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## External Apical Root Resorption in Patients Treated with Passive Self-Ligating System

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### 1. Introduction

External apical root resorption (EARR) is an unavoidable pathologic consequence of orthodontic tooth movement. It can be defined as an iatrogenic disorder that unpredictably occurs after orthodontic treatment, whereby the resorbed apical root portion is replaced with normal bone. EARR is a sterile inflammatory process that is extremely complex and involves various disparate components, including mechanical forces, tooth roots, bone, cells, surrounding matrix, and certain known biologic messengers (Krishnan & Davidovitch, 2006; Meikle, 2006). In the relationship between EARR and inflammatory cytokines, Zhang et al. (2003) indicated that interleukin (IL)-1 and tumour necrosis factor (TNF)-alpha are important for the induction and the further processing of mechanically-induced root resorption in the rat. Receptor activator of nuclear factor  $\kappa$ B ligand (RANKL) is a cytokine that belongs to the TNF family and is essential for the induction of osteoclastogenesis. Osteoblasts and bone marrow stromal cells produce this cytokine, and its signals are transduced by the specific receptor RANK, which is localized on the cell surface of osteoclast progenitors. The RANKL/RANK system has been suggested to play an integral role in osteoclast activation during orthodontic tooth movement. Shiotani et al. (2001) observed RANKL in osteoblasts, osteocytes, fibroblasts, and osteoclasts during the application of orthodontic forces. The RANKL/RANK system may regulate the natural process of root resorption in deciduous primary teeth (Lossdörfer et al., 2002). Therefore, these inflammatory cytokines contribute to alveolar bone remodeling and to resorption during orthodontic tooth movement and EARR.

The wire friction influences the forces acting in a continuous arch system. Damon (2006a) suggested that the nearly friction-free system, using the self-ligation brackets and high-tech wires, may not cause periodontal problems, including alveolar bone loss. Other studies reported that static friction measured in vitro is much less with a passive self-ligating system than with any other type of fixed appliance (Berger, 1990; Sims et al., 1993). The friction force disturb orthodontic tooth movement, thus, it is expected that influence for the periodontal tissue is different from the self-ligating brackets in the conventional appliances. We reported that GCF levels of substance P (SP), one of neuropeptides which cause the local inflammation, SP for the passive self-ligating system sites were significantly lower than for the teeth with conventional brackets at 24 hours (Yamaguchi et al., 2009). Thus, the passive

self-ligating system is useful to reduce the inflammation and pain resulting from orthodontic forces.

The purposes of this study were to measure EARR and the levels of RANKL in GCF in patients undergoing with self-ligating brackets compared with conventional appliances, and to compare them.

## 2. Materials and methods

### 2.1 Subject selection

Forty subjects were selected from patients seeking treatment in the Department of Orthodontics at the Nihon University School of Dentistry at Matsudo. Forty orthodontic patients (9 males, 31 females, mean age of  $18.5 \pm 4.6$  years) were enrolled in the study, after meeting the following criteria: (1) good general health; (2) lack of antibiotic therapy during the previous 6 months; (3) absence of anti-inflammatory drug administration in the month preceding the study; (4) healthy periodontal tissues with generalized probing depths  $\leq 3$  mm and no radiographic evidence of periodontal bone loss. Informed consent from the subjects was obtained after an explanation of the study protocol, which was reviewed by the ethic committee of Nihon University School of Dentistry at Matsudo (#10-019).

Two groups were set up, one 'conventional bracket' (CB) and another 'self-ligation bracket' (SL) groups. Twenty patients (4 males, 16 females) were treated with self-ligating brackets (Damon 3; Ormco, Japan, Tokyo, Japan). A matched control group of 20 patients (5 males, 15 females) was selected from the same registry and treated with the conventional brackets (.022-inch slot; Ormco. These controls were matched with the group for age, sex, and ANB, overjet, and overbite values before orthodontic treatment (T1).

The selection criteria for the subjects were the following.

1. Class I crowded malocclusion.
2. Four premolar extractions.
3. Excellent quality records.
4. Only patients with no history or evidence of tooth injury or wear, as shown on the charts and diagnostic records, were included.

### 2.2 Measurement of EARR and tooth position

To record the above parameters, the following measurements and evaluations were executed.

**Tooth length:** Tooth length of the maxillary central incisor at T1 and T2 was measured on the cephalograms from the incisal edge to the apex. When a difference in the length of the 2 adjacent maxillary central incisors was evident, the shorter root length was recorded. Baseline measurements of ANB angle, overjet (along the occlusal line), and overbite (perpendicular to the occlusal line) at T1 were made on the cephalograms.

