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Mechanobiological modeling can explain orthodontic tooth movement: Three case studies

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ABSTRACT

Progress in medicine and higher expectation of quality of life has led to a higher demand for several dental and medical treatments. This increases the occurrence of situations in which orthodontic treatment is complicated by pathological conditions, medical therapies and drugs. Together with experiments, computer models might lead to a better understanding of the effect of pathologies and medical treatment on tooth movement. This study uses a previously presented mechanobiological model of orthodontic tooth displacement to investigate the effect of pathologies and (medical) therapies on the result of orthodontic treatment by means of three clinically relevant case studies looking at the effect of estrogen deficiency, the effect of OPG injections and the influence of fluoride intake. When less estrogen was available, the model predicted bone loss and a rise in the number of osteoclasts present at the compression side, and a faster bone resorption. These effects were also observed experimentally. Experiments disagreed on the effect of estrogen deficiency on bone formation, while the mechanobiological model predicted very little difference between the pathological and the non-pathological case at formation sites. The model predicted a decrease in tooth movement after OPG injections or fluoride intake, which was also observed in experiments. Although more experiments and model analysis is needed to quantitatively validate the mechanobiological model used in this study, its ability to conceptually describe several pathological conditions is an important measure for its validity.

1. Introduction

Progress in medicine and higher expectation of quality of life have led to a higher demand for several dental and medical treatments (Rinchuse et al., 2007), making it more and more common for other medical conditions needing to be taken into account by the orthodontist when planning orthodontic treatment. The primary aim of orthodontic treatment is obtaining the correct occlusion, in order to improve chewing, esthetics and patient comfort. During treatment, tooth displacement is achieved by applying orthodontic forces to the tooth. Under the influence of these forces, the pressure side of the tooth root will experience bone resorption while bone formation will take place on the tension side. The coordination of these two processes through cellular communication results in permanent tooth displacement through the alveolar bone. Orthodontic treatment can be complicated by different pathological conditions and medical treatments.

Estrogen deficiency is a common cause of bone loss and an increased bone turnover rate, as demonstrated in a number of studies with rats, monkeys and humans (Cesnjaj et al., 1991; Parfitt et al., 1983; Whyte et al., 1982). Osteoporotic changes in the alveolar bone of rats were shown by Tanaka et al. (2002). The mechanism by which estrogen exerts its effect on bone remodeling is not entirely understood. However, a normal estrogen concentration may limit the size of the pre-osteoclast population by stimulating apoptosis (Rattanakul et al., 2003) and limit the number of osteoclasts further by decreasing the sensitivity of maturing osteoclasts to RANKL (Weitzmann and Pacifici, 2006). Since tooth movement is achieved through the resorption and formation of alveolar bone, pathologies affecting bone metabolism will most likely affect the outcome of orthodontic treatment.

As OPG binds to RANKL, making it inert, it is known to prevent bone resorption. While the benefits of OPG injections in systemic conditions like osteoporosis are clear, there are also possible uses for RANKL inhibitors like OPG in orthodontic tooth movement. It is often necessary to minimize undesired movement of teeth

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which are for example to be used as an anchor unit. Sometimes, teeth are subjected to unnecessary, but unavoidable, forces generated by parts of the orthodontic appliances they come in contact with. Tooth movement should be avoided in those cases. The use of RANKL inhibitors may also be used to prevent teeth from returning to their original position after finishing orthodontic treatment (Kohno et al., 2005).

The use of fluoride has already been a successful strategy for preventing tooth decay and caries; it is commonly added to tooth paste. In mineralized tissues, fluoride replaces the hydroxyl group of the hydroxy apatite crystals, forming fluoroapatite (Gonzales et al., 2011; Robinson and Kirkham, 1990). The structure of fluoroapatite is larger and less soluble then hydroxy apatite, making it more resistant to demineralization (Foo et al., 2007). Therefore, it is believed that systematic fluoride intake may prevent orthodontically induced root resorption (Gonzales et al., 2011; Foo et al., 2007), although it will probably decrease the rate of tooth movement.

