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Effectiveness of Non-Conventional Methods for Accelerated Orthodontic Tooth Movement

A Project submitted to
The college of Dentistry, University of Baghdad, Department of Orthodontics in Partial Fulfillment for the Bachelor of Dental Surgery
By

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Certifiation of the Supervisor

I certify that this project entitled "Effectiveness of Non-Conventional Methods for Accelerated Orthodontic Tooth Movement" was prepared by the fifth-year student Taha Ali Abdelhussein under my supervision at the College of Dentistry/University of Baghdad in partial fulfilment of the graduation requirements for the Bachelor Degree in Dentistry.

Supervisor's name:

Assit. Prof. Dr. Ali Mohammed Hameed

April, 2023

Dedication

I dedicate this research to all our professors at Baghdad College Of Dentistry in recognition of their great efforts. To my family for their unlimited support throughout all these years and to all our dear friends and colleagues ... Finally, my appreciation and thanks to everyone taught me a letter from my childhood until today.

Acknowledgment

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List of Abbreviations

1,25-DHCC	1,25-dihydroxycholecalciferol
Al-Ga -As	Aluminum- gallium-arsenide
ATP	Adenosine triphosphate
CBs	Conventional brackets
Cyclooxygenase-2	COX2
DO	Distraction osteogenesis
EGE	Epidermal growth factor
GCF	Gingival crevicular fluid
IGF-1	Tnsulin-like growth factor-1
Interleukin-1 beta	IL1β
Interleukin-6	IL-6
IVIg	Intravenous immunoglobulin
LED	Light emitting diode
LILT	Low intensity laser therapy
LLLT	Low level light therapy
MMPs	Matrix metalloproteinases
MOPs	Micro osteoperforations
OTM	Orthodontic tooth movement
PAOO	Periodontal accelerated osteogenic orthodontics
PDL	Periodontal ligament
PGE1	Prostaglandin E1
PGE2	Prostaglandin E2
PRF	Platelet rich fibrin
PRP	Platelet rich plasma
PRP	Platelet rich plasma
PTH	Parathyroid hormone

RAP	Regional accelerated phenomenon
Receptor activator of nuclear factor kappa B	RANK
Receptor activator of nuclear factor kappa B ligand	RANKL
SLBs	Self-ligating brackets
TIMPs	Tissue inhibitors of metalloproteinases
TNF-α	Tumor necrosis factor–alpha

Introduction

Orthodontic tooth movement (OTM) occurs when there is prolonged application of pressure to the tooth, tooth movement will occur as a result of bone remodeling around the tooth that it means bone is removed selectively in some areas and added in others **(Shivalinga *et al.*, 2012).**

The applied force is transmitted through the root and reach periodontal ligament and alveolar bone and will lead to tooth movement. OTM is typically divided primarily into three phases by clinical observation: the initial phase, the lag phase, and the post lag phase **(Krishnan and Davidovitch, 2006).**

The alveolar bone, periodontal ligament (PDL) and cementum are closely related structures in functions and development together, they form the periodontium which is very important for orthodontic tooth movement **(Jiang *et al.*, 2016).**

Orthodontic treatment currently does not only meet the demands of creating the functional harmony in occlusion and enhancing the aesthetic outlook but is should also be completed in the most effective duration that is accepted by both the patient and the orthodontist **(Patil and Singh, 2019).**

Prolonged treatment time in orthodontics is an unpleasant side effect for the patient and the clinician. Usually, 2-3 years of treatment are required for a case to be properly completed **(Graber *et al.*, 2017).**

Accelerating the OTM will decrease the treatment time so the risk of gingival inflammation, decalcification, dental caries, and especially external root resorption will reduce .To reduce the treatment time the rate of OTM should be increase **(Andrade *et al.*, 2014).** There are several techniques has been suggested to accelerate OTM. Based on the invasiveness these techniques can be categorized as surgical and non-surgical techniques. Selective surgical alveolar bone reduction can induces an increase in turnover of alveolar cancellous bone in localized area, suggesting a possible mechanism for acceleration of tooth movement. Another suggested mechanism could be attributed to the removal of the hyaline zone that formed shortly after force application, which allows earlier bone resorption needed for tooth movement **(Gkantidis *et al.*, 2014).**

Because original techniques have been very invasive and have been associated with increased morbidity of teeth, the research in this field has always followed an episodic trend. Techniques that are more recent offer less invasive approach such as the use of piezoelectricity and corticision **(Almpani and Kantarci, 2015).**

However, the use of surgical approaches is limited due to the invasiveness nature of some techniques in view of this, the most of research has focused on non-surgical techniques, these can be sub divided into physiological, biological and mechanical methods these techniques have ranged from systemic/local administration of biological molecules to innovative physical stimulation technologies such as resonance vibration, magnetic filed forces, cyclic forces, light electrical currents, low-intensity laser irradiation and photobiomodulation, all these approaches have shown favorable outcomes with varying degree of success **(Li *et al.*, 2018).**

Aim of the Study

The aim of this study is to provide an overview of the different non-conventional methods that can be utilize to accelerate OTM and discuss their potential shortcomings.

Chapter One: Review of literature

1.1 Biology of tooth movement

OTM occurs in the presence of a mechanical stimulus sequenced by remodeling of the alveolar bone and the periodontal ligament (PDL). OTM consists of three phases**:** initial phase, lag phase and post lag phase **(Zainal *et al.*, 2011).**

The initial phase consists of an immediate and rapid movement and occurs within 24 to 48 hours after the initial application of force to the tooth. The rate of movement is largely attributed to the displacement of the tooth in the PDL space, causing its compression and undermining bone resorption on the pressure side. Bone resorption occurs through osteoclastic activity by creating bone lacunae that will later be filled in by osteoblast cells **(Meeran, 2013)**.

The lag phase lasts 20 to 30 days and displays relatively little to no tooth movement. This phase is marked by PDL hyalinization in the region of compression where the blood supply is cut off. No subsequent tooth movement occurs until the cells complete the removal of all of the necrotic tissues. Once the PDL regenerates, tooth movement continues. The post lag phase follows the lag phase, during which the rate of movement increases **(Krishnan and Davidovitch, 2006).**

When tooth movement occurs, the fibers on the tension side are stretched and resist further movement. Light continuous tension causes elongation of fiber bundles and subsequent bone formation mediated by osteoblasts. Osteoblasts are differentiated from the local precursor cells, called mesenchymal stem cells. Mature osteoblasts form the osteoids, and the mineralization processes follow **(Sprogar *et al.*, 2008).**

Different cytokines and hormones are involved in the biological mechanism of tooth movement. Tumor necrosis factor–alpha (TNF-α), interleukin-1 beta (IL1β), interleukin-6 (IL-6), prostaglandin E2 (PGE2), and other inflammatory cytokines can facilitate osteoclastic bone resorption processes, through the activation of receptor activator of nuclear factor kappa B (RANK) and the receptor activator of nuclear factor kappa B ligand (RANKL)**(Masella and Meister, 2006; Pacios *et al.*, 2011)**.

