inflammatory markers were increased after the intervention of MOP. The rate of bone remodeling is directly proportional to the level of cytokines expressed.

The lower the level of cytokines, the slower the bone remodels and results in slower rate of tooth movement⁸⁶. Micro perforation might help in increasing the activity of cytokine and at the same time it stimulates the osteocyte cells which plays major role in mechano transduction. Studies by **Alikhani et al**⁹⁴ demonstrated that by performing MOP's in the area where tooth movement need to be accelerated, bone remodeling enables a greater rate of OTM. While clinical trials on animals and humans have proved promising results. In 2016 a randomized clinical trial was conducted in our department to evaluate the effects of micro-osteo perforation during enmass retraction in adult bimaxillary patients along with matched controls. All four first bicuspid were extracted after leveling and aligning. MOP's were performed on the day of extraction and retraction started on the same day. The rate of tooth movement was assessed for a period of 6 months. In the control group extraction of first premolar was done just before retraction and similar force levels were used in both the groups. The results of the trial showed an increased rate of tooth movement in the experimental group compared to control group. About 46% of extraction space closed within two month. Procedures like extraction itself can induce RAP, and may result in increased inflammatory markers and may result in accelerated tooth movement. In order to differentiate between acceleration of tooth movement

caused by extraction or micro perforation the groups were compared with matched controls. However the rate of tooth movement declined after two months¹. Therefore there was need for a second intervention after two months. Hence the present study was done to evaluate the effects of multiple intervention on the rate of tooth movement and root resorption.

In the present study extractions were done before aligning and leveling and TADs were placed for anchorage. MOPs were done from distal of canine to contra lateral canine between the roots of all anterior teeth. A depth of 3, 5, and 7mm of MOPs were done. Interdental area between each tooth was evaluated using OPG to assess for root parallelism and also to avoid root contact. If accidental root contact had happened, patient would have experienced pain. Chances of inadvertent root contact are very rare since the roots were upright and parallel before retraction. However, in case of accidental damage or root contact, damage is unlikely as documented in the literature by **Shakeel ahmed et al**⁷⁵.

The rate of tooth movement was evaluated from plaster models taken every month for a period of four months. The overall rate of tooth movement as shown in graph 1 showed constant increase in the rate of tooth movement. The mean rate of tooth movement in maxilla and mandible are depicted in graph 2. The mean rate of tooth movement between the first and second intervention shows statistical significance as shown in table 11.

The results of our study are in concurrence with **Sonal attri et al**¹⁴⁵ and Mani **Alikhani et al**⁹⁴ which showed a increased in rate of tooth

movement followed by MOPs using proper device. However, another study done by **Alkebsi et al 2018** also assessed the efficacy of MOPs in accelerating OTM. Our results are contradictory to their study as they concluded that MOPs did not enhance the rate of tooth movement. This could be due to the fact that a mini implant was used to perform MOPs in their study, where as in our study over all rate of tooth movement increased every month.

The cutting edge of the propel device is made of surgical grade SS which does not yield to breakage during use. It is made up of 17-4 martensitic stainless steel, that combines high strength and hardness with excellent corrosion resistance. On the other hand mini implants are designed to provide anchorage without causing damage to the cortical bone. **Baumgaertel¹¹** et al reported that buccal cortical bone thickness increased with the increase in distance from the alveolar crest in the mandible and maxillary anterior region. More cortical bone thickness in mandible than maxilla. This is evident from the results of our study as shown in table 4. The rate of tooth movement is more in maxilla compared to mandible and statistical significance owing to dense cortical bone in mandible.

The biologic mechanisms underlying the increased rate of tooth movement appear to involve amplification and acceleration of normal biologic processes after a bony injury. RAP decreases the period of hyalinization through the accelerated appearance of macrophages that remove the hyaline tissue.

Light forces are commonly used in orthodontics to achieve faster orthodontic tooth movement. High force levels do not necessarily increase tooth movement as overloading of periodontal tissue leads to hyalinization and ischemia. Hence 200gms of force using a calibrated Niti coil spring was used in our study.

