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Review

The role of osteocytes during experimental orthodontic tooth movement: A review

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ABSTRACT

Objective: To explore the types of orthodontic force-induced mechanical stimuli that regulate osteocyte function.
Design: In orthodontics, a tooth can be moved through the alveolar bone when an appropriate orthodontic force is applied. These mechanical loads stimulate cells within the bone tissue around the tooth. These cellular responses lead to bone resorption on the side of the tooth where the pressure has been applied and bone deposition on the side of the tooth experiencing tension. Recently, osteocytes were identified to function as mechano-sensory cells in bone tissue that direct bone resorption and bone formation. Based on recent literature, the proposed function of osteocytes during orthodontic tooth movement is explored with better understanding.
Results: Several stimuli regulating osteocyte function have been highlighted, and their potential roles in events initiating osteocyte sensing of orthodontic force have been explored in detail. The most popular hypotheses for osteocyte response include stress-induced bone matrix deformation/microcrack formation and fluid-flow shear stress.
Conclusions: Understanding osteocyte function under mechanical stress may have profound implications in future orthodontic treatments.

Contents

1. Introduction

In orthodontics, mechanical force is placed on a tooth so that it can be moved through the alveolar bone. These forces induce strain on the bone tissue surrounding the tooth, leading to cellular responses that result in bone tissue remodelling (Melsen, 1999; Krishnan & Davidovitch, 2006; Masella & Meister, 2006; Henneman, Von den Hoff, & Maltha, 2008). Bone resorption is seen on the side of the tooth that receives the pressure, whereas new bone is deposited on the side of the tooth that senses the tension (Fig. 1). Although bone remodelling was thought to be a delicate balance between the function of osteoblasts and osteoclasts, research has shown that other cells are involved in bone remodelling, most

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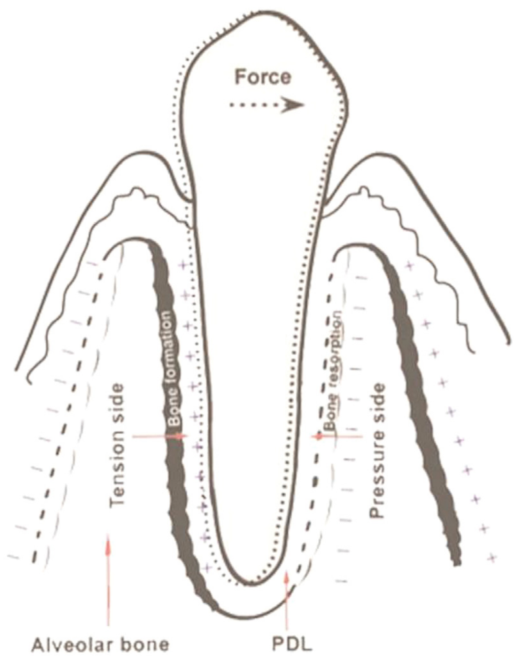

Fig. 1. A schematic diagram representing orthodontic tooth movement. The dotted arrow shows the direction of orthodontic force inducing tooth movement. Tooth movement is accompanied by alveolar bone remodelling. The side of the tooth where orthodontic pressure is applied shows alveolar bone resorption, whereas the side of the tooth where tension is applied shows alveolar bone formation. PDL: periodontal ligament.

notably osteocytes, which are now considered the most important players in the bone remodelling process (Klein-Nulend, Bakker, Bacabac, Vatsa, & Weinbaum, 2013; Bonewald, 2011) (Fig. 2a–e).

Osteocytes are the most numerous cells in bone tissue. They are derived from a select group of osteoblasts that have undergone a final differentiation, and they are encased within the lacunae of the mineralised bone matrix (Jande & Bélanger, 1973; Knothe Tate, Adamson, Tami, & Bauer, 2004). During the differentiation process, prospective osteocytes undergo progressive changes in morphology such that the cuboidal shape of the osteoblast gives way to the stellate shape of the mature osteocyte, with its multiple, slender, cytoplasmic processes (Nijweide, van der Plas, & Olthof, 1988; Palumbo, Palazzini, Zaffe, & Marotti, 1990). Osteocytes communicate with one another, with cells on the bone surface, and with cells in the bone marrow space through this highly organised network of cellular processes (Kamioka et al., 2001). Osteocyte processes are connected to each other through gap junctions, allowing for intracellular communication (Bonewald, 2005; Ishihara et al., 2012; Kamioka et al., 2007). Decades ago, osteocytes were considered inactive placeholder cells within the bone matrix. Recent data have shown that osteocytes are not passive cells, but instead, they are metabolically active and multifunctional. Several functions have been proposed for osteocytes, including osteolysis, regulation of mineralization, and mineral metabolism; they can act as mechano-sensory cells to detect mechanical stimuli produced from the mechanical loading of bones, and they are regulators of osteoblast and osteoclast function during bone remodelling (Lanyon, 1993; Feng et al., 2006; Lane et al., 2006; Dallas, Prideaux, & Bonewald, 2013; Jacobs, Temiyasathit, & Castillo, 2010).