1.2 Non-surgical approaches to accelerate orthodontic tooth movement

1.2.1 Biological methods

These methods include using pharmacological agents to accelerate tooth movement. These pharmacological agents have been used to alter the biological response to orthodontic forces **(Miles, 2017)**.

Pharmacological agents can interfere with the biochemical processes, which influence tooth movement during and stability after orthodontic treatment. As a result, the possibility to accelerate OTM where needed (such as in areas of space closure) and to decrease tooth movement where desired (to enhance the anchorage or to ensure tooth stability during the initial period of retention) has attracted considerable interest in the field **(Kouskoura *et al.*, 2017)**.

1.2.1.1 Epidermal growth factor (EGF)

It has long been demonstrated that EGF has catabolic effects on bone. In an organ culture study, high concentrations of EGF stimulated bone resorption in fetal rat long bone **(Lorenzo *et al.*, 1986)**.

Regulatory role of EGF in fibrous tissue remodeling in the periodontal ligament (PDL) has also been demonstrated **(Kimura *et al.*, 2013)**.

Regarding the influence of EGF administration on the OTM rate, studies in animals have shown that EGF administration has an additive effect on the rate of osteoclast genesis and recruitment, which leads to faster bone resorption and orthodontic movement acceleration **(Saddi *et al.*, 2008; Alves *et al.*, 2009)**.

The complex role of EGF in OTM remains to be explored even further before the conduction of any trials in humans **(Almpani and Kantarci, 2015).**

1.2.1.2 Prostaglandin (PGE)

Among the arachidonic acid metabolites, PGE2 is a pro-inflammatory factor, which is by far the most widely tested substance in terms of its capacity to modify OTM. Evidence, mainly derived from animal studies, points toward a positive effect of

PGE2 with respect to enhancing bone resorption and accelerating tooth movement **(Kale *et al.*, 2004).**

The mode of application of PGE2 is a major limitation as it involves repeated injection (due its short half-life) in combination with an anaesthetic solution to alleviate the hyperalgesia caused by injection of PGE2. Potential adverse effects (e.g., root resorption) linked to long-term administration of PGE2, as required in the context of orthodontic treatment, are possible given its mode of action but have not been evaluated so far **(Kouskoura *et al.*, 2017).**

It directly stimulate the production of osteoclast and form ruffled border to affect bone resorption. In addition, the level of PGE2 in Gingival crevicular fluid (GCF) reflect the biologic activity in periodontium during OTM, and it is significantly high in both the tension and compression side **(Dudic *et al.*, 2006).**

Prostaglandin E1(PGE1) is an anti-inflammatory factor it is another prostaglandin that has been reported to accelerate OTM it has also been seen to be induced by mechanical stress and cause bone remodeling. Even injection of minimal amounts of PGE1 can increase tooth movement significantly **(Patil *et al*., 2005).**

Yamasaki *et al* (1984) in their clinical study, injected prostaglandin E1 (PGE1) submucosal into the distal canine tooth during canine distalization and reported that tooth movement occurred twice as fast. They stated that it is an effective and safe method that can be used to accelerate tooth movement without causing any side effects other than mild pain in patients.

1.2.1.3 The parathyroid hormone

Parathyroid hormone (PTH) exerts its effects directly on osteoblasts and indirectly on osteoclasts through binding to the PTH type 1 receptor on osteoblasts, leading to expression of insulin-like growth factor-1 (IGF-1), which promotes osteoblastogenesis and osteoblast survival, and of receptor activator of RANKL, which promotes osteoclast activation. PTH is also likely interacting with bone lining cells promoting early osteogenesis **(Dobnig and Turner, 1995; Esbrit and Alcaraz, 2013).**

Recombinant PTH is clinically used for the treatment of osteoporosis and has been shown to mediate bone anabolic or catabolic effects depending on the circumstances of administration. Intermittent exposure to PTH seems to increase bone formation, while continuous and long-term exposure (longer than 1–2 years) enhances bone resorption **(Esbrit and Alcaraz, 2013)**.

Studies on the effects of PTH on tooth movement point toward a role of intermittent treatment with PTH in facilitating bone remodeling/turnover and therefore accelerating tooth movement. This is possibly occurring by PTH enhancing both osteoblast and subsequently also osteoclast activity **(Li *et al.*, 2013).**

Chronic elevation of PTH leads to pathological changes in multiple organs, especially the kidneys and bones. Thus, the safety remains a serious concern for its clinical application in orthodontic **(Li *et al*,. 2013).**

1.2.1.4 L-Thyroxine

Thyroid hormones play an imperative role in the regulation of cellular metabolism, proliferation and differentiation **(Meng *et al.*, 2011)**. L -Thyroxine is a synthetic thyroid hormone that is chemically identical to thyroxine **(Figure 1.1**), which is naturally secreted by the thyroid gland and has been used to treat thyroid hormone deficiency and occasionally to prevent the recurrence of thyroid cancer. Furthermore, thyroxine affects intestinal calcium absorption and, therefore, is indirectly involved in bone turnover. Hyperthyroidism or thyroxine medication can lead to osteoporosis **(Bartzela *et al.*, 2009)**.

Figure 1.1: SANDOZ Levothyroxine Sodium https://greenpharmacyonline.com/rxproducts/levothyroxine-sodium-

Because of the ability of thyroid hormones to act on the metabolism of nearly every cell in the body and especially of their indirect involvement in bone turnover **(Cray *et al.*, 2013)**, the possible effect of thyroxine on OTM has been examined in a relevant study on rats, the results showed that administration of 20 µg/kg i.p./day L thyroxine significantly increased the amount of OTM and the extent of root resorption as seen from scanning electron micrographs appeared to decrease with thyroxine administration **(Shirazi *et al.*, 1999)**.

Verna (2000) examined whether the rate of OTM is influenced by the general bone turnover capacity in another rat model. They obtained a high turnover by the general ad-ministration of L -thyroxine. The rate of tooth movement was higher in cases of high bone turnover and smaller in the rats with low bone turnover, in comparison to normal animals. Because of the fact that thyroxine medication can lead to osteoporosis, the seriousness of safety issues regarding its use for orthodontic purposes is quite high.

