Scholars Journal of Dental Sciences
Abbreviated Key Title: Sch J Dent Sci
ISSN 2394-4951 (Print) | ISSN 2394-496X (Online)
Journal homepage: https://saspublishers.com/journal/sjds/home

OPEN ACCESS

Methods of Accelerating Orthodontic Tooth Movement-A Literature Review

Sharath Kumar Shetty[1], Mahesh Kumar Y[2], Neeraj NS[3*], Vijayananda K. Madhur[4]

[1]Professor & HOD, Department of Orthodontics and Dentofacial Orthopaedics, K. V. G. Dental College and Hospital, Sullia, Karnataka, India
[2]Professor, Department of Orthodontics and Dentofacial Orthopaedics, K. V. G. Dental College and Hospital, Sullia, Karnataka, India
[3]Post Graduate Student, Department of Orthodontics and Dentofacial Orthopaedics, K. V. G. Dental College and Hospital, Sullia, Karnataka, India
[4]Reader, Department of Orthodontics and Dentofacial Orthopaedics, K. V. G. Dental College and Hospital, Sullia, Karnataka, India

***Corresponding author:** Neeraj NS
| **Received:** 02.03.2019 | **Accepted:** 05.03.2019 | **Published:** 30.03.2019
DOI: 10.36347/sjds.2019.v06i03.016

Abstract **Review Article**

Currently, fixed orthodontic treatment requires a long duration of about 2–3 years which is a great concern and poses high risks of caries, external root resorption, and decreased patient compliance. Thus, accelerating orthodontic tooth movement and the resulting shortening of the treatment duration would be quite beneficial. To date, several novel modalities have been reported to accelerate orthodontic tooth movement, including low-level laser therapy, pulsed electromagnetic fields, electrical currents, corticotomy, distraction osteogenesis, and mechanical vibration. However, pertinent results are inconclusive, and some are unreliable, which may bias clinician's understandings and mislead clinical practice. The aim of this review article is to conduct a review of current literature in order to update the knowledge about the methods of accelerating orthodontic tooth movement.
Keywords: orthodontic, caries, root resorption, corticotomy, osteogenesis.

INTRODUCTION

Comprehensive orthodontic treatment usually lasts for more than 1 year and a half when fixed appliances are used to treat moderate to severe cases of malocclusion [1], with a significant difference which can be affected by various factors [2, 3]. Accelerating orthodontic tooth movement has long been desired for its multiple potential benefits, including shorter treatment duration, reduced side effects such as oral-hygiene related problems, root resorption, and open gingival embrasure spaces [4-8], enhanced envelope of tooth movement, differential tooth movement, and improved posttreatment stability[9]. Moreover, most adult patients want to finish their treatment at the earliest opportunity due to social and aesthetic concerns [10]. Thus, accelerating orthodontic tooth movement and the resulting shortening of the treatment duration would be quite beneficial. Attempts have been made to accelerate alveolar bone remodeling which is crucial for the speed of orthodontic tooth movement. For that purpose, pharmaceuticals and various physical methods have been applied. Furthermore, surgical interventions at the alveolar process are supposed to cause an activation of the bone metabolism and consequently, speed up the orthodontic tooth movement [11].

Molecular mechanism

To achieve OTM, mechanical forces are applied on teeth. This initially causes fluid movement within the periodontal ligament (PDL) space and distortion of the PDL components (cells, extracellular matrix, and nerve terminals), setting into motion the process of release of a multitude of molecules (neurotransmitters, cytokines, growth factors, arachidonic acid metabolites etc.) which initiate alveolar bone remodeling. Orthodontic load strains nerve endings present in the PDL. These release in response a number of neuropeptides (substance P, vasoactive intestinal polypeptide, and calcitonin gene-related peptide-CGRP), which act on capillaries and cause the adhesion and migration of blood leukocytes into the area of compression [12]. Local hypoxia (unavoidably caused in areas of compression by occlusion of the PDL vessels) activates hypoxia-inducible transcription factor (HIF)-1a in endothelial cells and osteoblasts .And this leads to expression of downstream genes including VEGF (vascular endothelial growth factor) and receptor activator of NF-kB ligand (RANKL), which mediate the recruitment of peripheral blood mononuclear cells/osteoclast lineage cells from PDL capillaries and their conversion/activation into osteoclasts, respectively. Subsequently induce osteoclast terminal differentiation possibly through their action on RANK and RANKL expression [13]. Another chemokine ligand expressed

in the PDL under mechanical loading, CCL3, exerts its effects by interacting with chemokine receptors 1 and 5 (CCR1 and CCR5) present on the surface of osteoclasts and osteoblasts. The effects of chemokines seem to be of different nature depending on the receptor to which they bind, as the CCL3-CCR1 interaction leads to the induction of bone resorption by osteoclast recruitment, differentiation/activation [14]. Prostaglandins and leukotrienes are additional players in the process of tooth remodeling. PGE2 has different effects depending on the type of transmembrane receptor to which it binds. PGE2 can drive RANKL expression in osteoblasts (by binding to the EP2 or EP4 receptors), which subsequently leads to osteoclast activation [15], or drive bone mineralization by osteoblasts when binding to the EP1 receptor [16]. In addition, PGE2 has been shown to aid osteoclast formation [17] or lead to transient osteoclast inhibition when added to osteoclasts in vitro [18]. The two leukotrienes shown to be involved in tooth movement are LTB4 (leukotriene B4) and LTD4 (a cysteinyl leukotriene) [19], Both leukotrienes were found to significantly boost the recruitment and terminal differentiation/activation of osteoclasts through their effect on cytokine synthesis and in the presence of RANKL. Osteoblasts express IL-1b, IL-6, IL-11, TNFa and their receptors in response to compressive stress. IL-b shows an autocrine effect and enhances the phenomenon [20] plus induces osteoblasts to promote osteoclast activity (through induction of RANKL expression). IL-6 is involved in osteoclast recruitment and differentiation. TNFa directly stimulates the differentiation of osteoclast precursors to osteoclasts in the presence of M-CFS (which is a glycoprotein produced by fibroblasts and endothelial cells in response to growth factors and cytokines, such as PDGF, FGF, IL-1, and IL- 6). IL-11 enhances the expression of RANKL, a key molecule in osteoclast precursor differentiation, in osteoblasts. In areas of tension, growth factors (e.g., TGF-b) and cytokines (e.g., OPG) produced by PDL cells can induce apoptosis of osteoclasts [21] and tip the balance toward bone formation. One of the immediate responses of the PDL at sites of compression is also the rise in the level of matrix metalloproteinases (MMPs) which are produced by activated fibroblasts. MMPs either degrade collagen fibers (MMP-1 and MMP-8) or eliminate the degraded collagen (MMP-9 and MMP-2) to allow tooth movement [22, 23]. Chemokines mediate chemotaxis of leukocytes and bring about cellular differentiation. In the PDL, interaction between CCL2 (chemokine ligand 2) and CCR2 (chemokine receptor 2) have been found to mediate osteoclast precursor attraction to the sites of orthodontic force application and to osteoclasts and through secretion of cytokines such as IL-10 and TGF-b also play a key role in suppressing osteoclastic activity[24]. Balanced osteoclast activity is necessary to prevent uncontrollable osteolysis and control bone metabolism during OTM

Pharmacological Agents to Modulate Orthodontic Tooth Movement (OTM)

Pharmacological agents have the potential to interfere with the biochemical processes which govern tooth movement during, and stability after, orthodontic treatment. As a result, the possibility to accelerate/enhance OTM where needed (such as in areas of space closure) and to halt tooth movement where desired (to provide anchorage or to ensure positional tooth stability during the initial retention period) has attracted considerable interest in the field

Arachidonic acid metabolites

Among the arachidonic acid metabolites, PGE2 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 [25, 26]. Specific synthases are involved in the pathway of the synthesis of each type of prostaglandins (e.g., PGE and PGD synthases) and many of them have been cloned and could provide drug targets for the regulation of the synthesis of specific prostaglandins, such as PGE2 in the case of OTM [27]. In addition, it is possible that other PGs such as PGI2 may be involved in bone resorption providing further targets for drugs [28]. Another obvious group of drug targets are the identified receptors of specific prostaglandins (such as the receptors EP1, EP2, or EP4 of prostaglandin PGE2) and the design of selective agonists can provide pharmacological methods of modifying OTM through these receptors.

