Biological principles behind accelerated tooth movement

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Understanding the biology of tooth movement has great importance for developing techniques that increase the rate of tooth movement. Based on interpretations of data on the biology of tooth movement, the resulting accelerating techniques can be divided into two main groups: one group stimulates upstream events to indirectly activate downstream target cells, while the other group bypasses the upstream events and directly stimulates downstream target cells. In both approaches, there is a general consensus that the rate of tooth movement is controlled by the rate of bone resorption, which in turn is controlled by osteoclast activity. Therefore, to increase the rate of tooth movement, osteoclasts should be the target of treatment. In this article, both approaches will be reviewed and the biological limitations of each group will be discussed. (Semin Orthod 2015; 21:151–161.) © 2015 Elsevier Inc. All rights reserved.

Introduction

Orthodontic tooth movement is possible due to the remodeling ability of the surrounding bone and soft tissue. Without this remarkable biological phenomenon, the practice—indeed, the very concept—of orthodontics would not be possible. Yet, orthodontic appliances are not intentionally built to activate or inhibit specific remodeling pathways and specific cells. Rather, they are built to generate biomechanical force systems that produce the desired tooth and jaw movements needed to establish an ideal occlusion—regardless of the cellular mediators of the response. This begs the question, should we be designing orthodontic appliances to target specific remodeling pathways to move teeth and jaws into an ideal occlusion faster?

The biology of tooth movement is not a new field of inquiry. What is new is that we are now designing innovative appliances and treatments that optimize skeletal and dental target cell responses that produce controlled, safe accelerated tooth movement. By identifying and harnessing reactions of the target cells, we can develop two different approaches to accelerate the rate of tooth movement: directly stimulate the target cells by artificial, physical, or chemical means to increase their numbers and their activity, or indirectly stimulate the body to recruit and activate more target cells. In either scenario, identifying the target cells and understanding how they are activated are crucial.

Bone cells and their role in biology of tooth movement

Bone is a dynamic tissue that remodels in response to mechanical force. The cells that perform this response are distributed throughout the bone and each is specialized to perform specific functions needed to detect force (both its magnitude and direction), recruit cells that resorb bone at specific sites, and activate cells to

deposit new bone matrix and promote mineralization that will withstand mechanical force. The mechanosensors are osteocytes, which are by far the most numerous bone cells in the body, but are also the least well studied because they are embedded entirely within the bony matrix. The bone-resorbing cells are giant multinucleated osteoclasts, which are found on the bone surface at resorption sites. The bone-forming cells are osteoblasts, which spend their lives attached to the bone surface. Finally, inflammatory cells (specifically, T lymphocytes and macrophages) that reside in the bone marrow are important regulators of osteoclasts and osteoblasts.

Osteoblasts are mononuclear cells found along the surface of bones. They are derived from mesenchymal stem cells in the bone marrow and synthesize collagenous and non-collagenous proteins that form the organic bone matrix called osteoid. Inactive osteoblasts that cover bone surfaces, particularly in the adult skeleton, are called bone-lining cells. These cells are quiescent until growth factors or other anabolic stimuli induce them to proliferate and differentiate into cuboidal osteoblasts. While osteoblasts play an important role in maintaining the integrity of alveolar bone during tooth movement, they are not the cells that control the rate of tooth movement.

The osteocyte is a mature osteoblast embedded in lacunae within the bone matrix. Although immobile, osteocytes possess exquisitely fine processes, which traverse the mineralized matrix in tunnels called canaliculi, to make contact with other osteocytes, as well as with osteoblasts residing on the bone surface. Given their preponderance in bone, and their intricate three-dimensional network, osteocytes are key mechanosensors. Loading of bone results in strain, or deformation, in the matrix, including the lacunae and canaliculi. This deformation evokes osteocytic responses via fluid shear stress (produced by increased fluid flow in the lacuno-canalicular system) or electrical stream potential. Osteocytes orchestrate the overall remodeling response by secreting key factors, such as prostaglandins, nitric oxide, and insulin-like growth factors (IGFs), which activate osteoblasts and osteoclasts and the bone remodeling system. Under the influence of orthodontic forces, osteocytes play a critical role in detecting force and activating osteoclast–osteoblast coupling, but they are not the cells that regulate the rate of tooth movement.

