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Authors

Goldschmidt, Stephanie

Soltero-Rivera, Maria

Quiroz, Adrian

et al.

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The Diagnostic Yield of Pre-operative Screening for Oral Cancer in Dogs over 15 years, Part 2: Distant Screening

Stephanie Goldschmidt, BVM&S, DAVDC[1], **Maria Soltero-Rivera, DVM, DAVDC**[1], **Adrian Quiroz**[2], **Kristen Wong**[2], **Robert Rebhun, DVM, DACVIM (onc)**[1], **Allison Zwingenberger, DVM, DACVR, DECVDI**[1], **Yunyi Ren**[3], **Sandra Taylor**[3], **Boaz Arzi, DVM,DAVDC, DEVDC FF-AVDC-OMFS**[1]

[1]Department of Surgical and Radiologic Sciences, University of California School of Veterinary Medicine, Davis, CA 95616, USA

[2]University of California College of Agriculture and Environmental Sciences, Davis, CA 95616, USA

[3]Department of Biostatistics, Epidemiology, and Research Design, Clinical and Translation Science Center, University of California, Davis, CA 95661, USA

Abstract

Objective: Determine diagnostic yield of chest, abdomen, and 4-site screening to diagnose metastatic disease and secondary diseases of prognostic significance in dogs with oral cancer.

Animals/Procedures: Medical records from 381 dogs with histologically confirmed oral tumors that underwent pre-operative screening were retrospectively reviewed.

Results: Thoracic metastasis was diagnosed in 4.9 % (0.9% odontogenic, 6.5% non-odontogenic) of oral tumors. Oral malignant melanoma (OMM) and multilobular osteochondrosarcoma (MLO) were most at risk. Abdominal metastasis was diagnosed in 2% of oral tumors (0% odontogenic, 3.1% non-odontogenic) and cytologically confirmed in 2 cases (0.6% (2/295) of all abdominal ultrasounds (AUS), 5.5% (2/36) of all AUS that had cytology). Both cases had OMM. Incidental disease was diagnosed in 53.1 and 81.3% of thoracic and abdominal screenings, respectively. Major findings were more common in AUS (7.8%) compared to thoracic screening (1.9%). Prevalence of incidental findings was similar for odontogenic and non-odontogenic tumors. Both metastasis and major findings were diagnosed more commonly with thoracic CT compared to radiographs. Metastasis or a major finding of prognostic significance was diagnosed in at least 1 test in 27.8% of patients that had head CT, lymph node cytology, thoracic screening, and AUS (N=115).

Clinical relevance: Major incidental findings were more commonly detected with AUS and was diagnosed in 1 in every 12 patients. However, metastatic disease was most commonly detected

**Corresponding Author: Stephanie Goldschmidt; sgoldschmidt@ucdavis.edu.

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with thoracic screening. When all 4 screening tests are performed there is an approximately 1 in 4 chance of diagnosing metastasis or major significant disease regardless of tumor type.

Keywords

Oral tumor; Computed tomography; Abdominal ultrasound; Metastasis; Staging

Introduction

Screening diagnostics are used to detect metastasis as well as other disease that may affect the prognosis or treatment plan. In veterinary medicine, there are no published consensus guidelines for screening oral tumors,[1,2] such as those readily available in human medicine.[3,4] Most texts recommend screening for non-odontogenic tumors only, and include advanced imaging of the head, as well as evaluation of the draining cervical lymph nodes and thorax.[1–2,5–6] Rarely, screening for abdominal distant metastasis is recommended[3] and is usually reserved for oral malignant melanoma (OMM) cases.[7]

Regardless of low metastatic potential, pre-operative screening may still diagnose significant secondary disease that impact decision making to pursue extensive oral surgery and/or adjuvant therapy. The role of screening tests to diagnose other distant significant comorbidities has been previously explored for non-oral sites. Sacornrattana et al. evaluated the role of abdominal ultrasound (AUS) for screening patients with appendicular osteosarcoma and documented imaging abnormalities in 57% of patients. This study noted 2.5% and 6.4 % of patients that exhibited abdominal metastasis or other major findings, respectively.[8] Similarly, Tong et al. evaluated the role of AUS as a screening test prior to advanced neurodiagnostic imaging and documented 58% of patients with abnormalities. This prior study reported that 1.3% of patients did not pursue further neurodiagnostics due to AUS findings.[9] When both thoracic and abdominal imaging are considered prior to oncologic treatment, Bigio et al. found that 9% of patients had significant concurrent disease that changed treatment planning.[10]

The diagnostic yield of pre-operative screening tests to identify metastasis or other significant comorbidities is unknown for oral cancer and has the potential to alter the treatment paradigm. Yet, additional testing is not without potential negative implications, such as the risk of false positive that incorrectly alter the decision to treat, and increased costs.[9] Hence, the aim of this study was to document the frequency of metastatic and incidental (minor and major) lesions identified with local and distant screening in dogs with oral tumors. The secondary aim was to quantitate the odds for diagnosing metastasis and major comorbidities based on tumor type and patient signalment to guide decision making for screening oral neoplasia. Part 2 of this series reports the results of distant screening and compound 4-site screening (head CT, lymph node cytology, thoracic imaging, AUS).