Intravenous immunoglobulin (IVIg) preparations were shown to induce COX-2 mediated PGE2synthesis and cytokine production [29-31]. It is possible that local administration of these IVIg preparations could be used to modulate bone modeling through PEG2 induction and bypass some of the limitations of PEG2 injections The mode of application of PGE2 is a major limitation as it involves repeated injection (due its short half-life) in combination with an anesthetic 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[32].

Carageenan

Carrageenan (CGN) is a common polysaccharide food additive derived from seaweeds and is used for stabilizing, emulsifying and thickening processed food and dairy products, as well as in non-food products, such as pharmaceuticals, toothpaste, room deodorizers, or cosmetics [36]. CGN can activate inflammatory cells (such as resident or recruited macrophages, lymphocytes, dendritic cells, and other myeloid cells which respond to IL-8 or other

cytokine/chemokine stimuli and produce TNF-a, as well as other cytokines, potentiating the inflammatory response), while inhibiting apoptosis [33,36,37]. Temporary increases of subchondral osteoclasts have been observed following subcutaneous CGN injection [38]. This and the above-mentioned properties of carrageenan predispose CGN as a potential local drug to facilitate orthodontic tooth movement. Study conducted by Kavoli *et al.* indicated that injection of carrageenan can speed up tooth movement by about 58% and increase the presence of osteoclasts by 40%, after 21 days and carrageenan was introduced as an intervention capable of speeding up OTM, by increasing the inflammatory response and osteoclastic activity.

Parathormone

Parathormone (PTH) is a compound secreted by the parathyroid gland which binds to receptors on osteoblasts, activating them and leading to the expression of insulin-like growth factor 1 (IGF-1; somatomedin).This results in the proliferation of osteoblasts and, with the participation of the RANK ligand, osteoclast activation[39]. Depending on the frequency of administration, PTH may stimulate bone formation (intermittent therapy) or its resorption (exposure longer than 1–2 years)[40]. Two 12-day studies in rats confirmed that intermittent administration of PTH accelerated the mesialization of the 1st molar 1.6 times after administration of a dose of 0.25 μg/100 g into the subperiosteal area and 1.4 times as a result of subcutaneous administration of 4 μg/100 g m.c.10,11

Vitamin D

Another agent that may affect tooth movement is vitamin D. 1, 25-dihydroxycholecalciferol is the most active metabolite of this vitamin. It mainly has an anabolic effect on the bone tissue (to a small extent also catabolic)[41]. Similarly to PTH, sub-periosteal administration of vitamin D enhances the activity and proliferation of osteoblasts [42]. Collins *et al.* used calcitriol dissolved in DMSO (dimethylsulfoxide) − a compound that readily penetrates cell membranes, as well as has a high solubility coefficient for vitamin D) − administered daily into the periosteum [43-44]. After 3 weeks, the retraction range of the canines was 60% higher compared to the control group. Other researchers came to similar conclusions, this time testing the action of this vitamin on rats. They noticed an increased number of both osteoclasts and osteoblasts [45-47]. Kawakami and Takano-Yamamoto emphasized the continuation of intensified remodeling during the retention period as well.19 In turn, Kale *et al.* observed that distalization of the maxillary incisors increased by 23%.20 in a few clinical trials, acceleration of orthodontic tooth movement was also demonstrated [48].

Nicotine

Nicotine is generally absorbed into the human body by the inhalation of cigarette smoke within a few seconds, where its systemic stimulatory and psychoactive effect unfolds by binding to cell membrane-based nicotinic acetylcholine receptors (nAChR) of the nervous system[49,50]. Several in vivo and in vitro studies have found that nicotine can have a proinflammatory effect on periodontal tissues and influence bone metabolism. Nicotine has been shown to dose-dependently increase the expression of cyclooxygenase 2 (COX-2) in human gingival and periodontal ligament fibroblasts [51, 52]. Furthermore, several studies have indicated that prostaglandin E2 enhances the expression of proinflammatory cytokines by fibroblasts, in particular of IL-1β, IL-6 and IL-8 [53, 54]. A nicotine-induced increase in the production of prostaglandin E2 could thus provide an explanation for the significant nicotine-induced increase in interleukin expression observed. The major mechanism for osteoclast activation and differentiation is the interaction of RANKL with the RANK-receptor of osteoclast precursor cells [55]. Orthodontic tooth movement, on the other hand, is also enabled by a similar, but controlled (pseudo)inflammatory process within the periodontal ligament and bone. This leads to an increase in osteoclastogenesis and bone resorption in compression zones of the periodontal ligament, whereas the recruitment of osteoblasts with corresponding osteogenesis is increased in tensile zones, thus enabling stable tooth movement overall. The nicotine-induced increase in osteoclast activity and osteoclastogenesis explains the observed nicotine-induced increase of OIIRR as well as acceleration of orthodontic tooth movement within 14 and 28 days Research on suitable pharmacological substances and their safe delivery and usage to this end is currently intensively pursued [56,57]. Although nicotine could be administered systemically in a controlled fashion via a nicotine patch or administered locally by injection into the periodontal ligament [57], the severe detrimental side effects observed and to be expected (root resorptions, periodontal bone loss) as well as the clinically limited acceleration achieved (about 50%) most likely exclude nicotine as suitable drug for possible adjuvant therapeutic use in orthodontics

Surgical Methods for the Acceleration of the Orthodontic Tooth Movement

Orthodontic treatment aims to improve dentofacial function and aesthetics but patients often complain that it takes a long time to achieve optimal results. To overcome this, surgical techniques have been developed, 1, 2and 2approaches have been reported to facilitate the movement of teeth. The first is corticotomy in which cortical bone is cut to improve bony remodeling. Periodontally accelerated osteogenic orthodontics, which is a combination of selective alveolar decortications and alveolar augmentation, 3–5can be modified using selective piezosurgery to circumscribe theroots, 6and more recently, techniques for minimally invasive flapless corticotomy have been introduced.1, 2 The second approach is based on

distraction osteogenesis is a method described by Ilizarov to induce new bone to form by the mechanical stretching of pre-existing bone

Corticotomy

The aim of corticotomy is to cut the cortical layer of alveolar bone in order to induce local temporary osteopenia. The origins of the method date back to the end of the 19th century; however, Kole, who discussed the procedure in 1959, is considered the pioneer of corticotomy [58, 59]. According to his claims, cortical bone is the main obstacle to the orthodontic movement of teeth. This theory, referring to osteotomy, was to a certain extent rejected in 1983, when Frost discovered the regional acceleratory phenomenon (RAP), and in 1994 Yaffe *et al*. introduced this concept to periodontal literature [60, 61]. Small harmful stimuli (such as shallow bone incisions) activate the RANK/RANKL system.

In "weakened" bone tissue, 10–50 times faster remodeling is expected. This effect lasts for about 4 months (though it can last up to 6–24 months), with peak efficiency reached 1 or 2 months after surgery [62].The field of the procedure depends on the defect: vertical incisions are made between the roots of the teeth, horizontally, 2–3 mm above the apices, in order not to damage the bundles. The advantage of the method lies in the creation of a more stable anchorage, not involving teeth/ arches in the procedure. The brackets of the fixed appliance are bonded before the surgery. The cuts, after earlier retraction of the muco-periosteal flap, can be made with traditional rotational tools or a piezoelectric knife. Dibart *et al.* recommend the use of the latter, due to limited traumatization of tissues, greater precision of execution, and more extensive bone demineralization, which induces prolonged RAP [63].