In fact, it is the osteoclast that determines the rate of bone resorption and, therefore, the rate of tooth movement. These cells are the major bone-resorbing cells. They are specialized monocyte/macrophage family members that differentiate from hematopoietic stem cells in the bone marrow. Mature osteoclasts are giant multinucleated cells that form from the fusion of monocytic precursors. Terminal differentiation in this lineage is characterized by the acquisition of mature phenotypic markers, such as the calcitonin receptor and tartrate-resistant acid phosphatase (TRAP), and the appearance of an astounding ruffled border rich in proton pumps that acidify the bone surface to which the cells are attached, resulting in resorption pits.

When viewed physiologically, normal healthy bone remodeling is a tightly choreographed sequence of cellular activity. Mechanical force distorts osteocytes housed in lacunae and canaliculi, often producing micro-fractures, which are cleared out by osteoclasts. Osteoblasts follow to fill in the newly excavated site. Some of those osteoblasts become embedded in the new bone to form new osteocytes to replace those lost at the remodeling site. Thus, healthy strong bone that can withstand mechanical force applications is formed due to signaling between osteocytes, osteoclasts, and osteoblasts. As we will discuss below, a variation of this response, which incorporates immune cells and inflammatory cytokines, is key to understand the biology of tooth movement and develop approaches to accelerate tooth movement.

## Theories on biology of tooth movement

During recent years, many theories have been developed to explain the mechanism of tooth movement. In general, these theories split into two camps: one camp proposes that bone is the direct target of mechanical force (direct view), while the other camp proposes that it is the periodontal ligament (PDL) that is the key target (indirect view). According to the direct view model, compression stress generated in the direction of tooth movement directly stimulates osteoclasts, and tension stress in the opposite direction of tooth movement directly stimulates osteoblasts. Under this assumption, osteocytes may play a significant role by coordinating osteoclast and osteoblast activity. There is significant evidence against this proposal. First, bone does not recognize static

forces such as orthodontic forces.[1] Second, the lack of movement of implants and ankylosed teeth in response to orthodontic forces argues against the claim that bone is the target of orthodontic forces. Third, in experiments where bone is loaded directly, without interference of the PDL, compression stresses stimulate bone formation, not bone resorption.

Supporters of the indirect view of tooth movement propose that the PDL is the primary target of orthodontic forces. Consider the impossibility of moving an ankylosed tooth, which lacks a PDL. Based on this proposal, the PDL will exhibit areas of compression and tension in response to the application of orthodontic forces. Distribution of these areas varies depending on the different types of tooth movement, which in turn are controlled by the magnitude of the force and the moment applied to the tooth. Regardless of the type of tooth movement, if the duration of force application is limited to a few seconds, the incompressible tissue fluid prevents quick displacement of the tooth within the PDL space. However, if the force on a tooth is maintained, the fluid is rapidly squeezed out and the tooth displaces within the PDL space, leading to the compression of the

PDL. The immediate result of this displacement is the constriction of blood vessels in the compression site. Alteration in blood flow would cause a decrease in nutrition and oxygen levels (hypoxia). Depending on the magnitude of pressure and level of blood flow reduction, some of the cells will go through apoptosis, while some cells will die non-specifically, resulting in areas of necrosis (cell-free zone). It should be emphasized that apoptotic or necrotic changes are not limited to PDL cells, and some of the osteoblasts and osteocytes in adjacent alveolar bone also die in response to orthodontic forces. These sequences of events lead to an aseptic, acute inflammatory response with the early release of chemokines from local cells (Fig. 1). Chemokines are small proteins released by local cells that can attract other cells into the area. The release of chemokines in response to orthodontic forces facilitates expression of adhesion molecules in blood vessels and stimulates further recruitment of inflammatory and precursor cells from the microvasculature into the extravascular space.

