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Biphasic theory: breakthrough understanding of tooth movement

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ABSTRACT

Background: Research on the biology of orthodontic tooth movement has led to the prevailing compression-tension theory, which divides the response to orthodontic force into two opposing reactions spatially separated: on the compression side, osteoclasts resorb bone to create space for tooth movement, whereas on the tension side, osteoblasts form bone to restore the alveolar bone structure.
Methods: Here we take a critical look at the literature on how force-induced inflammation, the periodontal ligament, osteoclasts, and osteoblasts contribute to the biological reaction to orthodontic force. We introduce new evidence that supports a novel theory to explain the biology of tooth movement—the Biphasic Theory.
Results: The Biphasic Theory of Orthodontic Tooth Movement divides tooth movement into the initial Catabolic Phase, during which osteoclasts resorb bone at both compression and tension sites, and the Anabolic Phase, which occurs subsequently to restore alveolar bone to its pretreatment levels.
Conclusions: The Biphasic Theory of Tooth Movement successfully addresses shortfalls in the Compression-Tension Theory of Tooth Movement, provides clinicians with a better understanding of how orthodontic forces move teeth, and offers new targets for therapies aimed at accelerating tooth movement.

1. Introduction

Although studied for decades, the biology of orthodontic tooth movement remains the focus of intense investigation, as innovative technologies give us important insights into the molecular, cellular, and tissue responses to orthodontic force. This knowledge is important because it establishes the foundation of orthodontics, which relies on stimulating the movement of teeth through alveolar bone. Although the biological changes during tooth movement are the basis of any orthodontic treatment, optimizing this movement and reducing potential risk factors remain the main challenges for researchers and clinicians in this field. In this review, we introduce you to the Biphasic Theory of Orthodontic Tooth Movement and how we can better understand the effects of orthodontic forces on the teeth, the periodontal ligament (PDL), and the alveolar bone.

Although the tissue responses that enable orthodontic tooth movement are generally known, the mechanisms driving these responses remain unclear. Some of the unanswered questions include the following: How do orthodontic forces activate bone resorption and formation? Are the effects of orthodontic force direct or indirect? Does the PDL play a role in controlling the rate of tooth movement? To address these and other questions, we begin with an overview of how each type of bone cell functions.

2. Bone cells and their role in tooth movement

The key to understanding the Biphasic Theory is recognizing that alveolar bone is perhaps the most reactive skeletal tissue in the body. When orthodontic force is applied to a tooth, coordinated and calibrated signals travel from the tooth through the PDL to the alveolar bone. The bone cells that make tooth movement possible are the bone-forming osteoblasts, bone-resorbing osteoclasts, and mechanosensoring osteocytes.

Osteoclasts carry out the critical job of resorbing bone during orthodontic tooth movement. Formed through fusion of monocyte/macrophage precursor cells in the bone marrow, mature multinucleated osteocytes are distinctive cells. When mature, they express the calcitonin receptor [1], tartrate-resistant acid phosphatase (TRAP) [2], and cathepsin-K [3] and secrete an array of proteases to digest the extracellular matrix. Anatomically, mature osteoclasts are notable for

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the appearance of an elaborate ruffled border that is rich in proton pumps that acidify the bone surface causing bone resorption.

Osteoclasts are the main players in the initial Catabolic Phase. They control the rate of bone resorption during orthodontic treatment and, therefore, the rate of tooth movement [4]. However, the recruiting and activity of osteoclasts during orthodontic treatment require signals from several other cell types. Left unchecked, activated osteoclasts would resorb excessively the alveolar bone leading to pathology such as osteopenia and fractures. Because of the need for such tight regulation, osteoclasts cannot be the direct target of orthodontic forces. Instead, orthodontic forces must target the upstream regulators of osteoclastogenesis and osteoclast activation, such as inflammatory cytokines and chemokines [5]. These regulators are part of the osteoimmunology network that is active during normal physiological and pathological alveolar bone remodeling [6].

Osteoblasts are mesenchymal stem cell–derived mononuclear cells residing along bone surfaces. When mature, they synthesize osteoid, a mix of collagenous and noncollagenous proteins in the extracellular matrix. Of importance to the Biphasic Theory is the finding that inflammatory cytokines also trigger osteoblast proliferation and differentiation [7]. Inactive osteoblasts, known as bone-lining cells, are flat until growth factors or other anabolic stimuli induce activation and they become cuboidal. In the Biphasic Theory, osteoblasts are the main cells participating in the Anabolic Phase, and they have a limited role during the initial Catabolic Phase where they can activate osteoclasts through the RANKL (receptor activator of nuclear factor kappa-B ligand)-RANK pathway.

