Prevalence and types of tooth resorption in dogs with oral tumors

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Objective—To determine the prevalence and types of tooth resorption in dogs with oral tumors and to compare findings with those for control dogs.

Animals—101 dogs with oral tumors and 128 control dogs that did not have oral tumors and for which dental radiographs were available.

Procedures—Exclusion criteria for dogs included systemic disease, long-term administration of anti-inflammatory drugs, traumatic occlusion, severe semigeneralized or generalized periodontitis, and endodontic disease. For each dog with an oral tumor, histologic sections of biopsy specimens of tumors were examined. Dental radiographic images of dogs were examined, and the presence and type of tooth resorption were determined for each tooth. Statistical analyses were performed to compare data regarding prevalence of tooth resorption.

Results—Teeth at tumor sites in dogs with nonodontogenic tumors were significantly more frequently affected with external inflammatory resorption, compared with teeth at tumor sites in dogs with odontogenic tumors. Teeth at sites distant from tumors in dogs with oral tumors were 3.2 times as likely to have external surface resorption (OR, 3.2; 95% confidence interval, 1.3 to 7.9) and 83.4 times as likely to have external inflammatory resorption (OR, 83.4; 95% confidence interval, 9.7 to 719.6) as teeth in control dogs.

Conclusions and Clinical Relevance—Resorption of teeth at tumor sites and at sites distant from tumors was common in dogs with oral tumors. Results of the present study will contribute to an understanding of the complex effects of oral tumors on local and distant hard tissues. (Am J Vet Res 2012;73:1057–1066)
of a tumor, and detection of tooth resorption may have value in determination of diagnosis and prognosis.\textsuperscript{11-19}

The purpose of the study reported here was to evaluate the presence and types of tooth resorption in dogs with oral tumors. Teeth at tumor sites and at sites distant from tumors were evaluated to detect resorption, and findings were compared with those for control dogs.

Materials and Methods

Animals—Records in the database and pathology reports of the University of California-Davis School of Veterinary Medicine, Department of Pathology, Microbiology and Immunology from 1999 through 2010 were searched by use of the following keywords: canine oral mass, canine oral neoplasm, canine oral tumor, and canine oral epulis. Complete medical records of dogs with reports identified via the database search were reviewed. Dogs with chronic systemic disease, traumatic occlusion, or severe semigeneralized or generalized periodontitis and dogs that had long-term treatment with anti-inflammatory drugs (that might have had an effect on osteoclast and odontoclast activity\textsuperscript{12,20,21}) were excluded from the study reported here. Only dogs that had dental radiographs that included the entire side (right or left) of the jaw (mandible or maxillary region) in which the visible tumor was located and the contralateral side of that jaw were included in the study. For most dogs, radiographic images of the entire mouth were available. All dogs evaluated at the University of California-Davis School of Veterinary Medicine Dentistry and Oral Surgery Service from 1999 through 2010 had survey radiographs taken of the entire mouth and did not have an oral tumor were identified via database search and review of medical records. These dogs were included in the present study as control dogs and were subject to the same exclusion criteria as were dogs with oral tumors. The study reported here included 101 dogs with oral tumors and 128 control dogs that did not have oral tumors.

Procedures—Data obtained from medical records of each dog included breed, age, sex, weight, and visible location of tumor in the oral cavity. A veterinary pathologist (BM) examined H&E-stained and immunohistochemically (as needed) stained histologic sections of incisional and excisional biopsy specimens of tumors. For each dog, each tooth on dental radiographic images was examined using 3.5\texttimes magnification loupes for signs of tooth resorption by 2 observers (AN and BA) who were unaware of the diagnosis; a consensus opinion was reached regarding presence and type of resorption for each tooth. Tooth resorption was classified by type in accordance with previously published radiographic criteria for dogs.\textsuperscript{21} Teeth affected by severe periodontitis or endodontic disease (ie, fractured, luxated, or discolored teeth), as indicated in medical records, were excluded from analysis because these conditions commonly result in tooth resorption.\textsuperscript{21} If a tooth was affected concurrently with > 1 type of tooth resorption, it was classified as having the type of resorption that was most prominent.

