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The diagnostic yield of preoperative screening for oral cancer in dogs over 15 years, part 1: locoregional screening

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OBJECTIVE
Determine locoregional diagnostic yield of 4-site screening (head, neck, chest, and abdomen) to diagnose metastatic disease or clinically significant comorbid diseases in dogs with oral cancer.

ANIMALS
381 dogs with histologically confirmed oral tumors.

METHODS
Medical records from 381 dogs with histologically confirmed oral tumors that underwent preoperative screening were retrospectively reviewed.

RESULTS
Skull and neck CT scan was performed on 348 patients. Bone lysis was present in 74.4% of tumors. Oral squamous cell carcinoma, sarcomas, and T2-T3 (> 2 cm) tumors had a significantly ($P < .05$) increased incidence of lysis compared to odontogenic and T1 (< 2 cm) tumors, respectively. Minor incidental findings were present in 60.6% of CT scans. Major incidental findings were found in 4.6% of scans. The risk of diagnosing an incidental finding increased by 10% and 20% per year of age for minor and major findings, respectively. Lymph node metastasis was diagnosed with CT or cytology in 7.5% of cases (10.7% of nonodontogenic tumors, 0% of odontogenic tumors). Oral malignant melanoma, oral squamous cell carcinoma, and T3 tumors had the highest prevalence of metastatic disease at the time of staging. The presence of bone lysis was not associated with cervical metastasis.

CLINICAL RELEVANCE
Major incidental findings were rare (< 5%) but primarily included secondary extraoral tumors. Lymphatic metastasis was diagnosed in 10.7% of nonodontogenic tumors, but cytology was not performed in the majority of cases and often included only a single mandibular node. Therefore, these results likely underestimate the incidence of lymphatic metastasis. Guided lymph node sampling is highly recommended, especially for oral malignant melanoma, squamous cell carcinoma, and T2-T3 tumors.

Keywords: oral tumor, computed tomography, cervical metastasis, bone lysis, locoregional spread

Staging is an essential step in the work-up of oral tumors. Evidence of locoregional or distant metastasis informs prognosis and invariably influences the recommended care paradigm. However, in veterinary medicine, there is no standard guideline for staging oral neoplasia.[1] This is compounded by the high prevalence of odontogenic tumors that carry a relatively low, but not null,[2] metastatic risk, challenging the value of preoperative screening tests in this subtype of oral cancer. Conversely, many institutions perform staging at the time of tumor biopsy, utilizing the oral and maxillofacial imaging appearance and

metastatic status to help inform the pathologist.[3] Thus, evidence-based recommendations for screening of oral tumors as one entity is pragmatic.

At this juncture, most texts recommend evaluation of the draining cervical lymph nodes and thorax as standard work up for nonodontogenic tumors.[3–6] Yet, controversy surrounds how best to stage cervical lymph nodes to ensure metastasis is not missed,[1,7–12] as well as the need for radiographic versus CT screening to accurately diagnose pulmonary metastasis.[13]

Based on current literature, both cervical and thoracic screening with diagnostic imaging and/or histology appear to be high-yield diagnostic tests for nonodontogenic tumors. At the time of diagnosis, locoregional metastasis is reported from 7.1% to 42% for oral malignant melanoma (OMM), 0% to 29% for oral squamous cell carcinoma (OSCC), and 0% to 11.1% for oral fibrosarcoma. In addition, pulmonary metastasis is reported at 1.4% to 28% for OMM, 0% to 10% for OSCC, and 0% to 20.8% for oral fibrosarcoma.[14–27] This wide range in diagnostic yield is likely secondary to lack of standardized screening, which precludes firm conclusions on the true presence of metastatic disease at the time of staging for oral neoplasia. The most sensitive method is biopsy, followed by fine needle aspirate and diagnostic imaging characteristics. Both sensitivity and specificity increase in advanced disease.[7–13]

Recommendations to screen the abdomen for distant metastasis are rare[6] and are primarily made in relation to OMM.[14] To the authors' knowledge, OMM is the only oral tumor documented to metastasize to an abdominal organ, and overall, the risk appears relatively low.[15] This finding, however, may be due to the lack of routine abdominal staging.

Even in tumors that carry a low metastatic risk, preoperative screening may diagnose unrelated conditions that may affect the decision to pursue further treatment. Both odontogenic and nonodontogenic tumors have a higher prevalence in an older population.[14–30] Inherently, this population also has an increased risk of concurrent undiagnosed significant disease. The diagnostic yield of preoperative screening tests to identify metastasis or other significant comorbidities is unknown for oral cancer and could substantially impact decision-making to pursue extensive oral surgery (ie, maxillectomy or mandibulectomy). This is particularly impactful when postoperative reconstruction surgery using bone-morphogenic protein, a powerful growth factor with the potential to promote oncoproliferation of any remaining cancer cells, is planned.[31]

Although positive preoperative screening will undoubtedly impact therapeutic decision-making, it is not without potential negative implications such as the risk of false positive results that may inaccurately sway the decision to pursue treatment and increased medical costs without direct benefit.[32] Hence, the primary aim for part 1 of this study was to document the frequency of metastatic and incidental (minor and major) lesions identified with locoregional screening in dogs with oral tumors. The secondary aim was to quantitate the odds for diagnosing metastatic disease and major concurrent disease based on tumor type and patient signalment to guide risk-benefit analysis for screening oral neoplasia.