One of the chemokines that is released during tooth movement is monocyte chemoattractant protein-1 (MCP-1 or CCL2),[2] which plays an important role in recruiting monocytes. These
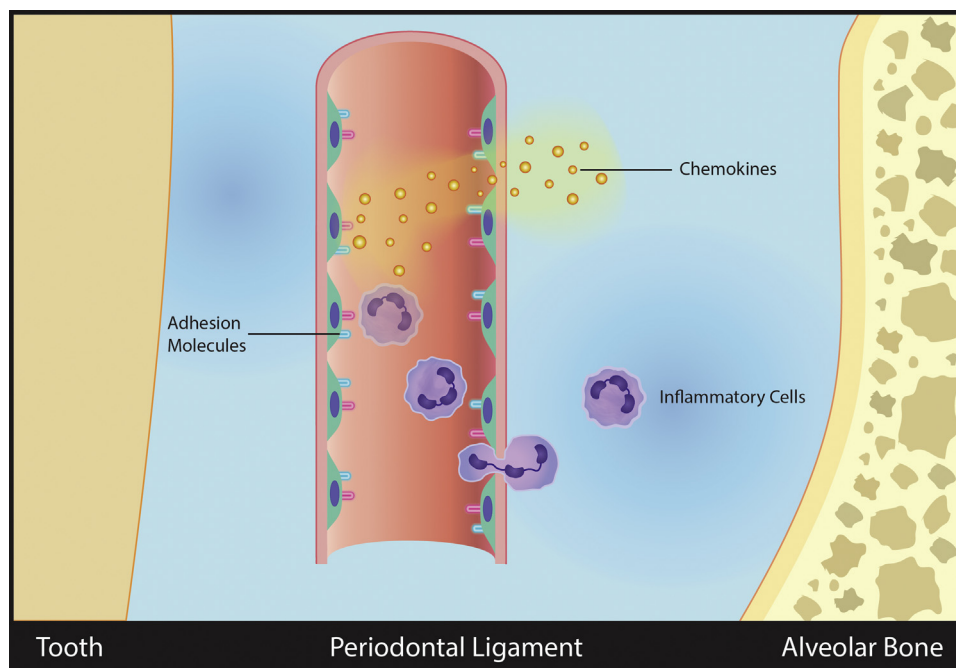
Figure 1. Schematic representation of increase in permeability of vessels, release of chemokines, expression of adhesion molecules, and recruitment of inflammatory and precursor cells during early events of orthodontic tooth movement.

cells leave the bloodstream and enter the surrounding tissue to become tissue macrophages or osteoclasts. Similarly, the release of CCL3 and[3] CCL5 (RANTES)[4] during orthodontic tooth movement leads to osteoclast recruitment and activation. Within the first few hours of orthodontic treatment, there is further release of a broader spectrum of inflammatory mediators. In addition to chemokines, cytokines are released during orthodontic treatment. These extracellular proteins play an important role in regulating the inflammatory process. Many cytokines are pro-inflammatory. They amplify or maintain the inflammatory response and activation of bone resorption. Importantly, other cytokines are anti-inflammatory and prevent an unrestrained inflammatory response. The main pro-inflammatory cytokines that are released during orthodontic tooth movement are IL-1α, IL-1β, TNF-α, and IL-6.[5] These cytokines are produced by inflammatory cells such as macrophages and by local cells such as osteoblasts, fibroblasts, and endothelial cells.

Another series of inflammatory mediators that are released during orthodontic tooth movement are prostaglandins (PGs) and neuropeptides. PGs are derived from the metabolism of arachidonic acid and can mediate virtually every step of inflammation such as vasodilation, increase vascular permeability, and adhesion of inflammatory cells. During orthodontic tooth movement, these mediators can be directly produced by local cells or by inflammatory cells in response to mechanical stimulation, or indirectly by cytokines. For example, TNF-α is a potent stimulator of PGE_2 formation.[6] Prostaglandins act locally at the site of generation and then decay spontaneously or are enzymatically destroyed.[7,8] Similar to PGs, neuropeptides can participate in many stages of the inflammatory response to orthodontic forces. Neuropeptides are small proteins, such as substance P, that transmit pain signals, regulate vessel tone, and modulate vascular permeability.[9] The importance of all these inflammatory makers can be appreciated in the role that they play in osteoclastogenesis.

