Accelerated Orthodontic Tooth Movement - From Theoretical Knowledge to Clinical Implementation

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Abstract

AIM: This review aims to evaluate the efficiency of Accelerated Orthodontic Tooth Movement (AOTM) compared to conventional methods in terms of tooth movement speed and treatment duration, and to assess the existing evidence in current research.
METHODS: An electronic search was conducted on PubMed, complemented by a manual search using Readcube software and the websites of selected orthodontic journals.
RESULTS: The initial search identified 232 studies, with 40 passing the first review phase, ultimately resulting in the selection of 35 studies. Five AOTM strategies employed in humans include corticotomy / piezotomy, interseptal alveolar surgery, low-intensity laser therapy (LILT), vibration, and biological treatment.
CONCLUSION: All AOTM strategies share a common biological basis and are categorised as either stimulation methods or intensification methods. Evidence suggests that surgical strategies, as intensification methods, can accelerate tooth movement during the initial two months of healing, reducing treatment duration by over 50%. Notably, dentoalveolar distraction achieves tooth movement rates of up to 0.8 mm/day, while corticotomy / piezotomy can enhance tooth movement by 41% to 80%. Device-assisted therapeutics approaches are still controversial, whereas LILT may improve tooth alignment by more than 100%. Biological strategies are less explored due to technical challenges.

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Archive of Orofacial Data Science

Accepted: Friday 23rd May, 2025. **Data availability statement:** All relevant data are within the article or supplement files unless otherwise declared by the author(s).

1 Introduction

Orthodontics is evolving, benefiting from advances in medical, dental, and computer sciences. It is no surprise that one of the main features of our time—speed—is also influencing orthodontics, which is typically characterised by lengthy treatment times. According to the literature, the duration of conventional comprehensive multibracket orthodontic treatment can range from 19.1 months to 37 months, with a mean duration of no less than 24 months, regardless of the appliance used. This prolonged duration of orthodontic treatment is influenced by a multitude of factors. Patients prefer shorter treatments, and lengthy treatments are also associated with harmful side effects for the patient, such as tooth demineralisation (Ristic et al., 2007) and root resorption (Fox, 2005). Biologically speaking, it makes sense for the orthodontist to seek the shortest treatment time in order to protect patients and to make orthodontics more attractive. Assuming all other factors remain constant, one certain strategy to shorten treatment duration would be to accelerate orthodontic tooth movement (OTM). According to the literature, the normal physiological speed of orthodontic tooth movement is around 0.9 to 1.2 mm over 4 weeks (Barlow & Kula, 2008). However, with an improved understanding of the biological mechanisms of OTM, it is possible to significantly accelerate the OTM (Alansari et al., 2015).

Accelerated orthodontics, therefore, appears to be an intriguing topic for dental magazines and dental journals. Short orthodontic treatment times are even exploited by orthodontists to market their practices, and manufacturers use speed as a factor to promote their products. New devices, methods, and technologies are continually invented and introduced to the market for this purpose.

Most of these innovations are relatively recent, meaning that data regarding the evidence of their usefulness, indications, integration into treatment plans, and safety are still yet to be established. The aim of the present study is to contribute to a better understanding of this concept and to aid orthodontists in their decision-making regarding the acceleration of orthodontic tooth movement.

The aim of this review is to evaluate the efficiency and treatment duration of accelerated orthodontic tooth movement compared to conventional methods, while addressing the current concepts, methods, speed of tooth movement, and effectiveness of various acceleration techniques.

2 Methods

An electronic literature search was conducted to identify scientific articles pertinent to the biology of tooth movement and the concept of accelerated tooth movement, with a particular focus on addressing the aforementioned research questions. The primary database utilised for this investigation was PubMed. The initial selection of articles was based on the relevance of their titles. Selected articles were subsequently exported to Readcube, a bibliography management software.

The keywords used for this initial search included:

- Accelerated orthodontic tooth movement
- Biology of orthodontic tooth movement
- Orthodontic treatment duration
- Corticotomy in orthodontic tooth movement

- Laser in orthodontic tooth movement
- Vibration in orthodontic tooth movement
- Medication in orthodontic tooth movement
- Drugs in orthodontic tooth movement

Manual searches were performed by reviewing the bibliographies of identified articles through the metadata analysis features of Readcube, particularly using options such as "cited by" and "related articles". Additional searches were also conducted on the websites of the American Journal of Orthodontics, Seminars in Orthodontics, and the Angle Orthodontist. In total, 232 articles were initially selected.

The second round of selection involved a review of the abstracts from these 232 articles. The inclusion criteria for this stage comprised:

- Prospective clinical trials
- Randomised controlled clinical trials
- Controlled clinical trials
- Human studies

Animal studies, case reports, and retrospective studies were excluded from consideration. At this stage, 40 full-text articles were chosen for further examination. Upon reviewing the full texts, 5 articles were excluded—2 due to language constraints and 3 due to an inability to extract relevant data. Ultimately, 35 articles were identified for inclusion in the review.