Methods

Data collection

Electronic medical records (EMRs) of dogs that were presented to University of California-Davis William R. Prichard Veterinary Medical Teaching Hospital for diagnostic work of a biopsy-diagnosed oral tumor between 2008 and 2022 were reviewed. The EMR used queries with the terms "oral tumor"; "mass, maxillary"; "mass, mandibular"; "mass, oral"; and "tumor, oral." Cases that were presented to the Dentistry and Oral Surgery Service from January 2013 to January 2023 were also manually reviewed to identify additional cases that were missed with query terms. Recruitment for both part 1 (locoregional spread) and part 2 (distant spread) was performed together. Thus, patients needed to meet inclusion for both parts of the study to be included, ie, had to have a form of locoregional screening (head and neck CT and/or lymph node cytology) and distant screening (abdominal ultrasound and/or thoracic imaging). Dogs with a historical nonoral neoplasm were excluded from the analysis. Only the first visit where screening was performed was reviewed.

Clinical patient data acquired from the EMR included sex, age, weight, if the oral tumor was identified incidentally, tumor histology, tumor location, and tumor size. Tumor size was classified based on the World Health Organization Tumor Node Metastasis grading system.[33] Briefly, T1 tumors are defined as < 2 cm in the largest dimension, T2 tumors are 2 to 4 cm, and T3 tumors are > 4 cm. Tumor location was classified as rostral maxilla, caudal maxilla, rostral mandible, or caudal mandible as previously described.[29] If the tumor was not directly overlying bone, and could not be classified, its exact location was reported. Location was also documented as right, left, or bilateral.

For each patient, the screening tests performed were recorded. Each screening test (head CT, cervical lymph node screening [CT or cytology], thoracic imaging, and abdominal ultrasound) was evaluated separately. Radiology and pathology reports were utilized for data collection.

Diagnostic yield of locoregional screening

For conventional head CT, the presence of bone lysis was recorded as yes/no, and the presence of incidental findings was documented. Incidental findings were recorded and categorized as minor or major **(Table 1)**.

For cervical lymph node (LN) screening, the appearance of the cervical LNs on CT was recorded as normal, enlarged, or metastatic based on the radiology report. The specific LNs that were described as

Table 1—Classification of incidental findings on head and neck CT scan.

Minor	Major
1. Dental disease	**1. Secondary mass in a nonoral location**
Periodontal disease	Thyroid, nasal, brain, other
Retained tooth roots	**2. Thyroid or parathyroid nodule**
Endodontic disease (periapical lucency)	**3. Osseous lesion in a distant site from the tumor**
Tooth resoprtion	**4. Suspect satellite metastasis to the tonsil or other intraoral site**
2. Aural disease	
Otitis externa	
Otoliths	
Otitis media	
3. Rhinitis	
4. Developmental anomaly	
5. TMJ osteoarthritis	
6. Salivary disease	
Sialolith	
Minor sialocele formation	
7. Dystrophic soft tissue mineralization	
8. Subcutaneous masses without contrast enhancement	
Favored lipoma or adenoma	

For each screening test, incidental findings were categorized and classified as minor or major.
TMJ = Temporomandibular joint.

abnormal were recorded. If cervical LNs were sampled with fine needle aspiration, the presence of metastasis was recorded as yes/no. When both CT scan and cytology were performed for locoregional staging, it was documented if the LNs that were sampled were described as abnormal or normal on imaging.

For all screening tests, classification of an incidental finding as major was based on consensus between board-certified specialists in radiology (AZ), medical oncology (RR), and dentistry and oral surgery (BA, MSR, SG) that this finding could indicate significant additional disease burden that would likely alter prognosis, lifespan, and treatment recommendations. Conversely, minor incidental findings were defined as a condition that was unlikely to change patient prognosis as well as findings consistent with a previously known medical condition.

Statistical analysis

Prevalence for tumor finding is calculated by sex, age, weight, tumor histology, tumor stage, and tumor location. When calculating prevalence, we did not remove any data point or merge any categories. For continuous variables, we report mean, SD, quantiles, and ranges; for categorical variables, we report the number of cases, total number, and frequency. Bivariate logistic regression analyses were performed to calculate ORs and 95% CIs. When calculating OR, we report the associated OR and *P* value. A contingency table was created to compare the presence of bone lysis and cervical metastasis. A χ^2 test was used to evaluate the association between these 2 variables. All analyses were conducted in R version 4.2.2.