Osteoclastogenesis

As previously discussed, osteoclasts are multinucleated giant cells that resorb bone and are derived from hematopoietic stem cells of the monocyte–macrophage lineage. After recruitment to the compression sites, osteoclast precursors begin to differentiate into osteoclasts (Fig. 2). Cytokines are important mediators of
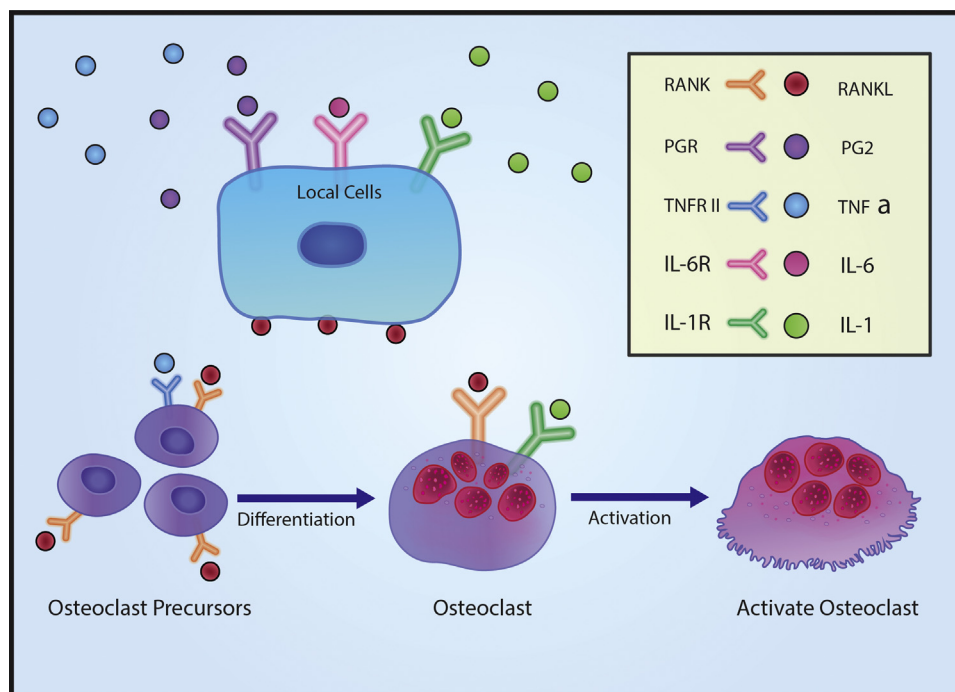
Figure 2. Schematic representation of interaction between RANKL expressed by local cells and inflammatory cells, and RANK expressed by precursor cells resulting in osteoclast differentiation.

this process. For example, TNF-α and IL-1 bind to their receptors, TNFRII[10] and IL-1R,[11] respectively, and directly stimulate osteoclast formation from precursor cells and osteoclast activation (Fig. 3). Additionally, IL-1 and IL-6[12] can indirectly stimulate local cells or inflammatory cells to express macrophage colony-stimulating factor (M-CSF) and receptor activator of nuclear factor κ-B ligand (RANKL). These ligands through cell-to-cell interactions bind to their respective receptors, c-Fms and RANK, which are both expressed on the surface of osteoclast precursors (Fig. 3).

Other inflammatory mediators that enhance osteoclast formation through enhancing RANKL expression by stromal cells are PGs, especially PGE_2.[13] As mentioned before, PGs can be produced by local cells directly in response to orthodontic forces or indirectly as downstream of cytokines such as TNF-α.

It should be emphasized that local cells normally try to down regulate osteoclastogenesis by producing a RANKL decoy receptor, osteoprotegerin (OPG).[14] Therefore, OPG levels in compression sites should decrease to enable tooth movement.