1.2.1.5 Calcitriol or 1,25-dihydroxycholecalciferol (1,25 DHCC)

This agent is a biologically active form of vitamin D and has a potent role in calcium homeostasis. A decrease in the serum calcium level stimulates secretion of PTH, which in turn increases the excretion of $(PO_{4)})^{3+}$, reabsorption of Ca^{2+} from the kidneys, and hydroxylation of 25-hydroxycholecaliferol to 1,25DHCC. The latter molecule has been shown to be a potent stimulator of bone resorption by inducing differentiation of osteoclasts from their precursors. It is also implicated in increasing the activity of existing osteoclasts. In addition to bone resorbing activity, 1,25-DHCC is known to stimulate bone mineralization and osteoblastic cell differentiation in a dose dependent manner **(Almpani and Kantarci, 2015).**

No obvious clinical, microscopic or biochemical side effects have been noted until now, but the safe use of this systemic factor in orthodontic movement should be further investigated. Nevertheless, the current way of administration of 1,25-DHCC with the use of frequent injections is also decreasing the clinical practicality of this factor in orthodontic patients **(Almpani and Kantarci, 2015).**

1.2.1.6 intravenous immunoglobulin (IVIg)

Intravenous immunoglobulin (IVIg) preparations are polyspecific and polyclonal immunoglobulin therapeutic preparations used as a replacement therapy in immunodeficient patients **(Schneider *et al.*, 2015).**

These IVIg preparations were shown to induce Cyclooxygenase-2 (COX2) mediated PGE2 synthesis and cytokine production. It is possible that local administration of these IVIg preparationscould be used to modulate bone modeling through PEG2induction and bypass some of the limitations of PEG2 injections **(Djoumerska *et al.*, 2015).**

1.2.1.7 Relaxin

Relaxin has been known as a pregnancy hormone. It is released just before child birth to loosen the pubic symphysis, this will allow widening of the birth canal for delivery. Administration of human relaxin may accelerate the early stages of OTM in rats **(Madan *et al.*, 2007)**.

Relaxin is a peptide hormone with strong effects on collagen turnover. In vitro studies have suggested that relaxin may have a direct effect on the PDL by means of decreasing the expression and release of collagen type I, increasing expression of certain matrix metalloproteinase (MMPs) and decreasing the expression of tissue inhibitors of metalloproteinases (TIMPs) in PDL cells **(Henneman *et al.*, 2008; Takano *et al.*, 2009).**

Another study suggest that human relaxin does not accelerate orthodontic tooth movement in rats; it can decrease the organization level of PDL, decrease PDL mechanical strength, and increase tooth mobility at early time points **(Madan *et al.*, 2007).**

Despite increased interest in the potential of relaxin to modulate OTM, effects on tooth movement and tooth stabilization could to date not be confirmed, neither clinically **(McGorray *et al.*, 2012)** nor in animal experiments **(Stewart *et al.*, 2005; Madan *et al.*, 2007).**

1.2.1.8 Osteocalcin

Osteocalcin is a non-collagenous matrix protein that is abundant in bone tissue and functions as a negative regulator of mineral apposition and bone formation due to its high binding strength with calcium and hydroxyapatite **(Tsao *et al.*, 2017).**

Hashimoto (2001), injected local osteocalcin to the maxillary first molars of rats, while applying mesial motion with a spiral spring, and evaluated tooth movement histologically for a period of 10 days In their results, they determined that local application of osteocalcin accelerated tooth movement and explained this with the increase of osteoclast on the pressure side in the early period and there is no side effects were reported.

1.2.1.9 Platelet rich plasma (PRP) and platelet rich fibrin (PRF)

Recently, there have been studies investigating the effect of PRP and PRF on OTM speed. Studies have reported that these applications can accelerate OTM **(Tehranchi *et al.*,2018).**

PRP is the plasma fraction obtained by centrifuging whole blood and containing a higher concentration of platelets than whole blood. It contains a high amount of platelets, growth factors, and coagulation factors in PRP **(Paoloni *et al.*, 2011).**

It has been reported that PRF has positive effects on bone healing, socket protection and acceleration of tooth movement **(Tehranchi *et al.*,2018).**

Liou (2016) reported in their research on humans that submucosal PRP injection can increase the speed of tooth movement without surgical application and alveolar bone loss. In his clinical study, he reported that local submucosal PRP injection was 1.7 times faster in maxillary and mandibular leveling and this acceleration was PRP dose-dependent. This PRP ratio (platelet count in PRP/platelet count in the blood) is <12.5. He stated that the ideal number of PRP platelets to be used to accelerate tooth movement should be 9.5–12.5 times the normal. On the other hand, PRP injection during enmasse retraction reduced alveolar bone loss by 71–77% on the pressure side, which is also dose-dependent. The optimal dose of PRP for optimal clinical performance is 11.0–12.5-folds, with submucosal injection of PRP accelerating orthodontic tooth movement and at the same time protecting the alveolar bone on the pressure side of orthodontic tooth movement.

A single dose of PRP injection is effective for 5–6 months. It has been reported that the most effective period of PRP injection in accelerating tooth movement is the second half of the 4th month after the injection (**Liou, 2016).**

1.2.1.10 Nitric oxide

Nitric oxide is synthesized from arginine by the enzyme nitric oxide synthase. It is a short-lived molecule that plays a key role in the regulation of some functions of the nervous, defense, respiratory, circulatory, and reproductive systems **(Brennan *et al*., 2003).**

Akin *et al*. (2004) in their study, reported a significant increase in multinucleated osteoclasts, howship lacunae, vascularization and OTM as a result of nitric oxide injection in rats

1.2.2 Biomechanical method

1.2.2.1 Self-ligating brackets

There are many advantages of self-ligating brackets (SLBs) as compared with conventional brackets (CBs) which include: dramatically reducing chair-side time, reducing the total treatment time, gaining better oral health, and reducing pain and discomfort **(Zhou *et al*, 2014).**

Active SLBs: which can exert force on the archwire, through spring clip

Passive SLBs : do not exert force and do not encroach on the slot lumen **(Figure 1.2).**

Figure 1.2: Passive and Active self-ligating brackets
(**Deepshikha *et al*.,2020)**

Examples of self-ligating systems include Damon® , Speed™, or In-Ovation®. In SLBs the friction between the archwire and bracket slot is reduced this will reduce the treatment time and the force required for tooth movement. There is no elastics in SLBs this will decrease plaque build-up. However, clinical trials and a number of systematic reviews using randomized controlled trials have concluded that SLBs do not show clinical superiority as compared to conventional brackets in term of expanding transversal dimensions, space closure, or orthodontic efficiency. Further high-level studies involving randomized, controlled, clinical trials are needed to confirm these results **(Yang *et al.*, 2017).**

1.2.3 Physiological / mechanical methods

1.2.3.1 Low level mechanical vibrations

Significant evidence from orthopedic research proposed that low level mechanical oscillatory signals (vibrations) affect bone metabolism positively, increasing the remodeling rate of long bones during adaptation to mechanical loading **(Rubin *et al.*, 2002) (Figure 1.3).**

Results from a study using a rodent model has showed that loading of dynamical vibration increase the rate of OTM about 15%, there is no negative side effects on the periodontium and surrounding tissues of the alveolar bone **(Nishimura *et al.*, 2008)** .

