Bone remodeling surrounding primary teeth in skeletally immature dogs

Letitia E. Randall a; F. Michael Beck b; Sarandeep S. Huja c

ABSTRACT
Objective: To quantify remodeling in the bone surrounding fully erupted primary teeth and to compare bone remodeling in the primary and permanent dentitions.

Materials and Methods: Two bone sections were obtained bilaterally from the maxilla and mandible of the primary molar region of approximately 5-month-old male beagle dogs. Histomorphometric methods were used to estimate the osteonal remodeling in the alveolar and basal regions of the tooth supporting bone. The following variables were calculated: mineral apposition rate (MAR, μm/d), mineralizing surface/bone surface (MS/BS, %), bone formation rate (BFR, %/y), and erosion surface/bone surface (ES/BS, %). Comparisons were made between jaws (maxilla vs mandible) and bone types (alveolar vs basal), and data analyzed by analysis of variance (ANOVA) and Tukey-Kramer tests. Remodeling (BFR) surrounding primary teeth was compared to existing data from bone surrounding permanent teeth.

Results: The mean and standard deviation BFR values (%/y) were as follows: mandibular alveolar, 44.10 (±26.89); maxillary alveolar, 3.54 (±3.57); mandibular basal, 22.65 (±14.65); and maxillary basal, 12.33 (±7.11). The mandibular BFR was significantly (P < .05) higher than the maxillary bone. The BFR of the alveolar bone of primary teeth was not significantly (P = .48) different from the alveolar bone supporting permanent teeth.

Conclusions: The remodeling rate of alveolar bone in skeletally immature dogs was greater in the mandible than in the maxilla and remained unaltered between primary and permanent dentitions. (Angle Orthod. 2011;81:931–937.)

KEY WORDS: Remodeling; Primary teeth; Bone; Alveolar process

INTRODUCTION
Bone remodeling is central to understanding growth and development and is the foundation of newer clinical procedures to accelerate orthodontic tooth movement. Alveolar bone is a dynamic osseous tissue that undergoes both modeling and remodeling. Bone modeling is an uncoupled process that results in a net change in the size or shape of osseous tissue.1 In contrast, bone remodeling is a coupled process of bone turnover of existing osseous tissue.2 Bone growth involves both modeling and remodeling events, and these distinct processes are central to understanding bone physiology and adaptation.3 In addition, newer clinical procedures to accelerate orthodontic tooth movement such as periodontally accelerated osteogenetic orthodontics and vibration have their biologic basis in altering the remodeling rate.4,5 The remodeling within the cortical compartment (intracortical) is described as secondary osteonal remodeling because the end result of remodeling process is the formation of new osteons with haversian systems in previously existing bone. These osteons are in contrast to the hemi-osteons that are typical of trabecular bone remodeling.6 Primary osteons result from bone formation de novo,7 whereas the secondary osteons are associated with replacement bone. Only recently have there been quantitative studies8,9 rather and descriptions10 of intracortical bone remodeling activity associated with permanent teeth in an animal model at various ages. It is known that the bone formation rate (BFR), which is a measure of the bone turnover or remodeling in bone supporting permanent teeth, is elevated to threefold to sixfold greater than the

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baseline remodeling rate in other parts of the appendicular skeleton, such as the long bones. For example, in the skeletally mature (1- to 2-year-old) dogs, the BFR is substantially higher than the BFR found at other sites such as the femur (6.4%/y). The same pattern is seen in aged (approximately 10-year-old) dogs, albeit the rate of turnover is drastically reduced to < 1% per year in the long bones.

The mechanism of this elevated remodeling rate in the alveolar process is unknown and is challenging to study. It has been suggested that the elevated remodeling is an adaptation mechanism for the functional forces that are transmitted from the teeth to the alveolar process. Microdamage is a known stimulus of remodeling, and it has been proposed that the elevated alveolar remodeling serves to repair microdamage in the alveolar process. However, there is no published data supporting the existence of larger amounts of microdamage in the alveolar process. One important piece of information that is lacking is the alveolar bone remodeling rates surrounding primary teeth. Should the remodeling rate in the bone surrounding primary teeth have a similar pattern to that described in the permanent dentition, it would provide mounting evidence that the presence of a tooth provides a unique environment which results in a localized region of steady state, elevated remodeling irrespective of the age and dentition of the animal.