Different approaches to accelerate the rate of tooth movement

The approach that a researcher selects to accelerate the rate of tooth movement depends on his or her interpretation of the data on the biology of tooth movement. A researcher who chooses to amplify body reactions to orthodontic forces may either try to increase the release of cytokines (if they believe that inflammatory responses of the PDL and bone are the key factor in controlling the rate of tooth movement) or optimize the mechanical stimulation (if they
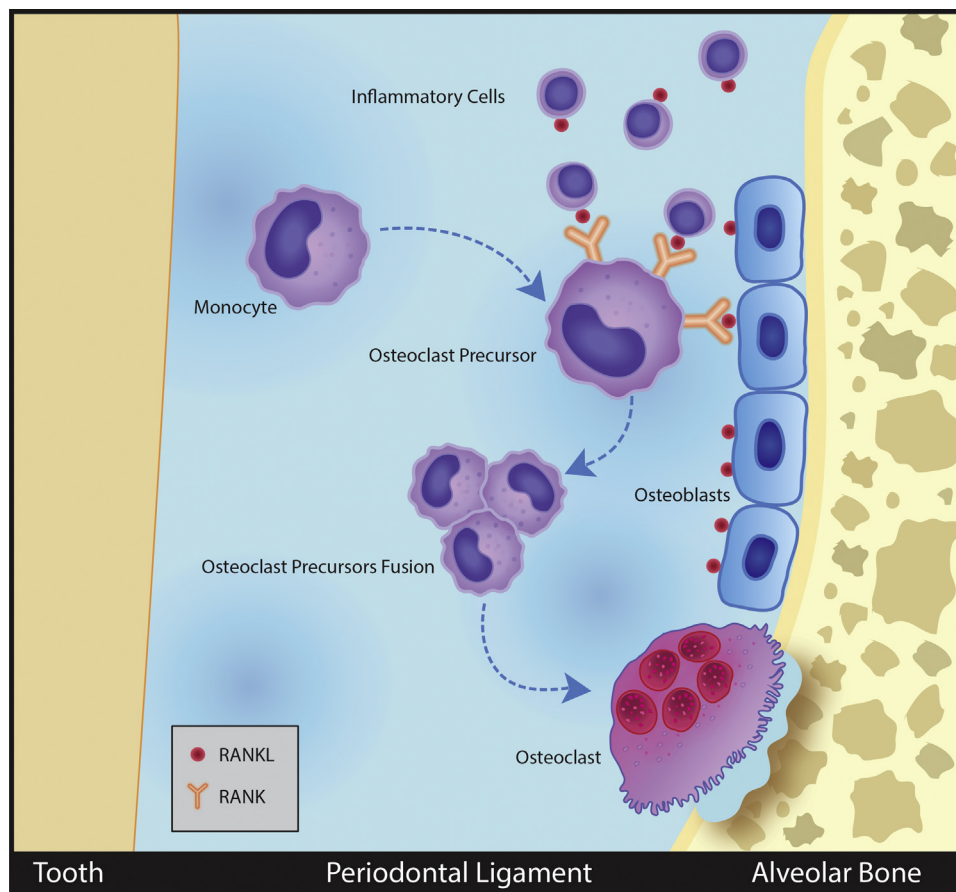
Figure 3. Diagram of the effect of cytokines on skeletogenesis. Cytokines can directly help in the differentiation or activation of osteoclasts from osteoclast precursor cells. Also, cytokines can stimulate local cells to express RANKL that interacts with its receptor (RANK) on precursor cells and help the development of osteoclasts.

believe that orthodontic tooth movement is a direct physiologic response to mechanical stimulation). On the other hand, another researcher who does not propose mimicking the body's response to orthodontic forces may choose instead to increase the rate of tooth movement by artificially increasing the number of osteoclasts. These approaches include local or systemic induction of different chemical factors or application of physical stimuli that can increase the number of osteoclasts independent of orthodontic forces. It should be emphasized that, in spite of some disagreement about initial trigger that starts the cascade of events leading to bone resorption and tooth movement, all theories agree that osteoclast activation is the main rate-controlling factor in orthodontic tooth movement.

Stimulation of cytokines to increase the rate of tooth movement

As previously discussed, orthodontic force induces an aseptic inflammatory response,[15] during which many cytokines and chemokines are activated and play a significant role in osteoclastogenesis. The importance of these molecules in controlling the rate of tooth movement can be appreciated through the dramatic results obtained from studies that block their effects. For example, injections of IL-1 receptor antagonist (IL-1Ra) or TNF-α receptor antagonist (sTNF-α-RI) result in a 50% reduction in the rate of tooth movement.[16] Similarly, tooth movement in TNF type II receptor-deficient mice is reduced compared to wild-type mice.[17] Animals that are deficient in CC chemokine receptor 2 (CCR2), which is a receptor for CCL2, or animals that are deficient in CCL3, demonstrate a significant reduction in orthodontic tooth movement and number of osteoclasts.[2] Likewise, non-steroidal anti-inflammatory drugs (NSAIDs) reduce the rate of tooth movement by inhibiting PG synthesis.[18] Inhibiting other derivatives of arachidonic acid, such as leukotrienes, also significantly decreases the rate of tooth movement.[19]

If inhibiting inflammatory markers decreases the rate of tooth movement, it is logical to assume that increasing their activity should significantly increase the rate of tooth movement. Indeed, injecting PGs into the PDL in rodents increases the number of osteoclasts and the rate of tooth movement.[20] Systemic application of misoprostol, a PGE_1 analog, to rats undergoing tooth movement for 2 weeks, significantly increases the rate of tooth movement.[21] Similarly, local injection of other arachidonic acid derivatives, such as thromboxane and prostacyclin,[22] increases the rate of tooth movement.