Statistical analysis—Statistical analysis of data included use of the \( \chi^2 \) test for homogeneity to compare numbers of affected and nonaffected dogs with respect to the presence and type of tooth resorption at tumor sites and sites distant from tumors. Similarly, associations between the presence and type of tooth resorption with type of tumor were analyzed. Duration of tumor presence (time from when a tumor developed or was noticed to time when radiographs of the mouth were obtained) differed among dogs, which likely influenced the extent of tooth resorption because tumors present for long periods can be larger, may involve more teeth, and may produce more factors that increase bone and tooth resorption, compared with tumors present for short periods. To compensate for this, the presence or absence of at least 1 affected tooth at each tumor site was used as a variable in the analysis (ie, a dog was considered to have a positive result for tooth resorption at the tumor site if at least 1 tooth at that tumor site had resorption).

Logistic regression was performed to evaluate presence and type of tooth resorption in teeth at sites distant from tumors (in dogs with oral neoplasia) versus data for control dogs. This analysis was controlled for age, sex, and body weight of dogs. Similarly, the presence and type of tooth resorption were compared between control dogs and dogs with nonodontogenic tumors and between control dogs and dogs with odontogenic tumors. These analyses were controlled only for age and weight of dogs because of the small number of dogs in these categories and because authors of another report\textsuperscript{24} found that there is no important association between sex of dog and presence of tooth resorption. Presence of resorption in teeth at sites distant from tumors was not compared among dogs with each type of tumor because the number of dogs with each type of tumor was small. Results were expressed as ORs and 95% CIs. Values of \( P < 0.05 \) were considered significant. Median and range values were reported for continuous data.

Results

Tissue origin and types of oral tumors—Nonodontogenic tumors were diagnosed in 55 of 101 (54.5%) dogs with oral tumors. Types of tumors in these dogs included SCC (n = 13 [23.6%]), fibrosarcoma (12 [21.8%]), osteosarcoma (7 [12.7%]), MM (7 [12.7%]), sarcoma (4 [7.3%]), carcinoma (4 [7.3%]), GCE (3 [5.5%]), plasmacytoma (2 [3.6%]), and mast cell tumor, melanocytoma, and PNT (1 [1.8%] dog each). Odontogenic tumors were diagnosed in 46 of 101 (45.5%) dogs with oral tumors; 23 (50.0%) of these dogs had POE (22 [47.8%]) had CAA, and 1 (2.2%) had compound odontoma. Characteristics of the 101 dogs with oral tumors and the 128 control dogs were summarized (Table 1).

Tooth resorption at tumor sites—in 6 dogs with nonodontogenic tumors (including 2 dogs with SCC, 1 dog each with MM and fibrosarcoma, and each of the dogs with mast cell tumor and PNT), no tooth was available for evaluation at the tumor site (because of tumor location [tumor did not arise from the gingiva]...
or teeth were missing or had been previously extracted at the site). Among the other 49 dogs with nonodontogenic tumors, 26 (53.1%) had at least 1 tooth with resorption at the tumor site (Table 2). In these dogs, 141 teeth at tumor sites were evaluated (median, 2 teeth/dog; range, 1 to 10 teeth/dog); of these, 57 (40.4%) teeth had resorption. Teeth at tumor sites most commonly had external inflammatory resorption; in dogs with osteosarcoma, all teeth at tumor sites that had resorption and had external inflammatory resorption (Figures 1 and 2; Tables 2 and 3). No significant differences were detected for the presence or type of tooth resorption at tumor sites among dogs with different types of nonodontogenic tumors.

In 3 dogs with odontogenic tumors (including 1 each of the dogs with CAA and POF and the dog with compound odontoma), no tooth was available for evaluation because of tumor location (tumor did not arise from the gingiva) or the fact that teeth were missing or had been previously extracted at the site; 6/55 and 3/46 dogs with nonodontogenic and odontogenic tumors, respectively). Within the tissue origin of an oral tumor, the total number of teeth at any type of tooth resorption does not equal the total number of dogs with specific types of tooth resorption because at least 1 dog had more than 1 affected tooth. Teeth at tumor sites in dogs with nonodontogenic tumors were significantly ($P = 0.046$) more likely to have external inflammatory resorption, compared with results for teeth at tumor sites in dogs with odontogenic tumors.

![Figure 1](image1.png)

**Figure 1**—Radiographic images of a 14-year-old dog evaluated because of extensive osteosarcoma of the left maxillary region. A—Lateral radiographic view of the left maxillary canine tooth. Notice the moth-eaten appearance of bone; all incisors and canine teeth and 3 premolar teeth have inflammatory resorption (white arrows). B—Lateral radiographic view of the right maxillary canine tooth. Notice the extensive inflammatory tooth resorption (white arrows).