Periodontally accelerated osteogenic orthodontics

Described by Wilcko *et al*. in 2001, the technique referred to as periodontally accelerated osteogenic orthodontics (PAOO) or accelerated osteogenic orthodontics (AOO) is a combination of conventional corticotomy with the implantation of bone graft material.3Wilcko *et al.* observed the process of remodeling remineralization and demineralization of the bone and demonstrated its relationship with the RAP, as described earlier [64]. After retraction of the muco-periosteal flap and incisions in selected areas, allogenic frozen and dried material is placed in the scars [65]. Insertion of the material allows bone density and mass to increase. This increases the possible range of tooth movement, the apical base and the arch envelope, and minimizes gum recessions, relapses and the need for extraction [66]. One indication is the presence of shortened roots, which could become shorter during traditional treatment [66]. Wilcko *et al.* presented many cases demonstrating the effectiveness of the method in accelerating the movement of teeth while improving the condition of periodontal tissues [68, 69].

Piezocision

To initiate the RAP phenomenon, one needs to perform a cut to the cortical layer of bone. In the traditional technique, this stage is preceded by the detachment of the muco- periosteal flap. This increases the risk of discomfort and postoperative pain. Park *et al*. and Kim *et al*. proposed performing the procedure without the flap retraction, but directly through the gum [70, 71]. An alternative combining limited invasiveness, enhanced precision and treatment of periodontal problems is piezosurgery (the piezocision technique), described in 2009 by Dibart *et al.* [72]. It combines cuts in the bone through the gingiva with a piezoelectric knife to create of submucosal tunnels for bone substitute material.

Micro-osteoperforations

This is another treatment modality based on the RAP.102. Micro-osteoperforations can also be combined with standard corticotomy or the PAOO technique. Clinically, the use of micro-osteoperforations significantly increases the expression of cytokines, which leads to a 60% shorter treatment time compared to a control group, and 2.3 times faster retraction of canines [73]. The procedure itself is described as effective, convenient, and less invasive than standard corticotomy [74]. Experiments conducted on an animal model show both a shorter therapy time and increased remodeling occurring within the cancellous bone [75-77]. Similar results were obtained during the treatment of mild crowding (a study on 24 patients resulted in a 47% shorter treatment time), orthodontic extrusion of palatally impacted canines (6 patients) and retroinclination of upper incisors with sufficient bone support [78-80]. Al-Naoum *et al.* in a group of 30 patients obtained an average speed of 0.74 mm/week (compared to 0.2 mm/week on the control side) during retraction of canines [112].

Accelerated tooth movement induced by physical stimulus

In recent years, numerous surgical and nonsurgical adjunctive procedures to accelerate OTM have been introduced. Surgical techniques like corticotomy have been reported to facilitate tooth movement in short term via inducing regional acceleratory phenomenon. However, the invasiveness and postoperative discomfort make patients less receptive to these techniques and restrict the routine application in clinics. Several nonsurgical adjuncts including laser therapy, electric current, pulsed electromagnetic fields and photobiomodulation are suggested to promote tooth movement.

Effect of laser therapy on orthodontic tooth movement

Low level laser therapy, at a cellular level, causes an increase in RANKL (Receptor Activator of Nuclear Factor Kappa B Ligand) in the periodontal ligament which, in turn, increases the differentiation of precursor cells into activated osteoclasts and potentially increases the rate of orthodontic tooth movement. Most clinical trials investigating canine retraction into premolar extraction sites reported a positive effect caused by laser irradiation on the rate of canine movement [82]. However, a well-designed study with a low risk of bias, found no difference between the laser and control groups [83]. This contradictory finding may be due to the different laser application protocols with the energy density being lower compared with the other studies [82]. The inclusion of this trial affects the results of meta-analysis as one paper indicated that low-intensity laser application had no effect on the rate of orthodontic tooth movement [84] whereas the other concluded that there was weak evidence that low laser therapy plus a corticotomy were associated with accelerated orthodontic tooth movement. However, further research is required before the dual therapy achieves routine application [82]. An additional issue requiring consideration is the possibly that the wavelength used was less important than the energy of the laser and this may vary with different animal species [85]. For example, in dogs, photoradiation seems to accelerate orthodontic movement at a radiant exposure of 5.25 J/cm2, whereas a higher dosage (35.0 J/cm2) movement is delayed [86].

Photobiomodulation (PBM)

Photobiomodulation, also known as low-level light therapy (LLLT), attempts to use low energy lasers (previously discussed) or light-emitting diodes (LED) to modify cellular biology by the exposure to light in the red to near-infrared (NIR) range (600–1000 nm). The evidence regarding PBM is limited to one trial using the OrthoPulseTM appliance which was conducted by a consulting orthodontist for the company (Biolux Research Ltd.). The study concluded that intraoral PBM increased the average rate of tooth movement resulting in a 54 per cent average decrease in alignment duration compared with a control [87]. However, there were confounding variables including the use of different brackets in the two test groups. The design of the study was poor, lacking appropriate and complete reporting, so that the overall quality of evidence supporting this intervention is currently very low [82].

Electric Currents

Exogenous electric currents have been employed in the last two decades. Both experimentally and clinically, in successful attempts to initiate osteogenesis in intact bones or to enhance bone apposition in healing of uncomplicated or nonunionfractures. In spite of this encouraging clinical evidence By using immunohistochemical techniques, we discovered that external electric currents increased bone and PDL cyclic nucleotide contents.“‘; a step leading toward heightened enzymatic phosphorylation reactions, synthetic and secretory activities, and an enhanced rate of tissue remodeling. Earlier”, 2X we studied the involvement of adenosine 3’.5’-monophosphate (cyclic AMP. CAMP) in the periodontal tissue response to orthodontic treatment and concluded that mechanical forces might not be the most efficient means to activate PDL and alveolar bone cells. That conclusion, coupled with the recent observation that electric current can activate a large number of cells in a small, well-delineated area,‘)’ led us to hypothesize that the application of electric currents to periodontal tissues during orthodontic treatment will potentiate the effect of the mechanical forces and lead to an enhanced rate of cell activation, tissue remodeling, and tooth movement. Teeth treated by force and electricity moved significantly faster than those treated by force alone. Histologic examination of the involved tissues revealed that the enhanced tooth movement resulted from resorption of bone as a result of the compressive force and the presence of the anode near the PDL compression site. The degree of new bone formation (as judged by the length of the newly formed bony trabeculae in the PDL) at electrically treated tension sites was higher than at the corresponding sites of teeth treated by force alone. These results suggest that orthodontic tooth movement may be accelerated by the use of force in conjunction with other biologically potent means which can generate a local response. Specifically, this study has demonstrated that electric currents, in the range of 10 to 20 microamperes, can be used successfully for this purpose [88].

Tooth Movement-Induced Osteoclast Activation, Regulated By Sympathetic Signaling

Orthodontic tooth movement changes the bone architecture through the stimulation of bone remodeling because bone is a dynamic tissue that can adapt its mass and architecture to mechanical loading [89-96]. The periodontal ligament is highly innervated by nerves, and experimental tooth movement (ETM) was shown to increase the number of nerve fibers containing neuropeptides, such as substance P and calcitonin gene-related peptide (CGRP)[97-][100]. Alteration of these nerve fibers is considered to be involved in pain transduction, inflammatory response, and periodontal ligament remodeling [101, 102]. These nerve fibers are also considered to be involved in bone remodeling. When a force was applied to a tooth, osteoclasts predominantly appeared in the alveolar bone within a few days [103,104]. Inferior alveolar nerve transection suppressed an increase in osteoclast appearance during ETM. This suggests that sensory nerves play an important role in bone resorptive activity during ETM [105]. Kondo *et al*. reported that bone loss induced by mechanical unloading is regulated by the sympathetic nervous system]. The sympathetic nervous system regulates bone remodeling through the β2-adrenergic

receptor [91, 92, 106, 107]. These studies have indicated that β2-adrenergic receptor mediates signaling in osteoblasts, which inhibits bone formation and increases osteoclastogenesis via receptor activator of nuclear factor kappa-B ligand (RANKL) expression [107,108].