Unfortunately, injection of PGs to increase the rate of tooth movement has limitations. First, due to their very short half-life, PGs must be delivered repeatedly. Second, local PGs injections can cause hyperalgesia due to release of histamine, bradykinin, serotonin, acetylcholine, and substance P from nerve endings.[23]

Another approach in increasing inflammatory mediators that will increase the rate of tooth movement is to stimulate the body to produce these factors at a higher level. The advantage of this approach is a coordinated increase in the level of all inflammatory mediators. As discussed before, many cytokines participate in response to orthodontic forces. Injecting one cytokine does not mimic the normal inflammatory response, which is a balance of pro- and anti-inflammatory mediators. However, the approach that safely triggers the body to produce higher levels of inflammatory mediators is not clear.

One may suggest that increasing the level of orthodontic force should increase the level of cytokine expression, since a higher magnitude of force produces greater trauma to the PDL and bone leading to higher levels of inflammation. In fact, increasing the force magnitude is accompanied by higher levels of cytokine and chemokine expression, but only to certain point. Increasing the magnitude of force beyond that point does not produce higher levels of inflammatory mediators or accelerated tooth movement.[24] This observation led to the conclusion that there is a "biological saturation point" in response to orthodontic forces. However, it should be emphasized that extremely high levels of forces may lead to the appearance of micro-fractures in bone that can stimulate further cytokine expression and bone resorption. While these forces are beyond the magnitude of orthodontic forces applied during orthodontic treatment, the observation highlights the possibility of stimulating a similar reaction in bone via another method, thus facilitating orthodontic tooth movement by increasing the rate of bone resorption.

Animal studies have shown that introducing small perforations in the alveolar bone [micro-osteoperforations(MOPs)] during orthodontic tooth movement can significantly stimulate the expression of inflammatory mediators. While application of orthodontic force beyond the saturation point does not elevate the expression and activation of inflammatory mediators beyond certain levels, adding MOPs to the area of tooth movement increases the level of inflammatory mediators.[25] This response is accompanied by a significant increase in osteoclast number, bone resorption, and localized osteopenia around all adjacent teeth, which could explain the increase in the rate and magnitude of tooth movement. One may argue that the effects of the shallow perforations on tooth movement are not a response to increased cytokine expression, but rather due to weakening of the bone structure. While the effects that perforations can have on the physical properties of the bone cannot be ignored, the number and diameter of these perforations are too small to have significant impact.[26] Similarly, a human clinical trial using a canine retraction model demonstrates that MOPs can amplify the catabolic response to orthodontic forces. Canine retraction in the presence of MOPs results in twice as much distalization in comparison with patients receiving similar orthodontic forces without MOPs. This increase in tooth movement is accompanied by an increase in the level of inflammatory mediators.[27]

Clinical studies demonstrate that increasing the number of MOPs significantly increases expression of inflammatory mediators and the magnitude of tooth movement.[28] Therefore, one should expect procedures such as orthognathic surgery, corticotomies, or piezocision would significantly increase the levels of inflammatory cytokines beyond those induced by MOPs. While increase in cytokine release is accompanied with higher rate of tooth movement, unfortunately, the increase in the expression of inflammatory mediators is not sustained for a long time. A significant decrease in cytokine activity is observed 2–3 months after any of these treatments. As a result, each of these procedures would need to be repeated during the course of orthodontic treatment, which renders some of the above-mentioned modalities impractical.

