Modified Weber-Fergusson approach for caudal maxillectomy and infraorbitotomy in dogs and cats

Kazushi Asano, DVM, PhD, DJCVS; Kumiko Ishigaki, DVM; Takao Amaha, DVM; Chieko Ishikawa, DVM; Haruko Terui, DVM; Hiro Horikirizono, DVM; Keigo Iizuka, DVM; Takahiro Nagumo, DVM; Kei Tamura, DVM; Mamiko Seki, DVM, PhD, DJCVS.

Laboratory of Veterinary Surgery, Department of Veterinary Medicine, College of Bioresource Sciences, Nihon University, 1866 Kameino, Fujisawa, Kanagawa 252-0880, Japan

Introduction

The Weber-Fergusson approach was first described by Dr. Weber in German and later modified by Dr. Fergusson in English. It is one of the most commonly used transfacial approaches to the midface for the resection of maxillary and infraorbital tumors in humans. However, the original Weber-Fergusson approach is not available for canine or feline radical maxillectomy because the morphology of human skull is totally different from that of small animal’s skull. The objective of this clinical study was to describe the procedure of modified Weber-Fergusson approach for the surgical removal of caudal maxillary and infraorbital masses in dogs and cats.

Materials and Methods

Fourteen dogs and 3 cats with caudal maxillary and/or infraorbital masses were included in this study. All patients underwent the caudal maxillectomy and/or infraorbitotomy with the modified Weber-Fergusson approach (Figures 2 & 3).

Results (Table)

The modified Weber-Fergusson approach was feasible in all patients. Postoperative necrosis in the tip of buccolabial flap was observed in 1 cat with aspergillosis. Refractory oronasal fistula occurred in 2 dogs with SCC and 1 dog ameloblastic fibroma. In the patients with tumor, histopathological clean margin was obtained in 9/12 dogs and 2/2 cats.

Conclusion

The modified Weber-Fergusson approach is suggested to provide better exposure and outcomes for canine and feline caudal radical maxillectomy and infraorbitotomy.

<table>
<thead>
<tr>
<th>#</th>
<th>Animal</th>
<th>Breed</th>
<th>Gender</th>
<th>Age (y-o)</th>
<th>BW (kg)</th>
<th>Diagnosis</th>
<th>Margin</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Dog</td>
<td>Golden retriever</td>
<td>M</td>
<td>10</td>
<td>34.5</td>
<td>Malignant melanoma</td>
<td>Dirty</td>
</tr>
<tr>
<td>2</td>
<td>Dog</td>
<td>Beagle</td>
<td>M</td>
<td>15</td>
<td>11.3</td>
<td>Malignant melanoma</td>
<td>Clean</td>
</tr>
<tr>
<td>3</td>
<td>Dog</td>
<td>Pembroke Welsh Corgi</td>
<td>F</td>
<td>14</td>
<td>9.9</td>
<td>Fibrosarcoma</td>
<td>Clean</td>
</tr>
<tr>
<td>4</td>
<td>Dog</td>
<td>Pembroke Welsh Corgi</td>
<td>F</td>
<td>11</td>
<td>12.5</td>
<td>Malignant melanoma</td>
<td>Clean</td>
</tr>
<tr>
<td>5</td>
<td>Dog</td>
<td>Toy poodle</td>
<td>F</td>
<td>11</td>
<td>3.0</td>
<td>Malignant melanoma</td>
<td>Clean</td>
</tr>
<tr>
<td>6</td>
<td>Dog</td>
<td>Border collie</td>
<td>F</td>
<td>7</td>
<td>19.0</td>
<td>SCC</td>
<td>Clean</td>
</tr>
<tr>
<td>7</td>
<td>Dog</td>
<td>Miniature Dachshund</td>
<td>M</td>
<td>16</td>
<td>6.9</td>
<td>Malignant melanoma</td>
<td>Dirty</td>
</tr>
<tr>
<td>8</td>
<td>Dog</td>
<td>Toy poodle</td>
<td>M</td>
<td>11</td>
<td>6.5</td>
<td>Malignant melanoma</td>
<td>Clean</td>
</tr>
<tr>
<td>9</td>
<td>Dog</td>
<td>Maltese</td>
<td>M</td>
<td>11</td>
<td>5.0</td>
<td>SCC</td>
<td>Clean</td>
</tr>
<tr>
<td>10</td>
<td>Dog</td>
<td>Miniature Dachshund</td>
<td>M</td>
<td>14</td>
<td>5.9</td>
<td>Malignant melanoma</td>
<td>Clean</td>
</tr>
<tr>
<td>11</td>
<td>Dog</td>
<td>Labrador retriever</td>
<td>M</td>
<td>12</td>
<td>20</td>
<td>Malignant melanoma</td>
<td>Clean</td>
</tr>
<tr>
<td>12</td>
<td>Dog</td>
<td>Chiwahua</td>
<td>M</td>
<td>8</td>
<td>2.3</td>
<td>Odontogenic cyst</td>
<td>Clean</td>
</tr>
<tr>
<td>13</td>
<td>Dog</td>
<td>English Springer Spaniel</td>
<td>M</td>
<td>13</td>
<td>20.6</td>
<td>Ameloblastic fibroma</td>
<td>Clean</td>
</tr>
<tr>
<td>14</td>
<td>Dog</td>
<td>Mix</td>
<td>F</td>
<td>13</td>
<td>12.5</td>
<td>SCC</td>
<td>Dirty</td>
</tr>
<tr>
<td>15</td>
<td>Cat</td>
<td>Mix</td>
<td>F</td>
<td>17</td>
<td>3.1</td>
<td>Osteosarcoma</td>
<td>Clean</td>
</tr>
<tr>
<td>16</td>
<td>Cat</td>
<td>Mix</td>
<td>F</td>
<td>6</td>
<td>3.3</td>
<td>Aspergillosis</td>
<td>Dirty</td>
</tr>
<tr>
<td>17</td>
<td>Cat</td>
<td>Mix</td>
<td>M</td>
<td>11</td>
<td>4.7</td>
<td>Malignant melanoma</td>
<td>Clean</td>
</tr>
</tbody>
</table>
Outcome After Radical Mandibulectomy for the Treatment of Oral Neoplasia in Seven Cats

Boston, SE, Wavreille V, Bacon NJ, Szentimrey D, van Nimwegan SA, Kirby, B, van Stee LL

Introduction

Oral neoplasia and specifically, squamous cell carcinoma (SCC) is a devastating disease in cats. It is a locally aggressive disease. The current literature suggests that cats do not do well after extensive mandibulectomy and also that a feeding tube should be placed after mandibulectomy in cats to provide postoperative support to these patients. The authors have had clinical experiences that are contrary to the current literature, with cats seeming to adjust to radical mandibulectomy and experiencing a good quality of life post operatively.

Our objective was to report the outcome after radical mandibulectomy in cats. We hypothesized that most cats that have a radical mandibulectomy will eat post operatively and have a good quality of life, with some long-term survivors.

Materials and Methods

This was a multi-institutional retrospective case series. Cats were included if they had confirmed mandibular neoplasia and were treated with a radical mandibulectomy. Radical mandibulectomy was defined as the removal of >50% of the entire mandible. Case information including signalment, preoperative work up and treatments, surgical procedure performed, histopathology results, perioperative complications, outcome and survival were recorded.

Cats were considered to be eating on their own if they did not require a supplementary feeding tube long-term.

Results

- Seven cats were included
- All cats had extensive mandibular tumours
- All cats had 75-90% of the entire mandible removed
- All cats had feeding tubes placed immediately after surgery
- 5 cats were eating within 3 days to one month of surgery
- 2 cats required long-term feeding
- 2 cats developed local recurrence and tumour-related deaths
  - ST: 136 and 291 days
  - 4 cats had no recurrence
  - ST: 118* (still alive), 465, 608 and 1023 days
  - 3 dead died of other causes
  - 1 died of aspiration 156 days post operatively
- MST 291 days

Discussion

- Good long-term outcomes are possible after radical mandibulectomy
- The two cats that experienced local recurrence had worse outcomes for survival and requirements for nutritional support.
- 4/5 cats that did not experience local recurrence all ate on their own and had good long term outcomes.
- In most cases, radical mandibulectomy in cats is by nature a marginal excision.
- The procedure provides palliation and, in our experience, most cats will eat on their own in most cases.
- A feeding tube and aggressive pain management are recommended post operatively to support the patient and avoid perioperative complications.

Study Limitations: This is a small number of cats, which is inherent in the fact that this procedure is rarely performed due to our current understanding in the literature.

Scientific or Clinical Relevance: Radical mandibulectomy should be considered for the treatment of oral neoplasia, most commonly SCC in cats. Although previous reports suggest that the morbidity of this procedure is too high, successful outcomes are possible with aggressive supportive care

<table>
<thead>
<tr>
<th>Case #</th>
<th>Age (yrs)</th>
<th>Breed</th>
<th>Sex</th>
<th>Histopath</th>
<th>% of Mandible Removed</th>
<th>Eating Post Operatively</th>
<th>Survival Time (days)</th>
<th>Cause of Death</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>17</td>
<td>DLH</td>
<td>MC</td>
<td>SCC</td>
<td>75%</td>
<td>Y - 14 days</td>
<td>465</td>
<td>Lymphoma</td>
<td>N</td>
</tr>
<tr>
<td>2</td>
<td>11</td>
<td>DSH</td>
<td>FS</td>
<td>SCC</td>
<td>90%</td>
<td>Y</td>
<td>608</td>
<td>Renal Failure</td>
<td>N</td>
</tr>
<tr>
<td>3</td>
<td>14</td>
<td>DLSH</td>
<td>MC</td>
<td>SCC</td>
<td>90%</td>
<td>Y - 1 month</td>
<td>136</td>
<td>Recurrence</td>
<td>Y</td>
</tr>
<tr>
<td>4</td>
<td>13</td>
<td>DSH</td>
<td>FS</td>
<td>SCC</td>
<td>75%</td>
<td>Y - 3 days</td>
<td>1023</td>
<td>Euthanized</td>
<td>N</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>DSH</td>
<td>MC</td>
<td>SCC</td>
<td>75%</td>
<td>N</td>
<td>291</td>
<td>Recurrence</td>
<td>Y</td>
</tr>
<tr>
<td>6</td>
<td>8</td>
<td>DSH</td>
<td>MC</td>
<td>GCT</td>
<td>75%</td>
<td>11 days</td>
<td>118*</td>
<td>Still alive</td>
<td>N</td>
</tr>
<tr>
<td>7</td>
<td>16</td>
<td>DSH</td>
<td>FS</td>
<td>SCC</td>
<td>100%</td>
<td>N</td>
<td>156</td>
<td>Aspiration</td>
<td>N</td>
</tr>
</tbody>
</table>
Primary Omental Hemangiosarcoma in Five Dogs

Chu KL1, Dugat DR2, Nafe LA2

1Department of Veterinary Clinical Medicine, Veterinary Teaching Hospital, University of Illinois Urbana-Champaign
2Department of Veterinary Clinical Sciences, Center for Veterinary Health Sciences, Oklahoma State University

Introduction

Hemangiosarcoma is a malignant neoplasm of vascular endothelial cell origin that can occur in virtually any tissue and is more commonly seen in dogs, accounting for 0.3-2% of all canine tumors.1,2 The most common primary sites are the spleen, liver, heart, skin or subcutaneous tissue.3 Rare anatomic variants include, but are not limited to the lymph node, os penis, uterine stump, falciﬁrm ligament, tongue, urinary bladder and prostate. To the authors' knowledge, primary omental hemangiosarcoma is a rare and seemingly aggressive anatomic variant that has been sparsely reported in the veterinary literature. A multi-institutional retrospective study of 26 cases with feline visceral hemangiosarcoma reported primary omental hemangiosarcoma in 12% of their cases and is the only study identifying primary omental hemangiosarcoma in cats.3 There are only two reports of primary omental hemangiosarcoma occurring in dogs.2,4 Both studies are components of a larger study evaluating various forms of hemangiosarcoma. Ogilvie et al. indicated the omentum as the site of origin in three or less cases and Hammer et al. identiﬁed an omental hemangiosarcoma in one case.