Figure 1.3: A, AcceleDent Aura. B, Patient wears the AcceleDent for 20 minutes per day by lightly biting on the mouthpiece **(Graber *et al*, 2017)**.

The exact biological mechanism underlying the anabolic effect of cyclic loading on bone metabolism is not fully understood. Several signaling pathways have been implied in the response of bone cells to mechanical vibrational loading **(Pavlin and Gluhak, 2001; Rubin *et al.*, 2006)**.

As early as 6 hours after the onset of oscillatory loading, a surge in the expression of genes for osteocalcin and dentin matrix protein was detected in the osteocytes of alveolar bone. These signaling pathways induced by mechanical vibrational forces could be triggered by fluid shear stress in osteocyte lacunae and canaliculi or by piezoelectric potentials which induced by bone bending, all of which can occur during these vibrations. In addition, bone microfractures at the level similar to or lower than microfractures exerted by physical activity, may be a contributing factor in the early response to vibrational forces loading **(Graber *et al.,* 2017).**

1.2.3.2 Low Intensity laser therapy

In the field of orthodontics, low intensity laser irradiation(LILT) has been utilized for several types of orthodontic applications, such as the reduction of post appliance adjustment pain **(Lim *et al.,* 1995)** or the treatment of traumatic ulcers in the oral mucosa **(Sun *et al.,* 2001).**

In addition to the previous application and according to the results of the histological analyses of most studies reported that LILT stimulates alveolar bone remodeling activities as indicated by the increased numbers and functions of osteoclasts and osteoblasts **(Sun *et al.,* 2001; Habib *et al.,* 2010; Altan *et al.,* 2010).**

The the lasers that are the mostly used for these interventions are Aluminum-gallium-arsenide (Al-Ga-As) diode lasers which have been proven to have a higher depth of tissue penetration in comparison to other modalities **(Khadra *et al.,* 2004) (Figure 1.4).**

Cruz *et al*. (2004) were the first to publish research results on the effect of LILT on the duration of dental movement in humans. According to their results, orthodontic movement of the treated teeth was accelerated due to the use of laser radiation. Since then, more clinical studies in humans have also revealed a significantly positive effect of low intensity laser radiation on the acceleration of OTM

Ninomiya *et al.* (2007) pointed out that the biological effect of the laser light depends on the characteristics of the light source such as wavelength, output power and energy density and different laser systems are associated with different biostimulatory effects .

Study made by **Fujita *et al*. (2008)** examined the effect of LILT and lightemitting diode (LED) irradiation on OTM. According to their results, the amount and rate of tooth movement were significantly greater in the laser irradiation group (day 3: 2.2-fold; day4: 2.0-fold; day 7: 1.5-fold) compared with the non-irradiation and LED irradiation groups. **(Kawasaki and Shimizu 2000)**.

Figure 1.4: Laser biostimulation on the buccal side of the canine **(Dakshina *et al*,. 2019).**

1.2.3.3 Photobiomodulation or Low-level Light therapy

Photobiomodulation is an emerging medical and dental technique in which exposure to light or LEDs stimulates cellular function leading to beneficial clinical effects. This technique is known as low-level light therapy or LLLT. The light spectrum may vary, but it falls in the infrared range. AGa-Al-As diode laser produces coherent light, whereas the light produced by the LED is incoherent. This technique has been based on the fact that cytochrome oxidase or complex IV – an enzyme which mediates the synthesis of Adenosine triphosphate (ATP) in cells – is upregulated by infrared light **(Kau, 2012)**.

During tooth movement, higher ATP availability boosts cell metabolism, leading to an increased remodeling process and accelerated tooth movement **(Oron *et al.*, 2007;Kau, *et al.*, 2013)**.

LLLT may also be enhancing OTM due to increased vascular activity, which is also promoted by light **(Tuby *et al.*, 2007)** and contributes to a more rapid boneturnover **(Vinck *et al.*, 2003).**

Studies have shown that the impact of the LLLT is also dependent on the wavelength and intensity of the emitted light **(Doshi and Bhad, 2012).** Nevertheless, according to the results of **Fujita *et al.* (2008)** infrared LED irradiation did not stimulate the velocity of tooth movement or osteoclastogenesis in rats.

Vinck *et al.* (2003). also reported in an in vitro study that infrared LED irradiation did not stimulate the proliferation of fibroblasts obtained from chicken embryos.

Conclusively, larger and longer clinical trials are required in order to be able to assess the validity of LLLT, the long-term stability of the produced outcomes and any potential adverse effects. Moreover, more research studies on a molecular level are also needed that would lead to a deeper understanding of the biological mechanisms involved, which would simplify and optimize the clinical applications of LLLT **(Almpani and Kantarci, 2015).**

1.3 Surgical methods for acceleration of the orthodontic tooth movement

A significant increase in bone turnover is seen after bone fracture and osteotomy. This is due to the induced regional accelerated phenomenon (RAP) **(Wilcko *et al.*, 2001).** As the bone turnover rate increases, it inadvertently increases the rate of alveolar bone remodeling. There is a reduction of density of bone, which, in turn will reduce the resistance to OTM **(Teixeira *et al.*, 2010)**.This is the logic behind the surgical approach and is most commonly used in adult patients, in cases where the treatment is time bound. However, surgical methods have disadvantages including **(Sharma *et al.*, 2019):**

- Surgical morbidity associated with the procedures
- Increased cost of the procedure has to be borne by the patient

- If not carried out properly chances of damage to the roots of adjacent teeth
- Chances of pain, infection, and swelling after the procedure if proper hygiene is not maintained.

1.3.1 Interseptal alveolar surgery (distraction osteogenesis)

Distraction osteogenesis (DO) involves gradual, controlled displacement of surgically created fractures (subperiosteal osteotomy) by incremental traction **(Ilizarov, 1988),** resulting in simultaneous expansion of soft tissue and bone volume due to mechanical stretching through the osteotomy **site (Figure 1.5) (Figure 1.6).** This ability to reconstruct combined deficiencies in bone and soft tissue makes the process unique and invaluable to all types of reconstructive surgeons **(Ilizarov, 1989).**

Sayin *et al*. (2004) investigated the clinical validation of this technique and substantiated that this procedure reduced the net orthodontic treatment time. However, a number of other complications have been associated with the distraction osteogenesis techniques, such as increase in gingival sulcus depth, tipping of the anchorage, retracted teeth and, more frequently, loss of pulpal vitality **(Liou and Huang, 1998; Sukurica *et al,* 2007)** and anchorage loss **(Sayin *et al,* 2004).**

