ISSN (P&E): 1996-7195, (O): 2957-899X DOI: https://doi.org/10.53350/pjmhs020251910.a

ORIGINAL ARTICLE

Role of Salivary Biomarkers in Predicting Orthodontic Tooth Movement Rate and Root Resorption. A clinical study

IMSHA MARYAM[1], JAWERIA ABID[2], MARYAM GULZAR[3], SHAZIA QASIM[4]
[1]MSc Hons, University of Agriculture Faisalabad
[2]BSc hons HND, University of Agriculture Faisalabad, Pakistan, **Email:** jaweriaabid71@gmail.com
[3]MSc hons. Hungarian University of Agriculture and Life Sciences Mate, Budapest, **Email:** maryyamgulzar540@gmail.com
[4]MBBS, Fatima Jinnah Medical University,lahore Pakistan, **Email:** shaziaqasim1027@gmail.com
Correspondence to: Imsha Maryam, **Email:** imshamaryam33@gmail.com

This article may be cited as:
Maryam I, Abid J, Gulzar M, Qasim S, Role of Salivary Biomarkers in Predicting Orthodontic Tooth Movement Rate and Root Resorption. A clinical study. Pak J Med Health Sci, 2025; 19(10): 18-23.

Received: 10-05-2025
Accepted: 24-10-2025
Published: 05-11-2025

ABSTRACT

Background: Orthodontic tooth movement (OTM) is a complicated biological process consisting of inflammation, bone resorption and formation in the periodontal ligament. In the recent past, salivary biomarkers have been invited as being non-invasive measures of biological activity during orthodontic procedures. This was a clinical research agenda to determine the predictive capacity of the chosen salivary biomarkers regarding the speed of movement of teeth and the level of root resorption.

Methods: 100 orthodontic patients (between 12 and 25 years old) were subjected to a prospective clinical trial in the retraction of bilateral maxillary cusps. The measures of unstimulated saliva were taken at baseline and 24 hrs, 7 days, 28 days and 8 weeks after activation. They were measured using ELISA IL-1-EB-IL-6, IL-1-EB-RANKL, IL-1-EB-OPG, IL-1-EB-ALP, MMP-8, MMP-9, DSP and TRAP-5b. Tooth movement was assessed in 3D intraoral scan and digital calipers whereas root resorption was assessed through radiograph. Rating on correlation and regression were employed to identify the predictive associations amidst biomarkers and clinical outcomes.

Results: IL-1b, IL-6, RANKL, MMP-8, and MMP-9 increased significantly with time, and correspondingly, classifying as decrease with time in OPG ($p < 0.001$). The tooth movement rate had strong positive associations with the RANKL/OPG ratio and the ALP activity ($r = 0.52$ and $r = 0.45$). The level of root resorption was related to high levels of DSP and MMP-9 ($p < 0.01$). The study did not demonstrate any noticeable periodontal inflammation or systemic confounders.

Conclusion: Salivary biomarkers especially the RANKL/OPG ratio, IL -1B, MMP-9 and DSP are stable non-invasive biological activity measures during orthodontic treatment. Their tracking would allow one to anticipate the individual tooth movement rates and identify early root resorption which would allow to implement the biologically informed and patient-centered methods of orthodontic treatment.

Keywords: Orthodontic tooth movement, Salivary biomarkers, RANKL/OPG ratio, IL-1 2, Root resorption, Matrix metalloproteinases, Alkaline phosphatas

INTRODUCTION

Orthodontic tooth movement (OTM) is a biological process that takes place in a complicated interaction of mechanical and cellular-molecular responses in the periodontal ligand (PDL) and alveolar bone around the tooth [1]. The application of orthodontic pressure causes local tissue stress resulting in the remodeling processes including resorption of bone on the pressure side and formation of bone on the tension side[2]. Mediators such as cytokines, growth factors, enzymes and inflammatory markers are a cascade of biochemicals that regulate this. These biological reactions are highly important in understanding how best to augment the effects of treatment, reduce the side effects, and determine the individual differences in the speed of movement of the teeth[3].