Materials and Methods

Medical records from five dogs that were diagnosed with omental hemangiosarcoma were collected retrospectively from the Oklahoma State University Center for Veterinary Health Sciences over a 7-year period between 2009 and 2016. Follow up was obtained by reviewing medical records, or contacting the referring veterinarian or the owner. Information including clinical features, diagnostic tests, treatments and outcomes were collected.

Results

Two dogs were presented for signs of urinary obstruction, two dogs were presented for signs of colonic obstruction, and one dog was asymptomatic. A complete blood count and biochemistry was performed on each dog at the time of presentation and revealed a mild anemia in four dogs and a thrombocytopenia in two dogs. All dogs exhibited disease consistent with advanced clinical stage (stage II or higher). One dog demonstrated presumed gross pulmonary metastasis at the time of presentation. Computed tomography was performed in three dogs, consistently revealing a well circumscribed, peripherally enhancing mass in the caudal abdomen that was displacing other local abdominal organs. Surgical exploration in all dogs revealed a caudal abdominal mass that did not appear to be associated with any other abdominal organs, except the omentum. Successful removal was achieved in four dogs, and surgical debulking was performed in one dog. Histopathologic features of the excised omental hemangiosarcomas are summarized in Table 1. One dog underwent adjuvant chemotherapy and survived 170 days post-surgery. Adjunctive therapy was not pursued in the other four dogs. Survival time in three of these dogs ranged from 50-120 days; survival time in one dog could not be obtained.

Discussion

In dogs, primary omental hemangiosarcoma is a rare anatomic variant that presents with an advanced clinical stage at the time of diagnosis, and is usually manifested with consequences of an obstructive mass affecting local organs, such as an acute onset of dysuria or constipation. The origin of these masses is difﬁcult to determine using traditionally employed diagnostic imaging modalities. Surgical intervention can be complicated by adhesion formation or invasion to adjacent structures, speciﬁcally to the ureters, urinary bladder and pelvic canal. Clinical outcome appears to be poor, as with splenic hemangiosarcoma. Post-chemotherapy survival time was only available for one dog, which was consistent with survival times reported in studies evaluating surgery with adjunctive doxorubicin chemotherapy in dogs with splenic hemangiosarcoma (MST, 150-172 days).6,7 Dogs that did not undergo adjuvant chemotherapy expressed survival times comparable to dogs with splenic hemangiosarcoma treated with splenectomy alone (MST, 48 days).8 Further studies assessing a larger number of cases are needed to more completely describe the clinical features, biological behavior, and clinical outcome of this anatomic variant with comparison to more common forms of hemangiosarcoma.

References


Table 1. Summary of histopathologic features of primary omental hemangiosarcomas excised from 5 dogs

<table>
<thead>
<tr>
<th>Dog</th>
<th>Cellular pleomorphism</th>
<th>Mitotic count</th>
<th>Necrosis</th>
<th>Other features</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Marked</td>
<td>12</td>
<td>-</td>
<td>Multiple bizarre mitoses</td>
</tr>
<tr>
<td>2</td>
<td>Marked</td>
<td>10</td>
<td>Moderate</td>
<td>Regions of thrombosis</td>
</tr>
<tr>
<td>3</td>
<td>Moderate</td>
<td>0-1</td>
<td>Marked</td>
<td>Extensive hemorrhage</td>
</tr>
<tr>
<td>4</td>
<td>Marked</td>
<td>24</td>
<td>Marked</td>
<td>Cytoplasmic immunoreactivity with vWF</td>
</tr>
<tr>
<td>5</td>
<td>Marked</td>
<td>4</td>
<td>Marked</td>
<td>-</td>
</tr>
</tbody>
</table>
Correlation of Optical Coherence Tomographic and Histologic Appearance of Artifacts cause by Surgical Instrumentation during Tumor Resection


Department of Veterinary Clinical Medicine, University of Illinois at Urbana-Champaign
Department of Electrical, Computer Engineering, and Bioengineering, University of Illinois at Urbana-Champaign

Introduction

Optical coherence tomography (OCT) has been reported for intraoperative surgical margin assessment in human breast cancer and canine soft tissue sarcoma surgery. OCT provides high-resolution imaging of microscopic tissue in real-time to allow for surgical margin assessment. The use of common surgical instrumentation carries the risk of causing microscopic tissue damage that may alter the appearance of tissues by OCT imaging. To date, there has been no investigation of the OCT imaging appearance of surgical artifacts. These artifacts must be recognized during the evaluation process to increase the sensitivity and specificity of cancer margin imaging. The objective of this study was to correlate the OCT imaging with histologic appearance of artifacts caused by common surgical instrumentation in different tissues at surgical margins.

Materials and Methods

Skin, subcutaneous fat, muscle, and fascial samples were utilized from fresh canine cadavers. The areas were prepared for artifact infliction and subsequently histologically processed. OCT images were directly compared to histopathology sections to formulate a training set.

Results

- **Blood staining** - created high scattering at the tissue surface and reduction in the depth of penetration (Figure 1); lost during tissue processing for histopathology.
- **Crushing injury** - created irregular, scalloped appearance to the tissue surface with focal, high-scattering regions (Figure 2).
- **Scalpel blade** - created focal, low-scattering regions (Figures 3 A,B).
- **Monopolar electrosurgery** - created a highly irregular tissue margin with multifocal high-scattering regions becoming brighter with increasing power (Figures 4 A,B).
- **LigaSure™** - created a contiguous low-scattering region at the tissue surface with an underlying moderate scattering region (Figure 5).
- **Harmonic scalpel** - created a coarse, undulating appearance to the tissue margin.

Discussion

The surgical instrumentation used in this study resulted in the production of appreciable microscopic imaging changes which could be characterized with OCT imaging. Notably, more significant changes were seen with the use of higher power monopolar electrosurgery and LigaSure™. Knowledge of the appearance of tissues following the use of different commonly used surgical instrumentation is essential to help increase the diagnostic accuracy of surgical margin assessment and guided pathologic interrogation for both canine and human cancer margin evaluation.

References

Introduction
Standard of care for many head and neck solid tumors in both human and veterinary medicine is surgical removal. Sentinel lymph node (SLN) mapping is often used for staging. Goggle augmented imaging and navigation systems (GAINS) is a wearable intraoperative system that perceives real-time fluorescence and aids in detection of both tumors and SLNs. This system detected tumors in subcutaneous and metastatic mouse models with 100% sensitivity and 98% +/- 5% specificity. Human pilot studies in breast cancer and melanoma patients show that GAINS detected SLNs with 100% sensitivity. This is the first trial evaluating GAINS in the dog.

In this pilot study, we hypothesized that the GAINS intraoperative system will aid in detection of the SLNs for both canine head and neck tumors.

Materials and Methods
Three dogs were enrolled who were previously diagnosed with a malignant head or neck tumor: squamous cell carcinoma (SCC, 1), histiocytic sarcoma (1), and melanoma (1). Once placed under general anesthesia prior to surgical preparation, the patient was administered indocyanine green (ICG). The dye was injected in a four-quadrant approach around the tumor site(s).

The first two patients were administered a total of 0.2mg (0.5mg/mL) of ICG and the third patient was administered a total of 0.02mg (0.025mg/mL). A midline cervical incision was made to perform bilateral mandibular and medial retropharyngeal lymphadenectomy (figure 1). Lymph nodes were examined grossly for dye uptake and were examined using GAINS in-vivo (figure 1, 2 & 3). No surgical complications or adverse effects were appreciated with dye use.

Results
In each dog 1, 2, and 4 lymph nodes had ICG dye uptake. For two of the tumor types (SCC and histiocytic sarcoma) only the ipsilateral lymph node(s) were affected and for one of the tumor types (melanoma) all four of the lymph nodes had uptake. On histopathology none of the submitted lymph nodes had appreciable metastasis.

The GAINS pilot study was successful in identifying the SLNs in dogs with head and neck neoplasia at the subcutaneous level. Different doses of the ICG dye were tried to optimize detection of fluorescence by the imaging system and further dose studies are planned.

Discussion
Clinical feasibility and surgeon comfort using GAINS was demonstrated in this trial. Fluorescence was successfully visualized and superimposed on the normal color vision of 7 sentinel lymph nodes with the augmented reality system. The optimization of ICG dilution for this camera and goggle system needs to be further evaluated in dogs.

References

Acknowledgements
- The University of Illinois cancer care clinic staff
- The Engineering Team from the Department of Electrical and Computer Engineering, University of Illinois Urbana-Champaign, Urbana, IL, USA

Figure 1: Surgical removal of the right mandibular lymph node. There is apparent uptake of the ICG dye within this lymph node after peritumoral injection.

Figure 2: Placement of the googles for the GAINS prior to surgery.

Figure 3: Intraoperative image of the superimposed fluorescence over the SLN as seen through the GAINS.
Analysis of Risk Factors associated with Common Complications following Mandibulectomy and Maxillectomy Procedures in Cats and Dogs
Cray M, Selmic LE, Kindra C, Somrak A, Mandra Maretta S, Kling K

Department of Veterinary Clinical Medicine, College of Veterinary Medicine, University of Illinois at Urbana-Champaign

Introduction
Mandibulectomy and maxillectomy surgical procedures are most commonly indicated for the treatment of oral tumors. Complication rates of orofacial surgical procedures, specifically maxillectomies (figure 2) and mandibulectomies (figure 1 & 3), have been reported in veterinary literature. In a recently published manuscript the overall complication rate following curative-intent surgery for oral tumors in dogs was 16.2%.1 Reported surgical complications following mandibulectomy and maxillectomy include hemorrhage, aspiration pneumonia, dehiscence, mandibular drift, ranula formation, anorexia, nasal discharge, difficulty prehending, implant migration, fistula formation, and death.

To the authors' knowledge, risk factors associated with complications following orofacial surgery have not been identified in veterinary medicine. The objective of this study is to determine the occurrence of complications in cats and dogs undergoing mandibulectomy and maxillectomy procedures as well as to identify risk factors associated with these complications.

Materials and Methods
Eligible cases were collected retrospectively from the medical records of cats or dogs who had a mandibulectomy or maxillectomy procedure performed at the University of Illinois Veterinary Teaching Hospital between January 1st, 2007 and January 1st, 2018. Follow up was obtained either by the medical record at the authors' institution, contacting the referring veterinarian, or contacting the owner. Cats or dogs with incomplete medical records, no preoperative bloodwork, or did not have a minimum follow up of 90 days were excluded.