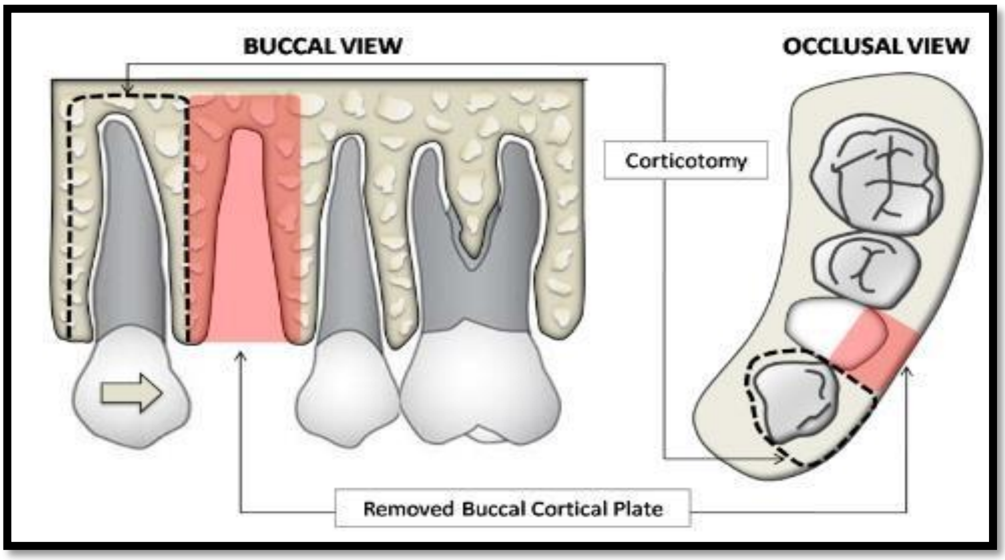

Figure 1.5: Surgical technique involving vertical and horizontal corticotomies. after removal of the buccal cortical plate in relation to the extraction socket the dentoalveolar segment will be used as transport unit to carry canine posteriorly **(Cherackal and Thomas, 2014).**

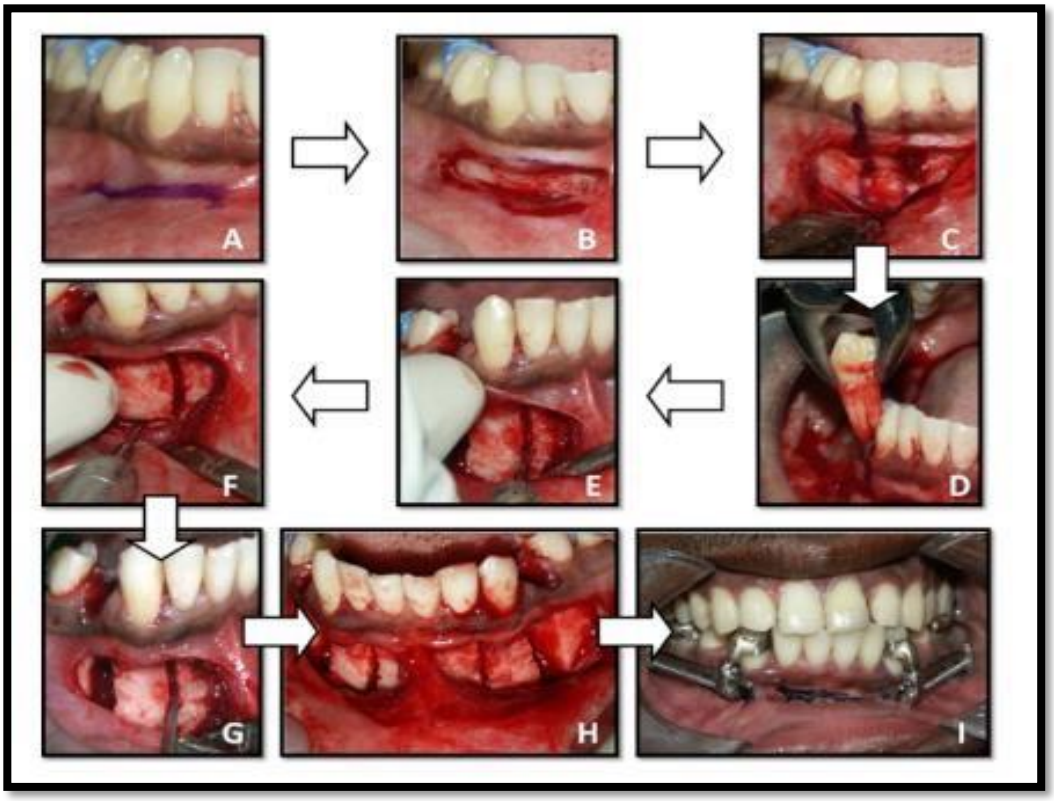

Figure 1.6: Sequential steps involved in the surgical technique for dentoalveolar distraction. (A) & (B) horizontal mucosal incision: (C) osteotomy lines and cortical holes marked; (D) first premolar extracted; (E) & (F) vertical and horizontal osteotomies and removed cortical plate; (G) osteotomes applied to mobilize the alveolar segment; (H) & (1) post surgery and appliance cementation **(Cherackal and Thomas, 2014)**.

1.3.2 Corticotomy

The procedure of corticotomy is surgical cut where only the cortical bone is involved, perforated or mechanically altered in a controlled surgical manner **(Murphy *et al.*, 2014) (Figure 1.7).** It can increase bone remodeling and creates transitory state of osteopenia that reduces bone density, which causes less resistance to tooth movement. It can be used in En-masse retraction, canine retraction, decrowding, molar uprighting, correction of a scissor bite, and rapid maxillary expansion **(lee, 2018).** However, corticotomy might engender marginal interdental bone loss, induces loss of the attached gingiva, infection, unfavorable changes in the appearance of the gingiva and associated with postoperative pain and swelling **(Chen *et al.*, 2020).**

Figure 1.7 :To perform corticotomies, the gingiva and the periosteum need to be elevated to expose the bone. The osteotomy cuts are made between the teeth and the bone surface will also be perforated between the osteotomy cuts (fig. B and D). The decorticated bone surfaces will be covered with a mixture of demineralized freeze dried bovine bone and plasma rich in blood platelets (fig.C and E). The surgical flap is closed and sutured **(Proffit *et al*,. 2019).**

1.3.3 Piezocision

Dibart *et al*.(2009) used piezocision to accelerate tooth movement through trans-mucosal corticotomy without flap elevation. This method used a piezoelectric knife to cut bones from a small tissue opening **(Figure 1.8).**

The knife can selectively cut the bone, thus preventing damage to adjacent soft tissue. If hard and soft tissue grafts are required, they can be placed by using a tunneling procedure (**Dibart *et al*., 2009).**

This technique can reduce about half of the total treatment time. The attachment level and pocket depth change minimally, but gingival scar tissue was observed and remained in most cases **(Strippoli *et al.*, 2019).** In addition, the visibility of piezocision was inferior than corticotomy because the of the small soft tissue opening. Thus, risk of iatrogenic root damage, devitalization of teeth and invasive root resorption must be paid attention **(Tunçer *et al.*, 2019).**