Results

Three hundred and 81 cases met the inclusion criteria for the study. Pure-breed dogs were more common (82.4%; 314/381) than mixed breed (17.6%; 67/381). Seventy-three different breeds were included. Golden (n = 43) and Labrador (52) Retrievers were the most common. Medium-large breed dogs were overrepresented with a median (range) weight of 26.7 (2.8 to 72.1) kg. There were 3.1% (12/381) intact females, 44.6% (180/381) spayed females, 6.3% (24/381) intact males, and 45.9% (175/381) castrated males. The median (range) age was 9 (0.4 to 18) years.

Most dogs (92.9%; 354/381) initially presented for evaluation of an oral mass, while the oral mass was considered an incidental finding in the remaining dogs. There were 31.5% (120/381) odontogenic and 68.5% (261/381) nonodontogenic tumors arising from multiple intraoral locations **(Table 2)**. Tumor size was reported in the EMR for 76.1% (290/381) of patients; 2.4% (7/290) were T0 with no visible gross disease (scar), 43.4% (126/290) had T1 (< 2 cm) tumors, 31.4% (91/290) had T2 (2 to 4 cm) tumors, and 22.8% (66/290) had T3 (> 4 cm) tumors. Unilateral tumors were most common with 41.2% (157/381) on the left and 46.2% (176/381) on the right. The remainder were bilateral (12.6%; 48/381).

Locoregional screening with head and neck conventional CT was performed in 91.3% (348/381) of dogs. LN cytology was performed in 43% (164/381) of dogs. Forty percent (40.4%; 154/381) of dogs had both a CT scan and LN cytology performed. The distribution of all locoregional and distant screening tests performed in the study group is shown elsewhere **(Supplementary Table S1)**.

Diagnostic yield of head and neck CT (n = 348)

Bone lysis was present in 74.4% (259/348) of all oral tumors. Bone lysis was common in most tumor types. In fact, peripheral odontogenic fibroma (POF), fibro-osseous lesions, tonsillar squamous cell carcinoma (SCC), infiltrative lipoma, and plasma cell tumor were the only tumor types associated with < 50% bone lysis. Conventional SCC, soft tissue sarcomas, and osteosarcoma had a significantly greater risk of bone lysis compared to odontogenic tumors. T2-T3 tumors had an increased risk of bone lysis compared to T1 tumors **(Table 3)**. Compared to caudal mandibular tumors, soft tissue lesions (OR, 0.08 [0, 0.2], $P < .001$) and multifocal lesions (OR, 0.05 [0, 0.4], $P = .007$) had a significantly decreased risk of bone lysis. The mean (range) age of patients with bone lysis was 8.9 (0.4 to 18) years. Age was mildly protective (OR, 0.89 [0.8, 1], $P = .005$) for risk of bone lysis. Both males and females had similar risks.

Incidental findings were present in 65.2% (227/348) of CT scans. Sixty percent (60.6%; 211/348) had at least 1 minor incidental finding and 4.6% (16/348) had a major incidental finding (Tables 3 and **4**). The majority (63.3%; 133/348) had 1 incidental finding, 31.4% (66/348) had 2 incidental

Table 2—Prevalence of tumor histologies and locations in the study group.