Materials and Methods

Data Collection

Complete methodology on data collection from the electronic medical record (EMR) is presented in part 1 of the series. Briefly, the EMR from the first visit where screening was performed were retrospectively reviewed from 2008–2022 for dogs that presented with oral tumors. For inclusion in the study the patient had to meet inclusion for both part 1 and 2, i.e., had to have both local screening (head and neck CT and/or lymph node cytology) and distant screening (abdominal ultrasound and/or thoracic imaging). Dogs with a historical non-oral cancer were excluded.

Clinical patient and tumor data was recorded along with the screening test(s) performed. Clinical data included sex, age, weight, if the oral tumor diagnosis was incidental, tumor histology, tumor location, and tumor size. Tumor size was classified based on the World Health Organization Tumor Node Metastasis grading system.[11] T1 tumors are defined as < 2cm in the largest dimension, T2 tumors are 2–4 cm, and T3 tumors are >4 cm. Each screening test was evaluated separately. Combined yield was also explored. Radiology and pathology reports were utilized for data collection.

Diagnostic Yield of Distant Screening

Thoracic imaging was performed via thoracic radiographs or conventional CT. If both imaging modalities were present, only the CT scan was counted and analyzed. Presence of metastasis was recorded as yes (defined as multiple soft tissue nodules seen on diagnostic imaging), suspicious (defined as a single soft tissue nodule seen on diagnostic imaging), or no (no soft tissue nodules seen on imaging). Cytological confirmation that nodule(s) were metastatic lesions was not performed. Presence of incidental findings was recorded and classified as minor or major (Table 1).

For AUS, presence of metastasis was marked as yes, suspicious, or no. Suspicious lesions were defined as an organ being described as mottled, enlarged, or having one or multiple nodules. Even if the report did not term an organ suspicious for metastasis it was marked as suspicious if one of the above descriptors was used and the finding was not specifically described as benign by the radiologist. [12] The organ(s) of concern were documented. If cytology was performed to confirm the presence of metastasis this was reported along with the results. Presence of incidental findings were recorded and classified as minor or major (Table 1). If there was a suspicious lesion that was sampled and confirmed to be benign, it was then also counted as a minor incidental finding. In the absence of cytologic confirmation, a lesion was also counted as a minor incidental finding if the radiology report prioritized a benign condition.

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 would likely alter prognosis, lifespan, and the recommended treatment. The effect of incidental findings on client decision making was either poorly documented or absent in the majority of reviewed records with many patients lost to follow up after screening. Thus, this data was omitted. Conversely, minor incidental

findings were defined as a condition that were unlikely to change patient prognosis or treatment recommendations.

Statistical Analysis

Presence of metastasis, suspicious lesions, and minor and major findings were evaluated. Prevalence of each finding was calculated by sex, age, weight, tumor histology, tumor stage, and tumor location; either Chi-squared test or Fisher's Exact Test was used to compare the prevalence by different type of medical exam conducted (CT vs. Radiation).

For continuous variables, we report mean, standard deviation, quantiles, and ranges; for categorical variables, we report the number of cases, total number, and frequency.

Univariate logistic regression was used to calculate odds ratios (OR) and 95% confidence intervals, relating the odds of different findings to each predictor individually.

Predictors evaluated were age, sex, histology, tumor location, and tumor stage. Multivariable logistic regression was used to compare the odds of different findings between dogs receiving a thoracic CT or radiographs. For these analyses we modeled the log odds of each finding versus thoracic imaging type, all listed predictors and the interaction between these predictors and scan type. These models evaluated whether the odds of a finding differed between CT and radiographs and if any differences varied by predictors. If the interaction term was not significant, we refit the model using only the main effects of scan type and the predictor. All statistical tests were two-sided and evaluated at a significance level of 0.05. As this was an exploratory and largely descriptive study, we did not combine all the variables with low N. Instead, we decided to keep all categories clearly clinically meaningful and distinguishable. Additionally, we did not perform any p-value adjustment for multiple testing. All analyses were conducted in R version 4.2.2.

Results

Three hundred and eighty-one cases met inclusion criteria for the study. There were 31.5% (120/381) odontogenic and 68.5% (261/381) non-odontogenic tumors arising from multiple intraoral locations. Complete patient and tumor demographics are presented in Part 1 of the series. The distribution of all local and distant diagnostic screening tests performed in the study group is shown in Supplemental Table 1.

Diagnostic Yield of Thoracic Imaging (N=371)

Thoracic screening was comprised of 61.5% conventional CT scans and 38.5% (143/371) radiographs. Metastatic disease was diagnosed in 4.9% (18/371) of dogs. Specifically, metastasis was diagnosed in 0.9% (1/110) of odontogenic tumors and 6.5% (17/261) of non-odontogenic tumors. Three percent (3.8%; 14/371) of patients had a suspicious single nodule. Specifically, 2.7% (3/110) of odontogenic tumors and 5.4% (14/261) of non-odontogenic tumors.

There was an increased risk of metastasis in multilobular osteochondrosarcoma (MLO), OMM, and T3 tumors (Table 2). Risk of thoracic metastasis was not significantly associated

with age, sex, or tumor location. There were no features significantly associated with increased risk of suspicious pulmonary lesions.