<table>
<thead>
<tr>
<th>Tissue origin</th>
<th>Variable</th>
<th>Any type of tooth resorption</th>
<th>External replacement resorption</th>
<th>External inflammatory resorption</th>
<th>External cervical root surface resorption</th>
<th>Internal surface resorption</th>
<th>Internal replacement resorption</th>
<th>Internal inflammatory resorption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonodontogenic</td>
<td>Dogs (n = 49)*</td>
<td>26 (53.1%)†</td>
<td>1 (2.0)</td>
<td>6 (12.2)</td>
<td>20 (40.8)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (2.0)</td>
</tr>
<tr>
<td></td>
<td>Teeth (n = 141)</td>
<td>57 (40.4%)</td>
<td>1 (0.7)</td>
<td>7 (5.0)</td>
<td>48 (34.0%)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Odontogenic</td>
<td>Dogs (n = 43)*</td>
<td>15 (34.9%)</td>
<td>2 (4.7)</td>
<td>8 (18.6)</td>
<td>9 (20.9%)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td></td>
<td>Teeth (n = 85)</td>
<td>30 (35.3%)</td>
<td>3 (3.5)</td>
<td>9 (10.6)</td>
<td>18 (21.2)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Values reported are number (%) of affected dogs or teeth.

Tooth resorption was classified by type in accordance with previously published radiographic criteria for dogs.™ Teeth affected by severe periodontitis or endodontic disease (ie, fractured, luxated, or discolored teeth), as indicated in medical records, were excluded from evaluation. If a tooth was affected concurrently with $>1$ type of tooth resorption, it was classified as having the type of resorption that was most prominent.

*Number of dogs does not equal number of dogs with a tumor of the tissue origin in the present study because no tooth was available for evaluation at the tumor site in some dogs (as a result of tumor location [tumor did not arise from the gingiva] or the fact that teeth were missing or had been previously extracted at the site; 6/55 and 3/46 dogs with nonodontogenic and odontogenic tumors, respectively).
with resorption at the tumor site (Table 2). In these dogs, 85 teeth at tumor sites were evaluated (median, 1.5 teeth/dog; range, 1 to 6 teeth/dog); of these, 30 (35.3%) teeth had resorption. In dogs with CAA, teeth at tumor sites that had resorption most commonly had external inflammatory resorption (Figure 3). In dogs with POF, teeth at tumor sites that had resorption most commonly had external replacement resorption. No significant differences were detected for the presence or type of tooth resorption at tumor sites between dogs with POF and dogs with CAA.

Teeth at tumor sites in dogs with nonodontogenic tumors had external inflammatory resorption significantly ($P = 0.046$) more frequently than did teeth at tumor sites in dogs with odontogenic tumors. There were no significant differences between teeth at tumor sites in dogs with nonodontogenic tumors and dogs with odontogenic tumors with respect to the total prevalence of resorption or prevalence of any other specific type of resorption.

**Tooth resorption at sites distant from tumors**—Among the 55 dogs with nonodontogenic tumors, 40 (72.7%) had at least 1 tooth with some type of resorption at sites distant from tumors (Table 4). In these dogs, 1,686 teeth at sites distant from tumors were
evaluated (median, 35 teeth/dog; range, 8 to 41 teeth/dog); of these, 193 (11.4%) teeth had resorption. Most commonly, teeth at sites distant from tumors had external replacement resorption. However, dogs with osteosarcoma had more teeth at distant sites with external inflammatory resorption (14/32) than with any other type of resorption (Figure 1; Table 3): half (7/14) of these teeth were located adjacent to the tumor site, and half (7/14) were located in the quadrant of the mouth contralateral to the visible tumor. In teeth of dogs with tumors other than osteosarcoma, external inflammatory resorption was not the most common type of resorption; teeth with external inflammatory resorption in these dogs were located adjacent to tumors (tooth with external inflammatory resorption in 1 of the dogs with plasmacytoma) or in quadrants of the mouth distant from tumors (all teeth with external inflammatory resorption in dogs with MM, carcinoma, melanocytoma, or GCE and most teeth with external inflammatory resorption in dogs with fibrosarcoma [Figure 2] or SCC).