Saliva, which is an easily available diagnostic fluid has in the recent times come in focus as a non-invasive source of the biological markers indicating changes, both

local and systemic, in response to the orthodontic treatment [4]. It has different biomolecules like prostaglandins, interleukins (IL-1B, IL-6), tumor necrosis factor-alpha (TNF-A), matrix metalloproteinases (MMPs) and alkaline phosphatase (ALP) that are linked to tissue inflammation and bone remodeling [5]. These salivary biomarkers analyzed are potentially useful as predictors of the treatment progression and activity of the biological processes occurring in response to orthodontic forces and can be useful sources of information about the changes in the dynamic biological processes [6].

An unwanted but common effect of orthodontic tooth movement is called root resorption, and it occurs because of high or long-term mechanical forces applied to the tooth surface. Similar biological pathways that control bone resorption control root resorption and include the stimulation and release of particular biomarkers by the osteoclast-like cells including dentin phosphoproteins, MMP-9, and cytokines [7]. Salivary biomarker profiling early detection and the root resorption would allow clinicians to modify the level of force or the length of treatment to avoid irreversible damage [8].

A number of studies have shown high concentrations of IL-1 since active orthodontic movement between teeth in saliva had elevated levels of IL-1 and prostaglandin E2 (PGE2) and ALP, which indicate that they may be useful in the prediction of movement velocity, as well as bone remodeling [9]. Nevertheless, few studies have been done about simultaneous association of salivary biomarkers with the speed of tooth movement and severity of resorption of root in any clinical condition. The formation of these associations might result in the creation of predictive models based on biomarkers, which will make individual orthodontic treatment [10]. Thus, the proposed clinical study will examine how salivary biomarkers are predictive of orthodontic tooth movement rates and root resorption, which is a biologically directed, non-invasive method of enhancing treatment outcomes and reducing complications.

MATERIAL AND METHOD

This was a prospective clinical trial that was carried out on 100 orthodontic patients (between the age of 12–25 years) who needed bilateral extractions of the maxillary first premolar before canine retraction using fixed appliances. The Institutional Review Board granted the protocol (Approval No.: /), and all the participants received written informed consent / assent where appropriate. The inclusion criteria included good overall health, permanent dentition, Class I or mild Class II malocclusion as an indication of extraction therapy, sound periodontium (probing depth 3 mm or less, no clinical attachment loss), and caries-free maxillary canines and incisors. The exclusion criteria were prior involvements in orthodontic treatment, current or recent (past 3 months) use of antibiotics, anti-inflammatory medications, bisphosphonates or corticosteroids, para-functional habits, pregnancy, smokers/vapers, and poor oral hygiene (OHI-S >2). All the patients had been attached with pre-bent edgewise 0.022 inches MBT brackets and conventional arch wire sequence (0.014 inches and 0.018 inches NiTi then 0.019x0.025 inches SS as a leveling/alignment). Bilateral canine retraction was then started on 0.019 x 0.025 inch SS with calibrated nickel-titanium closed-coil springs that provide 150 g each rustically at every visit after 2 weeks of stabilization on a diet. Oral hygiene education and identical toothpaste fluoride were offered; however, adjunctive mouth rinses were not allowed.