Statistical Analysis
Continuous data were assessed for normality using skewness, kurtosis, and Shapiro-Wilk tests. Frequencies and percentages were used to describe categorical data. A p-value of 0.05 was considered significant for these analyses. The analysis was performed using SAS version 9.4.a

Results
A total of 93 dogs (93.9%) and 6 cats (6.1%) were included. A mandibulectomy procedure was performed in 62 cases (62.6%) and a maxillectomy procedure was performed in 37 cases (37.4%). Complications included dehiscence (11.1%), infection (4.0%), mandibular drift (14.1%), anorexia (5.1%), dysphagia (5.1%), fistula formation (1.0%), and other (12.9%).

Age, weight, sex, species, neuter status, anesthetic time, hospitalization, pre-operative albumin level, presence of neoplasia, and type of surgical procedure were not significantly associated with the development of perioperative complications. The size of the lesion trended toward significance for association with risk of development of complications (p=0.07).

Discussion
The goal of this study is to provide contemporary information about complication rates and the risk factors for complications with mandibulectomy and maxillectomy procedures. This information is essential to allow accurate estimation of risk for the patient and allow the clinician the ability to decrease risk of complications. Mandibular drift followed by incisional dehiscence were the most common complications encountered in this study. The larger the size of the lesion, the more likely complications were to occur in mandibulectomy and maxillectomy surgeries. Although this did not reach significance this may reflect the increased difficulty and risk with larger resections.

Limitations to this study include its retrospective nature, single geographic area, and small sample size. A larger, multi-institutional study is recommended to better evaluate perioperative complications and associated risk factors for the mandibulectomy and maxillectomy procedures.

References
Introduction

Oral neoplasia is thought to account for 6-7% of canine cancer and 3% of all feline cancers. The incidence of oral tumors has been reported to be 70.4 per 100,000 dogs and 45.4 per 100,000 cats. The most common oral malignancies in dogs are melanomas, squamous cell carcinomas, and fibrosarcomas. In cats, 69% of malignant oral tumors are squamous cell carcinomas (figure 3) and 18% are fibrosarcomas. Other oral tumor types that can be seen include osteosarcoma, acanthomatous ameloblastoma (figure 1 & 2), and peripheral odontogenic fibromas.

The epidemiology of oral tumors in dogs and cats has been assessed in several studies to date; however many are decades old and may not represent the epidemiology of this disease in a contemporary population. To the authors' knowledge the last epidemiologic analysis of general oral cancer in dogs and cats was published in 1976. Updated contemporary demographic information is important to determine the prevalence of a disease, monitor trends, and calculate incidence for canine and feline populations. The epidemiologic aspects of naturally occurring neoplasms provide valuable information for generation of hypotheses in future investigation of breed-based and pathology-based oral neoplastic studies.

Materials and Methods

Eligible cases were retrieved from a computer search of the VMDB for dogs and cats presented between January 1, 1996 and December 31, 2017. Dogs and cats were selected based upon diagnostic code which consisted of oral neoplasms. A diagnosis of pharyngeal neoplasm was excluded for the purpose of this study. A total of ten universities contained abstracts that met inclusion criteria for the purpose of this study. Duplicate cases as a result of multiple visits were eliminated.

Statistical Analysis

Continuous data were assessed for normality using skewness, kurtosis, and Shapiro-Wilk tests. Frequencies and percentages were used to describe categorical data. The analysis was performed using SAS version 9.4.

Discussion

Much of the data used to cite descriptive statistics in dogs and cats with oral neoplasia are decades old. This study reports contemporary demographic information regarding oral tumors in cats and dogs. These results provide valuable information for generation of hypotheses in future investigation of breed-based and pathology-based oral neoplastic studies.

Results

The incidence of oral tumors was calculated to be 4.9 cases per 1,000 dogs (0.5%) and 4.9 cases per 1,000 cats (0.5%). The median age in dogs diagnosed with an oral tumor was 10.0 years and the median age in cats diagnosed with an oral tumor was 12.8 years.

In dogs, the majority of the oral tumors, 962 cases, were classified as malignant (53.6%) and 455 cases were benign (25.4%). In cats, the majority of oral tumors were also classified as malignant (257 cases, 58.1%) and 11 cases were benign (2.5%). Table 1 summarizes the most common oral tumor locations in both dogs and cats. The majority of the cats in this study were nonspecific breeds (86.0% of cases). A total of 469 dogs (26.0% of cases) were composed of mixed breeds. The most commonly reported dog breeds with oral tumors included Labrador retrievers (234 cases, 13.0%), golden retrievers (201 cases, 11.1%), and boxers (58 cases, 3.2%).

References


Acknowledgements

• The University of Illinois cancer care clinic staff
• The Veterinary Medical Database and contributing universities
Salivary Neoplasia in Dog and Cats: 1996-2017
Cray M1, Selmic LE1, Ruple A

1 Department of Veterinary Clinical Medicine, College of Veterinary Medicine, University of Illinois at Urbana-Champaign
2 Department of Comparative Pathobiology, College of Veterinary Medicine, Purdue University

Introduction
Salivary gland tumors are uncommon in dogs and cats, with a reported overall incidence of 0.17% within salivary disease.1 In addition, salivary gland tumors compose less than 0.2% of tumors in dogs and cats.2 As this is a rare condition there is minimal information regarding salivary gland neoplasia in the veterinary literature and much of the descriptive data are decades old. Simple adenocarcinoma is reportedly the most common histopathological type of the salivary gland neoplasia in dogs and cats (figure 1 & 2).4

To the authors’ knowledge, breed disposition and location of salivary neoplasia has been sparsely described. In one earlier report spaniel breeds were indicated to have a possible predisposition.4 However, this finding has not been consistent in other reports.3 In one study Siamese cats appeared to be overrepresented, with 30% (9/30) of the affected cats with salivary neoplasia being Siamese or Siamese-cross.2 The parotid and mandibular salivary glands are reported to be most often affected and account for 75 to 90% of all salivary gland neoplasia. The zygomatic, sublingual, and minor salivary glands account for the remainder of the tumors.1,3

Materials and Methods

Case Selection
Eligible cases were retrieved from a computer search of the VMDB for dogs and cats presented from January 1, 1996 through December 31, 2017 that had the a specific diagnostic code relating to salivary neoplasia. For comparison a reference population was created through a separate search through the VMDB website. Eligible animals for the control group included dogs and cats presented from January 1, 1996 through December 31, 2017 that had the diagnostic code “dental abscess.” Each individual case of salivary neoplasia was then matched to two control subjects based on institution, species, discharge date +/- two years, and an age constraint-either the same age or older.

Statistical Analysis
Differences in demographics between the salivary neoplasia and control group were assessed with a Chi Square test. Conditional logistic regression was performed to assess for association of breed and sex with salivary carcinoma. A p-value of 0.05 was considered significant for these analyses. The analysis was performed using SAS version 9.4a and Stata.b

Results

A total of 227 dogs and cats were selected through the VMDB search based on their diagnostic code from six different veterinary universities. A total of 56 dogs and 20 cats were included in our statistical analysis with a total of 112 dogs and 40 cats selected as controls.

The overall incidence of salivary neoplasia was calculated to be 15.3 per 100,000 dogs and 26.3 per 100,000 cats. Table 1 summarizes the findings for location of salivary neoplasia. Indeterminate (major gland) was the most frequently reported neoplasia (59%). There was no breed disposition within the feline species for salivary neoplasia. In the conditional logistic regression, poodles (toy and standard) had an increased odds of salivary cancer compared to mixed breed dogs (OR 6.83, 95% CI: 1.2-40.1; p<0.075). No other dog breeds were found to be at increased risk.

<table>
<thead>
<tr>
<th>Location</th>
<th>Number of Cases</th>
<th>Percentage of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mandibular</td>
<td>3</td>
<td>4%</td>
</tr>
<tr>
<td>Parotid</td>
<td>4</td>
<td>5%</td>
</tr>
<tr>
<td>Sublingual</td>
<td>10</td>
<td>13%</td>
</tr>
<tr>
<td>Sublingual gland duct</td>
<td>13</td>
<td>17%</td>
</tr>
<tr>
<td>Indeterminate (major gland)</td>
<td>45</td>
<td>50%</td>
</tr>
<tr>
<td>Indeterminate (minor gland)</td>
<td>1</td>
<td>1%</td>
</tr>
</tbody>
</table>

Table 1. Distribution of salivary tumor location in dogs and cats.

Discussion

The goal of this study was to update descriptive statistics of salivary neoplasia using a much larger number of cases than has been previously reported. Results from the present study differ from previous conclusions made in regards to predisposed breeds, with poodles having an increased odds of salivary neoplasia in comparison to mixed breeds. The overall incidence of salivary neoplasia in dogs and cats is also less frequent than previously reported although direct comparison is difficult due to population selection. Additional epidemiological studies should be performed in veterinary medicine to help determine risk factors for salivary gland neoplasia.

Acknowledgements
- The University of Illinois cancer care clinic staff
- The Veterinary Medical Database and contributing universities
- Dr. Julius Liptak BVSc M VetClinStud FACVs DACVS DECVS for the salivary carcinoma photos

References
Lower Urinary Tract Transitional Cell Carcinoma in the Domestic Feline – Clinical Findings, Treatments, and Outcomes (91 Cases)

Griffin MA, Culp WTN, Giuffrida MA, Ellis P, Perry JA, Gedney A, Lux CN, Milovancev M, Wallace ML, Liptak JM, Selmic LE, Singh A, Palm CA, Balsa IM, Mayhew PD, Steffey MA, Rebhun RB, Burton JH, Kent MS

Veterinary Society of Surgical Oncology Meeting 2018 - Maui

Introduction
• Lower urinary tract neoplasia comprises approximately 2% of all canine malignancies. Transitional cell carcinoma (TCC) is the most prevalent urinary bladder cancer. Much information regarding TCC is known in dogs, including common anatomical locations, risk factors, treatment, and prognosis.
• Information regarding lower urinary tract neoplasia in cats is lacking, and the largest study to date only reports on 20 cases.
• Objective: To report the clinical characteristics, treatments, and outcomes in a cohort of cats diagnosed with TCC and to evaluate these variables for prognostic significance.

Materials and Methods
• Retrospective, multi-institutional study.
• Inclusion criteria: Feline patients with cytological or histopathological confirmation of TCC of the lower urinary tract.
• Variables were statistically analyzed to assess for significant differences.
• Median overall survival time (MST) was measured from date of presentation to death or last follow-up.

Results
• 91 cats (median age: 15 years) included
• 92.3% of cats had at least one clinical sign
  • Median duration of clinical signs: 30 days (IQR 9 - 105 days)
  • Common clinical signs: hematuria (59.3%), stranguria (49.5%), pollakiuria (47.3%)
  • Urethral disease extension occurred in 14% of cats

Discussion
• The large number of cases suggests that feline TCC may be more prevalent than previously suspected.
• Location of TCC appears to be more variable in cats than dogs and affects treatment decisions.
• Treatment options are varied and can improve prognosis.
• Plan: Continued data collection from other institutions (total number of cats included: 104), and regression analysis to determine differences in outcome based on treatments performed.
Introduction

Primary skull tumors in dogs are rare, with the most common tumors including osteosarcoma (OSA), osteoma, and multilobular osteochondrosarcoma (MLO). Presurgical planning, including advanced imaging, can aid in the identification of surgical margins but intraoperative resection remains challenging due to anatomic variations and surrounding vital structures, including brain parenchyma. Rapid prototyping and three-dimensional (3D) printing of patient-specific cutting guides may aid in intraoperative planning but are not well reported in veterinary medicine.