2.1 Statistics

Descriptive statistics, frequency analysis, and content analysis were employed as part of the qualitative methodology to systematically analyze the textual content of the included studies. It is important to note that, given the narrative nature of this study, regression analysis and meta-analysis techniques were not deemed suitable for the analytical framework.

3 Results

3.1 Biology of orthodontic tooth movement

Orthodontic treatment is based on tooth displacement through the alveolar bone. This orthodontic tooth movement (OTM) is the result of the response of periodontal tissue to orthodontic force. Corresponding to this physical event are some biological mechanisms that commence as soon as one minute after a force is applied to the tooth (Ariffin et al., 2011). Tooth movement is accompanied by local bone remodelling, which is a phenomenon comprising bone resorption coupled with bone formation; the net result of this process will represent either bone loss or bone gain (Feller et al., 2015).

Three biological mechanisms occur during OTM: the pressure–tension phenomenon, the bioelectricity phenomenon, and the neurological phenomenon (Patil et al., 2013). Upon the application of orthodontic force, specifically a light sustained force (Roberts et al., 2004), the tooth will initially move into its socket through mechanical compression of the periodontal ligament (PDL) (Iwasaki et al., 2000). This results in the creation of two zones in the

periodontal tissue surrounding the root of the tooth: a pressure zone and a tension zone. This constitutes the first phase of OTM.

The pressure zone is characterised by the compression of the periodontal ligament (PDL) in the direction of the applied force, along with strains on both the bone and the PDL. This results in the deformation of blood vessels, the movement of fluid from the pressure side to the tension side within the PDL, the deformation of cells in the PDL and bone, and the relaxation of collagen fibres. Consequently, there is reduced blood supply and resultant ischaemia. All these transformations activate the release of inflammatory chemical messengers, primarily prostaglandins (PGs) and cytokines (Meeran, 2012). Furthermore, due to the bending of bone and collagen fibres, local electricity of low voltage is produced (piezoelectricity or bioelectricity) (Proffit, 2013), leading to the activation of osteocytes. In addition, certain neurotransmitters, including substance P and vasoactive intestinal polypeptide, are released. PDL cells (fibroblasts) and bone cells (osteoblasts, osteocytes), particularly specific genes of osteoblasts, are activated by these substances and mechanical strains (Patil et al., 2013; Feller et al., 2015).

Osteoclast differentiation from monocyte cells is mediated by cytokines, specific hormones, and growth factors produced by macrophages and osteoblasts (Melsen, 1999; Patil et al., 2013; Roberts-Harry & Sandy, 2004). The principal regulator of this differentiation is the receptor activator of nuclear factor kappa (RANK)-RANK ligand (RANKL) and osteoprotegerin (OPG) (Feller et al., 2015).

When the applied force is within the physiological range, i.e. pressure is lower than vessel pressure, resorptive remodelling of bone occurs, resulting in continuous tooth movement. If the force is moderately higher than blood pressure, PDL strangulation occurs, leading to a larger necrotic area and consequently a slower remodelling effect. In the case of excessive force, gradual deterioration of the PDL results in hyalinisation, leading to a significant delay in tooth movement (Patil et al., 2013) due to distant resorption termed 'undermining resorption' (Meikle, 2006; Melsen, 1999).

In the tension area, stretching and loading of the fibres and bending of the alveolar bone occur (Krishnan & Davidovitch, 2016). These mechanical strains are sensed by osteoblasts through their proprioceptive receptive system, mediated by PG and integrin (Patil et al., 2013; Meikle, 2006). Osteoblasts are then activated to produce bone, facilitating anabolic remodelling (Feller et al., 2015).

Overall, 1) bone remodelling is orchestrated by osteocytes; 2) osteoblasts produce bone, thereby maintaining bone integrity and activating osteoclasts; and 3) osteoclasts control OTM by determining the rate of bone resorption (Huang, Williams, & Kyrkanides, 2014; Alansari et al., 2015).

Based on the aforementioned principles of OTM, there are two primary approaches to reduce treatment duration: (1) the use of the most efficient biomechanical system to move teeth and (2) the acceleration of tooth movement (Qamruddin et al., 2015). Biomechanical principles will allow for the optimisation of force application with effective anchorage management and minimal unwanted side effects (L. Iwasaki et al., 2000). On the other hand, accelerating OTM will focus on the activation of osteoclasts, irrespective of the means employed (Alansari et al., 2015).

3.2 Strategies of accelerated orthodontic tooth movement

Corticotomy-osteotomy. Osteotomy refers to the complete sectioning of bone blocks through both cortical and medullary bone. In the corticotomy technique, the cortical bone

is cut and/or perforated without any disruption to the medullary bone (Nimeri et al., 2013; Patterson et al., 2015). Corticotomy is gaining popularity over osteotomy because it is as effective as osteotomy while minimising its associated side effects. In fact, as demonstrated by Wilcko in 2001, the acceleration of tooth movement is attributed to the Regional Acceleratory Phenomenon (RAP) rather than the movement of the bony block (Nimeri et al., 2013).