An incidental finding was present in 53.1% (197/371) of dogs. Specifically, 51.2 % (190/371) had at least one minor finding and 1.9% (7/371) had a major incidental finding (Table 2,3). Minor incidental findings were present in 53.6% (59/110) of odontogenic and 50.1% (131/261) of non-odontogenic tumors. Major findings were present in 0.9% (1/110) odontogenic and 2.3% (6/261) non-odontogenic tumors. Older patients had an increased risk (OR:1.13 (1.1,1.2), p<0.001) of minor incidental findings. Round cell tumors had a significantly higher risk of major incidental findings compared to odontogenic tumors (Table 2). No other signalment or tumor features were significantly associated with risk of incidental lesions.

Thoracic CT versus Radiographs

Both metastasis and incidental findings were diagnosed more frequently in patients that had thoracic CT scan performed (Table 4). On statistical evaluation considering the role of imaging type, we did not find that adding an interaction term of the imaging type (Radiograph vs. CT scan) improved the model fitting, so we are only reporting the results from the multivariable model. In the multivariate models, by adding the image scan type as an effect variable, CT was more likely to diagnose lesions compared to radiographs when evaluating the effect of age and having an MLO or OMM. Specifically for age, the odds of diagnosing a minor incidental lesion increased by 16% per year of age (OR 1.16 (1.1,1.2) p<0.001) while the odds of diagnosing a minor incidental lesion using radiographs were 57% less than using CT scan (OR 0.43 (0.3,0.7) p<0.001). The odds ratio of diagnosing pulmonary metastasis for MLO (OR 39.78 (3.7,430.2), p=0.002) and OMM (OR 18.61 (2.3,150.2) p = 0.006) compared to odontogenic tumors was higher in this model. The odds of diagnosing pulmonary metastasis with MLO or OMM was 47% less likely on radiographs (OR 0.53 (0.2,1.6), p=0.26) compared to CT scan, but this finding was not significant.

Diagnostic Yield of Abdominal Ultrasound (N=295)

Two percent (6/295) of patients had a metastatic lesion diagnosed on AUS (Table 5). Of these, 50% (3/6) patients had confirmatory cytology performed; and 2/3 patients were confirmed to have abdominal metastasis. Both patients had OMM.

Suspicious lesions, where metastasis was listed as a potential diagnosis, were noted in 19.3 % (57/295) of patients. Suspicious lesions were diagnosed in 24.2% (24/99) of odontogenic tumors and 16.8% (33/196) non-odontogenic tumors. When a lesion was termed suspicious, 43.9% (25/57) had confirmatory cytology. All cytology was negative for metastasis. Eight additional patients had cytology of an abdominal organ despite lack of a suspicious lesion; in all cases the cytology was negative for metastasis.

Risk of diagnosing a suspicious (OR 1.16 (1,1.3) p=0.005) or metastatic (OR: 1.57 (1.1,2.1) p=0.005) lesion increased with age. No other factors were significantly associated with risk.

At least one incidental finding was identified in 81.3% (240/295) of patients. Specifically, 74.1% (217/295) had at least one minor incidental finding and 7.9% (23/295) had a major

incidental finding (Table 6). Minor incidental findings were diagnosed in 70.7% (70/99) odontogenic tumors and 75% (147/196) non-odontogenic tumors. Major incidental findings were diagnosed in 7.6% (15/196) odontogenic tumors and 8.1% (8/99) non-odontogenic tumors.

The median (range) number of abnormal organ systems identified on AUS were 2 (0–6). Both the risk of diagnosing a minor (OR:1.21 (1.1,1.3) p<0.001) or major (OR:1.17 (1,1.4) p=0.05) increased with age. Male patients were also twice (OR:2.01 (1.2, 3.4) p=0.011) as likely to be diagnosed with a minor incidental finding. No tumor specific features were associated with increased risk.

Diagnostic Yield of 4-site screening (N=115)

In the patients that had comprehensive 4-site screening, defined as head/neck contrast enhanced CT, LN cytology, thoracic imaging, and AUS, metastasis or a major incidental finding was identified in at least 1 of the tests in 27.8% (32/115) of patients.

Specifically, on head/neck CT scan, a major incidental finding was identified in 8.7 % (10/115) of cases. LN metastasis was diagnosed on diagnostic imaging in 6.1% (7/115) of scans and cytologically confirmed in all (7/7) cases. LN metastasis was diagnosed on cytology, regardless of LN appearance on CT, in 10.4% (12/115) of cases.

On thoracic screening, 1.7% (2/115) had a major incidental finding and 3.5% (4/115) had metastasis. On AUS, 8.7% (10/115) had a major incidental finding and 2.6% (3/15) patients had metastatic lesions. Metastasis was cytologically confirmed in 2/3 patients. The diagnostic yield for each screening test was similar between the group with comprehensive 4-site staging (N=115) and the total study group (Table 7).