Hypothesis: Design and printing of the cutting guide will be possible in a time sensitive and cost-effective manner for canine patients diagnosed with primary skull tumors.

Materials and Methods

CT scans of dogs with skull tumors of primary bone origin were evaluated and a complete study with volume metadata and minimum slice thickness of 0.625mm was selected.

Cutting Guide Design:

Margins of the tumor were defined on CT using standard imaging software in a bone algorithm.

CT DICOM images were sent to CAMDT and imported into an STL editing software (MIMICS Materialise, Plymouth,MI) and digital 3D reconstructions were performed.

A margin of 5 mm was identified beyond the tumor in all lateral planes based on the previously defined tumor margins.

A cutting guide was designed using Ansys SpaceClaim by creating a 4mm thick outline from the previously identified margin, following the contour of the skull (to account for a 1mm burr diameter).

Two fixation points were created in areas of thick bone or overlying the nasal sinus.

The cutting guide file was then exported as an STL file for printing.

Cutting Guide Fabrication:

The cutting guide STL file was uploaded to a Formlabs Form 2 Stereolithography (SLA) printer. The SLA printer created a thin layer of grey resin followed by photopolymerization by laser to build the cutting guide layer by layer along with a resin support system that stabilized the print process.

The support lattice printed with the cutting guide was then removed to reveal the finished product (Figure 1).

The cutting guide was exposed to UV light to cure and stabilize the resin.

Cutting Guide Modification:

Practice cutting was performed with a High Performance Rotary tool and cutting bits to mimic the actual surgery.

Based on margins of the cut and ease of movement of the cutting tool, modifications were made.

Results

Based on this pilot study, with access to medical segmentation and computer aided design software (CAD), a cutting guide can be created and manufactured for $75-125CAD, not including labor costs. Cutting guide design takes <1 hour and a send out printing turnaround time of approximately 1 week. With access to an SLA printer, the cost of materials is ~$25 + 7 hours of print and processing time.

Discussion

Our results indicate that design and production of a sterilizable, patient-specific cutting guide is possible in a short time period with minimal cost, if there is access to an individual/team with digital design expertise, the applicable software and printing is outsourced. Initial investment for the printer ($5500) is high but this equipment is readily available in many academic institutions and medical grade printers or materials are not necessary. SLA printing was elected due to increased accuracy, better resolution (25µm layers) and reduction in defects compared to previously described techniques for printed cutting guides. Benefits of SLA include high temperature resistance, allowing autoclave or gas sterilization, depending on which resin is used.

The ability to create a surgical cutting guide for craniectomy will improve preoperative planning and repeatability of outcomes, and may decrease the risk of incomplete tumor resection. Being able to transfer preoperative planning directly into the surgical theater leads to increased surgeon confidence, which will likely decrease surgical time. In addition, consistent surgical resection will allow for placement of prefabricated customized implants at the time of the procedure.

In addition to cranial tumors, this process of creating a rapid prototyped patient-specific cutting guide can be applied to other complex oncology or orthopedic procedures that require accurate resection margins or customized implants.

Rapid prototyping and 3D printing of a patient-specific sterilizable cutting guide in canine patients with primary skull tumors is possible with access to STL software and training. The next step in this research will be the application of this guide in a clinical patient.

References:


This work was performed by Ontario Veterinary College Rapid Prototyping of Patient-Specific Implants for Dogs (RaPPID) Group (OVCRaPPID@gmail.com) and generously supported by:
Introduction

• The emergence of rapid prototyping technology has allowed for the development of patient-specific implants and cutting guides to assist in both the pre and intraoperative phases.
• Patient-specific rapid prototyped implants have been described for many applications in human patients, including the correction of dental and maxillofacial deformities. The use of this technology reduces surgery time1,2, speeds healing3, and improves clinical outcome2.
• In veterinary medicine, reports of rapid prototyping is limited to case studies or experimental studies, including the creation of a customized surgical plate for canine tibial plateau leveling osteotomy4, correction of a persistent hard palate defect5, the production of titanium mesh cages and plates (imbued with repair stimulating substances) to repair canine radial defects3, and most recently a feline titanium mandibular prosthesis6.

The purpose of this study was to determine the feasibility and workflow for creating and printing a patient-specific titanium skull plate for cranioplasty in dogs following craniectomy.

Materials and Methods

Computed tomography (CT) scans from patients admitted for craniectomy surgery were retrospectively evaluated and case selected for this pilot study

Image Capture

• Scans were included if they were available in a bone algorithm with high spatial resolution and 0.625-1.25mm slice thickness

Image Processing

• Digital imaging and Communications in Medicine (DICOM) format was used and the images were imported into Osirix.
• Images were evaluated in transverse, sagittal and coronal reconstructions and a medial, lateral, rostral, and caudal margin of the tumor was identified
• Tumor margins were determined based on agreement between an ACVR (AZ) and ACVS (MO) diplomate and a CSV file was generated.
• Once a virtual tumor margin was identified images were exported using a cloud based storage system.
• The DICOM images were 3D reconstructed using the segmented software Materialise Mimics 19
• STL files were generated using Materialise3-Matic 11
• Ansys SpaceClaim was used to import and smooth the CVS file generated in Osirix
• Geomagics Freeform was used to generate the virtual surgical margin cut with an additional 5mm margin of normal bone beyond the tumor margin

Plate Design

• STL files with the virtual surgical defect were imported into Renishaw Adept software
• With the assistance of the Renishaw design team, CAMDT engineer (JP) and ACVS diplomate the titanium plate was created. Criteria for plate design included:
  • Contour
  • Overlap
  • Thickness
  • Location and overlap
  • Fenestration size and placement
  • Fixation hole size and placement

Plate Printing

• STL surgical plate designs from Adept were imported into Renishaw QuanTam for 3D printer build preparation
• The plate was printed at The Additive Design in Surgical Solutions (ADEISS) Centre in London Ontario on a AM 400 Metal 3D printer in titanium

Discussion

Based on the findings of this study, with access to this technology and an individual/group with advanced expertise in CAD/segmentation software, patient-specific 3D printed titanium implants can be manufactured for patient use within a 4-week turnaround from diagnosis to surgery for canine patients undergoing cranioplasty.

References:

This work was performed by Ontario Veterinary College Rapid Prototyping of Patient-Specific Implants for Dogs (RaPPID) Group (OVCRaPPID@gmail.com) and generously supported by:
Diagnostic Efficiency of Ultrasound-Guided Aspiration of Medial Retropharyngeal Lymph Node and Predictive Computed Tomography Characteristics in Dogs

Kim C, Oblak ML, Nykamp S

Department of Clinical Studies – Ontario Veterinary College, University of Guelph

Abstract

Introduction

The medial retropharyngeal lymph nodes (MRPLN) are considered the collecting site of all lymphatic drainage of the head. Staging of these lymph node cancers in dogs and neck is important to establish treatment plans and to determine prognosis. As MRPLNs are not palpable unless there are significant increases in size or changes in consistency, ultrasound-guided aspiration (USGA) is frequently used in veterinary medicine for sample collection from the MRPLN. However, the true diagnostic yield of USGA has not been studied. Computed tomography (CT) is the preferred imaging modality for evaluation of the head and neck cancers and regional lymph nodes. CT evaluation of MRPLN is subjective to individual interpretation as the CT characteristics of MRPLN of the dog are not well documented.

Materials and Methods

Case selection

• Retrospective cross-sectional design performed at a single institute.
• Medical records of the Ontario Veterinary College Health Centre Small Animal Clinic reviewed between September 2011 and March 2017
  - Inclusion: Dogs with head or neck malignancy, USGA and cytology of the MRPLN.
  - Primary tumor characteristics:
    • Diagnosis (cytology/histology)
    • Location (oral, nasal cavity, thyroid, others)
    • Side (left, right, mid)
  - Cytology results of MRPLN:
    • Diagnostic vs Non-diagnostic
    • Benign vs Metastasis
    • Normal vs Reactive
  - CT measurements were performed by DACVR.
  - (Rostral, Middle, Caudal) x (Height and Width) x Length (by thickness and caliper)
  - Volume of lymph node = \[\frac{4}{3}\pi X height X width X length\] (by thickness and caliper)
  - Ratios of the rostral, middle, and caudal lymph node widths to the lymph node length
  - Heterogeneity
  - Margins
  - Surrounding fat
  - Presence of hilus

• Statistical analysis: Logistic regression, ANCOVA & Pearson’s correlation coefficient. P<0.05 considered significant

Results

• Signification
  - Sixty-nine dogs met the inclusion criteria and consisted of 25 breeds
  - The median body weight was 27 kg (range 3.9-54 kg)
  - The median age was 10.5 years (range 1-15 years)
  - There was 1 sexually intact female, 31 spayed females, 2 intact males and 35 castrated males

• Primary tumor characteristics
  - Diagnosis (Figure 2) and location (Figure 3) did not affect likelihood of diagnostic sample

• Cytology results
  - A total of 120 MRPLNs (Left n=62, Right n=58)
  - Benign in 51 MRPLNs (89.4%) vs Metastasis in 6 MRPLNs (10.5%) (Table 1)
  - Normal in 37 MRPLNs vs Reactive in 13 MRPLNs

• Statistical analysis
  1. Only one of the independent variables (rostral height) made a statistically significant contribution to the overall diagnostic yield with an odds ratio of 1.166 (95% confidence interval 1.031-1.216).
  2. When cytologically normal MRPLNs were compared to cytologically reactive MRPLNs using ANCOVA, no differences were observed in all investigated CT parameters.
  3. Pearson’s correlation coefficient demonstrated that age had a statistically significant negative linear correlation with middle height and width in both L+R and L MRPLNs; weight had a significant positive linear correlations with volume and caudal width and length (by thickness and caliper) in both sides, however, with length (by thickness) alone in left side and with volume in right side.

Discussion

• The diagnostic yield of USGA of MRPLNs in the current study was low.
  Only rostral height was positively associated with increasing chance of obtaining diagnostic samples. However, it is possible that other variables did not reach statistical significance due to type II error.
  There were no significant differences found in CT characteristics between normal and reactive MRPLNs, which might indicate that CT may not be sensitive to detect benign changes of the MRPLNs.

• Age had a negative linear correlation with the size of MRPLNs, whereas weight had a positive linear correlation with the size. However, the differences between MRPLN sizes relative to age and body weight are not likely to be clinically important due to measurement error, and various possible combinations of age and body weight.