Measurement of root length (EARR) and tooth position were performed according to the method of Brin and Bollen (2011).

Change in root length (EARR) of the maxillary central incisor was record as the difference between tooth lengths from T1 to T2.

Maxillary incisor movements were measured as the following. (1) The axial inclination of the maxillary central incisor to SN (I/SN) between T1 and T2. (2) The vertical and horizontal distances that the maxillary central incisor root was moved during orthodontic treatment (Table 1).

Parameter	CB group	SL group	<i>P</i> value
Male/female ratio	5/15	4/16	0.505
Mean age at T1 (y)	18.8 ± 4.5	18.3 ± 4.8	0.643
ANB (°)	3.3 ± 1.2	3.2 ± 1.3	0.544
Overjet (mm)	3.5 ± 1.4	3.4 ± 1.5	0.478
Overbite (mm)	3.3 ± 1.4	3.5 ± 1.3	0.377
Tooth length (mm)	26.8 ± 1.6	27.0 ± 1.7	0.682

Table 1. Descriptive parameters of the 2 groups at T1 (± SD)

### 2.3 GCF collection

GCF was collected from the mesial and distal sides of the upper central and lateral incisors. GCF sampling was performed using the method of Yamaguchi et al. (2006a), and collected at before (T1) and after (T2) orthodontic treatment. The tooth was gently washed with water, and then the sites under study were isolated with cotton rolls (to minimize saliva contamination) and gently dried with an air syringe. Paper strips (Periopaper, Harco, Tustin, CA, USA) were carefully inserted 1 mm into the gingival crevice and allowed to remain there for 1 minute, after which a second strip was placed at the same site. Care was taken to avoid mechanical injury. The contents were eluted out into 1x phosphate buffer saline (PBS) containing 0.1mM phenylmethylsulphonyl fluoride and stored at -80°C until further processing (Fig. 1).



Fig. 1. GCF was collected from the mesial and distal sides of the upper central and lateral incisors.

## 2.4 Enzyme immunoassay

The levels of RANKL and OPG were measured in duplicate using a commercial ELISA kit (Quantikine, R&D Systems, Inc., Minneapolis, MN, USA), with the results expressed as pg/ $\mu$ g of total protein in the GCF.

## 2.5 Statistical methods

Statistical analysis among the groups was performed using one-way ANOVA and Scheffe test to evaluate the statistical difference between each pair of groups.

## 3. Results

### 3.1 Measurement of EARR and tooth position

The 2 groups were matched for sex ( $P = 0.505$ ) and chronologic age at T1 ( $P = 0.643$ ). Good agreement was also found for the ANB angle ( $P = 0.544$ ), overjet ( $P = 0.478$ ) and overbite ( $P = 0.377$ ) at T1. The tooth lengths at T1 in both groups were similar:  $26.8 \pm 1.6$  in the CB group and  $27.0 \pm 1.7$  in the SL group ( $P = 0.6312$ ) (Table 1).

Table 2 showed that the duration of treatment was not significant between the CB group and the SL group ( $P = 0.891$ ). In both groups, the lengths were reduced at T2 (Table 2):  $24.6 \text{ mm} \pm 2.0$  in the CB group and  $26.2 \text{ mm} \pm 1.5$  in the SL group. Tooth lengths in the 2 groups were statistically different at T2 ( $P = 0.05$ ).

	CB	SL	<i>P</i> value
Duration of treatment (mo)	$24.4 \pm 2.1$	$24.8 \pm 1.3$	0.891
EARR (mm)	$2.2 \pm 1.4$	$0.80 \pm 0.7$	0.005 *
Change in $\angle$ SN ( $^{\circ}$ )	$-6.5 \pm 6.7$	$-6.1 \pm 7.2$	0.901
Apex ( $\dot{a}$ ) vertical movement (mm)	$-0.6 \pm 1.0$	$-0.5 \pm 1.3$	0.883
Apex ( $\dot{a}$ ) horizontal movement (mm)	$2.2 \pm 1.6$	$2.5 \pm 1.8$	0.750

Table 2. Comparison of changes ( $\pm$  SD) during mechanotherapy (T1-T2) in EARR and tooth position in the Conventional bracket and Self-ligation bracket groups (absolute values in parentheses)

The mean amount of root resorption of the maxillary central incisor measured on the lateral cephalogram was significantly greater in the CB group than the SL group at T2. This mean difference in EARR between the groups did reach statistical significance.