Effectiveness of Vibrational Stimulus to Accelerate Orthodontic Tooth Movement

Low-magnitude (LM; less than 1 g, where g = 9.81 m/s2) high-frequency (HF; 20–90 Hz) vibrations, such a mechanical signal, can positively influence skeletal homeostasis and stimulate an anabolic response in both weight-bearing [109] and non-weight-bearing [110] bone. In dental practice, several prospective randomised controlled clinical trials have recently investigated the effect on orthodontic tooth movement of supplemental vibration applied with fixed appliances for 20 min/day using a vibration device which delivers a force of 0.25 N (25.49 g) at a frequency of 30 Hz to the dentition [11-113]. Although some of these studies reported an increase in the rate of tooth movement when vibration was applied as an adjunct to orthodontic treatment, others demonstrated that supplemental vibration did not increase the rate of tooth movement. The anabolic effects of supplemental vibrational therapy on bone metabolism have been long recognized [114]. Its effectiveness in promoting suture growth and remodeling in craniofacial region has also been identified 115. A recent study indicates that vibration could accelerate OTM through promoting alveolar bone remodeling [116]. However, another experiment found that mechanical vibration did not increase the number of osteoclasts or rate of tooth movement [117]. It should be noted that distinguished difference of vibration frequency exists in these two animal studies (60 vs 5–20 Hz), indicating that vibratory stimulus could act in a frequency-dependent manner. Mechanical stimulation is known to activate NF-κB signals in osteoblasts and related cells and, thereafter, influences bone metabolism as a result of cellular and molecular interactions in osteoclasts, osteoblasts and osteocytes. Therefore, we hypothesised that a dynamic vibration force applied with a continuous static force would exert synergistic effects to activate bone modelling and remodeling through osteoclasts, osteoblasts and osteocytes, resulting in acceleration of orthodontic tooth movement Leethanakul *et al.* detected enhanced IL-1β secretion in gingival crevicular fluid in quadrant receiving vibrational stimulus compared to the control quadrant [118]. IL-1 could induce RANKL expression in osteoblasts and periodontal ligament cells, and also promote the differentiation of preosteoclast [119]. Interestingly, a well-designed animal study indicated that vibration could promote osteoclast formation via enhancing RANKL expression in periodontal tissue and thus facilitate alveolar bone remodeling and lead to faster tooth movement. These studies suggested that vibrational stimulus could accelerate OTM through promoting osteoclast formation and alveolar bone remodeling Vibratory stimulations have been proved to reduce pain perceptions in different fields]120,121]. Root resorption is one of the main complications in orthodontic treatment [122]. DeBiase *et al*. assessed the changes of root lengths after orthodontic treatment using periapical radiographs [123]. Based on current information, weak evidence suggests that vibrational stimulus is effective for accelerating tooth movement in canine retraction but not in the alignment phase. The effects of vibration on pain intensity and root resorption during orthodontic treatment are inconclusive.

Low frequency electromagnetic fields on orthodontic tooth movement

The results of different in vivo and in vitro studies show that the application of exogenous electromagnetic fields (EMF) affect the bone metabolism [124, 125]. Studies demonstrated that EMF can regulate the osteoblast proliferation and differentiation which may lead to reduction in the loss of bone mass and accelerate the bone formation in animal models [126]. This study was to evaluate whether a 50 Hz extremely low frequency electromagnetic field (ELF-EMF) affects the extent of orthodontic tooth movement in rats.. The effects of EMF on cells as well as on tissues are on both cellular and transcriptional levels SEMF group was significantly greater than that of Cg-Cnt but the largest extent of tooth movement was achieved in the PEMF group. Although Tengku *et al.* [127] reported that SEMF application did not enhance the orthodontic tooth movement; Sakata *et al*. [128] reported that the application of SEMF can accelerate the tooth movement in rats. On the other hand Showkatbakhsh *et al.* [130] reported that the accumulative toot movement was significantly larger in the PEMF group. Stark and Sinclair [131] reported that the rate of orthodontic tooth movement and bone deposition was increased after PEMF application Darendeliler *et al*. [129] reported that under PEMF, the coil spring induced tooth movement at a significantly higher extent than that of coil–magnet combination. Although there were some differences in relation with the duration and the frequency of EMF applications, our results are in accordance with the results of several studies [132]. EMF enhances DNA [135], RNA [134] and protein production in cell cultures [133] and short-term EMF application is suggested to cause accelerated calcium uptake in cartilaginous embryonic chick limbs [136]. On the other hand studies which evaluated the effects of EMF on bone and cartilage reported that EMF increased the rates of cellular division and metabolism, and thus promoted increased healing of bony and cartilaginous defects [137,138]. Although the precise mechanism of accelerated tooth movement after EMF applications is unclear, the beneficial therapeutic and cellular effects are thought to be contributed to the process of orthodontic tooth movement [139].

CONCLUSION

When reviewing the current evidence, one concluded that, of the non-surgical interventions, only low-level laser therapy provided some evidence of accelerating orthodontic tooth movement. However, a contrary review concluded that LLLT was unable to accelerate orthodontic tooth movement. Currently, the non-surgical methods are associated with very-low quality evidence. Further well-designed RCTs are required to determine whether non-surgical interventions may safely result in a clinically-important reduction in the duration of orthodontic treatment. Of the surgical interventions, a recent Cochrane review concluded that corticotomy appeared to show promise but the available evidence is of low quality indicating that future research is likely to change the estimate of any effect. A study in dogs, which investigated a corticotomy with a raised flap, demonstrated movement peaked at days and then decelerated. However, if a second surgery was performed, accelerated tooth movement was maintained. Similar results when performing a corticotomy with a raised flap were found in adults when canines were retracted following premolar extractions but the effect subsided four months following the procedure. As a result of these studies, the duration of the RAP seems to be in the range of two to three months, after which the rate of tooth movement returns to normal. Based upon the limited evidence available, the clinical significance of this temporary acceleration as part of the overall treatment time is questionable. In addition, there are significant additional surgical costs and associated morbidity and, combined with the short duration of the effect, this makes the application of corticotomies on a routine basis, unjustified.