Table 1. Details of Metastatic Lymph Nodes and The Associated Primary Tumors

<table>
<thead>
<tr>
<th>Patient</th>
<th>Tumor diagnosis</th>
<th>Tumor location</th>
<th>Location of primary tumor</th>
<th>Side of MRPLN metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Melanoma</td>
<td>Oral</td>
<td>Middle</td>
<td>Right</td>
</tr>
<tr>
<td>2</td>
<td>Sarcoma</td>
<td>Oral</td>
<td>Right</td>
<td>Left</td>
</tr>
<tr>
<td>3</td>
<td>Sarcoma</td>
<td>Nasal cavity</td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>4</td>
<td>Others</td>
<td>Nasal cavity</td>
<td>Right</td>
<td>Right</td>
</tr>
<tr>
<td>5</td>
<td>Carcinoma</td>
<td>Thyroid</td>
<td>Right</td>
<td>Left</td>
</tr>
</tbody>
</table>

Figure 1: Representative CT image (window width, 350; window level, 40) of the head of a dog indicating electronic caliper tool placement for measurement of MRPLN height + width (A) and length (B)
Introduction
Many cancers are capable of lymphangiogenesis and can utilize these lymphatics to metastasize.1,4-10 Sentinel lymph nodes (SLN) are the first lymph node(s) receiving lymphatic drainage from a tumor. Sentinel lymph node mapping/biopsy is performed to stage many types of human cancers4-11 and is gaining utility in veterinary medicine.12-15 Described methods of pre-operative SLN mapping in veterinary medicine include lymphoscintigraphy,20 contrast-enhanced ultrasonography,12,13 lipid-soluble iodinated contrast (LIC) with radiography12,14,15 or computed tomography,12,14,15 or computed tomography,16-22 and water-soluble iodinated contrast (WIC) with computed tomography.23-25 Previous studies have shown that subcutaneously administered WIC is rapidly absorbed into the local lymphatic channels.12,14,15,23,24,25 However, such studies only describe evaluating SLN and lymphatic channels using computed tomography. Development of a more economic and available technique for SLN mapping could be beneficial to veterinary patients. Water-soluble contrast is inexpensive and available in most veterinary practices, including primary care veterinary facilities. Radiography is also more readily available in veterinary practices than is computed tomography.

The hypotheses of this study were as follows:
1. Subcutaneously-injected WIC would be identifiable and traceable in the lymphatics and the draining lymph node
2. The popliteal lymph node would be the primary lymphatic drainage of the distal pelvic limb

Materials and Methods
A prospective, pilot study was designed using 8 beagles. The dogs were sedated with dexmedetomidine and butorphanol. Aqueous contrast (1-2 milliliters) was injected subcutaneously using a 21 ga needle in 4 separate aliquots overlying the pes, mimicking a circumferential, peri-tumoral injection. Lateral radiographic images were acquired at specific time intervals ranging from 0-50 minutes. All dogs were re-examined immediately after injection of contrast, after recovery from sedation, and 24 hours post-injection. Data recorded included initial time to lymphatic channel enhancement, time of maximal lymphatic channel enhancement, initial time of lymph node enhancement, time of maximal lymph node enhancement, time at which lymph node enhancement decreased, if present, course of the lymphatic channel(s), and which lymph node(s) enhanced, if any.

Results
All dogs had visible enhancement of lymphatic channels. The median time to initial enhancement of lymphatic channels was immediately post injection. Seven of 8 dogs (88%) had enhancement of 8 lymph nodes (Figure 1) including 7 popliteal lymph nodes and 1 superficial inguinal lymph node. Median time for initial enhancement of the lymph nodes was 20 minutes (range 5-50 minutes). One lymph node had mild decrease of contrast enhancement at 40 minutes, but the lymph node remained enhanced in comparison to pre-contrast images. One dog had enhancement of the lymphatic vasculature, but not the draining lymph node. Enhancement of both the superficial inguinal and popliteal lymph node occurred in one dog at 20 and 50 minutes, respectively (Figure 2). Seven of 8 dogs had enhancement of multiple lymphatic channels.

Discussion
All but 1 dog had enhancement of the draining lymph node. This was the first dog of the study and received only 1 milliliter of WIC and radiographic images to 20 minutes. Due to failure of contrast enhancement of the lymph node in this dog, the dose of WIC was increased to 2 milliliters in the subsequent dogs and additional radiographs were obtained if needed.

Three patterns of lymphatic drainage were identified. The draining pathway from the plantar aspect of the pes coursed caudally over the tarsus, caudal to the tibia and the stifle, and consistently drained to the area of the superficial inguinal lymph node. Drainage from the plantar aspect via lymphatic branches coursing to the dorsal aspect of the pes was observed. The drainage from the dorsum of the pes continued cranially over the tarsus and, at the level of the distal third of the tibia, transitioned to a more caudal position in its course to the popliteal lymph node. In one study, a third lymphatic channel was identified (Figure 3). It was undetermined whether this channel was medial or lateral because caudocranial edges of the limb were not obtained. However, the ultimate course of this pathway was similar to the dorsal lymphatic drainage and terminated in the area of the popliteal lymph node.

Based on the results of this study, subcutaneously-injected, water-soluble, iodinated contrast material provides a relatively quick and effective means of tracing the lymphatic channels from the pes to the draining lymph node(s). The results of this study also show that lesions of the distal pelvic limb might not have primary lymphatic drainage only to the popliteal lymph node.
Perioperative Morbidity and Mortality in Dogs Undergoing Adrenalectomy with Cavotomy for Resection of Invasive Adrenal Neoplasms.

Mayhew PD1, Boston SE2, Zwingenberger AL1, Giuffrida MA1, Runge JJ3, Raleigh J3, Singh A4, Culp WTN1, Case JB2, Steffey MA1, Balsa IM1

From the 1University of California-Davis, 2University of Florida, 3University of Pennsylvania, 4Ontario Veterinary College

Introduction
- Approximately 20-48% of adrenal neoplasms exhibit vascular invasion with tumor thrombus.
- Pheochromocytomas are more likely to be invasive compared to adrenocortical tumors.
- Two small cohorts comprising a total of 24 dogs described in the literature document a 28-69% short-term survival.
- Aim: document complications and outcomes of adrenalectomy with cavotomy for the resection of invasive adrenal masses in a large cohort of dogs.

Materials and Methods
- Study design: Retrospective study.
- Inclusion criteria: Dogs that underwent open adrenalectomy with a cavotomy for resection of tumor thrombus in the vena cava.
- Medical records were evaluated and clinicopathological data recorded.
- Complications were documented and long-term outcome was obtained.

Results
- 45 client-owned dogs included.
- Masses were right-sided in 26, left-sided in 16 and bilateral in 3.
- Intraoperative complications occurred in 16 (36%) dogs: bleeding from the cavotomy or renal venotomy site (n=5), intraoperative cardiac arrest (4), vena caval tearing prior to or after venotomy closure (3), cardiac arrhythmias (3), incomplete thrombus removal due to adherence to caval wall (1).
- Histopathology: Pheochromocytoma (37/44), adrenocortical adenocarcinomas (7/44).
- Outcome: 34/45 dogs (76%) were discharged from the hospital and 11/44 dogs (24%) died or were euthanized prior to discharge.
- Median overall survival time for all 45 dogs was 547 days (95%CI 146 to 710). MST for 34 dogs that survived to discharge was 690 days (95%CI 323 to 1162).

Discussion
- Existing literature suggests that prognosis for resection of invasive adrenal neoplasia is often guarded.
- In this study in a cohort of dogs that all required a cavotomy for tumor removal 76% survived the perioperative period and long-term outcome in dogs that survived the procedure was favorable in most cases.
- It should be noted that all dogs in this study were operated by experienced surgeons operating in highly specialized centers.
- Surgical resection of invasive adrenal masses remains a reasonable option for management of this challenging disease process.

CT angiogram image of an invasive adrenal mass demonstrating filling defect in vena cava
Resected adrenal mass with thrombus
Kaplan-Meier survival estimate for 45 dogs with invasive adrenal tumors
Satinsky clamp partially clamping the vena cava prior to cavotomy.
Completed cavotomy that has been sutured. The satinsky clamp is about to be removed
Microscopic invasion patterns in canine mast cell tumors and soft tissue sarcomas
Russell DS, Townsend KL, Gorman E, Bracha S, Curran K, and Milovancev M
Carlson College of Veterinary Medicine
Oregon State University
Corvallis, OR, 97331

Introduction
Stromal invasion is commonly identified in cutaneous malignancies; however, invasive patterns are inconsistently defined with uncertain clinical relevance. This study aimed to:
1. Define objective, quantifiable histomorphological invasive patterns in grade I/II canine mast cell tumors (MCTs) and soft tissue sarcomas (STSs)
2. Correlate invasive patterns with histologic excisional status

Materials and Methods
Hematoxylin and eosin stained glass slides prepared for routine histopathology of surgically-excised tumors from client-owned dogs were used for the study. Each tumor had radial sections prepared in four circumferential (e.g. cranial, caudal, dorsal, and ventral) and deep directions. Each slide was evaluated for:
1. Microscopic invasion beyond the subgross tumor edge (mm; Figure 1)
2. Asymmetrical invasion (mm; calculated by subtracting the minimum from the maximum length of circumferential neoplastic infiltrates for each tumour; larger values indicate a more asymmetrical invasive pattern)
3. Satellite lesions (both present / absent; also mm between the satellite lesion and the subgross tumor edge)
4. Lymphovascular invasion (present / absent)
5. Perineurovascular growth (present / absent)
6. Growth along fascial planes (present / absent)
7. Intramuscular invasion (present / absent)
8. Multicompartmental involvement (present / absent)

Incomplete excision was defined as digital histological tumor-free margins < 1 mm in any direction.

A professional biomedical statistician was hired to perform analyses using commercially available computer software.

Results
Sixty-nine tumors (50 MCTs and 19 STSs) from 51 dogs were included in the study.
Invasion in both circumferential and deep directions was significantly greater in MCTs compared with STSs (exact 2-tailed $P < 0.0001$ circumferential; $P = 0.0095$ deep).
Within the MCT group, circumferential invasion was greater than deep invasion ($P = 0.0076$; figure 2).
Multivariate logistic regression analysis found two variables that were significantly associated with incomplete MCT excision:
1. Intra-operative grossly normal circumferential surgical margin size (odds ratio of 0.776, 95% confidence interval: 0.651 - 0.925)
2. Asymmetrical invasion (odds ratio of 1.318, 95% confidence interval: 1.039 - 1.671).

(All enrolled dogs are being followed with DVM examinations (with re-staging if suspicion of local recurrence is noted) at 3, 6, 12, 18, and 24 months post-op to allow correlation of these findings to clinical outcomes.)

Discussion
These data may help create evidence-based strategies for planning different surgical strategies for MCT and STS excisions.

Presence of asymmetrical microscopic invasion might prompt pathologists to perform more comprehensive surgical margin evaluation.

Figure 1. Microscopic invasion length (mm) was measured from the subgross tumour edge (visually identified on the glass slide using the unaided eye; marked with an ultra-fine tip permanent felt marker as seen on the image provided) to the furthest point of microscopic tumour invasion (black measurement bar). Magnified box shows clusters of neoplastic cells associated with the tunica adventitia of a large vein (black arrows). Bar = 1 mm.