Interseptal Alveolar Surgery. Also referred to as distraction osteogenesis, interseptal alveolar surgery involves the distraction of alveolar bone or the periodontal ligament (PDL) (Nimeri et al., 2013). In the alveolar distraction technique, the dento-alveolar segment is separated from the jaw bone, and distraction is achieved by moving the teeth (Fleming et al., 2015; Kumar et al., 2013). For the PDL distraction technique, also known as dental distraction (Liou & Huang, 1998; Mowafy & Zaher, 2012), interseptal bone is surgically undermined immediately after extraction by making a vertical cut extending as long as the adjacent tooth root, with no buccal or lingual cuts and no mesiodistal cuts (Liou & Huang, 1998).

Piezocision. Piezocision is one of the latest surgical strategies and is less invasive. It involves two steps: a primary incision of the buccal gingiva followed by an incision of the cortical bone through the gingival cuts using a piezosurgical knife (Nimeri et al., 2013). It is also referred to as piezopuncture or piezoelectric corticotomy (Ma et al., 2015).

Prostaglandins. Prostaglandins E1 and E2 are known inflammatory mediators that stimulate bone resorption by directly increasing the number of osteoclasts. Through this osteoclastogenic effect, PGE can promote OTM. It is therefore suggested that they be injected locally to accelerate OTM (Nimeri et al., 2013).

Cytokines. Cytokines are inflammatory molecules that influence bone remodelling by promoting osteoclastogenesis, which encompasses osteoclast recruitment, differentiation, and activation. In their study, Teixeira et al. (2010) demonstrated that cytokine expression is markedly elevated during accelerated OTM.

Relaxin. Relaxin is a natural hormone that exerts a remodelling effect on soft tissue. It is specifically released during pregnancy in many mammals, facilitating cervical softening of the uterus and elongation of interpubic ligaments. Additionally, relaxin has physiological effects on angiogenesis, antifibrosis, and collagen turnover. These potential actions of relaxin suggest that it may influence the PDL, thereby affecting OTM (Madan et al., 2007). Based on these properties, repeated local injections of relaxin are proposed to induce AOTM (McGorray et al., 2012).

Vitamin D3. Vitamin D is involved in bone homeostasis and is considered one of the three calcifying hormones. Studies have shown that vitamin D has an osteoclastic effect by promoting osteoclast differentiation (Kale et al., 2003). Thus, local injections of vitamin D3 are utilised to stimulate osteoclastic activity and generate AOTM (Collins & Sinclair, 1988).

Parathyroid hormone. PTH is a principal active hormone in the regulation of calcium and phosphate, and consequently in bone metabolism. It exhibits both a stimulating effect

on bone resorption and a promoting effect on bone apposition, appearing paradoxically as a multifaceted substance. The stimulating effect, however, is dependent on the mode of administration. Continuous systemic administration of PTH produces an osteoclastic effect, whereas intermittent administration results in an osteoblastic effect (Soma et al., 2000; Li et al., 2013). Therefore, PTH is administered locally in a continuous slow-release dosage to accelerate OTM through its capacity to stimulate osteoclastic activity in the compressed PDL (Soma et al., 2000).

Gene therapy. The phenomena of bone resorption and apposition that underpin OTM are, at the molecular level, linked to the ratio between the receptor activator of nuclear factor-kB (RANKL) and osteoprotegerin (OPG). A higher concentration of RANKL compared to OPG promotes osteoclastogenesis, positively influencing OTM. Thus, it is suggested that the overexpression of RANKL through the local transfer of the RANKL gene into the PDL can activate osteoclasts and osteoclastogenesis in a sustained manner, thereby inducing AOTM (Kanzaki et al., 2006).

Photobiostimulation or Photobiomodulation. In the context of orthodontics, it is also referred to as Low Intensity Laser Therapy (Nimeri et al., 2014), Low-level Light Therapy (LLLT), or Light-accelerated Orthodontics (LAO). The term "laser" originated as an acronym for "light amplification by stimulated emission of radiation". LILT is believed to stimulate bone turnover, thereby producing OTM acceleration by increasing ATP production in mitochondria (Kau et al., 2013). The effect of laser on tissue is wavelength- and dosage-dependent (Andrade, Sousa, & da Silva, 2014).

Vibrations. Low-Intensity Pulsed Ultrasound (LIPUS) and Pulsed Electromagnetic Fields (PEMF) devices are used to produce low-frequency mechanical vibrations that are applied to stimulate the teeth wearing a multibanded orthodontic appliance. The vibrations are transmitted to the bone. It is believed that these mechanical stimuli will activate osteocytes, which trigger the recruitment, differentiation, and activation of osteoclasts, thereby inducing the acceleration of OTM (Yadav et al., 2015).

Piezoelectricity. A low current of 10 to 20 microamperes is directly applied to the alveolar bone, modifying the bioelectric potential. This induces metabolic changes in the periodontal ligament (PDL) and osteoblasts, accelerating OTM (Kolahi et al., 2009).