REFERENCES

1. Tsichlaki A, Chin SY, Pandis N, Fleming PS. How long does treatment with fixed orthodontic appliances last? A systematic review. Am J Orthod Dentofacial Orthop. 2016;149:308–18.
2. Fisher MA, Wenger RM, Hans MG. Pretreatment characteristics associated with orthodontic treatment duration. Am J Orthod Dentofacial Orthop. 2010;137:178–86.
3. Mavreas D, Athanasiou AE. Factors affecting the duration of orthodontic treatment: a systematic review. Eur J Orthod. 2008;30:386–95.
4. Brin I, Tulloch JF, Koroluk L, Philips C. External apical root resorption in Class II malocclusion: a retrospective review of 1- versus 2-phase treatment. Am J Orthod Dentofacial Orthop. 2003;124:151-6.
5. Sunku R, Roopesh R, Kancherla P, Perumalla KK, Yudhistar PV, Reddy VS. Quantitative digital subtraction radiography in the assessment of external apical root resorption induced by orthodontic therapy: a retrospective study. J Contemp Dent Pract. 2011;12:422-8.
6. Jiang RP, McDonald JP, Fu MK. Root resorption before and after orthodontic treatment: a clinical study of contributory factors. Eur J Orthod. 2010;32:693-7.
7. Richter AE, Arruda AO, Peters MC, Sohn W. Incidence of caries lesions among patients treated with comprehensive orthodontics. Am J Orthod Dentofacial Orthop. 2011;139: 657-64.
8. Ikeda T, Yamaguchi M, Meguro D, Kasai K. Prediction and causes of open gingival embrasure spaces between the mandibular central incisors following orthodontic treatment. Aust Orthod J. 2004;20:87-92.
9. Hassan AH, Al-Fraidi AA, Al-Saeed SH. Corticotomy-assisted orthodontic treatment: review. Open Dent J. 2010;4:159-64.
10. Rosvall MD, Fields HW, Ziuchkovski J, Rosenstiel SF, Johnston WM. Attractiveness, acceptability, and value of orthodontic appliances. Am J Orthod Dentofacial Orthop. 2009;135:276–7
11. Hoffmann S, Papadopoulos N, Visel D, Visel T, Jost-Brinkmann PG, Praeger TM. Influence of piezotomy and osteoperforation of the alveolar process on the rate of orthodontic tooth movement: a systematic review. Journal of Orofacial Orthopedics/Fortschritte der Kieferorthopädie. 2017 Jul 1;78(4):301-11.
12. Krishnan V, Davidovitch ZE. Cellular, molecular, and tissue-level reactions to orthodontic force. American Journal of Orthodontics and Dentofacial Orthopedics. 2006 Apr 1;129(4):469-e1.
13. De Albuquerque Taddei SR, Andrade Jr I, Queiroz-Junior CM, Garlet TP, Garlet GP, de Queiroz Cunha F, Teixeira MM, da Silva TA. Role of CCR2 in orthodontic tooth movement. American journal of orthodontics and dentofacial orthopedics. 2012 Feb 1;141(2):153-60.
14. Silvana R, Queiroz-Junior CM, Moura AP, Andrade Jr I, Garlet GP, Proudfoot AE, Teixeira MM, da Silva TA. The effect of CCL3 and CCR1 in bone remodeling induced by mechanical loading during orthodontic tooth movement in mice. Bone. 2013 Jan 1;52(1):259-67.
15. Mayahara K, Yamaguchi A, Takenouchi H, Kariya T, Taguchi H, Shimizu N. Osteoblasts stimulate osteoclastogenesis via RANKL expression more strongly than periodontal ligament cells do in response to PGE2. Archives of oral biology. 2012 Oct 1;57(10):1377-84.
16. Fujieda M, Kiriu M, Mizuochi S, Hagiya KI, Kaneki H, Ide H. Formation of mineralized bone nodules by rat calvarial osteoblasts decreases with donor age due to a reduction in signaling through EP1 subtype of prostaglandin E2 receptor. Journal of cellular biochemistry. 1999 Nov 1;75(2):215-25.
17. Collins DA, Chambers TJ. Prostaglandin E2 promotes osteoclast formation in murine hematopoietic cultures through an action on hematopoietic cells. Journal of Bone and Mineral Research. 1992 May;7(5):555-61.

18. Fuller K, Chambers TJ. Effect of arachidonic acid metabolites on bone resorption by isolated rat osteoclasts. Journal of Bone and Mineral Research. 1989 Apr;4(2):209-15.
19. Moura AP, Taddei SR, Queiroz-Junior CM, Madeira MF, Rodrigues LF, Garlet GP, Souza DG, Machado FS, Andrade Jr I, Teixeira MM, Silva TA. The relevance of leukotrienes for bone resorption induced by mechanical loading. Bone. 2014 Dec 1;69:133-8.
20. Koyama Y, Mitsui N, Suzuki N, Yanagisawa M, Sanuki R, Isokawa K, Shimizu N, Maeno M. Effect of compressive force on the expression of inflammatory cytokines and their receptors in osteoblastic Saos-2 cells. Archives of oral biology. 2008 May 1;53(5):488-96.
21. Kobayashi Y, Hashimoto F, Miyamoto H, Kanaoka K, Miyazaki-Kawashita Y, Nakashima T, Shibata M, Kobayashi K, Kato Y, Sakai H. Force-Induced Osteoclast Apoptosis In Vivo Is Accompanied by Elevation in Transforming Growth Factor β and Osteoprotegerin Expression. Journal of Bone and Mineral Research. 2000 Oct;15(10):1924-34.
22. Lekic P, McCulloch CA. Periodontal ligament cell populations: the central role of fibroblasts in creating a unique tissue. The Anatomical Record: An Official Publication of the American Association of Anatomists. 1996 Jun;245(2):327-41.
23. Cantarella G, Cantarella R, Caltabiano M, Risuglia N, Bernardini R, Leonardi R. Levels of matrix metalloproteinases 1 and 2 in human gingival crevicular fluid during initial tooth movement. American Journal of Orthodontics and Dentofacial Orthopedics. 2006 Nov 1;130(5):568-e11.
24. Zaiss MM, Axmann R, Zwerina J, Polzer K, Gückel E, Skapenko A, Schulze-Koops H, Horwood N, Cope A, Schett G. Treg cells suppress osteoclast formation: a new link between the immune system and bone. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology. 2007 Dec;56(12):4104-12.
25. Yamasaki K, Shibata Y, Fukuhara T. The effect of prostaglandins on experimental tooth movement in monkeys (Macaca fuscata). Journal of dental research. 1982 Dec;61(12):1444-6.
26. Leiker BJ, Nanda RS, Currier GF, Howes RI, Sinha PK. The effects of exogenous prostaglandins on orthodontic tooth movement in rats. American Journal of Orthodontics and Dentofacial Orthopedics. 1995 Oct 1;108(4):380-8.
27. Forsberg L, Leeb L, Thorén S, Morgenstern R, Jakobsson PJ. Human glutathione dependent prostaglandin E synthase: gene structure and regulation. FEBS letters. 2000 Apr 7;471(1):78-82.
28. Wang J, Yamamoto K, Sugimoto Y, Ichikawa A, Yamamoto S. Induction of prostaglandin I2 receptor by tumor necrosis factor α in osteoblastic MC3T3-E1 cells. Biochimica et Biophysica Acta (BBA)-Molecular and Cell Biology of Lipids. 1999 Oct 18;1441(1):69-76.
29. Trinath J, Hegde P, Sharma M, Maddur MS, Rabin M, Vallat JM, Magy L, Balaji KN, Kaveri SV, Bayry J. Intravenous immunoglobulin expands regulatory T cells via induction of cyclooxygenase-2–dependent prostaglandin E2 in human dendritic cells. Blood. 2013 Aug 22;122(8):1419-27.
30. von Gunten S, Cortinas-Elizondo F, Kollarik M, Beisswenger C, Lepper PM. Mechanisms and potential therapeutic targets in allergic inflammation: recent insights. Allergy. 2013 Dec;68(12):1487-98.
31. Djoumerska-Alexieva I, Roumenina L, Pashov A, Dimitrov J, Hadzhieva M, Lindig S, Voynova E, Dimitrova P, Ivanovska N, Bockmeyer C, Stefanova Z. Intravenous immunoglobulin with enhanced polyspecificity improves survival in experimental sepsis and aseptic systemic inflammatory response syndromes. Molecular medicine. 2015 Jan 1;21(1):1002-10.
32. Kouskoura T, Katsaros C, von Gunten S. The potential use of pharmacological agents to modulate orthodontic tooth movement (OTM). Frontiers in physiology. 2017 Feb 8;8:67.
33. Bhattacharyya S, Dudeja PK, Tobacman JK. Tumor necrosis factor alpha-induced inflammation is increased but apoptosis is inhibited by common food additive carrageenan. J Biol Chem. 2010;285(50):39511–22.
34. Tobacman JK. Review of harmful gastrointestinal effects of carrageenan in animal experiments. Environ Health Perspect. 2001;109(10):983–94.
35. Bhattacharyya S, Liu H, Zhang Z, Jam M, Dudeja PK, Michel G, Linhardt RJ, Tobacman JK. Carrageenan-induced innate immune response is modified by enzymes that hydrolyze distinct galactosidic bonds. The Journal of nutritional biochemistry. 2010 Oct 1;21(10):906-13.
36. Necas J, Bartosikova L. Carrageenan: a review. Vet Med. 2013;58(4):187–205.
37. Sfikakis PP. The first decade of biologic TNF antagonists in clinical practice: lessons learned, unresolved issues and future directions. Curr Dir Autoimmun. 2010;11:180–210.
38. Schett G, Stolina M, Bolon B, Middleton S, Adlam M, Brown H, Zhu L, Feige U, Zack DJ. Analysis of the kinetics of osteoclastogenesis in arthritic rats. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology. 2005 Oct;52(10):3192-201.
39. Dobnig H, Turner RT. Evidence that intermittent treatment with parathyroid hormone increases bone formation in adult rats by activation of bone lining cells. Endocrinology. 1995 Aug 1;136(8):3632-8.
40. Esbrit P, Alcaraz MJ. Current perspectives on parathyroid hormone (PTH) and PTH-related protein (PTHrP) as bone anabolic therapies. Biochemical pharmacology. 2013 May 15;85(10):1417-23.