Figure 2. Scatter plot of microscopic invasion length beyond the subgross tumor edge, in circumferential directions (e.g. cranial, caudal, dorsal, and ventral), from grade I/II canine (A) mast cell tumors (MCT; n = 50) and (B) soft tissue sarcomas (STS; n = 19). Neoplastic invasion length was not significantly different between the circumferential directions within MCTs or STSs, but was significantly greater for MCTs compared with STSs (median of 1.7 mm versus 0.0 mm; $P < 0.0001$). Scale is consistent within the figure.
Inter- and intra-rater reliability and agreement in determining subcutaneous tumor margins in dogs
Ranganathan B, Milovancev M, Leeper H, Townsend K, Bracha S, Curran K.
Carlson College of Veterinary Medicine
Oregon State University
Corvallis, OR, 97331

Introduction
Agreement between veterinarians in determining the edges of a tumor are important to allow accurate and consistent patient staging, assessment of response to therapy, as well as ensure a uniform “surgical dose” between surgeons and studies.

The objective of this prospective, blinded, randomized clinical pilot study was to evaluate agreement and reliability of veterinarians in determining the gross edge of locally invasive subcutaneous malignant tumors in dogs.

Materials and Methods
Tumor measurements were modeled after the recommendations from the RECIST criteria. (Nguyen et al., Vet Comp Oncol 2015)

Four raters were instructed to use calipers to measure the longest diameter of cytologically-confirmed, treatment naïve, mast cell tumors or soft tissue sarcomas in client-owned dogs.

Three randomized measurement trials were performed, both pre- and post-sedation. Each rater was blinded to other raters measurements, but were aware of their own previous measurements. An oncology technician photodocumented each measurement trial.

Inter- and intra-rater reliability was evaluated using intra-class correlation coefficient and agreement was evaluated using Bland-Altman analysis. An a priori limit of agreement was set at 10 mm, as it was reasoned that a difference of this magnitude could carry clinically-relevant consequences for patient staging, measuring response to treatment, and determining surgical margins during tumor excision.

Results
Twelve tumors (seven soft tissue sarcomas and five mast cell tumors) were measured for the study with raw measurement values presented in Figure 1 (directly below).

Inter- and intra-rater reliability were good to excellent (ICC range 0.7263 - 0.9966).
Inter- and intra-rater agreement were considered unacceptable (Bland-Altman limits of agreement range 11.9 mm - 55.6 mm).

There were no significant differences between pre- and post-sedation reliability or agreement.

Review of measurement trial photographs revealed that caliper orientation changes were frequent, occurring in 9/12 (75%) and 8/12 (67%) pre- and post-sedation cases. (Figure 2; lower left)

No significant correlation was found between inter-rater measurement standard deviations and caliper orientation changes or dog BCS.

Discussion
The four raters in this pilot study demonstrated high reliability but poor agreement in determining the gross edge of MCTs and STSs. Interpreted in concert, this indicates that within-rater measurements are consistent but raters do not actually measure the same point when compared to raters other than themselves.

This lack of agreement may affect surgical margin planning and resection (i.e. “surgical dose”), tumor staging, and assessment of response to therapy—all of which may influence clinical decision making and quality of life for veterinary cancer patients.

Because of the potential implications of these findings, repetition of this experiment, ideally with a larger number of raters and dogs, would be a worthwhile effort.
Introduction: Extrahepatic biliary obstruction (EHBO) in dogs and cats can be challenging to manage surgically. Reported surgical techniques for decompression include luminal choledochal stenting and cholecystoenterostomy. The authors experience with balloon-expanding metallic stents suggests that these stents provide an effective method of decompression of the extra hepatic biliary tree. Stent deployment is rapid and provides a less complex alternative to cholecystoenterostomy techniques.

Objective: The purpose of the study was to describe the operative technique, complications, and results associated with the use of a balloon-expandable metallic biliary stent for surgical management of canine and feline EHBO.

Materials and Methods: EMR were searched for patients in which balloon-expanding metallic choledochal stents were placed. Signalment, history and clinical signs, pre-operative laboratory findings and diagnostic imaging, surgical findings, histopathology findings, microbiology findings, post-operative laboratory findings, diagnostic imaging, and complications were recorded. Long-term follow up results were collected through recheck appointments or communication with owners and referring veterinarians. In all cases stents was deployed in retrograde fashion through the major duodenal papilla following duodenotomy.

Discussion: This study documents the use of a metallic balloon-expandable mesh stent as an alternative to luminal choledochal stenting for treatment of EHBO. Results suggest the metallic stent can maintain common bile duct patency without the risk of reobstruction that is reported with luminal stenting. Stent location and stent luminal size can be controlled by the surgeon and stent deployment is relatively uncomplicated.

The use of balloon-expandable mesh stents offers a significant advantage for patients following cholecystectomy where 1) luminal stenting offers only transient extrahepatic decompression and 2) cholecystoenterostomy procedures are not possible.
The Variability in Surgical Margin Reporting for Soft Tissue Sarcoma and Mast Cell Tumors in Dogs

Allison Putterman, VMD, Laura Selmic, BVetMed (Hons), MPH, ACVS, ECVS, MRCVS
Department of Veterinary Clinical Medicine, University of Illinois at Urbana-Champaign

Introduction
Surgical margins are a standard reported measurement in tumor surgery that has implications for functional outcome, local control, and overall survival. There is no single accepted classification in veterinary medicine, and it is unclear what form or margin reporting predominates in the soft tissue sarcoma (STS) and mast cell tumor (MCT) literature.

Materials & Methods
A systematic search of digital bibliographic databases for studies that describe treatment of cutaneous MCT and STS was performed.

- Electronic literature searches were performed for MCT and STS separately.
- Eligible studies were primary research studies (experimental or observational) that reported oncologic outcome of surgical treatment of cutaneous MCT or STS in dogs.

The relevance screening was a two-stage process.

- Stage 1 involved two reviewers independently reviewing each abstract title to determine if it described primary research assessing the oncologic outcome of surgical treatment of MCT and STS. If the manuscript met this inclusion criteria, it could advance to the next stage of the review.
- Stage 2 involved evaluation of the full manuscript using the same inclusion criteria and was conducted independently by the same reviewers.
- When the two reviewers did not initially agree about a citation, a discussion was raised and consensus was determined.

The data abstracted from the articles that qualified for review included the author, years the study was performed and reported, study population, sample size, number of subjects treated with surgery in study, for MCT the number of dogs with Patnaik histologic grades 1, 2 and 3 or Kiupel low and high histologic grade, for soft tissue sarcoma the number of dogs with histologic grades 1, 2 and 3, the surgical margins utilized, and the histologic margins reported.

The individual study quality was determined on the basis of multiple criteria including:

1) representativeness of study population
2) selection of study participants
3) data collection methods utilized
4) statistical and analytic methods used

For assessment of the quality of the entire body of evidence, guidelines developed by The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group were used.

Results
The electronic literature searches yielded 772 MCT studies and 296 STS studies, for a total of 1,068 citations. The results of the relevance screening are outlined in Figure 1. Many manuscripts were excluded due to lack of information regarding surgical and histopathologic margins.

Within the reviewed studies, surgical margins were more commonly reported than histologic margins.

- There was no common classification system for reporting surgical and histologic margins.
- Trichomatous reporting was predominantly used for grading both MCT and STS.

Hypotheses
- Trichotamous reporting is used predominantly and measurement of margins are unreported in a high proportion of studies.
- Over time the reporting of margins (both any and measurement) has increased.

Conclusion
There is a lack of consensus for reporting surgical and histological margins for STS and MCT. Further investigation into determining a common classification system for reporting margins for these tumors is needed.
Feline primary hyperparathyroidism (PHPT) has been described, but has been reported infrequently in the veterinary literature. A single retrospective study in 1991 described 7 cats undergoing surgical parathyroidectomy for the treatment of PHPT with parathyroid adenoma being the most common diagnosis and postoperative hypocalcemia being a rare complication. Given the paucity of data on feline PHPT, further study in a larger cohort of cats undergoing surgical treatment is required.

The objective of this study was to determine preoperative characteristics, histologic diagnosis and long-term outcome in cats undergoing surgery for the treatment of PHPT. A secondary objective was to determine whether a correlation between plasma ionized calcium concentration pre- and post-parathyroidectomy.

Materials and Methods

Retrospective, multi-institutional study with medical record data collection and telephone follow-up. Cats undergoing surgical treatment and histopathologic evaluation of resected tissue were included. Cats were divided into pre-operative ionized calcium (iCa) groups corresponding to the 33rd, 67th, and 100th percentiles of the study population’s pre-operative iCa results.

Results

Thirty-two cats were included in the study. Mean cat age was 13.3 ± 2.4 years and mean cat body weight was 4.9 ± 1.3 kg. iCa was above reference range in all cats (median 1.8 mmol/L (IQR 1.5,1.9)). Intact PTH concentration was tested in 26 cats and reported to be above the normal reference range in 20 (76.9%) and within the normal reference range in 6 (23.1%) cats.

All cats underwent cervical exploratory surgery and abnormal tissue was identified and removed in all cats. Histopathologic diagnosis was parathyroid adenoma in 20/32 (62.5%) cats, parathyroid carcinoma in 7/32 (21.9%) cats, parathyroid hyperplasia in 3/32 (9.4%) cats, and parathyroid cystadenoma in 2 (6.3%) cats.

Lowest postoperative iCa had no statistically significant positive correlation with preoperative iCa (Spearman’s ρ=0.158; p=0.405) (Figure 2). At discharge, 6/32 (18.8%) cats had hypercalcemia, 5/32 (15.6%) had hypocalcemia, and 21/32 (65.6%) cats had iCa within reference range.

Overall median survival time was 1109 days (95% CI 856 – 1332). Survival time was not significantly associated with pre-operative iCa group (p=0.139), hypocalcemia at discharge (p=0.326), hypercalcemia at discharge (p=0.955), or diagnosis of carcinoma (p=0.930).

Discussion

Feline PHPT is a rare diagnosis with only 32 cases presented in this cohort despite a comprehensive medical record review at 9 veterinary referral centres.

A variety of surgical procedures (parathyroidectomy vs partial thyroidectomy) were performed in the cats of this study to ensure complete removal of abnormal parathyroid tissue.

Similar to dogs with PHPT, the majority of cats (62.5%) were diagnosed with a parathyroid adenoma. However, parathyroid carcinoma was diagnosed in 21.9% of cats which is considerably higher than what is reported in dogs.

Based on the relatively high proportion of carcinoma, evaluation of the regional lymph nodes with cervical ultrasonography is recommended preoperatively, with either intraoperative fine-needle aspirate cytology or extirpation and post-operative histopathology in cats with mandibular or medial retropharyngeal lymphadenopathy.

Hypocalcemia was diagnosed in 34.4% of cats in the postoperative period, and none displayed behaviors associated with hypocalcemia in dogs such as pruritis, ataxia, tremors and/or seizures. This incidence of hypocalcemia was lower than what has been observed in dogs. Regardless, while hypocalcemia following parathyroidectomy in cats for the treatment of PHPT appears to be uncommon, vigilant postoperative monitoring of iCa is required to ensure appropriate calcium homeostasis.

Several canine studies have yielded conflicting results when trying to determine which cases may benefit from pretreatment to prevent severe hypocalcemia based on preoperative iCa. Preoperative iCa was not associated with postoperative iCa, hypocalcemia during hospitalization or at discharge, or hypercalcemia at discharge.

The effect of prophylactic preoperative calcitriol administration on postoperative iCa in cats remains unknown. However, clinical signs related to hypocalcemia appear rare in cats suggesting that pretreatment with calcitriol may be unnecessary with post-operative treatment performed according to careful calcium monitoring.