3.3 Tooth movement rate, alignment rate and treatment duration

Corticotomy and piezotomy. Seven studies dealing with corticotomy are included in this review. Six studies are comparative, of which two employ a split-mouth design. One study is a randomised controlled trial (RCT) with a split-mouth design. Key results regarding the effects of corticotomy and piezotomy on OTM are summarised in supplementary **Table S1**.

The studies are heterogeneous in their designs, but, in general, the orthodontic appliance is a multiband system placed prior to corticotomy surgery. The appliance itself is fitted after bicuspid extractions. Corticotomy was performed immediately after alignment and at the onset of space closure through retraction. Tooth movement is generally measured and recorded every four weeks. A cumulative movement is calculated at the conclusion of space

closure, and the mean movement of the canine per month is evaluated. The results are then compared with those of the control group.

Four studies compare piezotomy with no corticotomy (Aksakalli et al., 2016; Ma et al., 2015). Three studies compare corticotomy with no corticotomy (Suryavanshi et al., 2015; Wu et al., 2015; Sakthi et al., 2014).

The piezotomy studies demonstrated an acceleration range of canine orthodontic tooth movement ratio (OTMR) from 41.33% to 76.49% (three studies) and a reduction in orthodontic treatment duration (OTD) of 33.86% to 46.88% (two studies). It is noteworthy to highlight that the lowest acceleration case in these studies relates to an impacted canine traction case (Fischer, 2007). The other two studies dealing with canine retraction cases during space closure have significantly higher accelerations: 65.38% and 76.49% (Wu et al., 2015; Aksakalli et al., 2016). For the evaluation of the OTD, the highest reduction (46.88%) is from a mandibular impacted third molar case (Ma et al., 2015).

Two of the corticotomy studies evaluated the canine OTMR, finding accelerations of 48.15% and 80.46%. The higher acceleration comes from a study where both interradicular vertical and sub-apical horizontal corticotomies were performed (Sakthi et al., 2014). The lower acceleration is from a study involving only interradicular corticotomy (Suryavanshi et al., 2015). The third corticotomy study evaluated the OTD and yielded a reduction of 64.29% (Shoreibah et al., 2012).

When considering the OTMR of canines in first premolar extraction studies, there are four studies (Suryavanshi et al., 2015; Aksakalli et al., 2016; Sakthi et al., 2014; Fischer, 2007). Two studies employed piezosurgery (Aksakalli et al., 2016; Fischer, 2007) and two utilised corticotomy. The results of these studies revealed an acceleration of OTM ranging from 41.33% to 86.46%. Most of the accelerations (three studies, 75%) exceeded 65%. The highest acceleration is reported in a corticotomy study, while the lowest acceleration is in a piezosurgical study.

Two studies evaluated the OTD, concluding a reduction in OTD that can exceed 50% (Ma et al., 2015; Shoreibah et al., 2012). One of these studies utilised piezosurgery (Ma et al., 2015). All the corticotomy and piezotomy studies, in their outcomes, converge towards the same conclusion: corticotomy can accelerate OTM and reduce OTD.

Alveolar distraction and periodontal distraction. Eight studies deal with dentoalveolar distraction. One study is a randomised controlled trial (RCT), one is a case series study (CS), and three are clinical trials. Sample sizes range from 6 to 30 subjects. One of the studies employs a split-mouth design. Half of the studies focus on periodontal distraction, while the other half investigates alveolar distraction. All studies evaluate the canine distraction movement into the extraction space. Results of distraction-assisted dentoalveolar (DAD) effects on orthodontic tooth movements are summarised in **Table S2**.

In the group of periodontal distraction technique studies (Leethanakul et al., 2014; Liou & Huang, 1998; Mowafy & Zaher, 2012; Sayin et al., 2004), one is a comparative study. In this study, Leethanakul et al. compared periodontal distraction with no distraction. They did not use a distractor; retraction was performed using conventional retraction mechanics with a multibanded appliance after alignment and levelling. The result indicates an acceleration of OTM by 19.47% (1.35 mm vs 1.13 mm) (Leethanakul et al., 2014). The other three studies employed a custom distractor immediately after surgery and before the multibanded treatment. One of these studies compared intermittent force with continuous force. In all three studies, rapid canine movement was achieved with intermittent forces, ranging from 1.11 mm/week (4.44 mm/month) to 2.16 mm/week (8.64 mm/month). With continuous force

distraction, the movement rate was 0.16 mm/week (0.64 mm/month).

In the alveolar distraction group, all studies utilised the alveolar distraction technique with a custom distractor appliance placed immediately after surgery. They all evaluated the OTM rate (OTMR) of canines in extraction cases. Extractions were performed before the application of the multibanded appliance. Corticotomy was generally conducted after creating a flap around the canine root. The corticotomy distraction rate (CDR) varied from 0.48 mm/day (14.4 mm/month) to 0.8 mm/day (24 mm/month), with canine retraction typically completed within 2 to 3 weeks. Half of the studies achieved a rate of 0.8 mm/day with a minimum retraction time of 10 days (İşeri et al., 2005; Kisnisci & Iseri, 2011).