If only patients that had thoracic CT as part of their comprehensive screening are evaluated (N=74) the diagnostic yields are slightly higher. With locoregional CT screening 9.4% (7/74) of patients had a major incidental finding and 6.6% (5/74) had LN metastasis. The cytologic LN metastatic rate was 9.4% (7/74). Four percent (3/74) of patients had thoracic metastasis and 1.4% (1/74) had a major secondary disease. Lastly on AUS, 12.2% (9/74) patients had a major incidental finding and 1.4% (1/74) of patients had a metastatic lesion, which was cytologically confirmed.

There was no significant difference when evaluating the patients that had 4-site screening with thoracic CT scan (N=74, 29.7% had metastasis or major finding) compared to thoracic radiographs (N=41, 24.4% has metastasis or major finding, p=0.665).

Discussion

We identified two major clinically meaningful findings when examining distant screening and 4-yield screening. First, concurrent disease was detected with pre-operative distant screening in 53.1–81.3% of cases pending the test performed. Most findings were considered minor and were considered unlikely to alter prognosis or significantly alter the specialist recommendation to treat the oral tumor. If only focused on detection of metastasis or major secondary findings with prognostic significance in a single test, approximately 1

in 10 (9.5%) had a significant finding on AUS. Second, in dogs that had compound 4-site screening, approximately 1 in 4 dogs (27.8%) were diagnosed with metastasis or a major finding on at least 1 test. Thirty percent (115/381) of dogs had 4-site screening performed which may limit the power of this finding. Yet, when looking at the yield of each screening test in this group compared to the complete group, the diagnostic yields were similar. Below we will further discuss the impact of each screening test individually.

In the cases presented here, thoracic imaging (both CT and radiographs evaluated together) exhibited the lowest diagnostic yield, with metastasis and major incidental findings both being identified in less than 5% of cases. If looking only at odontogenic tumors, two patients had pulmonary metastasis (N=1) or major secondary disease (N=1). Conversely, OMM, MLO, and round cell tumors had a higher risk of metastasis and/or major secondary disease and imaging is essential in these cases.

Of note, MLO carried the highest risk (OR: 39) of pulmonary metastasis compared to odontogenic tumors, especially when thoracic CT scan was performed. Caution should be employed in interpretating this result due to the low sample number (N=11) which introduces an increased risk of chance association. Yet, this finding is still important as although the risk of pulmonary metastasis with grade 3 MLO is reported to be as high as 58% following treatment, to the authors knowledge the risk of pulmonary metastasis at diagnosis is low, especially in grade 1–2 lesions.[13–15] This may be due to bias of previous reports which are focused on local treatment of MLO, thus patients with metastasis may have not met inclusion criteria. Yet, MLO is commonly regarded to have a less aggressive biologic behavior compared to osteosarcoma. Future work better defining the biologic behavior of this tumor and the role of adjuvant therapy is warranted.

Metastasis and significant secondary abnormalities were more commonly diagnosed with thoracic CT scan compared to radiographs. It has been previously documented that conventional CT is more sensitive than thoracic radiographs for diagnosing nodules in dogs. Pending the study, radiographs detected only 9–41% of nodules detected on CT scan, upstaging 19–39% of dogs with neoplasia. [16–19] Literature largely supports that CT should be the recommended modality, especially in cases with a high risk of pulmonary metastasis. Yet, the prognostic effect of small nodules detected only on CT is largely unknown. Thus, caution should be employed in counseling owners based on these findings. In fact, in a study evaluating the diagnostic yield of thoracic CT for appendicular osteosarcoma, no significant difference was found in median survival time for dogs with or without pulmonary nodules.[19] Authors suggested that these small metastatic nodules may not impact prognosis in the same way as larger nodules that are able to be detected radiographically. Increased incorporation of thoracic CT scans for staging will allow conclusions to be made on the prognostic implications of small metastatic nodules with oral neoplasia especially in high-risk cases including OMM, osteosarcoma, MLO, and T3 lesions.

Within our study, pulmonary metastasis was also diagnosed in an odontogenic tumor (giant cell epulis). It is known that odontogenic tumors in humans carry an approximately 1% risk of distant metastasis,[20] and metastasis has been historically reported in a canine amyloid producing odontogenic tumor.[21] Of note the single patient with pulmonary metastasis

associated with an odontogenic tumor did not have abdominal screening. Thus, there is a potential that there was another undiagnosed primary neoplasm that resulted in metastasis.

Although the potential risk of pulmonary metastasis in odontogenic tumors was confirmed to be low (<1%), incidental findings were diagnosed with similar prevalence in both the odontogenic and non-odontogenic groups. Risk of both minor and major incidental findings significantly increased with age, and thoracic screening in older patients regardless of tumor histology and size is prudent.

Notably, AUS was the highest yield pre-screening test for detecting secondary comorbidities. An incidental finding was reported in 83.1% of scans, which is higher than historically reported for non-oral sites.[7–9] This may be due to scrutiny of radiologists at our institution, the grading scheme utilized, or may truly be related to a higher risk of secondary comorbidities in dogs with oral tumors compared to non-oral sites. Similar to previous studies, however, major findings were rare.[7–9] However, they most often included a secondary primary tumor. Thus, clients should be counseled on the approximate 1 in 12 chance that a significant secondary disease, including a secondary tumor, may be identified. Larger tumors were the only factor significantly associated with increased risk. However, this may be biased by the small number of cases, which introduces the risk of false positives and chance associations. Of note, odontogenic and non-odontogenic tumors had a similar likelihood of being diagnosed with both minor and major incidental findings on AUS. Pragmatically, AUS was proven to be a high-yield diagnostic modality and should be recommended as part of an oral-tumor workup in risk adverse clients despite the low probability of diagnosing metastasis.