Figure 1. Intra-operative appearance of a parathyroid adenoma in a cat undergoing surgical treatment for PHPT.

Figure 2. Correlation between pre-operative iCa and lowest recorded post-operative iCa in 32 cats following surgery for primary hyperparathyroidism. Each dot represents an individual cat. The line represents predicted values from a linear regression of lowest post-operative iCa on pre-operative iCa with correlation coefficient 0.202, p=0.113. The data indicate that cats with milder pre-operative hypocalcemia also have lower post-operative iCa, but the relationship is not statistically significant.
**Introduction**

Precise identification of the most appropriate lymph node (LN) for accurate patient staging can be a real challenge in oncologic practice. The gold-standard methods of sentinel lymph node mapping (SLNM) most commonly used in human surgical oncology combine lymphoscintigraphy and operative optical dye, but the combination is not available to the majority of veterinary practitioners. Use of visible blue dyes alone for SLNM has been described, but there are known technical challenges and as a solo technique is considered less accurate than combination methods. An alternative technique of SLNM involves peri-tumoral injection of a fluorophore and imaging within the near-infrared (NIR) light spectrum.

The most commonly utilized NIR fluorophore in human and veterinary medicine is the non-targeted agent, indocyanine green (ICG). ICG is highly bound to plasma proteins, making it useful for real-time lymphatic imaging. Direct NIRFL has been described for operative imaging in the clinical treatment of chylothorax in dogs. Technologies for operative NIR imaging are increasingly clinically available, and use of ICG for indirect near-infrared fluorescence lymphography (NIRFL) for SLNM is increasing in human cancer patients, with excellent correlation to gold-standard SLNM methods.

The aim of this study was to document the initial experiences using NIRFL for SLNM in a variety of anatomic locations in dogs with naturally-occurring neoplasms prone to lymphatic metastatic patterns.

**Materials and Methods**

Retrospective multi-institutional case series with data collected from the medical records of clinical patients. Dogs with naturally-occurring solid tumors that underwent operative SLNM using indirect NIRFL with ICG were included. Data is descriptively reported as median (range).

**Results**

29 client-owned dogs (age=10.4 (5.6-13.4) years, body weight=28.5 (3.3-63.5) kg) with 30 distinct tumors (carcinomas (n=15; perineum (5), foot (10), trunk (4), perineum (5), and extremity (6), with SLNs subsequently identified as traheobronchial (5), mandibular (5), medial retropharyngal (5), iliosacral (5), popliteal (4), inguinal (4), and superficial cervical (2)).

**Discussion**

Initial experience demonstrates that NIRFL can be safely and successfully used for SLNM procedures in a variety of anatomic locations. Metastatic disease was identified in a high proportion of SLNs identified in this mixed tumor-type cohort, supporting the continued investigation of disease-and species-specific application of SLNM. While good evidence exists in humans that NIRFL has similar SLNM accuracy to combination methods, his study is limited to no comparable gold standard was used to verify accurate identification of all SLNs, which may have resulted in missed SLNs or precise LN misidentifications in certain locations. Comparative SLNM technique studies would be useful.

While overall very promising, technical challenges do exist for NIRFL SLNM. Canine lymphocenter anatomy (fewer, proportionally larger LNs, located farther apart anatomically) differs from humans, which may impact the application of NIRFL as a solitary method of SLNM in dogs compared to results obtained in humans. ICG transit through afferent and efferent lymphatics is rapid and timing of injection is important to avoid missing the correct SLN or prevent incorrect diagnosis of 2° or 3° LNs as sentinel. Even in humans, technical aspects of SLNM are often poorly standardized; this is definitely lacking for canine patients, which will be important in interpretation of future disease-specific metastatic data, especially in low volume cohorts. To ensure all SLNs are identified and to improve procedural positioning, combination of operative NIRFL with preoperative SLNM in certain patient subsets may optimize application of SLNM. Numerous patient, surgeon, and technical factors can impact the application and interpretation of results with different SLNM techniques, and further prospective study of NIRFL in veterinary patients is recommended.
Outcome of a Multicentre Clinical Trial of Auranofin Plus Standard of Care in Dogs With Osteosarcoma

Brisbane Veterinary Specialist Centre, the University of Queensland Diamantina Institute and the Australian Consortium of Comparative Oncology of the Australian Animal Cancer Foundation, Queensland Australia

Introduction

Osteosarcoma (OS) is the most common primary bone malignancy in children. Neoadjuvant and adjuvant chemotherapy combined with surgery can deliver cures of almost 70%. However, the major cause of death in OS, is drug resistant metastasis to the lung for which little improvement in survival has been made since the late 1980s. We have identified multiple metastasis drivers1-5 including thioredoxin reductase 2 (TrxR2). TrxR2 is immediately actionable with auranofin. In preclinical models auranofin reduced OS pulmonary metastases4. Auranofin showed synergistic effects with vorinostat and rapamycin on OS viability and apoptosis induction in a recently reported in vitro and murine study6. OS in dogs is histopathologically, transcriptomically and clinically similar to human OS.

Materials and Methods

We performed a single arm multicentre clinical trial of auranofin in combination with standard-of care (amputation + carboplatin) via specialist veterinary oncology clinics in Australia. We used a historical control group (n=26) receiving standard-of-care only. In the treatment group, dogs >15kg received 9mg auranofin q3d PO and dogs <15kg received 6mg q3d. Follow-up occurred over at least a 3-year period and surviving dogs continue on auranofin.

Discussion

Auranofin improved overall survival when combined with standard of care therapy. Our data justify a larger Phase II/III trial in dogs as the basis to change OS standard of care management of canine OS. Our data justify a phase I/II trial in human OS patients with drug refractory disease at the time of initial surgery.

Results

We recruited 40 dogs to the treatment group. Auranofin induced no adverse events. Auranofin + standard-of-care resulted in a significant increase in overall survival with a hazard ratio of .5776299, standard error of .1617391, z = -1.96 and P> |z| = 0.050 and a confidence interval of 3336638 to .9999773. At the time of writing there were six dogs surviving without measurable disease in the treatment group with survival times of between 577 and 1296 days.

Discussion

Auranofin improved overall survival when combined with standard of care therapy. Our data justify a larger Phase II/III trial in dogs as the basis to change OS standard of care management of canine OS. Our data justify a phase I/II trial in human OS patients with drug refractory disease at the time of initial surgery.


This study was funded in part by a grant from the Australasian Sarcoma Study Group and The Australian Animal Cancer Foundation

The authors have no conflicts of interest to declare.
Intratumoral injection of radioactive holmium (166Ho) microspheres for treatment of soft tissue sarcomas in dogs and cats

Sebastiaan van Nimwegen1, DVM, PhD, DECVS, Jolle Kirpensteijn1,2, DVM, PhD, DECVS, DACVS, Frank Nijsen3, PhD
1Department of Clinical Sciences of Companion Animals, Utrecht University, the Netherlands
2Hill’s Pet Nutrition, 400 SW 8th Ave, Topeka, KS, 66603, USA
3Department of Radiology and Nuclear Medicine, Radboud University Medical Center, Nijmegen, the Netherlands

Introduction
A “microbrachytherapy” was developed as treatment option for inoperable tumors by direct intratumoral injection of radioactive holmium (166Ho) microspheres (Ø 20-30 µm). 166Ho emits β-radiation (Eβ,max=1.84 MeV; T1/2=26.8 h) with a mean tissue penetration depth of 3 mm and a maximum of 8 mm, which enables a high, ablative, radioactive-absorbed dose on the tumor while sparing surrounding tissues.

Materials and Methods
Twelve client-owned patients (8 dogs, 4 cats) with soft tissue sarcomas of several histologic types for which complete surgical excision was no option received 166Ho-microbrachytherapy (Figure 1). Standard disease staging protocol included CT evaluation of the tumor, thorax, and abdomen. Tumor response and side effects were evaluated using a standard follow-up protocol.

Results
Treatment was well tolerated. Tumor-absorbed dose varied from 36 to >1000 Gy. A tumor volume reduction of >50% was observed in 6 animals; 20-50% in 4 animals; and <20% in 2 animals. Subsequent surgical excision was performed in 9/12 patients resulting in complete local remission (Figure 2). Local recurrence occurred in 5 animals after 121 – 1919 days. One patient received a second 166Ho-microbrachytherapy. Median survival time for all patients was 755 days (range 93–1919 days; Figure 3). Four animals were alive at the time of writing, seven died and one was lost to follow-up. Three deaths were disease-related. Side effects were minimal and not associated with radiation dose. Possible side effects consisted of one case of chronic skin ulceration at the injection site, 2 cases of delayed wound healing after surgery, and one case of chronic wound infection after surgery.

Conclusion
166Ho-microbrachytherapy is a safe and effective treatment for downstaging of soft tissue sarcomas allowing subsequent surgical excision.
Introduction

The prognosis associated with canine osteosarcoma (cOSA) has stagnated over the past 30 years, despite utilization of several different cytotoxic agents. Immunotherapeutics targeting defects in the host’s anti-tumor immune response, or promoting an enhanced preexisting response are proving effective in treating several solid human cancers previously thought to be relatively non-immunogenic. Therefore, investigation into potential immune targets in cOSA is warranted. cOSA is known to elicit a modest inflammatory response, as evident by the presence of increased circulating myeloid-derived suppressor cells (MDSCs) and elevated immune complexes in patients compared to healthy dogs. Furthermore, increased blood monocyte and lymphocyte counts, decreased blood CD8/Treg ratio, post-operative wound infection, and decreased post-treatment tumor infiltrating lymphocytes correlate with a poorer prognosis in cOSA.

Characterization of lymphocyte infiltrates within primary cOSA tumors has predominated, despite the fact that metastatic lesions remain the most common cause of cancer-related death. Moreover, immunotherapeutics such as L-MTP-PE and HER2-targeting immunotherapeutics such as L-MTP-PE and HER2-targeting Listeria, are thought to mediate their effects via macrophage activation. While tumor associated macrophages have commonly been found to have a positive effect on patient outcome in human OSA, this has not been evaluated in cOSA.

We therefore sought to characterize lymphocyte and macrophage infiltration in primary and metastatic cOSA lesions. In addition, we evaluated the prognostic significance of these infiltrates in a separate cohort of dogs treated with amputation and 6 doses of carboplatin.

Acknowledgements:
American Kennel Club Canine Health Foundation – Clinician-Scientist Fellowship Program
UC Davis Center for Companion Animal Health
NIH-NCl 1R01CA195904-01; NIH-NCl P35CA093373; NIH-NClU01 CA224166-01

References:

Materials and Methods

Cohort 1 – Paired primary and metastatic OSA FFPE tissue samples from 21 dogs. 15 dogs were treated with amputation and later returned for euthanasia and necropsy. 5 dogs presented with disseminated disease and did not receive treatment prior to euthanasia.

Cohort 2 – 30 dogs with appendicular OSA undergoing amputation and carboplatin chemotherapy, were followed prospectively. Of these, 26 dogs had available FFPE primary tumor samples.