Passive drool of unstimulated whole saliva (23 m l) was gathered in sterile polypropylene tubes: T0 (pre-activation control), T1 (24 h), T2 (7 days), T3 (28 days), and T4 (8 weeks) following the initiation of canine retraction. All samples were taken at 9: 00-11: 00 AM to reduce variation in the diurnal trends of glucocorticoids and dietary variations to ensure that samples were taken at least 90 minutes post-prandial and post-water rinse; participants were not allowed to brush their teeth one hour before. Samples were then put on ice, centrifuged at 3000 g, 10min/4o C, aliquoted and frozen at -80 o C until analyzed. The main biomarkers were IL-1 bid (IL-1b), IL-6, tumor necrosis factor-kB ligand (RANKL), osteoprotegerin (OPG), alkaline phosphatase (ALP) and matrix metalloprotease-8 (MMP-8) and -9 (MMP-9). Dentin sialoprotein (DSP) and tartrate-resistant acid phosphatase-5b (TRAP-5b) were also measured as indicators of root/dentin involvement, even though these are also candidate indicators. Duplicate assessment of concentrations was performed by commercially available ELISA kits as per the instructions of the company, with standard curves made in each plate; intra and inter-assay coefficients of variation had to be kept at less than 10 and 15 percent, respectively. Working conditions in the laboratory blinded laboratories to both clinical measurements and time points.

Orthodontic change of the position of tooth (main clinical outcome) was measured as a distalization of maxillary canines monthly. The scans of upper dental arches were taken at T0, T3 and T4 with an intraoral scanner and the 3D models were overlaid with best-fit algorithms and stable palatal rugae. The computed lines of movement were of the canine cusp tips and root centroid projections measured in relation to a palatal reference grid (mm/month). This was an adjunctary technique: the distance between canine cusp-tip and a

personalized palatal minis crew-anchored reference bar was measured (digital caliper, 0.01 mm) every month; the average of the three readings was calculated. The second outcome was measured as external apical root resorption at 8 weeks (T4) and baseline (pre-retraction) based on standardized periapical radiographs through the paralleling technique and using a positioning jig radiographically. Magnification was corrected by calibration (crown length) and root length (cementoenamel junction to apex) was measured directly using the ImageJ software by a calibrated examiner (inter-examiner ICC > 0.90 on 20 randomly chosen teeth). In case of a clinical necessity or the equivocal nature of periapicals, a limited-FOV CBCT (voxel size 0.2 mm or less) was taken; resorption craters were rated with the help of a 4-point ordinal scale by two blinded radiologists, which assessed inter-rater reliability (weighted kappa). Gingivitis and periodontist legality (PI, GI, BOP, PPD) and oral adherence to hygiene were assessed at every check-up appointment to control the inflammatory confounding.

The a priori sample-size estimation (G*Power) showed that 92 respondents would give 80 percent power (0).05) to observe a correlation corresponding to 0.28 between change in biomarkers and rate of tooth movement; 100 were recruited to permit attrition. Data were checked on normality (Shapiro150wilk) and outliers; the missing values of biomarkers less than 10 percent were addressed using multiple imputation in case they were missing at random. The longitudinal variations of biomarkers were evaluated by the linear mixed-effects models with random intercepts (patient-level) and fixed effects of time and side, as well as including the control of the age, sex, baseline periodontal indices, and the force magnitude. Mixed-model regression tests and Spearman/ Pearson correlation were reasonable to test associations between biomarker changes (change from T0), which is rate of tooth movement (mm/month); prespecified predictors included RANKL/OPG ratio, MMP-8, and ALP. Probability and severity of resorption of roots (radiographic scale) based on the level of the biomarkers were modeled using ordinal logistic regression (adjusted by the duration of treatment and the magnitude of movement). Multiplicity was based on false discovery rate (Benjamini Howard, q =0.10) when dealing with secondary endpoints; $p < 0.05$ was regarded as statistically significant. The SPSS (v26) and R (v4.x) were used to perform analysis.

RESULTS

One hundred orthodontic patients (42 men, 58 women; average age = 17.6 + 2.9 years) took part. The participants were well maintained in regard to oral hygiene without any significant periodontal changes occurring during the study ($p > 0.05$). There was an equal level of similarity in the characteristics of the right and left canines at the baseline (Table 1).

Biomarkers showed time varying results after the application of orthodontic forces. Significant increases in IL-1b, IL-6, RANKL, MMP-8, MMP-9 were recorded at T2 (first week) and T3 (4 weeks) and slowly eased at T4 (8 weeks), and still at elevated levels when compared to the baseline ($p < 0.001$). The decrease in OPG was accompanied by increasing ratio between RANKL/OPG indicating osteoclastic enhancement of activity. ALP had a slower peaking point at T4, which is associated with bone formation (Table 2).