In Table 2, the axial movements of the central incisor—vertical and horizontal apical movements—are presented.

The 1/SN change between T1 and T2 indicated an increase in the axial inclination in the CB and SL groups (about 6°). Change in the axial inclination of the maxillary central incisor (1/SN) was not significant difference between the CB group and the SL group ( $P = 0.901$ ). The amounts of vertical movement of the apex were also not significant difference in both groups ( $P = 0.883$ ). For the horizontal movements of the apex, similar ( $P = 0.750$ ) amounts of distal palatal root movement were observed in both groups (Table 2).

### 3.2 GCF study

GCF volume has been correlated with inflammatory state, however, there was no statistically significant difference in the mean as for the volume of GCF between CB group and SL group at T1 (CB:  $0.41 \pm 0.06 \mu\text{l}$ , SL:  $0.39 \pm 0.09 \mu\text{l}$ ) and T2 (CB:  $0.40 \pm 0.07 \mu\text{l}$ , SL:  $0.42 \pm 0.05 \mu\text{l}$ ), respectively. In all of the patients, probing depths remained less than 2 mm and gingival health was excellent, with no gingival bleeding.

At T1, there were no significant differences in the mean RANKL value between the CB and the SL. However, the mean RANKL value in the CB was significantly higher in the SL at T2 ( $p < 0.05$ ). While, the mean OPG values for the CB and SL were not significantly difference between T1 and T2. (Fig. 2)

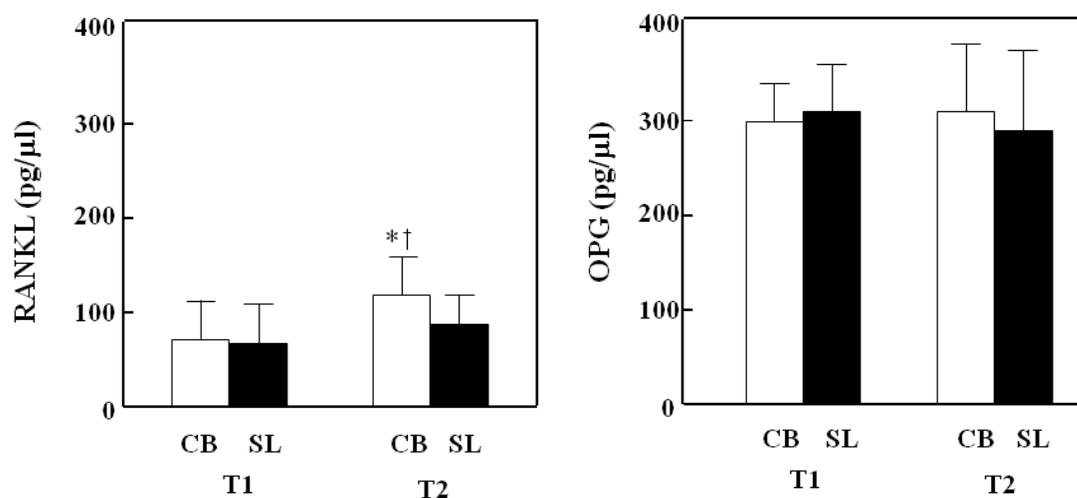


Fig. 2. Changes in RANKL and OPG concentrations in the GCF samples from the conventional brackets (CB) and self-ligating bracket (SL). Significant differences in concentrations between T1 and T2 are indicated with an \* ( $p < 0.05$ ), and between CB and SL with an † ( $p < 0.05$ ), correspondingly.

## 4. Discussion

In this study, the mean amount of root resorption of the maxillary central incisor measured on the lateral cephalogram was significantly greater in the CB group than the SL group at T2 (Table 2).

Considering to risk factor of EARR, according to Weltman et al. (2010) it are divided into the treatment-related and patient-related factors. Orthodontic treatment-related risk factors

include treatment duration (Segal et al., 2004; Sameshima & Sinclair, 2004; Fox, 2005), magnitude of applied force (Harris et al., 2006; Chan & Darendeliler, 2006; Barbagallo et al., 2008), direction of tooth movement (Costopoulos & Nanda, 1996; Parker & Harris, 1998; Han et al., 2005), amount of apical displacement (Segal et al., 2004; Fox, 2005), and method of force application [continuous vs intermittent (Weiland, 2003; Brezniak & Wasserstein, 2002), type of appliance (Brezniak & Wasserstein, 1993; Pandis et al., 2008), and treatment technique (McNab et al., 2000; Scott et al., 2008).