Recently, a modification of these techniques has been introduced where, after selective decortication in the form of lines and points, a resorbable bone graft is placed over the surgical sites. Falsely, the accelerating effect of these techniques has been attributed to the shape of the cuts made into the bone (block concept) and to the bone grafts.[29,30] As previously discussed in this article, the rate of tooth movement is controlled by osteoclast recruitment and activation which is controlled by cytokine release in response to trauma. While magnitude of trauma (number and depth of the cuts) can affect the magnitude of cytokine release, shape of trauma does not affect inflammatory response. Moreover, bone grafts do not increase osteoclast activation and as a result do not contribute to the increase in the rate of tooth movement. Therefore, while the application of bone grafts can help in increasing the boundary of tooth movement toward cortical bone, during routine orthodontic treatment where teeth are moved in trabecular bone, they are unnecessary.

Mechanical stimulation to increase the rate of tooth movement

Another methodology that has been suggested to increase the rate of tooth movement is the application of high-frequency low-magnitude forces.[31] The main assumption in this hypothesis is that bone is a direct target of orthodontic forces, and therefore by optimizing mechanical stimulation, it is possible to increase the rate of tooth movement. There are many flaws in this theory. As we discussed before, the assumption that tooth movement is the result of direct response of bone cells to mechanical stimulation is incorrect, which means that optimizing the mechanical stimulation based on bone cell activity, especially osteocytes, is not a correct approach. Based on this biological principle, application of vibration and orthodontic forces will never be able to move an ankylosed tooth. In addition, all studies in long bone and alveolar bone[24] demonstrate an osteogenic effects of these stimulants with increases in bone density without any resorptive effect, which logically should delay, rather than accelerate, the rate of tooth movement. It is possible that application of high-frequency low-magnitude forces during orthodontic movement stimulates a pathway far

different from its effect on bone. If that is true, the frequency-dependence of the stimulant is questionable, and literature in this field should not be used to justify applying vibration during tooth movement.

Heat, light, electric currents and laser to increase the rate of tooth movement

Early studies on the application of heat and light during orthodontic tooth movement[32] have demonstrated faster tooth movement. Similarly, animals exposed to longer hours of light also show an increase in the rate of tooth movement.[33] However, the magnitude of this acceleration was either small or could be explained more by systemic effect of the stimulant and not necessarily local effects.

Minute electric currents have been suggested to increase the rate of tooth movement. In this regard, some studies did not report any changes in the rate of tooth movement,[34] while others report significant increase.[35] Similarly, studies on static magnetic fields produce inconsistent results on the rate of tooth movement with some showing an increase[36] and others demonstrating no change in the rate of tooth movement.[37]

Based on the piezoelectric theory, some researchers suggest using a pulsed electro-magnetic field to accelerate tooth movement.[38] Indeed, animals that received this type of stimulation during orthodontic tooth movement demonstrate a faster rate of tooth movement.

Recently, more attention has been given to possible effect of low-level laser therapy (LLLT) on the rate of tooth movement. LLLT is a treatment that uses low-level lasers or light-emitting diodes to alter cellular function. LLLT is controversial in mainstream medicine with ongoing research to determine whether there is a demonstrable effect. Also disputed are the dose, wavelength, timing, pulsing, and duration.[39] The effects of LLLT appear to be limited to a specified set of wavelengths[40] and administering LLLT below a dose range does not appear to be effective.[26]

In general, the mechanism of action of LLLT is not clear and sometimes opposite to what is required for orthodontic tooth movement. For example, LLLT may reduce pain related to inflammation by dose-dependently lowering levels of PGE_2, IL-1, and TNF-α, decreasing the influx of inflammatory cells such as neutrophils, oxidative stress, and edema.[41] Another mechanism may be related in stimulating mitochondria to increase the production of adenosine triphosphate (ATP) resulting in an increase in reactive oxygen species, which influences redox signaling, which then affects intracellular homeostasis or cellular proliferation.[42] The final enzyme in the production of ATP by mitochondria, cytochrome-c oxidase, appears to directly respond to lasers, making it a possible candidate for mediating the properties of laser therapy.[43] Due to anti-inflammatory and osteogenic effects of LLLT, application of LLLT to increase the rate of tooth movement is controversial. While some studies demonstrate increased rates of tooth movement,[44] other studies did not see any effect.[45] The anti-inflammatory effect of LLLT should delay the tooth movement, while the proliferative effect may help increase the number of osteoblasts. On the other hand, some studies show an increase in the number of osteoclasts during LLLT application with orthodontic tooth movement,[46] which cannot be explained by a proliferative effect of lasers since osteoclasts arise from precursor cells and not proliferation of mature osteoclasts, as some have suggested. Further studies in this subject are clearly necessary.