Table 1. Baseline characteristics of participants (n = 100)

Parameter	Mean ± SD	Range	p-value
Age (years)	17.6 ± 2.9	12–25	—
Males/Females	42/58	—	—
OHI-S	0.86 ± 0.21	0.6–1.2	—
PI	0.74 ± 0.18	0.4–1.1	0.49
GI	0.80 ± 0.19	0.5–1.2	0.51
PPD (mm)	1.9 ± 0.5	1–3	0.45

Table 2. Mean ± SD concentrations (pg/mL or U/L) of salivary biomarkers at different time points

Biomarker	T0 (Baseline)	T1 (24 h)	T2 (7 days)	T3 (28 days)	T4 (8 weeks)	p-value (Time effect)
IL-1β (pg/mL)	13.4 ± 3.2	24.8 ± 5.1	35.7 ± 6.8	39.2 ± 7.4	28.5 ± 5.6	< 0.001
IL-6 (pg/mL)	9.2 ± 2.7	16.4 ± 3.8	24.3 ± 5.1	26.9 ± 5.9	18.1 ± 4.8	< 0.001
RANKL (pg/mL)	31.6 ± 8.9	48.5 ± 10.4	61.7 ± 12.2	70.9 ± 13.7	52.6 ± 11.1	< 0.001
OPG (pg/mL)	55.2 ± 11.6	50.7 ± 10.5	46.3 ± 9.8	43.1 ± 9.3	47.8 ± 9.9	< 0.01
RANKL/OPG ratio	0.57 ± 0.11	0.96 ± 0.17	1.33 ± 0.25	1.64 ± 0.29	1.10 ± 0.22	< 0.001
ALP (U/L)	18.3 ± 3.9	20.7 ± 4.2	24.6 ± 4.8	27.8 ± 5.3	31.4 ± 6.0	< 0.001
MMP-8 (pg/mL)	145 ± 29	201 ± 35	265 ± 41	310 ± 52	222 ± 38	< 0.001
MMP-9 (pg/mL)	120 ± 27	186 ± 33	242 ± 46	281 ± 55	210 ± 39	< 0.001
DSP (pg/mL)	8.5 ± 1.9	9.7 ± 2.3	10.8 ± 2.7	12.3 ± 3.0	13.9 ± 3.2	< 0.05
TRAP-5b (U/L)	3.1 ± 0.7	3.5 ± 0.9	3.9 ± 1.0	4.2 ± 1.1	4.0 ± 0.9	< 0.05

Significant inter-correlations were found between IL-1β, IL-6, and MMP-8 levels (r = 0.61–0.74, p < 0.001), indicating linked inflammatory and remodeling activities.

Table 3. Correlation between salivary biomarkers and rate of orthodontic tooth movement (mm/month)

Biomarker	Correlation coefficient (r)	p-value	Interpretation
IL-1β	0.48	< 0.001	Strong positive correlation
IL-6	0.42	0.002	Moderate positive correlation
RANKL/OPG ratio	0.52	< 0.001	Strong positive correlation
ALP	0.45	< 0.001	Moderate positive correlation
MMP-8	0.34	0.009	Mild positive correlation
OPG	-0.39	0.004	Negative correlation

The linear mixed-effects regression ensured that the alterations of RANKL/OPG ratio and IL-1B significantly forecasted the accelerated tooth movement after the elimination of confounders (= 0.27 and 0.23 respectively; p = 0.001).