Together with experiments, computer models might lead to a better understanding of orthodontic treatment and the pathologies affecting the outcome. Most existing models (Mengoni and Ponthot, 2010; Alcañiz, 1998; Bourauel et al., 1999; Bourauel et al., 2000; Schneider et al., 2002; Soncini and Pietrabissa, 2002) describing tooth movement are based on an empirical bone remodeling function derived from experiments. Moreover, the biological activity in the PDL and the alveolar bone is not taken into account. Taking into account this biology makes the model more complex, but makes it possible to more accurately describe the process. The work presented in this article builds on the mechanobiological model of tooth movement previously presented by the authors (Van Schepdael et al., 2012) and investigates three case studies: the effect of estrogen deficiency, the effect of OPG injections and the influence of fluoride intake.

2. Materials and methods

2.1. Model development

The mechanobiological model consists of a set of nine coupled non-linear partial differential equations, of the taxis–diffusion–reaction (TDR) type. The equations describe the concentration of various cells, growth factors, cytokines and matrix-components. The periodontal ligament consists of collagen fibers (m_c) and contains a large amount of fibroblasts (c_f). The alveolar bone consists of mineralized collagen, with m_m representing the degree of mineralization of the collagen. The bone has a small concentration of osteoblasts (c_b) and osteoclasts (c_l), constantly remodeling and renewing the bone. To coordinate bone remodeling, osteoclasts, osteoblasts and fibroblasts communicate through the RANKL-RANK-OPG signaling pathway. In the model, RANKL ($g_r = g_{rb} + g_{rf}$) is produced by fibroblasts (g_{rf}) and osteoblasts (g_{rb}), while OPG (g_o) is produced by osteoblasts only. The osteogenic differentiation of mesenchymal stem cells into osteoblasts is regulated by active TGF-β (g_b), also produced by osteoblasts and fibroblasts. Multinucleated osteoclasts are formed through the fusion of hematopoietic stem cells, which are present in the vascular matrix in the PDL and the bone.

Fibroblasts are modeled to respond to mechanical stretching by producing the osteogenic growth factor TGF-β, along with other osteogenic factors of the TGF-β superfamily (Wescott et al., 2007; Kimoto et al., 1999; Marotti 2000; Pinkerton et al., 2008). The upregulation of the TGF-β production results in the appearance of a high number of osteoblasts in and around the PDL. This leads to bone formation in the tension zones. Fibroblasts respond to compression by upregulating the production of RANKL (Kanzaki et al., 2002; Nishijima et al., 2006; Yamaguchi et al., 2006; Krishnan and Davidovitch, 2009). This results in a higher number of osteoclasts, which start resorbing the alveolar bone, making it possible for the tooth to move. More information concerning the biological assumption made in this model can be found in Van Schepdael et al. Van Schepdael et al., (2012) as well as in the online Supplementary material, and a more comprehensive overview of the biology of tooth movement can be found in Garant (2003), Krishnan and Davidovitch (2009), Krishnan and Davidovitch (2006) and Henneman et al. (2008).

The specific equations for all nine variables are represented below. More information on the parameters, equations and initial conditions can be found in Van Schepdael et al. (2012) and in the online Supplementary material. An overview of the origin and value of all parameters can be found in Table 1.Table 2 shows the initial values of all variables in the PDL and the bone.

Table 1
Overview of the parameters of the mechanobiological model, their value, unit and origin. (1) Derived from Geris et al. (2008). (2) Derived from Pivonka et al. (2008). (3) Derived from Pfeilschifter et al. (1998). (4) Derived from Sandberg et al. (1988).