Previous studies found that heavy forces produced significantly more EARR than light forces or controls (Harris et al., 2006; Chan & Darendeliler, 2006; Barbagallo et al., 2008). Chan and Darendeliler (2006) found that the mean volume of the resorption craters was 11.59 times greater in the heavy-force group than in the control group (significant). Heavy forces in both compression and tension areas produced significantly more RR than in regions under light compression and light tension forces. Barbagallo et al. (2008) also found that heavy force produced significantly more RR (9 times greater than the control) than light force (5 times greater than the control). Therefore, light force may have the advantage of prevention of occurrence of EARR.

According to Chen et al. (2010), the claim of reduced friction with self-ligating brackets is often cited as a primary advantage over conventional brackets (Damon, 1998b; Griffiths et al., 2005; Kim et al., 2008). This occurs because the usual steel or elastomeric ligatures are not necessary, and it is claimed that passive designs generate even less friction than active ones (Budd et al., 2008). Beger (1990) demonstrated that a significant decrease in the force level required for the self-ligating bracket when compared with elastomeric and steel-tie ligation in both metal and plastic bracket systems, and concluded that self-ligating bracket is less force needed to produce tooth movement by reduced friction (Beger, 1990).

During the process of root resorption, organic matrix proteins and cytokines are released into the gingival crevice. In this GCF study, the mean RANKL value in the CB was significantly higher in the SL at T2 ( $p < 0.05$ ) (Fig. 2). A recent study demonstrated that mRNA of RANK was detected in tissues involved in root resorption following subjection to orthodontic forces (Low et al., 2005). Furthermore, our laboratory reported that RANKL expression was increased by compression force *in vitro* and *in vivo*. Yamaguchi et al. (2006b) demonstrated that compressed PDL cells obtained from tissues with severe external apical root resorption may produce a large amount of RANKL and upregulate osteoclastogenesis *in vitro*. Nakano et al. (2011) observed RANKL immunoreactivity in rat odontoclasts with an orthodontic force of 50 g (heavy force) on day 7 *in vivo*. Nishijima et al. (2006) found an increased concentration of RANKL in GCF during orthodontic tooth movement, and the ratio of concentration of RANKL to that of OPG in the GCF was significantly higher than at the control sites. These studies suggest that during orthodontic tooth movement, OPG/RANKL/RANK system in the periodontal tissues is an important determinant regulating balanced alveolar bone resorption. Taken together, those findings and the present results, suggest that OPG/ RANKL/RANK system may play an important role in orthodontically root resorption. Furthermore, George and Evans (2009) demonstrated that the concentration of RANKL in GCF in severe and mild resorption were significant higher than that of no loss of root structure. Therefore, these findings and our present results, taken together, the self-ligating brackets may be a useful system for reduction of remarkable inflammation and EARR.

Despite claims regarding the clinical superiority of self-ligating brackets, evidence is generally lacking. Pandis et al (2008) and Scott et al. (2008) reported that there was no significant difference in EARR between CB and SL groups. Further studies should be carried out to investigate the advantage and disadvantage of self-ligating brackets in orthodontic treatment.

## 5. Conclusion

These results show that the mean amount of EARR and the GCF levels of RANKL were significantly lower in the Damon 3 appliance than conventional brackets. Therefore, self-ligating brackets may be a useful system for reduction of remarkable inflammation and EARR.

## 6. Acknowledgements

This research was supported, in part, by a Grant-in-Aid for Scientific Research from the Japan Society for the Promotion of Science (C:22592297).

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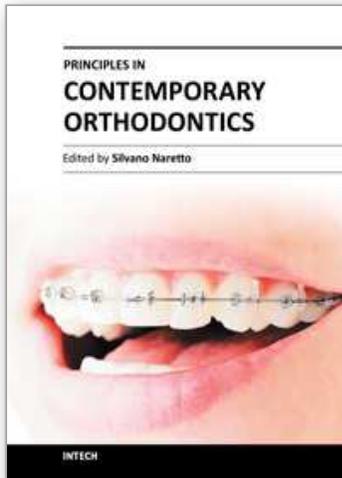
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Edited by Dr. Silvano Naretto

ISBN 978-953-307-687-4

Hard cover, 584 pages

**Publisher** InTech

**Published online** 25, November, 2011

**Published in print edition** November, 2011

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