Unfortunately, applying any of these physical stimuli to increase the rate of tooth movement at present suffers from a lack of evidence, an unknown mechanism and general impracticality. In addition, the magnitude of increase in the rate of tooth movement is not significantly high to justify their application. Nevertheless, this field has great potential for growth.

Chemical agents to increase the rate of tooth movement

If bone resorption is the key factor in controlling the rate of tooth movement, application of any agent that increases the rate of bone turnover should increase the rate of tooth movement. With this in mind, the application of parathyroid hormone (PTH), vitamin D3, corticosteroids, thyroxin, and osteocalcin have been examined. It should be noted that other factors, such as calcitonin or estrogens, can prevent bone resorption and decrease the rate of tooth movement.[47]

PTH is secreted by the parathyroid glands and increases the concentration of serum calcium by

stimulating bone resorption. A significant stimulation of the rate of tooth movement by exogenous PTH appears to occur in a dose-dependent manner, but only when it is continuously applied by either systemic infusion[48] or local delivery every other day in a slow-release formulation.[49] It should be noticed that although continuous elevation of PTH leads to bone loss, intermittent short elevations of the hormone level are anabolic for bone[50] and perhaps cannot increase the rate of tooth movement.

Vitamin D3 (1,25 dihydroxycholecalciferol) is another factor that can affect the rate of bone remodeling and therefore its possible effect on the rate of tooth movement has been studied. vitamin D3 regulates calcium and phosphate serum levels by promoting their intestinal absorption and reabsorption in the kidneys. Furthermore, it promotes bone deposition and inhibits PTH release. Based on these mechanisms, one would expect that vitamin D3 should decrease the rate of tooth movement. To the contrary, it has been shown that vitamin D3 can increase the rate of tooth movement if injected locally.[51] This effect can be related to the effect of vitamin D3 on increasing the expression of RANKL by local cells and therefore activation of osteoclasts.[52] Similarly, local injection of osteocalcin (a bone matrix component) caused rapid tooth movement due to attraction of numerous osteoclasts into the area.[53]

Corticosteroids are another group of chemical agents that have been suggested for accelerating the rate of tooth movement. While the anti-inflammatory effect of corticosteroids can decrease the rate of tooth movement, in the presence of cytokines such as IL-6 they may help stimulate osteoclastogenesis and cause osteoporosis.[31] Therefore, the effect of corticosteroids on tooth movement can vary depending on the dosage and whether they are administered before the expression of cytokines (induction period) or after their presence. While some studies demonstrate an increase in rate of tooth movement following corticosteroid treatment,[54] others did not report any changes.[55,56]

Another factor that may increase the rate of tooth movement is the thyroid hormone (thyroxin). Thyroxin affects intestinal calcium absorption, thus it is indirectly involved in bone turnover and induction of osteoporosis. It has been shown that exogenous thyroxin increases the rate of tooth movement,[57] which can be related to increase in bone resorption.

Recently, the hormone Relaxin has been used in rats to increase the rate of tooth movement. Relaxin is capable of reducing the organization level of connective tissues, facilitating rapid separation between adjoining bones. Unfortunately, no significant increase in the rate of tooth movement was observed.[58]

The application of chemicals to accelerate tooth movement suffers from many problems. First, all the chemical factors have systemic effects that raises questions about their safety during clinical application. Second, the majority of the factors have a short half-life; therefore multiple applications of the chemical are required, which is not practical. In addition, administration of a factor in a manner that allows an even distribution along the alveolar bone surface in the compression site is still a challenge. Uneven distribution can change the pattern of resorption and therefore the biomechanics of tooth movement.

Summary and future directions

While many seemingly random approaches have been taken to increase the rate of tooth movement, a successful approach should be based on solid biological principles where the target cells and mechanism to stimulate those cells are well defined. This would be possible only if theories on biology of tooth movement are revisited. A good accelerating technique should be affordable, repeatable, practical, efficient, and have no side effects on the periodontium, including roots and alveolar bone. At this moment, all the current approaches are suffering from one or more deficiencies, but it is not far from reality to claim that we are on the right track.

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