Parameter	Value	Unit	Origin
P_{ms}	3.42	ml cells^{-1} day^{-1}	From steady state conditions
Q_{md}	3.6	ml cells^{-1} day^{-1}	(1)
P_{cs}	2	g cells^{-1} day^{-1}	(1)
κ_c	13.55	ml g^{-1}	(1)
P_{csf}	2	g cells^{-1} day^{-1}	(1)
κ_{cf}	10	ml g^{-1}	(1)
A_{b0}	0.54	day^{-1}	(1) and stability analysis
α_b	2	ml cells^{-1}	(1) and stability analysis
d_b	0.18	day^{-1}	(1)
Y_{11}	3.27	cells ml^{-1} day^{-1}	(1)
H_{11}	10	ng ml^{-1}	(1)
m_{bt}	0.3	[dimensionless]	Estimated
C_{mh}	3.06	mm^2 day^{-1}	Estimated
Y_2	551.6	cells ng^{-1} day^{-1}	(2)
d_{l0}	0.7	day^{-1}	Using life span of osteoclast
D_f	0.25	mm^2 day^{-1}	(1)
A_{f0}	1.06	ml g^{-1} day^{-1}	(1)
A_{fs}	10	[dimensionless]	Estimated
α_f	1	ml cells^{-1}	(1)
d_f	0.11	day^{-1}	From steady state conditions
D_{gb}	6.13	mm^2 day^{-1}	(1)
G_{gb}	6.03	ng cells^{-1} day^{-1}	(1)
α_g	0.1	ml ng^{-1}	(3), (4)
E_{gb}	1	ng cells^{-1} day^{-1}	Estimated
d_{gb}	100	day^{-1}	(1)
P_{rs}	3440	ng ml^{-1} day^{-1}	(2)
R_1	9.15	ng cells^{-1}	(2)
d_{gr}	10.05	day^{-1}	(2)
B_{1r}	2.5	ml ng^{-1} day^{-1}	(2)
B_{1o}	1.67	ml ng^{-1} day^{-1}	(2)
E_{grf}	1	ng cells^{-1} day^{-1}	Estimated
D_{go}	4.58	mm^2 day^{-1}	Using molecular weight of OPG
P_{os}	6.83	ng cells^{-1} day^{-1}	(2)
κ_o	8.3	ml ng^{-1}	(2)
d_{go}	35	day^{-1}	(2)
D_2	248.5	[dimensionless]	From H_2
H_2	48.6	ml ng^{-1}	(2)
A	98	MPa	
B	1	MPa	
C	0.68	MPa	

Table 2
Initial values applied to the model domain.

	PDL	Alveolar bone	Unit
m_m	0	0.9	[dimensionless]
m_c	1	0.075	g ml^{-1}
c_b	0	3.2	cells ml^{-1}
c_l	0	2.3	cells ml^{-1}
c_f	1	0	cells ml^{-1}
g_b	0	2	ng ml^{-1}
g_{rb}	0	2.9	ng ml^{-1}
g_{rf}	0	0	ng ml^{-1}
g_o	0	6.2	ng ml^{-1}

$$\frac{\partial m_c}{\partial t} = \underbrace{P_{cs}[1-\kappa_c m_c]c_b}_{\text{production by osteoblasts}} + \underbrace{P_{csf}[1-\kappa_{cf} m_c]c_f}_{\text{production by fibroblasts}} \quad (1)$$

$$\frac{\partial m_m}{\partial t} = \underbrace{P_{ms}[1-m_m]c_b}_{\text{mineralisation by osteoblasts}} - \underbrace{Q_{md}c_l H(m_m)}_{\text{demineralisation by osteoclasts}} \quad (2)$$

$$\frac{\partial c_b}{\partial t} = \underbrace{\frac{Y_{11}g_b}{H_{11}+g_b}[1-m_m]H(\overline{m}_m - m_{bt})}_{\text{differentiation from MSC}} + \underbrace{A_{b0}m_m c_b[1-\alpha_b c_b]}_{\text{proliferation}} - \underbrace{d_b c_b}_{\text{apoptosis}} \quad (3)$$