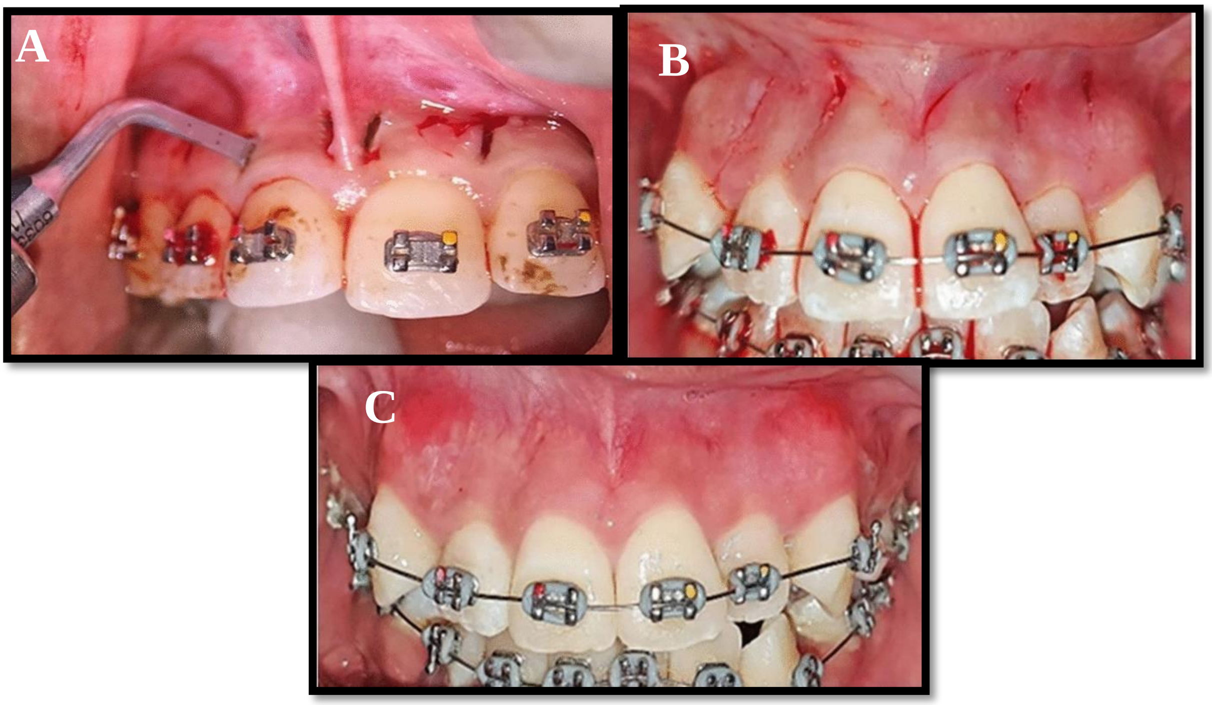

Figure 1.8: (A) Piezocision flapless corticotomy procedure performed on maxillary anterior teeth. The surgical blade no.1 with millimeter marker showed 3 mm depth of corticotomy (B) immediate after piezocision surgery, (C) healing response after1 week of surgery. **(Sultana *et al*,. 2022)**.

1.3.4 Micro-osteoperforations

Micro-osteoperforations (MOPs) involve a less invasive approach than corticotomy. The perforations are performed through the gingival tissues, penetrating the cortical plate . There is no need to raise a mucogingival flap, create any incisions or perform a tissue punch to access the cortical bone. The osteoperforations are performed with a bone screw, which is self-drilling and self tapping, and no pilot hole is necessary **(Graber *et al*,. 2017) (Figure 1.9) (Figure 1.10).**

Alikhani *et al*. (2013) conducted the first human clinical trial of this method, and they reported that the application of MOPs can increase the rate of canine retraction by 2.3-fold. However, a recent randomized clinical trial indicated that MOPs did not significantly increase tooth movements **(Alkebsi *et al*., 2018).**

About the location of MOPs, study has indicated that if MOPs placed at 3 mm away from teeth would not increase the rate of tooth movement **(Cramer *et al*., 2019)**. Although the bone density is decreased up to 4.2 mm, the principal effects did not extend to more than 1.5 mm away from the MOP **(van *et al*., 2019)**.

It has the advantage that it does not require periodontal surgery and can be implemented by orthodontists. Microperforation, if it is effective, would appear to be limited to specific areas rather than a whole arch or even all the anterior teeth because of the increasing effort to place so many screw holes (**Proffit *et al*,. 2019).**

Figure 1.9:Propel handheld disposable device used for MOPs **(Alikhani, 2013).**

Figure 1.10: Propel device by Propel Orthodontics. It has a surgical tip 1.6 mm in diameter and a usable length of up to 7.0 mm **(Keser and naini, 2022).**

1.3.5 Periodontal accelerated osteogenic orthodontics (PAOO)

PAOO can be used in treating moderate to severe crowding, cases requiring expansion, reduced periodontal tissues, molar intrusion and open bite correction as well as to improve post-orthodontic stability. It can prevent the need of extraction and decrease the risk of dehiscence and fenestration. The surgical cuts created vertical grooves from 2 to 3 mm below the alveolar crest to 2 mm beyond the apices of the roots and perform circular corticotomy to connect vertical cuts. Selective medullary penetration was performed to enhance bleeding **(Figure 1.11).** Bone grafts was placed in most areas that have undergone corticotomies. The volume of the graft material could be decided by the alveolar bone thickness and the direction of tooth movement. An immediate orthodontic force can be applied to the teeth. Initiation of the orthodontic force should not be delayed for more than 2 weeks after surgery and the duration of tooth acceleration is usually last for 4 to 6 months **(Amit *et al,* 2012).** PAOO can decrease treatment time and increases alveolar bone width and volume. The disadvantage of PAOO is similar to corticotomy **(Chen *et al,* 2020).**