The primary objective of this research is to characterize the secondary osteonal cortical bone remodeling in the jaws of skeletally immature (5-month-old) dogs in both the alveolar and basal bone supporting the primary dentition. The secondary objective of this paper is to compare the remodeling rate in bone surrounding primary teeth with those supporting fully erupted permanent teeth. We hypothesize that the bone surrounding primary teeth will demonstrate a similar pattern of alveolar bone remodeling that is observed in the permanent dentition.

MATERIALS AND METHODS

Four approximately 5-month-old, purpose bred, skeletally immature, male beagle dogs were purchased from Marshall Research Animals (North Rose, New York). Institutional Laboratory Animal Care and Use Committee approval was obtained, and the dogs were maintained in The Ohio State University Animal Facility. The dogs were fed standard dry chow and water ad libitum and were monitored for normal behavior and weight maintenance. Vital calcein bone labels (Sigma, St Louis, Mo), 5 mg/kg, were given intravenously 16 and 2 days prior to sacrifice. The calcein bone labels identify anabolic bone formation events of mineral apposition. The dogs were killed with intravenous injection of pentobarbital, as recommended by the American Veterinary Medical Association Panel on Euthanasia.

Bone blocks were obtained from the primary second and third molar region of the maxilla and mandible of each beagle dog. Standard histologic techniques were used to embed the bone blocks in resin (Polysciences Inc, Warrington, Pa). The blocks were sectioned buccolingually, through the center of the longitudinal axis of a tooth root using a band saw (Exakt 310, Exakt Technologies, Oklahoma City, Okla) with water lubrication. The blocks were cut/ground to approximately 80–100 µm in thickness. Two bone sections per tooth were obtained bilaterally from the maxilla and mandible (2 specimens/tooth × 2 bilateral teeth/jaw × 2 jaws/dog = 8 specimens per dog). An exception to the above was the one dog that had three specimens from the maxilla and five from the mandible; therefore, there were 15 specimens from the maxilla and 17 specimens from the mandible.

Histomorphometric Methods

Histomorphometry is a commonly used method for histologic quantification of the volumes and tissue dimensions involved in bone formation. The primary tooth and supporting bone sections were examined under an epifluorescent microscope at 100× for all parameters except interlabel width, which was examined at 200× (Olympus, BX 51, Tokyo, Japan) with the aid of a Merz grid. The Merz grid consists of six sinusoidal lines with 36 test points contained within a square. Each test point is a hit and represents area/volume. Each intercept represents perimeter or length and is the intersection of the sinusoidal line with a bone feature such as a double label. The sections were divided into alveolar and basal regions (Figure 1). In addition, we distinguished areas of remodeling and modeling in the bone (Figures 2 and 3). In the modeling areas, we only quantified the bone (hits) volume. In the remodeling areas we quantified both hits and intercepts.

Primary data on the following variables were collected: bone hits (BH), void hits (VH), bone and void intercepts (BI, VI), erosion surface intercept (ESI), double label intercept (DLI), single label intercept (SLI), and interlabel width (ILW, µm). Secondary data were calculated only from the remodeling primary data and included: mineral apposition rate (MAR, µm/d, ILW/14 days), mineralizing surface/bone surface (MS/BS, %), ([DLI + ½ SLI])×100/[DLI + SLI + VI]), erosion surface/bone surface (ES/BS, %, erosion surface intercept×100/[DLI + SLI + VI]), and bone formation...
rate (BFR, %/y, ([MAR * (DLI + 1/2 SLI)]/BV)*100)), where BV is bone volume. We only analyzed areas of intracortical bone, and secondary osteons were verified by brightfield and polarized light for the existence of a reversal line, appropriate size (200–300 microns), and collagen banding pattern. Modeling areas were excluded (Figures 2 and 3) with the objective of not including any primary osteons. We examined erosion cavities quantitatively which represent the resorption phase of the remodeling cycle. The analysis was performed by one examiner who was calibrated by an experienced histomorphometrist. The calibration resulted in an interclass correlation coefficient for intrarater reliability > 0.85, which is considered excellent in histomorphometry methods. All slides were blinded to the examiner. All histomorphometry nomenclature conformed to the recommendations of the American Society for Bone and Mineral Research.