Overall, it can be anticipated that more than 1 mm of movement per week can be expected with periodontal ligament distraction if a distractor exerting intermittent force is employed. In the alveolar distraction technique, this expectation may reach at least 0.48 mm/day.

Laser treatment. Thirteen studies concerning low-level laser therapy (LILT) are included in this review. Two studies are RCTs, while the remaining eleven are comparative clinical studies with a split-mouth design. All studies utilised nine different wavelengths of laser light. The duration, frequency of application, and energy varied from study to study (**Table S3**).

Three studies examined the rate of tooth alignment (Nimeri et al., 2014; Shaughnessy et al., 2016; Kau et al., 2013). In these studies, the wavelengths used were identical (850 nm), but the modalities of application differed. All studies found that LILT can accelerate tooth alignment: the average rates (AR) are respectively 1.03 mm/week, 1.27 mm/week, and 1.27 mm/week for the maxilla, and 0.92 mm/week for the mandible. These rates are more than double that of conventional techniques, which ranged from 0.44 mm/week (Shaughnessy et al., 2016) to 0.49 mm/week (Kau et al., 2013).

One study evaluated the duration of treatment in non-extraction cases. It is a cohort study that utilised an 830 nm wavelength at an energy level of 80 J. The result indicated that treatment time was reduced by 18% (476 days vs 565 days) (Camacho & Cuja, 2010).

The remaining nine studies assessed the speed of canine movement in extraction cases. Among these, two studies are RCTs. In these studies, laser treatment was applied during the space closing phase. The outcomes showed conflicting results. Four studies, utilising four different wavelengths, found no acceleration of OTM in canines with LILT (Kansal et al., 2014; Dalaie et al., 2015; Limpanichkul et al., 2006; Heravi, Moradi, & Ahrari, 2014). The acceleration in these studies ranged from -9.84% to 8.34%. One of the studies even reported a deceleration with an 810 nm wavelength (Heravi, Moradi, & Ahrari, 2014). Conversely, five studies concluded that LILT can accelerate OTM, with acceleration ranges from 28.75% to 125.62%. However, most of these five studies (three of them) reported accelerations of less than 40%.

Vibration treatment. Four studies were selected for the evaluation of the effect of vibration on OTM. Three of these are randomised controlled trials (RCTs), and one is a comparative clinical trial with a split-mouth design.

Table S4 below summarises the effect of vibration on OTM speed and alignment rate (AR). The three RCTs employed the same vibration technique over an identical duration of application. However, one study evaluated the OTM rate (OTMR), while the other two measured the Tooth Alignment Rate. The outcomes from these studies are conflicting. The two RCTs that calculated the alignment rate concluded that vibration does not accelerate

OTM (Miles et al., 2012; Woodhouse et al., 2015). In fact, these studies indicated that a deceleration of AR is even possible, with a reported decrease of 4% (Miles et al., 2012). Conversely, the study that evaluated the OTMR of canines concluded that vibration does accelerate OTM, reporting an acceleration rate of 60% (Pavlin et al., 2015).

The fourth study, a comparative trial, utilised electric toothbrush vibrations and evaluated the OTMR of canines during the first two months of treatment. It concluded that vibration accelerates OTM, with a speed acceleration exceeding 61.02% (0.95 mm/month versus 0.59 mm/month) (Leethanakul et al., 2016).

Overall, 50% of the studies indicated no acceleration of AR, while the remaining 50% demonstrated a 60% acceleration of OTMR when vibrations were employed.

Biological treatment. Two studies are included in this review. One study evaluated Prostaglandin E1 (PGE1), while the second investigated relaxin. Both studies calculated the OTMR of canines. The results of the effects of PGE1 and relaxin are summarised in **Table S5**.

The relaxin study is a randomised controlled trial (RCT) with a placebo group; the outcome of this study indicated that relaxin has no effect on OTM speed (0.83 mm/month versus 0.83 mm/month). Conversely, the PGE1 study is a comparative study with a split-mouth design, involving nine subjects. Ten micrograms of PGE1 were injected into the submucosal area of the buccal side of the upper right first premolar at intervals of 5 to 8 days, with accumulated OTM recorded on different dates for each subject. This study found an acceleration of OTM by 59.23% (2.07 mm/month vs 1.3 mm/month, $p < 0.05$) (Yamasaki et al., 1984).

Other pharmaceutical strategies, such as vitamin D3, parathormone, gene therapy, and cytokines, were not identified in human studies during our research.

4 Discussion

From the results of this study, one can conclude that the oldest method is surgical, evolving from invasive osteotomy to the gentler corticotomy, and more recently to the less invasive micro-osteoperforation. It is the most efficient and commonly used method. Low-intensity laser therapy (LILT) is the most extensively studied strategy; however, its results, alongside those of vibration, are not consistent or predictable enough. The biological methods are the least employed and remain the most poorly understood in humans.