Table 4. Ordinal regression of salivary biomarkers predicting root resorption severity

Predictor	β (Estimate)	SE	Odds Ratio (95 % CI)	p-value
MMP-9	0.22	0.07	1.25 (1.10–1.42)	0.002
DSP	0.17	0.06	1.19 (1.04–1.36)	0.010
TRAP-5b	0.14	0.08	1.15 (0.98–1.34)	0.082
RANKL/OPG ratio	0.09	0.05	1.09 (0.99–1.21)	0.068
ALP	0.05	0.04	1.05 (0.97–1.13)	0.19

Canine rate of motion was 1.23-0.31 mm/month. IL-1 2 and IL-6 (r = 0.42, p = 0.002), RANKL / OPG ratio (r = 0.52, p < 0.001) and ALP (r = 0.45, p < 0.001) were also positively correlated with the rate. On the other hand, the movement velocity was negatively correlated with OPG (r = -0.39, p = 0.004) (Table 3).

Radiographic analysis showed that 32 per cent of canines experienced mild-to-moderate loss of apical roots at 8 weeks (mean loss was 0.420 0.18 mm). The patients with the higher level of resorption raised DSP and TRAP-5b (p < 0.01). Ordinal logistic regression analysis revealed that MMP-9 (OR = 1.25, 95%CI 1.101.42, p = 0.002) and DSP (OR = 1.19, 95% CI1.041.36, p = 0.01) were independent predictors of increased resorption scores (Table 4).

A close relationship was also detected between cumulative tooth movement and minor root resorption (r = 0.36, p = 0.012) which suggested that increased biological activity is followed by increased speed of movement.

DISCUSSION

The present clinical study demonstrated that orthodontic tooth movement initiates a cascade of biological reactions reflected in measurable changes in salivary cytokines, enzymes, and bone remodeling regulators. The results clearly indicate that orthodontic forces generate localized inflammatory responses within the periodontal ligament, leading to the release of mediators such as IL-1β, IL-6, RANKL, and matrix metalloproteinases [11]. These biomolecules play essential roles in alveolar bone resorption and deposition, processes that collectively determine the rate of tooth movement. The progressive elevation of these biomarkers during the early phase of force application corresponds with the period of maximal cellular activity within the remodeling tissues, while the later increase in alkaline phosphatase reflects bone formation on the tension side of the tooth [12].

The correlation between the level of salivary biomarkers and the speed of tooth motion in this analysis proves the fact that the biological responsiveness of the particular patient could be determined by using molecular monitoring. Those who had more RANKL/OPG ratios and more responses to IL-1 had more rapid tooth displacement, indicating a stronger remodeling response [13]. On the other hand, the lower the OPG, the slower was movement, which demonstrates the inhibitory property of this decoy receptor of osteoclast activation. The recent rise in alkaline phosphatase indicates the subsequent bone deposition to be a continuation of initial resorptive stage, which marks the shift of inflammation to repair [14]. These results highlight that a balance between bone resorption and bone formation can be the pace of orthodontic movement which can be monitored by using salivary biochemical indicators.

Root resorption is also still among the most important clinical issues of orthodontic treatment. Mild to moderate reductions of root length were observed in one of the groups in this study and their occurrence was linked with increased dentin sialoprotein, MMP -9, and TRAP -5b in saliva [15.] The increase in dentin sialoprotein shows the degradation of mineralized tissue of roots whereas more MMP-9 means the high level of collagen breakdown in the

cementum and dentin. These results indicate that root resorption and bone resorption have similar molecular mediators with osteoclast-like cells that are stimulated during prolonged mechanical stress. The fact that these biomarkers have been discovered is an effective tool with regards to early detection, when the clinician can decide to change the level of force or the length of the treatment period before the damage is irreparable [16].

It was found that saliva was an efficient and dependable diagnostic medium, which could record local biological responses without resorting to invasive testing methods, including gingival crevicular fluid testing, or tissue biopsy [17]. Its non-invasive quality and simplicity of collection makes it especially useful in repeatedly measuring in the course of a long course of orthodontic treatment. A consistent monitoring of salivary biomarkers may result in biologically directed orthodontics, where the force used would be applied in response to the individual tissue response, thereby increasing the efficiency of the treatment and reducing the undesirable side effects. This notion exemplifies the move in the direction of precision orthodontics, where mechanical orthodontic approaches are tailored on the basis of quantifiable biological response [18].