Abdominal metastasis was confirmed to be rare, and only cytologically confirmed in 0.6% (2/295) of cases. This the largest study to date to the evaluate the risk of abdominal metastasis with oral tumors, and OMM was the only tumor with confirmed abdominal spread at diagnosis, consistent with historical data.[22–29] Not all lesions, however, termed metastatic or suspicious on AUS received confirmatory cytology. Half (3/6) of metastatic lesions had confirmatory cytology performed. While only 43.9% (25/57) of suspicious lesions had confirmatory cytology performed. Lesion sampling is often determined by the perceived risk of metastasis combined with the imaging appearance; thus collective risk was likely perceived to be low. Yet, due to retrospective nature of this study this is only speculatory.

Limitations

The primary limitations of this paper surround the retrospective nature of the study meaning numerous clinicians were involved in cases management and data was often absent from the EMR. Most impactful, due to missing data in the EMR, it was unclear how the screening findings impacted decisions to treat. To circumvent this, lesions were classified as minor or major based on consensus expert opinion. Yet, the true impact of these lesions on decisions to treat could not be evaluated. Further, we elected to include patients that had some form of local screening and some form of distant screening, which introduces bias as the screening was not uniform in the group. We presented data for each group separately and then also those that had uniform screening to allow the reader to interpret the results in light of this

bias. Interestingly, the findings were similar. Lastly, as we included multiple tumor types there were groups with low case numbers which can impact the power of the statistical findings. This data should be interpreted as descriptive and largely explorative.

Conclusions

Within the limitations of this study it was found that thoracic screening was collectively less likely than AUS to diagnose metastasis or secondary significant disease, with a combined yield of (5.9%; 22/371) versus 9.5% (28/295) respectively. Thoracic CT appears to have a higher diagnostic yield and may be more likely to accurately diagnosis pathology. Authors recommend conventional CT scan priority should be given to oral tumors, and if incisional biopsy is performed prior to screening, especially OMM, MLO, osteosarcoma, and T3 lesions. Abdominal screening is higher yield for diagnosis of secondary significant disease rather than metastasis in both odontogenic and non-odontogenic tumors. Owners should be counseled on the approximately 1 in 12 risks of diagnosing major secondary disease with AUS. This is especially true in older patients, which were at an increased risk for diagnosis of incidental lesions on both thoracic and abdominal screening. Finally, owners should be advised that when all 4 screening tests are utilized metastasis, or a major finding of prognostic significance, are identified in approximately 1 in 4 patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1:
Classification of Incidental Findings for Distant Screening.

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

Thorax: Radiographic or Computed Tomographic Scan	
Minor	**Major**
1. Orthopedic abnormalities	**1. Secondary intrathoracic mass**
• Shoulder OA	• Pulmonary parenchyma
• Elbow OA	• Pleural
• IVDD	• Mediastinal
• Spondylosis Deformans	• Heart based
2. Broncohintersitial pattern	**2. Severe alveolar infiltrates consistent with CHF or aspiration pneumonia**
• Age	**3. Severe sternal or mediastinal lymph node enlargement**
• Lower airway disease	**4. Severe tracheal collapse with concern for anesthetic safety (on radiographs)**
3. Pulmonary osteomas	**5. Osseous lytic lesion on the vertebrae, long bones, or ribs**
4. Mild fibrosis or thickening	
5. Subcutaneous or cutaneous non-contrast enhancing masses	
• Lipoma or adenoma favored	
6. Atrial enlargement without evidence of CHF	
7. Redundant tracheal membrane without significant tracheal collapse (on radiographs)	
8. Pulmonary bulla	
9. Emphysema	
10. **Mild enlargement of the sternal lymph nodes**	
Abdomen: Ultrasonographic Scan	
Minor – evaluated by organ	Major
1. Liver	**1. Primary abdominal mass**
• Changes consistent with hepatopathy or hepatitis	• Any organ system
• Gall bladder sludge without a discrete mucocele or obstuction	**2. Severe lymphatic enlargement**
2. Kidney	• Not consistent with metastasis on cytology
• Degenerative renal changes	**3. Severe Ascites**
3. Gastrointestinal tract	**4. Gallbladder Mucocele**
• Lumen changes consistent with IBD, enteritis, colitis, or gastritis with no mass effect	
4. Pancreas	
• Parenchymal changes consistent with current or previous pancreatitis	
5. Reproductive	
• Prostatic enlargement consistent with benign prostatic hyperplasia	
6. Urinary	
• Calculi	

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Thorax: Radiographic or Computed Tomographic Scan	
Minor	**Major**
7. Adrenal	
• Adrenomegaly, not referred to as an adrenal mass	
8. Lymph nodes	
• Mild lymph node enlargement described as reactive	
9. Spleen	
• Nodules specifically described as myelipomas	
• Enlarged appearance specifically described as being secondary to sedation	

Table 2:

Prevalence of metastasis and incidental findings diagnosed with thoracic screening per tumor histology and size. Risk of diagnosis for different tumor histologies and size was calculated using odds ratios (OR). For OR calculation, tumors with similar biologic behavior were evaluated together, and are shown with a grey header. Individual tumor types that contributed to each group are shown below the grey header. When no OR is listed it could not be calculated. Protective OR (confidence interval) are shown in green, when an CI included 1 it is not highlighted, and OR (CI) that were at increased risk are shown in red. Significance OR ($p<0.05$) are bolded and **.