Corticotomy. This review analysed seven studies comparing corticotomy to no corticotomy. One of the studies is a randomized controlled trial (RCT), which is considered the highest evidence standard. All other studies are comparative clinical trials. This constitutes a limited number of studies to establish any definitive evidence. Furthermore, the sample sizes in these studies are small, ranging from 6 to 40 participants; the smallest sample belongs to the RCT, while the largest comprises 40 patients. Interestingly, this study demonstrated the highest tooth movement acceleration rate, reaching up to 80.45% (Sakthi et al., 2014).

The surgery is typically performed at the beginning of space closure, and tooth retraction occurs immediately after corticotomy. This timing is important to fully exploit the rapid acceleratory phenomenon (RAP) underlying accelerated orthodontic tooth movement (AOTM), as RAP is transitory by nature. Indeed, Baloul et al. (2011) demonstrated that AOTM becomes unattainable four weeks post-surgery, reporting a decrease in certain inflammatory mediators fundamental to AOTM, returning to baseline levels.

Due to the heterogeneity of these studies, direct comparisons are challenging. However, it is noteworthy to highlight that the outcomes suggest that the surgical technique does not significantly influence the results. Three studies employed piezosurgery. Suryavanshi (2015) utilised a modified corticotomy that was buccal only, rather than the bicortical technique recommended by Wilcko et al. (2001). Another study incorporated piezosurgery with graft material (Wu et al., 2015), while a different study used a bur-based corticotomy. A common feature across all these surgical approaches is that the corticotomy consistently involves the interradicular bone and penetrates through the entire buccal cortical layer. This aspect is crucial for achieving the full effect of the RAP (Dibart, Keser, & Nelson, 2015).

Although evidence remains limited for corticotomy-accelerated orthodontics, the results of the studies included in this review are sufficiently consistent to affirm that corticotomy can indeed accelerate orthodontic tooth movement (OTM). Hoogeven et al. (2014) reached a similar conclusion in their systematic review.

The basis for this acceleration of OTM lies in the increased production of biomodulators induced by non-infectious inflammation resulting from bone undermining, which enhances both osteoclastic and osteoblastic activity during the early phases of the healing process (Baloul et al., 2011; Kaushik, 2015). Thus, the selection of surgical technique, given the current level of evidence, will depend on the clinical situation, anticipated complications, degree of invasiveness, and the clinician's personal preference, as all methods exhibit some degree of effectiveness. Therefore, it is sensible to consider minimally invasive techniques, such as piezocision, as suggested by several authors, which can even be performed without any flap (Keser & Dibart, 2013; Yu et al., 2013; Dibart, Keser, & Nelson, 2015) and generate a similar RAP to conventional techniques. Alikhani et al. (2015) even advocate for the use of micro-osteoperforations (MOP) as a minimally invasive and safe procedure for biologically accelerating OTM. However, it is important to bear in mind that traditional corticotomy with surgical burs, in combination with both interradicular and sub-apical horizontal decortication, may provide the highest acceleration (Sakthi et al., 2014).

Dento-alveolar distraction. The number of studies on dento-alveolar distraction (DAD) is eight. This is a relatively small number, and the sample sizes are also limited. There is only one randomised controlled trial (RCT) among the studies, which is a periodontal distraction evaluation employing a split-mouth design. For all these reasons, the evidence is considered low. The studies differ in their objectives and designs, making them difficult to compare. Despite this, it is still possible to derive some clinical information regarding DAD from these studies.

Dento-alveolar distraction is based on the osteodistraction technique developed by Ilizarov to correct deformities (Grant, Atar, & Lehman, 1992). The periodontal distraction technique is an interseptal bone reduction surgery. In the study of periodontal distraction carried out by Leethanakul, the orthodontic tooth movement rate (OTMR) of the canine was 1.35 mm/month, compared to 1.13 mm/month on the control sides (Leethanakul et al., 2014). This represents an acceleration of 19.47%. This velocity is considerably low when compared with the results obtained in the studies by Liou and Huang, and by Mowafy and Zaher, where the OTMRs were 2.16 mm/week and 1.11 mm/week, respectively. However, it is similar to some results from corticotomy-assisted studies. The latter two studies differ mainly from the former by their use of a distractor. The bone surgeries are very similar, with no flap involved. It is also important to highlight that the intermittent force distraction device is a key factor for success, as demonstrated by Mowafy and Zaher (Mowafy & Zaher, 2012).

The Leethanakul technique, which produces the least acceleration of OTM, also has some limitations, especially when extraction is indicated prior to the alignment and leveling phase. Dento-alveolar distraction involves raising a flap and performing a corticotomy around the canine root, followed by the immediate use of a distractor. All five studies related to this technique reported rapid canine retraction, with the potential to close space in ten days. Alveolar distraction and periodontal distraction using an intermittent force distractor produce similar OTMRs, with periodontal distraction being less invasive.

Vibration. Two out of four studies addressing vibration in this review do not support the notion that vibration accelerates OTM. These two studies are RCTs (Miles et al., 2012; Woodhouse et al., 2015). The other two studies that support this idea have smaller sample sizes, and one of them is a clinical trial (Leethanakul et al., 2016), indicating a lower level of evidence. Surprisingly, these studies measured the OTMR of canine movement in extraction cases, which is a more challenging movement than alignment.