Tumor histology	Rostral maxilla	Rostral mandible	Caudal maxilla	Caudal mandible	Rostral-caudal maxilla	Rostral-caudal mandible	Palate	Soft tissue: tongue/lip/ cheek/ tonsil	Multifocal	Percentage of all tumors
Odontogenic (n = 120)										**31.5% (120/381)**
POF (n = 44)	38.6% (17/44)	29.5% (13/44)	6.8% (3/44)	13.6% (6/44)	–	–	–	–	11.4% (5/44)	**11.5% (44/381)**
CAA (n = 62)	11.3% (7/62)	38.7% (24/62)	14.5% (9/62)	33.9% (21/62)	1.6% (1/62)	–	–	–	–	**16.3% (62/381)**
CEOT (n = 1)	–	–	100% (1/1)	–	–	–	–	–	–	**0.3% (1/381)**
Giant cell epulis (n = 1)	–	–	100% (1/1)	–	–	–	–	–	–	**0.3% (1/381)**
Odontoma (n = 1)	–	–	–	100 % (1/1)	–	–	–	–	–	**0.3% (1/381)**
Ameloblastic fibroma (n = 1)	–	–	100% (1/1)	–	–	–	–	–	–	**0.3% (1/381)**
Ameloblastic carcinoma (n = 5)	40% (2/5)	60% (3/5)	–	–	–	–	–	–	–	**1.3% (5/381)**
OF (n = 5)	–	20% (1/5)	20% (1/5)	40% (2/5)	20% (1/5)	–	–	–	–	**1.3% (5/381)**
Nonodontogenic (n = 261)										**68.5% (261/381)**
Conventional OSCC (n = 54)	20.3% (11/54)	20.3% (11/54)	24.1% (13/54)	11.1% (6/54)	7.4% (4/54)	20.3% (11/54)	–	11.1% (6/52) (3 tonsillar)	–	**14.2% (54/381)**
Papillary OSCC (n = 11)	54.5% (6/11)	27.3% (3/11)	9.1% (1/11)	9.1% (1/11)	–	–	–	–	–	**2.9% (11/381)**
Basaloid SCC (n = 2)	50% (1/2)		50% (1/2)							**0.5% (2/381)**
OMM (n = 74)	12.2% (9/74)	8.1% (6/74)	27% (20/74)	16.2% (12/74)	5.4% (4/74)	4.1% (3/74)	2.7% (2/74)	23% (17/74)	1.4% (1/74)	**19.4% (74/381)**
OFSA (n = 42)	47.6% (20/42)	4.8% (2/42)	21.4% (9/42)	4.8% (2/42)	14.3% (6/42)	4.8% (2/42)	2.4% (1/42)	–	–	**11% (42/381)**
Fibroma (n = 1)	–	–	–	–	–	–	–	100% (1/1)	–	**0.3% (1/381)**
Undifferentiated sarcoma (n = 15)	26.7% (4/15)	20% (3/15)	26.7% (4/15)	20% (3/15)	6.7% (1/15)		–	–	–	**3.9% (15/381)**
Hemangiosarcoma (n = 1)	–	–	–	100% (1/1)	–	–	–	–	–	**0.3% (1/381)**
Osteosarcoma (n = 1)	10% (3/30)	13.3% (4/30)	43.3% (13/30)	26.7% (8/30)	–	6.7% (2/30)	–	–	–	**7.9% (30/381)**
MLO (n = 11)	27.3% (3/11)	9.1% (1/11)	27.3% (3/11)	27.3% (3/11)	–	–	9.1% (1/11)	–	–	**2.9% (11/381)**
Myxosarcoma (n = 2)	–	50% (1/2)	–	–	50% (1/2)	–	–	–	–	**0.5% (2/381)**
Peripheral nerve sheath tumor (n = 2)	–	–	100% (2/2)	–	–	–	–	–	–	**0.5% (2/381)**
Infiltrative lipoma (n = 1)	–	–	100% (1/1)	–	–	–	–	–	–	**0.3% (1/381)**
Lymphoma (n = 2)	–	50% (1/2)	–	–	–	–	–	50% (1/2)	–	**0.5% (2/381)**
Mast cell tumor (n = 4)	–	25% (1/4)	–	–	–	–	–	75% (3/4)	–	**1% (4/381)**
Plasma cell tumor (n = 9)	22.2% (2/9)	33.3% (3/9)	33.3% (3/9)	–	–	–	–	–	11.1% (1/9)	**2.4% (9/381)**
Total percentage of tumors at each location	**22.3% (89/381)**	**20.2% (77/381)**	**22.6% (86/381)**	**17.3% (66/381)**	**4.7% (18/381)**	**4.7% (18/381)**	**1% (4/381)**	**7.3% (28/381)**	**1.8% (7/381)**	

The percent and number of location per each tumor type are shown. The percent and number of each tumor type that contributed to the total study are shown in the last column in bold. The percent and number of each tumor location that contributed to total study are shown in the last row in bold.

CAA = Canine acanthamatous ameloblastoma. CEOT = Calcifying epithelial odontogenic tumor. MLO = Multilobular osteochondrosarcoma. OF = Ossifying fibroma aka fibro-osseous lesion. OFSA = Oral fibrosarcoma. OMM = Oral malignant melanoma. OSCC = Oral squamous cell carcinoma. POF = Peripheral odontogenic fibroma.

findings, 4.8% (10/348) had 3 findings, and a single patient had 4 incidental findings.

The odds of diagnosing an incidental finding increased with age. Specifically, the risk of diagnosing a minor incidental finding significantly increased by approximately 10% per year of age (OR, 1.11 [1, 1.2], $P = .003$) and a major finding by approximately 20% per year of age (OR, 1.22 [1, 1.5], $P = .032$). Risk of diagnosing a minor or major incidental finding was not affected by sex. Rostral mandibular lesions

Table 3—Prevalence of bone lysis, incidental findings, or cervical metastasis with head and neck screening per tumor histology and size.