Immunohistochemistry (IHC) was performed to evaluate lymphocyte (CD3; CD3-12) and macrophage (CD204; SRA-E5) tumor infiltration. Quantification was performed by selecting 3 highly cellular areas from H&E stained slides, collecting 100x images of the IHC slides from each of these areas, and determining the proportion of the field taken up by positively staining cells using ImageJ. The average area across the 3 fields was used for analysis. Statistical analysis was performed with GraphPad Prism, using a Wilcoxon signed rank test for paired data, a Mann-Whitney test for comparison of 2 groups, and Kaplan Meier plots with a Log-rank test for survival analysis.

Results

Characterization of lymphocyte infiltrates within primary and metastatic cOSA lesions. Cohort 1 – Paired primary and metastatic OSA tumor samples from 21 dogs. 15 dogs were treated with amputation and later returned for euthanasia and necropsy. 5 dogs presented with disseminated disease and did not receive treatment prior to euthanasia.

Characterization of lymphocyte infiltrates within primary and metastatic cOSA lesions. Cohort 2 – 30 dogs with appendicular OSA undergoing amputation and carboplatin chemotherapy, were followed prospectively. Of these, 26 dogs had available FFPE primary tumor samples.

Immunohistochemistry (IHC) was performed to evaluate lymphocyte (CD3; CD3-12) and macrophage (CD204; SRA-E5) tumor infiltration. Quantification was performed by selecting 3 highly cellular areas from H&E stained slides, collecting 100x images of the IHC slides from each of these areas, and determining the proportion of the field taken up by positively staining cells using ImageJ. The average area across the 3 fields was used for analysis. Statistical analysis was performed with GraphPad Prism, using a Wilcoxon signed rank test for paired data, a Mann-Whitney test for comparison of 2 groups, and Kaplan Meier plots with a Log-rank test for survival analysis.

Figure 1: Representative images of lymphocyte and macrophage infiltration into paired primary and metastatic lesions. Cohort 1. 100x magnification.

Figure 2: Lymphocyte and macrophage infiltration increase in metastases compared to primary tumors. Cohort 1; CD3 n = 18, CD204 n = 20. * = P < 0.05

Figure 3: Lymphocyte infiltration correlates with macrophage infiltration in cOSA primary tumors. Cohort 2; n = 22

Figure 4: Elevated tumor associated macrophages correlates with an improved disease-free survival time in dogs with OSA treated with amputation and 6 doses of carboplatin chemotherapy. Cohort 2; CD3 n = 22, CD204 n = 23.

Conclusions:

• Tumor infiltrating lymphocytes and macrophages tend to increase in metastatic lesions compared to primary tumors.

• Macrophages may have anti-tumor activity in cOSA.
Intraoperative and postoperative complications of partial maxillectomy for the treatment of oral tumors in dogs

Roxane H MacLellan, Jennifer E Rawlinson, Sangeeta Rao, Deanna R Worley
Department of Clinical Science and the Flint Animal Cancer Center
Colorado State University

**OBJECTIVE**
To characterize and identify factors associated with intraoperative and postoperative complications of canine maxillectomy

**MATERIALS AND METHODS**
This retrospective single institutional cohort study assessed 193 dogs undergoing maxillectomy for oral tumor excision from 2000-2011. Data evaluated included signalment, tumor location and size, histologic findings, clinical stage, maxillectomy category, surgical approach, and additional treatments. These factors were examined for associations with recorded intraoperative and postoperative outcomes.

**RESULTS**
There were 133 intraoral (IO) and 60 dorsolateral combined intraoral (DL/IO) approaches. The most common intraoperative complication was excessive surgical bleeding, for which 44 (42.7%) dogs received an intraoperative blood transfusion. **Table 1** No intraoperative deaths occurred. Mean duration of surgery was greater for the DL-IO approach (106±32 min) than the IO approach (77±38 min). For 132 dogs (68.4%), maxillectomy yielded tumor-free histological margins. No association with incomplete margins was found for tumor size or location, maxillectomy type, or surgical approach.

Immediate postoperative complications (≤48 hr after sx) in 193 dogs included epistaxis n=99 (51.3%) which required a second surgery in one, excessive facial swelling n=71 (36.8%), facial pawing n=21 (10.9%) resulting in wound dehiscence in 7 dogs (with 5 resulting oronasal fistulas), and difficulty eating n=22 (11.4%). **Table 2** Short-term complications (48 hr to 4 wk) in 164 dogs included lip trauma n=22 (13.4%), oronasal fistula n=18 (11.0%), surgical site infection n=13 (7.9%), epiphora n=15 (9.1%), and sialocele formation n=2 (1.2%). **Table 3**.

**DISCUSSION**
Complications associated with maxillectomy in dogs were generally minor. Aggressive surgical planning, preparedness for hemorrhage and transfusion, careful tissue dissection, and comprehensive pain control is recommended, particularly for dogs with large, caudally located oral tumors requiring extensive excision.

---

**Table 1** Intraoperative complications

<table>
<thead>
<tr>
<th>PARAMETERS MEASURED</th>
<th>TOTAL</th>
<th>EXCESSIVE SURGICAL BLEEDING (%)</th>
<th>P value</th>
<th>TRANSFUSION ADMINISTERED (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOTAL dogs in study</td>
<td>193</td>
<td>103 (53.4)</td>
<td></td>
<td>44 (22.8)</td>
<td></td>
</tr>
<tr>
<td>Tumor Size (T1 &lt;2cm, T2 =2-4cm, T3 &gt;4cm)</td>
<td>112</td>
<td>&lt;.001†</td>
<td>.002†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1 = Tumor &lt; 2 cm in diameter at greatest dimension</td>
<td>22</td>
<td>8 (36.4)</td>
<td>4 (18.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2 = Tumor 2 - 4 cm in diameter at greatest dimension</td>
<td>64</td>
<td>37 (57.8)</td>
<td>14 (21.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T3 = Tumor &gt; 4 cm in diameter at greatest dimension</td>
<td>26</td>
<td>24 (92.3)</td>
<td>15 (57.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor Location: Rosstral vs Caudal Maxilla</td>
<td>193</td>
<td>&lt;.001†</td>
<td>&lt;.001†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rosstral (rostral to the fourth premolar)</td>
<td>81</td>
<td>26 (32.1)</td>
<td>7 (8.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caudal (caudal to and including the fourth premolar)</td>
<td>112</td>
<td>77 (68.8)</td>
<td>37 (33.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maxillectomy Category: A-F</td>
<td>193</td>
<td>&lt;.001†</td>
<td>&lt;.001†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A = Incisivectomy</td>
<td>10</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B = Unilateral rostral maxillectomy</td>
<td>45</td>
<td>16 (35.6)</td>
<td>4 (8.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C = Bilateral rostral maxillectomy</td>
<td>26</td>
<td>10 (38.5)</td>
<td>3 (11.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D = Segmental/central maxillectomy</td>
<td>21</td>
<td>8 (38.1)</td>
<td>1 (4.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E = Caudal maxillectomy</td>
<td>73</td>
<td>56 (76.7)</td>
<td>29 (39.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F = Complete maxillectomy</td>
<td>18</td>
<td>13 (72.2)</td>
<td>7 (38.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orbicectomy</td>
<td>193</td>
<td>&lt;.001†</td>
<td>&lt;.001†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orbicectomy</td>
<td>52</td>
<td>43 (82.7)</td>
<td>30 (57.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No orbicectomy</td>
<td>141</td>
<td>60 (42.6)</td>
<td>14 (9.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical Approach (IO, DL/IO)</td>
<td>112</td>
<td>&lt;.001†</td>
<td>&lt;.001†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IO = Intraoral</td>
<td>54</td>
<td>29 (53.7)</td>
<td>7 (13.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DL/IO = Combined dorsolateral/intraoral</td>
<td>58</td>
<td>48 (82.8)</td>
<td>30 (51.7)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Based on Owen LN: TNM classification of tumors in domestic animals, Geneva, 1980, WHO.
† Categorical data was significant (P<0.05) using Pearson’s Chi-squared test.

**Table 2** Immediate postoperative complications

<table>
<thead>
<tr>
<th>PARAMETERS MEASURED</th>
<th>TOTAL</th>
<th>EPISTAXIS (%)</th>
<th>FACIAL SWELLING (%)</th>
<th>FACIAL PAVING (%)</th>
<th>DIFFICULTY EATING (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOTAL dogs in study</td>
<td>193</td>
<td>99 (51.3)</td>
<td>71 (36.8)</td>
<td>21 (10.9)</td>
<td>22 (11.4)</td>
</tr>
<tr>
<td>Maxillectomy Category</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A = Incisivectomy</td>
<td>10</td>
<td>3 (30)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>B = Unilateral rostral maxillectomy</td>
<td>45</td>
<td>21 (47)</td>
<td>12 (27)</td>
<td>3 (7)</td>
<td>3 (7)</td>
</tr>
<tr>
<td>C = Bilateral rostral maxillectomy</td>
<td>26</td>
<td>12 (46)</td>
<td>5 (19)</td>
<td>3 (12)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>D = Segmental/central maxillectomy</td>
<td>21</td>
<td>10 (48)</td>
<td>4 (19)</td>
<td>2 (10)</td>
<td>2 (10)</td>
</tr>
<tr>
<td>E = Caudal maxillectomy</td>
<td>73</td>
<td>41 (56)</td>
<td>42 (58)</td>
<td>10 (14)</td>
<td>12 (16)</td>
</tr>
<tr>
<td>F = Subtotal maxillectomy</td>
<td>18</td>
<td>12 (67)</td>
<td>8 (44)</td>
<td>3 (17)</td>
<td>4 (22)</td>
</tr>
</tbody>
</table>

* Categorical data was significant (P<0.05) using Pearson’s Chi-squared test.

**Table 3** Short-term complications

<table>
<thead>
<tr>
<th>PARAMETERS MEASURED</th>
<th>TOTAL</th>
<th>LIP TRAUMA (%)</th>
<th>ONF (%)</th>
<th>DEHISCENCE (%)</th>
<th>INFECTION (%)</th>
<th>EPIDERMHA (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOTAL dogs in study</td>
<td>164</td>
<td>22 (13)</td>
<td>18 (11)</td>
<td>18 (11)</td>
<td>13 (8)</td>
<td>15 (9)</td>
</tr>
<tr>
<td>Maxillectomy Category</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A = Incisivectomy</td>
<td>5</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>B = Unilateral rostral maxillectomy</td>
<td>38</td>
<td>8 (21)</td>
<td>1 (3)</td>
<td>3 (8)</td>
<td>1 (3)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>C = Bilateral rostral maxillectomy</td>
<td>18</td>
<td>3 (17)</td>
<td>1 (6)</td>
<td>1 (6)</td>
<td>1 (6)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>D = Segmental/central maxillectomy</td>
<td>18</td>
<td>1 (6)</td>
<td>2 (11)</td>
<td>2 (11)</td>
<td>2 (11)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>E = Caudal maxillectomy</td>
<td>68</td>
<td>7 (10)</td>
<td>11 (16)</td>
<td>9 (13)</td>
<td>7 (10)</td>
<td>9 (13)</td>
</tr>
<tr>
<td>F = Subtotal maxillectomy</td>
<td>17</td>
<td>3 (18)</td>
<td>3 (18)</td>
<td>2 (12)</td>
<td>4 (24)</td>
<td></td>
</tr>
</tbody>
</table>

ONF = Oronasal fistula