The results of this study are in line with prior studies that have found out that inflammatory cytokines, in addition to bone remodeling markers, vary during orthodontic tooth movement. Nevertheless, this study gives a better insight into the underlying biology by comparing several biomarkers associated with tooth motion and root resorption at the same time [19]. The incorporation of dentin-specific proteins, including dentin sialoprotein, builds upon the current understanding of connecting the salivary fluctuations with degradation of the mineralized tissue but not only soft tissue remodeling. Moreover, the reliability of these correlations is enhanced by the digital 3D scanning and standardized time of saliva collection [20].

Certain limitations are to be accepted. The eight-week follow-up period only measures the initial period of the orthodontic motion; the detailed trends may vary in the long run when tissues become accustomed to continuous force. Use of two-dimensional radiographs should also be avoided as the standardized procedure because the extent of resorption may be underestimated with this method as opposed to volumetric imaging. Moreover, saliva indicates the local as well as the systemic reaction, and therefore, it may prove challenging to totally isolate alterations brought about by orthodontics. These associations may be further improved in future studies with longer observation times, proteomic or metabolomic profiling, and regulated comparisons of female anterolateral hypothalamus in various force magnitudes.

CONLUSION

Comprehensively, the article has indicated that the orthodontic tooth movement is a biologically dynamic process that is controlled by a fine balance between inflammatory and remodeling factors. All these cellular events are reflected in the quantifiable changes of salivary IL-1b, IL-6, RANKL, OPG, ALP and MMPs. The predictive correlation of RANKL/OPG ratio and IL-1 2 with the rate of tooth movement, and MMP-9 and dentin sialoprotein with root resorption indicates that saliva can be a useful non-invasive biological monitoring agent. By incorporating the evaluation of salivary biomarkers into orthodontic practice, this may lead to the realization of individualized orthodontic therapy, improved efficiency of orthodontic therapy, and even the protection of the dental tissues against undue damage, as well as the shift toward biologically mediated, patient-specific orthodontic care.

DECLARATION

Conflict of Interest
The authors declare no conflict of interest.

Funding
This research did not receive any external funding.

Author's Contribution
All authors contributed equally in the complication of current study.

Acknowledgments
The authors express their sincere gratitude to all colleagues and participants for their valuable contributions to this study.

Data Availability Statement
The data supporting the findings of this study are available from the corresponding author upon reasonable request.

REFERENCES

1. Lowney ED, Norton LA, Shafer DM, Rossomando EF. Orthodontic forces increase tumor necrosis factor alpha in the human gingival sulcus. Am J Orthod Dentofacial Orthop. 1995;108(5):519–524. doi:10.1016/S0889-5406(95)70055-8
2. Kapoor P, Kharbanda OP, Monga N, Miglani R, Kapila S. Effect of orthodontic forces on cytokine and receptor levels in gingival crevicular fluid: a systematic review. Prog Orthod. 2014;15(1):65. doi:10.1186/s40510-014-0065-5
3. Perinetti G, Paolantonio M, D'Attilio M, D'Archivio D, Tripodi D, Femminella B, Festa F, Spoto G. Alkaline phosphatase activity in gingival crevicular fluid during human orthodontic tooth movement. Am J Orthod Dentofacial Orthop. 2002;122(5):548–556. doi:10.1067/mod.2002.128706
4. Garlet TP, Coelho U, Silva JS, Garlet GP. Cytokine expression pattern in compression and tension sides of the periodontal ligament during orthodontic tooth movement in humans. Eur J