Total prevalence of resorption and prevalence of each type of tooth resorption in teeth at sites distant from tumors were not statistically compared for dogs with specific types of nonodontogenic tumors versus control dogs because the small number of dogs in each of these categories limited the value of such comparisons. Data for the total prevalence of tooth resorption and prevalence of each type of tooth resorption in dogs with nonodontogenic tumors were summarized (Table 5).

Among the 46 dogs with odontogenic tumors, 31 (67.4%) had at least 1 tooth with resorption at sites distant from tumors. In these dogs, 1,743 teeth at sites distant from tumors were evaluated (median, 40 teeth/dog; range, 12 to 41 teeth); of these, 202 (11.6%) teeth had resorption. These teeth most commonly had external replacement resorption (Tables 4 and 5).

Table 3—Total prevalence of resorption and prevalence of each type of resorption in teeth at tumor sites in 92 dogs with specific types of oral tumors.

<table>
<thead>
<tr>
<th>Type of oral tumor</th>
<th>Variable</th>
<th>Any type of tooth resorption</th>
<th>External surface resorption</th>
<th>External replacement resorption</th>
<th>External inflammatory resorption</th>
<th>External cervical root resorption</th>
<th>Internal surface resorption</th>
<th>Internal replacement resorption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteosarcoma</td>
<td>Dogs (n = 7)</td>
<td>6 (85.0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>6 (85.0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
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<tr>
<td>MM</td>
<td>Dogs (n = 6)*</td>
<td>3 (50.0)</td>
<td>0 (0)</td>
<td>1 (16.7)</td>
<td>2 (33.3)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
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<tr>
<td>Fibrosarcoma</td>
<td>Dogs (n = 11)*</td>
<td>7 (63.3)</td>
<td>0 (0)</td>
<td>2 (18.2)</td>
<td>5 (45.5)</td>
<td>0 (0)</td>
<td>1 (9.1)</td>
<td>0 (0)</td>
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<tr>
<td>SCC</td>
<td>Dogs (n = 11)*</td>
<td>14 (40.0)</td>
<td>0 (0)</td>
<td>3 (8.6)</td>
<td>10 (28.6)</td>
<td>0 (0)</td>
<td>1 (2.9)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>Dogs (n = 4)</td>
<td>1 (25.0)</td>
<td>0 (0)</td>
<td>1 (25.0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Carcinoma</td>
<td>Dogs (n = 4)</td>
<td>2 (50.0)</td>
<td>1 (25.0)</td>
<td>1 (25.0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
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<tr>
<td>Melanocytoma</td>
<td>Dogs (n = 1)</td>
<td>1 (100)</td>
<td>1 (100)</td>
<td>1 (100)</td>
<td>0 (0)</td>
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<tr>
<td>Plasmacytoma</td>
<td>Dogs (n = 2)</td>
<td>1 (50.0)</td>
<td>0 (0)</td>
<td>1 (50.0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
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<tr>
<td>GCE</td>
<td>Dogs (n = 3)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
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<tr>
<td>CAA</td>
<td>Dogs (n = 21)*</td>
<td>10 (47.6)</td>
<td>0 (0)</td>
<td>4 (19.0)</td>
<td>7 (33.3)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>POF</td>
<td>Dogs (n = 22)*</td>
<td>6 (27.3)</td>
<td>2 (9.1)</td>
<td>4 (18.2)</td>
<td>2 (9.1)</td>
<td>0 (0)</td>
<td>0 (0)</td>
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</tbody>
</table>

The dogs with mast cell tumor, PNT, and compound odontoma in the present study were not included in the table because no tooth was available for evaluation at the tumor site in those dogs.

*Number of dogs does not equal number of dogs with a tumor of the specific type in the present study, because no tooth was available for evaluation at the tumor site in some dogs (because of tumor location [tumor was not arising from the gingiva] or teeth were missing or had been previously extracted at the site; 1/7, 1/12, 2/13, 1/22, and 1/23 dogs with MM, fibrosarcoma, SCC, CAA, and POF, respectively). **Within the tumor type, total number of dogs with any type of tooth resorption does not equal the total number of dogs with specific types of tooth resorption because at least 1 dog had more than 1 affected tooth.

See Table 2 for remainder of key.
Total prevalence of resorption and prevalence of each type of resorption in teeth at sites distant from tumors were not statistically compared for dogs with specific types of odontogenic tumors versus control dogs because the small number of dogs in each of these categories limited the value of such comparisons. Data for specific types of oral tumors.