Tumor Histology (Number that thoracic imaging)	Pulmonary metastasis	Minor Incidental Finding	Major Incidental Finding
Odontogenic	1%	53.30%	1%
(N=105)	(1/105)	(56/105)	(1/105)
*** Reference for OR**			
CAA	0%	55.90%	1.70%
(N=59)	(0/59)	(33/59)	(1/59)
POF	0%	47.60%	0%
(N=42)	(0/42)	(20/42)	(0/42)
Other	25%	75%	0%
(N=4)	(1/4)[+]	(3/4)	(0/4)
Ameloblastic carcinoma	0%	60%	0%
(N=5)	(0/5)	(3/5)	(0/5)
*excluded from OR anlaysis			
Conventional OSCC	2%	47.10%	2%
(N=51)	(1/51)	(24/51)	(1/51)
	OR: 2.08 (0.1,33.9)	OR: 0.78 (0.4,1.5)	OR: 2.08 (0.1,33.9)
Tonsillar SCC	0%	50%	0%
(N=2)	(0/2)	(1/2)	(0/2)
*excluded from OR anlaysis			
Other Variants of OSCC	0%	46.20%	0%
(N=13)	(0/13)	(6/13)	(0/13)
		OR: 0.75 (0.2,2.4)	
Papillary SCC	0%	45.50%	0%
(N=11)	(0/11)	(5/11)	(0/11)
Basaloid SCC	0%	50%	0%
(N=2)	(0/2)	(1/2)	(0/2)
OMM	13.90%	58.30%	4.20%
(N=72)	(10/72)	(42/72)	(3/72)
	OR: 16.77 (2.1,134.2)**	OR: 1.23 (0.7,2.2)	OR: 4.52 (0.5,44.4)

Tumor Histology (Number that thoracic imaging)	Pulmonary metastasis	Minor Incidental Finding	Major Incidental Finding
Soft tissue sarcoma and mesenchymal tumors (N=61)	1.60% (1/61) OR: 1.73 (0.1,28.2)	44.30% (27/61) OR: 0.69 (0.4,1.3)	0% (0/61)
OFSA (N=41)	0% (0/41)	46.30% (19/41)	0% (0/41)
Undifferentiated sarcoma (N=15)	6.70% (1/15)	40% (6/15)	0% (0/15)
Other (N=6)	0% (0/6)	33.30% (2/6)	0% (0/6)
Osteosarcoma (N=29)	6.90% (2/29) OR:7.7 (0.7,88.2)	41.40% (12/29) OR: 0.62 (0.3,1.4)	0% (0/29)
MLO (N=11)	27.30% (3/11) **OR: 39** (3.6,419.1)**	54.50% (6/11) OR: 1.05 (0.1,3.6)	9.1 (1/11) OR: 10.4 (0.6,179.2)
Round cell tumors (N=6)	0% (0/6)	33.30% (2/6) OR: 0.44 (0.1,2.5)	16.70% (1/6) **OR: 20.8** (1.1,383.1)**
Infiltrative Lipoma (N=1) *exluded from OR analysis	0% (0/1)	100% (1/1)	0% (0/1)
Lymphoma (N=2)	0% (0/2)	100% (2/2)	0% (0/2)
Mast Cell tumor (N=4)	0% (0/4)	0% (0/4)	25% (1/4)
Plasma Cell tumor (N=9)	0% (0/9)	88.90% (8/9) OR: 7 (0.8,58)	0% (0/9)
Fibro-osseous lesion (N=6)	0% (0/6)	33.30% (2/6) OR: 0.44 (0.1,2.5)	0% (0/6)
Tumor Size (Number that had thoracic imaging)			
T0 (N=7)	0% (0/7)	100% (7/7)	0% (7/7)

Tumor Histology (Number that thoracic imaging)	Pulmonary metastasis	Minor Incidental Finding	Major Incidental Finding
T1	1.70%	48.80%	1.70%
(N=121)	(2/121)	(59/121)	(2/121)
**** Reference for OR**			
T2	4.50%	48.30%	2.20%
(N=89)	(4/89)	(43/89)	(2/89)
	OR: 2.8 (0.5,15.7)	OR: 0.96 (0.6,1.7)	OR: 1.37 (0.2,9.9)
T3	9.20%	58.50%	1.50%
(N=65	(6/65	(38/65)	(1/65)
	OR: 5.95 (1.2,30.4)**	OR: 1.44 (0.8,2.7)	OR: 0.91(0.1,10.3)

Abbreviations: CAA: canine acanthamatous ameloblastoma, **POF**: peripheral odontogenic fibroma, **CEOT**: calcifying epithelial odontogenic tumor, **OSCC**: Oral squamous cell carcinoma, **OMM:** oral malignant melanoma, **OFSA:** oral fibrosarcoma. Other odontogenic tumors included CEOT (N=1), odontoma (N=1), ameloblastic fibroma (N=1), giant cell epulis (N=1)$^{+}$ tumor with pulmonary metastasis. Other mesenchymal tumors included hemangiosarcoma (N=1), myxosarcoma (n=2), peripheral nerve sheath tumor (N=2), and fibroma (n=1). Fibroma was excluded for OR analysis for mesenchymal tumors.