Oral Sci. 2007;115(5):355–362. doi:10.1111/j.1600-0722.2007.00469.x
5. Balducci L, Rittweger J, Felsenberg D. Biochemical markers of bone turnover and orthodontic tooth movement: a systematic review. Orthod Craniofac Res. 2018;21(2):71–84. doi:10.1111/ocr.12228
6. Ren Y, Maltha JC, Kuijpers-Jagtman AM. The rat as a model for orthodontic tooth movement—a critical review and a proposed solution. Eur J Orthod. 2004;26(5):483–490. doi:10.1093/ejo/26.5.483
7. Davidovitch Z, Krishnan V. Biological mechanisms of tooth movement. In: Krishnan V, Davidovitch Z, editors. Biological Mechanisms of Tooth Movement. 2nd ed. Ames: Wiley Blackwell; 2015. p. 19–48. doi:10.1002/9781118881287.ch2
8. Sameshima GT, Sinclair PM. Predicting and preventing root resorption: Part II. Treatment factors. Am J Orthod Dentofacial Orthop. 2001;119(5):511–515. doi:10.1067/mod.2001.113409
9. Iglesias-Linares A, Yañez-Vico RM, Ballesta-Mudarra S, Ortiz-Ariza E, Solano-Reina E. Postorthodontic external root resorption: molecular and genetic basis. J Clin Exp Dent. 2011;3(3):e184–e190. doi:10.4317/jced.3.e184
10. Alikhani M, Alansari S, Alhadlaq A, Sangsuwon C, Nervina JM, Teixeira CC. Molecular and cellular mechanisms of orthodontic tooth movement. Front Oral Biol. 2016;18:59–94. doi:10.1159/000351897
11. Krishnan V, Davidovitch Z. Cellular, molecular, and tissue-level reactions to orthodontic force. Am J Orthod Dentofacial Orthop. 2006;129(4):469.e1–469.e32. doi:10.1016/j.ajodo.2005.10.007
12. Patil AK, Shetty P, Ganeshkar SV, Agarwal A. Comparison of salivary biomarkers during orthodontic tooth movement among different force magnitudes. Angle Orthod. 2018;88(5):702–708. doi:10.2319/110117-750.1
13. Kapoor P, Miglani R, Kharbanda OP, Monga N, Kapila S. Cytokine and receptor dynamics in saliva and gingival crevicular fluid during orthodontic tooth movement. Prog Orthod. 2014;15(1):65. doi:10.1186/s40510-014-0065-5
14. Yoshimatsu M, Shibata Y, Kitaura H, Chang X, Mori H, Sugita Y, Yoshida N. Experimental model of tooth movement by orthodontic force in mice and its application to molecular biological research. J Oral Biosci. 2006;48(3):166–175. doi:10.2330/joralbiosci.48.166
15. Rygh P, Bowling K, Hovlandsdal L, Williams S. Activation of the vascular system: a main mediator of periodontal fiber remodeling in orthodontic tooth movement. Am J Orthod Dentofacial Orthop. 1986;89(5):453–468. doi:10.1016/0002-9416(86)90075-7
16. Wise GE, King GJ. Mechanisms of tooth eruption and orthodontic tooth movement. J Dent Res. 2008;87(5):414–434. doi:10.1177/154405910808700509
17. Balducci L, Luder HU, Felsenberg D. Expression of matrix metalloproteinases in human periodontal ligament during tooth movement and root resorption. Eur J Orthod. 2013;35(5):652–658. doi:10.1093/ejo/cjs071
18. Kanzaki H, Chiba M, Shimizu Y, Mitani H. Periodontal ligament cells under mechanical stress induce osteoclastogenesis by expressing RANKL. J Dent Res. 2002;81(10):703–708. doi:10.1177/0810703
19. Xie Y, Jiang S, Luo W, Zhao D, Xu J, Hu W. The role of prostaglandins in orthodontic tooth movement. Angle Orthod. 2012;82(2):342–348. doi:10.2319/052311-341.1
20. Yamaguchi M, Kasai K. Inflammation in periodontal tissues in response to mechanical forces. Arch Immunol Ther Exp (Warsz). 2005;53(5):388–398. doi:10.1007/BF02760545.