41. Kouskoura T, Katsaros C, von Gunten S. The potential use of pharmacological agents to modulate orthodontic tooth movement (OTM). Frontiers in physiology. 2017 Feb 8;8:67.
42. Reichel H, Koeffler HP, Norman AW. The role of the vitamin D endocrine system in health and disease. New England Journal of Medicine. 1989 Apr 13;320(15):980-91.
43. Collins MK, Sinclair PM. The local use of vitamin D to increase the rate of orthodontic tooth movement. *Am J Orthod Dentofacial Orthop*. 1988;94:278–284.
44. Wood DC, Wood J. Pharmacologic and biochemical considerations of dimethyl sulfoxide. *Ann NY Acad Sci*. 1975;243:7–19.
45. Takano-Yamamoto T, Kawakami M, Kobayashi Y, Yamashiro T, Sakuda M. The effect of local application of 1,25-dihydroxycholecalciferol on osteoclast numbers in orthodontically treated rats. *J Dent Res*. 1992;71:53–59.
46. Kawakami M, Takano-Yamamoto T. Local injection of 1,25-dihydroxyvitamin D3 enhanced bone formation for tooth stabilization after experimental tooth movement in rats. *J Bone Miner Metab*. 2004;22:541–546.
47. Kale S, Kocadereli I, Atilla P, Aşan E. Comparison of the effects of 1,25 dihydroxycholecalciferol and prostaglandin E2 on orthodontic tooth movement. *Am J Orthod Dentofacial Orthop*. 2004;125:607–614.
48. Blanco JF, Diaz R, Gross H, Rodríguez N, Hernandez LR. Efecto de la administración sistémica del 1,25 Dihidrxicolecalciferol sobre la velocidad del movimiento ortodóncico en humanos. *Estudio Clínico Revista Odontos*. 2001;8:13–21.
49. Malhotra R, Kapoor A, Grover V, Kaushal S. Nicotine and periodontal tissues. Journal of Indian Society of Periodontology. 2010 Jan;14(1):72.
50. Matta SG, Balfour DJ, Benowitz NL, Boyd RT, Buccafusco JJ, Caggiula AR, Craig CR, Collins AC, Damaj MI, Donny EC, Gardiner PS. Guidelines on nicotine dose selection for in vivo research. Psychopharmacology. 2007 Feb 1;190(3):269-319.
51. Kirschneck C, Proff P, Maurer M, Reicheneder C, Römer P. Orthodontic forces add to nicotine-induced loss of periodontal bone. Journal of Orofacial Orthopedics/Fortschritte der Kieferorthopädie. 2015 May 1;76(3):195-212.
52. Chang YC, Tsai CH, Yang SH, Liu CM, Chou MY. Induction of cyclooxygenase-2 mRNA and protein expression in human gingival fibroblasts stimulated with nicotine. Journal of periodontal research. 2003 Oct;38(5):496-501.
53. Czuszak CA, Sutherland DE, Billman MA, Stein SH. Prostaglandin E2 potentiates interleukin-1β induced interleukin-6 production by human gingival fibroblasts. Journal of clinical periodontology. 1996 Jul;23(7):635-40.
54. Cho JS, Han IH, Lee HR, Lee HM. Prostaglandin E2 Induces IL-6 and IL-8 Production by the EP Receptors/Akt/NF-κB pathways in nasal polyp-derived fibroblasts. Allergy, asthma & immunology research. 2014 Sep 1;6(5):449-57.
55. Meikle MC. The tissue, cellular, and molecular regulation of orthodontic tooth movement: 100 years after Carl Sandstedt. The European Journal of Orthodontics. 2006 Jun 1;28(3):221-40.
56. Kouskoura T, Katsaros C, von Gunten S. The potential use of pharmacological agents to modulate orthodontic tooth movement (OTM). Frontiers in physiology. 2017 Feb 8;8:67.
57. Andrade IJR, Sousa AB, da Silva GG. New therapeutic modalities to modulate orthodontic tooth movement. Dental Press J Orthod. 2014; 19(6): 123–133.
58. Guilford SH. *Orthodontia or Malposition of the Human Teeth, Its Prevention and Remedy*. Philadelphia, PA: Spangler&Davis. 1893.
59. Köle H. Surgical operations of the alveolar ridge to correct occlusal abnormalities. *Oral Surg Oral Med Oral Pathol*. 1959;12:515–529.
60. Frost HM. The biology of fracture healing. An overview for clinicians. Part II. Clinical orthopaedics and related research. 1989 Nov(248):294-309.
61. Yaffe A, Fine N, Binderman I. Regional accelerated phenomenon in the mandible following mucoperiosteal flap surgery. Journal of periodontology. 1994 Jan;65(1):79-83.
62. Murphy KG, Wilcko MT, Wilcko WM, Ferguson DJ. Periodontal accelerated osteogenic orthodontics: A description of the surgical technique. *J Oral Maxillofac Surg*. 2009;67:2160–2166.
63. Mehra P. Corticotomy-facilitated orthodontics: Surgical considerations. In: Brugnami F, Caiazzo A, eds. *Orthodontically Driven Corticotomy: Tissue Engineering to Enhance Orthodontic and Multidisciplinary Treatment*. Hoboken, NJ: John Wiley & Sons. 2014.
64. Wilcko WM, Wilcko T, Bouquot JE, Ferguson DJ. Rapid orthodontics with alveolar reshaping: Two case reports of decrowding. *Int J Periodontics Restorative Dent*. 2001;21:9–19.
65. Ericsson I, Thilander B, Lindhe J. Periodontal conditions after orthodontic tooth movements in the dog. *Angle Orthod*. 1978;48:210–218.
66. Murphy NC, Wilcko MT, Bissada NF, Davidovitch Z, Enlow DH, Dashe J. Orthodontic applications of alveolus decortication. In: Brugnami F, Caiazzo A, eds. *Orthodontically Driven Corticotomy: Tissue Engineering to Enhance Orthodontic and Multidisciplinary Treatment*. Hoboken, NJ: John Wiley & Sons. 2014.
67. Montesinos FA, Linares TS, Pérez-Gasque BM. Accelerated Osteogenic Orthodontics™ for retreatment of a patient with diminished root length