The data from the immature dogs were compared with an existing data set of six skeletally mature (1- to 2-year-old) dogs which displayed a permanent dentition. The rationale for directly comparing within this paper the current data from bone surrounding primary teeth to those of permanent teeth was to assess the importance of the presence of a tooth on patterns of bone remodeling in the alveolar bone. The data on bone remodeling surrounding permanent teeth, though

Figure 1. Composite epifluorescent photomicrographs (each taken at magnification 12.5×) from skeletally immature (approximately 5-month-old) dog illustrating bone formation in the (A) mandible and (B) maxilla, surrounding a portion of the primary tooth (P) and developing permanent tooth (*). In Figure 1A, remodeling (R) is apparent in the alveolar and basal bone, and modeling (M) is seen near the apex of the primary tooth in (A) and buccal (B)/lingual (L) surfaces. The primary tooth root apex indicated the approximate anatomically separation of alveolar (A) and basal (Ba) bone. In Figure 1B, A indicates the alveolar region, and B indicates basal regions.
published, were collected in the same laboratory using identical histomorphometric methods.9

Statistical Analyses

Descriptive statistical analyses (means and standard deviations) were calculated for the secondary indices. The data were analyzed by repeated measures factorial analysis of variance (ANOVA) to examine the variation between locations (maxilla vs mandible) and between bone types (alveolar vs basal) as well as the interaction of locations/bone type. Post hoc testing for multiple comparisons was accomplished with the Tukey-Kramer method. The current data set was also compared with an existing data set9 of six skeletally mature (1- to 2-year-old) dogs using the same methods. P < .05 was considered statistically significant for all comparisons.

RESULTS

Descriptive statistics for histomorphometric variables for the skeletally immature dogs are presented in Table 1.

Mineral apposition rate. MAR was statistically greater (P = .01) in the mandible than in the maxilla, but not different between alveolar and basal bones (P = .13) (Table 1). With the alveolar and basal bone regions combined, MAR for the maxilla and mandible were 1.5 μm/d (SE = 0.1) and 2.1 μm/d (SE = 0.1), respectively. The jaw/bone type interaction for MAR was also not significant (P = .14).

Mineralizing surface/bone surface. MS/BS was significantly greater in the mandible (P = .01) than in the maxilla, while the difference between the alveolar/ basal (P = 0.24) and the jaw/bone type interaction (P = .10) was not significant. With the alveolar and basal bone regions combined, MS/BS for the maxilla and mandible were 3.8% (SE = 0.9%) and 12.1% (SE = 0.9%), respectively.

Erosion surface/bone surface. ES/BS represents the percentage of bone that is resorbing (Figure 4) to the total bone surface that is available. Like MAR and MS/BS, only the difference between jaws was statistically significant (P = .01), with ES/BS being greater in the mandible, while the difference between bone types (P = .99) and jaw/bone type interaction (P = .78) was not. With the alveolar and basal bone regions combined, ES/BS was 5.0% (SE = 1.9%) for the maxilla and 23.2% for the mandible (SE = 1.8%).

Bone formation rate. BFR represents the product of the rate of mineralization and the surface that is available for mineralizing. The differences of BFR between jaws (P = .005) and the jaw/bone type interaction were both statistically (P = .02) significant, being greater in the mandible than in the maxilla, while the difference between alveolar/basal was not (P = .16) significant. With the alveolar and basal bone regions combined, BFR was 7.9% per year (SE = 4.6%/y) for the maxilla, and 33.4% per year (SE = 4.5%/y) for the mandible.

Comparison of bone remodeling in the alveolar bone surrounding primary and permanent teeth. MAR was not significantly different (P = .34) for the alveolar bone supporting the primary and permanent dentitions (Table 2). However, the MAR for the skeletally immature and mature mandibles was significantly (P = .003) higher than the age combined maxillas and
there was a jaw/age interaction \((P = .003)\). MS/BS for the adult was significantly higher for the alveolar bone supporting the primary and permanent dentitions \((P < .01)\). There was a significant difference for jaw \((P < .01)\), however there was no significant jaw/age interaction \((P = .31)\). BFR was not significantly different \((P = .48)\) for the primary and permanent dentitions. However, there was a significant difference for the jaw \((P < .01)\) and jaw/age interaction \((P < .01)\).

**DISCUSSION**

This study quantifies intracortical, secondary osteonal bone remodeling in the bone surrounding the primary dentition from maxilla and mandible of skeletally immature dogs. The main findings of this study are as follows. First, in bone surrounding the primary dentition the histomorphometric variables that reflect bone remodeling in the mandible are significantly higher than those in the maxilla. Second, the mean remodeling rates for bone supporting the primary and permanent dentitions are not significantly different. With the current literature about BFR in skeletally immature dogs mainly focused on the rib, femur, and trabecular bone,\textsuperscript{18–20} our analysis focused

### Table 1. Means and Standard Deviations (SD) of Histomorphometric Variables for the Maxilla and Mandible for Bone Surrounding Primary Teeth\(^*\)

<table>
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<tr>
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<th>Maxilla</th>
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<th>Mandible</th>
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<td>Mean</td>
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<td>0.3</td>
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<td>0.5</td>
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<td>0.5</td>
<td>17</td>
<td>33.4</td>
<td>23.9</td>
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\(^*\) MAR indicates mineral apposition rate; MS/BS, mineralizing surface/bone surface; ES/BS, erosion surface/bone surface; BFR, bone formation rate.