Osteocytes are mature osteoblasts immobilized within the mineralized bone matrix [8]. They contact each other and cells on the bone surface via a fine network of cellular processes housed in canaliculi. Their intricate three-dimensional network enables osteocytes to serve as mechanosensors to detect mechanical load and signal osteoclasts and osteoblasts to reshape bone to fit the mechanical demand.

Although it is clear that osteocytes are critical for normal bone remodeling, their precise role in the Biphasic Theory is unclear. They may play a role in the Catabolic Phase by activating osteoclasts. Evidence from transgenic mice with nonfunctional osteocytes have significantly fewer osteoclasts and less orthodontic tooth movement compared with normal mice, indicating that alveolar bone osteocytes are vital for cellular communication during tooth movement [9]. It is also probable that osteocytes function in the Anabolic Phase to coordinate osteoblast activation [10]. Interestingly, there is crosstalk between osteocytes and the PDL during tooth movement, suggesting another possible mechanism for osteocytes to influence tooth movement [11].

3. Biphasic theory of orthodontic tooth movement

Tooth movement results from tightly regulated responses of osteoclasts, osteocytes, and osteoblasts to orthodontic forces. Specifically, evidence points to the conversion of orthodontic forces into temporally sequenced catabolism followed by anabolism in alveolar bone. Taken together, the data on tooth movement led us to develop the Biphasic Theory of Tooth Movement to not only explain the biological consequences of orthodontic treatment, but to also guide researchers to develop accelerated, efficacious, and safe orthodontic treatments.

The Biphasic Theory states that orthodontic tooth movement results from two sequential phases of alveolar bone remodeling induced by orthodontic force. The Catabolic Phase precedes the Anabolic Phase, with distinct cellular and molecular events establishing the limits for each phase.

4. The Catabolic Phase of tooth movement

4.1. Classical theories of initiation of tooth movement

Orthodontic forces and couples generate stresses that are transmitted through the PDL to the alveolar bone to produce tooth movement. According to the classical theories, the biology of tooth movement rests on three pillars:

1. Cells involved: Compression activates osteoclastogenesis and osteoclast activation, whereas tension activates osteoblasts; therefore, osteoclasts should populate compression sites and osteoblasts should populate tension sites.
2. Location: The catabolic and anabolic responses occur independently of each other in the PDL, on opposite sides of the tooth.
3. Timing: Although independent, the catabolic and anabolic phases occur simultaneously, because both compression and tension occur simultaneously.

Numerous proposals explaining the initial events leading to catabolism at compression sites fall into two main camps: 1) The Direct Theory proposes that bone cells (especially osteocytes) are the direct target of orthodontic forces, and 2) the Indirect Theory proposes that the PDL is the direct target of orthodontic forces (Fig. 1). Importantly, there is agreement in both theories that osteoclasts are the target cells that resorb bone, and therefore, are the cells that control the rate of tooth movement.

Based on stress responses in weight-bearing bones, Direct Theory proponents suggest that there are two possible mechanisms by which direct loading activates osteocytes. First, osteocytes detect different components of normal, physiological stress (such as matrix deformation) and direct the bone-remodeling machinery to strengthen bone in line with the direction of the stress. This is accomplished by triggering osteoclasts to remove weakened bone and osteoblasts to rebuild new load-tolerant bone at the site of greatest weakness. Second, osteocytes detect higher, pathologic stress by sensing microfractures in the matrix, resulting in increased bone remodeling at the damaged site.

Although the osteocyte-driven bone-remodeling response to physiologic or pathologic stress is accepted for weight-bearing bones, applying the Direct Theory to alveolar bone remodeling triggered by orthodontic forces is questionable. Experiments in long bones and alveolar bone demonstrate that osteocytes cannot detect static forces at physiologic levels [13,14]. Because orthodontic forces are static and within physiologic limits, this argues against orthodontic tooth movement being a physiological adaptation to mechanical stimulation. Moreover, dental implants used as orthodontic anchorage do not move when a static force is applied, suggesting that the Direct Theory is not correct.

Perhaps orthodontic forces stimulate tooth movement by inducing microfractures in bone [15]. The possibility that this is the main mechanism triggering tooth movement is low because, as with implants, orthodontic force cannot move an ankylosed tooth. Thus, the presence of microfractures is not sufficient for orthodontic force to move teeth. Moreover, the relationship between force magnitude and tooth movement is not linear, and soon after applying orthodontic force, the bone-remodeling rate reaches a saturation point. If microfractures are the trigger for tooth movement, higher forces should continually increase the rate of movement, without ever reaching a saturation point [16]. It should be emphasized that although application of pathological, high-magnitude forces may damage the bone around an implant to the point of failure, high-magnitude forces do not move an implant. Taken together with the fact that physiological, low-magnitude

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