Teeth with resorption in dogs with CAA and POF most commonly had external replacement resorption (Figure 4; Table 4). Teeth with external inflammatory resorption in these dogs were most commonly located in quadrants of the mouth distant from tumors.

Of the 128 control dogs, 64 (50.0%) had at least 1 tooth with resorption (Table 4). In these dogs, 5,104 teeth were evaluated (median, 42 teeth/dog; range, 19 to 42 teeth/dog); of these, 344 (6.7%) teeth had resorp-
tion; these teeth most commonly had external replacement resorption. No internal replacement resorption, internal inflammatory resorption, or internal surface resorption was detected in teeth of control dogs.

No significant differences in the total prevalence of resorption or prevalence of each type of resorption were detected for teeth at sites distant from tumors in dogs with odontogenic tumors versus dogs with nonodontogenic tumors. No significant difference was detected between the total prevalence of resorption in teeth at sites distant from tumors in dogs with oral tumors and the prevalence of resorption in teeth of control dogs. However, teeth at sites distant from tumors in dogs with oral tumors were 3.2 times as likely to have external surface resorption (OR, 3.2; 95% CI, 1.3 to 7.9) and 83.4 times as likely to have external inflammatory resorption (OR, 83.4; 95% CI, 9.7 to 719.6) as teeth in control dogs. Teeth at sites distant from tumors in dogs with nonodontogenic tumors were 169.8 times as likely to have external inflammatory resorption (OR, 169.8; 95% CI, 15.7 to 1,831.9) as teeth in control dogs. Teeth at sites distant from tumors in dogs with odontogenic tumors were 6.7 times as likely to have external surface resorption (OR, 6.7; 95% CI, 2.5 to 17.7) and 34.7 times as likely to have external inflammatory resorption (OR, 34.7; 95% CI, 3.8 to 316.0) as teeth in control dogs.

**Discussion**

Results of the present study indicated that oral tumors may cause external inflammatory resorption of teeth at tumor sites and sites distant from tumors because dogs with tooth resorption not caused by tumors (ie, dogs with systemic disease, periodontitis, endodontic disease) were excluded. Tooth resorption develops in humans with benign or malignant tumors but is more commonly associated with slow-growing benign tumors (especially ameloblastoma, ossifying fibroma, and central giant cell granuloma). Tumor-related tooth resorption is most commonly associated with sarcomas and is rarely associated with SCC or fibrosarcoma in humans. In contrast, results of the present study indicated that dogs with nonodontogenic tumors (most of which were malignant) had tooth resorption at tumor sites more often than did dogs with benign odontogenic tumors (53.1% and 34.9% of dogs, respectively). Reports of tooth resorption in dogs with oral tumors are rare, but tumor-associated dental disruption is reported to develop in 60% of dogs with malignant tumors.

However, results of the present study and those of other study were difficult to compare because dental disruption was not clearly defined in that other study. External inflammatory resorption was detected in teeth at tumor sites more commonly than was any other type of tooth resorption in dogs with odontogenic (20.9% of dogs; 21.2% of teeth) and nonodontogenic (40.8% of dogs; 34.0% of teeth) tumors. Teeth at tumor sites in dogs with nonodontogenic tumors had external inflammatory resorption significantly more frequently than did teeth of dogs with odontogenic tumors. External inflammatory resorption was detected in more teeth at tumor sites than was any other type of resorption in dogs with nonodontogenic tumors and in dogs with CAA. No type of tooth resorption predominated in the teeth of dogs with POE. This is consistent with the different biological behaviors of these 2 types of benign odontogenic tumors; CAA is more biologically aggressive and locally invasive than is POE. Although small numbers of dogs with each type of tumor (especially nonodontogenic tumor types) were included in the present study, teeth at tumor sites in dogs with osteosarcoma seemed to have a higher prevalence of external inflammatory resorption (75.0%), compared with teeth at tumor sites in dogs with other types of tumor. In 1 study, osteosarcomas in humans had a higher expression of markers of bone remodeling than did any other type of bone-related tumor investigated. Although, to the authors’ knowledge, no specific data regarding tumor-related tooth root resorption have been reported.