Tumor histology/size (number that had head CT, LN cytology)	Bone lysis	Metastatic LN on CT	Metastatatic LN on cytology	Minor incidental finding	Major incidental finding
Odontogenic (n = 98, 23) reference for OR	**69.4% (68/98)**	**0% (0/98)**	**0% (0/23)**	**66.3% (65/98)**	**3.1% (3/98)**
CAA (n = 54, 12)	90.7% (49/54)	0% (0/54)	0% (0/12)	66.7% (36/54)	3.7% (2/54)
POF (n = 40, 9)	37.5% (15/40)	0% (0/40)	0% (0/9)	72.5% (29/40)	2.5% (1/40)
CEOT (n = 1, 1)	100% (1/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)
Giant cell epulis (n = 1, 0)	100% (1/1)	0% (0/1)	–	0% (0/1)	0% (0/1)
Odontoma (n = 1, 1)	100% (1/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)
Ameloblastic fibroma (n = 1, 1)	100% (1/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)
Ameloblastic carcinoma (n = 5, 1) (excluded from OR anlaysis)	100% (5/5)	0% (0/5)	0% (0/1)	40% (2/5)	0% (0/5)
Conventional OSCC (n = 47, 29)	**89.4% (42/47) OR, 3.71* (1.3, 10.3)**	**6.4% (3/47)**	**17.2% (5/29)**	**63.8% (30/47) OR, 0.9 (0.4, 1.9)**	**4.3% (2/47) OR, 1.41 (0.2–8.7)**
Tonsillar SCC (n = 2, 2) (excluded from OR anlaysis)	0% (0/2)	50% (1/2)	50% (1/2)	100% (2/2)	0% (0/2)
Other variants of OSCC (n = 12, 5)	**100% (12/12)**	**0% (0/12)**	**0% (0/5)**	**50% (6/12)** OR, 0.36 (0.1, 1.2)	**0% (0/12)**
Papillary SCC (n = 10, 3)	100% (10/10)	0% (0/10)	0% (0/3)	40% (4/10)	0% (0/10)
Basaloid SCC (n = 2, 2)	100% (2/2)	50% (1/2)	50% (1/2)	50% (1/2)	0% (0/2)
OMM (n = 67, 50)	**55.2% (37/67) OR, 0.54 (0.3, 1)**	**14.9% (10/67)**	**22% (11/50)**	**65.7% (44/67) OR, 0.97 (0.5, 1.9)**	**11.9% (8/67) OR, 4.29* (1.1, 16.8)**
Soft tissue sarcoma and mesenchymal tumors (n = 59, 30)	**84.7% (50/59) OR, 2.45* (1.1, 5.6)**	**5.1% (3/59)**	**6.7% (2/30)**	**50.8% (30/59) OR, 0.53 (0.3, 1)**	**1.7% (1/59) OR, 0.55 (0.1, 5.4)**
OFSA (n = 41, 18)	80.5% (33/41)	4.9% (2/41)	0% (0/18)	51.2% (21/41)	0% (0/41)
Fibroma (n = 1, 0) (excluded from OR anlaysis)	0% (0/1)	0% (0/1)	–	100% (1/1)	0% (0/1)
Undifferentiated sarcoma (n = 13, 9)	100% (13/13)	0% (0/13)	11.1% (1/9)	53.8% (7/13)	7.7% (1/13)
Hemangiosarcoma (n = 1, 1)	100% (1/1)	0% (0/1)	0% (0/1)	100% (1/1)	0% (0/1)
Myxosarcoma (n = 2)	100% (2/2)	50% (1/2)	–	50% (1/2)	0% (0/2)
Peripheral nerve sheath tumor (n = 2, 1)	50% (1/2)	0% (0/2)	0% (0/1)	0% (0/2)	0% (0/2)
Osteosarcoma (n = 27, 15)	**96.3% (26/27) OR, 11.47* (1.5, 88.5)**	**0% (0/27)**	**0% (0/15)**	***40.7% (11/27) OR, 0.35* (0.1, 0.8)***	**3.7% (1/27) OR, 1.22 (0.1, 12.2)**
MLO (n = 11, 3)	**100% (11/11)**	**0% (0/11)**	**0% (0/3)**	**81.8% (9/11) OR, 2.28 (0.5, 11.2)**	**9.1 (1/11) OR, 3.17 (0.3, 33.4)**
Round cell tumors (n = 5, 4)	**60% (3/5) OR, 0.66 (0.1, 4.2)**	**0% (0/5)**	**25% (1/4)**	**40% (2/5) OR, 0.34 (0, 2.1)**	**0% (0/5)**
Infiltrative lipoma (n = 1, 0) (exluded from OR analysis)	0% (0/1)	0% (0/1)	–	0% (0/1)	0% (0/1)
Lymphoma (n = 2, 2)	50% (1/2)	0% (0/2)	50% (1/2)	100% (2/2)	50% (1/2)
Mast cell tumor (n = 3, 2)	66.7% (2/3)	0% (0/3)	0% (0/2)	0% (0/3)	0% (0/3)
Plasma cell tumor (n = 8, 2)	**37.5% (3/8) OR, 0.26 (0.1, 1.2)**	**0% (0/8)**	**0% (0/2)**	**75% (6/8) OR, 1.52 (0.3, 8)**	**0% (0/8)**
Fibro-osseous lesion (n = 6, 0)	**33.3% (2/6) OR, 0.22 (0, 1.3)**	**0% (0/5)**	**–**	**83.3% (5/6) OR, 2.5 (0.3, 22.6)**	**0% (0/6)**
Tumor size (number that had head CT, LN cytology)					
T0 (n = 7, 5)	*14.3% (1/7) OR, 0.1* (0.0.8)*	14.3% (1/7)	20% (1/5)	100% (7/7)	28.6% (2/7) OR, 10.5* (1.5, 71.6)
T1 (n = 113, 44) (reference for OR)	62.8% (71/113)	0.9% (1/113)	2.3% (1/44)	66.4% (75/113)	3.5% (4/113)
T2 (n = 84, 36)	81% (68/84) OR, 2.36* (1.2, 4.6)	1.2% (1/84)	2.8% (1/36)	65.5% (55/84) OR, 0.93 (0.5, 1.7)	6% (5/84) OR, 1.73 (0.4, 6.7)
T3 (n = 61, 34)	82% (50/61) OR, 2.9* (1.3, 6.3)	14.8% (9/61)	29.4% (10/34)	57.4% (35/61) OR, 0.69 (0.4, 1.3)	4.9% (3/61) OR, 1.38 (0.3, 6.4)