Saritha sivarajan et al¹⁴² evaluated the rate of canine retraction using multiple MOPs and found only a small difference in tooth movement. Whereas in our study after the second intervention there was an increase in the rate of tooth movement (graph 3).

Aboul-ela³ et al. investigated on rate of canine retraction with corticotomy- facilitated orthodontics. Results showed that the rate of space closure peaked during the first 2 months and reduced by the end of the 4th month. The study by **Jonathan nicozis**⁴¹ stated that the RAP phenomenon lasted only for 8-10 weeks using MOP. .

Cho²⁵ et al also reported that the mean tooth movement increased to 4.41 times and 2.44 times in the maxilla and mandible, respectively, after applying 24 decortication dots with flap surgery in dogs. Therefore, it is logical to come to the conclusion that as the number of perforation are increased causing more damage and recruits more osteoclast thereby accelerated tooth movement.

Acceleration in tooth movement is evident in our study. This correlates with the findings of **Alikhani et al**⁸⁸, who reported that 4 mops were able to increase the rate of tooth movement more than 2 folds when

compared to one osteoperforation. In our study total of 40 micro perforations were performed in maxilla and mandible. Increase in the magnitude of trauma to the bone increases the duration of the RAP. The acceleration of tooth movement is relative to the magnitude of the insult. This is evident as there was statistically significant difference between the first and second intervention (table 10)

Yamile Zamora Escobar⁴⁶ compared canine distalization using micro osteoperforation and he reported that increase in rate of tooth movement by 41 percentage on the experimental side.

Frost⁵¹ observed a direct correlation between the severity of surgical insult and intensity of the healing response are attributed it to RAP. This is a temporary window of increased localized remodeling in an effort to rebuild surgical site. **Mcbride**⁹⁷ evaluated how different amounts of surgical insult affect the bone around treated teeth in an animal study. He concluded that increased surgical insults produce less dense and less mature bone due to increased osteoclastic activity. Increased surgical insults in our study 20 MOPs were performed in each arch. Therefore, it is evident that the accelerated tooth movement in the MOPs group is not due to reduced bony tissue or transient osteopenia as in corticotomy but by activating the patient's own biology.

In our study the rate of acceleration was significantly less than those reported by wilcko⁸⁹. The corticotomy procedure invoke the RAP wherein the effect is expected to last for 4-6 months. This may be due to high insult to

the bone. So repeated interventions are needed for the steady acceleration of tooth movement when performing micro osteo perforation.

Anchorage plays a crucial in orthodontics. To avoid unwanted tooth movements and maintain treatment success, these reciprocal forces must be minimal. Anchor losses by mesial movement of molars during space closure after premolar extractions are common. The study by **Badri thiruvengadachari**^{3, 4} who reported a mean anchorage loss of 1.6 mm in maxilla and 1.7 mm in mandible in samples without TADs in canine retraction. Therefore in our study tad assisted anchorage were employed to avoid anchor loss.

Some studies suggest that accelerated orthodontics can cause root resorption. However literature evidence is scant in terms of root resorption caused by MOPs. Our study also tested the effect of MOPS on root resorption. **Emmanuel Chan**²² evaluated the effects of MOP's on orthodontic root resorption with micro-CT. In their study, MOP's were associated with greater root resorption crater volumes compared with the controls. Premolars treated with MOPs demonstrated greater root resorption in all 4 surfaces than the control side. The cause of resorption in their study is unclear as it may be either due to MOP or buccal tipping force, whereas the results of our study showed no difference in root resorption between pre and post retraction except for laterals which was clinically significant (table 11).