**Figure 4**—Radiographic images of an 8-year-old dog evaluated because of POE grossly visible at the right mandibular first molar tooth. A—Radiographic image of the caudal aspect of the right mandible; there is no bone or tooth involvement. B—Radiographic image of the premolar teeth of the left mandible. Several teeth have external surface (arrows) and external replacement (arrowheads) resorption. External surface resorption may be the initial stage of resorption likely to progress to external replacement resorption, which is present in the mesial root of the left mandibular third premolar tooth in this image.
in human or veterinary medical literature, root surfaces of teeth at sites of benign tumors (typically teeth adjacent to tumors) are usually resorbed in a smooth manner.\textsuperscript{5,6,10,22} In contrast, resorption of teeth at sites of malignant tumors is irregular, involves multiple areas of tooth roots, results in a spike-like shape of roots, and causes floating of teeth (ie, lack of bony support).\textsuperscript{5,6,10} This pattern of tooth root resorption at sites of malignant tumors may be attributable to external inflammatory resorption of tooth roots.\textsuperscript{21}

Although radiographic evidence of bone resorption in 50 dogs with incisive or maxillary neoplasia reported by other authors' (bone resorption detected in 11/14 dogs with fibrosarcoma, 9/11 with SCC, 3/3 with MM, and 36/41 with any type of malignant tumor) seemed to differ from findings of the present study regarding tooth resorption in dogs with oral tumors, the mechanisms involved in bone and tooth resorption are likely similar. Resorption of teeth at tumor sites is likely attributable to direct trauma (eg, pressure\textsuperscript{22}), indirect tissue damage causing local inflammation (eg, ischemia), tumor-associated inflammation,\textsuperscript{12,19,20} or production of factors by tumor cells,\textsuperscript{25} that stimulate activity of osteoclasts and odontoclasts in periodontal ligaments (which initiates external tooth resorption\textsuperscript{24}). Several factors that stimulate osteoclasts to resorb bone and odontoclasts to resorb tooth roots have been identified, some of which are produced during inflammation; these factors modulate the function of OPG, RANKL, and RANK, which regulate osteoclast and odontoclast maturation and activity.\textsuperscript{12,13,19,20,26,27} Increased production of IL-1, IL-6, and tumor necrosis factor-α induces bone resorption via effects on OPG, RANKL, and RANK. This seems to be similar to the process responsible for tooth resorption.\textsuperscript{19}

Changes in expression of OPG, RANKL, and RANK have been detected in odontogenic tumors (most commonly ameloblastoma\textsuperscript{15,16,25,27}) of humans. Similar findings have been reported for some nonodontogenic oral tumors in humans.\textsuperscript{20–31} To the authors’ knowledge, findings regarding expression of OPG, RANKL, and RANK in oral tumors of dogs have not been reported. However, hypercalcemia in dogs with CAA may be associated with increased circulating concentrations of parathyroid hormone–related peptide, which may also result in osteoclast-mediated bone resorption,\textsuperscript{32} and cells in other types of tumor involving bone in dogs often express RANKL.\textsuperscript{33}

Cats with oral tumors have increased odds for root resorption in teeth at sites distant from tumors.\textsuperscript{34} No such predisposition was found for dogs with any type of oral tumor, dogs with nonodontogenic tumors, or dogs with odontogenic tumors in the present study. Although external replacement resorption was the most common type of resorption in teeth at sites distant from tumors in dogs of the present study, results did not statistically differ from those for control dogs. However, teeth at sites distant from tumors in dogs with an oral tumor of any type were more likely to have external surface and external inflammatory resorption, compared with teeth in control dogs. Although this finding was similar to findings for teeth in dogs with odontogenic tumors, teeth at sites distant from tumors in dogs with nonodontogenic tumors were more likely to have only external inflammatory resorption, compared with teeth in control dogs.