Risk for different tumor histologies and sizes was calculated using OR with odontogenic tumors as the reference. For OR calculation, tumors with similar biological behavior were evaluated together and shown in bold. Individual tumor types that contributed to each group are shown below the bold header. When no OR is listed, it could not be calculated. OR (CI) that were protective are underlined, OR (CI) that had a CI that included 1 are not in italics or bold, and OR (CI) that had increased risk are italicized.

CAA = Canine acanthatmous ameloblastoma. CEOT = Calcifying epithelial odontogenic tumor. LN = Lymph node. OFSA = Oral fibrosarcoma. OMM = Oral malignant melanoma. OSCC = Oral squamous cell carcinoma. POF = Peripheral odontogenic fibroma.

*Significant OR ($P < .05$).

Table 4—Incidental findings detected on head/neck CT scan.

Findings	Prevalence	Comments
Minor incidental findings		
Dental disease	35.1% (122/348)	
Aural disease	28.7% (100/348)	
Rhinitis	3.4% (12/348)	
TMJ osteoarthritis	2.3% (8/348)	
Salivary disease	2% (7/348)	
Other	14.4% (50/348)	Developmental anomaly, signs of previous trauma, subcutaneous masses, ectopic mineralization
Major incidental findings		
Secondary mass	2.3% (8/348)	Meningioma (n = 2), carotid body tumor (n = 1), mass in ventricle (n = 1), thyroid mass (n = 4)
Thyroid nodule	1.1% (4/348)	
Distant osseous lesion	0.9% (3/348)	TMJ (n = 1) occipital bones (n = 1), hard palate (n = 1)
Suspect satellite metastasis	0.3% (1/348)	Tonsillar metastasis

had a significantly increased risk (OR, 2.83 [1.3, 6.2], P = .01) of minor incidental lesions compared to caudal lesions. Unilateral lesions were protective compared to bilateral lesions (left side: OR, 0.2 [0, 0.7], P = .015; right side: OR, 0.25 [0.1, 0.8], P = .024) for diagnosing a major incidental finding. No other location was significantly associated with an increase or decreased OR for incidental findings. The odds of diagnosing a minor incidental finding were significantly lower for osteosarcoma while the odds of diagnosing a major incidental finding were significantly higher for OMM (Table 3). No other tumor type or feature was significantly associated with a change in risk for incidental findings on CT scan.

Diagnostic yield cervical LN staging (n = 358)

Locoregional staging comprised of either cytology alone (2.8%;10/358), conventional neck CT alone (54.1%;194/358), or both CT and cytology (43%,154/358).

Twelve percent (12.8%; 21/164) of cases that had cytology performed had confirmed metastasis. Specifically, 0% (0/24) of odontogenic tumors and 15% (21/140) of nonodontogenic tumors had confirmed metastasis on cytology. The most common LN to be aspirated was the mandibular LN (MLN; 95.1%; 156/164). In most cases, these were the only LN sampled either ipsilateral (n = 77) or bilateral (68) to the tumor. Rarely, the medial retropharyngeal LN (MRLN) (7) or the superficial cervical (4) lymph node was also sampled in addition to the MLN. The remainder had only the MRLN or superficial cervical LN sampled.

On CT scan, 5.2% (18/348) of scans had LNs described as metastatic. Specifically, 0% (0/98) of odontogenic tumors, 0% (0/6) of fibro-osseous lesions, and 7.4% (18/244) of nonodontogenic tumors had metastasis diagnosed on CT scan. For the LNs described as metastatic, 72.2% (13/18) had confirmatory cytology performed. Of these, 92.3% (12/13) had aspiration performed on the LN described as metastatic on imaging. In the remaining case (1/13), the ipsilateral MLN was sampled, although the MRLN was the LN described as metastatic on CT. All sampled LNs were cytologically metastatic (100%; 13/13).