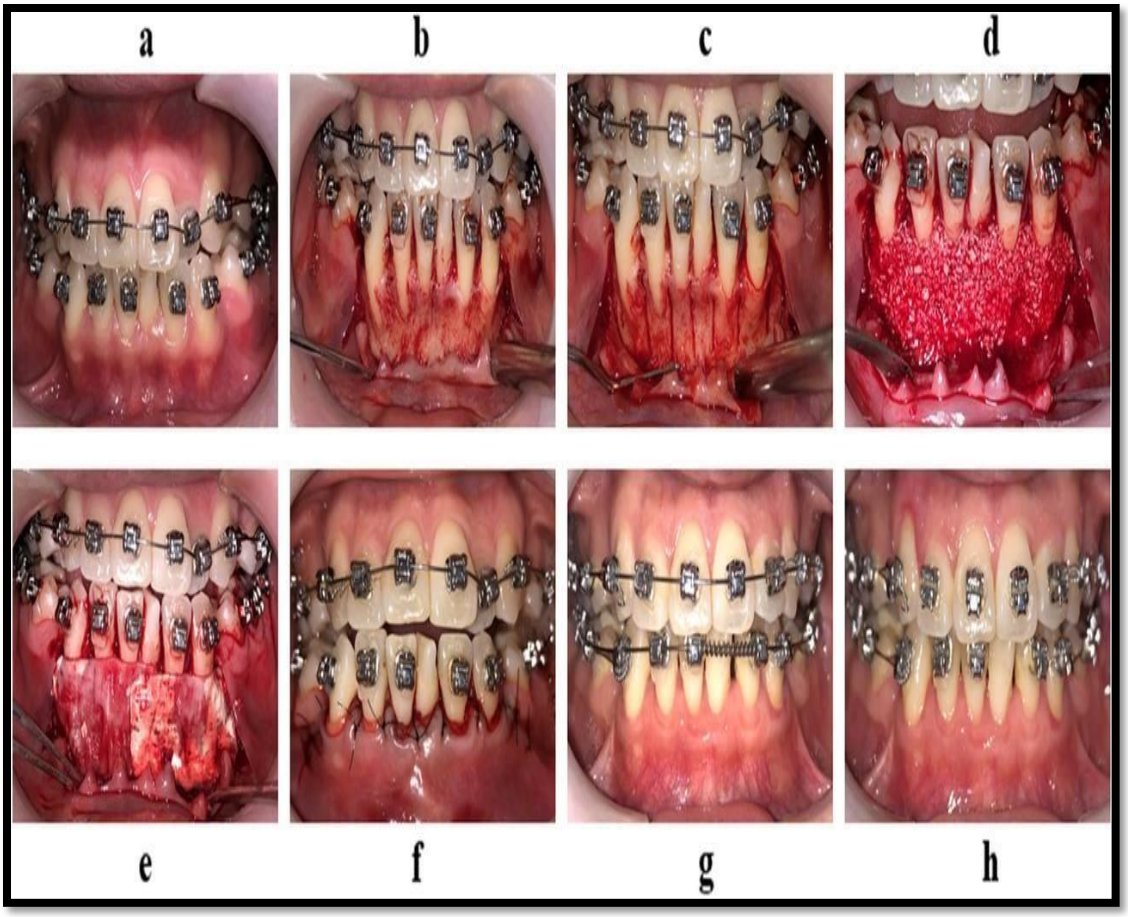

Figure 1.11: Surgical procedure of PAOO (a) presurgical treatment (b) full-thickness flap reflection (c) performing corticotomies in the inter-radicular space (d) placement of grafting materials on the surface of alveolar bone (e) collagen membrane covering the grafting materials (f) interrupted sutures (g) six-month follow-up (h) twelvemonth follow-up **(Chen *et al*,. 2022).**

1.3.6 Corticision

Kim *et al.* (2009) proposed a surgical technique called corticision by performing flapless corticotomy transmucosally. This method is to create a vertical cut starting 5 mm from the papillary gingiva and up to two thirds of the root length by a reinforced scalpel and mallet. In an animal study, histologic findings showed that corticision could activate the catabolic remodeling in the direction of tooth movement **(Figure 1.12) (Figure 1.13).** The overall effect of corticision reached the peak at the second months and drops at the third months **(Park, 2016).** The surgical procedure is less invasive. However, it is not able to place grafts during the procedure. A single-site corticision could not induce clinical or histologic changes **(Murphy *et al.*, 2014).**

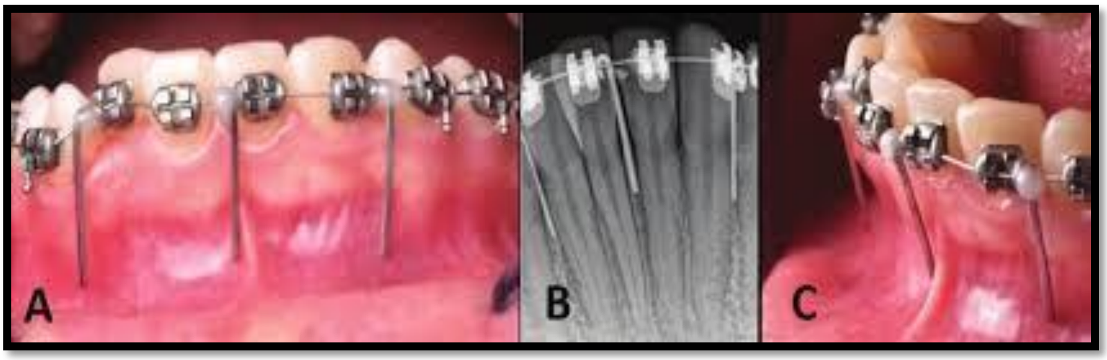

Figure 1.12:Three metallic guides were used before taking digital radiographs: Clinical appearance of the metallic guides from a frontal view (a) Radiological appearance of these pins (b) Lateral view of the metallic guides (c) **(Sirri *et al.*, 2020).**

Figure 1.13:Three vertically oriented corticisions were performed using the surgical blade no 15 (a) The surgical mallet was used over surgical scalpels (b)The clinical appearance following the minimally invasive intervention (c). Each corticision had a 4-5 mm length and 3-4 mm depth **(Sirri *et al.*, 2020).**

Chapter two

2.1 Discussion

In an attempt to reduce treatment time, there are several techniques has been suggested to accelerate OTM. Based on the invasiveness these techniques could be surgical or non-surgical techniques.

The original surgical techniques have been very invasive and have been associated with increased morbidity of teeth. The most of research has focused on non-surgical technique and have ranged from administration of biological molecules to innovative physical stimulation technologies such as resonance vibration, low level laser therapy and photobiomodulation, all these techniques have shown favorable outcomes with varying degree of success **(Li *et al.*, 2018).**

Administration of pharmacological substances one of the methods used for acceleration of orthodontic tooth movement. These substances include: Epidermal growth factor which has catabolic effect on bone by increasing the rate of osteoclastgensis, prostaglanding is a potent stimulator of bone resorption but it is associated with adverse effect like root resorption and pain on local injection, PTH facilitate bone remodeling by enhancing both osteoblast and osteoclast but there is a potential risk that chronic elevation of PTH may leads to pathological changes in multiple organs, especially the kidney and bones, thyroxine is indirectly involoved in bone turnover through it's effect on intestinal calcium absorption. However, because thyroxine medication can lead to osteoporosis, the seriousness of safety issues is quite high**(Almpani and Kantarci, 2015).**

DHCC inducing differentiation of osteoclast from their precursor and stimulate bone reosorption in a dose dependent manner. The local administration of IVIg can modulate bone modeling through PGE2 induction and bypass some of the limitation of PGE2 injection. Osteocalcin local application may accelerate tooth movement and there is is no side effect reported of osteocalcin **(Almpani and Kantarci, 2015).**

Liou (2016) reported in their research that submucosal PRP injection can increase the speed of tooth movent without surgical application and alveolar bone loss, he reported that local submucosal PRP injection was 1.7 faster in maxillary and mandibular leveling and this acceleration was PRP dose dependent. Nitric oxide is important in bone turnover and regulation of pulpal blood flow. **Akin *et al.* (2004)** reported significant increase in osteoclast, howship lacunae, vascularization and OTM as a result of nitric oxide injection in rats.