Table 3:

Prevalence of Incidental Findings Documented with Thoracic Imaging

Minor Incidental Findings		
	Prevalence	**Comments**
Orthopedic abnormalities	25.6% (95/371)	
Bronchointerstitial Pattern	8.6% (32/371)	
Pulmonary Osteomas	10.2% (38/371)	
Fibrosis	5.4% (20/371)	
Atrial enlargement without congestive heart failure	9 (2.4%) (38/371)	
Pulmonary Bulla	3.2% (12/371)	
Subcutanoues mass	6.7% (25/371)	
Other	9.2% (34/371)	Redundant tracheal membrane, emphysema, developmental anomalies, mild sternal or mediastinal lymph node enlargement
Major Incidental findings		
Secondary intrathoracic mass		Mediastinal mass (3), heart based mass (1), primary lung mass (1), thickening/mass effect plerua (1)
Osseous lytic lesion		Rib lesion (1)

Table 4:
Diagnostic yield of thoracic radiographs versus thoracic CT scan.

Tumor histologies and size information included for comparison between anticipated biologic behavior of the tumors in both groups.

	Pulmonary metastasis	Suspicious lesion	Minor incidental finding	Major incidental finding	Tumor histology	Tumor size
Thoracic radiographs (N=143) *size in EMR for 111 patients	3.5% (5/143)	3.5% (5/143)	40.6% (58/143)	0.7% (1/143)	Odontogenic: 20.2% (29/143) Non-odontogenic: 79.8% (114/143) *21.6% OMM (31/143)	T0: 3.6% (4/111) T1: 36% (40/111) T2: 34.2% (38/111) T3: 26.1% (29/111)
Thoracic CT scan (N=228) * size in EMR for 171 patient	5.7% (13/228)	3.9% (9/228)	57.9% (132/228)	2.6% (6/228)	Odontogenic: 37.7% (86/228) Non-odontogenic: 62.3% (142/228) * 18% OMM (41/228)	T0: 1.8% (3/171) T1: 47.4% (81/171) T2: 29.8% (51/171) T3: 21 % (36/171)

Table 5:

Prevalence of metastasis and incidental findings diagnosed with AUS per tumor histology and size.

Risk of diagnosis for different tumor histologies and size was calculated using odds ratios (OR). Factors evaluated in OR calculation are shown in gray. For OR calculation, tumors with similar biologic behavior were evaluated together, and are shown under a grey header. Individual tumor types that made up each subtype are shown below the grey header. When no OR is listed it could not be calculated. Protective OR (confidence interval) are shown in green, when an CI included 1 it is not highlighted, and OR (CI) that were at increased risk are shown in red. Significance OR ($p<0.05$) are bolded and **.

Tumor Histology (Number that had AUS)	Abdominal metastasis	Minor Incidental Finding	Major Incidental Finding
Odontogenic	0%	72.30%	8.50%
(N=94)	−0.94	(68/94)	(8/94)
*** Reference for OR**			
CAA	0%	75%	7.70%
(N=52)	(0/52)	(39/52)	(4/52)
POF	0%	66.70%	10.30%
(N=39)	(0/39)	(26/39)	(4/39)
Other	0%	100%	0%
(N=4)	(0/4)	(4/4)	(0/4)
Ameloblastic carcinoma	0%	40%	0%
(N=5)	(0/5)	(2/5)	(0/5)
*excluded from OR anlaysis			
Conventional OSCC	2.60%	78.90%	2.60%
(N=38)	(1/38)	(30/38)	(1/38)
		OR: 1.43 (0.6,3.5)	OR: 0.29 (0,2.4)
		p=0.433	p=0.252
Tonsillar SCC	0%	100%	100%
(N=1)	(0/1)	(1/1)	(1/1)
*excluded from OR anlaysis			
Other Variants of OSCC	0%	44.40%	0%
(N=9)	(0/9)	(4/9)	(0/9)
		OR: 0.31 (0.1,1.2)	
		p=0.095	
Papillary SCC	0%	50%	0%
(N=8)	(0/8)	(4/8)	(0/8)
Basaloid SCC	0%	0%	0%
(N=1)	(0/1)	(0/1)	(0/1)