Forty-four percent (44.8%;156/348) had cervical LNs described as enlarged on CT. Fifty-eight percent (58.9%; 92/156) of cases that had enlarged LNs on CT scan had confirmatory cytology performed. The aspirates were obtained from a LN that was described as enlarged on the imaging report in 82.6% (76/92) of cases. Most often, only the MLNs were sampled despite other cervical LNs also being described as enlarged. In 17.4% (17/92) of cases the aspirates were obtained from LNs described as normal on the CT scan. Most often (88.2%; 15/17 cases), the MLNs were aspirated even though MRLNs were enlarged. In 7.6% (7/92) of cases, with enlarged LN where cytology was performed, metastasis was diagnosed. Taken together, for cases that had both CT and cytology performed (n = 194), metastasis was diagnosed with cytology in 10.3% (20/194) of cases.

Collectively, metastasis was diagnosed on either CT scan or cytology in 7.5% (27/358) of cases, 10.7% (27/253) of nonodontogenic tumors, and 0% of odontogenic tumors and fibro-osseous lesions. The OR could not be calculated for the risk of cervical metastasis. Of note, OMM, OSCC, and T3 tumors had the highest reported cervical metastatic rate (Table 3). Cervical metastasis was present in 4.6% (12/259) of tumors that had bone lysis and 6.7% (6/83) tumors that did not. The presence of bone lysis was not significantly (P = .44) associated with the presence of cervical metastasis.

Discussion

This study quantified the types and frequency of metastasis and incidental findings using locoregional screening. The risk of regional lymph node metastasis was highest in OMM, OSCC, and T3 tumors. Regional metastasis was not diagnosed in any odontogenic tumors. Lymph nodes that were deemed metastatic on CT were highly likely to be cytologically metastatic, and those that were enlarged were 7.6% likely to be metastatic on cytology. Yet, not all enlarged LNs were sampled, and normal LNs were rarely sampled. Thus, determining the true sensitivity and specificity of CT to predict metastasis in this retrospective study was not feasible.

The body of literature supports that contrast-enhanced CT should not be solely relied on to evaluate the metastatic status of cervical LNs due to poor sensitivity.[34–37] Consistent with historical data, our data also supported that LN size was inconsistent in predicting metastasis within this study with enlarged lymph nodes only being cytologically metastatic in < 10% of samples. However, only 58.9% of cases with enlarged LNs on CT scan had confirmatory cytology performed and of these the aspirate was performed on the enlarged LN in only 82.6% of cases. Further, there was a high prevalence of both periodontal disease and aural disease in the study group, which can also result in enlarged lymph nodes confounding the diagnostic imaging findings as well as the imaging-cytologic correlation.

Thus regardless of imaging appearance, cytology, at a minimum, should be performed for diagnostic screening of lymphatic metastasis. For cytology, however, it is critical that either the sentinel[38] or all draining lymph nodes are aspirated. Oral drainage is unpredictable with both contralateral spread and drainage to lymphocentrums other than the lateralized mandibular node reported.[6–8,34] Sentinel lymph node (SLN) mapping techniques, which identify the LNs most likely to harbor metastatic disease, have been introduced and validated in canine oral tumors, allowing for more accurate locregional screening.[34,39,40] Despite these advancements, sampling of the lateral MLN due to its easily accessible location is currently regarded as "common practice." This was observed in the current retrospective data set, where even in the face of other cervical lymph nodes described as abnormal on imaging, only the MLN were aspirated. Lack of accurate LN screening precludes true prevalence and prognostic information to be gained, introduces bias, and limits conclusions from this study.

Importantly, within the limitations of the data, the highest metastatic risk was associated with OMM, OSCC, and T3 tumors and lowest for sarcomas, consistent with historical data.[15–27] Furthermore, cytology had a higher yield than CT scans for diagnosing metastasis. However, these data are likely biased, as clinicians were more likely to sample LN of concern based on physical examination or imaging appearance. Caution should be employed in only prioritizing guided cytology for specific tumor types based on this data set as aspiration was performed in less than half the cases and only in a subset of draining cervical LNs; thus, occult metastasis was likely missed. Further, in tumors at high risk of cervical metastasis, the pathology of the SLN should be considered for gold standard diagnosis.[1,8,9,11,12]

Interestingly, the presence of bone lysis was not associated with the presence of cervical metastasis. This is concordant with data on OMM, where even though bone lysis was found to be a significant prognostic factor for median survival time, locoregional metastasis rate was similar regardless of the presence or absence of lysis.[41] However, this finding may also be biased by the high prevalence of bone lysis and low prevalence of cervical metastasis in the group. Bone lysis was apparent in nearly 75% of cases and prevalent amongst a variety of tumor types. Malignant tumors, specifically OSCC, soft tissue sarcomas, and osteosarcoma, had significantly increased odds risk of bone lysis compared to odontogenic tumors in agreement with historical data.[42] Yet, bone lysis was present in almost all tumor types. Furthermore, soft tissue lesions not overlying bone had significantly decreased risk of lysis, and nearly a quarter of OMM was in a soft tissue region, which may have diluted the findings for this tumor type specifically.