In spite of the huge focus on the acceleration of orthodontic tooth movement, there were only 2 human studies investigating the effect of local pharmacological agents on the acceleration of OTM. There were much more animal studies on the same topic. The obvious reason was the risk of side effects that accompany the tested interventions. From the systematic review, Relaxin **(McGorray *et al.*, 2012)** and Prostaglandin **(Yamasaki *et al*., 1984)** were tested on humans. Prostaglandin showed a marked increase in OTM. The study was divided into 3 phases in which all phases showed acceleration of OTM in intervention sides, yet the study was considered having a high risk of bias. The study wasn't a randomised controlled study, and the sample size wasn't enough for each phase **(Eltimamy *et al,*. 2019).**

The use of self ligating brackets (SLBs) may reduce the treatment time as the frection between the arch wire and breacket slot is reduced and the force required also reduced. However, clinical trials and a number of systematic reviews using randomized controlled trials have concluded that SLBs do not show superiority as copared to conventional bracket in term of expanding tranversal dimension , space closure or orthodontic efficiency **(Yang *et al.*, 2017).**

The results of the histological analyses of most studies reported that Low level laser therapy (LILT) stimulates alveolar bone remodeling activities as indicated by the increased numbers and function of osteoclast and osteoblast. Study made by **Fujita *et al.* (2008)** reported that the rate of tooth movement were significantly greater in the laser irradiation group (Day 3: 2.2-fold; day 4: 2.0- fold ; day 7: 1.5fold).

Significant evidence from orthopedic research proposed that low level mechanical vibration affect bone metabolism positively **(Rubin *et al.*,2002).** Loading of dynamical vibration increase the rate of OTM about 15%, there is no negative side effects on the periodontium and surrounding tissues of the alveolar bone **(Nishimura *et al*., 2008).**

Photobiomodulation or low level light therapy (LLLT) may also enhance orthodontic tooth movement due to increased vascular activity, which also promoted by light and contributes to a more rapid bone turnover. This technique has been based on the fact that cytochrome oxidase or complex IV- an enzyme which mediates the synthesis of ATP in cells is upregulated by infrared light. During tooth movement, higher ATP availability boosts cell metabolism, leading to an increased remodeling process and accelerated tooth movement **(Kau, 2012).**

Currently, the non-surgical methods are associated with very-low quality evidence. Further well-designed RCTs are required to determine whether nonsurgical interventions may safely result in a clinically-important reduction in the duration of orthodontic treatment **(Miles, 2017)**.

Distraction osteogenesis is a surgical method that lead to formation of new bone with no side effect like reduce in alveolar height and change in soft tissue but lead to increase gingival sulcus depth and tipping of the anchorage. Human study found that the speed of tooth movements was about 1.6 times faster than control side **(Leethanakul *et al.*, 2014).**

Corticotmoy can increase bone remodeling and create transitory state of osteopenia that reduces bone density, which cause less resistance to tooth movement. However, corticotomy might engender marginal interdental bone loss, induces loss of attached gingiva, infection and associated with postoperative pain and swelling **(Chen *et al.*, 2020).**

piezocision appeared to be minimally invasive an effective method to reduce the orthodontic treatment time in similar effect to corticotomy. The attachment level and pocket depth change minimally. However, the visibility of this technique was inferior to cortictomy. Thus risk of iatrogenic tooth damage, devitalization of teeth and invasive root resorption **(Tunçer *et al.*, 2019).**

The micro-osteoperforation resolves most of the problems associated with conventional surgical methods and unlike other less invasive surgical methods, it can be performed by the orthodontist using commonly available orthodontic appliance to increase the rate of tooth movement and also help adjust the anchorage.However, a recent randomized clinical trial indicated that MOPs did not significantly increase tooth movements **(Alkebsi *et al.*, 2018).**

Periodontal accelerated osteogenic orthodontics (PAOO) can prevent the need of extraction and decrease the risk of dehiscence and fenestration. It can decrease the treatment time and increase alveolar bone width and voulum. The disadvantage of PAOO is similar to corticotomy **(Chen *et al.*, 2020)**.

Some of the surgical techniques described are gaining popularity (MOPs, piezocision), whereas others (distraction osteogensis, corticision) are not, due to limited applications, patient discomfort, or the invasiveness of the technique **(Keser and Naini, 2022).**

Piezocision and PAOO have the advantage of grafting during the surgery, which allows for improvement of the hard and soft tissues and preventing periodontal defects which might occur due to a thin alveolar bone. Piezocision, MOPs, and corticision are flapless approaches it is not able to place grafts during the procedure and are less invasive than PAOO. Mallet use in corticision is traumatic for the patient. MOPs seem to be the least invasive application. PAOO appears to be the most invasive approach. Then use of the Piezoelectric knife appears to have a greater impact on bone metabolism and creates a greater response to injury when compared to other techniques. The depth of the injury created during these procedures has a direct effect on the intensity of bone remodeling. Therefore, it plays a very important role in the effectiveness of the techniques **(Keser and Naini, 2022)**.

Chapter three

3.1 Conclusion

1- At present, there is insufficient evidence to support the use of the majority of approaches reported to accelerate OTM.

2- Non-surgical approaches can be difficult to apply in everyday practice due to the use of expensive and specialized equipment and the need for regular and repeated administration of the intervention.

3- The local administration of systemic regulatory factors for accelerated OTM has been linked with an increased risk for root resorption and pain.

4- Physical stimulation techniques, though, appear to be less prone to adverse effects. They are noninvasive, pain free and in general more attractive to orthodontic patients and clinicians.

5- surgical approaches to accelerating OTM associated with significant invasiveness, exposing the patient to additional stress and postoperative pain especially in techniques that require mucoperiosteal flaps such as cortictomies and PAOO.

6- Some minimally invasive surgeries such as MOP and piezoincision seems to be most promising; However, the MOP technique still requires more evidence to prove its effectiveness.

7- With proper selection of surgical methods, we can shorten the orthodontic treatment time and prevent unexpected side effects.

3.2 Suggestions

1- Conduct survey study among Iraqi orthodontists about most used technique for accelerate OTM.

2- Survey study for orthodontic patients about most acceptable method for accelerate OTM.

3- Cost benefit study for different acceleration methods.

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