The objectives of this review are to describe the main types of mechanical stimuli that modulate osteocyte function, including stimuli that may result from the application of orthodontic forces, and to discuss recent literature implicating osteocyte function during bone remodelling. Although the intention of this review is to provide an insight into how osteocytes react to orthodontic

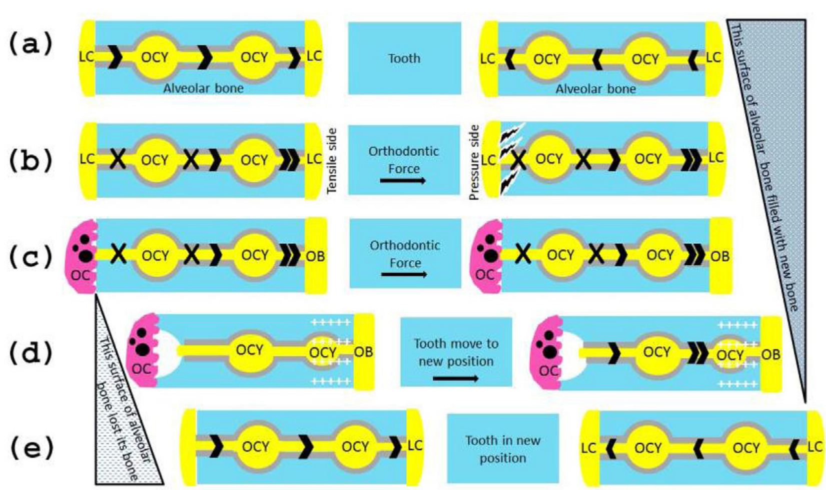

Fig. 2. A schematic diagram of the regulation of bone remodelling events by osteocytes during the application of orthodontic force. (a) In the steady state, normal mechanical use ensures a basal level of fluid flow through the lacunar-canalicular pores of the alveolar bone that surrounds the tooth. This basal flow keeps the osteocytes viable and ensures basal osteocyte activation and signalling, thereby suppressing osteoblastic activity as well as osteoclastic attack. (b) During the application of orthodontic force to move the tooth in the direction indicated by the arrow, two deformed sides within the bony socket of the alveolar bone are created: compressive deformation on the side receiving pressure and tensional deformation on the opposite side. On the pressure side, the orthodontic force induces micro-damage (indicated by lightning bolts). The accumulation of micro-damage interferes with canalicular fluid flow by disrupting the canaliculi, severing osteocyte processes, and leading to osteocyte apoptosis. Osteocytes are inactivated by the lack of fluid flow (as indicated by "X" through the canaliculi), while other osteocytes localised in the region where fluid flow shear stress is enhanced are over-activated by the fluid that has escaped from the pressure side (indicated by the double-headed arrow). On the tension side, the orthodontic force enhances the fluid flow towards the tooth; thus, the osteocyte is over-activated by the increased fluid flow shear stress (indicated by double-headed arrow). Other osteocytes localised in the region of decreased fluid flow shear stress, are inactivated by the lack of fluid flow shear stress (as indicated by "X" through the canaliculi). (c) In regions lacking fluid flow shear stress and micro-damage, osteoclast recruitment occurs, suggesting that osteocyte signals support osteoclast recruitment. In regions of enhanced fluid flow shear stress, fluid flow through the lacunar-canalicular network leads to the release of osteoblast-recruiting signals, and osteoblast recruitment occurs. (d) In regions lacking fluid flow shear stress and micro-damage, osteoclasts resorb damaged bone until they reach undamaged bone. This facilitates tooth movement in the indicated direction. In regions with enhanced fluid flow shear stress, osteoblasts form new bone. **(e)** Once tooth movement is complete and orthodontic force is removed, bone remodelling occurs around the tooth, and the alveolar bone returns to its normal, steady state. LC: lining bone cell; OB: osteoblast ; OC: osteoclast ; OCY: osteocyte.