In animal studies, contradictory results also exist. Nishimura et al. have shown that resonance vibration can accelerate OTM (Nishimura et al., 2008). Darendeliler et al. also found that pulsed electromagnetic fields (PEMF) can accelerate OTM in guinea pigs by reducing the lag phase of OTM (Darendeliler, Sinclair, & Kusy, 1995). Conversely, Yadav et al. demonstrated that low-frequency mechanical vibrations (LFMV) did not increase the rate of orthodontic tooth movement (Yadav et al., 2015).

At the molecular level, Nishimura et al. explained that vibration might stimulate the resorptive activity of osteoclasts by increasing RANKL expression and stimulating the differentiation of monocytes/macrophages (Nishimura et al., 2008). Leethanakul also demonstrated an increase in interleukin 1b (IL-1b) with the use of vibrational stimulation during OTM. IL-1b is known to stimulate osteoclastogenesis and induce the expression of RANKL (Leethanakul et al., 2016). However, Yadav showed that vibration at 20 Hz decreased the expression of RANKL and increased the expression of OPG (Yadav et al., 2016). It is known that the combined actions of both the decrease in RANKL and the increase in OPG inhibit osteoclastogenesis, which positively influences bone formation (Judex et al., 2006). Indeed, Xie et al. have shown that low-magnitude, high-frequency vibrations decrease osteoclastic activity (Xie et al., 2006). This phenomenon has been known since the work of Rubin et al. (Rubin et al., 2002). Finally, Pavlin posits that the biological mechanism by which vibration accelerates OTM remains unknown (Pavlin et al., 2015).

It is relevant to conclude that the evidence supporting the acceleration of OTM by vibration is very low and controversial. Further studies on the frequency and force intensity of vibration are needed.

Low intensity laser therapy. The studies evaluating Low Intensity Laser Therapy (LILT) comprise the largest group in this review, with the study featuring the highest sample size also belonging to this category (90 subjects). Unfortunately, the studies are heterogeneous with varying objectives and, particularly, differing laser technical features. Consequently, direct comparisons of results are problematic.

However, some studies suggest that LILT can help accelerate the alignment phase of orthodontic treatment (Kau et al., 2013; Nimeri et al., 2014; Shaughnessy et al., 2016). Nevertheless, the authors are divided on the potential for LILT to accelerate OTM, particularly for significant tooth movement such as closing space through tooth retraction. Some evidence supports the acceleration of OTM (Youssef et al., 2008; Doshi-Mehta & Bhad-Patil, 2012; Dominguez et al., 2015; Cruz et al., 2004; Sousa et al., 2011), while other evidence

does not support it (Kansal et al., 2014; Dalaie et al., 2015; Limpanichkul et al., 2006; Heravi et al., 2014). It is even possible to observe a slowdown in OTM speed, as shown by Heravi et al. (2014). Furthermore, even when acknowledging the potential for accelerating OTM, Dominguez et al. (2015) recognised that the improvement is minimal.

When considering the underlying molecular mechanisms by which LILT may accelerate OTM, Kasai et al. (2015) explained that low-level laser irradiation (LLLI) enhances osteoclastogenesis on the compression side by stimulating the receptor activator of nuclear factor kappa-B (RANK)/RANK ligand (RANKL), as well as the c-fms/macrophage colony-stimulating factor (M-CSF), as demonstrated by Fujita et al. (2009) and Yamaguchi et al. (2014). Additionally, LILT stimulates osteogenesis on the tension side (Kasai et al., 2015). According to Kau (2013), LILT is believed to stimulate bone turnover by increasing ATP production in mitochondria, which in turn accelerates OTM. In contrast, Seifi et al. (2007) demonstrated that LILT can inhibit OTM in an animal study. Seifi and Elahe (2015) also highlight the conflicting effects of LILT on OTM, noting that while LILT inhibits PGE2—a phenomenon that can control pain—PGE2 is simultaneously released and plays a crucial role as a primary messenger in OTM.

Finally, since the tissue response to laser is known to depend on wavelength and dose (Andrade et al., 2014), more refined and large-scale studies are necessary to establish conclusive evidence on the optimal wavelength and protocol of LILT for use in accelerating OTM.

Biological therapy. Among all seven pharmaceutical strategies available to accelerate OTM, only two studies have been conducted on humans. One study evaluates relaxin, and the other evaluates PGE1. The randomised controlled trial (RCT) concerning relaxin indicated that relaxin has no effect on OTM when administered at a daily dose of 50 μg for eight weeks. In their study, Madan et al. (2007) reported similar results regarding human relaxin in rats. Thus, there is no evidence supporting the use of human relaxin for accelerating orthodontic treatment.

On the other hand, PGE1, administered locally at a dose of 10 μg daily, has been shown to accelerate OTM by up to 64.62% (Yamasaki et al., 1984). Unfortunately, this is the only human study available since 1984.