Van Gemert⁸² in his thesis study claimed that the extent of the micro-damage and the most pronounced effects on bone produced by MOP

placement extend no more than 1.5 mm from the placement site. MOPs induce a small and momentary distant demineralization extending at least 3mm from the placement site. If there is sufficient inter radicular space and roots surfaces are away from the mop site the chances of root resorption can be minimized. In our study MOPs with 7mm depth are placed more apical. In the cervical region inter radicular distance is less and the effect might be transmitted to the root surface. Cervical region is mainly composed of acellular cementum which is not capable of repair. Apical region is composed of cellular cementum capable of repair by recruiting osteoclast cells¹¹⁰. To reduce the risk of root resorption MOPs were placed more apically. Since the inter radicular distance is more and the roots are fairly upright.

In our study we evaluated the EARR using CBCT. Pre retraction CBCT and post retraction CBCT were taken. The reliability of our method of assessing root resorption with CBCT is supported by a recent study (COUTNEY AMAN 2018). Similarly **Yaqi deng**¹⁶⁶ studied on reliability of CBCT on root resorption. He concluded that root resorption established in CBCT was more reliable and accurate than the two dimensional approach. Amount of root resorption was more in maxillary lateral incisors, maxillary central incisors and mandibular anterior teeth. Our results were in concordance with their study, as maxillary lateral incisor showed more EARR than maxillary central and canine (table 11).

The effect of micro-osteoperforations and other techniques related to surgically assisted tooth movement on root resorption has been unclear. RAP

decreases the period of hyalinization and also the resultant osteoporotic environment has less mechanical resistance against tooth movement through the alveolar bone. This should theoretically minimize hyalinization of the periodontal ligament. It is possible that excessive localized activation of osteoclasts, as seen after surgical procedures such as micro-osteoperforations, can lead to an increase in odontoclastic activity¹¹⁰.

The mechanism of tooth movement is multifaceted and need strictly coordinated regulation of pdl, osteoclasts, osteocytes and osteoblasts. Hence future studies with larger sample size to strengthen the findings of the present study should be carried out.

Summary & Conclusion

SUMMARY AND CONCLUSION

In this study we evaluated the effects of Micro osteoperforation on the rate of tooth movement during enmasse space closure with two interventions. The study was completed at the end of four months. The results of this clinical trial show that there is an increase in the rate of tooth movement. However the effects decline after 8 weeks. This implies that there is a need for repeated interventions.

The effect of micro osteoperforations on root resorption was also evaluated in our study using CBCT data. The results show that maxillary lateral incisor had more predisposition to root resorption than maxillary centrals and canines.

Micro osteoperforation could be a reliable method for accelerating orthodontic tooth movement but it incurs additional costs and repeated interventions.

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Annexures

ANNEXURE – I



RAGAS DENTAL COLLEGE & HOSPITAL

(Unit of Ragas Educational Society)

Recognized by the Dental Council of India, New Delhi

Affiliated to The Tamilnadu Dr. M.G.R. Medical University, Chennai

2/102, East Coast Road, Uthandi, Chennai - 600 119. INDIA

Tele : (044) 24530002, 24530003 - 06. Principal (Dir) 24530001 Fax : (044) 24530009

TO WHOM SO EVER IT MAY CONCERN

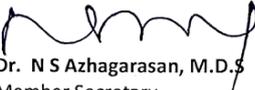
Date: 18-01-19

Chennai.

From,

The Institutional Review Board,
Ragas Dental College and Hospital,
Uthandi, Chennai-600119.

The Dissertation topic titled "THE IMPACT OF MICRO OSTEO PERFORATION ON THE RATE OF TOOTH MOVEMENT AND ROOT RESORPTION" submitted by Dr. BAJATH . B has been approved by the Institutional Review Board of Ragas Dental College & Hospital.


Dr. N S Azhagarasan, M.D.S
Member Secretary,
Institutional Ethical Board,
Ragas Dental College and Hospital,
Uthandi, Chennai-600119.

ANNEXURE – I



Urkund Analysis Result

Analysed Document: THESIS FINAL.docx (D47709584)
Submitted: 2/7/2019 8:57:00 PM
Submitted By: baji.jan@gmail.com
Significance: 2 %

Sources included in the report:

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