### Table 2. Means and Standard Deviations (SD) for the Maxilla and Mandible (Alveolar) for Bone Surrounding Primary and Permanent Teeth

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<tr>
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<td>Mean</td>
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<tr>
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<td>0.6</td>
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<td>0.3</td>
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<td>23.2</td>
<td>11.2</td>
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<tr>
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<td>1.7</td>
<td>1.3</td>
<td>24</td>
<td>19.3</td>
<td>11.8</td>
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<td>19.3</td>
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<tr>
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<td>3.6</td>
<td>24</td>
<td>37.6</td>
<td>7.4</td>
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<tr>
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\(^*\) MAR indicates mineral apposition rate; MS/BS, mineralizing surface/bone surface; BFR, bone formation rate.

\(^*\) From the study by Huja et al.\textsuperscript{9}
on quantitative data of the alveolar and basal bone surrounding primary teeth.

In this study, the maxillary alveolar bone surrounding primary teeth demonstrated lower than expected bone activity for all histomorphometric variables. We also found that the mandibular BFR was fourfold greater than the maxilla, a greater difference than previously reported. This difference in the BFR is likely due to the maxillary alveolar bone having threefold to fivefold smaller bone volume. The alveolar width in many areas of the maxilla was less than 200 μm, and therefore osteonal remodeling was unlikely to occur. Four sections of the maxillary alveolar bone yielded a BFR of 0% per year, and this contributed to the overall lower results for dynamic variables in the maxilla. However, with increasing age and transition to the permanent dentition, the thickness of the alveolar process increases and allows for osteonal remodeling developing in the alveolar process.

While BFR was significantly higher in the mandible than in the maxilla, there was also a jaw (maxilla/mandible) and bone type (alveolar/basal) interaction for BFR. The first interaction indicated that the maxillary alveolar bone had a lower BFR than the maxillary basal bone. The second interaction was that the maxillary basal bone had lower BFR than the mandibular alveolar bone. We speculate this interaction was caused by the wide difference in morphology between mandibular alveolar bone and maxillary alveolar bone.

MAR was also statistically different between the maxilla and mandible of the skeletally immature dogs. While these values reflect actual differences, the biological significance, if any, of these differences has to be interpreted with caution. It should be noted that a wide range (eg, 0.5–2.0 μm/d) of MAR exists. We observed that the erosion process (ES/BS) was higher in the mandible than in the maxilla. This is a reflection of remodeling being a coupled process. Therefore, the erosion should follow the pattern of bone formation.

The erosion cavities are bone resorption sites related to the active bone remodeling during the process of tooth eruption. Our findings are consistent with histology and descriptions reported in the literature. The presence/absence of erosion cavities can be used as a means to study the impact of bisphosphonates on alveolar bone remodeling and tooth eruption. The effect of bisphosphonates on osteoclasts may limit the formation of erosion cavities needed to create an eruption path. The literature offers information supporting the assumption that bisphosphonates delay or inhibit eruption, but whether it is through the decrease of erosion cavities remains unknown. When the alveolar bone of the immature dogs was compared to prior data of alveolar bone from mature dogs, MAR and BFR were not significantly different. Unlike MAR and BFR, MS/BS was significantly greater in the mature dogs than in the immature dogs. We believe it may be related to the larger areas of erosion in the skeletally immature dogs.

It is unclear as to the nature of the stimulus that the presence of a tooth may provide to the surrounding tissues. However, the high bone remodeling rate can be considered as an adaptation mechanism for maintaining a primary or permanent tooth in bone. Furthermore, decreased treatment time would be considered as a significant advance in how orthodontic treatment is provided. Current studies on corticotomies and vibration-induced accelerated tooth movement indicate that the osteopenia induced by injury is a result of increased remodeling and serves as the basis of decreased treatment time. A thorough understanding and control of bone remodeling could serve as a foundation for future treatments in orthodontics.

CONCLUSIONS

- The remodeling rate of alveolar bone supporting primary teeth is greater in the mandible than in the maxilla.
- There is no difference in the rate of bone turnover in the bone supporting the primary vs the permanent dentition.

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