Only primarily soft tissue lesions (tonsillar SCC, infiltrative lipoma), plasma cell tumors, fibro-osseous lesions, and POF had bone lysis in < 50% of the tumors that underwent imaging. Of interest, nearly 40% of POF had bone lysis detected on CT scans. This tumor is often described as not having the ability to invade bone.[5,6,29] However, our study is consistent with other imaging studies[43] of odontogenic tumors that report the alveolar bone lysis in POF. It is unclear if the biologic behavior of POF is more aggressive than previously considered or, alternatively, if periodontal disease was being interpreted as neoplasia-induced bone lysis. Both cone beam and conventional CT are superior to radiographs for detecting bony lysis in both veterinary and human patients.[44–48] Thus, the increased sensitivity of this imaging modality may have contributed to this finding. Future studies focused on the histologic origin of POF and the ability of POF to extend into underlying bone should be explored.

Of note, both the extent of bone involvement and soft tissue infiltration are crucial for understanding the extent of the tumor as well as for surgical planning. Although all CT scans included in the study were conventional CT scans (ie, not cone beam), we elected to focus on reporting the presence of bone lysis only as this feature is a documented prognostic factor.[20,21] However, this should not be interpreted as a recommendation to not fully evaluate the lesion in both a bone and soft tissue algorithm before and after contrast administration. Conventional rather than cone-beam CT should be utilized to assess oral tumors, as the latter has inherently poor contrast resolution and the use of IV contrast with this modality has not been validated.[49,50]

Incidental findings were common and diagnosed in 62.5% of scans. Unsurprisingly, the most common incidental findings included periodontal disease and ear disease, consistent with previous point prevalence studies[51,52] of canine diseases. Other diseases were rare (<5%). The high prevalence of periodontal disease in particular is interesting for 2 reasons. First, it makes the diagnostic interpretation of alveolar bone lysis and lymph node enlargement complicated, as it is unclear if these changes are secondary to periodontitis or neoplasia, representing an important limitation of this research. Second, there is a growing body of evidence that microbial dysbiosis, such as that seen in periodontal disease, is associated with the initiation and progression of cancer in humans. [53–55] The high prevalence of both

periodontal disease and oral cancer in tandem may suggest that periodontal disease is involved in oncogenesis in dogs and is a risk factor for oral cancer that warrants further exploration.

Major findings were less frequent than minor findings (<5%), yet they included a secondary mass in 8 patients that were unlikely to be identified with common oral diagnostics such as dental radiographs or cone-beam CT scans as both imaging modalities have poor soft tissue detail and the neck and brain are often excluded due to field of view restrictions.[49,50] When factoring in the risk of additional disease, major incidental findings should be a separate but added risk to the risk of metastatic disease. This further supports that contrast-enhanced conventional CT scan, or analogous advanced imaging, including both the head and neck, should be regarded as the standard for preoperative work up for oral cancer.

The primary limitation of this paper is its retrospective nature, meaning data regarding tumor biology and the yield of staging was potentially omitted from the EMR. We chose to include only patients who would meet the criteria for both part 1 and part 2, thus potentially omitting important diagnostic imaging data from the study group. There was a variety in case management and a variety of radiologists and pathologists interpreting the screening results, which may introduce some bias, compared to a single panel of reviewers. Further, we accepted less than ideal screening modalities (head CT rather than LN cytology/pathology) for historical reference, as we wanted to report the diagnostic yield of locoregional screening over an extended time period, which introduces bias as the true metastatic risk was likely underestimated. We determined, based on our clinical experience and investigator consensus, what would be a major or minor finding but did not compare this to the likelihood of an owner to pursue a procedure. Several patients were lost to follow-up after the initial staging, and it was unclear if the decision to move forward was based on finances, extent of oral surgery, or findings from staging. Thus, it was elected to not explore this as a factor, thus limiting the "classification" of if a finding truly was medically major for that case. Finally, we elected to include both odontogenic and nonodontogenic tumors as a single group, which likely diluted the diagnostic yield of each staging test. We also had certain tumor types with small numbers, which elevates the percent shown (Tables 2–4) despite only 1 to 2 having positive results. We presented data separately for each category and specific tumor type with both percent and number to allow the reader to critically evaluate the data. Many institutions perform staging at the time of tumor biopsy, thus looking at oral tumors as one entity is pragmatic for decision-making.

We conclude that contrast-enhanced conventional CT scan including head and neck is of strategic importance for staging of both odontogenic and nonodontogenic oral tumors. Locoregional spread is most common in OMM, OSCC, and T3 tumors, and guided LN cytology/pathology of the SLN, or all cervical LNs, is recommended. Even within the limitations of this study and inclusion of odontogenic tumors, cervical metastasis was detected in 12.8% of sampled LNs and true occult metastatic risk is likely higher. Authors recommend thorough cervical screening of all nonodontogenic tumors.

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Supplementary Materials

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