and absence of the maxillary central incisor. *Saudi Dent J*. 2015;27:228–234.
68. Wilcko MT, Wilko WM, Bissada NF. An evidence-based analysis of periodontally accelerated orthodontic and osteogenic techniques: A synthesis of scientific perspective. *Semin Orthodont*. 2008;14:305–316.
69. Wilcko WM, Wilcko MT, Bouquot JE, Ferguson DJ. Accelerated orthodontics with alveolar reshaping. *J Ortho Practice*. 2000;10:63–70.
70. Park YG, Kang SG, Kim SJ. Accelerated tooth movement by Corticision as an osseous orthodontic paradigm. *Kinki Tokai Kyosei Shika Gakkai Gakujyutsu Taikai Sokai*. 2006;48:6.
71. Kim SJ, Park YG, Kang SG. Effects of Corticision on paradental remodeling in orthodontic tooth movement. *Angle Orthod*. 2009;79:284–291.
72. Dibart S, Keser EI. Piezocision™. In: Brugnami F, Caiazzo A, eds. *Orthodontically Driven Corticotomy: Tissue Engineering to Enhance Orthodontic and Multidisciplinary Treatment*. Hoboken, NJ: John Wiley & Sons. 2014.
73. Pobanz JM, Storino D, Nicozisis J. Orthodontic acceleration: Propel alveolar micro-osteoperforation. *Orthotown*. 2013;5:22–25.
74. Alikhani M, Raptis M, Zoldan B, Sangsuwon C, Lee YB, Alyami B, Corpodian C, Barrera LM, Alansari S, Khoo E, Teixeira C. Effect of micro-osteoperforations on the rate of tooth movement. American Journal of Orthodontics and Dentofacial Orthopedics. 2013 Nov 1;144(5):639-48.
75. Sanjideh PA, Rossouw PE, Campbell PM, Opperman LA, Buschang PH. Tooth movements in foxhounds after one or two alveolar corticotomies.*Eur J Orthod*. 2010;32:106–113.
76. Baloul SS, Gerstenfeld LC, Morgan EF, Carvalho RS, Van Dyke TE, Kantarci A. Mechanism of action and morphologic changes in the alveolar bone in response to selective alveolar decortication- facilitated tooth movement. *Am J Orthod Dentofacial Orthop*. 2011;139(Suppl 4):83–101.
77. Sebaoun JD, Kantarci A, Turner JW, Carvalho RS, Van Dyke TE, Ferguson DJ. Modeling of trabecular bone and lamina dura following selective alveolar decortication in rats. *J Periodontol*. 2008;79:1679–1688.
78. Charavet C, Lecloux G, Bruwier A, Rompen E, Maes N, Limme M, Lambert F. Localized piezoelectric alveolar decortication for orthodontic treatment in adults: a randomized controlled trial. Journal of dental research. 2016 Aug;95(9):1003-9.
79. Fischer TJ. Orthodontic treatment acceleration with corticotomyassisted exposure of palatally impacted canines. *Angle Orthod*. 2007;77:417–420.
80. Lee JK, Chung KR, Baek SH. Treatment outcomes of orthodontic treatment, corticotomy-assisted orthodontic treatment, and anterior segmental osteotomy for bimaxillary dentoalveolar protrusion. *Plast Reconstr Surg*. 2007;120:1027–1036.
81. Al-Naoum F, Hajeer MY, Al-Jundi A. Does alveolar corticotomy accelerate orthodontic tooth movement when retracting upper canines? A split-mouth design randomized controlled trial. *J Oral Maxillofac Surg*. 2014;72:1880–1889.
82. Gkantidis N, Mistakidis I, Kouskoura T, Pandis N. Effectiveness of non-conventional methods for accelerated orthodontic tooth movement: a systematic review and meta-analysis. J Dent. 2014;42:1300–19.
83. Limpanichkul W, Godfrey K, Srisuk N, Rattanayatikul C. Effects of low-level laser therapy on the rate of orthodontic tooth movement. Orthod Craniofac Res. 2006;9:38–43.
84. Long H, Pyakurel U, Wang Y, Liao L, Zhoua Y, Lai W. Interventions for accelerating orthodontic tooth movement: A systematic review. Angle Orthod. 2013;83:164–171.
85. Seifi M, Shafeei HA, Daneshdoost S, Mir M. Effects of two types of low-level laser wave lengths (850 and 630 nm) on the orthodontic tooth movements in rabbits. Lasers Med Sci. 2007;22:261–4.
86. Goulart CS, Nouer PR, Mouramartins L, Garbin IU, de Lizarelli Fatima Zanirato R. Photoradiation and orthodontic movement: Experimental study with canines. Photomed Laser Surg. 2006;24:192–196.
87. Shaughnessy T, Kantarci A, Kau CH, Skrenes D, Skrenes S, Ma D. Intraoral photobiomodulation-induced orthodontic tooth alignment: a preliminary study. BMC Oral Health. 2016; 16:3.
88. Davidovitch Z. Tooth movement. Critical Reviews in Oral Biology & Medicine. 1991 Oct;2(4):411-50.
89. Ehrlich PJ, Lanyon LE. Mechanical strain and bone cell function: a review. Osteoporos Int. 2002;13:688-700.
90. Bikle DD, Sakata T, Halloran BP. The impact of skeletal unloading on bone formation, Gravit Space. Biol Bull. 2003;16:45-54.
91. Hino K, Nifuji A, Morinobu M, Tsuji K, Ezura Y, Nakashima K, Yamamoto H, Noda M. Unloading-induced bone loss was suppressed in gold-thioglucose treated mice. Journal of cellular biochemistry. 2006 Oct 15;99(3):845-52.
92. Kondo H, Nifuji A, Takeda S, Ezura Y, Rittling SR, Denhardt DT, Nakashima K, Karsenty G, Noda M. Unloading induces osteoblastic cell suppression and osteoclastic cell activation to lead to bone loss via sympathetic nervous system. Journal of Biological Chemistry. 2005 Aug 26;280(34):30192-200.
93. Marenzana M, Chenu C. Sympathetic nervous system and bone adaptive response to its mechanical environment. J Musculoskelet Neuronal Interact. 2008;8(2):111-20.
94. Lanyon L, Skerry T. Perspective: postmenopausal osteoporosis as a failure of bone's adaptation to