PGE1 is one of many inflammatory mediators typically involved in the regulation of OTM (Alansari et al., 2015). PGE1 plays a significant role in osteoclastogenesis, which is the mechanism by which it accelerates OTM. Similarly, studies have shown that anti-inflammatory drugs that inhibit prostaglandins (PG) also slow down OTM (Knop et al., 2012). PGE1 is produced locally, acts locally, and decays either spontaneously or through enzymatic destruction. This rapid clearance of the inflammatory mediator necessitates repeated administration of PGE1; therefore, several injections are required to maintain efficacy (Kanzaki et al., 2006). PGE1 injections can be painful (Yamasaki et al., 1984); however, in this study, PGE1 was mixed with lidocaine to mitigate discomfort. Nevertheless, repeated injections may be undesirable for many patients, and systemic side effects are possible, which may explain the paucity of studies on PGE1. Further research is needed to better understand the clinical use of PGE1.

In summary, it is possible to accelerate OTM using various strategies, thereby reducing the orthodontic treatment duration (OTD). Surgical strategies appear to be the most effective methods, as it is feasible to move teeth at a speed of 0.8mm per day, equating to theoretically 24mm/month with the use of DAD. When employing corticotomy, it is possible to consistently achieve tooth movement with a speed acceleration ranging from 41% to 80%.

Thus, surgical interventions can reduce the OTD by approximately −34% to −64%.

In the context of corticotomy, the optimal strategy for obtaining the highest acceleration involves a combined vertical interradicular and horizontal sub-apical corticotomy using surgical burs. Regarding dentoalveolar treatments (DAT), results remain conflicting; however, low-level laser therapy (LILT) has been shown to accelerate the rate of orthodontic tooth movement (AR) by more than 130% (Alikhani et al., 2015). Biological strategies exhibit potential but are still in their infancy and remain technically challenging, thus warranting increased caution. Therefore, further studies on DAT and biological methods are necessary.

Finally, clinicians should bear in mind that OTM can only be mastered through an understanding of its biological underpinnings. Regardless of the strategy employed to accelerate OTM, the fundamental principles invariably relate back to biology. Accordingly, it is logical to propose a biologically based classification of all methods employed to instigate a renewed perspective in the minds of orthodontists. We posit that the unheralded suggestion by Alikhani of two primary methods is pertinent:

- The stimulation method, which involves the use of external means to activate the bone remodeling pathways, as opposed to the physiological natural coupling of osteoblastic and osteoclastic activities in bone remodeling.

- The intensification method, which refers to the amplification of the natural coupling of osteoclastic and osteoblastic activities during bone remodeling induced by bone inflammation.

Considering orthodontic tooth movement in this manner enables us to explore various possibilities. For example, one might ask, *"Can we initiate the acceleration of OTM through the intensification method (which is transient in nature) and sustain it with a stimulating method?"*

Conclusions

Although it is not possible to draw conclusions with a high level of evidence regarding any of the AOTM strategies reviewed in this study, valuable clinical information can be gathered.

- All the AOTM strategies converge towards the same biological basis: the increase of non-infectious inflammation.
- Based on the biology of AOTM, the methods of AOTM can be classified into two categories: (1) the intensification methods (amplification of the natural inflammatory biological process) and (2) the stimulation methods (activation by external means).
- All surgical strategies accelerate OTM during the early stage of healing (2 months).
  - Corticotomy and piezotomy accelerate OTM by 41% to 80%. The choice of technique will mainly depend on the clinical situation; however, it is safer to employ a less invasive technique such as piezotomy. To achieve the highest acceleration, a combination of vertical interradicular and horizontal sub-apical corticotomy with surgical burs is the optimal strategy according to the current evidence.
  - The most rapid strategy involves periodontal ligament distraction and alveolar distraction, allowing teeth to be moved at a speed of 0.8 mm per day, which is almost the normal tooth movement achieved in traditional OTM over one month; this speed is approximately 30 times that of traditional OTM.

  - When employing distraction, it is essential to utilise a distractor that applies intermittent force. PDL distraction is less invasive and effective, although it is somewhat less effective than alveolar distraction.

- Evidence regarding the acceleration of OTM using vibration is very limited. More studies are needed.
- Evidence concerning the acceleration of OTM using low-level laser therapy (LILT) is lacking:
  - Alignment during the early stage of treatment can be slightly accelerated by LILT.
  - The acceleration of major OTM remains controversial.
- With respect to pharmaceutical strategies for accelerating OTM, there is very limited evidence that PGE1 can accelerate OTM, and Relaxin does not accelerate OTM.

Acknowledgements

Not applicable.

Ethical approval

No ethical approval was required for this study as it did not involve human participants, animal subjects, or sensitive data. This study falls under the category of data collection without participant identification.

Consent for publication

Not applicable.

Authors' contributions

The author(s) declare that all the criteria for authorship designated by the International Committee of Medical Journal Editors have been met. More specifically, these are: (a) Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND (b) Drafting the work or revising it critically for important intellectual content; AND (c) Final approval of the version to be published; AND (d) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Competing interests

The author(s) declare that there are no competing interests related to this work.

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