The finding of the present study that teeth at sites distant from tumors in dogs with odontogenic tumors had a higher prevalence of external surface resorption, compared with teeth in control dogs is difficult to explain. External surface resorption has been considered to be the initial stage of resorption likely to progress to external replacement resorption.\textsuperscript{21} This may have been the case in dogs of the present study. External inflammatory resorption of teeth distant from tumors was commonly detected in dogs of the present study, particularly in dogs with nonodontogenic tumors (especially osteosarcoma). This finding was suggestive of a systemic, rather than a local, effect of tumors. Results of studies\textsuperscript{29–31,34} reported in the human medical literature indicate that concentrations of several proangiogenic, proinflammatory cytokines are increased systemically (serum concentrations) and locally (saliva concentrations) in men with head and neck cancer or SCC. Therefore, it is possible that blood, saliva, or both deliver factors that increase resorption of teeth at sites distant from tumors. Increased concentrations of certain proinflammatory cytokines (eg, IL-1β) have a long-lasting effect on gingival fibroblasts, leading to increased osteoclastogenesis.\textsuperscript{36} However, it was possible that teeth distant from tumors in dogs of the present study were primarily affected with mild to moderate periodontitis\textsuperscript{10,20–22}; mild to moderate periodontitis might have been more common in dogs with oral tumors than in tumor-free control dogs of the present study. Endodontically compromised teeth commonly have some degree of external inflammatory resorption.\textsuperscript{10,21,22} Therefore, it was possible that teeth distant from tumor sites in dogs of the present study were endodontically compromised; this possibility was supported by the finding that different types of internal resorption (especially internal surface resorption) were detected in teeth distant from tumor sites in some dogs with oral tumors but not in control dogs. Internal resorption is generally associated with chronic endodontic disease.\textsuperscript{10,22,37} The possibility that teeth in dogs with tumors in the present study were not primarily endodontically compromised cannot be ruled out. However, the lack of internal resorption in teeth of control dogs indicated that tumors might have caused changes in the endodontic system of teeth in dogs with oral tumors. It was also not possible to rule out increased mechanical forces\textsuperscript{38} (because dogs with oral tumors may have preferred to chew food using teeth at sites distant from tumors, which would increase occlusal forces at those sites) as a cause of tooth resorption at sites distant from tumors in dogs of the present study.

Despite the low numbers of dogs with specific types of tumors in the present study, results were highly suggestive that malignant and aggressive oral tumors (ie, nonodontogenic tumors and CAA) may have biological behaviors that cause particular types of tooth resorption, as indicated by the finding that dogs with these types of tumors had a high prevalence of external inflammatory resorption (in teeth at tumor sites and in teeth distant from tumor sites). Therefore, further investigation is warranted regarding expression of
factors that increase bone and tooth resorption in oral tumors (especially those associated with function of OPG, RANKL, and RANK) and concentrations of those factors in saliva and gingival crevicular fluid.\(^{19}\) In the field of human oncology, determination of the activities of OPG, RANKL, and RANK is considered potentially useful for predicting the degree of bone remodeling and tooth root resorption.\(^{10}\) Degree of bone remodeling and tooth root resorption can indicate the biological aggressiveness and clinical behavior of tumors and the potential responses of patients to treatments.\(^{17,18,38}\)

Limitations of the present study could have affected findings. Limitations of conventional dental radiography for evaluation of tooth resorption are well-known.\(^{10,11,19}\) In the present study, this method of evaluation more likely resulted in underdiagnosis rather than overdiagnosis of tooth resorption. However, assignment of the most prominent type of tooth resorption as a final diagnosis in the rare instances in which teeth were concurrently affected with different types of resorption might have resulted in underdiagnosis of some types of tooth resorption. Additionally, findings for control dogs regarding tooth resorption in the present study were not completely in agreement with those reported for dogs from this same hospital population in another study.\(^{21}\) This was most likely attributable to the exclusion criteria (dogs with periodontitis, endodontic disease, or other disease- and treatment-related causes of tooth resorption\(^{11,12,19}\) were excluded) used in the present study. This may also be the reason for the disparity among results of the present study and those of other studies\(^{13} \) regarding the prevalence of specific types of oral tumors in dogs.

Although there was no significant difference in the prevalence of tooth resorption between dogs with odontogenic tumors and those with nonodontogenic tumors in the present study, teeth at tumor sites most commonly had external inflammatory resorption and this type of resorption more commonly affected dogs with nonodontogenic tumors than dogs with odontogenic tumors. The odds of external surface and external inflammatory resorption were higher for teeth distant from tumor sites in dogs with oral tumors than were the odds of those types of resorption for teeth of control dogs. Therefore, radiography of an entire mouth may be needed to properly plan comprehensive treatment\(^{8}\) of a dog with an oral tumor.

Results of the present study contribute to an understanding of the complex effects of oral tumors on local and distant hard tissues in dogs. Further studies that involve the use of molecular techniques are warranted to improve understanding of the biological behavior of oral tumors in dogs.\(^{16}\)

References