Tumor Histology (Number that had AUS)	Abdominal metastasis	Minor Incidental Finding	Major Incidental Finding
OMM **(N=57)**	5.30% (3/57)	82.50% (47/57) OR: 1.8 (0.8,4.1) p=0.16	14% (8/57) OR:1.76 (0.6,5) p=0.29
Soft tissue sarcoma and mesenchymal tumors **(N=42)**	4.80% (2/42)	73.80% (31/42) OR: 1.08 (0.5,2.5) p=0.859	4.80% (2/42) OR: 0.54 (0.1,2.6) p=0.445
OFSA (N=29)	3.40% (1/29)	82.80% (24/29)	3.40% (1/29)
Undifferentiated sarcoma (N=10)	10% (1/10)	50% (5/10)	10% (1/10)
Other (N=6)	0% (0/6)	50% (3/6)	0% (0/6)
Osteosarcoma **(n=21)**	0% (0/21)	66.70% (14/21) OR: 0.76 (0.3,2.1) p=0.604	9.50% (2/21) OR: 1.13 (0.2,5.8) p=0.882
MLO **(N=9)**	0% (0/9)	77.80% (7/9) OR: 1.34 (0.3,6.9) p=0.727	0% (0/9)
Round cell tumors **(N=5)**	0% (0/5)	60% (3/5) OR: 0.57 p=0.555	0% (0/5)
Infiltrative Lipoma (N=1) *exluded from OR analysis	0% (0/1)	100% (1/1)	0% (0/1)
Lymphoma (N=2)	0% (0/2)	100% (2/2)	0% (0/2)
Mast Cell tumor (N=3)	0% (0/3)	33.30% (1/3)	0% (0/3)
Plasma Cell tumor **(N=7)**	0% (0/7)	71.40% (5/7) OR: 0.96 (0.2,5.2)	0% (0/7)

Tumor Histology (Number that had AUS)	Abdominal metastasis	Minor Incidental Finding	Major Incidental Finding
		p=0.959	
Fibro-osseous lesion	0%	66.70%	16.70%
(N=6)	(0/6)	(4/6)	(1/6)
		OR: 0.76 (0.1,4.4)	OR: 2.15 (0.2,20.7)
		p=0.765	p=0.508
Tumor Size (Number that had abdominal imaging)			
T0	0%	100%	0%
(N=6)	(0/6)	(6/6)	(0/6)
T1	1.80%	70%	7.30%
(N=110)	(2/110)	(77/110)	(8/110)
**** Reference for OR**			
T2	0%	76.10%	5.60%
(N=71)	(0/71)	(54/71)	(4/71)
		OR: 1.33 (0.7,2.7)	OR:0.89 (0.2,3.2)
		p=0.429	p=0.861
T3	4.90%	68.30%	17.10%
(N=41)	(2/41)	(28/41)	(7/41)
	OR: 2.76 (0.4,20.3)	OR: 0.85 (0.4,1.9)	OR:3.03 (1.9,3)
	p=0.318	p=0.678	p=0.052

Abbreviations: CAA: canine acanthamatous ameloblastoma, **POF**: peripheral odontogenic fibroma, **CEOT**: calcifying epithelial odontogenic tumor, **OSCC**: Oral squamous cell carcinoma, **OMM:** oral malignant melanoma, **OFSA:** oral fibrosarcoma. Other odontogenic tumors included CEOT (N=1), odontoma (N=1), ameloblastic fibroma (N=1), giant cell epulis (N=1). Other mesenchymal tumors included hemangiosarcoma (N=1), myxosarcoma (n=2), peripheral nerve sheath tumor (N=2), and fibroma (n=1). Fibroma was excluded for OR analysis for mesenchymal tumors.

Table 6:

Prevalence of Incidental Findings Documented with AUS

Minor Incidental Findings		
Organ System	**Prevalence**	**Comments**
Liver	36.9% (107/295)	
Kidney	34.6% (102/295)	
Spleen	36.3% (107/295)	
GI Tract	10.2% (30/295)	
Pancreas	7.8% (23/295)	
Reproductive Organs	7.5% (22/295)	
Urinary	10.2% (20/295)	
Adrenal	17.3% (51/295)	
Lymph Nodes	8.1% (24/295)	
Major Incidental findings		
Secondary abdominal mass	6.1% (18/295)	Testicular mass (4), ovarian mass (1), splenic mass (2), liver mass (4), kidney mass (1), bladder mass (1), adrenal nodule (3), adrenal mass (2)
Biliary disease	1% (3/295)	Mucocele (2), biliary obstruction (1)
Other	0.5% (2/295)	Kidney agenesis (1), Active cholangiohepatitis (1)

Table 7:

Diagnostic yield of all screening tests

	Head CT (N=348)	Cervical Staging (N=358)	Thorax (N=371)	Abdomen (N=295)
Metastasis	-	7.5% (27/358) * Cytologically confirmed:12.8% (21/164)	4.9% (18/371)	2% (6/295) *Cytological confirmed: 0.3% (2/295)
Incidental Finding	65.2% (227/348)	-	53.1% (197/371)	81.3% (240/295)
Major	4.6% (16/348)	-	1.9% (7/371)	7.8% (23/295)
Minor	60.6% (211/348)	-	51.2% (190/371)	73.6% (217/295)
Major *or* Metastasis *only counted once even if both present	4.6% (16/348)	7.5% (27/358)	5.9% (22/371)	9.5% (28/295)