functional loading: a hypothesis. Journal of Bone and Mineral Research. 2001 Nov;16(11):1937-47.
95. Kondo H, Ezura Y, Nakamoto T, Hayata T, Notomi T, Sorimachi H, Takeda S, Noda M. MURF1 deficiency suppresses unloading-induced effects on osteoblasts and osteoclasts to lead to bone loss. Journal of cellular biochemistry. 2011 Dec;112(12):3525-30.
96. Ishijima M, Tsuji K, Rittling SR, Yamashita T, Kurosawa H, Denhardt DT, Nifuji A, Noda M. Resistance to unloading-induced three-dimensional bone loss in osteopontin-deficient mice. Journal of Bone and Mineral Research. 2002 Apr;17(4):661-7.
97. Kato J, Wakisaka S, Kurisu K. Immunohistochemical changes in the distribution of nerve fibers in the periodontal ligament during an experimental tooth movement of the rat molar. Acta Anat (Basel). 1996;157:53-62.
98. Norevall LI, Forsgren S, Matsson L. Expression of neuropeptides (CGRP, substance P) during and after orthodontic tooth movement in the rat. Eur J Orthod. 1995;17: 311-25.
99. Saito I, Ishii K, Hanada K, Sato O, Maeda T. Responses of calcitonin gene-related peptide-immunopositive nerve fibres in the periodontal ligament of rat molars to experimental tooth movement. Arch Oral Biol. 1991; 36:689-92.
100. Vandevska-Radunovic V, Kvinnsland S, Kvinnsland IH. Effect of experimental tooth movement on nerve fibres immunoreactive to calcitonin gene-related peptide, protein gene product 9.5, and blood vessel density and distribution in rats. Eur J Orthod 1997; 19:517-29.
101. Brown DF, Moerenhout RG. The pain experience and psychological adjustment to orthodontic treatment of preadolescents, adolescents, and adults. Am J Orthod Dentofacial Orthop. 1991;100:349-56.
102. Deguchi T, Yabuuchi T, Ando R, Ichikawa H, Sugimoto T, Takano-Yamamoto T. Increase of galanin in trigeminal ganglion during tooth movement. J Dent Res. 2006;85:658-63.
103. Rygh P. Ultrastructural cellular reactions in pressure zones of rat molar periodontium incident to orthodontic tooth movement. Acta Odontol Scand. 1972;30:575-93.
104. Yokoya K, Sasaki T, Shibasaki Y. Distributional changes of osteoclasts and pre-osteoclastic cells in periodontal tissues during experimental tooth movement as revealed by quantitative immunohistochemistry of H(+)-ATPase. J Dent Res. 1997;76:580-7.
105. Yamashiro T, Fujiyama K, Fujiyoshi Y, Inaguma N, Takano-Yamamoto T. Inferior alveolar nerve transection inhibits increase in osteoclast appearance during experimental tooth movement. Bone 2000;26:663-9.
106. Takeda S, Karsenty G. Central control of bone formation. J Bone Miner Metab. 2001;19:195-8.
107. Takeuchi T, Tsuboi T, Arai M, Togari A. Adrenergic stimulation of osteoclastogenesis mediated by expression of osteoclast differentiation factor in MC3T3-E1 osteoblast-like cells. Biochem Pharmacol. 2001;61:579-86.
108. Elefteriou F, Ahn JD, Takeda S, Starbuck M, Yang X, Liu X, et al. Leptin regulation of bone resorption by the sympathetic nervous system and CART. Nature. 2005;434: 514-20
109. Woodhouse NR, DiBiase AT, Johnson N, Slipper C, Grant J, Alsaleh M, Donaldson AN, Cobourne MT. Supplemental vibrational force during orthodontic alignment: a randomized trial. J Dent Res. 2015;94:682–9.
110. DiBiase AT, Woodhouse NR, Papageorgiou SN, Johnson N, Slipper C, Grant J, Alsaleh M, Cobourne MT. Effect of supplemental vibrational force on orthodontically induced inflammatory root resorption: a multicentre randomized clinical trial. Am J Orthod Dentofac Orthop. 2016;150:918–27.
111. Zawawi KH. Patients' acceptance of corticotomy-assisted orthodontics. Patient Prefer Adherence. 2015;9:1153–8.
112. Kalemaj Z, Debernard IC, Buti J. Efficacy of surgical and non-surgical interventions on accelerating orthodontic tooth movement: a systematic review. Eur J Oral Implantol. 2015;8:9–24.
113. Showkatbakhsh R, Jamilian A, Showkatbakhsh M. The effect of pulsed electromagnetic fields on the acceleration of tooth movement. World J Orthod. 2010;11:e52–6.
114. Rubin C, Turner AS, Muller R, Mittra E, McLeod K, Lin W, Qin YX. Quantity and quality of trabecular bone in the femur are enhanced by a strongly anabolic, noninvasive mechanical intervention. J Bone Miner Res. 2002;17:349–57.
115. Peptan AI, Lopez A, Kopher RA, Mao JJ. Responses of intramembranous bone and sutures upon in vivo cyclic tensile and compressive loading. Bone. 2008;42:432–8.
116. Nishimura M, Chiba M, Ohashi T, Sato M, Shimizu Y, Igarashi K, Mitani H. Periodontal tissue activation by vibration: intermittent stimulation by resonance vibration accelerates experimental tooth movement in rats. Am J Orthod Dentofac Orthop. 2008;133:572–83. 14. Bowman SJ. The effect of vibration on the rate of leveling and alignment. J Clin Orthod. 2014;48:678–88.
117. Yadav S, Dobie T, Assefnia A, Gupta H, Kalajzic Z, Nanda R. Effect of low-frequency mechanical vibration on orthodontic tooth movement. American Journal of Orthodontics and Dentofacial Orthopedics. 2015 Sep 1;148(3):440-9.
118. Leethanakul C, Suamphan S, Jitpukdeebodintra S, Thongudomporn U, Charoemratrote C. Vibratory stimulation increases interleukin-1 beta secretion during orthodontic tooth movement. Angle Orthod. 2016;86:74–80.

119. Teixeira CC, Khoo E, Tran J, Chartres I, Liu Y, Thant LM, Khabensky I, Gart LP, Cisneros G, Alikhani M. Cytokine expression and accelerated tooth movement. J Dent Res. 2010;89:1135–41.
120. Lundeberg T, Nordemar R, Ottoson D. Pain alleviation by vibratory stimulation. Pain. 1984;20:25–44.
121. Roy EA, Hollins M, Maixner W. Reduction of TMD pain by high-frequency vibration: a spatial and temporal analysis. Pain. 2003;101:267–74.
122. Weltman B, Vig KW, Fields HW, Shanker S, Kaizar EE. Root resorption associated with orthodontic tooth movement: a systematic review. Am J Orthod Dentofac Orthop. 2010;137:462–76.
123. DiBiase AT, Woodhouse NR, Papageorgiou SN, Johnson N, Slipper C, Grant J, Alsaleh M, Cobourne MT. Effect of supplemental vibrational force on orthodontically induced inflammatory root resorption: a multicentre randomized clinical trial. Am J Orthod Dentofac Orthop. 2016;150:918–27.
124. Akpolat V, Celik MS, Celik Y, Akdeniz N, Ozerdem MS. Gynecol Endocrinol. 2009;25:524–529.
125. Yamamoto Y, Ohsaki Y, Goto T, Nakasima A, Lijima T. J Dental Res. 2003;82:962–966. Available from: http://dx. doi.org/10.1177/154405910308201205
126. Tanizawa T, Yamaguchi A, Uchiyama Y, Miyaura C, Ikeda T, Ejiri S, Nagai Y, Yamato H, Murayama H, Sato M, Nakamura T. Bone. 2000;26(1):43–53.
127. Tengku BS, Joseph BK, Harbrow D, Taverne AA, Symons AL. Eur J Orthod. 2000;22:475–487.
128. Sakata M, Yamamoto Y, Imamura N, Nakata S, Nakasima A. J Orthod. 2008;35:249–254.
129. Darendeliler MA, Zea A, Shen G, Zoellner H. Aust Dental J. 2007;52:282–287.
130. Showkatbakhsh R, Jamilian A, Showkatbakhsh M. World J Orthod. 2010;11:52–56.
131. Stark TM, Sinclair PM. Am J Orthod Dentofacial Orthop. 1987;91:91–104.
132. Chen Q. Zhonghua Kou Qiang Yi Xue Za Zhi. 1991;26:7–10.
133. Farndale RW, Murray JC. Calcified Tissue Int. 1985;37:178–182.
134. Liboff AR, Williams T Jr, Strong DM, Wistar R Jr. Science. 1984;24:818–820.
135. Rodan GA, Bourret LA, Norton LA. Science. 1978;10:690–692.
136. Colacicco G, Pilla AA. Calcified Tissue Int. 1984;36:167-174.
137. Martin RB, Gutman W. Calcified Tissue Int. 1978;5:23
138. Norton JB, Young SO, Kenner GH. Clin Orthop. 1977;48:915-923.
139. Bassett CA, Pilla AA, Pawluk RJ. Clin Orthop Relat Res. 1977;124:128-143.